Study Protocol & Statistical Analysis Plan

Quality Control of CE-Certified Phonak Hearing Aids - 2020_43

NCT04723173

<< QUALITY CONTROL OF CE-LABELLED PHONAK HEARING SYSTEMS >>

Clinical Study Protocol

QUALITY CONTROL OF CE-LABELLED PHONAK HEARING SYSTEMS.
(AGEK 1; SPIRIT #1)

[A methodical evaluation of new CE-labelled Phonak Hearing Systems is intended to be conducted on hard of hearing participants to grant quality control prior to product launch. The aim of the investigation series is to ensure zero-defect overall performance of the new hearing systems as well as maximum benefit for the participant with the devices in comparison to previously outstanding Phonak Hearing Systems and to equivalent competitor devices. The Phonak Hearing System comprises hearing aids of different form factors, acoustic couplings, wireless accessories (e.g. remote control) and fitting software. Both objective laboratory measurements will be conducted as well as subjective evaluations of the devices in daily life will be undertaken. This will be a controlled, single blinded and randomised active comparator clinical evaluation which will be conducted mono centric at Sonova AG Headquarters based in Stäfa.]

Study Type:	Clinical trial with Medical Device (MD)
Study Categorisation:	Risk category according to LHR A
Study Registration:	Intended registry after approval: clinicaltrials.gov and Swiss Federal Complementary Database
Study Identifier:	CH-PH-Marketing-Validation
Sponsor:	Sonova AG Contact person: Katrin Manella Laubisrütistrasse 28 CH-8712 Stäfa Email: katrin.manella@phonak.com (preferred contact) Phone: 058 928 45 10
Principal Investigator:	Bernhard Buschle , Laubisrütistrasse 28, CH-8712 Stäfa, Phone: 058 928 4421 Email: bernhard.buschle@phonak.com
Investigational Product:	MD risk class IIA: Phonak Hearing Systems (comprising hearing aids, acoustic couplings and fitting software), Wireless Accessories (Receiver) MD risk class I: Wireless Accessories (transmitters).
Protocol Version and Date:	V1.3, 17.12.2019

than the applicable Competent Ethics Committee(s) and Regulatory Authority(ies) without prior written authorisation from the sponsor except to the extent necessary to obtain informed consent from those who will participate in the study.

Signature Page(s)

(AGEK 1.1; ICH E6 6.1)

ICH E6: Have signature pages with name and title of the person(s) authorised to sign the protocol and the protocol amendment(s) for the sponsor or of the medical expert (if applicable), the investigator responsible for conducting the trial, the statistician (if applicable)

Study number	www.clinicaltrials.gov as soon as approved by Competent Ethics Committee (CEC)
Study Title	Quality Control of CE-Labelled Phonak Hearing Systems

Sponsor: **Sonova AG (contact person: Katrin Manella)**

Stäfa/17.12.2019 — Place/Date

Signature

Principle Investigator: **Bernhard Buschle**

Stäfa/17.12.2019 — Place/Date

Signature

Local Principal Investigator at study site*:

I have read and understood this trial protocol and agree to conduct the trial as set out in this study protocol, the current version of the World Medical Association Declaration of Helsinki, ICH-GCP guidelines or ISO 14155 norm and the local legally applicable requirements.

Site: Sonova AG, Laubisrütistrasse 28, 8712 Stäfa

Principal Investigator: Bernhard Buschle

Site: Sonova AG, Laubisrütistrasse 28, 8712 Stäfa

Principal Investigator: Bernhard Buschle

Stäfa/17.12.2019 — Place/Date

Signature

**Note:* In multicentre studies, this page must be individually signed by all participating Local Principal Investigators.

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STUDY SYNOPSIS

(ClinO, Appendix 3, 1.1, 2.1, 3.1, 4.1; Appendix 5, 2b; AGEK Summary)

Sponsor **Principle Investigator**	Sonova AG (contact person: katrin.manella@phonak.com), Laubisrütistrasse 28, 8712 Stäfa, 058 928 45 10 Bernhard Buschle (bernhard.buschle@phonak.com), Laubisrütistrasse 28, 8712 Stäfa, 058 928 43 12
Study Title:	Quality Control of CE-Labelled Phonak Hearing Systems
Study ID:	CH-PH-Marketing-Validation
Protocol Version and Date:	Version 1.3, 17.12.2019
Trial registration:	After approval by CEC in: • clinicaltrials.gov • Swiss Federal Complementary Database
Study category and Rationale	MD risk class IIA: Phonak Hearing Systems (comprising hearing aids, acoustic couplings and fitting software), Wireless Accessories (receiver), Smartphone Applications MD risk class I: Wireless Accessories (transmitters). All investigational devices are CE-labelled and their application is done according to the specialised information.
Clinical Phase:	"Phase of final inspection" (directly prior to launch)
Background and Rationale:	Phonak Hearing Systems pass through different development and study stages. At an early stage, feasibility studies are conducted to investigate new algorithms, features and functions in an isolated manner. If the benefit is proven, their performance is then investigated regarding interdependency between all available algorithms, features and functions running in parallel in a hearing aid (pivotal/pre-validation studies) and, as a result, they get optimized. Afterwards, and prior to product launch, the Phonak Hearing Systems undergo a final quality control in terms of clinical trials in the way as planned for this study ("phase of final inspection").
Primary Objective(s): **Secondary Objective:**	Zero-defect overall performance of the new Phonak Hearing Systems: • Technical: Sound quality, system stability and no distortions/artefacts/interruptions/feedback/system noise or other malfunctions occur. • Audiological: In the lab (objective: Standardised speech intelligibility measures in quiet/noise, threshold measures, cognitive measures, simulations of various listening situations, interviews) and in the users' everyday life (subjective: questionnaires). • Handling: Rate of applicability, size, robustness, look-and-feel. Product benchmark: Comparison of new Phonak Hearing Systems to previous outstanding Phonak models and to competitor devices according to primary objectives.
Outcome(s):	• Lab trials: Objective and subjective test results • Home trials: Subjective test results
Study design:	Active comparator study, controlled, single blinded, randomised, cross-over or parallel design.

Inclusion / Exclusion criteria:	Participants fulfilling all of the following inclusion criteria are eligible for the study: • Adult hearing impaired persons (minimum age: 18 years) with and without (experience with) hearing aids • Good written and spoken (Swiss) German language skills • Healthy outer ear (without previous surgical procedures) • Ability to fill in a questionnaire (p/eCRF) conscientiously • Informed Consent as documented by signature The presence of any one of the following exclusion criteria will lead to exclusion of the participant: • Contraindications to the MD in this study, e.g. known hypersensitivity or allergy to the investigational product • Limited mobility and not in the position to attend weekly appointments • Limited ability to describe listening impressions/experiences and the use of the hearing aid • Inability to produce a reliable hearing test result • Massively limited dexterity • Known psychological problems • Central hearing disorders
Measurements and procedures:	Pure tone audiogram, speech intelligibility in quiet and noise, threshold measurements, cognitive measurements, rating of sound simulation, questionnaires, interviews.
Study Product / Intervention:	MD risk category I and IIA
Control Intervention (if applicable):	MD risk category I and IIA
Number of Participants with Rationale:	In total, a maximum of 210 subjects will participate per year. According to experience, 6 clinical trials (main studies) with a maximum of 30 subjects per study are conducted for a quality control of the Phonak Hearing Systems prior to product launch. Additionally, a pre-study with 5 Sonova internal (normal hearing and/or hearing impaired) persons may takes place to proof the respective study concept in advance if necessary.
Study Duration:	10 years (01.10.2015 – 31.10.2025)
Study Schedule:	Month Year of First-Participant-In: October 2015 Month Year of Last-Participant-Out: October 2025
Investigator(s):	Bernhard Buschle, Marie Lewerenz, Josephine Hollenbach, Claudia Zent, Claudia Pfister Sonova AG, Laubisrütistrasse 28, 8712 Stäfa, Phone: 058 928 01 01
Study Centre(s):	Single-centre (Sonova AG, Stäfa)
Statistical Considerations:	Sample size according to experience and to established specialized literature. Descriptive statistics: Frequency distribution, mean and standard deviation, median and quartile, boxplot, histogram, scatterplot. Inferential statistics: t-Test, Mann-Whitney-U-Test, Wilcoxon-Test, correlation coefficient (Pearson, Spearman) .
GCP Statement:	This study will be conducted in compliance with the protocol, the current version of the Declaration of Helsinki, the ICH-GCP or ISO EN 14155 (as far as applicable) as well as all national legal and regulatory requirements.

STUDY SUMMARY IN LOCAL LANGUAGE

In dieser Studienreihe findet eine methodische klinische Evaluation von neuen CE-zertifizierter Phonak Hörsystemen zur Qualitätskontrolle vor dem jeweiligen Produktlaunch statt. Das Ziel der Untersuchungen ist es, mithilfe von hörgeschädigten Studienteilnehmern, eine fehlerfreie Leistungsfähigkeit des gesamten Phonak Hörsystems zu gewährleisten. Das Phonak Hörsystem umfasst Hörgeräte unterschiedlicher Formfaktoren, akustische Ankopplung, drahtloses Zubehör (z.B. Fernbedienung) sowie die Anpass-Software. Des Weiteren wird die Sicherstellung des maximalen Nutzens für den Träger des Hörsystems anhand von objektiven Labormessungen sowie von subjektiven Bewertungen beim Tragen im Alltag angestrebt. Im Zuge dieser Untersuchungen werden die neu entwickelten Phonak Produkte mit ihren Vorgängermodellen sowie mit Mitbewerberprodukten verglichen. Diese klinische einfachblinde Studienserie erfolgt unter kontrollierten, randomisierten Bedingungen am Hauptsitz der Sonova AG in Stäfa.

ABBREVIATIONS

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

AE	Adverse Event
ANL	Acceptable Noise Level
BTE	Behind-The-Ear device
CA	Competent Authority (e.g. Swissmedic)
CEC	Competent Ethics Committee
CRF	Case Report Form
CU	Categorial Unit
ClinO	Ordinance on Clinical Trials in Human Research *(in German: KlinV, in French: OClin)*
CTCAE	Common terminology criteria for adverse events
dB	Decibel
DD	Device Deficiencies
DM	Digital Modulation
DSUR	Development safety update report
eCRF	Electronic Case Report Form
pCRF	Paper Case Report Form
FM	Frequency Modulation
GCP	Good Clinical Practice
GöSa	Göttinger Satztest
IB	Investigator's Brochure
ITE	In-The-Ear device
Ho	Null hypothesis
H1	Alternative hypothesis
HFG	Humanforschungsgesetz (Law on human research)
HIBAN	Hearing Instrument Body Area Network
HMG	Heilmittelgesetz
HRA	Federal Act on Research involving Human Beings
IMP	Investigational Medicinal Product
IIT	Investigator-initiated Trial
ISO	International Organisation for Standardisation
ITT	Intention to treat
KlinV	Verordnung über klinische Versuche in der Humanforschung *(in English: ClinO, in French OClin)*
LPTh	Loi sur les produits thérapeutiques
LRH	Loi fédérale relative à la recherche sur l'être humain
MD	Medical Device
MUSHRA	Multi-Stimulus Test with Hidden Reference and Anchor
N/A	Not Applicable
OClin	Ordonnance sur les essais cliniques dans le cadre de la recherche sur l'être humain *(in German : KlinV, in English : ClinO)*

OLSA	Oldenburger Satztest
PI	Principal Investigator
PL	Project Leader
PM	Product Manager
PPT	Phoneme Perception Test
REM	Real-Ear Measurement
RIC	Receiver-In-The-Channel device
SDV	Source Data Verification
SNR	Signal-to-Noise Ratio
SOP	Standard Operating Procedure
SPC	Summary of product characteristics
SPL	Sound Pressure Level
SRT	Speech Reception Threshold
SUSAR	Suspected Unexpected Serious Adverse Reaction
TEN test	Threshold-Equalizing-Noise test
TMF	Trial Master File
UAT	User Acceptance Test
UCL	UnComfortable Level
WaKo	Einsilber-Reimtest nach von Wallenberg und Kollmeier

STUDY SCHEDULE

(AGEK 4.2; SPIRIT #13; ICH E6 6.4.2)

Studies are organized in, a potential pre-study if needed, and the main study itself. A pre-study would be organized as follows:

Study Period	Screening	Pre-study appointments		Follow-up (final appointment)
Visit Number	1	2	3	4
Time [hrs]	1.5	2	2	2
Audiological History	x			
Physical Examination of Ear and Ear Canal	x	x	x	x
Audiogram	x			x
Tinnitus Matching	x			x
Check In- /Exclusion Criteria	x			
Decision Subject Participation	x			
Subject Information and Informed Consent	x			
Encoded Subject ID	x			
eCRF Screening	x			
eCRF Audiometry	x			x
Randomisation	x			
Hearing System Fitting	x	x	x	
Objective and Subjective Measurements		x	x	(x)
eCRF Objective and Subjective Measurements		x	x	(x)
Introduction to Handling		x	x	
Scheduling Next Visit		x	x	
eCRF Final Appointment				x
Capture of Adverse Events and Device Deficiencies	x	x	x	x

Table 1a: Pre-study: N = max 5

Study Period	Screening	Study appointments										Final Appointment
Visit Number	1	2	3	4	5	6	7	8	9	10	11	12
Time [hrs]	1.5	2	2	2	2	2	2	2	2	2	2	2
Audiological History	x											
Physical Examination of Ear and Ear Canal	x	x	x	x	x	x	x	x	x	x	x	
Audiogram	x											x
Tinnitus Matching	x											x
Check In- /Exclusion Criteria	x											
Decision Subject Participation	x											
Subject Information and Informed Consent	x											
Encoded Subject ID	x											
eCRF Screening	x											
eCRF Audiometry	x											x
Randomisation	x											
Hearing System Fitting	x											
Objective and Subjective Measurements		x	x	x	x	x	x	x	x	x	x	(x)
eCRF Objective and Subjective Measurements		x	x	x	x	x	x	x	x	x	x	(x)
Introduction to Handling		x	x	x	x	x	x	x	x	x	x	
Scheduling Next Visit	x	x	x	x	x	x	x	x	x	x	x	
eCRF Final Appointment												x
Capture of Adverse Events and Device Deficiencies	x	x	x	x	x	x	x	x	x	x	x	x

Table 1b: Main study: N = max 30 (no pre-study subjects)

1. STUDY ADMINISTRATIVE STRUCTURE

(ICH/E6 6.1.2-6.1.7; AGEK 1.1; SPIRIT 5a-d)

This section contains complete contact details.

1.1 Sponsor, Sponsor-Investigator

(ICH/E6 6.1.2; AGEK 1.1; SPIRIT 5b)
ICH: Name and address of the sponsor …..

The Sponsor is the company Sonova AG, represented by Katrin Manella. Sonova AG will provide the study budget, the staff, the spatial resources, the measurement equipment and the investigational products (hearing systems).

Company: Sonova AG, Stäfa
Contact: Katrin Manella, M.Sc.
Address: Laubisrütistrasse 28, 8712 Stäfa
Phone: 058 928 45 10
Email: katrin.manella@phonak.com
Role: Financier

1.2 Principal Investigator(s)

(ICH/E6 6.1.5, 6.1.6; AGEK 1.1; SPIRIT 5a-d)
ICH: Name and title of the investigator(s) who is (are) responsible for conducting the trial, and the address and telephone number(s) of the trial site(s).

In Sonova AG, the Validation Team undertakes a final quality control of the Phonak Hearing Systems in terms of clinical trials ("final inspection stage"). Each Validation Team member is qualified to take on the role as an Investigator (except of the administrative assistant, Claudia Pfister). The functions as the Principle Investigator is taken on by:

Site: Sonova AG, Stäfa
Contact: Bernhard Buschle, B.Sc. (phone: 058 928 4421)
Address: Laubisrütistrasse 28, 8712 Stäfa
Email: bernhard.buschle@phonak.com
Role:

- Study design
- Data collection
- Data analysis
- Report

1.3 Statistician ("Biostatistician")

(ICH/E6 6.1.7; SPIRIT 5a-d)
ICH: Name(s) and address(es) of the clinical laboratory(ies) and other medical and/or technical department(s) and/or institutions involved in the trial.

The role as the Statistician is adopted by the Principle Investigator.

1.4 Laboratory

(ICH/E6 6.1.7; SPIRIT 5a-d)
ICH: Name(s) and address(es) of the clinical laboratory(ies) ……. involved in the trial.

The study will take place in the labs of the Headquarter of Sonova AG, Laubisrütistrasse 28, 8712 Stäfa (see, 11_QualifikationPrüfort_V1.0_30.06.2015).

1.5 Monitoring institution

(ICH/E6 6.1.2; SPIRIT 5a-d)
ICH: Name and address of the …. monitor (if other than the sponsor).

Site: Sonova AG, Stäfa.
Every Sonova employee who is qualified in the domain of audiology research and who is not part of the study team is capable to take on the role of the Monitor.
Contact: Katrin Manella, M.Sc. (phone: 058 928 45 10)
Address: Laubisrütistrasse 28
8712 Stäfa
Email: katrin.manella@phonak.com

1.6 Data Safety Monitoring Committee

(ICH/E6 6.1.7; SPIRIT 5a-d)
ICH: Name(s) and address(es) of the clinical laboratory(ies) and other medical and/or technical department(s) and/or institutions involved in the trial.

N/A

1.7 Any other relevant Committee, Person, Organisation, Institution

(ICH/E6 6.1.7; SPIRIT 5a-d)
ICH: Name(s) and address(es) of the clinical laboratory(ies) and other medical and/or technical department(s) and/or institutions involved in the trial.

N/A

2. ETHICAL AND REGULATORY ASPECTS

(ICH/E6 6.12; AGEK 11; SPIRIT #24, 5)
ICH: Description of ethical considerations relating to the trial.

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

2.1 Study registration

(ClinO, Art. 1d, 64; SPIRIT #2a-b)

This study will be registered at clincaltrials.gov as a primary register and, additionally, it will be registered in the Swiss Federal Complementary Database as soon as the ethics application is approved by the CEC.

2.2 Categorisation of study

(ClinO, Art. 19, 20, App 3, 1.1)
The study is a clinical trial with MD risk category I (wireless accessories (transmitters and receivers)) and risk category IIA (hearing aids, acoustic couplings (receivers, tubes, earpieces) and fitting software). All medical devices in this trial are CE-labelled and the application is done according to the specialized information.

2.3 Competent Ethics Committee (CEC)

(ClinO, Art 24-29; SPIRIT #24)

The responsible investigator ensures that approval from an appropriately constituted CEC is sought for the clinical study.

Reporting duties and allowed time frame have to be abided concerning 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. No changes are 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 will be submitted within one year after study end. Amendments are reported according to chapter 2.10.

2.4 Competent Authorities (CA)

(ClinO, Art. 23, 27, 30-39, 42, 43, 46-48, 57; SPIRIT #24)

There is no need for a CA approval or other local requirements because this study is of risk category according to LHR A.

(ClinO, Art. 5; AGEK 11; ICH E6 6.12, 6.2.5)
ICH: A statement that the trial will be conducted in compliance with the protocol, GCP and the applicable regulatory requirement(s).

The study will be carried out in accordance to the protocol and with principles enunciated in the current version of the Declaration of Helsinki, the guidelines of Good Clinical Practice (GCP) issued by ICH, in case of medical device: the European Directive on medical devices 93/42/EEC and the ISO Norm 14155 and ISO 14971, the Swiss Law and Swiss regulatory authority's requirements. The CEC and regulatory authorities will receive annual safety and interim reports and be informed about study stop/end in agreement with local requirements.

2.5 Declaration of interest

(ClinO, Art. 3b; SPIRIT #28)

In accordance to ISO 14155 and KlinV, Art. 3b scientific integrity will be preserved. Therefore, any potential conflicts of interest, including financial, that interfere with the conduct of this clinical investigation or interpretation of the according results could be disclosed.

2.6 Patient Information and Informed Consent

(ClinO, Art. 7-9, Art. 15-17, Appendix 3, 1.4, 2.4, 3.4, 4.3, Appendix 4, 3.6; AGEK submission checklist item 5; SPIRIT #26, 32)

The investigators 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 may withdraw from the study at any time and that withdrawal of consent will not lead to consequences for the participant. The participant must be informed that his medical records may be examined by authorized individuals.

All participants for the study will be provided a participant information sheet and a consent form describing the study and providing sufficient information for participant to make an informed decision about their participation in the study. The participants will be given enough time (minimum time frame for this study: 1 week) for their participation decision. The patient information sheet and the consent form will be submitted to the CEC to be reviewed and approved.

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

2.7 Participant privacy and confidentiality

(ClinO, Art. 18; ICH/E6 6.10; AGEK 12.2, SPIRIT #27)
ICH: The sponsor should ensure that it is specified in the protocol or other written agreement that the investigator(s)/institution(s) will permit trial-related monitoring, audits, IRB/IEC review, and regulatory inspection(s), providing direct access to source data/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 audiological 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 measurement data in the computer files.

For data verification purposes, authorised representatives of the Sponsor, a competent authority (e.g.

Swissmedic), or an ethics committee may require direct access to parts of the measurement records relevant to the study, including participants' audiological history.

2.8 Early termination of the study

(ClinO Art. 47; ICH/E6 6.4.6; SPIRIT #21b)

ICH: A description of the "stopping rules" or "discontinuation criteria" for individual participants, parts of trial and entire trial.

The Sponsor or the Principle Investigator 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

2.9 Protocol amendments

(ClinO, Art. 29, 34, 55; SPIRIT #25)

Every person who is involved in the study performance is able to draft an amendment. All amendments have to be reviewed and signed by the Principle Investigator of the main study site before they get forwarded to the responsible approval institution.

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 if applicable to the CEC within the Annual Safety Report (ASR).

3. BACKGROUND AND RATIONALE

(ICH 6.2; AGEK 3; SPIRIT #6)

This section includes any statements that rely on existing knowledge or published information concerning the study.

3.1 Background and Rationale

(ICH/E6 6.2; AGEK 3.1; SPIRIT #6)

Phonak Hearing Systems pass through different development and study stages. At an early stage, feasibility studies are conducted to investigate new ideas in the form of algorithms, features and functions in an isolated manner. If the benefit of a new idea is proven, its performance is then investigated regarding interdependency between all available algorithms, features and functions running in parallel in a hearing aid (pivotal/pre-validation studies). Consequently, optimizations are undertaken according to the outcomes. Afterwards and prior to product launch, the complete Phonak Hearing Systems undergo a final quality control, amongst others, in terms of clinical trials conducted in a standardized manner by the Phonak Validation Team ("final inspection stage").

For years, the Phonak Validation Team could build extensive knowledge regarding quality control and clinical investigations. During the past three years, a series of studies for the final quality control of the Phonak Hearing Systems has been conducted based on the approved ethics proposal KEK ZH-Nr.2013-0144 "Strukturiertes Post Market Clinical Follow-up (PMCF) zur Qualitätsbeurteilung der ersten Palio3 Feature-, Funktions- und Produktgeneration." [37]. The planned study series within this proposal builds on the experiences of the previous studies in the same way. Please find a brief summary of the study series covered by the past ethics proposal below:

No.	Title	Status	Primary Objective	Secondary Objective	N	Methodology
1	Baseline	completed	Loudness, sound quality, speech intelligibility with individual hearing instrument prescription	Speech intelligibility in noise	22	p/eCRFs, WaKo, Freiburger, OLSA, PPT, sound simulations, REM
2	Palio3 - Active Occlusion Control (AOC)	omitted	x	x	x	x
3	HABS	completed	Acceptance of the automatic program during the individual daily life	Perception of artifacts, efforts on fine tuning, sound balance	66	p/eCRFs, Freiburger, OLSA, PPT, sound simulations, MUSHRA, paired comparison, REM
4	Low Frequency amplification in open fittings	completed	Speech intelligibility	Sound balance	20	p/eCRFs, WaKo, OLSA, PPT, sound simulations, REM
5	Sprachverständlichkeit in schwierigen Hörsituationen	omitted	x	x	x	x
6	System Validation Palio3 CR(M)T	completed	High user's satisfaction with the loudness and sound quality	Increase of hearing instrument acceptance after long-term experience (4wks), efforts on fine tuning, additional benefit from accessories, objective speech intelligibility, frequency of hardware defects	60	p/eCRFs, Freiburger, OLSA, PPT, sound simulations, REM
7a 7b	Palio3 HdO Systeme Palio3 IdO Systeme	running	Equality of the form factors regarding loudness and sound quality perception with individual hearing instrument prescription	Increase of hearing instrument acceptance after long-term experience (4wks), efforts on fine tuning, additional benefit from accessories, objective speech intelligibility, frequency of hardware defects	53	p/eCRFs, Freiburger, OLSA, PPT, sound simulations, REM
8a 8b	Palio3 (Bi)CROS CRT Palio3 (Bi)CROS IdO	running	Objective speech intelligibility in noise	Increase of hearing instrument acceptance after long-term experience (5wks), efforts on fine tuning, subjective speech intelligibility	32	p/eCRFs, Freiburger, OLSA, PPT, sound simulations, REM
9	Palio3 Power	To be planned	Equality or improved performance of the new power devices compared to appropriate predecessor regarding loudness and sound quality perception with individually calculated prescription	New system works reliable and no malfunctions occur	40	p/eCRFs, Freiburger, OLSA, PPT, sound simulations, REM

10	Benchmark	omitted	x	x	x	x

Table 2: Overview of study series: KEK ZH-Nr.2013-0144.

3.2 Investigational Product (treatment, device) and Indication

(ICH/E6 6.2.1; AGEK 2; SPIRIT #6)
ICH: Name and description of the investigational product(s).

All hearing systems (Phonak and competitor) are CE-labelled MD of risk category I and IIA. All MDs (hearing instruments, earpieces and wireless accessories) are bearing product names and unique serial numbers for an unambiguous assignment and retracing of the product to the subject. The hearing systems will be set and fine-tuned to the individual hearing loss and needs of the subject by using the corresponding fitting software (table 3) in accordance to the specialised information whereof the latest version can always be printed out of the Phonak Fitting Software, Target.

Manufacturer	Fitting Software
Phonak	Target
Oticon	Genie
Widex	Compass
Siemens	Connexx
Starkey	Inspire
Audio Service	Connexx

Table 3: Overview of hearing instrument companies with their appropriate fitting software.

Hearing Instruments:

In general, the hearing instruments themselves can be separated in different form factors: In-The-Ear (ITE), Receiver In Canal (RIC) and Behind-The-Ear (BTE) including different acoustic couplings depending on the hearing loss and on the anatomical conditions of the hearing aid user, see figures 1-4 below (source: http://www.phonak.com/ch/b2c/de/products/hearing_instruments/styles-10.html and https://www.phonakpro.com/content/dam/phonak/gc_us/Documents/Product/RIC/RIC%20Acoustic_Coupling_Guide_028-0555-03.pdf, status: 07.05.2015).

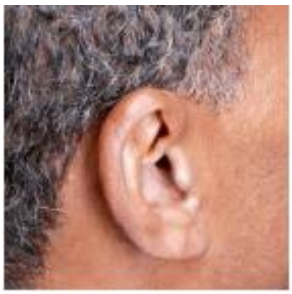

Figure 1: In-The-Ear (ITE)

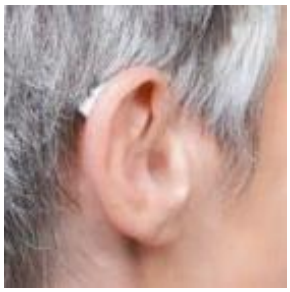

Figure 2: Receiver In Canal (RIC)

Figure 3: Behind-The-Ear (BTE)

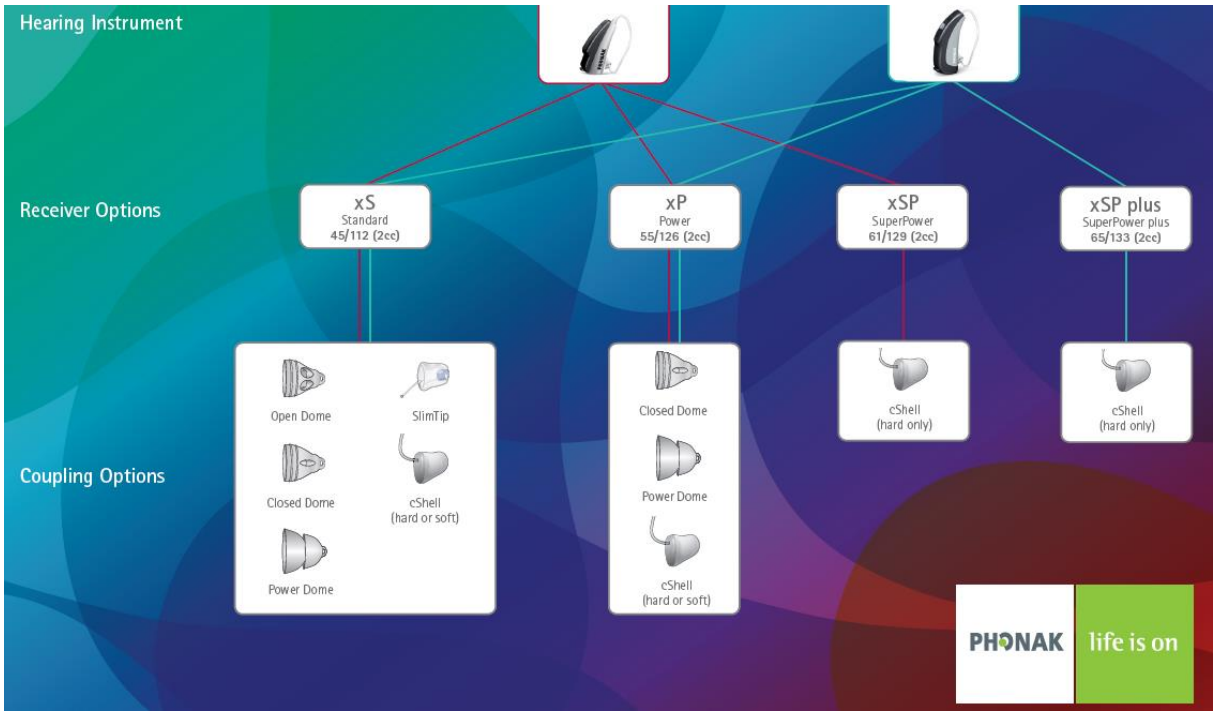

Figure 4: Different acoustic couplings offered by Phonak (receiver and coupling options/earpieces).

Earpieces:

Together with a BTE or RIC, the earpiece is a system which is also of medical device risk category IIA. Without the merge of the earpiece and hearing aid the earpiece has no medical harness.

Wireless Accessories:

The Phonak Wireless Accessories comprise various solutions to simplify the volume adjustment as well as the program switching in a hearing aid but also to enhance speech intelligibility in noisy environments, in making phone calls or in bridging distances between a talker and the hearing aid user like in class/conferences/lectures. The signal processing is based on frequency modulation (FM) technology, digital modulation (DM) technology, bluetooth (direct streaming, e.g. from the cell phone to the hearing instrument) and/or a specific signal processing algorithm developed by Phonak itself, the HIBAN (hearing instrument body area network), respectively. The subsequent current Phonak Wireless Accessory solutions are MD of risk class I: Phonak ComPilot, Phonak PilotOne, PhonakCompilot Air, RemoteControl App, Roger Pen, Roger Clip-On Mic, Roger for Education and their corresponding receivers. Phonak products which are no MD but which are also investigated are: Phonak DECT, Phonak EasyCall, Phonak RemoteMic and Phonak TVLink (figure 5, source: http://www.phonak.com/com/b2c/en/products/wireless-accessories.html, status: 18.05.2015). They also have a unique serial number for an unambiguous assignment and retracing of the product to the subject. The intended purpose is also according to the instruction manual.

Figure 5: Some examples of Phonak Wireless Accessories.

3.3 Preclinical Evidence

(ICH/E6 6.2.2; SPIRIT #6a)
ICH: A summary of findings from nonclinical studies that potentially have clinical significance …..

For MD this entry is only applicable if needed for pre-marketed / marketed devices needing Swissmedic notification (Guidance on the biological evaluation of medical devices is given in ISO 10993). Therefore, this entry is not applicable for this study.

3.4 Clinical Evidence to Date

(ICH/E6 6.2.2; SPIRIT #6a)
ICH: A summary of findings from … and from clinical trials that are relevant to the trial.

There is no available clinical research data to date on the investigational product.

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

(ICH/E6 6.2.4; SPIRIT #6a)
ICH: Description of and justification for the route of administration, dosage, dosage regimen, and treatment period(s).

The hearing instruments will be set and fine-tuned to the individual hearing loss and needs of the subject in accordance to established audiological test methods and according to the best knowledge and conscience of trained staff. The Sonova Validation Team is experienced in hearing instrument fitting for more than 15 years.

3.6 Explanation for choice of comparator (or placebo)

(AGEK 11.3; SPIRIT #6b)

In this study, hearing instruments of previous Phonak generations or competitors are compared with the latest Phonak hearing aid technology to evaluate the current overall product status.

3.7 Risks / Benefits

(ClinO, Appendix 4, 3.5; Art 25d2; ICH/E6 6.2.3; AGEK 11.1; SPIRIT #6a; MD: ISO 14155 Annex A & ISO 14971)
ICH: Summary of the known and potential risks and benefits, if any, to human subjects.

There are five known risks:

1. Infections can be caused by injuries of the ear canal which can occur by the placement of the acoustic coupling (e. g. receiver, earpiece) to the outer ear canal or by the placement of an ITE device. Therefore, the ear canal will be thoroughly checked and assessed during the study.

2. Pressure points can be caused by the hearing aid or the acoustic coupling. In case of pressure points, the hearing aid should not be worn until it healed up. The cause of the pressure point would then be investigated.

3. Tinnitus can be cause by wearing of the hearing aids. An existing tinnitus can be temporarily amplified. If the tinnitus doesn't improve after several days of not wearing the hearing aid, an assessment with an independent doctor (ENT) is necessary.

4. A headache can occur, especially for new hearing aid users. If a headache appears, the subject is instructed to interrupt the hearing aid use until the audiologist applies a new fitting (e.g. reduced gain level) to acclimatize the subject to the devices.

5. The hearing aid can reach a high maximum power output (MPO). The MPO will be set accordingly to clinical expertise at a level that no injuries can occur.

3.8 Justification of choice of study population

(ClinO, Art 25d4, Art. 15-17; ICH/E6 6.2.6; AGEK 11.2)
ICH: Description of the population to be studied.

In this study, adult hearing impaired persons with different degrees of hearing loss will participate. The sound processing in the inner ear significantly differs between normal hearing and hearing impaired persons and, furthermore, is dependent on the degree of the hearing loss. For this reason, the sound quality and the benefit of new hearing systems, which can be individually fitted to a hearing loss, can only be reliably evaluated by appropriate hearing impaired persons.

In addition, both persons with hearing aid experience (i.e. owning hearing aids) and without this experience can participate. Hearing impaired persons are categorized as a vulnerable population since in both cases (with and without hearing aid experience), they might expect a benefit from the study participation in the form of, e.g. a cheaper acquisition of the newest hearing system technology directly from the Sonova AG which is not possible.

4. STUDY OBJECTIVES

(ICH/E6 6.3; AGEK 3; SPIRIT #7)
ICH: A detailed description of the objectives and the purpose of the trial.

4.1 Overall Objective

A successive methodical evaluation of new CE-Labelled Phonak Hearing Systems (hearing instruments, acoustic couplings, wireless accessories and fitting software) on hard of hearing participants will be conducted to grant quality control prior to product launch.

4.2 Primary Objective

The study seeks primarily to grant zero-defect overall performance of the new Phonak Hearing Systems.

4.3 Secondary Objectives

Secondary objectives are to assess efficacy of the new Phonak Hearing Systems compared to previously outstanding Phonak Hearing Systems and to competitor devices.

4.4 Safety Objectives

With regard to a continuous improvement of the various algorithms running in parallel in a hearing systems, the study aims to assess long-term safety of the Phonak Hearing Systems.

5. STUDY OUTCOMES

(ICH/E6 6.4.1; AGEK 4.1; SPIRIT #12)
ICH: A specific statement of the primary endpoints and the secondary endpoints, if any, to be measured during the trial.

This section includes a description of the overall, primary and secondary objective(s) of the study including the specific measurement variable and analysis metric.

5.1 Primary Outcome

Zero-defect overall performance of the new Phonak Hearing Systems:

- Technical: Sound quality, system stability, no distortions/artefacts/interruptions/feedback/ system noise or other malfunctions occur.
- Audiological: In the lab (objective: standardised speech intelligibility measures in quiet and in noise, threshold measures, cognitive measures, simulations of various listening situations, interviews) and in the users' everyday life (subjective: questionnaires (p/eCRF)).
- Handling: Rate of applicability, size, robustness, look-and-feel.

Dependent on the investigational device and the corresponding focused algorithm, feature or function

(aim) the appropriate audiological testing method will be chosen (for details, see table 4):

Performance	Aim	Method	Result [unit]
Technical	Assessment of sound quality	Subjective Rating Scale [31, 32]	Point on a scale
	Assessment of system stability	Quantitative Questionnaires [29]	Yes/No replies and open-ended
	Survey of audibility of distortions, artefacts, interruptions, feedback, system noise or other malfunctions	Quantitative Questionnaires [29]	Yes/No replies and open-ended
Audiological	Determination of hearing threshold of pure tones	Pure Tone Audiometry [30]	Yes/No replies
	Assessment of speech intelligibility in quiet	Freiburger Sprachtest [10, 30]	Discrimination [%]
	Assessment of speech intelligibility in noise	Oldenburger Satztest (OLSA) [11, 12]	Speech intelligibility threshold in noise [dB SNR]
	Assessment of speech intelligibility in quiet or in noise	Einsilber-Reimtest nach von Wallenberg und Kollmeier (WaKo) (quiet/noise) [13]	Discrimination [%]
	Assessment of speech intelligibility in quiet or in noise	Göttinger Satztest (GöSa) (quiet/noise) [14]	SRT in quiet [dB], in noise [dB SNR]
	Determination of threshold of fricatives	Phoneme Perception Test (PPT) [15-18]	Detection, Distinction and Recognition Threshold [dB SPL]
	Judgment which of the entities in pairs is preferred or has a greater amount of some quantitative property	Paired Comparison [19]	Preference or point on a scale
	Subjective evaluation of the audio quality of a defined sound	Multi-Stimulus Test with Hidden Reference and Anchor (MUSHRA) [20]	Point on a scale
	Determination of acceptable noise intensities while listening to speech	Acceptable Noise Level (ANL) Test [21, 22]	Tolerated SNR [dB]
	Assessment of the subjectively perceived loudness of a test signal	Categorial Loudness Scaling [23]	Loudness [CU]
	Assessment of the real-ear performance of hearing aids	Real-Ear Measurement (REM) [24]	Frequency Response [magnitude and phase of the output as a function of frequency]
	Determination of individual information or circumstances regarding hearing system and/or listening situation	Interviews: Qualitative and Quantitative (ad hoc list of questions, semi-standardized, standardized or normed), Focus Groups [29]	Narrative, open/closed replies, ranking, single/multiple choice, or point on a rating scale
	Quantitative assessment of a person's perception of facts or circumstances regarding hearing system	Semantic Differential Analysis/ Polarity Profile [25]	Point on a scale
	Determination of a present tinnitus	Tinnitus Pitch and Loudness Matching [26]	Tinnitus frequency/pitch [Hz] and sensation level [dB SL].
	Assessment of a person's perception of a specific listening situation through selected hearing systems or hearing aid programs	Simulations of Various Listening Situations (in Car/Cafeteria/Reverberation) via Loudspeakers including Preference Rating or Subjective Rating Scale	Preference or point on a scale
	Determination of localization capabilities with and/or without hearing systems	Localization Test in Quiet, Noise, Reverberation. [27]	Average RMS localization error [°], back-front confusions [%]
	Determination of dead regions in the cochlear	TEN (Threshold-Equalizing-Noise) Test [28]	Detection of pure tones presented simultaneously with a wide band noise (TEN) which produces the same level of masking [dB NPS] throughout audiogram frequencies (250 – 10k Hz)
	Assessment of a hearing aid user's affection by objective occlusion (closed ear canals)	Occlusion Measurement and Leakage Measurement using REM method [36]	Frequency Responses [magnitude and phase of the output as a function of frequency] => Level differences [dB] and Level Loss [dB]
	Assessment of real-time individual information regarding	MobEval [33, 34, 35]	Logging of predefined HI parameters, time [h/min/s],

	hearing system and/or listening situation via Phonak App on Smartphone in daily life		open/closed replies or single/multiple choice
Other	Assessment of third-party disability and the role of social support in hearing care	Quantitative Data through Questionnaires (e.g., IOI-HA-SO [40], SOS-HEAR [41])	Score on Likert Rating Scales
	Assessment of cognitive influences on speech perception	Cognitive Measures, e.g. for Working-Memory Capacity (e.g., Reading Span [38]), Executive Functioning and Attention (e.g., Stroop Task), Overall Cognitive Ability (e.g., MoCA [39])	Performance Level [%-correct responses or time-to-complete outcomes]
	Subjective Assessment of Listening Effort and Hearing Fatigue	Questionnaires about Listening Effort in Everyday Life (e.g., CTO [42]), Rating Scales of Effort perceived during above listed Audiological Tests	Score on a Continuous Rating Scale or on a Likert Rating Scale
	Objective Assessment of Listening Effort and Spare Capacity	Response Delays during above listed Speech Intelligibility Tests; Dual-Task Paradigms with Speech Intelligibility as primary task and a Cognitive Outcome Measure as the Secondary Add-On Task (e.g., Assessment of Cognitive Capacity for tasks of Selective Attention or Working Memory during the Primary Task [43, 44, 45])	SRT [%] and Errors [%] or Response Times [ms]

Table 4: Primary outcome table.

5.2 Secondary Outcomes

Product benchmark: Comparison of new Phonak Hearing Systems to previous models and to competitor devices according to primary objectives in accordance to table 4.

5.3 Other Outcomes of Interest

Other outcomes of interest are side-effects.

5.4 Safety Outcomes

N/A

6. STUDY DESIGN

(ICH/E6 6.4; AGEK 4; SPIRIT #8)

6.1 General study design and justification of design

(ICH/E6 6.4.2, 6.4.5; AGEK 4.2; SPIRIT #8)
ICH: The scientific integrity of the trial and the credibility of the data from the trial depend substantially on the trial design.
ICH: A description of the type/design of trial to be conducted (e.g., double-blind, placebo-controlled, parallel design) and a schematic diagram of trial design, procedures and stages.
ICH: The expected duration of subject participation, and a description of the sequence and duration of all trial periods, including follow-up, if any.

A methodical evaluation of new CE-Labelled Phonak Hearing Systems is intended to be conducted on hard of hearing participants to grant quality control prior to product launch in spring or in fall per year. The aim of the investigation is to continuously ensure zero-defect overall performance of the new hearing systems as well as maximum benefit for the participant with the devices in comparison to previously outstanding Phonak Hearing Systems and to equivalent strong competitor devices across 10 years (October 2015 to 2025). This will be a controlled, single blinded (participants), randomised (testing method), cross-over (investigational product) active comparator study which will be conducted mono centric at Sonova AG Headquarters based in Stäfa.

In total, a maximum of 210 adult subjects will participate per year.If necessary, there will be a pre-study with a maximum of five internal (normal hearing or hearing impaired) subjects before the main study to prove the actual study design . A pre-study will be considered if there are adjustments away the normal audiological standard regarding the methode, setup, subject group etc. If a pre-study is necessary will be decided by the principal investigator. . Then, according to experience, 6 clinical trials (main studies) with a maximum of 30 subjects per study each of two months duration, are conducted for a quality control of the Phonak Hearing Systems. Typically, each participant gets a series of weekly appointments of 1.5 to 2 hours (lab trials), respectively, including the fitting procedure of the hearing system as well as the objective tests. Between the weekly appointments, the home trials take place so that the subjects can test the devices in their daily life in accordance to some questionnaires either pCRF or eCRF. In dependence on the form factor of an investigational product, which provide different gain levels, participants with appropriate hearing losses ranging from mild, moderate, severe to profound need to be recruited. Testing takes place in one of the three double-walled sound-attenuating booths (Validation Room 1, 2 and 3, see section 9.2.1).

Despite of the well-defined study protocol, some limitations of the study design are inherent. For example, it is not possible to blind the investigational product during the home trial. Especially the housing/naming of competitor devices are revealing their identity. During the lab trials, the participants are fully blinded. An additional limitation of the study design are software updates during the study for both the fitting software and the hearing systems. As soon as quality problems occur, such as acoustic feedback problems or artefacts, for example, a device deficiency form is filled in and the devices get revised leading to different firmware versions across the study which need to be considered during the data analysis.

6.2 Methods of minimising bias

(ICH/E6 6.4.3; AGEK 4.3; SPIRIT #16, 17)
ICH: A description of the measures taken to minimize/avoid bias, including: Randomization, Blinding.
In order to minimize bias:

1. Strictly defined hearing instruments settings will be taken for:
   A. Lab Trial: All objective lab tests will be performed in a lab setting of the hearing instruments. The lab setting for each hearing instrument will be defined in appointment 1 after performing the first fit to the individual hearing loss of the subject as proposed by the Phonak Fitting Software, and, if necessary, a fine tuning only in gain level.
   B. Home Trials: If necessary, for the Home Trials the hearing instruments will be fine-tuned based on the individual hearing loss and pre-calculation (lab setting). The fine tuning comprises every option offered in the fitting software as it can typically be applied by the hearing care professionals in the market.
2. No investigator change per subject during the study, if possible (exceptions: sickness, vacation, advanced training).
3. Uniform and extensive training of the whole study team and monitor prior to study start.
4. Use of electronic database eClinicalOS (Merge) for direct data capture by the investigators during the lab trial and by the study participants during home trial (reduction of pCRFs to the greatest possible extent).
5. Close meshed monitoring of subject appointments conducted by new investigators.
6. To avoid learning effects, subjects cannot jump from one study to the next (minimum break of six months, at least).
7. To avoid training effects, standardized test methods are applied according to their instructions.
8. Sensitizing the investigators to bias (e.g. Halo-Effects).
9. Orthogonal design of the questionnaires (p/eCRF) to fulfil the criteria for test quality (objectivity, validity, reliability).
10. Reduction of order effects – randomized order of the test procedure of the subjective judgments, the objective tests and the hardware comparisons.
11. Limited information will be given to the subjects regarding the test products and the features.
12. In order to ensure a high satisfaction of the subject, the physical position in and on the ear must be comfortable and it must be ensured that the subject can operate the device well (e. g. putting the hearing aids on, changing batteries, switching on/off). These aspects will be observed and checked throughout the study sections so that they are not the form factor to cause any bias in results, especially subjective results.

6.2.1 Randomisation

Randomization and concealment of randomization list is generated by the Principle Investigator using a script written in the program MatLab. The randomization is applied to all investigational products for both the lab trials and the home trials. Furthermore, the order of the test method used per visit is liable to a randomization.

6.2.2 Blinding procedures

Trial participants will be blinded after assignment to interventions. During the lab trials, the subjects will not know which hearing system they are wearing because the investigators will mount the hearing instruments covered to the subjects ear. During the home trials, the labelling on the housing will be covered by a sticker, if possible. Nevertheless, the brand of the device might be identified by the subjects due to the shape of the housing (limited blinding).

6.2.3 Other methods of minimising bias

To the greatest possible extent validated questionnaires (p/eCRF) come into operation. However, specifically adapted questionnaires are inevitable to validly capture the appropriate information needed.

6.3 Unblinding Procedures (Code break)

(ICH/E6 6.4.8; AGEK 4.2; SPIRIT #17b)
ICH: Maintenance of trial treatment randomization codes and procedures for breaking codes.

A subject coding list is safely stored and can be used to break the code, if necessary. Also the randomization lists can be used to identify the subject and his specific measurement order, if applicable.

7. STUDY POPULATION

(ICH/E6 6.2.6, 6.4.6; AGEK 3.2, 5; SPIRIT #9, 10, 15, 16, 21)
ICH: Description of the population to be studied.

This section describes the population to be studied.

7.1 Eligibility criteria

(ClinO, Art 25d5; ICH/E6 6.5.1&6.5.2; AGEK 5.2&5.3; SPIRIT #10)
ICH: Subject inclusion and exclusion criteria.

Only adult subjects will participate. In the pre-study normal hearing persons as well as hearing impaired persons will participate whereas in the main study merely hearing impaired subjects will be involved.

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

- Adult (minimum age: 18 years) hearing impaired persons both with and without (experience with) hearing aids
- Good written and spoken (Swiss) German language skills
- Healthy outer ear (without previous surgical procedures)
- Ability to fill in a questionnaire (p/eCRF) conscientiously
- Informed Consent as documented by signature

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

- Contraindications to the MD in this study, e.g. known hypersensitivity or allergy to the investigational product
- Limited mobility and not in the position to attend weekly appointments
- Limited ability to describe listening impressions/experiences and the use of the hearing aid
- Inability to produce a reliable hearing test result

- Massively limited dexterity
- Known psychological problems
- Central hearing disorders

7.2 Recruitment and screening

(ClinO, Art 25, Appendix 3, 1.4 & 1.6; AGEK 5.1; SPIRIT #15)

At Sonova AG Headquarters, a subject database is existing which is currently containing approx. 1000 hearing impaired subjects (various degrees of hearing loss) from circumjacent cantons. Furthermore, this database is containing hearing impaired employees from Sonova AG (internal subjects). The database is permanently extended (study independently) with new subjects recruited via different paths and screened by qualified Audiologists employed at Sonova AG:

- Phonak homepage (status 22.11.2019): https://www.phonak.com/ch/de/hoerverlust/feldstudie-anmeldung.html
- Flyer Phonak Feldstudien (see attachment: 4b1_Flyer_Phonak_Feldstudien.pdf)
- Campaign "Probanden werben Probanden" (see attachment: 4b2_Kampagne_Probanden_werben_Probanden.pdf)
- Advertisement in magazine Decibel (see attachment: 4b3_Inserat_Decibel.pdf)
- Links at homepages from organization of hearing impaireds, e.g.:
    - ProAudito (status 19.05.2015): http://www.proaudito-zuerich.ch/fileadmin/customer/Medien/Home_und_Aktuell/pdf/Inserat_Phonak_sucht_Probanden.pdf
    - Audiopädagogik.ch (status 19.05.2015): http://www.audiopädagogik.ch/phonak-sucht-probanden-ab-sofort/

After the study approval by the CEC and after a subsequent successful Initiation Visit undertaken by the monitor, the subject recruiting by contacting potential candidates can be started. At this initial contact, the time expenditure and the availability period will be discussed in advance. In case of a positive reply, the participant information as well as the informed consent form is sent to the potential study participant by post or email one week prior to the screening appointment, at least, and the subject is invited via telephone or email for an assessment of his hearing at Phonak HQ. The audiological history of a subject and a pure tone audiogram as well as a speech audiogram is recorded, the inclusion and exclusion criteria are requested and open questions concerning the study itself, the participant information and the informed consent form are replied before the decision about a study participation is made and the signed document is collected by the investigator. If a participant quotes hearing a tinnitus, a Tinnitus Pitch and Loudness Matching is executed to determine its frequency and intensity (section 5.1, table 4).

Internal subjects are personally contacted or via email to request their availability and interest in pre-study participation. The screening process is the same as for the external participants. The internal subjects participate on a voluntary basis during their regular working time and contribute to an investigational benefit for the company. In case of any non-attendances of the study, no employment consequences will occur.

All the selected participants will be listed and encoded in a password locked file. Only the study personal and the monitor have access to this file. For all study related appointments at Sonova AG, the participants receive an expense allowance of 25 CHF/hour during the lab trials, of 12.50 CHF per questionnaire (p/eCRF) which is filled in during the home trials (assumed duration of 30 min) and a train ticket (2nd class) from their home address to Sonova AG, Laubisrütistrasse 28, 8712 Stäfa, by the end of the study.

Please note that from the 6th July 2015 on, the Sonova AG is the family brand as well as the employer and the Phonak AG is the main brand of Sonova's different brands. The Validation Team works for the brand Phonak AG and, therefore, evaluates Phonak Hearing Systems. For this reason, both brands Sonova AG and Phonak AG have the same address and can both officially be used printed on the recruiting material.

7.3 Assignment to study groups

(AGEK 5; SPIRIT #16)

The assignment of the participants is done by chance. The first participants who state their participation and fulfil the inclusion criteria are picked.

7.4 Criteria for withdrawal / discontinuation of participants

(ClinO, Art 9; ICH/E6 6.5.3; SPIRIT #21b)

Subject withdrawal criteria (i.e., terminating investigational product treatment/trial treatment) and procedures specifying: a) When and how to withdraw subjects from the trial/ investigational product treatment. c) Whether and how subjects are to be replaced.

If a subject will be withdrawn (e. g. withdrawal of informed consent, non-compliance, disease progression, safety etc. or study or routine procedure must be stopped, e. g. due to safety concerns), a final assessment of the ear and ear canal will be carried out and all products as well as all study material (e.g. pCRFs) that had been used have to be returned by the participant to the study site. The participants participate on a voluntary basis and can abort the participation on the study at any point of the study. The withdrawn participant will be replaced by another voluntary employee, if needed. The measurement results of the withdrawn participants will be excluded of the evaluation if the results are not complete to be included in the analysis. A new participant has to pass each study trial from the beginning.

8. STUDY INTERVENTION

(SPIRIT #11)

8.1 Identity of Investigational Products (treatment / medical device)

(ICH/E6 6.2.1, 6.4.2, 6.4.4; AGEK Checklist 2, item 3)

ICH: A description of the trial treatment(s) and the dosage and dosage regimen of the investigational product(s).

This section describes all trial treatments for each arm of the study.

8.1.1 Experimental Intervention (treatment / medical device)

ICH: Name and description of the investigational product(s).

All investigational devices are CE marked and based on the latest Phonak Hearing System portfolio (all form factors and performance levels, see http://www.phonak.com/ch/b2c/de/products/hearing_instruments.html, status 20.05.2015). This includes MD of risk category IIA: Phonak Hearing Systems comprising hearing aids, acoustic coupling (receiver and earpiece), fitting software and of risk category I: Wireless accessories (transmitters and receivers). The application is done according to the specialised information.

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

ICH: Name and description of the investigational product(s).

Previous outstanding Phonak Hearing Systems as well as equivalent strong competitor devices.

8.1.3 Packaging, Labelling and Supply (re-supply)

ICH: Also include a description of the dosage form, packaging, and labelling of the investigational product(s).

N/A

8.1.4 Storage Conditions

All MD and MD supplies have to be stored according to standard procedures as mentioned in the

manufacturer directions. The hearing aids will be stored in their hearing aid cases (dry and dust-free). There are no special environmental conditions necessary for storage.

8.2 Administration of experimental and control interventions

(ICH/E6 6.4.4)

8.2.1 Experimental Intervention

ICH: Description of and justification of the treatment(s) to be administered, including the name(s) of all the product(s), the dose(s), the dosing schedule(s), the route/mode(s) of administration, and the treatment period(s), including the follow-up period(s) for subjects for each investigational product treatment/trial treatment group/arm of the trial.

Please find the description of route, dose, study procedure and the utilization period of the investigational medical devices in chapter 3.5, 5, 6.1 and in the section STUDY SCHEDULE.

8.2.2 Control Intervention

ICH: Description of and justification of the treatment(s) to be administered, including the name(s) of all the product(s), the dose(s), the dosing schedule(s), the route/mode(s) of administration, and the treatment period(s), including the follow-up period(s) for subjects for each investigational product treatment/trial treatment group/arm of the trial.

Same as in 8.2.1.

8.3 Dose / Device modifications

(SPIRIT #11b)

N/A

8.4 Compliance with study intervention

(ICH/E6 6.6.3; AGEK Checklist 2, item 2; SPIRIT #11c)
ICH: Procedures for monitoring subject compliance.

N/A

8.5 Data Collection and Follow-up for withdrawn participants

(ICH/E6 6.5.3; AGEK 9.2; SPIRIT #18b)
ICH: ……..b) The type and timing of the data to be collected for withdrawn subjects. d) The follow-up for subjects withdrawn from investigational product treatment/trial treatment.

The subjects participate on a voluntary basis and can abort the participation on the study at any point of the study. The withdrawn participant will be replaced by another voluntary employee. The measurement results of the withdrawn participants will be included to the evaluation if data are complete for the appropriate trial. The new participant has to pass each study trial from the beginning.

8.6 Trial specific preventive measures

(ICH/E6 6.6.2; AGEK 9; SPIRIT #11d)
ICH: Medication(s)/treatment(s) permitted (including rescue medication) and not permitted before and/or during the trial.

To avoid discomfort through too loud output levels of the hearing aids which could harm the subjects ear, the uncomfortable level (UCL) will be measured within the pure tone audiogram during the screening appointment. The UCL will be used for the fitting of the hearing aids to ensure a comfortable maximum power output.

After fitting the hearing aids to the individual hearing loss of the subject, the subjective acceptance of loud input signals will be tested (tolerance test) to ensure that the individual maximum power output (based on the UCL measurement) of the hearing aids is guaranteed and accepted by the subject.

8.7 Concomitant Interventions (treatments)

(ICH/E6 6.6.2; AGEK 9; SPIRIT #11d)
ICH: Medication(s)/treatment(s) permitted (including rescue medication) and not permitted before and/or during the trial.

N/A

8.8 Study Drug / Medical Device Accountability

(ICH/E6 6.4.7; AGEK Checklist 2, item 1; SPIRIT 11c)
ICH: Accountability procedures for the investigational product(s), including the placebo(s) and comparator(s), if any.

The accountability for the MD is ascribed to both the according Project Leader (PL) of the Research & Development Department and the Product Manager of the Marketing Department in the Sonova AG, Stäfa. The PL and the PM are also the persons addressed in case of any device deficiencies (receivers of the device deficiency form).

8.9 Return or Destruction of Study Drug / Medical Device

(AGEK Checklist 2, item 1; SPIRIT 11c)

At the end of the study during the final appointment, all study devices will be returned to the according PI.

9. STUDY ASSESSMENTS

(ICH/E6 6.7, 6.8; AGEK 6, 7; SPIRIT #18a)

This section includes a description of the procedures, measurements, collections and storage of samples taken.

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

A study maybe a combination of a pre-study, if neccesary, and a main study where of both include objective and subjective measurements. A maximum of 5 subjects will take part in the pre-study and a maximum of 30 will take part in the main study which does not include the pre-study participants. Please note the following tables repeat those of section STUDY SCHEDULE.

Study Period	Screening	Pre-study appointments		Follow-up (final appointment)
Visit Number	1	2	3	4
Time [hrs]	1.5	2	2	2
Audiological History	x			
Physical Examination of Ear and Ear Canal	x	x	x	x
Audiogram	x			x
Tinnitus Matching	x			x
Check In- /Exclusion Criteria	x			
Decision Subject Participation	x			
Subject Information and Informed Consent	x			
Encoded Subject ID	x			
eCRF Screening	x			
eCRF Audiometry	x			x

Randomisation	x			
Hearing System Fitting	x	x	x	
Objective and Subjective Measurements		x	x	(x)
eCRF Objective and Subjective Measurements		x	x	(x)
Introduction to Handling		x	x	
Scheduling Next Visit		x	x	
eCRF Final Appointment				x
Capture of Adverse Events and Device Deficiencies	x	x	x	x

Table 1a: Pre-study: N = max 5

Study Period	Screening	Study appointments										Final Appointment
Visit Number	1	2	3	4	5	6	7	8	9	10	11	12
Time [hrs]	1.5	2	2	2	2	2	2	2	2	2	2	2
Audiological History	x											
Physical Examination of Ear and Ear Canal	x	x	x	x	x	x	x	x	x	x	x	
Audiogram	x											x
Tinnitus Matching	x											x
Check In-/Exclusion Criteria	x											
Decision Subject Participation	x											
Subject Information and Informed Consent	x											
Encoded Subject ID	x											
eCRF Screening	x											
eCRF Audiometry	x											x
Randomisation	x											
Hearing System Fitting	x											
Objective and Subjective Measurements		x	x	x	x	x	x	x	x	x	x	(x)

eCRF Objective and Subjective Measurements		x	x	x	x	x	x	x	x	x	X	(x)
Introduction to Handling		x	x	x	x	x	x	x	x	x	x	
Scheduling Next Visit	x	x	x	x	x	x	x	x	x	x	x	
eCRF Final Appointment												x
Capture of Adverse Events and Device Deficiencies	x	x	x	x	x	x	x	x	x	x	x	x

Table 1b: Main study: N = max 30 (no pre-study subjects)

9.2 Assessments of outcomes

ICH: Specification of the efficacy parameters. Specification of safety parameters.

This section includes a description of each endpoint, what variables will be assessed/observed and how it will be done, including any related processes to promote data quality. In general, the standard measurement equipment gets calibrated by certified specialists sent out by the appropriate company to Sonova AG once per year. Study specific adjustments of the measurement tools get calibrated by the responsible study team member. Prior to study start, the PI uniformly trains the study team according to the study protocol, which is documented in a training log. Every measurement method used in this study is conducted according to its instruction. In this way, potential damages of a participants ears caused by unexpected loud sound levels are eliminated. Prior to every measurement, the participants absolve a training session to minimize a bias induced by training or learning effects. These data are not part of the analysis.

9.2.1 Assessment of primary outcome

ICH: Methods and timing for assessing, recording, and analysing of efficacy & safety parameters.

Procedure: After a successful screening as described in section 7.2, the data serving as primary outcomes are collected in a series of appointments lasting 1.5 to 2 hours each for the lab trials and one week for the home trials taking place between the lab trial appointments. The subjective and objective measurements that are applied to grant zero-defect overall performance of the new Phonak Hearing Systems regarding technical stability, audiological performance and handling are listed in section section 5.1. The general procedure of a lab trial can be described in a flow chart as follows:

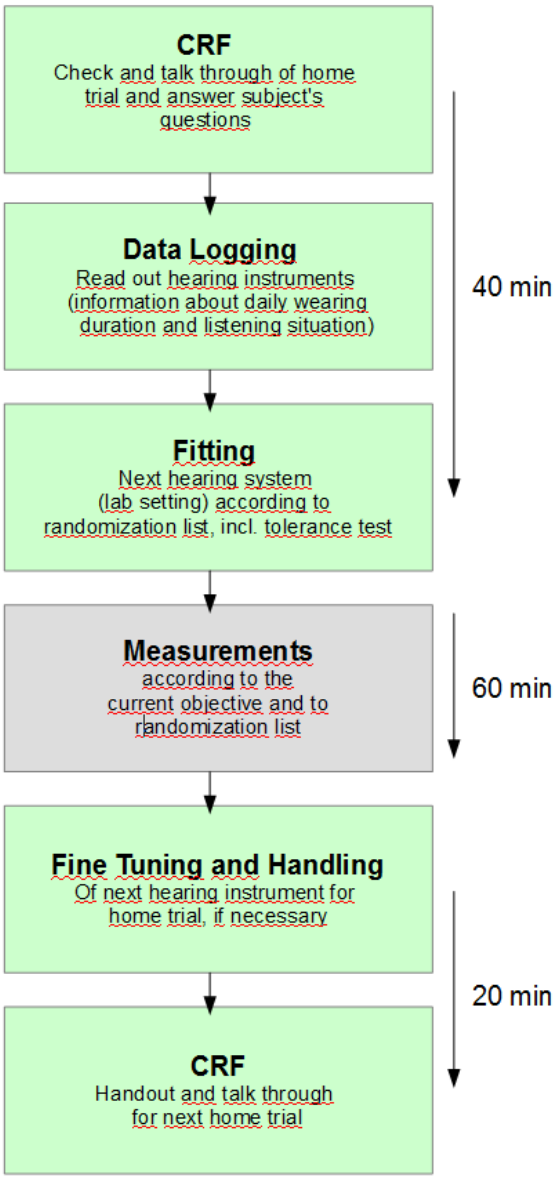

Figure 6: Schematic procedure of a lab trial.

Testing takes place in one of the three double-walled sound-attenuating booths (Validation Room 1, 2 and 3). Participants are tested individually. All of them comfortably sit on a chair in the middle of the room and are consistently instructed what their task is both written in terms of standardized instructions and verbally to ensure that the task is understood. Then, stimuli (speech: words, numbers or sentences in quiet or in a specific background noise, also music or sound simulations, like an in car situation, in a cafeteria or in a reverberated room) are presented with a computer and loudspeakers of a number and of a defined arrangement according to the test method used, see figures 7 and 8. In case of a closed-set speech test, the participant are instructed to choose an answer on a touch screen. In case of an open-set task, the participant is asked to verbally repeat the things understood.

Instead of loudspeaker presentations also headphone presentations simulating hearing aids (single features or functions) as well as sound situations by pre-recorded sound files can be presented to the participant. The advantage is a highly controlled listening situation and a simple possibility to quickly switch between different hearing aids (or settings) in case of a paired comparison or a MUSHRA task which use subjective rating on a rating scales to evaluate different dimensions.

Measurement methods: The measurement method that comes into operation depends on the particular question that needs to be answered during an appointment. Most important aims for ensuring a high quality hearing system are both a maximum *speech understanding* in every listening situation and a good *sound quality*.

Speech understanding can be assessed by standardized speech tests both in quiet and in noise (see figure 7, 8 and section 5.1, table 4). To evaluate speech intelligibility in quiet, different normed speech tests are available, such as the Freiburger, GöSa and WAKO. These methods are complemented with a new methodology, the Phoneme Perception Test (PPT), a language independent test, assessing a participant's detection, distinction and recognition threshold for single fricatives (high frequent sounds like /s/, /sh/, /f/) which are mostly affected by a hearing loss. In addition to speech understanding in quiet, speech intelligibility in noisy surroundings needs to be evaluated. The OLSA method as well as the GöSa in noise, the WAKO in noise and the Acceptable Noise Level (ANL) test provide a basis. Another important topic is the localization capability of a hearing aid user to know from which direction a sound origins from. The Localization Test delivers appropriate results.

Sound quality is evaluated by using methods of subjective rating on a rating scale using the Paired Comparison method or the MUSHRA. Furthermore, sound quality can be rated using qualitative and quantitative questionnaires (p/eCRF) during both the home trials and the lab trials or by conducting structured interviews, unstructured interviews or group discussions where the data collected are of narrative character. In this way data can be supplemented by some information that could not be captured using the standardized test methodologies.

The Real-Ear Measurement (REM) tool is an objective methodology to measure the hearing instrument's frequency response under real ear conditions. A Real-Ear-Measurement includes the established real ear measurements of REUG (real ear unaided gain), REAG (real ear aided gain), REIG (real ear insertion gain) and RECD (real ear coupler difference). For the real ear measurement a soft silicone probe tube is thread through the custom product vent. The individual length of the probe tube is measured via otoscopy. The tip of the probe tube has to be placed in the residual ear canal volume of the participants ear. After the insertion of the custom product in the participants ear, the ear canal gets stimulated by an acoustic source from an exterior sound source. With the probe tube in the residual ear canal the frequency response is recorded.

Further tests used are the Categorial Loudness Scaling a psychoacoustic method to capture the individual subjective loudness perception, the TEN test to evaluate dead regions in the cochlear, cognitive measures to assess hearing fatigue and listening effort, occlusion measurements to investigate occlusion effects mainly occurring in ITE devices.

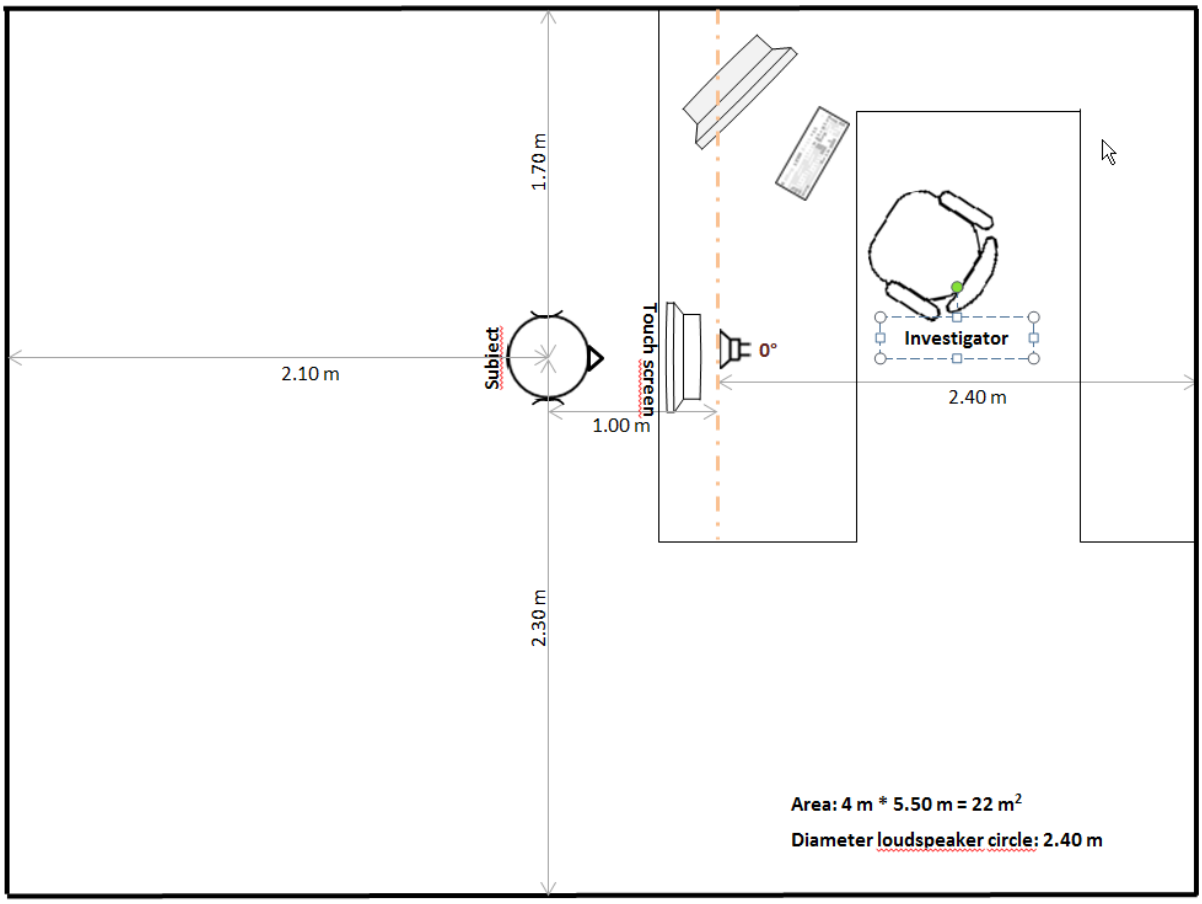

Figure 7: Measurement setup: Freiburger, WAKO and GöSa in quiet, PPT, Categorial Loudness Scaling. Both study participant and PI in sound-attenuating booth.

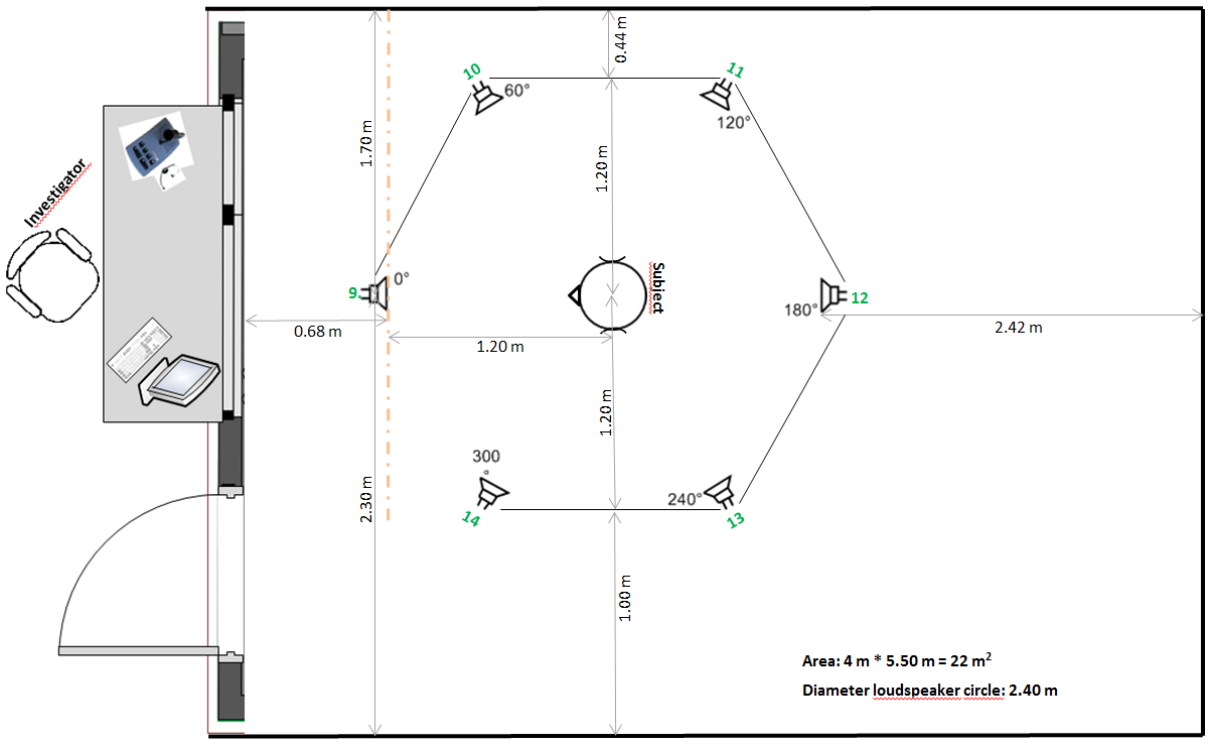

Figure 8: Measurement setup: OLSA, WAKO and GöSa in noise, sound simulations (e.g. in car/cafeteria/reverberation), localization test. Subject in sound-attenuating booth, PI outside.

9.2.2 Assessment of secondary outcomes

ICH: Methods and timing for assessing, recording, and analysing of efficacy & safety parameters.

The secondary outcomes are assessed in the same way as the primary outcomes (see section 9.2.1).

9.2.3 Assessment of other outcomes of interest

ICH: Methods and timing for assessing, recording, and analysing of efficacy & safety parameters.

Other outcomes of interest like side-effects will be carefully investigated, evaluated and documented.

9.2.4 Assessment of safety outcomes

ICH E6 6.8: Specification of safety parameters. The methods and timing for assessing, recording, and analysing safety parameters

9.2.4.1 Adverse events

Basically, all participants will be instructed to immediately report any problems, oddness or difficulties which occurred with or through the testing devices by contacting the appropriate investigator. Additionally, the investigator will request the same after each home trial at the beginning of the subject appointment. Any feedback will be recorded in the appropriate eCRF in the clinical database eClinicalOS (see eCRF_AdverseEvent_V1.0_30.06.2015).

9.2.4.2 Laboratory parameters

N/A

9.2.4.3 Vital signs

N/A

9.2.5 Assessments in participants who prematurely stop the study

Withdraw without Adverse Event: If a subject is withdrawn from the study without having an AE, an audiogram will be recorded in a final appointment and the outer ear will be controlled to ensure that there are no damages through the study.

Withdraw with Adverse Event: If a subject is withdrawn in case of an AE, a referral to an independent doctor will be carried out. In accordance with the subject and the doctor, an additional appointment will be arranged to record a status update.

9.3 Procedures at each visit

Each study part follows the same pattern:

- Screening
- Pre-study or main study
- Final appointment

This pattern ensures the best method to not unnecessarily extend the study and to not perform tests with participants, which are not needed. For that reason first a pre-study is conducted with only a few participants to proof the study concept and the scientific interrogation behind it. If the results of the pre-study are promising, the main study will start.

9.3.1 Screening appointment

- Mapping to an encoded and randomized subject ID
- Discussion of the subject information and signing of the informed consent which were sent in advance by post or email
- Recording of the subject's audiological history
- Ear and ear canal assessment (otoscopy)
- Hearing test (pure tone and speech audiometry)
- In case of tinnitus: Tinnitus Pitch and Loudness Matching
- Explanation of in-/exclusion criteria
- Decision if patient can participate in the trial regarding to the in-/exclusion criteria
- eCRF Screening
- eCRF Audiometry
- Scheduling of the next visit

9.3.2 Pre-study appointment

- Ear canal assessment
- Fitting of hearing instrument (randomized) and documentation in eCRF
- Measurements objective and subjective (randomized), see section 5.1 and 9.2.1
- Fine tuning hearing instrument, if necessary
- Introduction to handling of hearing system (randomized)
- Introduction to CRF
- Signing of the device delivery form
- Schedule next visit
- eCRF Adverse Event, if applicable

9.3.3 Main study appointments

A main study appointment will only be executed if the pre-study results were promising. The procedure for the main study appointments is the same as for the pre-study appointments (see section 9.2.1).

9.3.4 Final appointment

- Ear canal assessment

- Hearing test (pure tone)
- In case of tinnitus: Tinnitus Pitch and Loudness Matching and comparison with the outcome of the screening. If the intensity is increased, a referral to an independent doctor will be carried out. In accordance with the subject and the doctor, an additional appointment will be arranged to record a status update
- Calculation and signing of the compensation form
- Signing of the device return form
- Collecting all study material
- Hand out of study feedback form
- eCRF Adverse Event, if applicable

10. SAFETY

(ClinO Art. 37-43; ICH/E6 6.8; ISO14155 8.2.5, A.14; AGEK 4.1; SPIRIT # 22, 30)

Description of plans for collecting, documenting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct.

10.1 Drug studies

N/A

10.2 Medical Device Category C studies

N/A

10.3 Medical Device Category A studies

10.3.1 Definition and Assessment of safety related events

All hearing systems are CE-labelled, i.e. the safety of the user is granted. However, the hearing aid can reach a high maximum power output (MPO) which can be louder than the user's threshold of uncomfortable levels is. For this reason, the MPO will always be set accordingly to clinical expertise at a level so that no injuries can occur. Consequently, neither during the measurements nor in the daily routine the safety of the participants will be compromised.

In order to ensure that each MD works correctly, every device will be checked before each application by the appropriate investigator. Furthermore, the participant is instructed to take note of any unexpected incidences (e.g. redness or swelling of the outer ear) and to document these in the questionnaires (p/eCRF). Pressure points are also controlled by the investigator at the beginning and at the end of an appointment. In the case that wearing the test devices in the time between the appointments becomes uncomfortable or even painful, the subjects are instructed not to wear the devices anymore and to contact the investigator for information and, if necessary, a doctor.

Furthermore, the participants are advised not to wear the device if a setting is not acceptable or tolerable, but to contact the investigator for an additional appointment. If any unexpected incidences occur during the lab trials the participant will be encouraged to immediately report the issue to the investigator.

10.3.2 Reporting of Safety related events

Reporting to Sponsor: Health hazards that require measures are reported to the Sponsor within 24 hours upon becoming aware of the event. If any unexpected AEs are to occur (e.g. chronic pain in the ear canal after MD application), the event has to be documented in the AE eCRF. Depending on the event, a decision needs to be made whether the participation in the study has to be interrupted or

even cancelled. If required, a referral to an independent doctor is to be carried out. An additional appointment will be arranged with the test participant (e.g. after one to two weeks) in order to record and document the status update.

Reporting to authorities: In Category A studies it is the investigator's responsibility to report health hazards requiring measures to the local Ethics Committee within 2 days.

11. STATISTICAL METHODS

(ICH/E6 6.9; AGEK 8; SPIRIT # 14, 20)
Statistical considerations
ICH: A description of the statistical methods to be employed, including timing of any planned interim analysis(ses).

This section describes the statistical considerations done for the study and the level of significance that will be used. The traceability of the study data is warranted for both the pre-study and the main study at any time. This means that an unauthorized and an accidentally change, deletion or copy of the gathered and analysed data is excluded. In case of a pre-study, the data are collected in a paper based manner. In case of the main study, the data are gathered both paper based and electronically whereat the paper based data are all fed into the clinical database eClinicalOS by the respective investigator as soon as possible and the source data verification is undertaken by the monitor (see section 12.1 for data handling details).

11.1 Hypothesis

This is a methodical evaluation in which new hardware and software technologies of Phonak products shall be compared with previous outstanding Phonak Hearing Systems and with equivalent competitor devices regarding a zero-defect overall performance and a maximum audiological benefit for the user. Hence, this study will not test a specific hypothesis.

11.2 Determination of Sample Size

ICH: The number of subjects planned to be enrolled. In multicentre trials, the numbers of enrolled subjects projected for each trial site should be specified. Reason for choice of sample size, including reflections on (or calculations of) the power of the trial and clinical justification.

Based on numerous publications in the field of audiology research using standardized measurement methods testing hearing impaired subjects as well as on Sonova AG's extensive study experience, a number of maximum 20 subjects per study is sufficient to obtain statistically significant results on a significance level of 5%.

In the case of the pre-study a maximum of 5 subjects is included, since merely the study concept needs to be proved, and no inferential but only descriptive statistics is carried out. Later, during the main study, both descriptive and inferential statistics are executed. In the past, typically 20 subjects participated per study leading to significant results approaching the primary objective (zero-defect overall performance of the new Phonak Hearing Systems). To tackle the secondary objective (product benchmark) a number up to 30 subjects have taken part in several previous investigations. This case is founded in the fact that a study design of parallel groups, either containing 10 or 15 subjects each, is applied as soon as more than one competitor device is compared to the Phonak Hearing System. For this reason, an appropriate number of subjects will be included during the planned investigations.

11.3 Statistical criteria of termination of trial

ICH: A description of the "stopping rules" or "discontinuation criteria" for individual participants, parts of trial and entire trial.

After each pre-study an analysis is performed. The corresponding results are the basis for the further progress of the main study which might be adjusted accordingly, if necessary.

11.4 Planned Analyses

ICH: A description of the statistical methods to be employed, including timing of any planned interim analysis(ses).

In a first step, the distribution of the collected subjective and objective data is verified. Based on this outcome (normally distributed yes/no) and depending on the scale level (nominal, ordinal, interval or rational) of the variables, descriptive statistics is executed in the form of determining the mean value and standard deviation or the median and quartile, respectively. Furthermore, diagrams for visualization are compiled such as boxplots, histograms and scatterplots. Then, after a determination of the measurement variables regarding their relationship or their difference, inference statistics is executed by applying the appropriate parametric or non-parametric test depending on the data's distribution either using the correlation coefficient (Pearson, Spearman), t-Test, Mann-Whitney-U-Test, or the Wilcoxon-Test. Generally, a significance level of 5% is pursued.

11.4.1 Datasets to be analysed, analysis populations

ICH: The selection of subjects to be included in the analyses (e.g., all randomized subjects, all dosed subjects, all eligible subjects, evaluable subjects).

The data of all participants and measurement methods will be analysed. Subgroups typically composed are hearing loss dependent groups (mild, moderate, severe, profound) and groups depending on their experience level wearing hearing instruments or using accessories (non-experienced, short-term, experienced, long-term user). In case of a subject withdrawal, only complete data sets of a measurement method will be used as part of the statistical analysis.

11.4.2 Primary Analysis

The primary analysis will be done by the statistician continuously during the study to capture any unexpected issues soon as possible. As soon as a test has been accomplished by every subject, these data will be fully analysed. By the end of the study, the final analysis across the tests and the subjects will be executed.

11.4.3 Secondary Analyses

The secondary analysis is done in the same way as the primary analysis.

11.4.4 Interim analyses

ICH 6.9.1: ..... including timing of any planned interim analysis(ses).

Interim analyses are continuously executed. Firstly, after the pre-study. Secondly, during the main study as soon as the first participant has been seen. Then, the data are analysed as described in section 11.4.2.

11.4.5 Safety analysis

The safety analysis will be permanently done during the study by the PI.

11.4.6 Deviation(s) from the original statistical plan

(ICH/E6 6.9.6)
ICH: Procedures for reporting any deviation(s) from the original statistical plan (any deviation(s) from the original statistical plan should be described and justified in protocol and/or in the final report, as appropriate).

Deviation(s) from the original statistical plan will be described and justified in a protocol and in a final report, as appropriate.

11.5 Handling of missing data and drop-outs

(ICH/E6 6.9.5; AGEK 8.5; SPIRIT 20c)
ICH: Procedure for accounting for missing, unused, and spurious data.

If data records are complete from subjects who dropped out of the study early, these data will also be used in the analysis. If the data sets are not complete, they will not be integrated at all.

12. QUALITY ASSURANCE AND CONTROL

(ICH/E6 6.11, 6.13; AGEK 12; SPIRIT #19, 23, 27)
ICH: Quality Control and Quality Assurance Procedures

This section describes how quality is assured and controlled.

12.1 Data handling and record keeping / archiving

ICH: Data Handling and Record Keeping

All data and documents recorded during the study are only accessible to the clinical study team and to the monitor. The personal data, the source data of measurements, the documents inclusive all notes get coded and monitored. The code list for the codification is safely kept within the clinical study team. The coded study data are to undergo a continuous comprehensive analysis during the study. A final report is to be written after the study is finished and is available to Sonova AG. During the study as well as afterwards, different password protected platforms are used to collect, save and archive the data and documents as listed below.

A. Computers:
   All computers used to conduct measurements and to electronically capture data are password protected. The measurement tools used dispose of an automatic data storage. Furthermore, all data permanently get transferred to the study database eClinicalOS, see below.

B. eClinicalOS, Merge:
   The database eClinicalOS is a unified, cloud-based system that offers all the electronic data capture and study coordination capabilities needed. Each study team member and the monitor own an account. Furthermore, each subject can get an account to fill in eCRFs during the home trials if they have internet access at home.

C. Lockable filing cabinet:
   Each study team member owns a lockable filing cabinet to store the subject files with the paper based documents.

D. Lockable shelf:
   A lockable shelf is available to store the essential documents and the site documents (ISF, TMF) during the study.

E. Safe:
   Keys of the filing cabinets and of the shelf are retained in a safe with a security code overnight. Furthermore, the coding list of the subjects is stored there.

F. SharePoint:
   SharePoint is a Microsoft Web Application used by Sonova AG to store documents and export files from the Phonak Fitting Software.

G. Archive (minimum of 10 years):
   At the end of the study, all of the collected data, either collected in paper form or electronically, are saved in a trial master file (TMF) in a folder and on CD or DVD which are stored in a lockable stock in the cellar at Sonova AG, Stäfa.

12.1.1 Case Report Forms

(ICH/E6 6.4.9)
ICH: The identification of any data to be recorded directly on the CRFs (i.e., no prior written or electronic record of data), and to be considered to be source data.

Study data is recorded both with paper and with electronic Case Report Forms (p/eCRF). For each

enrolled study participant a CRF is maintained. CRFs are kept current to reflect the subject's status at each phase during the course of study. Participants cannot be identified in the CRF by name or initials and birth date but an appropriate coded identification is used, e.g. VP10SL15 containing the subject number and the study identifier.

All study team members are authorized for the CRF entries and it is assured that any authorised person can be identified both for pCRFs and eCRFs. If pCRFs are used, the investigator's acronym as well as the subject ID is filled in and data are entered into an electronic file for analysis by the respective investigator and data get monitored by the assigned monitor. In case of a self-evident corrections, either the subject does it by himself or the investigator undertakes the correction by crossing out the word/sentence with a single horizontal line and by adding the correction including his personal identifier and the date.

12.1.2 Specification of source documents

(ICH/E6 6.4.9)
ICH: The identification of any data to be recorded directly on the CRFs (i.e., no prior written or electronic record of data), and to be considered to be source data.

Source data are available at the site to document the existence of the study participants and can be found as described in section 12.1. The source data include the original documents relating to the study as follows:

- Demographic data / audiological history
- Visit dates
- Informed Consent Forms
- Randomisation number
- AEs/SAEs
- Device Deficiencies (DD)
- Results of relevant measurements
- Directly recorded data in p/eCRFs

12.1.3 Record keeping / archiving

(ICH/E6 6.13)
ICH: Data Handling and Record Keeping

All study data will be archived for a minimum of 10 years after study termination or premature termination of the clinical trial. The location of storage is on SharePoint as well in the archive at Sonova AG, Stäfa, as explained in section 12.1, subsections F and G.

12.2 Data management

(ICH/E2; AGEK 12.2; SPIRIT #19)

This section describes plans for data entry, coding, security, and storage, including any related processes to promote data quality.

12.2.1 Data Management System

The data management is carried out as described in section 12.1. Data management systems that are applied are the database eClinicalOS (Merge), the SharePoint Web Application (Microsoft) and the SQL server (Microsoft). The eClinicalOS system gets verified and validated by the study team in the form of User Acceptance Tests (UAT) prior to each study start to ensure a proper working of the solution for the user. In addition, the study team owns a permanent SharePoint site which is verified as well as validated and the filing of the documents follows a predefined scheme. The SQL server working in the background is controlled by the IT at Sonova AG, Stäfa.

12.2.2 Data security, access and back-up

Data security is fully granted, the access is limited to specified persons and both systems eClinicalOS and SharePoint undergo a daily backup on appropriate servers.

12.2.3 Analysis and archiving

Data are extracted via the Microsoft SQL server and can be converted to an arbitrary format, e.g. xls file. For the data analysis, different programs are used such as Microsoft Excel, SPSS, Statistica and MatLab. Archiving is done according to section 12.1, subsections F and G, for a minimum of 10 years.

12.2.4 Electronic and central data validation

The data is validated by the monitor.

12.3 Monitoring

(AGEK 12.1; SPIRIT #23)

The extent and nature of monitoring activities based on the objective and design of the study is defined in a study specific monitoring plan. Every Sonova employee who is qualified in the domain of audiology research and who is not part of the study team can be assigned to the role of the Monitor. Typical monitoring activities are:

- Initiation Visit (see 12a_Initiation_Visit.pdf)
- Routine On-Site Monitoring Visit (source data verification, data monitoring in eClinicalOS including queries, random attendance of subject appointments) (see 12b_Routine_OnSite_Monitoring_Visit.pdf)
- Close Out Visit (see 12c_Close_Out_Visit.pdf)

The source data/documents are accessible to the monitor and questions are answered during monitoring. Each monitoring visit is documented in the form of a monitoring report.

12.4 Audits and Inspections

(ClinO, Art. 58, 59; AGEK 12.1; SPIRIT #23)

At Phonak, regular annual audits of the trial conduct take place. This process is strictly independent from investigators and the Sponsor. The study documentation and the source data/documents are accessible to the auditors/inspectors (also CEC and CA, if applicable) and questions are answered during the inspections. All involved parties have to keep the participants' data strictly confidential.

12.5 Confidentiality, Data Protection

(ClinO, Art. 18, 58; SPIRIT #27, 29)

Direct access to source documents will be permitted for purposes of monitoring (12.3), audits and inspections (12.4) (ICHE6, 6.10). Confidentiality and data protection is granted since access to the original data is only allowed to the study team, the monitor and the auditor. In case of publications by Sonova AG, the data is anonymized and no conclusion can be made to the subjects. Single exception are subjects serving as testimonals of a specific product. All testimonials agree with publication plans revealing their identity (e.g. photo or video) in written form (see 13_Testimonial_Agreement.pdf).

12.6 Storage of biological material and related health data

(ClinO, Art. 18; HVF Art. 28-32; SPIRIT #33)

N/A

13. PUBLICATION AND DISSEMINATION POLICY

(ICH/E6 6.15)
ICH: Publication policy, if not addressed in a separate agreement.

Basically, all subject data are anonymized. The trial results are documented in a final report which is

handed out to relevant employees of the Sonova AG. Furthermore, trial outcomes are communicated to study participants in the form of presentations during a subject follow-up event taking place twice per year after a product launch. In addition, the results can be published in an industry magazine, in a peer reviewed journal or as field study news on the Sonova AG homepage (https://www.phonakpro.com/ch/b2b/de/evidence/publications/field-study-news.html). The study results also can support product claims to be found in brochures for the hearing care professionals and the end user.

14. FUNDING AND SUPPORT

(ClinO, Art. 25i; ICH/E6 6.14; SPIRIT #4)

This section provides a brief statement of sources and types of financial, material, and other support for the trial.

14.1 Funding

(ClinO, Art. 25i)
ICH: Financing and insurance if not addressed in a separate agreement.

All sources and types of financial support for the study is provided by the Sponsor, Sonova AG.

14.2 Other Support

(ClinO, Art. 25i)
ICH: Financing and insurance if not addressed in a separate agreement.

All material is provided by the Sponsor, Sonova AG.

15. INSURANCE

(ClinO Art 12, 13; ICH/E6 6.14, AGEK 10.3; SPIRIT #30)
ICH: ….and insurance if not addressed in a separate agreement.

Category A studies are exempt hence no insurance is required. However, insurance will be provided by the Sponsor, Sonova AG: Police (Nr. CHCANA00770) „Versicherung für klinische Versuche in der Humanforschung“ beim Versicherungsbroker KESSLER & CO AG Forchstrasse 95, CH-8032 Zürich. A copy of the specific certificate for each study part is filed in the ISF and in the TMF.

16. REFERENCES

(ICH/E6 6.2.7)
ICH: References to literature and data that are relevant to the trial, and that provide background for the trial.

List of the references cited in the protocol.

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17. APPENDICES

ICH: (NOTE: Since the protocol and the clinical trial/study report are closely related, further relevant information can be found in the ICH Guideline for Structure and Content of Clinical Study Reports.)

All attached documents are listed in 0b_Checkliste_KlinV_Kat_A_d_V1.0_30.06.2015.pdf.