Clinical Investigation Plan (CIP)

Investigation code	CBAS5477
Version	1.0
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Post-market clinical follow-up of a magnetic bone conduction implant (Cochlear™ Baha® Attract System)

A multicentre, open, prospective clinical investigation.
6 months investigation with an 18 months follow-up period.

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A change to this section is not a substantial protocol amendment.

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A change to this section is not a substantial protocol amendment.

Synopsis

Name of Sponsor	Cochlear Bone Anchored Solutions AB
Investigation code	CBAS5477
Investigational title	**Post-market clinical follow-up of a magnetic bone conduction implant (Cochlear™ Baha® Attract System)**
Design	A multicentre, open, prospective clinical investigation. 6 months investigation with an additional 18 months follow-up period.
Device tested in the investigation	Cochlear™ Baha® Attract System
Rationale for conducting the investigation	The rationale behind this post-market clinical follow-up investigation is to collect data regarding the usability and clinical performance of the Baha Attract System in subjects with hearing impairment that are candidates for Baha surgery: • to evaluate the efficacy of the Baha Attract System in terms of hearing performance compared to the unaided situation and compared to a pre-operative test situation using the sound processor on a Baha Softband; • to evaluate the mid- and long-term safety of the Baha Attract System.
Primary objective	To compare the hearing performance with the Baha Attract System (aided) and the unaided hearing performance.
Secondary objective(s)	• To compare the hearing performance with the Baha Attract System and the hearing performance with the same sound processor on a Baha Softband. • To compare health status and health-related quality of life and utility scores before and after use of the Baha Attract System. • To compare self-reported assessment of hearing aid outcome before and after use of the Baha Attract System. • To collect surgical information. • To investigate if the Sound Processor Magnet strength and magnetic force required for retention changes over time. • To collect information regarding pain, discomfort, numbness and soft tissue status. • To monitor implant survival. • To collect Adverse Events and device deficiencies.
Duration of subject participation	24 months
Inclusion criteria	• Adult subject, i.e. ≥ 18 years of age • Conductive or mixed hearing loss in the ear to be implanted:

	○ Bone conduction thresholds with a pure tone average PTA4 of < 30 dB hearing level (mean of 500, 1000, 2000 and 4000 Hz). **OR** Single-sided sensorineural deafness (SSD): ○ **European sites:** Bone conduction thresholds with a pure tone average PTA4 of < 30dB hearing level (mean of 500, 1000, 2000 and 4000 Hz) in the good ear. ○ **US sites:** Air conduction thresholds with a pure tone average PTA4 of ≤ 20 dB hearing level (mean of 500, 1000, 2000 and 3000 Hz) in the good ear **OR** Subject is indicated for an AC CROS but—for some reason—cannot or will not use an AC CROS. • No previous bone conduction implant on the side of the skull to be implanted. • Signed informed consent.
Exclusion criteria	• Subjects that are scheduled for simultaneous bilateral implant surgery. The investigation is limited to subjects with unilateral use of the Baha Attract System (however, bilateral hearing loss is not an exclusion criterion). • Suitable implant position for the BI300 Implant (4 mm or 3 mm) not found during surgery due to insufficient bone quality and/or bone thickness. • Less than 3 mm soft tissue thickness at the planned implant site. • Subjects that have received radiation therapy at the same side of the skull where the Baha Attract System will be positioned. • Condition that could jeopardise osseointegration and/or wound healing as judged by the investigator (e.g. osteoporosis, psoriasis, use of corticosteroids). • Uncontrolled diabetes as judged by the investigator. • Condition that may have an impact on the outcome of the investigation as judged by the investigator. • Unable to follow investigational procedures (e.g. to complete quality of life scales). • Participation in another investigation with pharmaceuticals and/or medical device.
Number of subjects	52
Primary assessment(s)	Free-field hearing tests: Threshold audiometry PTA4 (mean of 500, 1000, 2000 and 4000 Hz)
Secondary assessments	• Free-field hearing tests: - Threshold audiometry: 250, 500, 1000, 2000, 3000, 4000, and 6000 Hz - Adaptive speech recognition in noise (50% performance)

	- Speech in quiet (50dB, 65dB and 80dB SPL) • BC Direct thresholds • Questionnaires: - Health Utility Index (HUI) - Abbreviated Profile of Hearing Aid Benefit (APHAB) - The Speech, Spatial and Qualities of Hearing Scale (SSQ) • Surgical information: - Skin thickness - Surgery time - Soft tissue flap thinning - Bone removal/polishing - Implant stability quotient (ISQ) • Sound processor selection • SP Magnet selection • Magnet retention force • Questions regarding: - Daily use of sound processor (hours) - Magnetic retention - Change of Soft pad
Safety evaluation	• Pain/discomfort • Numbness • Soft tissue status • Loss/removal of Implant and/or Implant Magnet • Device deficiency • Concomitant medication • Adverse Events and Adverse Device effect • Serious Adverse Events and Serious Adverse Device effect

Flow chart - see next page

Flowchart

Procedures and timing	**Visit 1** Softband test	**Visit 2** Surgery	**Visit 3** Suture removal	**Visit 4** Fitting	**Visit 5**	**Visit 6**	**Visit 7**	**Visit 8**	**Visit 9**
Day/Week/Month[1]	**Pre-op**	**D 0**	**D 10**	**W 4**	**W 6**	**W 12**	**M 6**	**M 12**	**M 24**
Time window			± 5d	± 1w	± 1w	± 2w	± 4w	± 4w	± 4w
Demographics	X								
Medical history	X								
Nicotine use	X								
Audiogram[2]	X								
Eligibility criteria	X								
Informed consent	X								
Soft tissue thickness	X	***or*** X							
Health Utility Index (HUI)[3]	X[4]						X		X
Abbreviated Profile of Hearing Aid Benefit (APHAB)[3]	X[4,5]						X[6]		X[6]
The Speech, Spatial and Qualities of Hearing Scale (SSQ)[3]	X[4,5]						X[6]		X[6]
BC Direct using BFS	X[7]			X[8]					
Selection of sound processor	X								
Change of sound processor				X[9]	X[9]	X[9]	X[9]	X[9]	X[9]
Fitting of sound processor	X[7]			X[8]					
Fine tuning of sound processor					X[9]	X[9]	X[9]	X[9]	X[9]
Free field thresholds	X[5,7]			X[8]			X[8]	X[8]	X[8]
Speech recognition in noise	X[5,7]			X[8]			X[8]	X[8]	X[8]
Speech recognition in quiet	X[5,7]			X[8]			X[8]	X[8]	X[8]
Home test of sound processor on Softband	X →								
Surgery		X							
Surgery time		X							
Soft tissue thinning		X							
Bone polishing/removal		X							
Implant stability quotient		X							
Suture removal (if applicable)			X						
SP Magnet selection				X					
Magnetic retention force				X	X	X	X	X	X
Change of SP Magnet					X[9]	X[9]	X[9]	X[9]	X[9]
Questions regarding: • Daily use of sound processor • Magnet retention • Change of Soft pad					X	X	X	X	X
Pain/discomfort					X	X	X	X	X
Numbness			X	X	X	X	X	X	X
Soft tissue status			X	X	X	X	X	X	X
Loss/removal of Implant or Implant Magnet			X	X	X	X	X	X	X
Device deficiency		X	X	X	X	X	X	X	X
Adverse Events		X	X	X	X	X	X	X	X
Concomitant medication/treatment	X	X	X	X	X	X	X	X	X
Extra visit									

[1] The time between visits will be calculated from Visit 2 (time 0); [2] Only if the last audiogram that was performed on the subject is older than 6 months; [3] To be completed by the subject; [4] Before Softband test; [5] Unaided; [6] Aided; [7] With sound processor on Softband; [8] With Baha Attract System; [9] If needed.

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Abbreviations

ADE	Adverse Device Effect
AC	Air conduction
AE	Adverse Event
APHAB	Abbreviated Profile of Hearing Aid Benefit
Baha	Bone anchored hearing system
BC	Bone Conduction
BFS	Baha Fitting Software
BI	Baha Implant
BP	Baha Processor
CIP	Clinical Investigation Plan
CRF	Case Report Form
dB	Decibel
FDA	Food and Drug Administration
FS	Fitting Software
HRQL	Health-Related Quality of Life
HUI	Health Utility Index
Hz	Hertz
ICH	International Conference on Harmonisation
ITT	Intention To Treat
ISO	International Organisation for Standardisation
ISQ	Implant Stability Quotient
MedDRA	Medical Dictionary for Regulatory Activities
MRI	Magnetic Resonance Imaging
PP	Per Protocol
PTA	Pure Tone Average
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SNR	Speech to Noise Ratio
SP	Sound Processor
SPL	Sound Pressure Level
SSD	Single-sided Sensorineural Deafness
SSQ	The Speech, Spatial and Qualities of Hearing Scale
USADE	Unanticipated Serious Adverse Device Effect

Appendices

Appendix 1 Osstell ISQ Quick Guide

1 Introduction

1.1 Background

Bone conduction implants such as the Baha® system were first clinically described in 1977 by Tjellström et al.[1], and since then more than 100 000 patients have been treated with this technique. The traditional Baha system consists of a titanium implant, which connects to a sound processor via a skin-penetrating abutment. The sound processor transforms sound into vibrations that are transmitted via the abutment and titanium implant to the skull bone and then to the cochlea. Although Baha treatment has been proven to be a safe and effective treatment for patients with a mixed or conductive hearing loss or single-sided sensorineural deafness, a large proportion of Baha candidates refuse to undergo Baha surgery, mainly due to aesthetic concerns related to the percutaneous abutment. Other candidates may not be suitable for a percutaneous Baha due to being—for medical reasons or other—unable to perform the daily cleaning that the percutaneous abutment requires.

The clinical investigation outlined in this Clinical Investigation Plan (CIP) will assess the usability and clinical performance of a magnetic bone conduction implant, Cochlear™ Baha® Attract System. The device aims to reduce the perceived barriers for Baha candidates by providing a non-skin penetrating bone anchored hearing device. This gives Baha candidates a treatment option with improved cosmetic outcomes and minimal aftercare. In the Baha Attract System, the sound processor connects to a non-percutaneous implant through a transcutaneous coupling. The transcutaneous coupling consists of an implanted magnet, which is fixated to the osseointegrating titanium implant underneath the soft tissues, and an external magnet placed on top of the skin. The sound processor attaches to the external magnet via a snap coupling. The transducer of the sound processor transforms sound into vibrations which are conducted through the soft tissues and via the titanium implant to the skull and onwards to the cochlea.

The Baha Attract System is intended for patients (adults and children) with conductive or mixed hearing loss or single-sided sensorineural deafness. Patients should have sufficient bone quality and quantity to support successful implant placement.

The Baha Attract System is CE marked and has been in clinical use in Europe since September 2013, and received FDA clearance in the US in November 2013. This post-market clinical follow-up investigation aims to evaluate the usability and the mid- to long-term performance of the Baha Attract System in terms of hearing outcomes and safety. The investigation will also provide input to future product developments in the area of transcutaneous bone conduction hearing.

1.2 Rationale

The rationale behind this post-market clinical investigation is to collect data regarding the usability and clinical performance of the Baha Attract System in subjects with hearing impairment that are candidates for Baha surgery:

- to evaluate the efficacy of the Baha Attract System in terms of hearing performance compared to the unaided situation and compared to a pre-operative test situation using the sound processor on a Baha Softband;
- to evaluate the mid- to long term safety of the Baha Attract System.

1.3 Objectives

1.3.1 Primary objective

To compare the hearing performance with the Baha Attract System (aided) and the unaided hearing performance.

1.3.2 Secondary objectives

- To compare the hearing performance with the Baha Attract System and the hearing performance with the same sound processor on a Baha Softband.
- To compare health status, health-related quality of life and utility scores before and after use of the Baha Attract System.
- To compare the self-reported assessment of hearing aid outcome before and after use of the Baha Attract System.
- To collect surgical information.
- To investigate if the Sound Processor Magnet strength and magnetic force required for retention changes over time.
- To collect information regarding pain, discomfort, numbness and soft tissue status.
- To monitor implant survival.
- To collect Adverse Events and device deficiencies.

2 Statement of compliance

2.1 Ethical requirements for the conduct of the investigation

The investigation will be conducted in accordance with the ethical principles as described in the latest version of the Declaration of Helsinki adopted by the World Medical Association.

The Clinical Investigation Plan (CIP), the informed consent form and any other written information that will be given to subjects will be submitted to the appropriate ethics committee/institutional review board.

2.2 Regulatory requirements for the conduct of the investigation

The investigation does not need approval from regulatory authorities within EU since the devices used in the investigation are CE marked for the intended use described in this CIP.

In the US, the devices used in the investigation are registered as 510(k) medical devices in accordance with the Food, Drug, and Cosmetic Act for the intended use described in this CIP. Hence, the investigation does not need to be approved by the FDA in accordance with the premarket notification process.

The investigation will be conducted in accordance with applicable local regulations, e.g. data protection legislation.

2.3 Updates

The appropriate ethics committee/institutional review board shall after initial approval of the investigation receive the following information, when applicable:

- Status reports and written summary of the investigation as required by the ethics committee/institutional review board
- Documentation required in order to apply for an extension
- Documentation required in order to apply for a substantial amendment to the CIP or the informed consent form
- Report(s) with new information that may affect the safety of the subjects or the conduct of the investigation

Protocol amendments must be approved by concerned ethics committee/investigational review board and regulatory authorities (if applicable).

2.4 Quality standards

The staff at the investigational site and the Sponsor shall follow the guidelines provided in the ISO standard 14155:2011 '*Clinical investigation of medical devices for human subjects – Good clinical practice*'.

In the US, the FDA recognise ISO 14155:2011 with the following exceptions:

- Sections 4.5.2-5, 7.1.2: Institutional review board membership and procedures must follow US regulations
- Sections 4.7.3.4, 4.7.4-5: Informed consent content and procedures must follow US regulations
- Sections 6.4.1, 8.2.4.5.j-k, 8.2.5, 9.7-8. Annex A.14, Annex F: Adverse event reporting procedures must be consistent with US regulations

3 Medical devices used during and after the investigation

3.1 Device tested in the investigation

The device tested in the investigation is the Cochlear™ Baha® Attract System. The device is CE marked in the EU and registered as a 510(k) device in the US for the intended use described in this CIP.

The Cochlear Baha Attract System incorporates implantable and external parts as illustrated in Figure 1. The implantable parts include the BI300 Implant and the BIM400 Implant Magnet, which is intended to be fixated to the BI300 Implant. The external parts include the Sound Processor Magnet (SP Magnet), which, together with the Implant Magnet, constitute the transcutaneous coupling. The SP Magnet incorporates a soft material (Soft pad) at the tissue facing surface that is designed to distribute the pressure over the skin. The Baha Sound Processor attaches to the SP Magnet via a snap coupling.

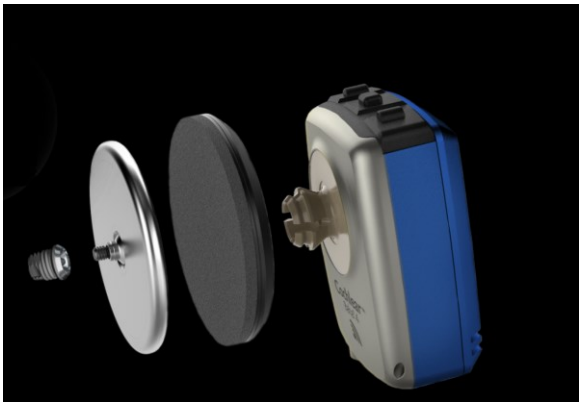

Figure 1. *From left to right: BI300 Implant, BIM400 Implant Magnet, SP Magnet with Soft pad, and sound processor.*

The different parts of the Cochlear™ Baha® Attract System are described in more detail below:

- **BI300 Implant** (Article # 92128, 92129)

  The BI300 Implant is a screw-shaped titanium implant with a titanium dioxide-blasted surface (TiOBlast™). The implant has a diameter of 4.5 mm and is available in two different lengths, 4 mm and 3 mm. The implant is intended to be fixated and become osseointegrated in the skull bone. The BI300 Implant is delivered sterile for single-use.

- **BIM400 Implant Magnet** (Article # 93550)

  The BIM400 Implant Magnet comprises an implantable hermetically sealed titanium casing (round shape, diameter: 27 mm, surface area: 5.7 cm^2) including two magnets (north and south pole) in half ring shape. The Implant Magnet is fixated to the BI300 Implant with a fixation screw and lies completely under the skin. The Implant Magnet is delivered sterile for single-use.

Figure 2. *Implant Magnet*

- **SP Magnet** (Article # 93561, 93562, 93563, 93564, 93565, 93566[1])

  The SP Magnet consists of a plastic casing (round shape, diameter: 30 mm, surface area: 7 cm^2), which holds two magnets (north and south pole) in half ring shape. The SP Magnet is intended to hold the sound processor in place over the Implant Magnet. The sound processor attaches to the SP Magnet by means of a snap connection. The SP Magnet is available in six different strengths to suit different soft tissue thicknesses and patient life style. The soft tissue facing portion of the SP Magnet is covered by a soft material, the Soft pad. The SP Magnet is delivered unsterile; sterilisation is not necessary.

Figure 3. *SP Magnet*

- **Soft pad** (Article # 94175)

  The part of the SP Magnet that is in contact with the skin is covered by a Soft pad. The intention of the Soft pad is to better distribute the pressure and improve the comfort for the patients. The Soft pad is disposable and can be easily removed and replaced by the patient when it becomes worn or dirty.

Figure 4. *Soft pad*

- **Sound Processor**

  The Baha Sound Processor attaches to the SP Magnet via a snap coupling. The Cochlear™ Baha 4 Sound Processor, BP110 Sound Processor or future generation regulatory approved Cochlear Baha sound processors shall be used in the investigation. Sound processor fitting shall be performed using Cochlear™ Baha® Fitting Software 4.0 or future generation Baha Fitting Software.

3.2 Other devices used in the investigation

- **Indicator for Baha Attract** (Article # 93571) – Used during surgery to identify the correct positioning of the Implant, SP Magnet and sound processor before surgery.

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[1] 93566 SP Magnet 6 is pending regualtory approval/clearance in Europe and US. The device will be regulatory approved before use in the investigation.

- **Implant Magnet template** (Article # 94071) – Used during surgery to ensure correct positioning of the Implant Magnet in relation to the bone, i.e. to assess size, position and angulation of the Implant Magnet in the bone.
- **Bone bed indicator** (Article # 93572) – Used during surgery to determine if polishing of the bone is required. The Bone bed indicator is used to identify any uneven bone parts around the BI300 Implant that could interfere with the implant casing. The instrument is placed into the BI300 Implant and then turned around a full circle. A lever arm will then identify any uneven bone surface that could interfere with the Implant Magnet casing when attached. Any such uneven part (bump) should be removed before placing the Implant Magnet.
- **Soft tissue gauge 6mm** (Article # 95070[2]) – A tool used during surgery to ensure that the soft tissue thickness does not exceed the recommended maximum of 6 mm and, when applicable, identify the need for surgical soft tissue thinning.

Figure 5. *Surgical tools. From left to right: Indicator for Baha Attract, Implant Magnet template, Bone bed indicator, Soft tissue gauge.*

- **Surgical instruments for the BI300 Implant 4mm and 3mm** – Used for the implantation of the implant.

For more information regarding tools needed for surgery, see the Surgery Guide for the Cochlear™ Baha® Attract System, and the Baha Attract System Product catalogue insert.

- **Baha Softband** – Used to fixate the sound processor to the skull during the 1-2 weeks test period before surgery and for pre-operative aided hearing tests.
- **Safety Line** – Used to secure the sound processor and the SP Magnet in case of loss of magnetic retention.
- **Cochlear Baha Fitting Software 4.0** – Used to customise the sound processor to an individual subject.

All the above devices are CE marked in the EU and registered as 510(k) devices in the US for the intended use described in this CIP.

In addition, a new **Force Measuring Tool** will be used in the investigation to measure the magnetic retention force of the SP Magnet. The device will be CE marked in the EU as a Class I product and listed as a Class I medical device in the US before use in the investigation.

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[2] *95070 Soft tissue gauge 6 mm is pending regualtory approval/clearance in Europe and US. The device will be regulatory approved before use in the investigation.*

3.3 Manufacturer of devices tested and used in the investigation

Cochlear Bone Anchored Solutions AB, Mölnlycke, Sweden.

3.4 Treatment after the completion of the investigation

The subjects will be able to continue with the Baha Attract System after the investigation.

4 Subjects and subject protection

4.1 Selection of subjects

4.1.1 Inclusion criteria

A subject will be eligible for inclusion in the investigation if he/she meets all of the criteria below:

- Adult subject, i.e. ≥ 18 years of age
- Conductive or mixed hearing loss in the ear to be implanted:
  - Bone conduction thresholds with a pure tone average PTA4 of < 30 dB hearing level (mean of 500, 1000, 2000 and 4000 Hz).

  OR

  Single-sided sensorineural deafness (SSD):
  - **European sites:** Bone conduction thresholds with a pure tone average PTA4 of < 30dB hearing level (mean of 500, 1000, 2000 and 4000 Hz) in the good ear.
  - **US sites:** Air conduction thresholds with a pure tone average PTA4 of ≤ 20 dB hearing level (mean of 500, 1000, 2000 and 3000 Hz) in the good ear **OR** Subject is indicated for an AC CROS but—for some reason—cannot or will not use an AC CROS.
- No previous bone conduction implant on the side of the skull to be implanted.
- Signed informed consent.

4.1.2 Exclusion criteria

A subject will be excluded from participation in the investigation if he/she meets **any** of the criteria below:

- Subjects that are scheduled for simultaneous bilateral implant surgery. The investigation is limited to subjects with unilateral use of the Baha Attract System (however, bilateral hearing loss is not an exclusion criterion).
- Suitable implant position for the Baha BI300 Implant (4 mm or 3 mm) not found during surgery due to insufficient bone quality and/or bone thickness.
- Less than 3 mm soft tissue thickness at the planned implant site.
- Subjects that have received radiation therapy at the same side of the skull where the Baha Attract will be positioned.
- Condition that could jeopardise osseointegration and/or wound healing as judged by the investigator (e.g. osteoporosis, psoriasis, use of corticosteroids).
- Uncontrolled diabetes as judged by the investigator.
- Condition that may have an impact on the outcome of the investigation as judged by the investigator.
- Unable to follow investigational procedures (e.g. to complete quality of life scales).
- Participation in another investigation with pharmaceuticals and/or medical device.

4.1.3 Number of subjects

52 subjects will be included in the investigation.

4.2 Subject enrolment and Informed consent

Before a subject is asked to sign an informed consent form, an investigator must explain the following to the potential investigational subject:

- The rationale, aims and objectives of the investigation
- Risks and benefits
- Alternative treatments
- Extent of the subject's involvement
- That the subject can withdraw his/her consent at any time
- That the confidentiality of subject data will be maintained at all time

The subject will be given time for consideration and must have the possibility to ask any questions before signing the informed consent form. Signed and dated informed consent from potential subjects must be obtained before any investigational procedure can be performed. The subject will receive a copy of the signed informed consent. The investigator will (after informed consent has been obtained) assign a unique enrolment number to the subject.

4.3 Randomisation

Not applicable

4.4 Discontinuation

- Subjects are free to discontinue their participation in the investigation at any time.
- Subjects may be discontinued from the investigation at any time at the discretion of the investigator.

Subjects who themselves discontinue from the investigation should always be asked about the reason(s) for the discontinuation and the presence of any Adverse Events. If possible, the subject should always be seen and assessed by an investigator. Any Adverse Event should be followed up.

4.5 Replacement of subjects

If a subject discontinues participation in the investigation, he/she will not be replaced.

4.6 Insurance

In case of any damage or injury occurring during the participation in the investigation, the Sponsor has contracted an insurance company (Willis), which will cover the liability of the Sponsor, the investigators and other persons involved in the investigation. The Sponsor may use a local insurance company, where applicable, according to national legislation.

5 Design of the clinical investigation

The investigation is designed as an international multicentre, open, prospective clinical investigation. The investigation comprises a 6-month investigation with an additional 18-month follow-up period.

5.1 Rationale for the design of the clinical investigation

This investigation is designed to collect data regarding the usability and clinical performance of the Baha Attract System in subjects with hearing impairment that are candidates for Baha surgery.

The investigation will be performed in an open design since it is not possible to perform the investigation in a blinded fashion. The main evaluations of the investigation, i.e. free-field hearing tests, are relevant and objective methods.

This investigation is expected to demonstrate that the Baha Attract System performs within its intended use and is a suitable treatment for patients with a conductive or mixed hearing loss or single-sided sensorineural deafness.

While the Baha Attract System is approved for use in both adults and children, this investigation is limited to adult subjects. The paediatric population constitutes an inhomogeneous patient group (age-related), and currently there are no audiological tests that are suitable for comparisons across age ranges and across multiple countries/languages. Performance evaluation of the Baha Attract System in children should be performed as separate investigations.

5.2 Variables

5.2.1 Primary efficacy variable

Free-field hearing tests: Thresholds audiometry – Pure Tone Average PTA4 (Mean of 500Hz, 1000Hz, 2000Hz and 4000Hz).

5.2.2 Secondary efficacy variables

The secondary efficacy variables will be evaluated as follows:

- Free-field hearing tests:
  - Threshold audiometry (pure tones): 250, 500, 1000, 2000, 3000, 4000 and 6000Hz
  - Adaptive speech recognition in noise (50% performance)
  - Speech in quiet (50dB, 65dB and 80dB SPL)
- BC Direct thresholds
- Questionnaires:

- Generic quality of life scale: Health Utility Index (HUI):
    - *Health related quality of life score for overall health*
    - *Vision score*
    - *Hearing score*
    - *Speech score*
    - *Ambulation/mobility score*
    - *Dexterity score*
    - *Self-care score*
    - *Emotion score*
    - *Cognition score*

- Abbreviated Profile of Hearing Aid Benefit (APHAB):
    - *Ease of Communication*
    - *Reverberation*
    - *Background Noise*
    - *Aversiveness*
    - *Global score*

- The Speech, Spatial and Qualities of Hearing Scale (SSQ)

- Surgical information:
    - Skin thickness
    - Surgery time
    - Soft tissue flap thinning
    - Bone polishing/removal
    - Implant stability quotient (ISQ)

- Sound processor selection
- Choice of SP Magnet
- Magnetic retention force (dynamometer)
- Questions regarding:
    - Daily use of sound processor (hours)
    - Magnetic retention
    - Change of Soft pad

5.2.3 Safety variables

- Pain/discomfort
- Numbness
- Soft tissue status

- Loss/removal of Implant and/or Implant Magnet
- Device deficiency
- Concomitant medication
- Adverse Events and Adverse Device Effect
- Serious Adverse Events and Serious Adverse Device Effects

5.2.4 Demographics and baseline variables

- Demographics
- Medical and surgical history
  - Type of hearing loss
  - Aetiology of hearing loss
  - Current conventional hearing aid
  - Current/previous medications and treatments
- Nicotine use
- Audiogram
- Skin thickness

5.3 Investigational flowchart

Procedures and timing	**Visit 1** Softband test	**Visit 2** Surgery	**Visit 3** Suture removal	**Visit 4** Fitting	**Visit 5**	**Visit 6**	**Visit 7**	**Visit 8**	**Visit 9**
Day/Week/Month[1]	**Pre-op**	**D 0**	**D 10**	**W 4**	**W 6**	**W 12**	**M 6**	**M 12**	**M 24**
Time window			± 5d	± 1w	± 1w	± 2w	± 4w	± 4w	± 4w
Demographics	X								
Medical history	X								
Nicotine use	X								
Audiogram[2]	X								
Eligibility criteria	X								
Informed consent	X								
Soft tissue thickness	X	***or*** X							
Health Utility Index (HUI)[3]	X[4]						X		X
Abbreviated Profile of Hearing Aid Benefit (APHAB)[3]	X[4,5]						X[6]		X[6]
The Speech, Spatial and Qualities of Hearing Scale (SSQ)[3]	X[4,5]						X[6]		X[6]
BC Direct using BFS	X[7]			X[8]					
Selection of sound processor	X								
Change of sound processor				X[9]	X[9]	X[9]	X[9]	X[9]	X[9]
Fitting of sound processor	X[7]			X[8]					
Fine tuning of sound processor					X[9]	X[9]	X[9]	X[9]	X[9]
Free field thresholds	X[5,7]			X[8]			X[8]	X[8]	X[8]
Speech recognition in noise	X[5,7]			X[8]			X[8]	X[8]	X[8]
Speech recognition in quiet	X[5,7]			X[8]			X[8]	X[8]	X[8]
Home test of sound processor on Softband	X →								
Surgery		X							
Surgery time		X							
Soft tissue thinning		X							
Bone polishing/removal		X							
Implant stability quotient		X							
Suture removal (if applicable)			X						
SP Magnet selection				X					
Magnetic retention force				X	X	X	X	X	X
Change of SP Magnet					X[9]	X[9]	X[9]	X[9]	X[9]
Questions regarding: • Daily use of sound processor • Magnet retention • Change of Soft pad					X	X	X	X	X
Pain/discomfort					X	X	X	X	X
Numbness			X	X	X	X	X	X	X
Soft tissue status			X	X	X	X	X	X	X
Loss/removal of Implant or Implant Magnet			X	X	X	X	X	X	X
Device deficiency		X	X	X	X	X	X	X	X
Adverse Events		X	X	X	X	X	X	X	X
Concomitant medication/treatment	X	X	X	X	X	X	X	X	X
Extra visit									

[1] The time between visits will be calculated from Visit 2 (time 0); [2] Only if the last audiogram that was performed on the subject is older than 6 months; [3] To be completed by the subject; [4] Before Softband test; [5] Unaided; [6] Aided; [7] With sound processor on Softband; [8] With Baha Attract System; [9] If needed.

6 Procedures

6.1 Subject demographics

The following demographic data will be recorded at the baseline visit, Visit 1:

- Date of birth (month and year)
- Gender
- Ethnic background
- Weight and height

6.2 Medical history

The following subject characteristics will be recorded at the baseline visit, Visit 1:

- Type of hearing loss
- Aetiology of hearing loss
- Current conventional hearing aid
- Relevant medical and surgical history during the past five years as judged by the investigator
- Current concomitant medication and treatments

6.3 Nicotine use

Use of nicotine should be assessed using the following scale:

0	Does not smoke	
1	Less than 10 cigarettes/day	Low consumption
2	Between 11 and 20 cigarettes/day	Medium consumption
3	Between 21 and 40 cigarettes/day	High consumption
4	More than 40 cigarettes/day	Very high consumption

6.4 Audiogram

Unaided audiometric threshold measures (including both air- and bone conduction thresholds) should demonstrate that the subject has a conductive or mixed hearing loss or single-sided sensorineural deafness. An existing audiogram may be used as long as it has been completed during the last six months. The subject's pre-operative Pure Tone Average PTA4 (mean of 500, 1000, 2000 and 4000Hz) should be recorded to ensure the subject meets the inclusion criteria.

6.5 Soft tissue thickness

At Visit 1 or Visit 2, the surgeon should measure the soft tissue thickness at the planned implant site. A hypodermic needle, a clamp and a ruler should be used. Topical anaesthetic may be used at the discretion of the investigator. Local anaesthetic given as a subcutaneous injection should **not be used prior to** soft tissue thickness measurement since the thickness will be affected. In order to obtain a correct measurement, care must be taken to not depress the skin with the needle, fingers and/or clamp.

Subjects with a soft tissue thickness of less than 3 mm should be excluded from the investigation. Subjects with a soft tissue thickness exceeding 6 mm at the planned location of the Implant Magnet will require surgical thinning of the soft tissue flap.

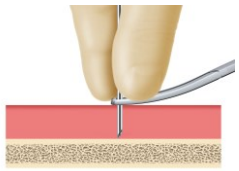

Figure 6. *Measuring soft tissue thickness*

6.6 Health Utility Index (HUI)

The Health Utilities Index (HUI®) is a generic preference-based system for measuring comprehensive health status and health-related quality of life (HRQL). HUI provides descriptive evidence on multiple dimensions of health status, a score for each dimension of health, and a HRQL score for overall health. Health dimensions include vision, hearing, speech, ambulation/mobility, pain, dexterity, self-care, emotion and cognition. Each dimension has 3-6 levels.

The subjects will complete the HUI Mark 3 (HUI3) at Visit 1, 7 and 9.

At Visit 1, the subjects will complete the HUI3 questionnaire prior to the Softband test.

6.7 The Abbreviated Profile of Hearing Aid Benefit (APHAB)

The APHAB is a 24-item self-assessment inventory that evaluates the benefit experienced by the subject when using hearing amplification compared to the unaided situation. The APHAB produces a global score and scores for four subscales: ease of communication (EC), reverberation (RV), background noise (BN), and aversiveness (AV).

The subjects will complete the APHAB questionnaire at Visit 1, 7 and 9.

At Visit 1, the subjects shall complete the questionnaire prior to the Softband test. At Visit 1, the questionnaire shall be answered with respect to the subject's **unaided** hearing.

At Visit 7 and 9, the subjects shall complete the questionnaire for the **aided** situation (with the Baha Attract System).

6.8 Speech, Spatial, and Qualities of Hearing Scale (SSQ)

The Speech, Spatial, and Qualities of Hearing (SSQ) questionnaire is designed to measure self-reported auditory disability across a wide variety of domains, reflecting the reality of hearing in the everyday world. It covers:

- Hearing speech in a variety of competing contexts
- The directional, distance and movement components of spatial hearing
- Segregation of sounds and attending to simultaneous speech streams
- Ease of listening
- The naturalness, clarity and identifiability of different speakers, different musical pieces and instruments, and different everyday sounds

The subjects will complete the SSQ at Visit 1, 7 and 9.

At Visit 1, the subjects shall complete the SSQ questionnaire prior to the Softband test. At Visit 1, the SSQ shall be answered with respect to the subject's **unaided** hearing, even for subjects with a previous hearing device.

At Visit 7 and 9, the subjects shall complete the questionnaire for the **aided** situation (with the Baha Attract System).

6.9 Sound processor selection

Based on results from BC Direct tests (see section 6.10 for details) performed with the sound processor on a Baha Softband at Visit 1, the audiologist will select an appropriate Baha sound processor for the subject. The Baha BP110 Sound Processor, the Baha 4 Sound Processor or future generation regulatory approved sound processors shall be used. If deemed necessary, the audiologist shall adjust the sound processor gain until satisfied, as judged by the investigator and subject.

During the selection process all the three free-field tests must be performed on the selected sound processor and the chosen setting, i.e:

- Threshold audiometry – free field
- Adaptive speech recognition in noise
- Speech recognition in quiet

The selected sound processor should be used during the Softband testing period and then attached to the SP Magnet at Visit 4. The subject will receive a user manual for the selected sound processor.

If the subject is unsatisfied or experiences extensive feedback noise, the audiologist may switch to a more powerful sound processor.

6.10 Bone Conduction (BC) Direct

BC Direct is a tool in the Cochlear Baha Fitting Software to establish the unmasked bone condition threshold with tones presented through the sound processor. At Visit 1, BC Direct data shall be collected with the selected sound processor on a Baha Softband and shall be used to calculate the fitting (settings) of the sound processor for the Softband test period (see section 6.15). BC Direct and the fitting procedure will also be performed at Visit 4 when the subject will start to use the sound processor connected to the SP Magnet.

Baha Fitting Software 4.0 or future generation Baha Fitting Software will be used. Feedback management (part of Fitting Software) should be used when fitting the device.

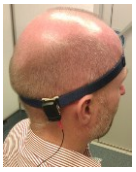

Figure 7. *Performing BC Direct on Softband.*

6.11 Fine tuning of Baha sound processor

If the subject experiences problem with the performance of the sound processor (e.g. feedback, loudness, poor sound quality) the audiologist should change the sound processor settings utilising Baha Fitting Software 4.0 or future generation Baha Fitting Software. BC Direct should be performed and the sound processor should be re-prescribed. **The same procedure shall also be performed each time a subject requires a change of the SP Magnet.**

6.12 Free field pure tone thresholds

The purpose of this test is to establish the hearing thresholds for pure tones presented in free field through a speaker in front position (0 degrees azimuth) according to the so-called ascending or modified Hughson-Westlake method. During the test, the signal processing of the sound processor shall be set to omnidirectional mode. The test shall be performed with the non-test ear blocked (in case or normal or near-normal hearing or a large assymetry with the non-test ear having significantly better hearing thresholds).

At Visit 1, free-field thresholds shall be measured for the unaided situation and with the selected sound processor on a Baha Softband. At Visit 4, 7, 8 and 9, the same test shall be performed with the selected sound processor and selected SP Magnet.

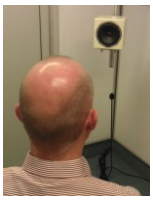

Figure 8. *Free field front speaker position.*

6.13 Speech recognition of words in quiet

The purpose of this test is to establish the test subject's maximum speech recognition in quiet. The speech test in quiet shall be performed using phonetically balanced words presented from the front (0 degrees azimuth). The test material shall be single syllable words and presented at 50, 65 and 80 dB sound pressure level (SPL) and scores shall be recorded as % correct words at each presentation level. During the test, the signal processing of the sound processor shall be set to omnidirectional mode. The test shall be performed with the non-test ear blocked (in case or normal or near-normal hearing or a large assymetry with the non-test ear having significantly better hearing thresholds).

At Visit 1, the speech in quiet test shall be performed for the unaided situation and with the selected sound processor on a Baha Softband. At Visit 4, 7, 8 and 9, the same test shall be performed with the selected sound processor and selected SP Magnet.

6.14 Adaptive sentence recognition in noise

The purpose of this test is to establish the test subject's ability to recognise speech in the presence of background noise. The adaptive speech test in noise shall be conducted using validated lists of phonetically balanced sentences, with speech presented from the front (0 degrees azimuth) and noise from the back (180 degrees azimuth). The noise shall be kept constant at 65 dB SPL, and the speech shall be adapted in 2 dB steps to establish the speech-to-noise ratio (SNR) providing a 50% level of understanding. During the test, the signal processing of the sound processor shall be set to omnidirectional mode. The test shall be performed with the non-test ear blocked (in case or normal or near-normal hearing or a large assymetry with the non-test ear having significantly better hearing thresholds).

At Visit 1, the speech in noise test shall be performed for the unaided situation and with the selected sound processor on a Baha Softband. At Visit 4, 7, 8 and 9, the same test shall be performed with the selected sound processor and selected SP Magnet.

6.15 Test of Sound Processor on Softband

Between Visit 1 and Visit 2 (pre-operatively), the subjects will use the Baha Softband to test the sound processor during 1-2 weeks in different daily listening situations in order to get an impression of the hearing improvement he/she might anticipate post-surgery with the sound processor connected to the SP Magnet. The subject will use the selected sound processor as described in section 6.9. Instructions regarding use of the Baha Softband are described in the user manual for the product.

6.16 Surgery

Surgery will be performed at Visit 2 in accordance with the procedure described in the Surgery Guide for the Baha Attract System. Surgery may be performed under general anaesthesia or by using local anaesthetic at the discretion of the investigator. The following information will be collected:

- **Surgery time**
  The surgery time is measured from the time from first incision to suture closure.

- **Soft tissue thinning performed**
  Surgical thinning of the soft tissue flap must be performed if the thickness exceeds 6 mm. If soft tissue thinning is performed, the extent of flap thinning (in mm) shall be recorded.

- **Bone polishing/removal performed**
  Any use of bone polishing to accommodate the Implant Magnet shall be recorded.

- **Implant stability quotient (ISQ)**
  Implant stability shall be measured during surgery using resonance frequency analysis. The measurement renders an implant stability quotient (ISQ) value between 1 and 100. The measurement shall be performed at the implant level after inserting the BI300 Implant and before attaching the Implant Magnet to the Implant. The highest and lowest ISQ value out of two perpendicular measurements shall be recorded, ISQ High and ISQ Low. The Osstell ISQ instrument and SmartPeg Type 30 (Osstell, Gothenburg, Sweden) shall be used. The procedure for obtaining ISQ values is described in Appendix 1.

After surgery, the subject will receive instructions as for how to take care of the skin in accordance with local practice. The subject will also receive a Magnetic Resonance Imaging (MRI) card, which contains information to professional health care providers regarding the implanted magnet.

6.17 Removal of sutures

The sutures shall be removed at Visit 3 (i.e. 10 days after surgery), if applicable. The surgeon/surgical nurse will determine if the wound requires further wound dressings, and if so, extra visit(s) will be scheduled, until the wound is considered healed.

6.18 Baha sound processor fitting on SP Magnet

The Baha sound processor that was selected during the initial sound processor selection at Visit 1 (see Section 6.9) will be fitted with the SP Magnet to the implant at Visit 4 (i.e. 4 weeks after surgery). A suitable SP Magnet shall be selected as described in Section 6.19. Sound processor fitting shall be performed in accordance with the information in the Fitting Guide (Baha Fitting Software 4.0 or later generation). If the wound is not considered sufficiently healed, as judged by the surgeon/surgical nurse, the installation shall be delayed to a scheduled subsequent visit or extra visit, when the site is considered sufficiently healed.

The subject will receive a User Guide, which contains important information regarding the device.

6.19 SP Magnet selection

Initial SP Magnet selection shall be performed at the time of fitting the Baha sound processor to the SP Magnet at Visit 4 (see Section 6.18). During follow-up, a change to a stronger or weaker SP Magnet may be required. A decision regarding SP Magnet strength shall be made at Visit 4-9 and at any extra visit. SP Magnet selection shall be performed in accordance with the procedure described in the SP Magnet Selection Guide for the Baha Attract System. When selecting an SP Magnet it is important to choose the SP Magnet that provides the best possible retention while still being comfortable for the subject.

If a subject requires an SP Magnet change, BC Direct shall be performed with the new SP Magnet and the device shall be re-prescribed.

6.20 Magnetic retention force

The magnetic retention force of the SP Magnet shall be measured at Visit 4-9 and at any extra visits including a change of SP Magnet. A specific Force Measuring Tool (dynamometer) shall be used. The measurement will be repeated three times. For each measurement the SP Magnet should be placed on the skin above the Implant Magnet and the measurement should be performed after one minute in order for the Soft pad to be compressed.

6.21 Daily use, retention, change of Soft pads

At Visits 5-9 subjects will be asked about the following topics:

- **Daily use of sound processor**
  Average hours of daily use (hours/day) during the last week before Visit 5, and during the last month before Visit 6-9.
- **Insufficient retention (number of episodes)**
  Number of times the device fell off during the last week before Visit 5-9?
- **Change of Soft pads (frequency)**
  Number of times the subject changed the Soft pad during the last week before Visit 5, and during the last month before Visit 6-9?

6.22 Pain/discomfort

The subject will be asked about the level of discomfort and/or pain at Visits 5-9 using the following scale:

- Which of the following alternatives corresponds best to the subject's experience with the Baha Attract System?

  0 = No discomfort and/or pain. Normal daily use of sound processor.

  1 = Slight discomfort and/or pain, not significantly affecting daily use of sound processor.

  2 = Discomfort and/or pain, reducing daily use of sound processor.

  3 = Excessive discomfort and/or pain, preventing use of sound processor.

6.23 Soft tissue status

At Visit 3-9, the investigator will examine the soft tissue at the implant site. In case of signs of e.g. inflammation, infection, skin necrosis or scar hypertrophy, the event shall be reported on the Adverse Event page in the CRF. If any treatment is provided, it shall also be recorded on the Concomitant medication page in the CRF.

6.24 Numbness

Subjects will be assessed for any presence of numbness around in the implant area at Visits 3-9. The following scale will be used:

1. No numbness
2. Numbness within 2 cm from the implant (center of the inner magnet)
3. Numbness within and beyond 2 cm from the implant (center of the inner magnet)

Numbness will be assessed by means of a pin and a cotton swab. Randomly picked locations in and around the implant area (within and beyond 2 cm from the centre of the implant magnet) will be tested by gently touching the skin with the pin and the cotton swab. The scale above shall be used to score the subject's sensation to stimulus with the pin and with the cotton swab.

6.25 Loss/Removal of Implant and/or Implant Magnet

Any loss or removal of the BI300 Implant and/or BIM400 Implant Magnet should be recorded on the Adverse Events page in the Case Report Form (CRF), together with the reason for the loss or removal.

6.26 Device deficiency reporting

The definition of a device deficiency is an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance.

A device deficiency should be reported to the Sponsor. A device deficiency that could have lead to a Serious Adverse Event (SAE) should be reported immediately (see next section).

6.27 Adverse Event (AE) and Serious Adverse Event (SAE)

6.27.1 Definitions

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the medical device used in the investigation*. This definition includes events related to the procedures involved.
Adverse Device Effect (ADE)	Adverse event related to the use of medical device used in the investigation*. • This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. • This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.
Serious Adverse Event (SAE)	A SAE** is an adverse event that: • results in death • is life-threatening • requires inpatient hospitalisation or prolongation of existing hospitalisation • results in persistent or significant disability/incapacity • is a congenital anomaly/birth defect • has led to a **important medical event** that may have jeopardised the subject or may have required an intervention to prevent one of the above characteristics/ consequences. These can include complaints that might have led to a medical occurrence if o suitable action had not been taken or o intervention had not been made or o if circumstances had been less fortunate. NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.
Serious Adverse Device Effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a serious Adverse Event
Unanticipated Serious	Serious adverse device effect which by its nature, incidence, severity or

Adverse Device Effect (USADE)	outcome has not been identified in the current version of the risk analysis report
Device deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance NOTE Device deficiencies include malfunctions, use errors, and inadequate labelling.

* The definition is broader than the definition in ISO14155:2011 since it includes all clinical investigations regardless if the medical device(s) is an investigational device or not.

** The definition is broader than the definition in ISO14155:2011 since it includes important medical event as a reportable event (see 6.26.3).

6.27.2 Handling and reporting of AEs

Subjects will be carefully monitored during the investigation for possible AEs and appropriate treatment of the subject will be initiated.

Any AE observed will be fully investigated by the investigator and documented in the case report form (CRF) including assessment of severity (mild, moderate or severe) and relationship to the medical device.

6.27.3 Reporting of SAEs and device deficiency that could have lead to a SAE

An investigator should report within 24 hours, after being aware of the event, an SAE or a device deficiency that could have lead to a SAE. The report should be sent as an e-mail attachment to Cochlear Bone Anchored Solutions AB. Instructions and contact information is available on the SAE form.

6.27.4 Reporting to ethics committees/investigational review boards

SAEs/SADEs/USADEs and device deficiencies that could have led to a SAE should be reported to ethics committees/investigational review boards in accordance with local requirements.

6.28 Concomitant medication and treatments

All medications and treatments given, whether or not to treat AEs/ADEs, must be recorded in the appropriate section of the CRF.

6.29 Extra visit(s)

Extra visit(s) may be a scheduled visit in order to change wound dressing or to follow-up any complications. These visits will be recorded on extra pages in the CRF. The following information will be recorded:

- Date
- Reason for extra visit
- Procedures and/or treatment used
- Staff that conducted the visit (surgeon, surgical nurse or audiologist)

7 Risk and benefits of the devices and the clinical investigation

7.1 Anticipated clinical benefits

The Baha Attract System is regulatory approved/cleared for the intended use in the present investigation. With the Baha Attract System, the subjects will be able to benefit from the Baha sound processor without an abutment penetrating the skin, thus providing cosmetic advantages compared to a traditional Baha. In addition, with the Baha Attract System, there is reduced need for daily cleaning to maintain a healthy implant site compared to a percutaneous Baha, and risk of adverse tissue reactions related to the percutaneous passage are eliminated.

It is expected that the audiological performance of the Baha Attract System will be similar to, or somewhat better than, Baha on a Softband. The performance in the high frequency range are likely to be slightly lower for subjects with the Baha Attract System compared to the percutaneous solution, due to transcutaneous attenuation of the vibrations through the skin.

Participation in the investigation requires slightly more frequent follow-up visits for the subject than what is normally required, and the duration of the visits will be slightly longer than normal. The more frequent visits will provide the subject the opportunity to more frequently interact with the treating physician. Subjects will receive compensation for travelling expenses made for extra visits to the clinic.

7.2 Residual risks associated with the device and procedures

Risks associated with the transcutaneous coupling that cannot be completely eliminated include magnetic retention difficulties, pressure-related skin complications and pain/discomfort. The system has been designed to minimise these risks. For example:

- The SP Magnet has been designed with a Soft pad on the soft tissue facing surface to evenly distribute the pressure, thus minimising the occurrence of peak pressure areas.
- To minimise the risk of pressure-related complications, the transcutaneous coupling has been designed such that the average pressure over the skin should not exceed 0.4 N/cm^2 (capillary blood pressure) and peak pressures should not exceed 0.6 N/cm^2 (diastolic blood pressure).
- The surgeons are instructed to carefully thin the soft tissue flap during surgery if the skin thickness exceeds 6 mm, to ensure good magnetic retention.
- Subjects with a soft tissue flap thickness of less than 3 mm are not included in the investigation.
- Sound processor loading shall be performed at 4 weeks post surgery. However, if the wound is not sufficiently healed, loading should be delayed.
- The investigators and the subjects will be instructed to carefully select an appropriate SP Magnet by balancing the magnet retention to avoid any skin problems.

The surgical procedure associated with the Baha Attract System is described in the Surgery Guide for the Baha Attract System. The guide has been developed by the Sponsor together with a group of experienced Baha surgeons.

Tests have demonstrated that the Implant Magnet in combination with the BI300 Implant is MRI conditional for up to 1.5 Tesla. Subjects that receive the Baha Attract System will receive an MRI card, for use by radiologists to evaluate and plan any MRI examination. Subjects that have received radiation therapy at the same side of the skull where the Baha Attract will be positioned are excluded from the investigation.

7.3 Risks associated with participation in the clinical investigation

As with any surgical products, there is a risk that unanticipated Adverse Events may occur. The subjects will be closely monitored in the investigation and instructed to contact the responsible investigator if they experience any untoward effect.

7.4 Risk/benefit assessment

The risks are acceptable when weighed against the benefits of the intended performance of the devices used in the investigation.

8 Statistical consideration

8.1 Statistical Design and Objectives

8.1.1 Primary statistical objectives

To compare the Baha Attract System to unaided hearing, via measurement of the following variables in free-field hearing tests:

- Threshold audiometry: PTA4 (mean of 500, 1000, 2000 and 4000Hz)

8.1.2 Secondary statistical objectives

- To compare the Baha Attract System to unaided hearing, via measurement of the following variables:
  - Thresholds audiometry: 250, 500, 1000, 2000, 3000, 4000, and 6000 Hz
  - Adaptive speech recognition in noise (50% performance)
  - Speech perception in quiet (50dB, 65dB and 80dB SPL)
  - HUI Mark 3
  - APHAB
  - SSQ

- To compare the Baha Attract System to the situation where the same sound processor is worn on a Baha Softband, via measurement of the following variables:
  - Threshold audiometry: PTA4 (mean of 500, 1000, 2000 and 4000Hz)
  - Threshold audiometry: 250, 500, 1000, 2000, 3000, 4000 and 6000 Hz
  - Adaptive speech recognition in noise (50% performance)
  - Speech perception in quiet (50dB, 65dB and 80dB)

- Description of all Adverse Events, device deficiencies, surgical variables, demographics, baseline variables, pain, numbness, soft tissue status, implant loss and questions.

- To investigate if the choice of SP Magnet and magnetic retention force changes over time.

8.2 Sample size calculation

8.2.1 Sample size calculation for the primary efficacy analysis:

In order to achieve 90 % power to detect a clinically significant difference of 10 dB in free-field hearing thresholds between the unaided situation and the Baha Attract System at the 6 months visit with Fisher's non-parametric permutation test for paired observation, two-sided test with significance level 0.05, on the ITT population 20 evaluable subjects are needed assuming a within subject standard deviation (SD) of 13.0 dB. The within subject SD for change in PTA4 has been estimated to 12.3 dB in a previous study within Cochlear comparing unaided hearing with a BP100 sound processor on a

Softband versus unaided hearing[2]. To compensate for a 10% drop out rate in the study 22 subjects should be included in the investigation.

8.2.2 Sample size calculation for the for the secondary analysis

In order to achieve 90 % power to detect a clinically significant change of 1.5 dB in free-field hearing thresholds from Softband to the Baha Attract System at the 6 months visit with Fisher's non-parametric permutation test for paired observation, two-sided test with significance level 0.05, on the ITT population 46 evaluable subjects are needed assuming a within subject SD of 3 dB. The within subject SD for change in PTA4 has been estimated to 2.89 dB in a previous study within Cochlear comparing outcomes with a BP100 sound processor on a Softband versus on an abutment[2].

8.2.3 Overall sample size considerations

In order to achieve 90% power both for the primary analysis (PTA4, Baha Attract vs. unaided) and the secondary analysis of the primary variable (PTA4, Baha Attract vs. Softband), 46 evaluable subjects are needed. To compensate for a 10% drop out rate in the study 52 subjects will be included in the investigation.

8.3 Analysis sets – populations

The Intention-to-Treat population (ITT) will include all subjects who have received the surgical intervention.

The Per Protocol population (PP) will include subjects that have completed the investigation according to the protocol. Subjects that were incorrectly included or were considered major protocol violators should be removed from the PP population.

The Safety population consists of all surgically treated subjects.

The final definition of the analysis sets (ITT, PP and Safety) will be taken at the clean file meeting before database lock.

8.4 General statistical methodology

Since all included subjects will have measurements of the primary and important secondary efficacy variables for unaided hearing, with the sound processor on a Softband and with the Baha Attract System, all statistical analyses will be paired. All statistical analyses will be non-parametric. In order to choose the most powerful test, the Fisher's non-parametric permutation test for paired observations[3] will be used for all paired analyses of continuous variables. The permutation tests use the measured values and not only the ranks in the calculations. For paired analysis of dichotomous and ordered categorical variables the Sign test will be used.

The analyses will be performed in the following priority:

1. Baha Attract System vs. Unaided
2. Baha Attract System vs. the sound processor on a Baha Softband

The main efficacy analysis will be performed on the ITT population and complementary efficacy analyses will be performed on the PP population. The main analysis will be performed after the 6 month visit. A complementary analysis will be performed 18 months after the main analysis (24-month visit). All significance tests will be two-sided and performed at the 5% significance level.

The distribution of continuous variables as well as change in continuous variables will be given as n, mean, SD, SEM, Median, Min and Max and the distribution of dichotomous and categorical variables will be given as number and percentages.

Adverse Events, Device deficiencies, Surgical variables, Demographics Baseline, Questions, Magnetic force and Magnet strength variables will only be analysed descriptively.

8.5 Efficacy analysis

8.5.1 Primary efficacy analysis

Primary efficacy analysis will be determined by analysis of change in free-field threshold audiometry: PTA4 (mean of 500, 1000, 2000 and 4000Hz), from unaided versus Baha Attract System at the 6 months visit for the ITT population, using Fisher's two-sided non-parametric permutation test for paired observations at a significance level of 0.05.

8.5.2 Secondary efficacy analyses

Comparison regarding change from unaided hearing to Baha Attract System will be done according to the general methodology with Fisher's non-parametric permutation test for paired observations for the following variables:

- Threshold audiometry: PTA4 (Mean of 500, 1000, 2000 and 4000 Hz) at 4 weeks, 12 and 24 months
- Threshold audiometry: 250, 500, 1000, 2000, 3000, 4000 and 6000 Hz at 4 weeks, 6, 12 and 24 months
- Adaptive speech recognition in noise (50% performance) at 4 weeks, 6, 12 and 24 months
- Speech in quiet (50dB, 65dB and 80dB) at 4 weeks, 6, 12 and 24 months
- HUI3 at 6 and 24 months
- APHAB at 6 and 24 months
- SSQ at 6 and 24 months

Comparison of the Baha Attract System with the same sound processor worn on a Softband will be done according to the general methodology with Fisher's non-parametric permutation test for paired observations for the following variables:

- Threshold audiometry: PTA4 (Mean of 500, 1000, 2000 and 4000 Hz) at 4 weeks, 6, 12 and 24 months
- Threshold Audiometry: 250, 500, 1000, 2000, 3000, 4000 and 6000 Hz at 4 weeks, 6, 12 and 24 months
- Adaptive speech recognition in noise (50% performance) at 4 weeks, 6, 12 and 24 months
- Speech in quiet (50dB, 65dB and 80dB SPL) at 4 weeks, 6, 12 and 24 months

All secondary efficacy analyses will be two-sided and conducted at the 0.05 significance level.

All secondary efficacy analyses will be performed for both the ITT population and PP population.

8.6 Adverse Event analyses

Adverse Events will be analysed descriptively for the Safety population. Implant survival will be analysed and illustrated with a Kaplan-Meier survival curve.

Adverse Events and Serious Adverse Events will be coded with the MedDRA dictionary and tabulated by Preferred Term-code and System Organ Class-code and treatment.

8.6.1 Analyses of Safety variables

All safety variables will be analysed descriptively for the Safety population.

8.7 Analyses of Surgical, Demographics and Baseline variables

The Surgical, Demographics and Baseline variables will be analysed descriptively for the ITT population and PP population.

8.8 Analyses of concomitant medications and treatments

Concomitant medications will be coded and tabulated by treatment.

8.9 Interim analysis

No interim analyses are planned. In addition to the main analysis at 6 months, only a follow-up analysis after 24 months is planned.

8.10 Statistical Analysis Plan

A statistical analysis plan (SAP) with detailed statistical analyses specified for all variables and time points will be written and signed before the database lock.

9 Administrative Aspects

9.1 Training

The Sponsor will organise an initiation visit before study start. The visit will cover: the CIP, investigational procedures including the informed consent process, instructions regarding CRF completion and any other matters or queries related to running the investigation at the site.

The principal investigator will ensure that appropriate training relevant to the investigation is given to the medical, nursing and other staff involved at the clinic and that new information of relevance to the performance of this investigation is forwarded to the staff involved.

9.2 Investigational data

9.2.1 Case Report Form (CRF)

Data Collection will be done by using a paper document (pCRF) or electronic system (eCRF) for each subject on which information will be reported. Specific instructions on how to complete the CRF will be provided to the investigator and other site staff. Completed CRFs will be reviewed and signed by an investigator.

9.2.2 Source data

Source data is defined as all the information in original records, certified copies of original records of clinical findings, observations, or other activities in a clinical investigation, necessary for the reconstruction and evaluation of the clinical investigation.

The CRF could be source data and before the initiation of the investigation the principal investigators should together with the monitor complete the template ‘Origin of source data’ stipulating where source data should be recorded at the investigational site.

9.2.3 Data management

A data management plan will be written that describes the overall data handling process including data validation, clarification of data and the clean file process.

The database management system iDataFax will be used. It will allow automated CRF tracing, facilitate data entry, provide easy data export into SAS and to Sponsor. It meets all the FDA (21 CFR§11) and ICH requirements.

All outstanding questions regarding data should be handled during the clean file meeting. After declaring clean file the data will be locked.

9.3 Archiving

The Sponsor and principal investigator shall maintain the investigation documents as required by the applicable regulatory requirements.

9.4 Device accountability

Access to the devices used in the investigation shall be controlled and the devices shall be used according to this CIP.

The principal investigator or authorised designee shall keep records documenting the device identity (batch number/serial number or unique code), use of the device and disposal of the device (if applicable) in accordance with standard procedures at the hospital and in accordance with local regulations.

9.5 Quality control

9.5.1 Monitoring

The Sponsor will appoint a monitor that will visit sites during the investigation. The monitor will be appropriately trained and informed about the nature of the investigation, ISO 14155:2011 and applicable regulatory requirements.

The monitor will verify the informed consent of participating subject, that the investigational team is adhering to the protocol and that data are accurately recorded in the CRF.

The monitor must have direct access to source data.

9.5.2 Audit

Audits of the clinical investigation may be conducted by the Sponsor or third party designated by the Sponsor to evaluate compliance with the CIP, written procedures, ISO-14155:2011 and applicable regulatory requirements.

9.6 Clinical Investigation Plan

9.6.1 Deviations from Clinical Investigation Plan

Any deviation from the CIP will be recorded together with an explanation of the deviation. Deviations will be reported to the Sponsor, who is responsible for analysing them and assessing their

significance. The appropriate ethics committee/institutional review board and regulatory authorities (if applicable) will be informed of any significant protocol deviations.

9.7 Suspension or premature termination

The Sponsor may suspend or prematurely terminate either an individual investigation site or the entire clinical investigation for significant and documented reasons. A principal investigator may suspend or prematurely terminate participation in the clinical investigation at the investigational site for which he/she is responsible.

9.8 Publication policy

The result of this study will be published. Authors of the primary publication based on this study must fulfil the criteria defined by the International Committee of Medical Journal Editors (ICMJE).

The primary publication must be published before any secondary publications are submitted for publication.

9.9 Timetable

First subject in:	Q1 2014
Last subject in:	Q3 2014
Last subject out:	Q3 2016

End of investigation is defined as ‘last subject last visit’.

10 Bibliography

1. Tjellström A, Håkansson B, Lindström J, et al. Analysis of the mechanical impedance of bone-anchored hearing aids. *Acta Otolaryngol* 1980;89:85-92
2. Hedin A, Flynn M. Investigation of potential impact of TBaha passive regarding hearing performance, Sweden: Cochlear Bone Anchored Solutions AB; 2013, 615077.
3. Good P. Permutation Tests. A Practical Guide to Resampling Methods for Testing Hypotheses. Springer, Inc New York (2000), page 51-52.

11 Signed agreement – Sponsor

Title	**Post-market clinical follow-up of a magnetic bone conduction implant (Cochlear™ Baha® Attract System)** A multicentre, open, prospective clinical investigation. 6 months investigation with an 18 months follow-up period
Investigation code	CBAS5477
Version	1.0
Version date	22 NOV 2013

Signature of Cochlear Bone Anchored Solutions

I agree to the terms of this clinical investigation protocol, including all appendices.

Signature:

_____	_____
Mark Flynn Director of Research and Applications	Date (dd-MMM-yyyy)

12 Signed agreement – coordinating investigator

Title	**Post-market clinical follow-up of a magnetic bone conduction implant (Cochlear™ Baha® Attract System)** A multicentre, open, prospective clinical investigation. 6 months investigation with an 18 months follow-up period
Investigation code	CBAS5477
Version	1.0
Version date	22 NOV 2013

Signature of Coordinating investigator

I agree to the terms of this clinical investigation protocol, including all appendices.

Signature:

_____ _____

Dr Emmanuel Mylanus
Radboud University Nijmegen Medical Centre
Nijmegen
Netherlands

Date (dd-MMM-yyyy)