# Study Protocol and Statistical Analysis Plan

# Evaluating the safety and effectiveness of Sonova's self-fitting method for hearing aids

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## 1 Background

As part of the FDA Reauthorization Act of 2017, the FDA was directed to establish an Over-The-Counter (OTC) hearing aid category, and the agency issued a proposed rule in October of 2021. The proposed rule addresses the conditions for sale of hearing aids, and includes certain requirements for device performance, safety, design, and labeling. The proposed category is intended for individuals age 18 and older, who have a mild to moderate hearing loss.

In advance of the final ruling, Bose submitted a De Novo application in 2018 for the SoundControl Hearing Aid, from which the FDA implemented a new classification product code: QDD-Self fitting Air Conduction hearing aid. This application was approved in October of 2018, and since that time, two additional devices have been submitted and ap- proved under the QDD category: Jabra Enhance Plus (GN Resound) and BHA100 Series Braun Clear Hearing Aid (Kaz USA, Inc., a Helen of Troy company).

Sonova believes that OTC hearing aids can be a first step for many people who otherwise would not seek professional help for their hearing loss. This study is necessary to obtain clinical data supporting the safety and effectiveness of Sonova's self-fitting method, which will support an application for 510(k) clearance from the FDA. This study will use the HelloGO devices, which is the OTC/self fitting device developed by Sonova and currently only distributed in Australia.

## 2 Objectives

The primary effectiveness objective of this investigation is to demonstrate that individuals age 18+ with self-perceived mild tomoderate hearing loss are able to achieve non-inferior APHAB-global benefit scores when using a device fit with Sonova's self-fitting method compared to the same device fit by a professional.

The secondary effectiveness objective of this investigation is to demonstrate that individuals age 18+ with self-perceived mild to moderate hearing loss are able to achieve non-inferior dB SNR (Signal-to-Noise Ratio) loss scores as measured by the QuickSiN test, when using a device fit with Sonova's self-fitting method compared to the same device fit by a professional.

## 3 Description of the investigational device

The HelloGO Hearing Device is a one-size-fits-most form factor designed for individu- als 18 years of age and older, with mild to moderate hearing loss. Through a compan- ion app called HelloGO Hearing, the end user can set-up their devices by selecting a sound profile in the app that is suitable for their level of hearing, or they can choose to purchase a "pro upgrade," where

they can have their devices fine-tuned through fitting software with a hearing care professional. In both scenarios the app also serves as a remote control.

The intended use of the HelloGO hearing devices is to amplify and transmit sound to the ears and hereby compensate for hearing loss. The devices used in this investigation will be the means by which to evaluate subjective and objective benefit of the self-fitting created by the end-user using the App, as compared to an HCP-created fitting following best practices.

The intended patient population for the HelloGO hearing device and the HelloGO app are individuals 18 years or older with self-identified mild to moderate hearing loss. As part of the screening process for this study, potential participants are required to undergo audiological testing to confirm mild to moderate hearing loss.

## 4 Design of the clinical investigation

This investigation is a randomized, double-blinded crossover study with two treatments(self-fitting vs. professional-fitting), two treatment sequences, and two periods. Treatments include a device fit by the user with Sonova's self-fitting method and the same device fit by a professional following clinical best practices. This is a non-inferiority study, comparing the self- fitting method to the professional fitting method, therefore, the professional fitting method will serve as the comparator and the control.

## 5 Risks and benefits of the investigational device and clinical investigation

There are minimal risks associated with both the investigational device and participating in the clinical investigation. Identified risks are no greater than those associated with the daily use and wear of approved, available hearing aids.
The benefits of participating in the investigation include the possibility of hearing sounds that have not been previously heard, such as speech and environmental sounds, which may improve communication in daily life. Additionally, participation in this study will help to inform future developments and improvements in hearing device technology.
Subjects experience the benefit of personal satisfaction for participating in research to improve hearing instrument technology, which has the potential to make future HelloGO use more convenient. Subjects will also be compensated for their time in participating in this study.

There are no known or anticipated risks to subject hearing ability associated with participa- tion in the study. All sounds used in this study will be presented at safe listening levels.
While using HelloGO the following are possible occurrences:
•Cerumen impaction
•Discomfort, pain, or soreness
•Sweat or moisture accumulation in the ear canal or pinna
•A feeling of pressure or fullness in the ear
•Blisters, itching, sores, or rashes in the ear canal or pinna
•Headache
•Redness of tissue

The research personnel will review all of these risks with the subjects and answer any questions they have.
This is a non-significant risk study following the abbreviated IDE requirements set forth in 21 C.F.R. § 812.2 (b)(1). HelloGO is not a significant risk investigational device as defined in 21 C.F.R. § 812.3 (m).

## 6 Endpoints

Primary effectiveness endpoint: Abbreviated Profile of Hearing Aid Benefit (APHAB) global benefit score, which is derived by subtracting the aided APHAB global score from the unaided APHAB global score. The APHAB is an externally developed and validated questionnaire that is available for use by both researchers and clinicians to assess hearing aid benefit (Cox and Alexander, 1995). The measure comprises 24 items distributed equally across four subscales ('Ease of Communication,' 'Reverberation,' 'Background Noise,' and 'Aversiveness'). These subscales were designed to assess the benefits of hearing aids for speech communication in a variety of listening environments, in addition to capturing the impact of bothersome loud sounds.

Secondary effectiveness endpoint: dB SNR loss score. QuickSiN, the testing procedure that measures dB SNR loss, is an adaptive test of an individual's ability to understand speech in noise. The test adapts the relative levels of noise and speech to determine the signal-to-noise ratio (SNR) at which the individual can correctly identify 50% of key words. This test was independently developed and validated and is available for use by clinicians and researchers (Killion, et al., 2004).

These outcomes closely match those of a recent study for a product cleared under the Self-Fitting Hearing Aid classification 510(k) K213424.

## 7 Inclusion and Exclusion Criteria

Inclusion criteria for participant selection:
•18-80 years of age
•Target 67-75%first-time hearing aid users, 25-33% ex-perienced hearing aid users
•Mild to moderate bilateral hearing loss
•Ability to use a smartphone
•Fluent in English; ability to read and write in English
•Willing and able to provide informed consent
•Willing to upload smartphone app to personal phone

Exclusion criteria:
The presence of any one of the following exclusion criteria will lead to the exclusion of the subject:
•Self-reported ear-related pathology (otorrhea w/in 90days, dizziness, sudden hearing loss or worsening ofhearing w/in 90 days, otalgia)
•Visible deformity of the ear
•Chronic, severe tinnitus
•Unilateral hearing loss

## 8 Measurements and procedures

This is a crossover design in which participants will spend two weeks wearing devices that are professionally programmed according to the participant's audiogram, and two weeks wearing devices that are en- tirely self fit. The order of fitting will be randomized in a 1:1 allocation ratio.

Participants will complete the QuickSiN speech test in all three condi- tions: unaided, aided with professional fitting, and aided with self-fitting. They will also complete the APHAB questionnaire in all three conditions.
Real Ear Aided Responses (REAR) will be measured following the initial fittings as well as at each follow up visit.
See table below for schedule of events.

| Appointment | Trial Day | Variables recorded |
|---|---|---|
| 1 | 1 | • Unaided APHAB<br>• Unaided QuickSiN<br>• Initial fittings for both treatments<br>• REAR for both treatments |
| 2 | 2-7 | N/A: First set of devices dispensed following a wash-out period |
| 3 | 16-21 | • Adverse Event assessment<br>• APHAB with first treatment<br>• QuickSiN with first treatment<br>• REAR with first treatment<br>• Blinding assessment |
| 4 | 30-35 | • Adverse Event assessment<br>• APHAB with second treatment<br>• QuickSiN with second treatment<br>• REAR with second treatment<br>• Blinding assessment |

## 9 Statistical design and analysis

Sample size is driven by the difference in APHAB global benefit scores between self-fitting and the professionally-fitted hearing aid. Assuming that the average difference score, APHABself - APHABprof is -5.0, and the standard deviation of the difference score is 14, 40 subjects with APHAB global scores in both periods are needed to demonstrate with 90% power the non-inferiority against the margin of -12.5 using Mixed Model ANOVA, setting one-tailed lpha=0.025.

Anticipating an attrition rate of no more than 10%, to minimize the impact of imputed data on the overall efficacy conclusion, 44 subjects will be enrolled and those randomized will enter into the Intent to Treat population.

In terms of examining safety, the proportion of subjects experiencing any Adverse Device Effect will be a key safety endpoint. A sample size of 40 provides a 95% Clopper-Pearson confidence interval with a half-width no wider than 0.133 when the observed sample proportion is 0.20 or less. In other words, we can be 95% confident that the true population proportion of Adverse Device Effects is no greater than 0.133 larger than the observed sample proportion when the sample size is 40 and the sample proportion is 0.20 or less.
Note that this sample size is slightly higher than that included in 510(k) K213424, which included the same endpoints and a similar crossover design.
The analysis populations are as follows:
Intent to Treat: All participants randomized.
Safety: All participants randomized who receive one or more study device kits.
Data will be entered immediately following participant completion of the assigned tasks. Unaided and both aided responses will be analyzed for each participant for the APHAB global benefit and dB SNR loss scores. The two aided conditions will be analyzed for non-inferiority as per the statistical plan**.**
The APHAB global benefit score recorded during the self-fitting will be compared to the APHAB global benefit score recorded during the professional-fitting by way of a 2-period, crossover, repeated measures mixed model, where APHAB score is the dependent variable, treatment sequence is the between-subjects factor, Period is the within-subjects factor and treatment (Self-Fit/Professional-Fit) is the repeated measures factor.
The hypotheses are: H0: μself – μprof < -12.5 Ha: μself – μprof ≥ -12.5,
where μself represents the mean APHABself score in the population and μprof represents the mean APHABprof score in the population.
The observed treatment effect will be compared to the non-inferiority margin of -12.5 by way of pre-planned TEST or ESTIMATE statements using SAS PROC GLM or PROC MIXED.
The carryover effect will be tested by means of a RANDOM statement on the subject nested within sequence effect.
The planned analysis will be done by an expert biostatistician who has previous experience with FDA clinical trials.
The dB SNR loss score recorded during the self-fitting will be compared to the dB SNR loss score recorded during the professional fitting by way of a 2-period,crossover, repeated measures mixed model, where dB SNR loss score is the dependent variable, treatment sequence is the between-subjects factor, Period is the within-subjects factor and treatment (Self-fit/Professional-Fit) is the repeated measures factor.
The carryover effect will be tested by means of a RANDOM statement on the subject nested within sequence effect.
All analyses will be completed by an expert biostatistician who has previous experience with FDA clinical trials.
At each return lab visit, the sub-investigator A will notate any device deficiencies or possible adverse events as reported by the participant in the participant study folder.
If any AE are reported, the severity and scope will be reviewed and the study manager/sponsor, along with the PI will decide on the appropriate follow up.
Treatment-emergent Adverse Events will be attributed to the treatment condition(self-fit or professional fit) of the device being evaluated. The number and proportion of subjects reporting any Adverse Event, any Adverse Device Effect, any Serious Adverse Event, or any Serious Adverse Device Effect will be summarized by treatment condition and overall. The incidence of Adverse Events by AE term will be summarized by treatment condition and overall.
Missing aided APHAB global benefit scores and db SNR loss scores for either visit 3 or 4 will be subjected to multiple imputation. Originally, missing data is assumed to be monotone and Missing at Random (MAR). Multiple imputation approach will follow fully-conditional specifica-

tion, Multiple Imputation of Chained Equations. There will be a minimum of 100 iterations of missing data, and these iterations will be combined according to Rubin's (1987) rules. Sensitivity analysis of the MAR assumption will be based on pattern-mixture model (Molenberghs and Kenward, 2007)

## 10 Investigation Duration

The total expected duration of the clinical investigation is six months, with the expected duration for each participant to be 5 weeks.

## 11 Data handling and management

Electronic or paper based CRFs will be used to capture the participants' answers to the APHAB questionnaire. If electronic, the questionnaire will be available in the EDC system and the participant will be able to read question and choose answer. If paper based, the participant will answer each question and the results will be transferred to the EDC by the investigator. All 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. All study team members are authorized for the CRF entries and it is assured that any authorized person can be identified both for pCRFs and eCRFs. If pCRFs are used, the investigator's initials and subject ID are documented and data are entered into an electronic file for analysis by the respective investigator and data will be 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.
The results for the QuickSiN objective measure will be taken from the computer used to complete the test and imported into the EDC system or transferred via an excel or csv file. Real Ear Measurements will be imported from the verification system and stored as an excel file.
The EDC system is password protected and has an audit trail. Only the PI and sub-investigators will have access for inputting data.

## 12 Amendments to the CIP

Any necessary amendments to the CIP will be communicated to the study manager/sponsor. A new version of the CIP will be written, with the necessary changes and justification, and the PI will be trained on the amendments. The amended CIP will go through the approval process and necessary signatures obtained from the study manager/sponsor, PI, and statistician. The amended CIP will be uploaded to the eQMS system as an additional revision.

## 13 Deviations from clinical investigation plan

Deviations from the CIP to protect the rights, safety and well-being of human participants under emergency circumstances may proceed without prior approval of the sponsor and the EC – such deviations will be documented and reported to the sponsor representative (Study Manager) and the EC as soon as possible. Apart from that the investigator is not allowed to deviate from this CIP unless that deviation does not influence the investigation data.

## 14 Device accountability

Study devices must be returned to Sonova at the completion of the study.
Sonova, in its capacity as sponsor, will maintain a log of all investigational devices, including the date of shipment from Sonova to the site, serial number, receiving study site, and date returned to Sonova.

The site will maintain a log of the devices provided by Sonova, including the date of receipt, serial number, date of fitting, participant identification, date of return to site by participant, and date returned to Sonova. Sonova will provide each site a template with which to record such information.
If a device needs to be replaced due to a device deficiency, the PI or sub-investigator will add the new device serial number, date of receipt, and date of return of the defective device on the Device Accountability Log.
In the case of a device deficiency, the Adverse Event-Device Deficiency form will be completed by the study manager and the PI or sub-investigators together.

## 15 Informed consent process

Informed consent will be obtained from participants prior to any study participation in accordance with the IRB guidelines. The participants will be granted sufficient time to read through the consent in full and ask any questions they have before signing. After the participant signs the consent form, the researcher will sign and provide a copy to the participant. This process will take place in a private office located at the study site.

Informed Consent will only be obtained by investigation participants who can provide informed consent themselves before enrollment.

## 16 Adverse events, adverse device effects and device deficiencies

Device deficiencies and all **adverse events (AE)** including all **serious adverse events (SAE)** are collected, fully investigated and documented in the source document and appropriate case report form (CRF) during the entire investigation period, i.e. from participant's informed con-sent until the last protocol-specific procedure, including a safety follow-up period (ISO-14155, 2020). Documentation includes dates of event, treatment, resolution, assessment of serious-ness and causal relationship to device and/or investigation procedure.
Information on AEs is systematically collected during the regular investigation visits, and phone calls (if applicable).
The investigator(s) will follow-up on a biweekly basis with any participant experiencing an AE until either a) the participant reports resolution of the AE or b) 8 weeks have passed since the participant's final visit. If, however, the participant's condition worsens throughout the 8 week follow-up period, the investigator will continue to follow-up biweekly until the AE is resolved or the participant's condition stabilizes over an 8 week period.
The reporting of Serious Adverse Events and Device Deficiencies follows the Regulation (EU) 2017/745 and the MDCG 2020-10/1 Safety Reporting in Clinical Investigations of Medical Devices under Regulation (EU) 2017/745.
The causality assessment of the SAE will be conducted according to MDCG 2020-10/1 Safety Reporting in Clinical Investigations of Medical Devices under Regulation (EU) 2017/745.

## 17 Vulnerable populations

This investigation will not include any vulnerable populations.

## 18 Suspension or premature termination of the clinical investigation

The study will be terminated if the majority of the participants are not able to wear the devices for the study visit.
The study will be terminated if the participants or researchers are exposed to safety risks other than those outlined in this document.
The study may be terminated in the event natural disasters, widespread outbreak of illness, compromised structure of the investigation site, etc. that would make continuation of the study

impossible or impractical. The study will be suspended within 5 days of determination that the study or device put participants at an unreasonable risk.
If a participant is suspended, terminated, or withdraws from the study, their data can be traced with their unique study identification number.
According to the FDA, follow-up is required for participants who experience Serious Adverse Events. Follow up will be conducted by the study manager and/or the PI until the nature of the event is resolved.

## 19 Publication policy

The clinical investigation will be registered in clinicaltrials.gov, a publicly accessible database, as required by U.S. regulations.
The results of the clinical investigation will be published on clinicaltrials.gov no later than one calendar year following the final participant appointment.
An internal report of the results of this investigation will be completed and uploaded to eQMS.