CLINICAL INVESTIGATION PLAN

Front-End Processing 3.0 - Noise reduction, Transient Reduction, Scene Classifier

Study ID: [redacted]
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SIGNATURE OF THE PRINCIPAL INVESTIGATOR

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Investigator's Statement

The signature below constitutes the approval of this Clinical Investigation Plan and its attachments and provides the necessary assurances that this clinical investigation will be conducted according to all stipulations of this CIP, including all statements regarding confidentiality, and according to local legal and regulatory requirements as applicable according to the most recent version of the Declaration of Helsinki and all relevant national and international regulations.

By signing below, I accept that any amendment to this study and relative documentation will be implemented only upon mutual agreement with MED-EL and upon official approval by the relevant Ethics Committees.

		Date	0	1	J	A	N	2	0	0	0
Principal Investigator´s signature	Place		Day		Month			Year			

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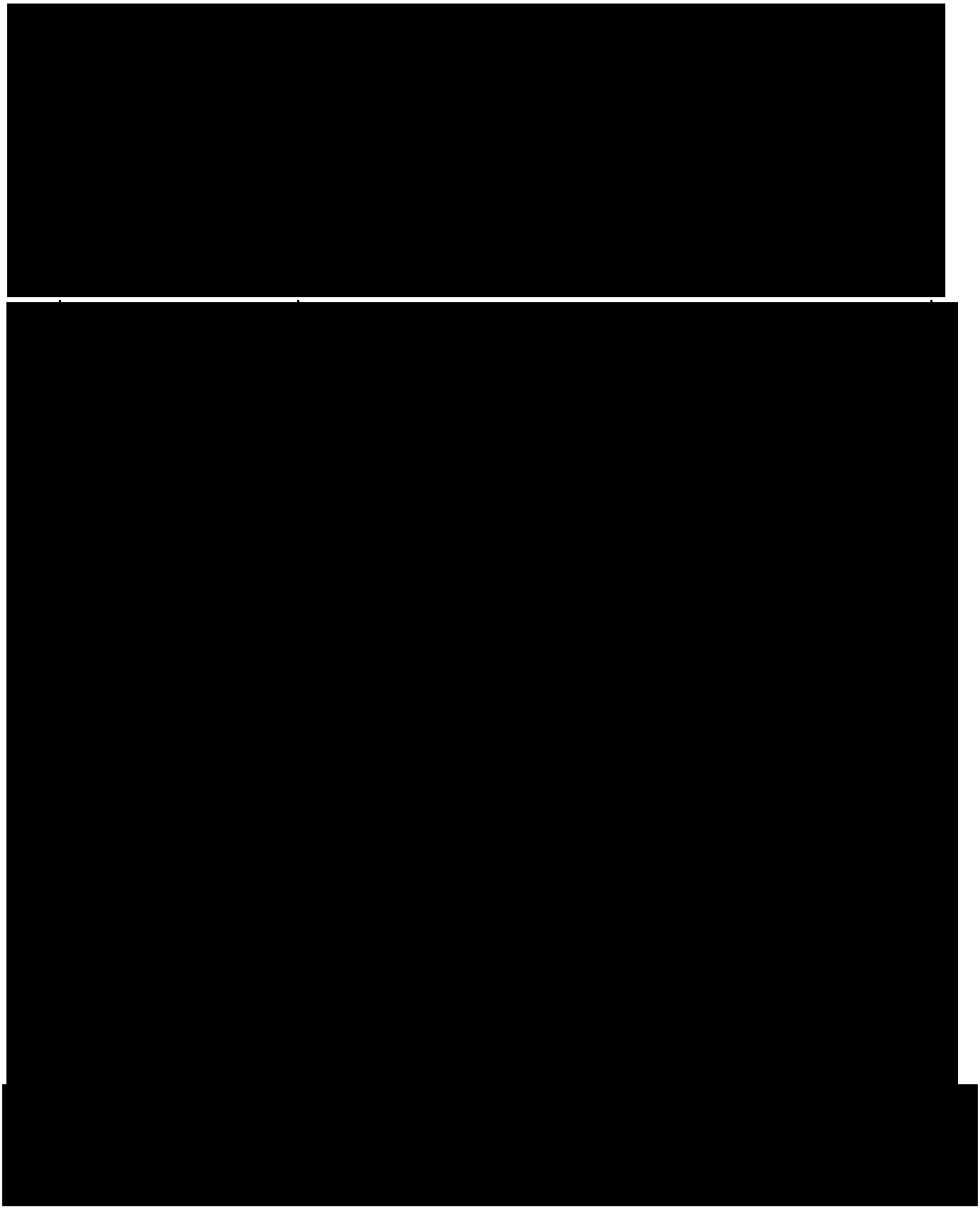
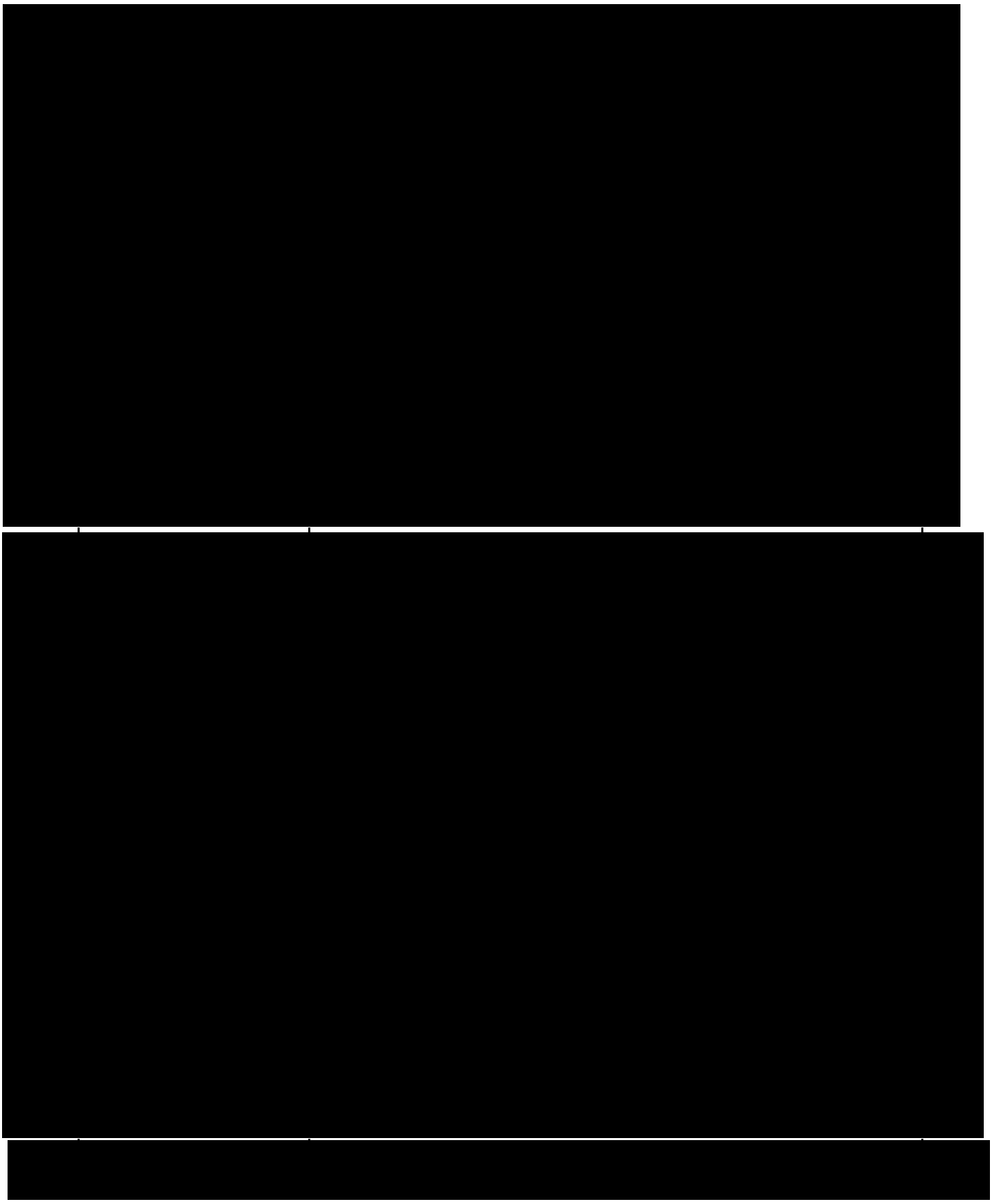
1 ABBREVIATIONS AND GLOSSARY

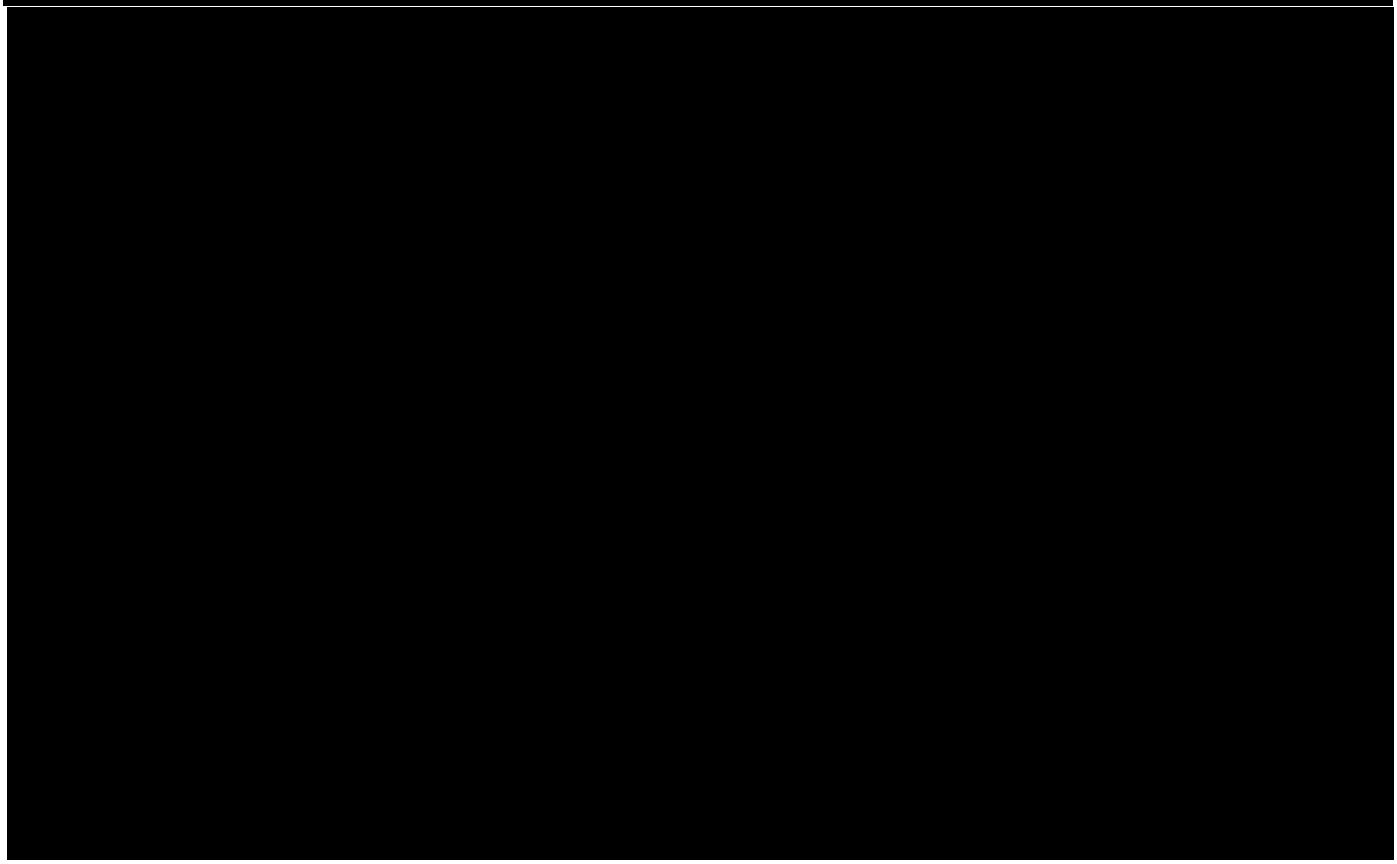
1.1 Abbreviations

Abbreviation	Definition
ACALES	Adaptive Categorical Listening Effort Scaling
ADE	Adverse Device Effect
AE	Adverse Event
ASC	Automatic Scene Classifier
ASM	Automatic Sound Management
APSQ	Audio Processor Satisfaction Questionnaire
CI	Cochlear Implant
CIP	Clinical Investigation Plan
CRF	Case Report Form
DD	Device Deficiency
FEP	Front-end Processing
HISQUI	Hearing Implant Sound Quality Index
IB	Investigator Brochure
ICF	Informed Consent Form
IEC	Independent Ethics Committee
ISF	Investigator Site File

OLSA	Oldenburger Sentence Test (Oldenburger Satztest)
NR	Noise Reduction
PI	Principal Investigator
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SNR	Signal-to-Noise Ratio
SOP	Standard Operating Procedure
SRT	Speech Reception Threshold
SSQ12	The Speech, Spatial and Qualities of Hearing Scale (short version with 12 questions)
TMF	Trial Master File
TR	Transient Noise Reduction
USADE	Unanticipated Serious Adverse Device Effect
WNR	Wind Noise Reduction







Test interval	Test Condition	Test performed
First visit (upgrade)	SONNET (must be the current audio processor)	Speech tests in quiet (Freiburg Monosyllables)
		Questionnaires
	SONNET 2	• Fitting of all audio processor configurations • Speech test in quiet in all 6 configurations • Subject sent home with two configurations (randomised across subjects)
		Note: the subjects' SONNET stays at the clinic until the study is completed (or subject is withdrawn)
Second visit	SONNET	Speech tests in noise (S0N0)
	SONNET 2	• Readout and save data logging

		• Questionnaires • Speech tests in noise (S0N0) in all 6 configurations • Speech tests in noise (S0N0T0) in the SONNET configuration and SONNET 2 configuration 1 and 2
		• Subject send home with two configurations (randomised across subjects)
Third visit	SONNET	Speech tests in noise with 5 loudspeakers (S0, ±N45, ± N135)
	SONNET 2	• Readout and save data logging
		• Questionnaires • Speech tests in noise 5 loudspeakers (S0, ±N45, ±N135) in all 6 configurations
		• Subject send home with two configurations (randomised across subjects)
Fourth visit	SONNET 2	• Readout and save datalogging
		• Questionnaires • Subjective ratings
		• Subject send home with two configurations (randomized across subjects)
Fifth visit	SONNET 2	Readout and save datalogging (
		Subjective ratings
	Give back the subject's SONNET	

Table 1. Study overview

3 INTRODUCTION

3.1 Literature Review

Cochlear implant (CI) users have experienced a steady improvement in their speech perception scores through the last decades (Zeng, 2004; Zeng, Rebscher, Harrison, Sun, & Feng, 2008). Nowadays, many CI users perform at ceiling in sentence tests in quiet (i.e. > 90%), and many CI users successfully converse over the telephone (Zeng, 2004; Zeng et al., 2008). Although the introduction of fine structure coding strategies and bi-directional microphones have improved the hearing performance in more challenging listening conditions, CI users still face considerable challenges when listening in background noise, reverberating surroundings (Cacace, Kleine, Holt, & Dijk, 2016; Finke, Strauss-Schier, Kludt, Buchner, & Illg, 2017).

In contrast to normal hearing people, cochlear implant users typically need a signal-to-noise ratio (SNR) of at least +5 dB, but often up to +20 dB to reach a 50% speech reception threshold (SRT) (Nelson, Jin, Carney, & Nelson, 2003; Stickney, Zeng, Litovsky, & Assmann, 2004; Zeng et al., 2008). Importantly, CI users' speech reception scores in noise often drop remarkable compared their scores in quiet (Finke et al., 2017; Schafer & Thibodeau, 2004; Wolfe & Schafer, 2008) which may lead to a considerable increase in listening effort and a loss in quality of hearing. CI users tend to have even more difficulties speech understanding if exposed to fluctuating noise (e.g. slamming doors, clattering dishes) than in stationary noise or noise with relatively low temporal variations (e.g. car engine) (Fu & Shannon, 1999; Nelson et al., 2003; Stickney et al., 2004; Zeng & Galvin, 1999). Therefore, the improvement of speech understanding in noise is still a very important topic in the CI field.

Early CI development aiming at enhancing speech recognition, have focused on increasing number of channels and the stimulation rate and improving the signal-processing strategies and the electrode design. Considerable improvements were also reached by improved front-end processing methods. MED-EL cochlear implants incorporate the Automatic Sound Management (ASM). This technology provides a wide input dynamic range and to some extent protection from sudden loud sound to cochlear implant users which is achieved by a dual loop automatic volume control and automatic gain control. Additionally, dual, omni-directional or adaptive directional microphones, and remote microphone technologies can improve signal quality by optimizing the acoustic signal. In combination with pre-processing algorithms, the signal can be enhanced for different environments, for instance by automatically identifying sounds, and thus customized for the individual user. A common approach is to use two omni-directional microphones to form fixed or adaptive directional microphones, also known as beamforming. With the SONNET, MED-EL introduced ASM 2.0 including wind-noise reduction and microphone directionality and significant improvements in speech performance could be shown (Hagen et al., In submission). With the most recent audio processor, SONNET 2, ASM 3.0 including new front-end features were incorporated: the noise reduction, the transient noise reduction and an automatic scene classifier.

3.2 Previous Clinical Experience

The SONNET 2 is an approved medical device indicated for individuals suffering severe to profound hearing loss. This study is designed to test speech perception quiet and in noise using different front-end processing features and collect subjective feedback on these new features by the use of different questionnaires (details are described in Section 10.2). Detailed information on the device can be found in Section 4.

3.3 Rationale

Similar to previous studies on audio processor and software development, this study investigates the new front-end features incorporated in the most recent audio processor SONNET 2.

This study is planned as an active post-market follow-up with an approved product bearing a CE mark, within its intended use.

Subjects will undergo the study-specific speech in quiet and speech in noise test and will complete questionnaires. This design will allow to a direct comparison of objective and subjective measures to test the new front-end features.

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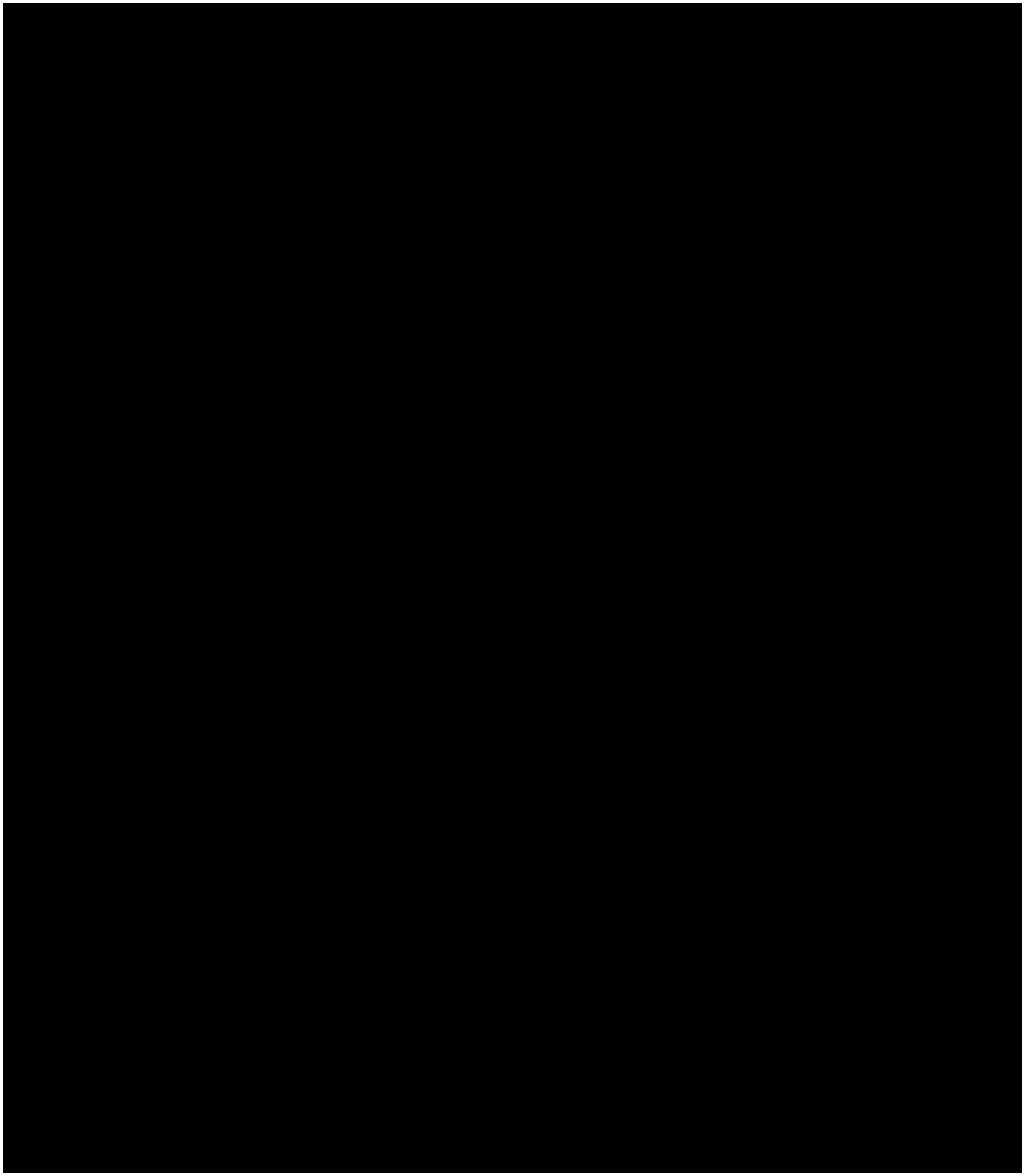
4 INVESTIGATIONAL DEVICE DESCRIPTION



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4.2 Storage

SONNET 2 audio-processor will be stored at the clinic according to the provision of the User Manual (see Section 21.1, Appendix 1 for details). The previous SONNET audio-processor will be stored at the clinics under the responsibility of the Investigator. An accountability log will be set-up to track the subjects' devices.

4.3 Accountability Procedures

Subjects will receive a SONNET 2 for the duration of the study. The audio processor will be handed over at the first study visit. To control for the SONNET 2 use during the study, the subject's audio processor will remain in the centre during active study participation and and will be given back after completing the study (see section 4.2 for details regarding the SONNET audio-processor retaining and storage procedure). If the subject discontinuous the study for any reasons, the subject will get back their own audio processor in the original setting (I.e. SONNET) without unnecessary delay. Might re-fitting be required the procedure

will be implemented according to the centre clinical routine procedures for follow up fitting. The details of the procedure will not be recorded as part of the study.

After study completion (all visits attended) the participants have the choice to keep the SONNET 2 processor or return it. The choice will be recorded during the last visit and will be descriptively analysed as study outcome.

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[redacted]

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4.6 Study population

This study aims to enrol experienced adult users of the MED-EL cochlear implant system.

- **Target population**: adults of both sexes suffering from sensorineural hearing loss as specified in the SONNET 2 Intended Use (IU) in the User Manual (See Section 21.1, Appendix 1 for details)
- **Accessible population**: target population matching all inclusion and exclusion criteria as defined in section 8.1
- **Intended population**: accessible population that can be recruited by the study site appointed for this study
- **Actual population**: intended population enrolled in the study without considering drop-out or withdrawal
- **Analytic population**: actual population meeting all criteria for analysis

the study population is identified with the analytic population.

4.7 Study Procedures

This study is performed in experienced adult users of the MED-EL Cochlear Implant System and involves an upgrade of the audio processor. Additionally, speech tests and questionnaires outside the clinical routine will be implemented.

For a detailed description of all study procedures, see Section 11.

4.8 Fitting

This study will involve fitting sessions in order to set the maps with the various configurations of front-end processing available for the SONNET 2.

Fitting will generally follow the clinical practice at the centre. Particular front-end features will be enabled/disabled for the four configurations.

Table 2 Overview of the different SONNET 2 fitting configurations

Audio Processor	Configuration	ASC	WNR	Beam-former	AGC Compression	AGC Sensitivity	NR	TR
SONNET	Default	N/A	Mild	NAT	3:1	75%	N/A	N/A
SONNET 2	OPUS 2	Off	Off	OMNI	3:1	75%	N/A	N/A
SONNET 2	SONNET (default)	Off	Mild	NAT	3:1	75%	N/A	N/A
SONNET 2	SONNET 2/1	Off	Mild	NAT	3:1	75%	Mild	Mild
SONNET 2	SONNET 2/2	Off	Mild	NAT	3:1	75%	Strong	Strong
SONNET 2	SONNET 2/3	Mild	Mild	Auto (NAT)	3:1	75%	Auto (Off-Mild)	Auto (Off-Mild)
SONNET 2	SONNET 2/4	Strong	Strong	Auto (OMNI-ABF)	3:1	75%	Auto (Off-Strong)	Auto (Off-Strong)

4.9 Permitted Concomitant Treatments

Medications that are considered necessary for the subject's welfare and are not specifically prohibited may be given at the discretion of the Investigator.

5 STUDY OBJECTIVES

5.1 Primary Objectives

Comparison between the speech reception thresholds in the OLSA test in noise (S0N0) of the SONNET 2 programmed as a SONNET and the SONNET 2 (setting 1; ASC off, mild WNR, mild NR, mild TR).

5.2 Secondary Objectives

- Comparison between the speech reception thresholds in the OLSA test in noise across all audio processors and audio processor settings.
- Comparison between the speech reception in quiet (Freiburg Monosyllables Test) across all audio processors and audio processor settings.
- Comparison of subjective user satisfaction, sound quality, quality of hearing, and listening effort across audio processors and audio processor settings

5.3 Study Outcome Measures

5.3.1 **Primary outcome measures**

The primary outcome measure is speech intelligibility in the S0N0 set-up in the OLSA speech test in noise. For a description of the test setup see Section 10.2.3

5.3.2 **Secondary outcome measures**

Performance of the SONNET 2 will be assess with different combinations of frontend processing features under different environmental test conditions using the following tests:

- Speech performance
  - ❖ Freiburg Monosyllabic test in quiet; speech presented from the front
  - ❖ Oldenburg Sentence Test in noise in the set-ups
    - ➢ S0N0
    - ➢ S0N0T0
    - ➢ S0, ±N45, ± N135
- Quality of hearing in real life
  - ❖ HISQUI19

- SSQ12

- Device handling
  - Data Logging
  - APSQ

- Subjective Rating
  - ACALES
  - Subjective Sound Quality Rating
  - Product Specific questionnaire

6 HYPOTHESES

6.1 Hypotheses for the Primary Objectives

The primary objective of this study is to show non-inferiority of SONNET2 in a OLSA in noise speech test (S0N0) compared to the SONNET. The margin of non-inferiority is set to 2 dB SNR (Hey, Hocke, Hedderich, & Müller-Deile, 2014; Nogueira, Rode, & Buchner, 2016).

- Verbal formulation

Hypothesis H_0 (Null Hypothesis):

Speech perception with the SONNET 2 in its default setting in the OLSA in noise (S0N0) is inferior to the speech perception in the same test condition with the SONNET.

Hypothesis H1 (Alternative Hypothesis):

Speech perception with the SONNET 2 in its default setting in the OLSA in noise (S0N0) is non-inferior to the speech perception in the same test condition with the SONNET.

- Mathematical formulation

H_0: $\mu 1 - \mu 2 \geq \Delta$ (2 dB SNR)

H_1: $\mu 1 - \mu 2 < \Delta$ (2 dB SNR)

Where:

μ1 = SONNET mean OLSA in noise (S0N0) results for the study population expressed in dB SNR

μ2 = SONNET2 mean OLSA in noise (S0N0) results for the study population expressed in dB SNR

6.2 Hypotheses for the Secondary Objectives

The secondary objectives of this study are to provide additional evidence on the performance of SONNET 2-specific front-end features. Thus, the analyses are of an explorative nature and will not influence the results of the primary outcome of the study. Due to the exploratory nature of the secondary objectives, no hypothesis is formulated a priori.

7 STUDY DESIGN

7.1 Type of Study

This study has been planned as a mono-centric, open label, prospective longitudinal study where each subject acts as his/her own control.

The SONNET 2 is an incremental innovation to the SONNET audio processor with additional front-end processing features which are designed to improve patient performance in specific auditory environments. The study is designed to prospectively follow-up experienced SONNET users who received the SONNET 2. As intra-individual control, subjects will be acutely tested with the SONNET in the same test conditions as with the SONNET 2.

7.2 Study Population

This study will be performed with experienced users of MED-EL cochlear implants (defined as a minimum experience of 6 months with a MED-EL cochlear implant and their current audio processor) who will be followed-up for fife study specific visits to the test centre.

7.3 Sample Size Calculation

The primary objective of this study is to show non-inferiority of SONNET2 in a OLSA in noise speech test (S0N0) compared to the SONNET. The margin of non-inferiority is set to 2 dB SNR (Hey et al., 2014; Nogueira et al., 2016).

Comparable data of the final report "Performance of Cochlear Implant Patients with Microphone Directionality and Wind Noise Reduction with the "SONNET" of the OLSA in noise speech test (S0N0) were used as basis for the sample size calculation (Hagen et al., In submission):

OPUS2	mean: 0.589 dB;	± SD: 1.586 dB vs.
SONNET natural-MILD	mean: -0.088 dB;	± SD: 1.463 dB

The sample size was estimated using the formula on noninferiority (Chow, Shao, & Wang, 2008):

$$N = (1 + \frac{1}{r})(\sigma \frac{Zcrit + Zpwr}{(\mu A - \mu B) - \Delta})^2$$

Assuming a non-inferiority margin of 2 dB (Δ), with an alpha-level of 0.025 (noninferiority, one-sided) and a power of 90%, a minimum sample size of 13 subjects was calculated (Zcrit is the normal quantile for the 0.025 alpha level, and Zpwr is the normal quantile for the 90%

power). To allow for possible dropouts (approximately 20%) and to provide additional safety and efficacy data, a maximum of 30 subjects will be included in this study.

7.4 Duration of the Study

Subject enrolment is scheduled to last for 15 months. If the minimum number of subjects is not achieved, enrolment may continue until the minimum number of subjects is reached or for an additional 9 months.

7.5 Management of Deviations from the CIP

Investigational sites shall inform the Monitor immediately about any deviations as they become aware of them. In addition, compliance to the CIP is verified by the Sponsor through monitoring sessions according to the study Monitoring Plan provisions.

Deviations that potentially affect the study outcome are recorded and listed in the final Clinical Investigation Report.

7.6 Protocol Amendments

Major Amendments shall be submitted to the relevant IEC(s) and NCA(s). Amendments may be implemented only after IEC(s) and, if required, NCA(s) approval has been obtained.

Amendments that are intended to eliminate an apparent immediate hazard for the subjects enrolled in the study may be implemented prior to receiving the relevant IEC(s) approval. However, in this case, approval shall be obtained as soon as possible after implementation.

No changes in the study procedures shall be affected without the mutual agreement of MED-EL, the Investigator and the Coordinating Investigator (if applicable). All changes shall be documented in the form of signed protocol amendments, or as a revised protocol. Changes to the protocol may require notification to or approval by the relevant IEC(s) before implementation. Local regulatory requirements shall be followed.

The Monitor is responsible for the distribution of protocol amendment(s) to the Investigator(s) and those concerned within the conduct of the study. The Investigator is responsible for the distribution of all amendments to the staff involved at his centre.

8 STUDY ENROLMENT AND WITHDRAWAL

8.1 Selection Criteria

8.1.1 Inclusion criteria

- A minimum of 18 years old
- Experienced user (≥ 6 months) of a MED-EL cochlear implant (C40+ and later model)
- Experienced user of a MED-EL SONNET audio processor (≥ 6 months)
- Post-lingual onset of bilateral severe to profound sensory-neural hearing loss
- Unilateral CI user
- A minimum of 10 active electrodes
- A minimum of 40% speech recognition in the Freiburg Monosyllables test in quiet at 65 dB SPL (at the last time tested)
- Fluent in German (the language of the test centre)
- Signed and dated ICF before the start of any study-specific procedure.

8.1.2 Exclusion criteria

- Lack of compliance with any inclusion criteria
- CI user with contralateral hearing equal to or better than 60 dB (PTA measured at 500, 1000, and 2000Hz)
- EAS user (user of an EAS audio processor)
- Implanted with C40X and C40C
- Implanted with an ABI or Split electrode array
- Known allergic reactions to components of the investigational medical device
- Unstable psychological status
- Anything that, in the opinion of the Investigator, would place the subject at increased risk or preclude the subject's full compliance with or completion of the study

8.2 Strategies for Recruitment and Retention

The pro-active recruitment can be performed by identification of potential study participants from the clinic database and invitation of such patients.

Subjects will be enrolled into the study by signing the informed consent upon being properly informed by the investigator. Subjects will retain a copy of the Informed consent form (ICF).

These recruitment activities will be conducted by the PI or delegated site staff.

8.3 Treatment Assignment Procedures

All subjects participating in this study will receive an upgrade to the SONNET 2 and undergo the same test regime (including tests with the SONNET 2 and SONNET audio processor).

8.4 Subject Identification

A subject willing to sign the ICF voluntarily at the screening visit will be considered enrolled into the study.

Thus, each subject will receive a code, which identifies them uniquely on all study related documents. This code constitutes the subject identification number according to the following scheme:

The subject will receive a subject identification number according to the scheme depicted in Table 3. The subject identification number shall be used henceforth to identify the subject on all study related documents.

Table 3: Coding of subjects entered into the study after signing and dating the ICF

The subjects of this study won't be replaced unless they are found not compliant with the inclusion/exclusion criteria prior to the first study specific tests. In this case, a non-compliant subject can be withdrawn and replaced. The replacing subject selected in place of a non-compliant one, will undergo the same approval procedure performed for the replaced subject and will receive a new unique identifier code (see section 8.2 for details about the enrolment procedure).

8.5 Early Withdrawal

8.5.1 Reason for Early Withdrawal

The Investigator may decide to withdraw a subject from the study for one of the following reasons upon agreement with MED-EL:

- Health issues (e.g. occurrence of SAEs, subject's death, etc.)
- Further participation would cause an unacceptable risk to the subject
- The subject moved away
- The subject does not comply with the CIP (e.g. s/he does not attend the visits on schedule; she/he does not communicate relevant medical issues to the Investigator, etc.)

In accordance with the Declaration of Helsinki (Fortaleza, 2013), subjects are free to terminate their participation in the study at any time for any or for no reason, without prejudicing their basic right to receive the best treatment available for them.

If a subject decides to withdraw early, he/she must return the SONNET 2 audio processor.

8.5.2 Handling of Early Withdrawal

Withdrawal of any subjects shall be recorded by the Investigator in the appropriate CRF "Early Withdrawal". If a subject decides to withdraw from the study, every effort should be made to contact him/her and to obtain information about the reason(s) for discontinuation and/or any AEs experienced. Subjects withdrawing prematurely won't be followed-up actively unless they suffer from an ongoing AE. In the case of an ongoing AE, the procedure described in section 8.8 of this CIP shall be followed.

8.6 Early Termination or Suspension of the Study

8.6.1 Reason for early termination or suspension of the study

The study may be suspended or early terminated by MED-EL for any of the following reasons:

- Suspicion or recognition of unexpected, significant and/or unacceptable risks for the subjects
- Insufficient adherence to protocol requirements
- Data that are not sufficiently complete and/or evaluable

- Plans to modify, suspend or discontinue the development of the investigational medical device

8.6.2 Handling of Early Termination or Suspension of the Study

The study may be suspended or early terminated either in all or in specific study sites, depending on the circumstances.

If the study is prematurely terminated or suspended, MED-EL will promptly inform the Investigators/institutions, the relevant IEC(s) and NCA(s) of the termination or suspension and state the reason(s) for the termination or suspension.

8.7 Replacement Policy

Subjects withdrawn from the study won't be replaced. Might the minimal sample size to evaluate the primary objective not be reached due to study drop-out or withdrawal, the enrolment is allowed to continue upon reaching the minimum number of subjects needed for such purpose in the analytical population as define in section 7.2.

8.8 Follow-Up Strategy

8.8.1 Premature Discontinuation

This study is designed to be conducted with a CE-marked investigational medical device which will be used solely within the approved indication.

Upon regular conclusion or premature discontinuation of the study, subjects won't be actively monitored unless a subject suffers from an ongoing AE.

Non-device or -procedure-related AEs that are ongoing at the time of a subject's end of active participation in the study will not be followed-up. Ongoing AEs will be recorded as ongoing and lost-to-follow-up at the time of a subject's end of active participation in the study.

Device- or procedure- related (ADEs, SADEs, and USADEs) or SAEs that are ongoing at the time of a subject's end of active participation in the study will be followed-up for a maximum of eight weeks. The PI will schedule a follow-up visit with the subject within the 8 weeks after the end of active participation. The subject may however decline to be followed-up. If the subject declines a follow-up visit, the unresolved AEs will be recorded as ongoing and lost-to-follow-up. Additionally, any unresolved AEs at the time of the follow-up visit will be recorded as ongoing and lost-to-follow-up.

9 STUDY SCHEDULE

Audio Processor	Configuration	**Visit 1**	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**
		Speech in quiet (S0)	Speech in noise (S0N0 & S0N0T0)	Speech in noise	Subjective Ratings	Subjective Ratings
SONNET	Default SONNET	✓	✓	✓	**x**	**x**
SONNET 2	OPUS 2	✓	✓	✓	✓	✓
SONNET 2	Default SONNET	✓	✓	✓	✓	✓
SONNET 2	SONNET 2/ Configuration 1[1]	✓	✓	✓	✓	✓
SONNET 2	SONNET 2 Configuration 2[1]	✓	✓	✓	✓	✓
SONNET 2	SONNET 2 Configuration 3[1]	✓	✓	✓	**x**	**x**
SONNET 2	SONNET 2/ Configuration 4[1]	✓	✓	✓	**x**	**x**
Questionnaires		SONNET: APSQ HISQUI SSQ	SONNET 2: SONNET 2[2] Questionnaire HISQUI SSQ	SONNET 2: SONNET 2[2] Questionnaire APSQ HISQUI SSQ	SONNET 2: SONNET 2[2] Questionnaire HISQUI SSQ	SONNET 2: SONNET 2[2] Questionnaire HISQUI SSQ

Take home 2 programs

1 Details on all SONNET 2 configurations are described in Table 2
2 The questionnaire will be completed for the SONNET 2 in the SONNET default configuration and one of the four SONNET 2 configurations (which will be randomised across subjects).

9.1 Screening and Upgrade Visit (1st study visit)

Potential subjects will be approached and asked for their willingness to participate in the study. If they indicate interest, they will be informed about the study in detail, receive the information and consent form. The investigator will perform a chart review to determine suitability of the subject.

If the subject voluntarily signs the consent and all inclusion/exclusion criteria are fulfilled the subject will be enrolled in the study. Appropriate fitting for the subject's SONNET will be confirmed according to clinical routine and then receive the upgrade to the SONNET 2. The SONNET 2 will be fitted based on the most current clinical map of the subject. Adjustments to the fitting map imported can be made if deemed necessary according to the clinical routine procedures. Adjustments to the fitting maps across the study visits are possible if deemed necessary according to the clinical routine procedures. Clinical maps will be recorded as part of the study.

For the duration of the study, the subject's own audio processor will be stored at the study site, and only be used at the follow-up test intervals by the subjects.

9.1.1 **Testing with the current audio processor (SONNET):**

- Speech test in quiet
- User satisfaction and subjective rating via questionnaires

9.1.2 **Testing with the SONNET 2:**

- Speech test in quiet
  - ❖ Set-up as an OPUS 2
  - ❖ Set-up as an SONNET (without new front-end features)
  - ❖ Setting 1: ASC off, mild WNR, mild NR, mild TR
  - ❖ Setting 2: ASC off, mild WNR, strong NR, strong TR
  - ❖ Setting 3: ASC mild, mild WNR, auto NR, auto TR
  - ❖ Setting 4: ASC strong, strong WNR, auto NR, auto TR
- Set the data logging in all configurations to zero
- MAESTRO Export of all SONNET 2 configurations
- Send subject home with two SONNET 2 configurations (randomized across subjects) and make sure data logging is on when the subject is send home
-

9.2 Follow-up Visit 1 (2nd study visit)

The first follow-up visit will be scheduled 2 weeks (±1 week) after the first study visit.

During this visit, fittings of the SONNET and the SONNET 2 sor will be confirmed prior to any study test and only adjusted if needed.

9.2.1 Testing with the current audio processor (SONNET):

- Speech test in noise (S0N0)

9.2.2 Testing with the SONNET 2:

- User satisfaction and sound quality rating via questionnaires
- MAESTRO Export of all SONNET 2 configurations including the data logging information
- Speech test in noise (S0N0)
  - ❖ Set-up as an OPUS 2
  - ❖ Set-up as an SONNET (without new front-end features)
  - ❖ Setting 1: ASC off, mild WNR, mild NR, mild TR
  - ❖ Setting 2: ASC off, mild WNR, strong NR, strong TR
  - ❖ Setting 3: ASC mild, mild WNR, auto NR, auto TR
  - ❖ Setting 4: ASC strong, strong WNR, auto NR, auto TR
- Speech test in noise (S0N0T0)
  - ❖ Set-up as an SONNET (without new front-end features)
  - ❖ Setting 1: ASC off, mild WNR, mild NR, mild TR
  - ❖ Setting 2: ASC off, mild WNR, strong NR, strong TR
- Reset the data logging in all configurations
- Send subject home with two SONNET 2 configurations (randomized across subjects) with data logging set to zero

9.3 Follow-up Visit 2 (3rd study visit)

The first follow-up visit will be scheduled 2 weeks (±1 week) after the second study visit.

During this visit, fittings of the SONNET and the SONNET 2 or will be confirmed prior to any study test and only adjusted if needed.

9.3.1 Testing with the current audio processor (SONNET):

- Speech test in noise (S0, ±N45, ± N135)

9.3.2 Testing with the SONNET 2:

- User satisfaction and sound quality rating via questionnaires
- MAESTRO Export of all SONNET 2 configurations including the data logging information
- Speech test in noise (S0, ±N45, ± N135)
  - ❖ Set-up as an OPUS 2
  - ❖ Set-up as an SONNET (without new front-end features)
  - ❖ Configuration 1: ASC off, mild WNR, mild NR, mild TR
  - ❖ Configuration 2: ASC off, mild WNR, strong NR, strong TR
  - ❖ Configuration 3: ASC mild, mild WNR, auto NR, auto TR
  - ❖ Configuration 4: ASC strong, strong WNR, auto NR, auto TR
- Reset the data logging in all configurations
- Send subject home with two SONNET 2 configurations (randomised across subjects) with data logging set to zero

9.4 Follow-up Visit 3 (4th study visit)

The first follow-up visit will be scheduled 2 weeks (±1 week) after the third study visit.

During this visit, fittings of the SONNET 2 will be confirmed prior to any study test and only adjusted if needed.

9.4.1 Testing with the SONNET 2:

- User satisfaction and sound quality rating via questionnaires
- MAESTRO Export of all SONNET 2 configurations including the data logging information
- Subjective sound quality ratings (S0N0T0) and the ACALES test in noise (S0N0) to evaluate the NR and TR for the following audio processor configurations
  - ❖ Set-up as an OPUS 2
  - ❖ Set-up as an SONNET (without new front-end features)
  - ❖ Configuration1: ASC off, mild WNR, mild NR, mild TR
  - ❖ Configuration 2: ASC off, mild WNR, strong NR, strong TR
- Reset the data logging in all configurations

- Send subject home with two SONNET 2 configurations (randomised across subjects) with data logging set to zero

9.5 Follow-up Visit 4 (5th study visit)

The first follow-up visit will be scheduled 2 weeks (±1 week) after the fourth study visit.

During this visit, fittings of the SONNET 2 will be confirmed prior to any study test and only adjusted if needed.

9.5.1 **Testing with the SONNET 2:**

- User satisfaction and sound quality rating via questionnaires
- MAESTRO Export of all SONNET 2 configurations including the data logging information
- Subjective sound quality ratings (S0, ±N45, ± N135, T135 ipsilateral to the CI) and the ACALES test in noise (S0, ±N45, ± N135) to evaluate the NR and TR for the following audio processor configurations
  - ❖ Set-up as an OPUS 2
  - ❖ Set-up as an SONNET (without new front-end features)
  - ❖ Configuration 1: ASC off, mild WNR, mild NR, mild TR
  - ❖ Configuration 2: ASC off, mild WNR, strong NR, strong TR

9.6 Early Termination Visit

If a subject withdraws from the study, he or she can do so during a regular study visit. In this case, the subject gives back the SONNET 2 audio processor and the centre gives him/her back their own SONNET audio processor and ensures that fitting is appropriate. In case a subject withdraws from the study outside of a study visits, an early termination visit shall be scheduled to follow-up on any potential open issues and document reasons for the withdrawal. During this visit, the subject gives back the SONNET 2 audio processor and the centre gives him/her back their own SONNET audio processor and ensures that fitting is appropriate. In any case, the case report form "Early Withdrawal Form" will be completed.

9.7 Unscheduled Visit(s)

In the case of any unexpected events, subjects may present at the clinic in-between regular study visits. During unscheduled visits the CRF "Unscheduled visit" shall be completed.

10 EQUIPMENT AND TEST METHODOLOGIES

10.1 Equipment

10.1.1 **MAESTRO Software**

Within the MED-EL Cochlear Implant System, MAESTRO 8 is used to program system components in order to achieve an optimal benefit for each individual implant patient. MAESTRO 8 consists of the software application, the installation program, and the accompanying labelling (instructions for use and CD labelling). Like its predecessor MAESTRO 7, MAESTRO 8 is designed and developed via the Microsoft .NET Framework and intended to be run on a personal computer that has a Microsoft Windows™ operating system installed. To communicate with implants and audio processors MAESTRO 8 uses the MAX Programming Interface which is connected via the standard USB 2.0 interface to the personal computer on which the software is running.

With MAESTRO 8 it is possible to program the new SONNET 2 audio processor and the new front-end processing features can be activated. The SONNET 2 audio processor comes equipped with various new ASM features (e.g. noise reduction, transient reduction, and automatic scene classification).

As MAESTRO 8 is a component of the MED-EL Cochlear Implant System, all indications stated for the MED-EL Cochlear Implant System are applicable.

MAESTRO 8 is intended to be used:

- In a clinical or office environment by persons adequately skilled and trained to perform all intended tasks
- With patients who received one of the intended MED-EL cochlear implants
- Installed on a Personal Computer running a version of the supported Microsoft Windows operating system
- All tasks which can be performed are described in the MAESTRO 8 manual.

10.2 Tests/Material

10.2.1 **Impedance Field Telemetry (IFT)**

A telemetry recording will be performed according to the procedures explained in the MED-EL Fitting Guide. The impedance field telemetry (IFT) recording ensures the proper function of the implant and measures impedances on all electrodes as well as the ground path.

These data form the basis of every clinical map and are necessary to interpret differences between fitting maps.

10.2.2 Speech testing in quiet

The Freiburg Monosyllabic test is an open-set monosyllabic word test and is widely used to test adults in German-speaking countries (K.-H. Hahlbrock & Zöllner, 1970; K. H. Hahlbrock, 1970). It consists in total of 20 lists with 20 words each. Each patient shall perform a training starting the actual testing. The results scored in this training session will not be analysed. The test lists will be allocated according to a randomization procedure. The analysis evaluates the number of correctly repeated words in % correct at a fixed presentation level. Speech is presented at 65dB SPL. The test shall be performed in quiet.

10.2.3 Speech testing in noise

In this study speech audiometry in noise will be performed using Oldenburger matrix sentence tests (Wagener, Brand, & Kollmeier, 1999a, 1999b; Wagener, Kühnel, & Kollmeier, 1999).

Oldenburger matrix sentence tests are available as measurement modules of the Oldenburger Measurement Application (OMA) (Hörtech GmbH). Matrix sentence tests will be used in the study, due to the sensitivity and applicability in a two-language study. Speech audiometry with the Oldenburger matrix sentence test using speech test material in the national language of the study site.

The test is used to assess the 50% speech-recognition threshold (SRT50 in dB SNR), which is a measure of the level difference at which speech can be identified at half the time in presence of simultaneous masking noise.

The sentences of matrix tests all are composed with the same structure. Test lists with 20 or 30 items are generated from several such sentences. The words are taken in a seemingly random fashion from an inventory (a matrix) of 50 words (10 words per category).

10.2.4 Subjective user ratings

10.2.4.1 *Audio Processor Satisfaction Questionnaire (APSQ)*

The APSQ is a validated general questionnaire which is designed to assess the handling of MED-EL devices. It assesses the wearing comfort, sound quality, and other device-specific factors related to the audio processor. The APSQ will be filled out by the patients at the first visit for the OPUS 2 before they get the SONNET and at the third visit for the SONNET.A copy of the completed questionnaire shall be sent to the study monitor. A copy of the completed questionnaire shall be sent to the study monitor.

10.2.4.2 *Hearing Implant Sound Quality Index 19 (HISQUI19)*

The Hearing Implant Sound Quality Index 19 (HISQUI19) is a self-administered questionnaire to quantify the individual perceived sound quality of hearing implanted patients in daily life (Amann & Anderson, 2014). The questionnaire consists of 19 seven-level Likert items ranging from “always (99%)” to “never (1%)”. Added percentage values shall support the answering. Eight additional items assess the current sound sensation of the patients implanted. The HISQUI19 takes about 15 minutes to complete. It will be filled out by the patients at the first visit for the OPUS 2 before they get the SONNET and at the third visit (final visit) for the SONNET. Documentation of the results shall be recorded in the appropriate sections of the case report forms. A copy of the completed questionnaire shall be sent to the study monitor.

10.2.4.3 *SSQ12 (Speech Spatial Qualities) in German*

The speech, spatial, and qualities of hearing (SSQ) questionnaire is used in its shorter 12-question version (Noble, Jensen, Naylor, Bhullar, & Akeroyd, 2013). The short version of the SSQ questionnaire provides similar results to the full version comprising 49 questions. A conversion formula between the abbreviated and full versions has been provided previously (Noble et al., 2013). The SSQ questionnaire is a sensitive and specific measure to assess the impact of hearing loss on speech perception, sound localization, and QoL. The SSQ12 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.

SSQ12 has a scale from 0 (not at all) to 10 (perfectly) and allows to rate every answer everywhere inside that scoring frame.

The SSQ12 will be filled out by the patients at the first visit for the OPUS 2 before they get the SONNET and at the third visit for the SONNET. A copy of the completed questionnaire shall be sent to the study monitor.

10.2.4.4 *SONNET 2 questionnaire*

A study specific questionnaire was developed to investigate how the four new SONNET 2 fitting configuration compare to the previous SONNET settings. The questionnaire covers different everyday situations (e.g. conversations in a cocktail party setting, speech different background noise situations, music etc.). The subjects are asked to state which fitting

configuration is preferred and give a reason why. Additionally, there are blank spaces which each subject can state situations which are important to each individual, state their preferred fitting and also tick why a particular fitting was preferred.

10.2.4.5 *Subjective sound quality rating*

In addition to questionnaires, subjects are asked to subjectively rate the sound quality of the different fitting configuration. The subjective sound quality of the different SONNET 2 configurations will be assessed on a visual analogue scale (VAS) for a range of signals comprising different samples of speech, music, and background noises. The subject will have to rate the perceived quality on different scales, compared to a reference condition.

10.2.4.6 *ACALES Test*

To evaluate the listening effort induced by different configurations, the ACALES test will be performed (Krueger & Schulte, 2017). In this test, the subject will listen to speech in noise and rate the subjectively perceived listening effort on a scale from “effortless” to “extremely effortful”. Depending on the rating of the subject, the level of the speaker will be varied adaptively while the noise level is kept constant. This test will be performed in different fitting configurations.

11 STUDY PROCEDURES

11.1 Demographics and Medical Data

The Investigator will record age and gender of the subject. Demographic data will be recorded in the appropriate section of the CRF at the screening visit and confirmed at every subsequent visit by the Investigator, as applicable

11.2 Medical History

Generally, the Investigator will record the medication history according to clinical standards in order to evaluate whether the subjects fulfils indication and inclusion criteria and does not fulfil any contraindications or exclusion criteria for CI surgery in general and for the study participation in particular. Results from the examination will be reported in the respective CRFs as applicable.

11.3 Medication

The Investigator will record the medication history according to clinical standards in order to evaluate whether the subject fulfils indication and inclusion criteria of the study. Results from the examination will be reported in the respective CRFs as applicable.

11.4 Compliance with the Selection Criteria

During the screening visit the Investigator thoroughly evaluates whether a subject meets the selection criteria and can be enrolled into the study. This does not imply that the subject needs to perform any kind of study specific testing. In case a subject meets the criteria and is willing to participate, the Investigator will explain all the involved procedures, risks and benefits of the clinical investigation understandably and will answer all upcoming questions. The subject will read the ICF, sign and date it. A written copy of the ICF will be given to the subject and can be taken home. The compliance of the subject with the study inclusion and exclusion criteria will be documented in the appropriate section of the CRF at each visit by the Investigator.

11.5 Special Tests/Procedures

11.5.1 **Fitting procedure**

Appropriate fitting for the subject's SONNET will be confirmed according to clinical routine and then receive the upgrade to the SONNET 2. The SONNET 2 will be fitted based on the most current clinical map of the subject. Adjustments to the fitting map imported can be made if deemed necessary according to the clinical routine procedures. Adjustments to the fitting maps across the study visits are possible if deemed necessary according to the clinical routine procedures. Clinical maps will be recorded as part of the study.

11.5.1.1 *Telemetry (IFT) recording*

Perform a routine telemetry recording as explained in the MAESTRO user guide. There are no parameters to be adjusted. Save the telemetry recording in MAESTRO and rename it according to the following scheme: "*SubjectID_IFT_visit name*".

11.5.1.2 *MCL and THR recording*

The standard fitting procedure as implemented at the study centre as per clinical routine will be used to determine MCL and THR levels. Briefly, THR and MCL levels are measured using verbal feedback from the patient. THR levels may be obtained using an ascending presentation, followed by a standard bracketing procedure. MCLs are obtained through a method referred to as loudness scaling. The level of current is gradually increased, while the patient reports on the level of loudness and comfort. Ideally, MCL levels should also be balanced across the electrode array. Loudness balancing requires comparison on at least two electrodes at a time until all MCLs are perceived as equally loud. After adjusting the parameters according to the subject's needs, save the THR and MCL recording in MAESTRO and rename it according to the following scheme: "*SubjectID_THRs_visit name*" and "*SubjectID_MCLs_visit name*".

11.5.2 **Speech testing**

11.5.2.1 ***Freiburg Monosyllables***

The Freiburg Monosyllables in quiet will be implemented according to the routine testing approach at the study centre. The results are recorded and expressed in % correct and reported in the CRFs.

11.5.2.2 *OLSA*

The Oldenburger Matrix Sentence Test will be performed according to the specification in the case report form (e.g. order of configuration etc.). Prior to the test lists, a training round will be performed at each visit. Noise level will be fixed to 60 dB SPL and the speech level will be adaptive.

The OLSA will be performed indifferent set-ups (also see Figure 1):

- S0N0

Speech and noise signal are both presented from the front of the subject (0° angle).

- S0N0T0

Speech, noise and transient noise are presented from the front of the subject (0° angle).

- S0, ±N45N, ± N135

Speech in presented from the loudspeaker in front of the subject (0°angle). Stationary noise presented from +45° and -45° angle and +135° and -135° angle.

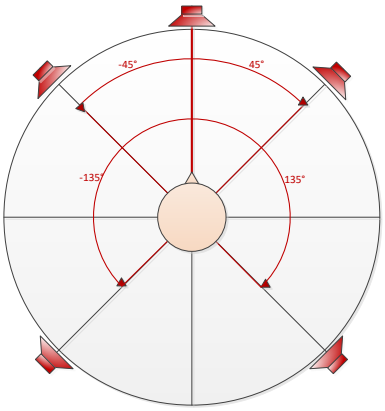


Figure 1 Loudspeaker set-up

11.5.3 **Subjective user ratings**

11.5.3.1 *Audio Processor Satisfaction Questionnaire (APSQ)*

The APSQ will be completed by the subject. An instruction is given in the questionnaire document. These data are considered source data.

11.5.3.2 *Hearing Implant Sound Quality Index 19 (HISQUI19)*

The HISQUI will be completed by the subject. An instruction is given in the questionnaire document. These data are considered source data.

11.5.3.3 *SSQ12 (Speech Spatial Qualities) in German*

The SSQ12 will be completed by the subject. An instruction is given in the questionnaire document. These data are considered source data.

11.5.3.4 *SONNET 2 questionnaire*

The SONNET 2 Questionnaire will be completed by the subject. An instruction is given in the questionnaire document. These data are considered source data.

11.5.3.5 *Subjective rating*

11.5.3.6 *ACALES Test*

To evaluate the listening effort induced by different configurations, the ACALES test will be performed. In this test, the subject will listen different sound files and rate the subjectively perceived listening effort on a scale from “effortless” to “extremely effortful”. Depending on the rating of the subject, the level of the signal will be varied adaptively while the noise level is kept constant,

The ACALES will be performed in different set-ups (also see Figure 1):

- S0N0

Speech and noise are both presented from one loudspeaker being in front of the subject (0° angle).

S0, ±N45, ± N135 ±Speech is presented from the loudspeaker in front of the subject (0°angle). Stationary noise is presented from +45° and -45° angle and +135° and -135° angle.

11.5.3.7 *Subjective sound quality rating*

The subjective sound quality of the different configurations will be assessed on a visual analogue scale (VAS) for a range of signals. The subject will have to rate the perceived quality on different scales, compared to the reference condition (Set-up as an SONNET (without new front-end features).

- Overall quality: Scale ranging from ‘Much better’ to ‘Much worse’

- Listening effort: Scale ranging from ‘Much less effortful’ to ‘Much more effortful’
- Listening comfort: Scale ranging from ’Much more comfortable’ to ’Much less comfortable’
- Annoyance of background signal: Scale ranging from ‘Much less annoying’ to ‘Much more annoying’
- Acceptability of the program (no reference necessary): ‘Not acceptable’ to ‘Very acceptable’

11.5.4 **Scientific data export**

After each take home period, the data of all configurations is exported and saved using the scientific export of MEASTRO. This data contains, among others, the logging data information (e.g., the processor usage, exposure time in the different audio environments, etc.) and enables to draw a relation between subjective ratings (questionnaires) and exposure to various audio environments during the take home periods.

[redacted]

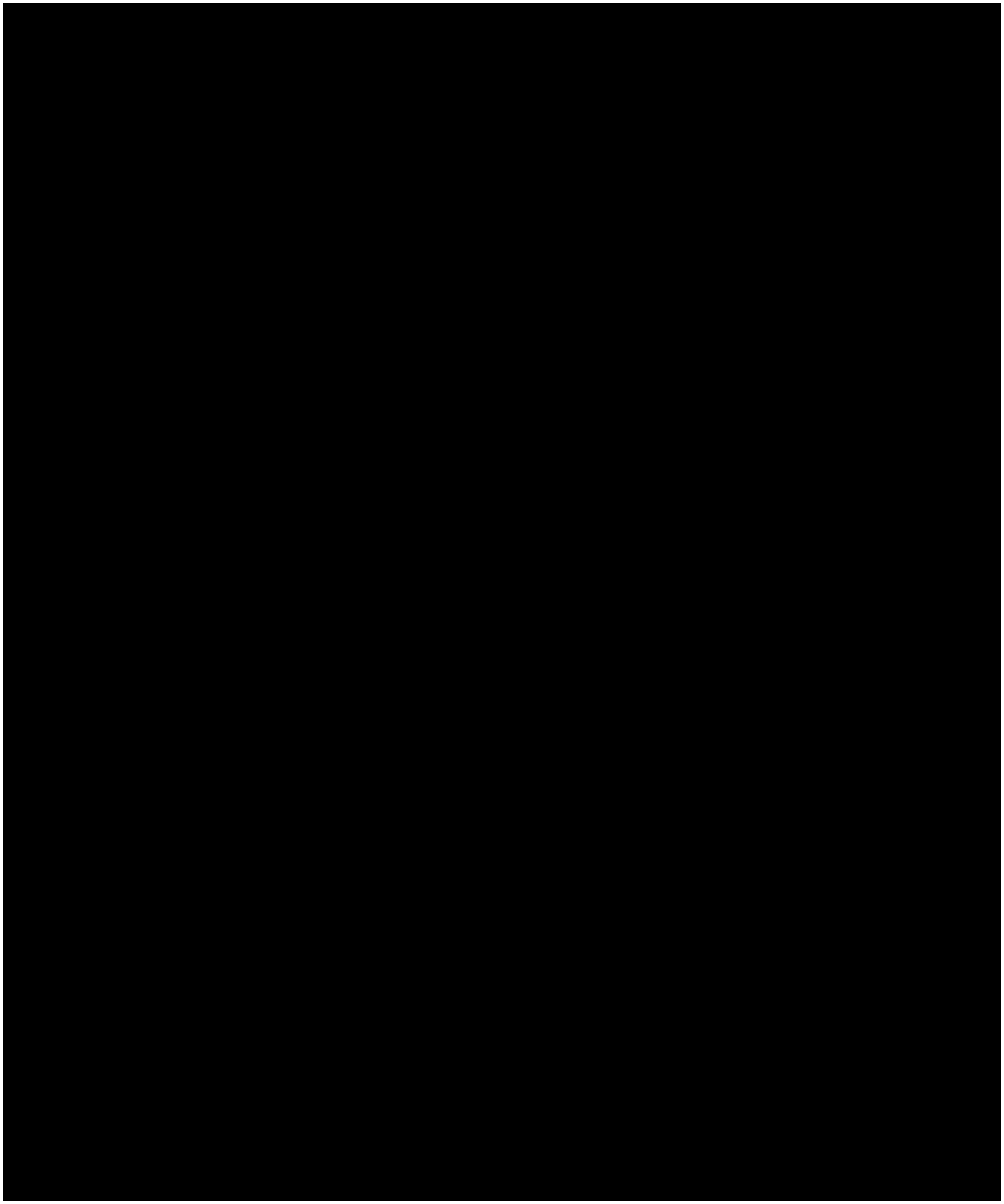
11.6 Randomization

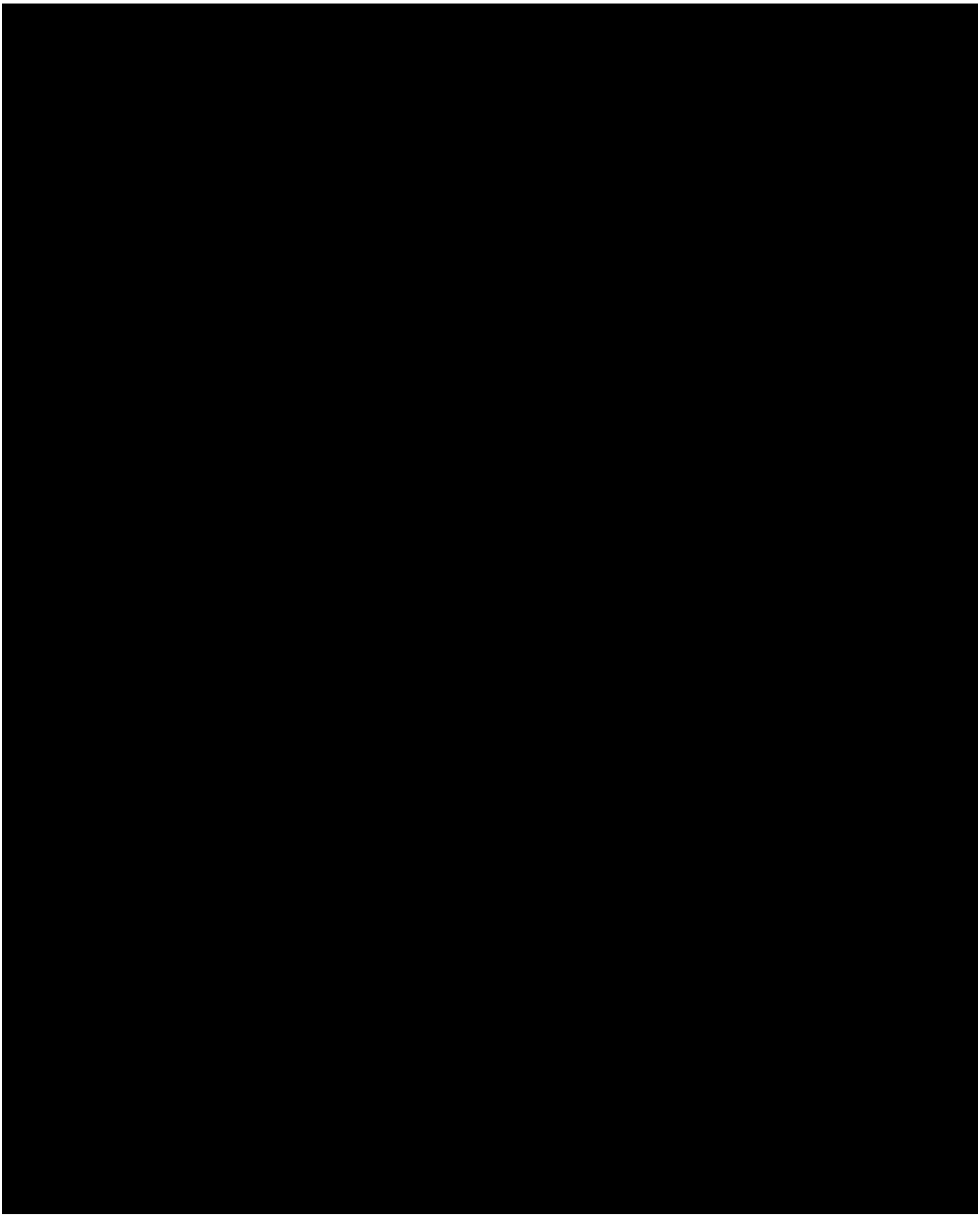
The order of the audio processor testing (see Section 9 for details) will be randomised for each subject and study visit. Additionally, it will be randomised, which audio processor configurations will be taken home after a particular visit. These randomizations will be performed to avoid any sequence-effects (e.g. training effect, fatigue effect). The particular fitting configuration and the order of the test procedures is verbally stated in the respective CRFs for each subject and each study visit. Hence, no de-randomisation procedure is necessary.

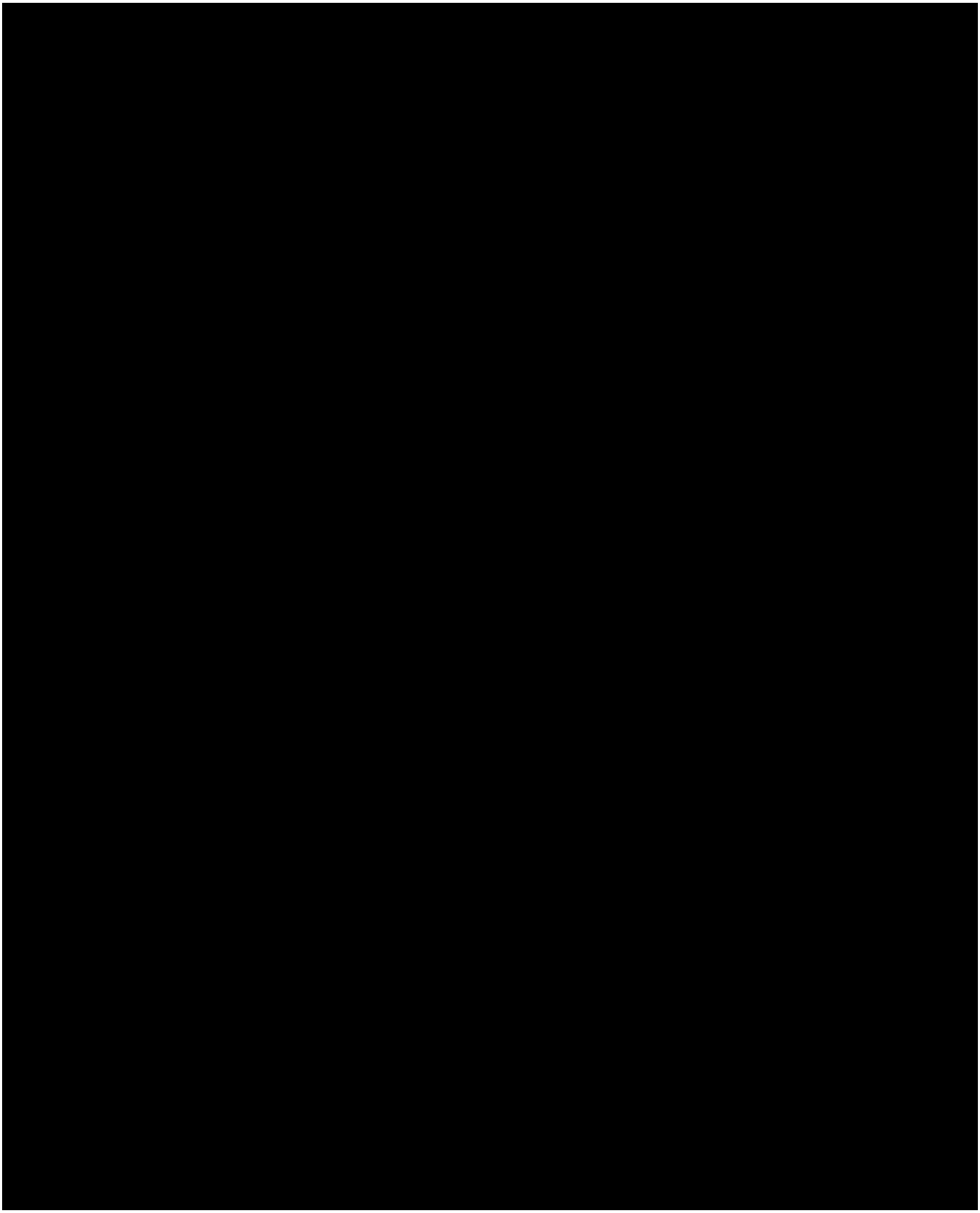
[redacted]

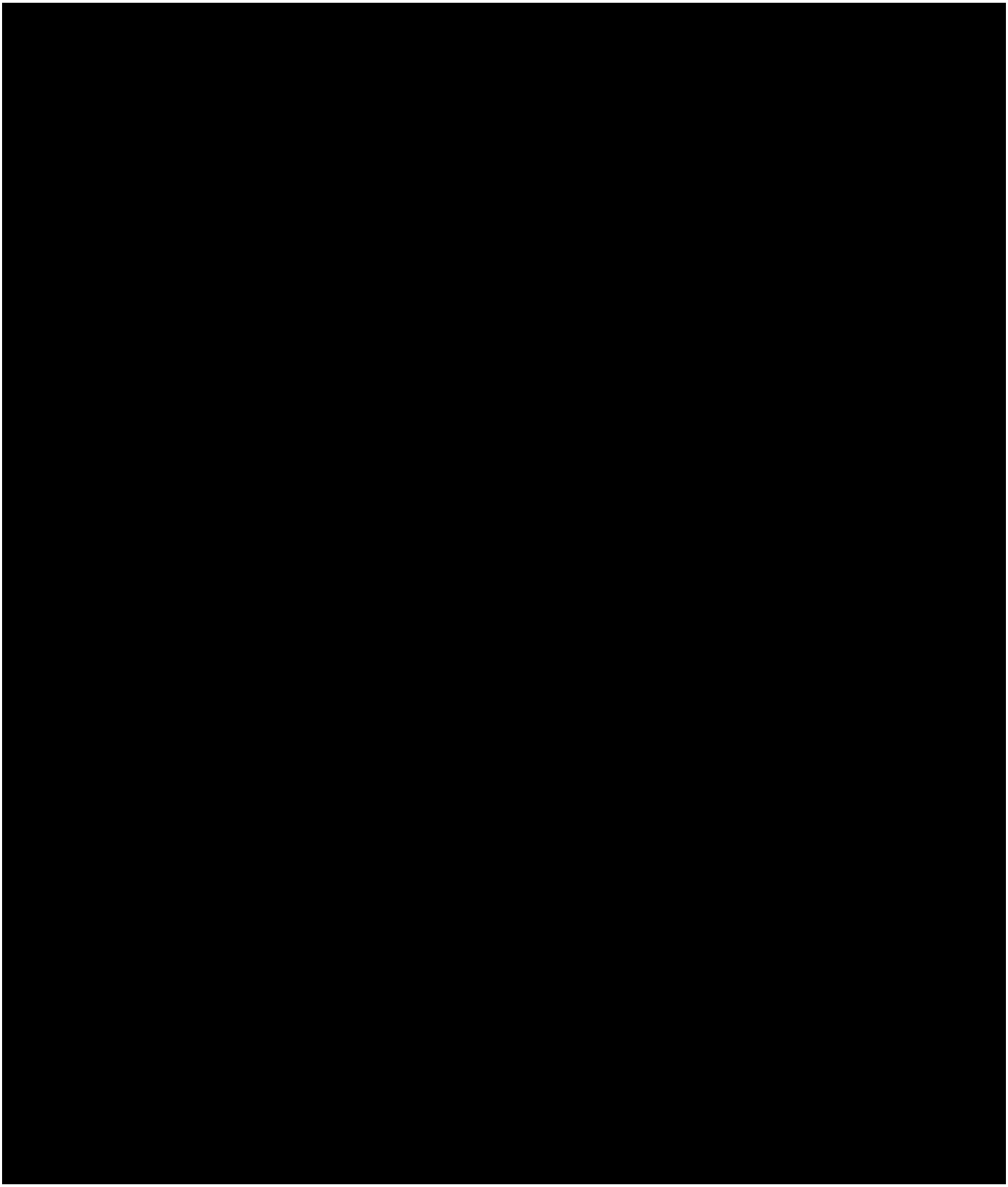
[redacted]

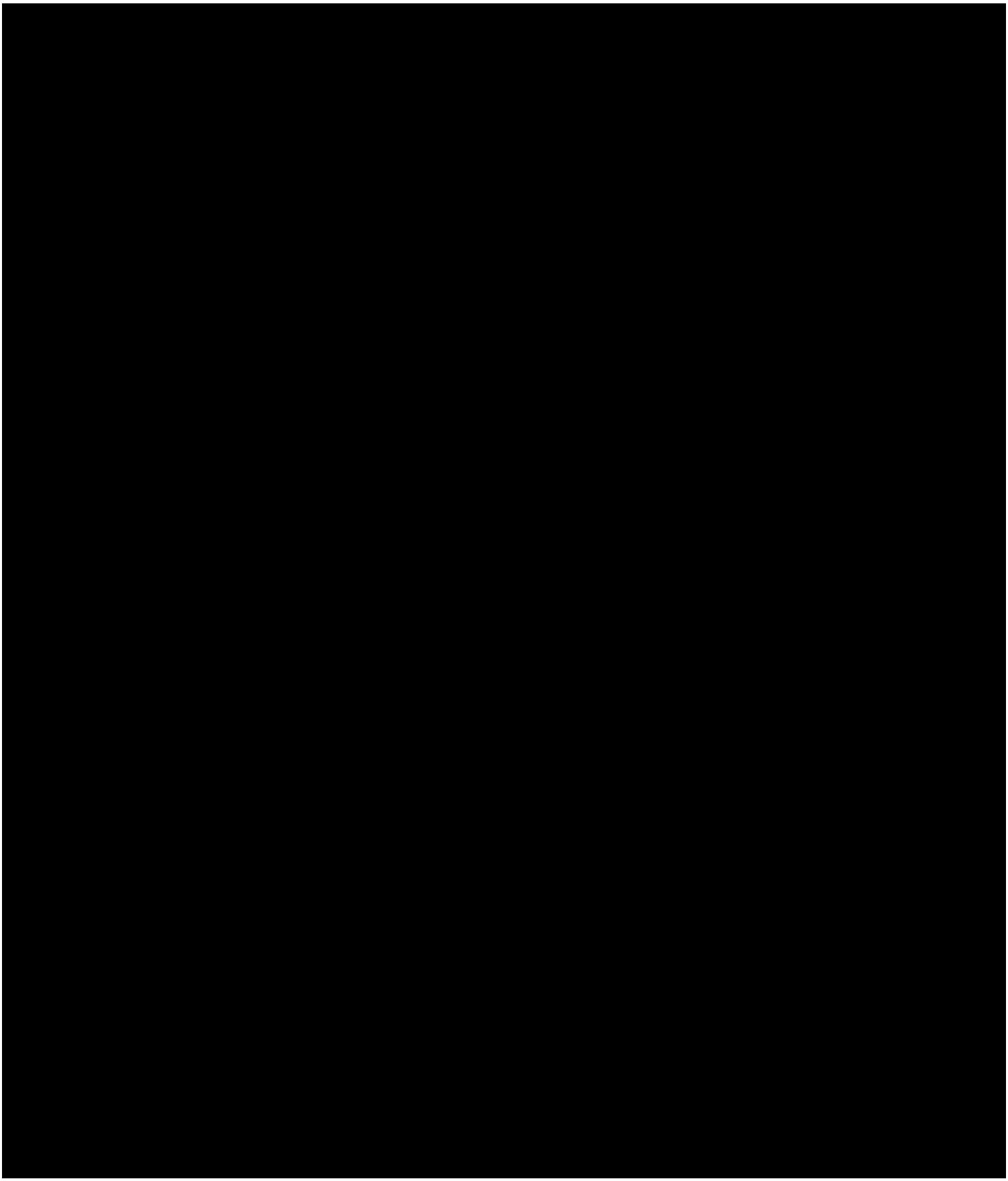
[redacted]

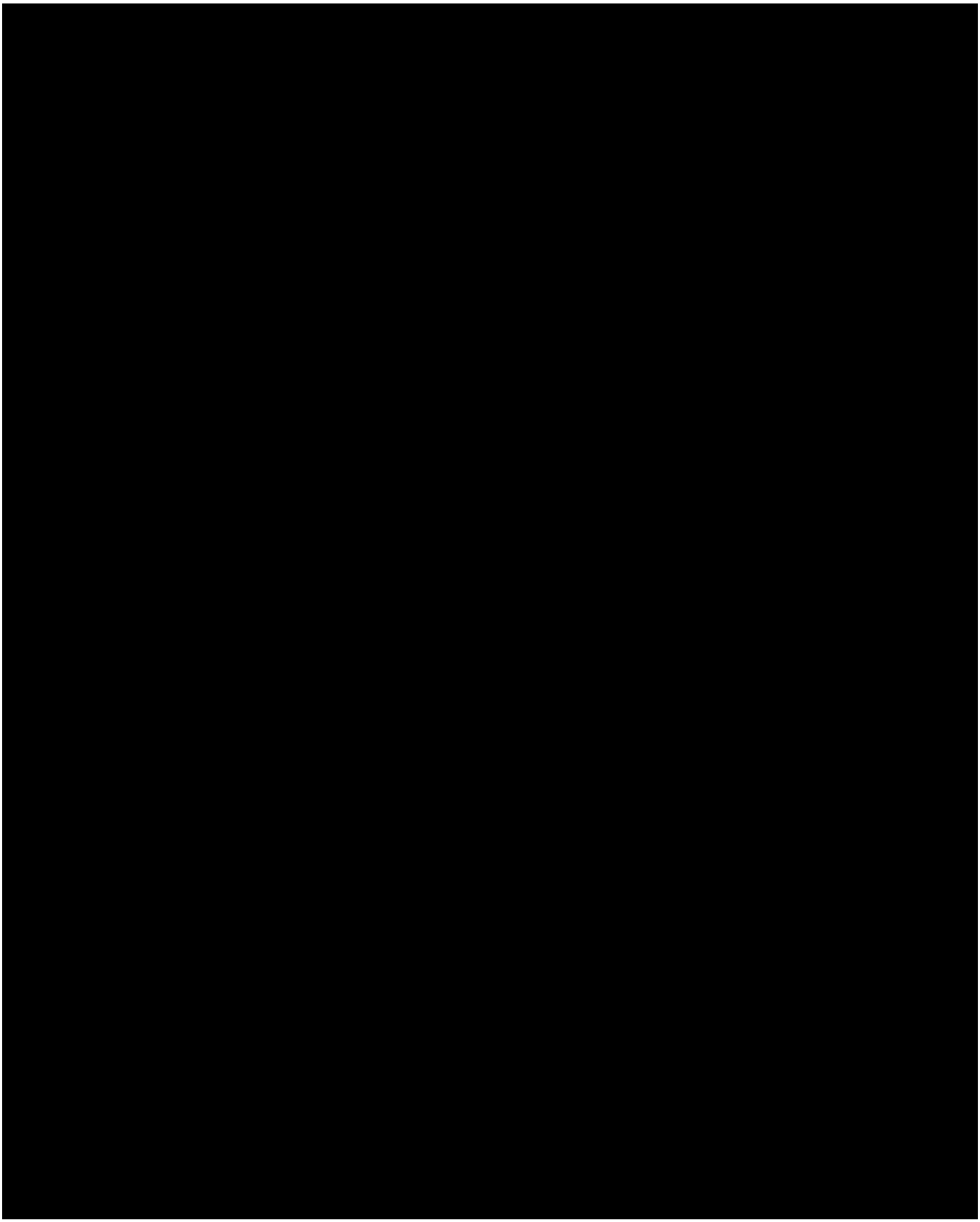












13 STUDY MONITORING

The Monitor is appointed by MED-EL and is responsible for monitoring this investigation in accordance with the relevant MED-EL SOPs (SOPs), the principles of ISO 14155:2011, the most recent version of the Declaration of Helsinki and all national and international requirements.

A detailed description of the Monitoring activities can be found in the “Monitoring Plan”.

14 DATA HANDLING AND RECORD KEEPING

The study site is responsible to ensure the accuracy, completeness, legibility, and timeliness of the data reported. All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data. Dark ink (preferentially BLUE INK) is required to ensure clarity of reproduced copies. When making changes or corrections, cross out the original entry with a single line, and initial (or sign) and date the change. DO NOT ERASE, WRITE OVER, OR USE CORRECTION FLUID OR TAPE ON THE ORIGINAL.

14.1 Source Data

The participating study centres will store all source data acquired during the study according to routine procedures. If source data is recorded directly on a CRF, this shall be stated.

14.2 Study Records

During the study, the Investigator will maintain complete and accurate documentation of the study procedures, including medical records, records detailing the progress of the study for each subject, test reports, CRFs, signed ICFs, correspondence with the relevant IEC(s) and NCA(s), the Monitor, the Clinical Support Staff, the Clinical Research Manager or MED-EL in general, serious adverse reports and information regarding subject screening, enrolment, discontinuation, and completion of the study.

Data on subjects collected on CRFs will be documented in an anonymous fashion in such a way that a subject will not be identifiable from the information recorded on the CRF. The confidentiality of those documents, which could identify the subjects, shall respect the subjects' privacy and the standard of confidentiality in accordance with the applicable regulatory requirements. The study site will maintain a subject identification code list.

14.3 Case Report Forms (CRFs)

In compliance with the principles of ISO 14155:2011, the Declaration of Helsinki as amended in Fortaleza (2013) and all national and international requirements, the medical records, medical notes and other source documents have to be clearly marked and permit easy identification of participation by an individual in the specified clinical trial.

All study data will be documented by the Investigator directly into the CRF provided by MED-EL.

The PI may designate authority to complete the CRF to appropriately qualified staff. This has to be documented by completing and signing the "Delegation of Responsibility Log". At study closure, if not present already, hardcopies of the finalized CRFs are generated and signed to

confirm the accuracy and completeness of all the data. A full audit trail of all changes to CRF data shall be available.

14.4 Record Retention

Upon completion of the study, the Investigator shall maintain all study records in a safe and secure location.

All study related documents shall be kept by the Investigator for the maximum period of time required by local regulations. No study document shall be destroyed without prior written agreement between the Investigator and MED-EL. Should the Investigator decide to assign the study documents to another party, or move them to another location, MED-EL and the Coordinating Investigator (if applicable) shall be notified.

The Investigator is responsible for archiving all source documents and the study documentation (including copies of the CRFs) as required by national laws and regulations. The Investigator will retain all study records according to the Clinical Investigation Agreement.

If the Investigator is withdrawn or decides to leave the study (for any reason), the records shall be transferred to another person whose designation has been mutually agreed. The written notification of this transfer shall be sent to MED-EL and the Coordinating Investigator (if applicable).

All data archived during the clinical study will be completely accessible for medical purposes to the staff of the associated study centres. The publication policy concerning the results of the clinical study is described in section 19.

14.5 Data Management

A detailed description of the data management designed for this study, including methods and data cleaning can be found in the “Data Management Plan”.

- Quality Control and Quality Assurance

Quality assurance and quality control principles in full accordance with ISO 13485 will be applied to all the processes of this clinical study.

MED-EL will implement and maintain written clinical quality procedures to ensure that the clinical investigation is designed, conducted and monitored, and that data are generated, documented, recorded and reported in compliance with the relevant MED-EL SOPs, the principles of ISO 14155:2011, the Declaration of Helsinki as amended in Fortaleza (2013) and all national and international requirements.

Furthermore, MED-EL will maintain records to document the compliance of all parties involved in this clinical study and ensure that the auditing requirements in accordance with

the relevant MED-EL SOPs and ISO 14155:2011 are met. Significant exceptions will be documented and justify as appropriate.

15 STATISTICAL ANALYSIS

15.1 Statistical Analysis Methods

Descriptive statistics will be calculated to report patients' baseline characteristics (e.g. age, gender) and to describe test outcomes. The mean, standard deviation (SD) and/or median with range (minimum and maximum) will be used to describe quantitative data; absolute and relative frequencies will be used to present qualitative data.

Inferential statistics: Data will be analysed based on the objectives and the formulated hypotheses described in sections 5 and 6. To choose whether a parametric or a non-parametric test shall be applied, the Kolmogorov-Smirnov test and a graphical examination will be used before to check the data distribution.

15.1.1 **Primary Objectives**

A difference between SONNET2 in a OLSA in noise speech test (S0N0) and the SONNET shorter than 2 dB SNR (∆) is not seen as a clinically relevant difference (Hey et al., 2014; Nogueira et al., 2016). A statistical significant difference will be examined applying Student's t-test or Wilcoxon signed-rank test.

15.1.2 **Secondary Objectives**

15.1.2.1 ***Speech performance***

Speech performance of the SONNET2 will be assessed with different combinations of frontend processing features under different environmental test conditions using the following tests:

- Freiburg Monosyllabic test in quiet; speech presented from the front
- Oldenburg Sentence Test in noise in the set-ups:
  - ❖ S0N0
  - ❖ S0, N0, ±N45, ± N135

A statistical significant difference will be examined applying Student's t-test or Wilcoxon signed-rank test.

15.1.2.2 ***Subjective feedback***

- Quality of hearing in real life

- ❖ HISQUI19
- ❖ SSQ12

- Device handling
  - ❖ Data Logging
  - ❖ APSQ

- Sound Quality
  - ❖ ACALES
  - ❖ SONNET 2questionnaire

The secondary objectives are exploratory and will be analysed descriptively. If applicable (i.e. if total score and/or subscales are existing), a statistical significant difference between the different test intervals will be examined applying Student's t-test or Wilcoxon signed-rank test.

15.2 Plan for Interim Analyses

No interim analysis is planned.

15.3 Handling of Missing Data

Missing data will be treated as missing values.

15.4 Reporting Conventions

Statistical significance is set to $p \leq 0.05$. The corresponding confidence level is 95%.

15.5 Presentation of Data

The results of the data analyses may be presented in tables and/or displayed in graphs depending on their nature and meaning.

15.6 Computer Systems and Packages

IBM SPSS Statistics 24 (IBM, Armonik, New York) and STATISTICA 13 will be used for the analyses. Graphs will be created in Microsoft Office Excel (http//www.microsoft.com).

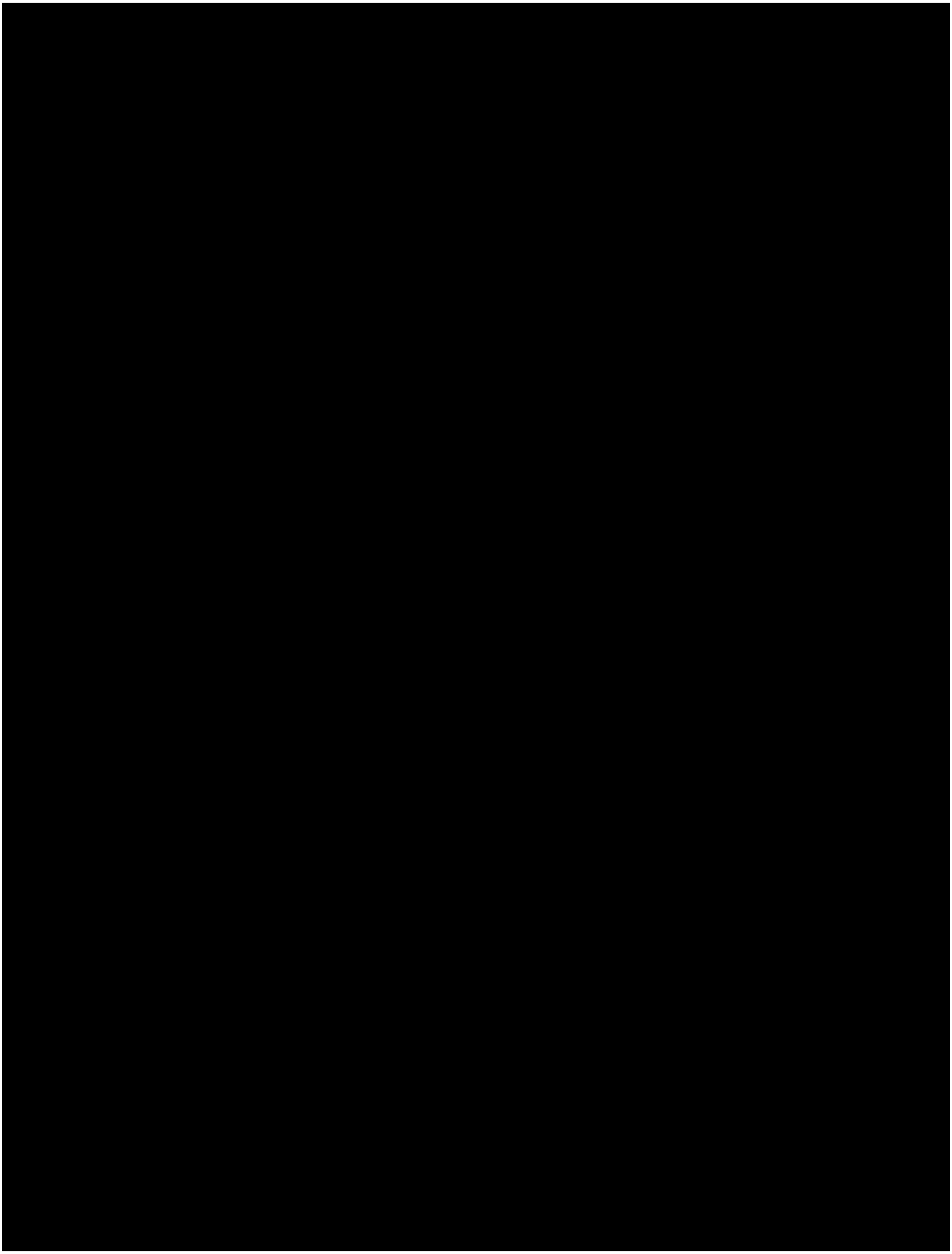
A more detailed description of the statistical analysis planned for this study, including methods and sampling are described in the "Statistical Analysis Plan".

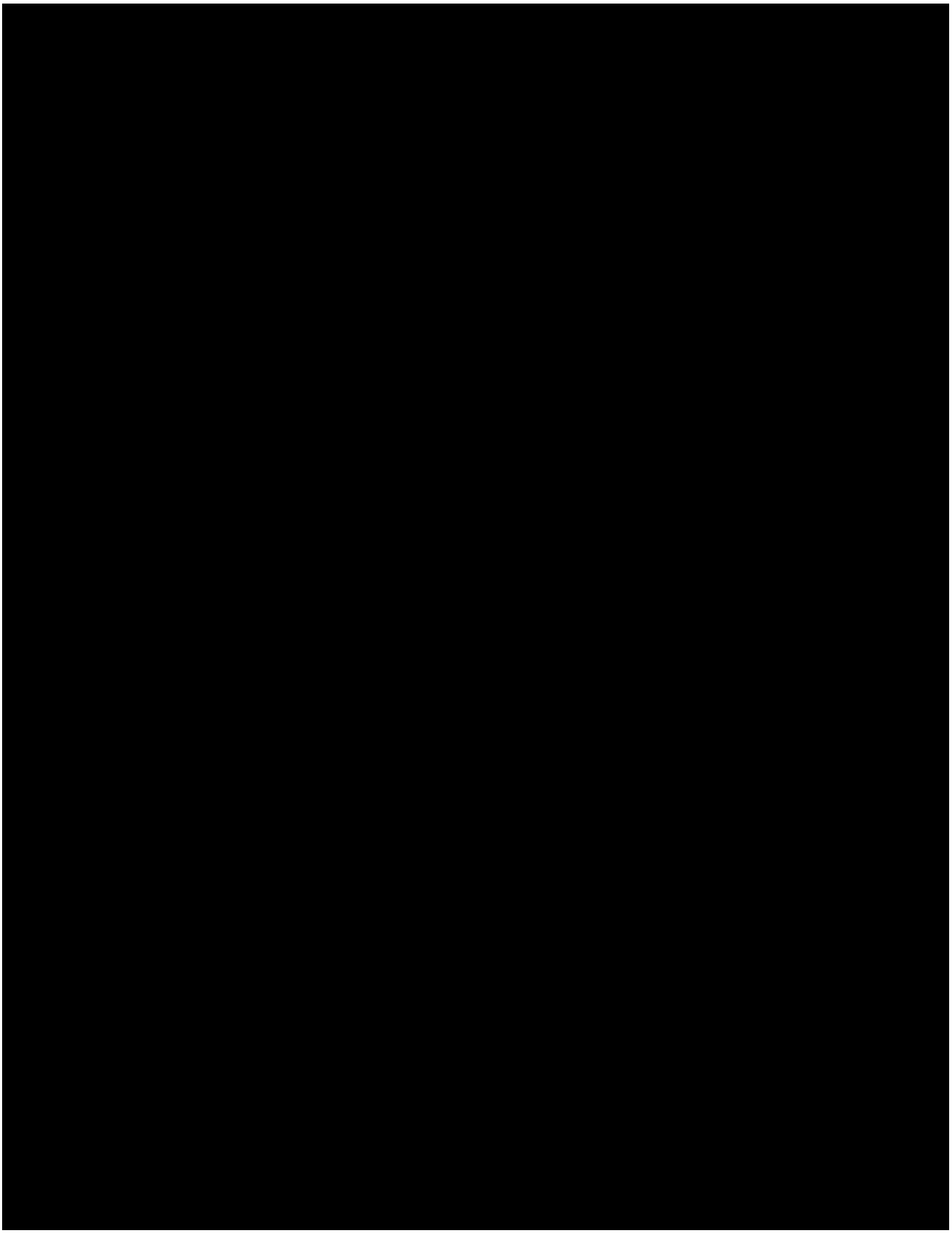
16 STUDY CLOSE-OUT

The study close-out comprises the following activities. Ensuring that:

- All essential documents are complete and up-to-date
- All Case Report Forms are completed
- All outstanding queries are resolved
- The current status of all on-going Adverse Events is documented
- Arrangements are made for archiving and record retention
- All materials are appropriately disposed of
- Notification to the relevant Independent Ethics Committee (IECs)

The Monitor will notify the Investigator when the entire study is complete. A letter to the Investigator will be sent notifying them of a “closed status” following completion of all requirements of the Study Plan and regulatory bodies.





18 ETHICS AND PROTECTION OF HUMAN SUBJECTS

18.1 Ethical and Regulatory Considerations

The Coordinating Investigator (if applicable) and MED-EL or their designees will submit the protocol for review by the relevant IEC(s) and NCA(s), according to national legislation, and agree to provide the relevant IEC(s) and NCA(s) with all appropriate materials. No subject will be admitted to this study until appropriate relevant IEC(s) and NCA(s) approval of the protocol has been received and the Investigator has obtained the signed and dated ICF. Appropriate reports on the progress of this study will be made to the relevant IEC(s) and NCA(s) by MED-EL and the Coordinating Investigator (if applicable), in accordance with applicable local regulations and in agreement with the policy established by the relevant IEC(s) and NCA(s) as well as with MED-EL relevant SOPs. The Coordinating Investigator (if applicable) and MED-EL will inform the relevant IEC(s) and NCA(s), if appropriate, of subsequent protocol amendments and any AE occurring during the study as described in section 12. The Investigator shall ensure that the study will be carried out in compliance with the protocol, the principles of ISO 14155:2011, the Declaration of Helsinki as amended in Fortaleza (2013) and all national and international requirements.

18.2 Informed Consent Process

Acquisition of consent is the step by which subjects are enrolled into the study. No study specific procedures shall be performed unless the information and consent process was conducted and fully documented by signing and dating the ICF. Only the PI or study personnel expressly acting on behalf of the PI (as reported in the relevant Delegation of Responsibilities Log) may administer consent. The person conducting the information conversation shall speak the native language of the subject. This person will thoroughly explain to the subject the purpose and methods of the study, the background and the present knowledge of the study treatment with special reference to known activity and side effects. The person conducting the information conversation shall also ensure that the following requirements are fulfilled:

- The subject shall be provided with the ICF consistent with the protocol version used and approved by the relevant IEC(s)
- The subject shall be thoroughly informed about risks, contraindications and expected benefit of the investigational treatment
- The subject will be given sufficient time and opportunity to inquire about the details of the trial and to discuss and decide on their participation in the study with the Investigator.
- The written consent shall be obtained before the enrolment in the study.

- The subject and the Investigator with whom they discussed the ICF will sign and date the ICF. A copy of the signed ICF will be kept by the subject and the original filed in the ISF unless otherwise agreed.
- The subject may refuse treatment either before or at any time during the study. Refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled. Similarly, the Investigator and/or MED-EL will be free to withdraw the subject at any time for safety or administrative reasons.
- Any other requirements necessary for the protection of the human rights of the subject will also be explained, according to the principles of ISO 14155:2011, the Declaration of Helsinki as amended in Fortaleza (2013) and all national and international requirements.
- The subject shall be given information about whom to contact for answers to questions pertinent to the research and the research subject's rights, and whom to contact in the event of a research-related injury.
- If the ICF is updated to include protocol changes, all the subjects affected by such changes shall sign and date a new ICF mirroring such changes, with the following exceptions:
  - ❖ The subject is clearly not affected by the changes
  - ❖ The changes do not have any clinical and/or ethical relevance (reformulation of sentences maintaining the same meaning, spelling, etc.)
  - ❖ The subject has already completed the study

The above requirements shall also apply with respect to informed consent obtained from a subject's legally authorized representative.

18.2.1 Subjects needing legally authorized representatives

Informed consent may be given by the legally authorized representative only if a subject is unable to make the decision to participate in a clinical investigation (e.g. infant, child and juvenile, seriously ill or unconscious subject, mentally ill person, mentally handicapped person). In such cases, the subject shall also be informed about the clinical investigation within his/her ability to understand.

18.2.2 Subjects unable to read or write

Informed consent shall be obtained through a supervised oral process if a subject or legally authorized representative is unable to read or write. An independent witness shall be present throughout the process. The written informed consent form and any other information shall be read aloud and explained to the prospective subject or his/her legally authorized representative and, whenever possible, either shall sign and personally date the informed consent form. The witness also signs and personally dates the informed consent form

attesting that the information was accurately explained and that informed consent was freely given.

18.3 Subject Confidentiality

The study protocol, documentation, data, and all other information generated will be kept in strict confidence. No information concerning the study or the data will be released to any unauthorized third party, without prior written approval of MED-EL.

The Investigator will guarantee that all persons involved will respect the confidentiality of any information concerning the investigation subjects.

All parties involved in a clinical investigation will maintain the strict confidentiality to assure the protection of privacy of a subject participating in the clinical investigation. Likewise, the appropriate measures shall be taken to avoid the access of non-authorized persons to the trial data. The processing of the personal data on the subjects taking part in this trial, shall comply with the local law on privacy.

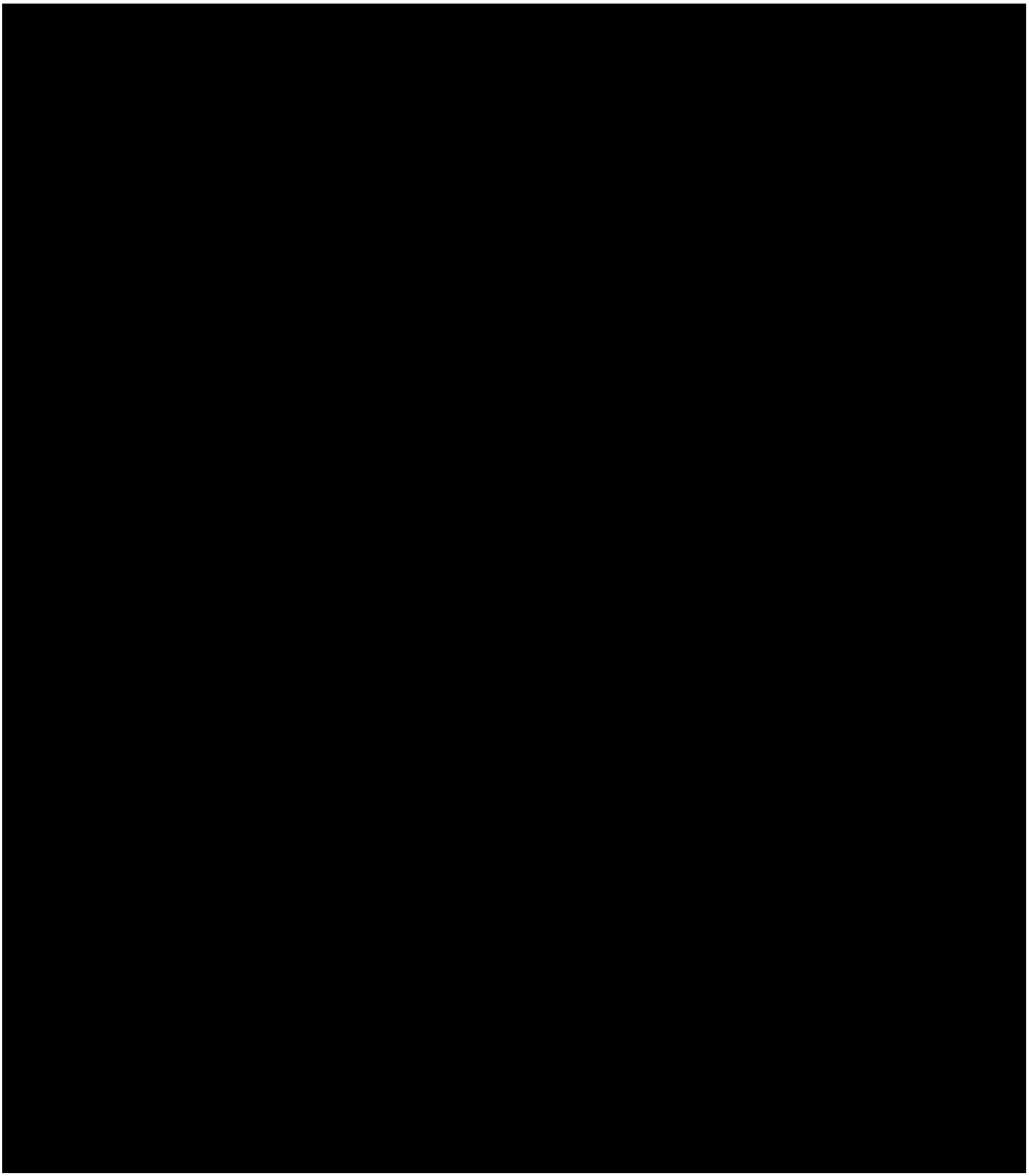
All information provided to the Investigator by MED-EL will be kept strictly confidential and confined to the clinical personnel involved in conducting the trial. Such personnel will be informed of the confidential nature of the information. It is recognized that this information may be communicated in confidence to the relevant IEC(s). In addition, no reports or information about the trial or its progress will be provided to anyone not involved in the trial other than MED-EL or in confidence to the relevant IEC(s), except if required by applicable law, regulation or court order.

In the event the Investigator is requested or required by applicable law, regulation or court order to disclose any confidential information contained in this protocol, such Investigator shall give prompt notice to MED-EL, so that MED-EL may seek a protective order or take other measures reasonable in light of the circumstances.

All data provided to MED-EL will be identified by a unique subject ID, thereby ensuring that the subject's identity remains unknown. The subjects should be informed in writing, that their data will be stored and analysed in a computer, with confidentiality maintained in accordance with local regulations.

The subjects should also be informed in the form of a written documentation that authorized representatives of MED-EL and/or regulatory authorities may require access to those parts of the site records (relevant to the study), including medical history, for data verification.

The Investigator is responsible for keeping a subject identification list of all subjects screened and enrolled.



20 REFERENCES

Amann, E., & Anderson, I. (2014). Development and validation of a questionnaire for hearing implant users to self-assess their auditory abilities in everyday communication situations: the Hearing Implant Sound Quality Index (HISQUI19). *Acta Otolaryngol, 134*(9), 915-923. doi:10.3109/00016489.2014.909604

Cacace, A. T., Kleine, E. d., Holt, A. G., & Dijk, P. v. (2016). Scientific foundations of audiology : perspectives from physics, biology, modeling, and medicine.

Chow, S.-C., Shao, J., & Wang, H. (2008). *Sample size calculations in clinical research*. Boca Raton: Chapman & Hall/CRC.

Finke, M., Strauss-Schier, A., Kludt, E., Buchner, A., & Illg, A. (2017). Speech intelligibility and subjective benefit in single-sided deaf adults after cochlear implantation. *Hear Res, 348*, 112-119. doi:10.1016/j.heares.2017.03.002

Fu, Q. J., & Shannon, R. V. (1999). Effect of acoustic dynamic range on phoneme recognition in quiet and noise by cochlear implant users. *J Acoust Soc Am, 106*(6), L65-70.

Hagen, R., Stark, T., Radeloff, A., Anderson, I., Nopp, P., Aschbacher, E., . . . Rak, K. (In submission). Microphone directionality and wind noise reduction enhance speech perception in users of the MED-EL SONNET audio processor. *Ear and Hearing*.

Hahlbrock, K.-H., & Zöllner, F. (1970). *Sprachaudiometrie*: Thieme.

Hahlbrock, K. H. (1970). *Sprachaudiometrie: Grundlagen und praktische Anwendung einer Sprachaudiometrie für das deutsche Sprachgebiet*: Thieme Georg Verlag.

Hey, M., Hocke, T., Hedderich, J., & Müller-Deile, J. (2014). Investigation of a matrix sentence test in noise: Reproducibility and discrimination function in cochlear implant patients. *International Journal of Audiology, 53*(12), 895-902. doi:10.3109/14992027.2014.938368

Krueger, M., & Schulte, M. (2017). Development of an adaptive scaling method for subjective listening effort. *The Journal of the Acoustical Society of America, 141*(6), 4680-4693. doi:10.1121/1.4986938

Nelson, P. B., Jin, S. H., Carney, A. E., & Nelson, D. A. (2003). Understanding speech in modulated interference: cochlear implant users and normal-hearing listeners. *J Acoust Soc Am, 113*(2), 961-968.

Noble, W., Jensen, N. S., Naylor, G., Bhullar, N., & Akeroyd, M. A. (2013). A short form of the Speech, Spatial and Qualities of Hearing scale suitable for clinical use: the SSQ12. *Int J Audiol, 52*(6), 409-412. doi:10.3109/14992027.2013.781278

Nogueira, W., Rode, T., & Buchner, A. (2016). Spectral contrast enhancement improves speech intelligibility in noise for cochlear implants. *J Acoust Soc Am, 139*(2), 728-739. doi:10.1121/1.4939896

Schafer, E. C., & Thibodeau, L. M. (2004). Speech recognition abilities of adults using cochlear implants with FM systems. *J Am Acad Audiol, 15*(10), 678-691.

Stickney, G. S., Zeng, F. G., Litovsky, R., & Assmann, P. (2004). Cochlear implant speech recognition with speech maskers. *J Acoust Soc Am, 116*(2), 1081-1091.

Wagener, K., Brand, T., & Kollmeier, B. (1999a). Development and evaluation of a German sentence test part II: Optimization of the Oldenburg sentence test. *Zeitschrift Fur Audiologie, 38*, 44-56.

Wagener, K., Brand, T., & Kollmeier, B. (1999b). Development and evaluation of a German sentence test part III: Evaluation of the Oldenburg sentence test. *Zeitschrift Fur Audiologie, 38*, 86-95.

Wagener, K., Kühnel, V., & Kollmeier, B. (1999). Development and evaluation of a German sentence test I: Design of the Oldenburg sentence test. *Zeitschrift Fur Audiologie, 38*, 4-15.

Wolfe, J., & Schafer, E. C. (2008). Optimizing the benefit of sound processors coupled to personal FM systems. *J Am Acad Audiol, 19*(8), 585-594.

Zeng, F. G. (2004). Trends in cochlear implants. *Trends Amplif, 8*(1), 1-34. doi:10.1177/108471380400800102

Zeng, F. G., & Galvin, J. J., 3rd. (1999). Amplitude mapping and phoneme recognition in cochlear implant listeners. *Ear Hear, 20*(1), 60-74.

Zeng, F. G., Rebscher, S., Harrison, W., Sun, X., & Feng, H. (2008). Cochlear implants: system design, integration, and evaluation. *IEEE Rev Biomed Eng, 1*, 115-142. doi:10.1109/RBME.2008.2008250

21 Appendices

21.1 Appendix 1

User Manual for "SONNET 2 (Me1510) and SONNET 2 EAS (Me1520) audio processors"