CLINICAL INVESTIGATION PLAN (CIP)

Clinical accuracy validation of the medical body composition analyzer seca mBCA 555 in comparison to seca mBCA 515

BCA-21 (clinical investigation code)

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seca gmbh & co. kg
Hammer Steindamm 3-25
22089 Hamburg | Germany
(sponsor)

DECLARATION OF SPONSOR

This Clinical Investigation Plan (CIP) was subject of critical review and has been approved by the sponsor and its representatives. The information it contains is consistent with:

- ⇨ the Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects; last revision Fortaleza, Brazil, October 2013
- ⇨ the DIN EN ISO 14155:2012
- ⇨ Guideline for good clinical practice E6(R1)
- ⇨ the German Medical Device Act, MPKPV (Verordnung über klinische Prüfungen von Medizinprodukte)
- ⇨ §20 German Medical Device Act

The investigator will be supplied with details of any significant or new findings, including AE's, relating to the administration of the medical device.

seca gmbh & co. kg
Hammer Steindamm 3-25
22089 Hamburg | Germany

Hamburg 26.02.2019
place, date

Frederik Vogel
CEO Development & Manufacturing

Hamburg 26.2.2019
place, date

Robert M. Vogel
CEO Sales & Marketing

Hamburg 25.2.2019
place, date

i.V. Björn Jensen
Björn Jensen
R&D, Statistician

DECLARATION OF PRINCIPAL INVESTIGATOR

I confirm that I have read the Clinical Investigation Plan (CIP), Investigator's Brochure (IB), informed consent of the subject, and referenced documents of the CIP entitled:

Clinical Investigation Plan Title:	Clinical accuracy validation of the medical body composition analyzer seca mBCA 555 in comparison to seca mBCA
Clinical Investigation Plan No.:	BCA-21

I agree that the documentation contains all the necessary information to conduct this study. I will conduct this study as outlined herein, in accordance with

- ⇨ the Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects; last revision Fortaleza, Brazil, October 2013
- ⇨ the DIN EN ISO 14155:2012
- ⇨ Guideline for good clinical practice E6(R1)
- ⇨ the German Medical Device Act, MPKPV (Verordnung über klinische Prüfungen von Medizinprodukte)
- ⇨ §20 German Medical Device Act

The study will be started only in the case that a favorable opinion of the responsible Ethical Committee (EC) and a successful request for waiving the authorization of the clinical trial to the Competent Authority (CA) has been obtained.

I will provide all study personnel under my supervision with copies of the CIP and any amendments, and access to all information provided by seca gmbh & co. kg. I will discuss the material with them to ensure that they are fully informed about the medical device and the study.

Institute of Transfusion Medicine
Center for Diagnostics
University Medical Center Hamburg-Eppendorf
Martinistraße 52
20246 Hamburg | Germany

Hamburg, 25.2.2019

place, date

Dr. Sven Peine
Head of Institute

Sponsor:	seca gmbh & co. kg Hammer Steindamm 9-25 22089 Hamburg | Germany
Clinical investigation site:	Institute of Transfusion Medicine Center for Diagnostics University Medical Center Hamburg-Eppendorf Martinistraße 52 20246 Hamburg | Germany
Principal investigator:	Dr. Sven Peine Head of Institute for Transfusion Medicine Center for Diagnostics University Medical Center Hamburg-Eppendorf Martinistraße 52 20246 Hamburg | Germany
Statistics / data management:	Björn Jensen seca gmbh & co. kg Hammer Steindamm 9-25 22089 Hamburg | Germany
Project management / monitoring:	Kristin Klückmann seca gmbh & co. kg Hammer Steindamm 9-25 22089 Hamburg | Germany
Medical Device:	seca medical body composition analyzer seca mbca 515 and 555
Regulatory status:	The seca mbca are non-invasive medical devices class IIa in accordance with rule 10 of the MDD 93/42/EEC Annex IX. While the seca mBCA 515 is CE approved (CE 0123), the mBCA 555 will be applied without CE mark.
Regulatory information:	This Investigation Protocol (CIP) will be conducted in accordance with: - the Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects; last revision Fortaleza, Brazil, October 2013 - the DIN EN ISO 14155:2012 - Guideline for good clinical practice E6(R1) - the German Medical Device Act, MPKPV - §20 German Medical Device Act The study will be started only in the case that a favorable opinion of the responsible Ethical Committee (EC) and the confirmation from the "Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)" that no approval must be granted (exception for approval according to §20 German Medical Device Act) was obtained.

STUDY SYNOPSIS

Title of study:	Clinical accuracy validation of the medical body composition analyzer seca mBCA 555 in comparison to seca mBCA 515
Study code:	BCA-21
Study purpose:	The mBCA 515 was compared to the gold standard methods MRI, DXA, ADP, D2O- and NaBr-dilution in previous clinical investigations (BCA-01, BCA-02, BCA-20) to generate prediction equations for calculating body composition (FFM, SMM, ECW, TBW and VAT) in different populations. Furthermore, normal ranges for body composition were generated based on the previous study BCA-03 conducted at the UKE. The mBCA 555 is a new body composition analyzer measuring bioimpedance in standing position developed by seca. In order to apply prediction equations and normal ranges from previous clinical investigations BCA-01, BCA-02, BCA-03 and BCA-20 to the new mBCA 555 it shall be compared to the mBCA 515.
Objectives:	Primary objective is to test whether the mBCA 515 prediction equations can be applied to the new mBCA 555. If necessary, to proof substantial equivalence, prediction equations should be adjusted for the mBCA 555. Secondary objective is to compare Impedance, phase angle, reactance and resistance for different frequencies in order to clarify if normal ranges for BIVA and phase angle generated with the mBCA 515 need to be adjusted for the new mBCA 555.
Study design:	Population based cross-sectional observational study
Study population:	120 healthy adults
Inclusion criteria:	male and female subjects, 18 years and older, subjects need to be able to sign the informed consent and privacy policy
Exclusion criteria:	acute disease pregnancy intake of diuretics edema diagnosed by inspection and palpation of lower limbs paralysis e.g. after a stroke neurodegenerative diseases e.g. ALS tumors in treatment amputation electronic implants e.g. pacemaker probands who cannot provide an ICF by themselves probands who might be dependent from the sponsor or the investigation site current alcohol abuse active prostheses electronic life-support systems, e.g. artificial heart, artificial lung portable electronic medical devices, e.g. ECG devices or infusion pumps metallic implants

Study conduct:

After measuring body height each subject will undergo 4 mBCA measurements.
Every 2nd subject will be measured in the following order:
1) mBCA 515
2) mBCA 555
3) mBCA 515
4) mBCA 555

The other subjects will be measured in reverse order:
1) mBCA 555
2) mBCA 515
3) mBCA 555
4) mBCA 515

Study statistics:

The aim of the study is a comparison of the investigational device mBCA 5555 with the predicate device seca mBCA 515. It shall be tested, if formulas for the mBCA 515 can be used for the investigational device. Formula corrections shall be generated if they are required.

The null hypothesis (H0) is: Impedances measured with the mBCA 555 are the same as when measured with the mBCA 515. The alternative hypothesis (H1) is therefore: Impedances measured on both devices differ for the same subject.

The α-level for type I error for wrongly accepting H1 while H0 is valid is set to 5%. The β-level for type II error for wrongly staying with H0 while H1 is valid is set to 20%. The power 1-β is therefore 80% with a significance level of 5% using a two sided test statistic. These values apply to each individual variable. The total error rate therefore is larger.

For the calculation of the effect that shall be detected in the study, error propagation was calculated. Formulas for phase angle, ECW, TBW, FFM, SMM (segmental and total) and VAT were taken into account. It was calculated how much variation of impedances is needed to gain an error of 0.1 SEE. (For phase angle the accuracy of 0.5° was used instead of the SEE.)

For the estimation of the standard deviation of measurements, results of an internal comparison with the mBCA 515 were used. The upper limit of the 95% confidence interval of the standard deviation was used.

The calculation of sample size was performed according to „Statistik und Forschungsmethoden", 4th edition, Eid et al., pages 239 – 240.

The sample size was taken from that variable that required the highest number of samples. The sample size is 113 subjects.

ABBREVIATIONS AND DEFINITION OF TERMS

AE	Adverse Event
BCA	Body Composition Analysis
BfArM	Federal Institute for Drugs and Medical Devices
BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index
CI	Clinical Investigation, synonym term is "clinical study" or "study"
CIP	Clinical Investigation Plan, synonym term is "study protocol" or "protocol"
CRF	Case Report Form
DIN	German Industrial Norm
ECW	Extra Cellular Water
FM	Fat Mass
FFM	Fat Free Mass
ICF	Informed Consent Form
ICW	Intra Cellular Water
mBCA	medical Body Composition Analyzer
MDD	Medical Device Directive
MPKPV	Medical Device Clinical Investigation Regulation
R	Resistance
SAE	Serious Adverse Events
SMM	Skeletal Muscle Mass
TBW	Total Body Water
VAT	Visceral Adipose Tissue
Xc	Reactance
Z	Impedance

CIP REVISION HISTORY

Revision number	Revision date	Explanation	Comment
1.0	07-12-18	First revision	

CONTENT

1. GENERAL INFORMATION

1.1 Bioelectrical Impedance Analysis

The use of bioelectrical impedance analysis (BIA) is widespread both in healthy subjects and patients. BIA allows the determination of the fat-free mass (FFM), skeletal muscle mass (SMM), fat mass (FM), extracellular water (ECW) and total body water (TBW) when using appropriate population, age or pathology-specific BIA equations and established procedures. BIA equations are based on validation studies where BIA is compared with reference methods such as Air Displacement Plethysmography (ADP), Dual-Energy X-Ray Absorptiometry (DXA), Magnetic Resonance Imaging (MRI) and isotope dilution.[1]

1.2 Study Rationale

The predicate device seca mBCA 515 was compared to the gold standard methods MRI, DXA, ADP, D2O- and NaBr-dilution in previous clinical investigations in Kiel (Germany) and New York City (USA) to generate prediction equations for calculating body composition (FFM, SMM, ECW, TBW and VAT) in different populations. Furthermore, normal ranges for body composition were generated in a previous study conducted at the UKE. [2,3,4]

The mBCA 555 is a new body composition analyzer measuring bioimpedance in standing position developed by seca.

In order to apply prediction equations and normal ranges from previous clinical investigations to the new mBCA 555 it shall be compared to the mBCA 515 in a healthy population.

1.3 Regulatory Information

The seca mbca are non-invasive medical devices class IIa in accordance with rule 10 of the MDD 93/42/EEC Annex IX. While the seca mBCA 515 is CE approved (CE 0123), the mBCA 555 will be applied without CE mark.

References

[1] Kyle G, Bosaeus I, De Lorenzo AD, Deurenberg P, Elia M, Gomez JM, Lilienthal heitmann B, Kent-Smith L, Melchior JC, Pirlich M, Scharfetter H, Schols AMWJ, Pichard C. ESPEN Guidelines. Bioelectrical impedance analysis – part I: review of principles and methods. Clin Nutr 2004; 23:1226-43.

[2] Bosy-Westphal A. et al., "Quantification of whole-body and segmental skeletal muscle mass using phase-sensitive 8-electrode medical bioelectrical impedance devices", Eur J Clin Nutr. 2017 Mar 22. doi:10.1038/ejcn.2017.27

[3] A. Bosy-Westphal et al., "What makes a BIA equation unique? Validity of eight-electrode multifrequency BIA to estimate body composition in a healthy adult population", European Journal of Clinical Nutrition (2013) 67, S14-S21; doi:10.1038/ejcn.2012.160

[4] S. Peine et al., "Generation of normal ranges for measures of body composition in adults based on bioelectrical impedance analysis using the seca mBCA", International Journal of Body Composition Research 2013 Vol. 11 No. 3 & 4: 67–76

This Investigation Protocol (CIP) will be conducted in accordance with:

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- the DIN EN ISO 14155:2012
- Guideline for good clinical practice E6(R1)
- the German Medical Device Act, MPKPV
- §20 German Medical Device Act

The study will be started only in the case that a favorable opinion of the responsible Ethical Committee (EC) and the confirmation from the "Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)" that no approval must be granted (exception for approval according to §20 German Medical Device Act) was obtained.

1.4 Study Objectives

Primary objective is to test whether the mBCA 515 prediction equations can be applied to the new mBCA 555. If necessary, to proof substantial equivalence, prediction equations should be adjusted for the mBCA 555.

Secondary objective is to compare Impedance, phase angle, reactance and resistance for different frequencies in order to clarify if normal ranges for BIVA and phase angle generated with the mBCA 515 need to be adjusted for the new mBCA 555.

1.5 Study Design

The study BCA-21 is a cross-sectional observational study.

1.6 Study Schedule

As soon as the study BCA-21 is approved by the local ethical committee of the Ärztekammer Hamburg and the BfArm the subject recruitment will start. The measurement period is estimated with 3 months. The measurement duration per subject is 25 minutes.

1.7 Requirements on study procedure

Please refer to chapter 4. Study procedure in this document.

1.8 Requirements on study population

Only subjects who meet the following inclusion and exclusion criteria shall be included in the study BCA-21:

Inclusion criteria:

- male and female subjects 18 years and older,
- subjects need to be able to sign the informed consent form

Exclusion criteria:

- acute disease
- intake of diuretics
- edema diagnosed by inspection and palpation of lower limbs
- paralysis e.g. after a stroke
- neurodegenerative diseases e.g. ALS

- tumors in treatment
- amputation
- electronic implants e.g. pacemaker
- probands who cannot provide an ICF by themselves
- probands who might be dependent from the sponsor or the investigation site
- current alcohol abuse
- active prostheses
- electronic life-support systems, e.g. artificial heart, artificial lung
- portable electronic medical devices, e.g. ECG devices or infusion pumps
- metallic implants

Subjects are recruited at the blood donor service of the Institute of Transfusion Medicine. All subjects need to be suitable for blood donation according to "Hämotherapie-Richtlinien nach §§ 12 a und 18 TFG", chapter 2.1.4 "Untersuchung zur Eignung als Spender und zur Feststellung der Spendetauglichkeit". Blood donors are considered to be healthy. Blood donation does not have happened before examination.

1.9 Subject Discontinuation Criteria

All subjects have the right to withdraw consent without prejudice at any time during the study. If a subject withdraws consent, the investigator should make a reasonable effort to determine the cause for withdrawal of consent. For these subjects, as well as for subjects who require permanent discontinuation from examination with the medical device, the investigator should make a reasonable effort to complete all required study procedures. All information should be documented in the subject's source data documents and on the Case Report Form (CRF). A subject who discontinues treatment will not be replaced. The subject's participation in this study should be permanently discontinued as a result of:

- formal withdrawal of informed consent
- investigator concludes that it is in the subject's best interest to discontinue study procedures
- presence of other medical conditions that prohibit continuation of study procedures
- subject is willingly or inadvertently non-compliant to any of the CIP procedures in the opinion of the investigator

1.10 Study Discontinuation Criteria

Study is discontinued only if irreversible failure of devices for measurement of body composition cannot be compensated.

2. INVESTIGATIONAL DEVICES

The seca medical Body Composition Analyzers (mBCA) 555 and 515 are mainly used in hospitals, medical practices and inpatient care facilities.

The functions weighing and bioimpedance measurement support qualified users in the assessment of the subject's health status.
The seca mBCA are no diagnostic devices. To make an accurate diagnosis, in addition to the results of the seca mBCA, targeted examinations must be ordered by the physician and their results taken into account.

In order to analyse the bioimpedance measurement the corresponding seca application software is needed.

The software records weight, height and bioelectric impedance measurements and derivable parameters, e.g. fat-free mass (FFM), for automatic calculation. The results are displayed graphically and assist the attending physician with the following medical issues:

- documentation of weight changes
- documentation of body composition and its changes
- documentation of the nutrition status and its changes
- documentation of the fluid status and its changes
- documentation of therapy progress e.g. in the framework of a multimodal nutrition and exercise therapy

2.1 Predicate device: mBCA 515

Figure 1: mBCA 515

Technical Data

General:

- Dimensions (W×H×D): 976 × 1,251 × 828 mm
- Display type: 8.4" touch-screen display, can be swiveled 180° to the left and right
- Power supply: Power adapter
- Voltage: 100 V – 240 V
- Interfaces: seca 360° wireless, USB 2.0, Ethernet
- Microsoft® Windows® compatible printer via seca 115 PC software
- Medical device class IIa
- CE approved

Bioelectrical Impedance Analysis:

- Measurement method: 8-point Bioelectrical Impedance Analysis
- Type of electrode: Stainless steel, six pairs of hand electrodes, two pairs of foot electrodes
- Measurement frequencies: 1; 1.5; 2; 3; 5; 7.5; 10; 15; 20; 30; 50; 75; 100; 150; 200; 300; 500; 750; 1,000 kHz
- Measurements: Impedance (Z), Resistance (R), Reactance (Xc), Phase angle (φ)
- Measurement range Impedance: 10 Ω to 1,000 Ω
- Measurement segments: Right arm, left arm, right leg, left leg, right half of body, left half of body, torso
- Measurement current: 100 µA
- Measurement time: max. 90 seconds for 19 frequencies

The seca mBCA 515 has an integrated calibrated scale with a maximum load of 300kg. More information about the technical data for the scale and technical modifications can be found at the instruction for use for doctors and assistants at chapter 13.

PC software seca analytics 115:
The device mBCA 515 does not have "on-board" subject or user management. To manage subject files and user accounts, the device must be connected to a PC on which the seca 115 PC software is installed. Subject files can be created directly on the device to manage measured results. The subject files are stored in the database of the seca analytics 115 PC software supplied.

Recording weight and height:
The device uses an electronic scale. Weight is recorded across 4 load cells. Height is recorded via wireless transmission from the seca 274 length measuring device.

Bioimpedance measurement:
Bioimpedance is measured according to the 8-point method. The flow of the low alternating current and the measurement of impedance are performed for each side of the body using a pair of foot electrodes and a pair of hand electrodes. The hand electrodes are attached at different heights so that persons with different heights can adopt the ideal position on the device for a bioimpedance measurement.

2.2 Investigational device: mBCA 555

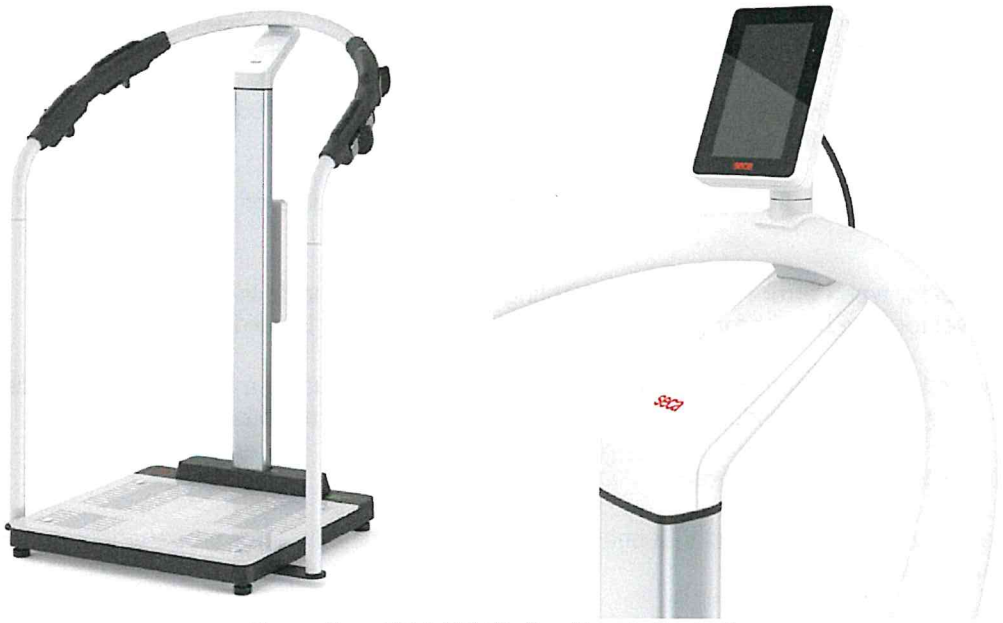

Figure 2: mBCA 555 (left: without display)

Technical Data

General:
- Dimensions (W×H×D): 840 × 1,280 × 655 mm
- Display type: 4,3 inch TFT touch screen with a 16:9 format, can be swiveled 180° to the left and right
- Power supply: Power adapter
- Voltage: 100 V – 240 V
- Interfaces: seca 360° wireless, WiFi, Ethernet
- Medical device class IIa

Bioelectrical Impedance Analysis:

- Measurement method: 8-point Bioelectrical Impedance Analysis
- Type of electrode: Stainless steel, four pairs of hand electrodes, two pairs of foot electrodes
- Measurement frequencies: 1, 2, 5, 10, 20, 50, 100, 200 and 500 kHz
- Measurements: Impedance (Z), Resistance (R), Reactance (Xc), Phase angle (φ)
- Measurement range Impedance: 10 Ω to 1,000 Ω
- Measurement segments: Right arm, left arm, right leg, left leg, right half of body, left half of body, torso
- Measurement current: 100 µA
- Measurement time: 30 seconds

The seca mBCA 555 has an integrated calibrated scale with a maximum load of 300kg. More information about the investigational device can be found in the investigator´s brochure.

2.3 mBCA Device Accountability

The mBCA 515 and 555 devices are delivered and installed by the sponsor. The responsible staff at the Clinical Investigation Site stores the product in a secure, limited access area under normal temperature and humidity conditions. After completion of the CI the devices are to be returned to the sponsor.

3. STUDY STATISTICS

The aim of the present study is a comparison of the investigational device mBCA 555 with the predicate device mBCA 515. It shall be tested, if formulas for the mBCA 515 can be used for the mBCA 555. Formula corrections shall be generated if they are required.

The null hypothesis (H0) is: Impedances measured with the mBCA 555 for adults are the same as when measured with the seca mBCA 515.

The alternative hypothesis (H1) is therefore: Impedances measured on both devices differ for the same subject.

The α-level for type I error for wrongly accepting H1 while H0 is valid is set to 5%.
The β-level for type II error for wrongly staying with H0 while H1 is valid is set to 20%.

The power 1-β is therefore 80% with a significance level of 5% using a two sided test statistic. These values apply to each individual variable. The total error rate therefore is larger.

The effect that shall be detected

For the calculation of the effect that shall be detected in the study, error propagation (uncertainty propagation) was calculated.

Formulas for phase angle, ECW, TBW, FFM, SMM (segmental and total) and VAT were considered. It was calculated how much variation of impedances is needed to gain an error of 0.1 SEE. (For phase angle the accuracy of 0.5° was used instead of the SEE.) For each impedance-value that formula was used that showed the highest dependency on impedance variations. This results in the following impedance changes that shall be detected in the study.

Variable	Change that causes 0,1 SEE change in the formula [Ω]
R5RS	8,89
R5LS	8,89
R50RS	5,19
R50LS	5,19
R50RA	2,22
R50LA	2,26
R50RL	1,94
R50LL	1,93
R50T	0,26
Xc50RS	1,04
Xc50LS	1,04
Xc50RA	0,72
Xc50LA	0,59
Xc50RL	0,45
Xc50LL	0,43
Xc50T	0,07

Table 1: impedance changes that shall be detected in the study

Estimated standard deviation

For the estimation of the standard deviation (sd) of measurements, results of an internal comparison with the mBCA 515 were used. 18 subjects were measured with the seca mBCA 515 and with two different prototype versions of the mBCA 555. The version "GND" used the same impedance correction that is used in the seca mBCA 515. The version "INT11" uses the impedance correction that is currently in development („ZampHautSG"). The upper limit of the 95% confidence interval (CI) of the standard deviation was used for further calculations.

Calculation of sample size

The calculation of sample size was performed according to „Statistik und Forschungsmethoden", 4th edition, Eid et al., pages 239 – 240. Using a two sided test statistic, formula (F 8.7b) becomes:

$$\mu_0 + z\left(1-\frac{\alpha}{2}\right)\cdot\frac{\sigma_X}{\sqrt{n}} = \mu_1 + z(\beta)\cdot\frac{\sigma_X}{\sqrt{n}}$$

Solving the equation for n gives:

$$n = \left(\frac{\left(z\left(1-\frac{\alpha}{2}\right) - z(\beta)\right)\sigma_X}{\mu_1 - \mu_0}\right)^2$$

The value μ_0 describes the effect under the null hypothesis: $\mu_0 = 0$, the value μ_1 is the effect that shall be detected and σ_X is the estimated standard deviation of the measurement.

Considering the different impedance variables and both devices, the following sample sizes were calculated:

Variable	Effect to be detected [Ω]	GND 95% CI of sd [Ω]	sample size [Ω]	INT11 95% KI of sd [Ω]	sample size [Ω]
R5RS	8,89	10,25	10,43	7,95	6,26
R5LS	8,89	12,40	15,25	8,04	6,42
R50RS	5,19	8,44	20,74	5,89	10,10
R50LS	5,19	10,82	34,10	7,22	15,16
R50RA	2,22	7,05	78,99	6,09	58,92
R50LA	2,26	8,56	112,99	5,21	41,85
R50RL	1,94	3,99	33,25	4,14	35,70
R50LL	1,93	3,73	29,40	4,47	42,23
R50T	0,26	0,71	58,48	0,62	44,04
Xc50RS	1,04	2,51	45,67	1,89	25,88
Xc50LS	1,04	2,65	50,68	0,97	6,80
Xc50RA	0,72	1,57	37,30	1,44	31,26
Xc50LA	0,59	1,87	80,42	0,71	11,56
Xc50RL	0,45	0,57	12,35	0,54	11,00
Xc50LL	0,43	0,59	14,70	0,56	12,83
Xc50T	0,07	0,20	62,09	0,25	100,69

Table 2: sample size calculation

The largest sample size is required for R50LA using the „GND"-device. 113 subjects are required.

Sample size: n = 113

4. STUDY PROCEDURE

In total, 2 measuring stations will be installed at the Clinical Investigation Site. One measuring station consists of a seca mbca 515, a laptop with the seca analytics software 115 and a height measuring instrument. The second measuring station is the mBCA 555 with an additional PC software. An examination time of 25 minutes is required per subject.

Subject insurance will be acquired.

4.1 Recruitment

Subjects are recruited at the blood donor service of the Institute of Transfusion Medicine. Blood donors are asked by the investigator to join the clinical investigation. A TV screen and display stands inform the blood donors about the clinical investigation in general.

A subject will only be admitted to the study if all inclusion and none of the exclusion criteria are met. Potential subjects will be screened for study eligibility. A subject is considered enrolled after:

- Written Informed Consent is obtained
- Meeting Inclusion and Exclusion criteria

4.2 Consent

An investigator will explain to the subjects the nature, significance and implications of the study prior to any Clinical Investigation related examination. The investigator will explain all methods, rules of

conduct and any restrictions which may apply. Possible effects and side effects will be discussed. Subjects will be informed that they are free to withdraw from the study at any time, without giving any reason for doing so. They must be able to understand the full implications of their decision.

All participants will sign an informed consent form as evidence of consent.
The subject information sheet and the informed consent form of each participant will be filed in the Investigator Site File. A second original (or copy) of the signed consent form and a copy of the information sheet will be handed to the subjects after signature and before enrollment.

4.3 Examinations

The investigation takes place during the opening hours of the blood donor service on Monday, Tuesday and Friday from 07:00 a.m. to 02:00 p.m. as well as on Tuesday and Wednesday from 12:00 a.m. to 07:00 p.m. The examination takes around 25 minutes and needs to be performed before blood donation.
The following table shows the examination schedule:

	Examination schedule	responsible	time in minutes
preparation			**5**
1.	read Informed Consent Form	subject	
2.	check inclusion and exclusion criteria	investigator	
3.	sign Informed Consent Form incl. Consent for processing personal data	subject & investigator	
4.	take off jacket and other heavy clothes	subject	
5.	empty trouser pocket	subject	
6.	take off shoes and socks	subject	
source data			**2**
7.	enter patient name and ID in source data doc.	investigator	
8.	enter date of examination, date of birth and gender in source data doc.	investigator	
9.	check if signed Informed Consent Form is available	investigator	
create subject file in PC software seca analytics 115			**1**
9.	start seca analytics 115	investigator	
10.	login as user named "BCA-21"	investigator	
11.	create new subject file	investigator	
12.	enter subject ID, gender, date of birth and select the ethnicity	investigator	
13.	save subject data	investigator	
mBCA 515 measurement			**3**
14.	start mBCA 515	investigator	
15.	go to patient tab	investigator	
16.	enter subject ID and click on search	investigator	
17.	select subject to be measured	investigator	
18.	go to weight & height tab	investigator	
19.	ask subject to take shoes off	investigator	
20.	measure subject height with seca 274 and send it wirelessly to the mBCA 515	investigator	
21.	ask subject to take socks off	investigator	
22.	step on mBCA 515 glassplattform	subject	
23.	weight is measured and BMI is calculated automatically	mBCA	
24.	click on BIA tab	investigator	
25.	State whether the subject meets the mBCA contraindications or not	investigator	
26.	**Yes:** the measurement is **not** performed.	investigator	
27.	**No:** the procedure continues. The dialog window for positioning the patient appears.	investigator	

	Examination schedule	responsible	time in minutes
28.	Ensure that the patient is standing on the device correctly: **Test point** / **Characteristics** Hands: • Hands must be clean • Same pair of hand electrodes on left and right • Select the pair of hand electrodes such that arms are extended but not under strain • Finger spacers of the hand electrodes between the middle finger and ring finger on both sides Feet: • Stand on device with bare feet • Feet must be clean • Heels on the rear foot electrodes • Balls of feet on the front foot electrodes Position: • Upright position • Knees slightly bent • Do not move during the measurement	investigator	
29.	If the patient is in correct contact with an electrode pair, the corresponding electrode indicator on the touchscreen display will be green. As soon as all the electrode indicators on the touchscreen display are green, a countdown to the start of measurement appears. Measurement starts automatically.	mBCA	
30.	Remaining measurement time is displayed.	mBCA	
31.	As soon as the measurement ends, the message "End of measurement" appears.	mBCA	
32.	Press the continue button	investigator	
33.	enter PAL value and waist circumference	investigator	
34.	Press the save button	investigator	
35.	check in seca analytics 115 if measurement data was saved	investigator	
measurement with mBCA 555			**3**
36.	start PC software for mBCA 555	investigator	
37.	enter subject ID	investigator	
38.	select handrail position	investigator	
39.	step on mBCA 555 glassplattform	subject	
40.	Ensure that the patient is standing on the device correctly: **Test point** / **Characteristics** Hands: • Hands must be clean • Same pair of hand electrodes on left and right • Select the pair of hand electrodes such that arms are extended but not under strain • Finger spacers of the hand electrodes between the middle finger and ring finger on both sides Feet: • Stand on device with bare feet • Feet must be clean • Heels on the rear foot electrodes • Balls of feet on the front foot electrodes Position: • Upright position • Knees slightly bent • Do not move during the measurement	investigator	
41.	If the patient is in correct contact with an electrode pair, start the measurement with the PC software	investigator	
42.	As soon as the measurement ends, the message "BIA measurement: OK" appears --> measurement must be saved manually	investigator	
measurement repetition			**6**
43.	repeat mBCA 515 measurement	subject & investigator	
44.	repeat mBCA 555 measurement	subject & investigator	
postprocessing			**5**
45.	explain results (if required)		
46.	put on shoes and socks		
47.	pick up personal other belongings		
total time needed for examinations:			***25***

After measuring body height each subject will undergo 4 mBCA measurements.
Every 2nd subject will be measured in the following order:

1) mBCA 515
2) mBCA 555
3) mBCA 515
4) mBCA 555

The other subjects will be measured in reverse order:
1) mBCA 555
2) mBCA 515
3) mBCA 555
4) mBCA 515

Demographic data

The patient record contains date of birth, gender and ethnic origin.

Anthropometric data

Body height is measured by the digital height measuring instrument seca 274.

Figure 3: seca 274

5. RISK MANAGEMENT

The risk management of the seca mBCA 515 was carried out in accordance with ISO 14971. The risk analysis was developed by a risk management team, which consists of members of the following sections:

- Research and development
- Quality Management
- Quality Assurance
- Product Management
- Sales
- Customer Service
- Safety Representative for Medical Devices
- Project Manager

5.1 Summary of risk analysis, including identification of residual risks

The risks or hazards that may occur during the course of the Clinical Investigation were evaluated and analyzed separately in following 2 sections:
- risks of the device
- risks during Clinical Investigation for the operator, subject and third persons

5.1.1 Risks of the predicate device

The risk management of the mBCA 515 was performed according to EN ISO 14971. The risk analysis comprises a detailed analysis of potential risks that may affect the safety and performance of the mBCA. For each identified risk the manufacturer seca gmbh & co. kg defined the probability of occurrence and the potential of the consequences. The hazards were evaluated and risk reduction measures were implemented to reduce the risks. All hazards, that were rated as "not acceptable" could be rated as "acceptable" after risk reduction measures.
The remaining risk because of the weak measurement current for patients with electronic implants is low, but the patient group was still contraindicated.
The mBCA 515 fulfills the requirements of EN 60601 and IEC 62133.
Detailed information can be found in the reference documents D1-D2.

5.1.2 Risks during the Clinical Investigation for the operator, subject and third persons

All examinations will be performed by trained personnel only. The contra-indications, precautions and warnings are listed in chapters 5.2 and 5.3 of this CIP.

5.2 Contra-indications for the mBCA

Bioimpedance measurements may not be performed on persons exhibiting the following characteristics:
- electronic implants, e.g. cardiac pacemakers
- active prostheses

Bioimpedance measurements may not be performed on persons who are connected to one of the following devices:
- electronic life-support systems, e.g. artificial heart, artificial lung
- portable electronic medical devices, e.g. ECG devices or infusion pumps

Bioimpedance measurements may only be performed on persons exhibiting the following characteristics after discussion with the attending physician:
- cardiac arrhythmias
- pregnancy

5.3 Precautions and Warnings for the mBCA

The following precautions and warnings should be considered when measuring the body composition with the seca mBCA:

Hazard to patient, damage to device
- Technical modifications may not be made to the device.
- The device does not contain any parts for servicing by the user. Please only have maintenance, technical checks and repairs performed by seca.

Risk of electric shock
- Never touch the power supply with wet hands.
- Make sure that the power cable is not crushed and cannot be damaged by sharp edges.

Hazard to patient (seca mBCA 515)
- Subject the device to a hygiene treatment after each measurement
- The mBCA 515 is not designed to be a rising aid. Assist people with limited mobility, e.g. when they are getting up from a wheelchair.
- Ensure that the weighing platform is dry before the patient steps onto it.

- Ensure that the patient does not step directly onto the edges of the weighing platform.
- Ensure that the patient steps onto the weighing platform slowly and safely.

Risk of infection
- Before and after every measurement, wash your hands to reduce the risk of cross-contamination and nosocomial infections.

Damage to device
- Make sure that fluids never get inside the device. These can destroy the electronics.
- Switch off the device before you disconnect the power pack from the power supply.
- Do not subject the device to shocks or vibrations.
- Do not place the device in direct sunlight and make sure that it is not placed in the direct proximity of a heat source. The excessive temperatures could damage the electronics.
- Use only chlorine and alcohol-free disinfectants which are explicitly suitable for acrylic sheet and other sensitive surfaces (active ingredient: quaternary ammonium compounds, for example).
- Do not use aggressive or abrasive cleaning agents.
- Do not use organic solvents (e.g. white spirit or petroleum spirit).

6. SAFETY ASSESSMENT

6.1 Definitions

Adverse Event
An adverse event (AE) is any untoward medical condition in a subject while participating in a clinical trial and which does not necessarily have to have a causal relationship with the use of the medical device. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. Symptoms or medically significant laboratory or instrumental abnormalities of a pre-existing disease, should not be considered as AE. Anticipated symptoms associated with tumor inflammation like fever, tumor pain, redness should not be considered as a medical device related AE. However, occurrences of new symptoms, as well as worsening of pre-existing conditions or events, drug interactions or the significant worsening of disease under investigation that is not recorded elsewhere in the CRF under specific efficacy assessment, are also considered as AEs.

Serious Adverse Event
A Serious Adverse Event (SAE) is defined as an AE, which falls into one or more of the categories listed below:

- ⇨ results in death
- ⇨ is life-threatening
- ⇨ requires in subject hospitalization or prolongation of existing hospitalization
- ⇨ results in persistent or significant disability/incapacity, where disability is defined as a substantial disruption of a person's ability to conduct normal life functions, either reported or defined as per judgment
- ⇨ is a congenital anomaly / birth defect

Complaint
A complaint is defined as an AE, which is not an untoward medical condition in a subject, but may comprise a technical defect or problem with the medical device.

6.2 Legal Aspects

For the documentation and reporting of AE and SAE the requirements as defined in the "*Medizinprodukte-Sicherheitsplan-Verordnung (MPSV)*" must be followed. This means, that both the

investigator and the sponsor must immediately inform the BfArM about any SAE, independently from the causal relationship with the medical device or the medical procedure applied. The relevant reporting form, which must be used, is available on the homepage of the BfArM (www.bfarm.de) in section "*Medizinprodukte/Formular*" and will be provided to the investigator in advance.

6.3 Documentation

All AEs will be reported from the time subject signs informed consent through study completion or premature discontinuation and must be documented on the Adverse Event page of the CRF. If an AE is considered serious, both the Adverse Event page of the CRF and the SAE Report Form must be completed.

Any ongoing AE should be followed up until the earliest occurrence of one of the following:

- ⇨ AE is resolved
- ⇨ AE is stabilized if it has not been resolved within 30 days from the last measurement with the medical device. Documentation of stabilization must be recorded in the subject's source data documents.

Complaints must be documented in the source documents and the CRFs providing more detailed information about the specific issues of the complaint (e.g. technical problem with the medical device).

6.4 Reporting

The investigator must report all SAEs immediately by E-Mail to the sponsors following E-Mail-Address: kristin.klueckmann@seca,com. The sponsor has to inform the BfArM immediately about any SAE. The SAE contact information for reporting SAEs or death as well as the reporting form is provided in the Investigator Site File.

A follow-up SAE form will be filled in by the investigators if important follow-up information (i.e., diagnosis, outcome, causality assessment, results of specific investigations) is made available after submission of the initial form. The follow-up SAE form will be sent to the sponsor. The investigator will submit, on request, copies of all these reports to the relevant EC. All AEs and complaints must be reported within the investigation plan report, after the CI was terminated and evaluated.

7. ETHICAL COMMITTEE / COMPETENT AUTHORITY / STANDARDS

7.1 Ethical Committee (EC)

Prior to initiation of the study, the sponsor or authorized party will submit the study protocol, ICF, and any other documents that pertain to subject information to the EC. The favorable opinion from the Committee must be documented in a letter to the sponsor specifying the protocol number, protocol version, documents reviewed, and date the committee granted the approval.

The sponsor must submit and, where necessary, obtain approval from the EC for all subsequent protocol amendments and changes to the ICF. The investigator must immediately notify the competent authority and EC from SAEs occurring at the site, as well as other AE reports received from the sponsor, in accordance with local procedures.

7.2 Competent Authority (CA)

In accordance with of the German Act on Medical Devices (MPG) the competent federal higher authority can waive the authorization in case of clinical trials of medical devices with a low safety risk. The medical device investigated in this clinical investigation meets the requirements as a device with a low safety risk. Prior to start of the study a request for waiving the authorization of the clinical trial will be submitted to the Competent Authority by the Sponsor.

7.3 Applicable standards

Please refer to chapter Regulatory Information in this document.

7.4 Subject privacy and confidentiality of data

Confidentiality of data shall be observed by all parties involved at all times throughout the CI. All data shall be secured against unauthorized access. The privacy of each subject and confidentiality of his/her information shall be preserved in reports and when publishing any data. The principal investigator or institution shall provide direct access to source data during and after the CI for monitoring, audits EC review and regulatory authority inspections. As required, the principal investigator or institution shall obtain permission for direct access to source data documents from the subject, hospital administration and national regulatory authorities before starting the CI.
Case report forms (CRF) will be filled out, signed and dated by the clinical investigation site. CRF only contain pseudonymized data. Completed CRF pages will be collected by the Sponsor after data have been monitored according to the monitoring plan for data analyzes.

8. SUBJECT DATA

8.1 Informed Consent

Prior to the beginning of the study, the investigator must have the written EC approval for the informed consent form and any other information provided to the subject. Before undertaking any study-related procedures with subjects, the purpose and nature of the study as well as possible adverse effects must be explained to them in understandable terms for the subject, parents or legal representatives and written informed consent must be obtained from each participant. Each informed consent will be signed and personally dated by the subject. Each subject will receive a copy of the signed informed consent.

8.2 Case Report Form (CRF)

The study sites will collect at least the data required for transfer into the CRF on the source data. Next, site staff will transfer the study data from the source documents into the CRF. After completion each CRF page will be printed and signed by an investigator or authorized designee. In case of any changes to the CRF the applicable CRF page will be printed and signed again. After conduct of the source data verification the study monitor will collect the CRFs. A copy of the CRFs stays at the investigations site. CRFs must be completed for all subjects who sign ICF even if the subject fails to complete the study. No section of the CRF is to be left blank without an appropriate explanation by the investigator, since the lack of such explanation may necessitate discarding an otherwise usable observation. Data reported on CRFs should be consistent with source data documents when applicable, or the discrepancies should be explained. Any correction or deletions are to be made by crossing out with a single line (so it´s still legible), then initialing and dating by the investigator or other authorized person. The use of correction fluids to "white-out" mistakes in data entry is not permitted. The investigator should ensure the accuracy, completeness, legibility, and timelines of the data

reported to the sponsor in the CRFs and in all required reports. The CRF shall be signed and dated by the principal investigator or his/her authorized designees.

9. MONITORING / INSPECTIONS / AUDITS

9.1 Monitoring

The sponsor will assign a study monitor to maintain contact with the investigator and will visit the study site for the purpose of discussing and/or retrieving data in order to comply with DIN EN ISO 14155:2012 guidelines. An initiation visit will be conducted by the sponsor and the study monitor to discuss the protocol and the obligations of both the sponsor and the investigator. The investigator must allow the study monitor to perform periodic, interim monitoring visits. The purpose of these visits is to review the CRFs at regular intervals throughout the study to verify adherence to the protocol, and the completeness, consistency and accuracy of the data being entered on them. The study monitor should have access to subjects' records needed to verify the entries on the CRFs for source data verification. The investigator should be available at some time during the interim monitoring visit to review the data and resolve any queries. The investigator agrees to co-operate with the study monitor to ensure that any problems detected in the course of these visits are resolved. The study monitor will perform a close-out visit at the conclusion of the investigator's involvement in the study.

9.2 Inspections / Audits

The Investigator will make all pertinent records available, including source data documentation, for inspection by the EC competent authorities and for auditing by the sponsor after appropriate notification. The verification of CRF data must be made available by direct inspection of source data documents. This information will be considered as confidential.

10. ADMINISTRATIVE PROCEDURES

10.1 Amendments

No change to the protocol may be made without the joint agreement of both the Investigator and the sponsor. Any amendment to the original protocol will be made by the sponsor. The written amendment must be submitted to the EC and the investigator must await the approval before implementing the changes. If in the judgment of the EC the investigator, and/or the sponsor, the amendment to the protocol substantially changes the study design and/or increases the potential risk to the subject and/or has an impact on the subject's involvement as a study participant, the currently approved written informed consent form will require similar modifications. In such cases, informed consent will be renewed for subjects enrolled in the study before continued participation.

10.2 Publication policy

All unpublished documentation (including the protocol, CRF, and Investigator's Brochure) given to the investigator is strictly confidential. All recipients must agree not to disclose the information herein contained to any person without the prior written authorization of the sponsor. The investigator agrees that the sponsor maintains the right to use the results of this study in their original form and/or in a global report for submission to governmental and regulatory authorities of any country.

10.3 Study Report

The final study report will be prepared according to the DIN EN ISO 14155:2012. The final study report will be prepared regardless of whether the study is completed or prematurely terminated. The sponsor and the Principal Investigator will sign the final report after review. The final report will be provided to the EC, the competent authority and upon re-quest, to all the investigators.

10.4 Confidentiality

All information provided to the Principal Investigator dealing with the medical device will be regarded as confidential.

APPENDIX

Instruction for use
A1 BA_seca 515_BH_17-10-07-626-002b_11-2016S.pdf
A2 BA_seca 514_515_mBCA_AH_17-10-07-627-005b_12-2016B.pdf

Declaration of Conformity
B1 DoC_17-10-09-289c_seca_515.pdf

Labels
C1 5157021009_20160915.pdf

Risk Management
D1 050712_Risikomanagement_Bericht_mbca.pdf
D2 Risikoanalyse_mBCA 515.pdf