

CLINICAL STUDY PROTOCOL

STUDY TITLE

CLINICAL EVALUATION OF THE EFFICACY OF A FOOD SUPPLEMENT ON BODY WEIGHT AND PERCEIVED FOOD CRAVING: A RANDOMIZED, DOUBLE-BLIND, PARALLEL-GROUP, PLACEBO-CONTROLLED STUDY

PROTOCOL REFERENCES

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GENERAL INFORMATION

SPONSOR

Name and Address:

ROELMI HPC S.R.L., Via Celeste Milani 24/26 – 21040 Origgio (VA), Italy

Authorized Signatory:

Carolina Galli, R&D Specialist

INVESTIGATORS AND SITES

Study Setting:

Multicenter

Principal Investigator Coordinator:

Dr. Achiropita Curti, Clinical Nutritionist

Principal Investigator:

Dr. Ana-Maria Calin-Necula, gastroenterologist

Co-Investigators:

Nicoleta Dumitru, senior efficacy clinical trial technician and senior safety clinical trial technician

Luminita Hudicovschi, senior efficacy clinical trial technician and senior safety clinical trial technician

Principal Study center:

Complife Romania SRL, Strada Orzari 92A, 021554 - Bucuresti, Romania

Other Study Centers and Associated Co-Investigators:

The number of study sites and associated co-investigators will be defined, as appropriate to ensure the proper conduct of the study, during the study start-up phase and documented in a separate document, subject to review and approval by the Sponsor, the Principal Investigator Coordinator, the Project Manager, and the Ethics Committee (see Annex 1 for the list of potential study centers).

Other laboratories:

None

MANAGEMENT

Responsible Person:

Dr. Roberta Villa, Project Manager

Facility Name and address:

Complife Italia S.r.l.; office in Viale Indipendenza, 11 - 27100 Pavia (PV), Italy

Headquarters: Via Guido Rossa, 1 - 20024 Garbagnate Milanese (MI), Italy



PROTOCOL APPROVAL

The undersigned acknowledge having read and understood the Clinical Study Protocol. They hereby agree to its content and commit to conduct or oversee the study in full compliance with this Protocol, the Declaration of Helsinki, Good Clinical Practice (GCP), and applicable regulatory requirements.

AUTHORIZED SIGNATORY OF THE SPONSOR

Date and Signature:

27/03/2026 *Roberta Villa*

PRINCIPAL INVESTIGATOR COORDINATOR

Date and Signature:

27/03/2026 *Achille Curi*

RESPONSIBLE FOR STUDY MANAGEMENT

Date and Signature:

Roberta Villa Digitally signed by
Roberta Villa
Date: 2026.03.26
+5.59.22 +01'00'



PROTOCOL AMENDMENTS

All protocol amendments must be jointly approved and signed by the Sponsor, the Principal Investigator Coordinator, and the Project Manager of the study.

Deviations during the study will be reviewed to determine whether they require a formal amendment or justify study termination.

AMENDMENTS HISTORY

Clinical Study Protocol Version and Date of issue:

00, 19/02/2026

Description:

First release

Clinical Study Protocol Version and Date of issue:

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Description:

Minor changes



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1. PROTOCOL SUMMARY

The aim of this study is to evaluate the efficacy of a food supplement on body weight and perceived food craving. To reach this goal, a double-blind, randomized, parallel-group, placebo-controlled clinical study is planned to be performed on 66 healthy subjects, aged between 18 and 45 years, with overweight and self-perception of excessive food craving, under the supervision of a board-certified Clinical nutritionist. 33 subjects will assume the active product and 33 subjects the placebo for 84 days according to the instruction for use. Specific assessments will be carried out before and after T14, T28, T56 and T84 days of product intake. The occurrence of adverse events will be also recorded.

2. BACKGROUND AND RATIONALE

Overweight and obesity represent one of the primary global public health challenges, being associated with an increased risk of metabolic disorders such as insulin resistance, dyslipidemia, and type 2 diabetes. It is widely recognized that even moderate weight loss (~5%) can yield clinically significant benefits for the metabolic profile and quality of life. However, poor adherence to dietary programs—often linked to hunger, food cravings, and postprandial glycemic fluctuations—limits the long-term effectiveness of nutritional interventions^{1,2}. In this context, the use of phytocomplex-based dietary supplements capable of modulating nutrient absorption, appetite regulation, and energy metabolism represents a promising supportive strategy in weight management programs. SelectSIEVE® Libra is a phytonutritional complex derived from *Salvia officinalis* L. and *Morus alba* L. leaf extracts, two plants traditionally used in Mediterranean and Asian folk medicine to control glucose and lipid metabolism. The extraction technology applied allows for a standardized natural composition, rich in polyphenols and bioactive phytochemicals, including rosmarinic acid, flavonoids, phenolic acids, and 1-deoxynojirimycin (1-DNJ). From a biological perspective, the active principles of the complex act through complementary mechanisms relevant to body weight control: inhibition of carbohydrate digestive enzymes, particularly α -glucosidase, resulting in slowed glucose absorption and attenuation of postprandial glycemic peaks; modulation of lipid metabolism by reducing adipogenesis and promoting lipolysis; inhibition of hepatic gluconeogenesis and improvement of peripheral glucose uptake, mediated by AMPK activation and increased expression of the GLUT4 transporter; and regulation of appetite and satiety signals through the modulation of leptin and adiponectin, along with inhibitory activity on MCH1 receptors involved in the central control of food intake^{3,4,5,6}. Preclinical evidence shows that SelectSIEVE® Libra can increase GLUT4 expression in differentiated adipocytes in a dose-dependent manner and stimulate physiological insulin secretion, suggesting an improvement in glucose homeostasis.^{7,8} In preliminary clinical study, these effects translate into a significant reduction in postprandial glucose levels, better control of the insulin response, and a decrease in signals associated with hunger and food cravings.⁹ Furthermore, controlled clinical trial conducted on overweight subjects with evidence of food craving have demonstrated that daily intake of the complex, in association with a controlled dietary regimen, leads to a significant reduction in cravings, improved perceived satiety, and a decrease in BMI and fat mass, with a positive impact on quality of life. These results support the scientific rationale underlying the clinical study and justify the use of SelectSIEVE® Libra as a nutritional support in weight management programs.¹⁰

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8. Internal Technical Report "Evaluation of the insulinotropic capacity of a compound", 06/02/2020, ROELMI HPC srl proprietary data.
9. Internal Technical Report "Effect of extracts of Mulberry leaves (*Morus alba*) and Sage (*Salvia officinalis*) on glucose and insulin metabolism", 30/07/2020, ROELMI HPC srl proprietary data.
10. Fogacci F, Veronesi M, Di Micoli A, Bove M, Cicero A.F.G. "Effect of a combined mulberry-sage dietary supplement on food craving and body weight: a pilot clinical trial". *Progress in Nutrition* 2023; Vol. 25, N. 3: e2023047 DOI: 10.23751/pn.v25i3.13469.



3. OBJECTIVES

3.1. Primary objective

The primary objective of this study is to evaluate the efficacy of the product in reducing body weight.

Primary end-points:

- Body weight (Kg)
- Body Mass Index (BMI) (Kg/m²)

3.2. Secondary objectives

The secondary objective of this study is to assess the efficacy of the product on additional anthropometric and body composition parameters potentially associated with body weight reduction.

Additionally, the study will evaluate participants' self-perceived changes in food craving control, appetite-related sensations, body perception, overall well-being, and product acceptability through a self-assessment questionnaire.

Secondary end-points:

- Waist circumference (cm)
- Hip circumference (cm)
- Fat Mass (FM) (Kg)
- Self-evaluation questionnaire (polytomous question with four possible answers)

4. STUDY DESIGN

The study will be double-blind, randomized, parallel-group, placebo-controlled: half of the subjects will be allocated to the active product and half of the subjects will be allocated to a placebo. Subjects will take the assigned food supplement for 84 days according to the directions for use.

4.1. Randomization

A restricted randomization list will be generated by an independent technician using the appropriate algorithm ("Wei's urn") of the PASS 11 software (PASS, LLC. Kaysville, UT, USA) and stored in a secure location. The Principal Investigator or designated personnel will dispense the products according to the generated randomization list.

4.2. Blinding

The study will be double-blind, meaning that subjects, Principal Investigator and collaborators are kept masked to products assignment. The products will be supplied in the same packaging with no obvious differences between the products (see Annex 2).

5. INVESTIGATIONAL PRODUCTS

5.1. Composition

Active

SelectSIEVE®LIBRA (Salvia officinalis extract – 60%, Morus alba (white mulberry) extract – 40%), Maltodextrin, Magnesium stearate. White HPMC capsule size 0

Allergens: None

Placebo

Maltodextrin, Magnesium stearate. White HPMC capsule size 0

Allergens: None

The food supplement is compliant to the current national and international legislation (The sponsor is responsible for providing a statement to this regard).

5.2. Dosage and direction of use

Subjects will take two capsules per day, half an hour before dinner, with a glass of water.

5.3. Supply and storage

The products will be supplied by the Sponsor.

If shipped without a pallet, the delivery address is: Complife S.r.l., Via Monsignor Angelini, 21, 27028, S. Martino Siccomario (PV), Italy.

If shipped on a pallet, the delivery address is: Complife S.r.l., Via Guido Rossa, 1, 20024 Garbagnate Milanese (MI), Italy.



The contact person is Sabrina Martinazzo (@: segreteriapavia@complifegroup.com; T: +39 0382 25504).

Products will be stored at room temperature protected from direct light, heat and source of water safe place with restricted access.

6. STUDY POPULATION

6.1. Sample size

The study will be performed on 66 (60 + 6, considering a 10% drop-out) subjects.

6.1. Subjects' enrolment

Subjects are enrolled according to specific inclusion and exclusion criteria listed in the sections below.

All inclusion and exclusion criteria are checked by the Principal Investigator or designated personnel. The Principal Investigator maintains a record of all subjects who are enrolled and who are considered screen-failed (i.e., subject who signs the informed consent form and is not enrolled) and for each subject, the primary reason for not enrolling is recorded. Subjects enrolled are identified by a unique code that remains personal and cannot be associated to another subject during the study.

6.1.1. Inclusion criteria

1. Healthy male and female subjects
2. 90% Caucasian subjects; 10% mixed-ethnicity subjects
3. Subjects aged between 18 and 45 years (extremes included)
4. Subjects who are overweight at screening (at the recruitment, BMI between 25 kg/m² and 29.9 kg/m², according to the World Health Organization (WHO) BMI Classification)
5. Subjects with stable body weight at screening, defined as a fluctuation of no more than ± 2 kg during the one-month screening phase, with body weight assessed every 14 days
6. Subjects with a stable, light-to-moderate physical activity level (e.g., routine daily mobility such as walking ≥ 30 minutes/day or equivalent), not engaged in competitive sports or structured training programs that may significantly influence body weight or body composition, and willing to maintain their habitual activity level throughout the entire study duration
7. Subjects who commit not to change their daily routine throughout the entire study period (screening and experimental phases)*
8. Subjects with self-perceived excessive food craving at screening, defined as a score ≥ 6 on a 0–10 Visual Numeric Scale (VNS).
9. Subjects registered with the national public health system in the country where the study is conducted
10. Subjects certifying the truthfulness of the personal data disclosed to the investigator
11. Subjects able to understand the language used in the investigation centre and the information given by the investigator
12. Subjects able to respect the instructions given by the investigator as well as able to respect the study constraints and specific requirements
13. Subjects on stable pharmacological therapy (except for the pharmacological therapy in the non-inclusion criteria) for at least one month without any changes expected or planned during the study
14. Subjects informed about the test procedures who have signed a consent form and privacy agreement.

* Subjects will complete a daily food and physical activities diary to monitor their habitual diet and quotidian/physical activity. Diaries will be collected during the one-month screening period and at each month of treatment (T28, T56, and T84).

6.1.2. Exclusion criteria

1. Subjects who do not meet the inclusion criteria
2. Menopausal or perimenopausal subjects
3. Subjects with any acute, chronic, or progressive disease or condition that may interfere with the study data or that the investigator considers dangerous to the subject or incompatible with the requirements of the study**



4. Subjects currently following a weight-loss diet/program or who started a structured diet/exercise program within the last 3 month
5. Subjects participating or planning to participate in other clinical trials
6. Subjects who participated in a similar study without respecting an adequate washout period (at least one month)
7. Subjects that have food intolerances or food allergies to ingredients of the study product
8. Subjects under pharmacological treatments that are considered incompatible with the study requirement by the investigator ***
9. Subjects who are currently using food supplement(s) and/or products with the same activity as the study product, or who haven't observed an adequate washout period (at least one month)
10. Subjects admitted to a health or social facility
11. Subjects planning a hospitalization during the study
12. Subjects not able to be contacted in case of emergency
13. Subjects deprived of freedom by administrative or legal decision or under guardianship
14. Subjects who have or have had a history of alcohol or drug addiction
15. Subjects with eating disorders (i.e. bulimia, psychogenic eating disorders, etc.)
16. Subjects breastfeeding, pregnant or not willing to take necessary precautions to avoid pregnancy during the study (for the women of childbearing potential).

** Including malignancy, severe cardiovascular disease, severe hepatic or renal impairment, neurological or psychiatric disorders, serious infections, autoimmune diseases or any medical condition that may affect body weight, appetite, or eating behavior or any condition considered by the Principal Investigator to interfere with the study.

*** Including the use of medications known to affect body weight, appetite, or eating behavior or any medication considered by the Principal Investigator to interfere with the study.

6.2. Subject withdrawal and discontinuation

In compliance with the Declaration of Helsinki, subjects have the right to withdraw from the study at any time and for any reason. In all cases, the Principal Investigator or designated personnel should try to contact the subject as soon as possible for a final assessment to: i) document the subject's decision on the informed consent form, ii) record the reason(s) for withdrawal on the data collection sheet, iii) evaluate the subject's clinical condition, if relevant iv) provide appropriate therapeutic measures if necessary (e.g., management of adverse events or concomitant conditions), v) collect any investigational product provided to the subject.

If a subject misses a scheduled visit, the Principal Investigator or designated personnel will attempt to contact the subject by phone on two separate occasions. If the subject cannot be reached after these attempts, they will be considered lost to follow-up. These contact attempts and their outcomes will be documented in the source document. The Principal Investigator may also decide to withdraw a participant from the trial early if the subject no longer meets the eligibility criteria, fails to comply with the protocol, or is deemed unsuitable to continue the study. This may occur, for example, in the event of illness, pregnancy, or the occurrence of an Adverse Event (AE) or Serious Adverse Event (SAE), particularly if the Principal Investigator considers that the subject's health may be at risk or if concomitant treatments required are incompatible with the continuation of the trial. In such cases, the Sponsor will be notified immediately, and a detailed report explaining the reason for withdrawal will be forwarded as soon as possible. Any early termination related to an AE or SAE will be monitored until its resolution.

The sponsor has the right to exclude any subject from the trial for major protocol violations, administrative reasons, or other justifiable reasons.

However, a high dropout rate may compromise or invalidate the interpretability of the study. Therefore, premature exits without valid reasons should be minimized and carefully documented in the case report form, the final report, and, if applicable, in the AE form. Each premature exit will be categorized as follows: i) violation of inclusion and exclusion criteria, ii) occurrence of an AE, iii) occurrence of an SAE, iv) withdrawal of consent, v) lost to follow-up, vi) non-adherence to the protocol, vii) other reason (to be clearly specified).

Withdrawn/lost to follow-up/drop-out subjects will not be replaced.

Further details regarding safety reporting and management are provided in Paragraph 12.



6.3. Subject full participation

Study completion is achieved when a subject has completed all treatment and has attended all scheduled visits.

7. ETHICAL CONSIDERATIONS

7.1. Risk and benefit

The food supplement administered in this study is in compliance with current food legislation and is composed of ingredients with a well-established history of safe use in humans.

No adverse effects are expected under the indication of use. However, as with any food product, the possibility of individual reactions cannot be completely excluded. If applicable, information regarding the presence of any substances that may cause hypersensitivity will be provided prior to participation.

The potential benefits associated with the use of the product are related to body weight reduction and improvement of other anthropometric and body composition parameters potentially associated with body weight reduction.

Additionally, another potential benefit may be an improvement in self-perceived food craving, body perception, and overall well-being.

7.2. Compliance with the Declaration of Helsinki

The study will be conducted in accordance with the ethical principles for the medical research (Ethical Principles for Medical Research Involving Human Subjects, adopted by the 18th WMA General Assembly Helsinki, Finland, June 1964 and amendments).

7.3. Informed Consent

During the recruitment phase, the Principal Investigator or designated personnel will explain to each subject the nature, purpose, potential benefits, and possible risks of participation in the study. The investigator must ensure that the subject has understood all relevant aspects of the study. Sufficient time will be provided to allow questions to be asked and answered.

After this discussion, subjects will be asked to carefully read and sign the study information sheet and informed consent form, and the privacy agreement pursuant to art. 13 of EU Regulation 2016/679.

The informed consent form, approved by the Sponsor, will be prepared in two versions: a version in English and a version in the local language, written in terms readily understandable to the subject. Only the version in the local language will be presented to and signed by study participants.

The informed consent form, approved by the Sponsor, will contain all required elements in language that is readily understandable to the subject. Each original consent form, personally signed and dated by both the subject and the investigator conducting the consent discussion, will be retained by the investigator. A copy will be provided to the subject. Subjects will be informed that they have the right to withdraw their consent.

The consent form may need to be revised during the study, either because important new information has become available that may be relevant to the safety of the subjects, or because of protocol amendments. It is the investigator's responsibility to ensure that the amended form is signed by all subjects who are subsequently entered into the study, as well as by those who are already in it. This is documented in the same way as previously described.

7.4. Confidentiality and Data Protection

All information, data, and results of the study are strictly confidential, and all individuals with access to such data are informed of this obligation.

In accordance with the applicable law on data protection (EU Regulation 679/2016), the personal data, which may be special, including date of birth, sex, race, etc., the information resulting from clinical studies and on health status are processed in confidence, only for research purposes in relation with this study. If the results arising from the clinical study should be published or disseminated in scientific journals or conferences, this is done in a manner that preserves confidentiality. For this purpose, relevant subject data may be forwarded to the Sponsor or its partners abroad. In each case, subject data will be pseudonymised and identified only by a code number and initials. The Principal Investigator will be responsible for maintaining the list of codes that links each subject's number with their identity.

In all cases, nominative information shall not be transmitted to the Sponsor. If a subject's name appears on a document required by the Sponsor (e.g., photographs), the name will be permanently blacked out by the site personnel, leaving only the initials visible and annotating the subject number for identification.

The data will remain strictly confidential and will not be made public. However, at any time during or after the study, health authorities may be granted direct access to the records to verify the accuracy of the collected information. In



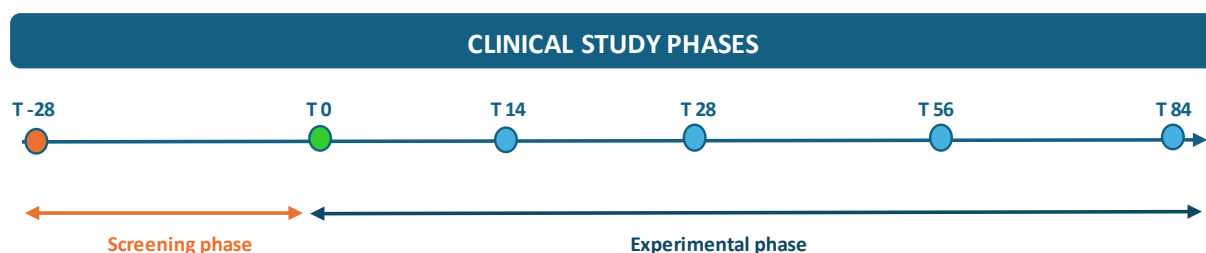
such cases, subject identity may be disclosed. All individuals granted access to these records are bound by professional secrecy.

8. STUDY SCHEDULE AND PROCEDURES

The study is structured into two phases: a one month of screening phase prior to product intake, followed by 84 days of treatment. Clinical visits are planned at T-28 (Initial visit), T0 (baseline visit), and follow-up visit at T14, T28, T56 and T84 (final visit).

8.1 Timeline diagram

A schematic flow diagram is provided below:



8.2. Summary of study visits and procedures

The following table summarizes the planned visits and procedures:

Procedures	T-28	T0	T14	T28	T56	T84
Signature of informed consent and privacy statement of screened subjects	X	-	-	-	-	-
Verification of subject eligibility	-	X	X	X	X	X
Collection of subjects' demographic data and variables relevant to eligibility assessment	X	-	-	-	-	-
Distribution of diaries	X	X	-	-	-	-
Collection of diaries	-	X	-	X	X	X
Randomization to treatment	-	X	-	-	-	-
Distribution of products	-	X	-	X	X	-
Measurement of Waist circumference, Hip circumference, Body weight, Fat Mass (FM) and calculation of Body Mass Index (BMI).	-	X	X	X	X	X
Completion of the self-assessment questionnaire by subjects	-	-	X	X	X	X
Collection and counting of products	-	-	-	X	X	X
Monitoring of Tolerability	-	-	X	X	X	X

8.3. Initial visit (T-28)

Potential subjects will be identified within the volunteer database by appropriately authorized personnel (designated by the Investigator, in accordance with applicable data protection regulations) and invited to participate in the study. At the initial visit, the Principal Investigator or designated personnel will verify whether each subject meets the inclusion and exclusion criteria and will collect demographic data along with all variables relevant to eligibility assessment. Subjects will be informed about the study procedures and will be asked to sign the informed consent form and the authorization for personal data treatment. From this visit, a one-month screening period will begin, during which each participant's body weight will be monitored to assess weight stability. Body weight will be measured at the initial visit (T-28), reassessed after 14 days (self-recorded by the participant), and confirmed at the baseline visit. During this visit, a retrospective diary of eating habits and physical activity will be completed to collect information on dietary habits and physical activity.



Subjects will also be provided with a daily food and physical activity diary to record their habitual dietary intake and lifestyle patterns (to be completed every 14 days) during the screening period, in order to ensure that their habits do not change.

The Principal Investigator or designated personnel will schedule the date of the baseline visit.

8.4. Baseline visit (T0)

After 28 ± 2 days from the initial visit, subjects will return to the study site and will be visited by the Principal Investigator or designated personnel who will verify whether each participant meets all inclusion and exclusion criteria, including confirmation of stable body weight. Subjects will return the completed diaries from the screening phase.

Body weight, waist circumference, hip circumference, and Fat Mass will be measured. Body Mass Index (BMI) will be calculated.

According to the predefined randomization list, 33 subjects will be allocated to the active product group and 33 subjects to the placebo group. Each subject will receive a quantity of product sufficient for at least 28 days of treatment. Subjects will be instructed to take two capsules per day, 30 minutes before dinner, with a glass of water, for 84 consecutive days. They will also be provided with diaries to record their habitual dietary intake and physical activity throughout the entire study period (the diaries will be completed every 14 days and returned monthly).

Participants will be instructed to return any unused product after 1 month, at the follow-up visit T28.

The Principal Investigator or designated personnel will set the date of the follow-up visit.

8.5. Follow-up visit (T14: after 14 ± 2 days)

After 14 days (± 2 days) of product intake subjects will be visited by the Principal Investigator or designated personnel who will assess whether each participant still meets all inclusion and exclusion criteria.

Body weight, waist circumference, hip circumference, and Fat Mass will be measured. Body Mass Index (BMI) will be calculated. The subjects will complete a self-evaluation questionnaire.

The Principal Investigator or designated personnel will set the date of the follow-up visit.

8.6. Follow-up visit (T28: after 28 ± 2 days)

After 28 days (± 2 days) of product intake subjects will be visited by the Principal Investigator or designated personnel who will assess whether each participant still meets all inclusion and exclusion criteria.

The subjects will return the completed diaries. Body weight, waist circumference, hip circumference, and Fat Mass will be measured. Body Mass Index (BMI) will be calculated. The subjects will complete a self-evaluation questionnaire.

To assess the compliance, unused product samples will be collected and counted. Subjects will receive enough amount of the same product for at least 28 days of treatment, and they be advised to bring back the advanced products at the next visit.

The Principal Investigator or designated personnel will set the date of the follow-up visit.

8.7. Follow-up visit (T56: after 56 ± 2 days)

After 56 days (± 2 days) of product intake subjects will be visited by the Principal Investigator or designated personnel who will assess whether each participant still meets all inclusion and exclusion criteria.

The subjects will return the completed diaries. Body weight, waist circumference, hip circumference, and Fat Mass will be measured. Body Mass Index (BMI) will be calculated. The subjects will complete a self-evaluation questionnaire. To assess the compliance, unused product samples will be collected and counted. Subjects will receive enough amount of the same product for at least 28 days of treatment, and they be advised to bring back the advanced products at the next visit.

The Principal Investigator or designated personnel will set the date of the final visit.

8.8. Final visit (T84: after 84 ± 2 days)

After 84 days (± 2 days) of product intake subjects will be visited by the Principal Investigator or designated personnel who will assess whether each participant still meets all inclusion and exclusion criteria.

The subjects will return the completed diaries. Body weight, waist circumference, hip circumference, and Fat Mass will be measured. Body Mass Index (BMI) will be calculated. The subjects will complete a self-evaluation questionnaire. To assess the compliance, unused product samples will be collected and counted.

NOTES:

The tolerability of the product will be monitored through the reporting of adverse events throughout the entire duration of the study (see paragraph 12).



9. TREATMENT COMPLIANCE

The Principal Investigator and designated personnel will keep a record of products given to subjects and unused products received by subjects during the visits.

Any returned product will be destroyed according to current internal procedures.

Compliance will be calculated as follows:

$$\text{Compliance to treatment} = \frac{\text{number of intake product}}{\text{number of product to intake}} \times 100$$

Subjects will be defined as compliant if they use 80 –120% of the treatment regimen over the 84 days period.

10. ENDPOINTS

10.1 Primary endpoints

10.1.1 Body weight

Body weight will be monitored using a scale. Measurements will be expressed in Kg.

10.1.2 Body Mass Index (BMI)

Body Mass Index (BMI) is an anthropometric index used to classify body weight status. It is calculated using the formula:

$$\text{BMI} = \frac{\text{weight}}{\text{height}^2}$$

where weight is in kilograms and height is in meter.

10.2 Secondary endpoint

10.2.1 Waist circumference

Waist circumference will be measured using a tape. The measurement will be taken with the subject in a standing position, breathing normally, with arms relaxed at the sides. The tape will be positioned horizontally at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest. Results will be recorded in centimeters (cm).

10.2.2 Hip circumference

Hip circumference will be measured using a tape. The measurement will be taken on a subject in a standing position, with the muscles relaxed. The circumference will be measured at the most prominent point of the glutes. Results will be recorded in centimeters (cm).

10.2.3 Fat Mass (FM)

Fat Mass (FM) will be assessed using the BIA 101 ASE device, a Bioelectrical Impedance Analysis (BIA) tool. Measurements will be taken with the Hand-Foot Tetrapolar Technique, with the subject in a supine position and electrodes placed on the right hand and foot. This technique evaluates body composition by analyzing electrical conductivity, providing an estimate of fat mass. Measurements will be expressed in kilograms (kg).

Extracellular Water (ECW), Intracellular Water (ICW), and Lean Mass will also be monitored and are expected to remain stable.

10.2.4 Self-assessment

Subjects are asked to reply to a self-assessment questionnaire (17 questions) to assess the efficacy perceived and the pleasantness of the product. Responses are provided spontaneously, without external influence.

The four possible answers will be: Completely Agree – Agree – Disagree - Completely Disagree (see Annex 3)

11. SUPPORT MATERIAL

None

12. SAFETY ASSESSMENT

The tolerability of the product will be closely followed by the study Principal Investigator during the study. Subjects will have access to the investigator via a contact phone number provided with the study information sheet in case of



intolerance reactions. If a subject reports an event, the Principal Investigator will establish whether it is product-related. If so, report it as an adverse reaction. Any unexpected side effects related to the product will be reported to the sponsor. At the investigator's discretion, the subject may be withdrawn from the study, in which case the side effect will be monitored until it is resolved.

12.1. Causality assessment

There are five levels of causality that can be used to determine whether the event is related to the product.

- Very likely

Clinical signs suggest a link with the product. The reaction follows a clear temporal sequence in relation to the time of product use and rechallenge is positive.

- Likely

Clinical signs suggest a link with the product; the reaction follows a definite reasonable temporal sequence from the time of the product intake and there hasn't been a rechallenge or results of rechallenge are ambiguous. Or clinical signs suggest a link with the product; the reaction follows a partially reasonable or unknown temporal sequence from the time of the product intake and rechallenge is positive. Or, clinical signs only partially suggest or do not suggest a link with the product, the reaction follows a definite reasonable temporal sequence from the time of the product intake and rechallenge is positive.

- Not clearly attributable

Clinical signs suggest a link with the product; the reaction follows a definite reasonable temporal sequence from the time of the product intake and rechallenge is negative. Or clinical signs suggest a link with the product; the reaction follows a partially reasonable or unknown temporal sequence from the time of the product intake and there hasn't been a rechallenge or results of rechallenge are ambiguous. Or clinical signs only partially suggest or do not suggest a link with the product; the reaction follows a definite reasonable temporal sequence from the time of the product intake and there hasn't been a rechallenge or results of rechallenge are ambiguous. Or clinical signs only partially suggest or do not suggest a link with the product; the reaction follows a partially reasonable or unknown temporal sequence from the time of the product intake and rechallenge is positive.

- Unlikely

Clinical signs suggest a link with the product; the reaction follows a partially reasonable or unknown temporal sequence from the time of the product intake and rechallenge is negative. Or clinical signs only partially suggest or do not suggest a link with the product; the time sequence between use of the product and occurrence of the symptoms is compatible; and rechallenge is negative. Or clinical signs only partially suggest or do not suggest a link with the product; the reaction follows a partially reasonable or unknown temporal sequence from the time of the product intake and there hasn't been a rechallenge or results of rechallenge are ambiguous. Or clinical signs only partially suggest or do not suggest a link with the product; the reaction follows a partially reasonable or unknown temporal sequence from the time of the product intake and rechallenge is negative.

- Excluded

Causality can only be excluded if another aetiology has been medically validated or if the time sequence between exposure and the occurrence of signs is incompatible. In case of adverse events, subjects can also contact the Principal Investigator or designated personnel if necessary. If required, they would be assessed by the specialist who would perform the clinical assessment and decide the appropriate measures to take (i.e. medical treatment, withdrawal ...).

12.2. Recording and evaluation of adverse reactions

For each sign, intensity, location, duration (hours, minutes), and frequency are recorded. Moreover, the investigator collects all discomfort or reactions reported by the subjects. Each time a sign (physical or functional) appears (new sign or worsened compared to the baseline evaluation i.e. evaluation on the first day of the study), a reaction is recorded. All the reactions observed by the specialist and reported by the subject are recorded. The following information are recorded: i) subject characteristics, ii) details about study product (product code or name, date of first use, way of use), iii) description of the reaction (functional and physical signs, intensity of the signs, location, date/time of onset, timeframe between product use and onset of the reaction, date/time of end or duration (hours, minutes), frequency, diagnosis/nature of the reaction), iv) significant medical history, v) concomitant events: cutaneous diseases, medical treatments, products application, food, external factors (weather conditions), other diseases, vi) outcome and actions taken (way of use modification, temporary interruption, definitively discontinuation, medical treatment, care), and viii) relationship to the product (causality assessment). This assessment is done in conjunction with clinical expertise, and knowledge of the product (type of product, conditions of use...).



12.3. Documentation of Adverse Event and Serious Adverse Event

All Adverse Events considered likely to be related to the study product, as well as all Serious Adverse Events, will be documented in the data collection sheet and included in the report of the study. If no Adverse Events occur, the report will explicitly state that no side effects were observed during the study.

12.4. Notification to the Sponsor

Any adverse events occurring during the study or after the study will be reported to the Sponsor's vigilance officer by e-mail carolina.galli@roelmihpc.com with a copy to the project manager, using the appropriate notification forms. Serious adverse events will be reported within 24 hours of observation, and adverse events related to the product will be reported as soon as possible. If pictures of the reactions are available, these will be included in the notification.

12.5. Follow-up procedures

Any adverse events or serious adverse events related to the product will be followed up until they are resolved or stabilised. To inform the sponsor's vigilance officer of any new information, the investigator will use the appropriate forms, which will be filled in with the results collected from the examination carried out. Reports of hospitalisation will be enclosed with the notification form.

12.6. Definitions

Adverse Event (AE): An Adverse Event is any untoward medical occurrence in a clinical investigation subject administered a test product and that does not necessarily have a causal relationship with this treatment. 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 test product, whether related to the test product.

Serious Adverse Event (SAE): A Serious Adverse Event is any untoward medical occurrence that: i) results in death, ii) is life-threatening, iii) requires inpatient hospitalization or prolongation of existing hospitalization, iv) results in persistent or significant disability/incapacity, or v) is a congenital anomaly/birth defect.

13. DATA HANDLING AND RECORD KEEPING**13.1. Data collection**

Data will be recorded in paper and/or electronic data collection sheets. The Principal Investigator, or appropriately qualified staff authorized by the Investigator, will be responsible for completing the data collection sheets. Paper forms will be completed in blue ballpoint pen, while electronic data capture will be performed using Microsoft® Office 365. The Principal Investigator will review the data collection sheets and all adverse event reporting forms, attesting to the accuracy and completeness of the information. Any corrections made to the data collection sheets or source documents must be performed by the responsible staff member or an authorized delegate in a manner that does not obscure the original entry. For paper forms, all corrections must be dated and initialled by study site personnel. For electronic data capture, all modifications will be automatically tracked. Where the reason for a correction is not self-evident, an explanatory note must be provided.

Data entry and quality control will be performed by two different persons. The Principal Investigator remains ultimately responsible for all recorded data.

In line with Good Clinical Practice, the following definitions apply to clarify the nature and origin of recorded information:

- **Source Data:** all original records and certified copies of original records of clinical findings, observations, or other activities necessary for the reconstruction and evaluation of the trial. Source data are contained within source documents (i.e., original records or certified copies).
- **Source Documents:** original documents, data, and records, such as subject files, data collection sheets, notes, or evaluation checklists.

13.2. Quality assurance

All study-related files (including data collection sheets, the protocol, results, the final report, and other study documents) are subject to quality assurance procedures in compliance with regulatory requirements. Investigating sites authorize inspections by Regulatory Authorities and audits or controls by the Sponsor, granting access to raw data as needed.



13.3. Archiving and Retention

An original copy of all study documentation (signed protocol, Sponsor's safety assessment letter, case report forms, raw data, administrative file including all correspondence, etc.) will be retained in the records of Complife Srl for 10 years. The archives will only be destroyed after receipt of written and signed authorization from the Sponsor. However, documents will be kept for a longer period if required by applicable regulatory requirements or by agreement with the Sponsor. The Investigator must take appropriate measures to prevent accidental or premature destruction of these documents. Archiving arrangements will be defined at site close-out. The Sponsor will inform Complife Srl in writing when the documents are no longer required to be kept.

14. STATISTIC

14.1. Study population for analysis

The analysis will be conducted on the Per Protocol population. The per-protocol (PP) population is defined as all subjects who will complete the study without any major protocol violations. Subjects will be excluded from the per-protocol population if: they miss the one or more evaluation visit; or they do not used the product properly during the study period (as reported by the subject itself).

Any drop-outs and the reason for each drop-out will be reported in the final report.

14.2. Descriptive analysis

Demographic data and eligibility variables will be collected and reported in a Microsoft® Excel spreadsheet together with the randomization list and will be summarized using: i) mean value and/or median value; ii) standard error and/or interquartile range; iii) minimum value; iv) maximum value.

Endpoint variables will be recorded in a Microsoft® Excel spreadsheet, graphically represented, and analyzed using: i) mean value and/or median value; ii) standard error and/or interquartile range; iii) minimum value; iv) maximum value; v) individual variation or percentage variation versus baseline; vi) mean and/or median variation versus baseline.

14.3. Inferential statistical analysis

To assess the efficacy of the product, inferential statistical analyses will be performed on the endpoints with the exception of the self-evaluation questionnaires.

For each endpoint, appropriate parametric or non-parametric technique will be applied to compare active and placebo product and to evaluate their effect over time.

No inferential analysis by subgroup will be provided.

The significance level (α) will be set at 0,05.

Statistical analysis will be performed using NCSS 10 data analysis (Copyright © 1983-2015, NCSS, LLC.) or RStudio (Copyright © 2009-2025 Posit Software, PBC).

15. ADMINISTRATIVE ASPECTS

15.1. Publication policy

The results of the study as well as any other data disclosed or generated in the context of the study are confidential. Any publication in relation to the study shall be subject to Sponsor's prior written approval and authorization of the Principal Investigator of the study.

15.2. Contractual and financial agreements

The Principal Investigator and the Sponsor sign a clinical study agreement prior to the start of the study, outlining overall sponsor and investigator responsibilities in relation to the study. Financial remuneration covers the cost per included subject, based on the calculated costs of performing the study assessments in accordance with the protocol, and the terms of payment are described in the contract.

15.3. Insurance

Product liability insurance may be provided by the Sponsor.



ANNEX 1- List of Potential Study Sites

Complife Italia SRL

- Piazzale Siena 11, 20146 – Milano (MI), Italy
- Via Fratelli Signorelli 159, 20024 – Garbagnate Milanese (MI), Italy
- Via Angelini 21, 27028 – S. Martino Siccomario (PV), Italy
- Corso San Maurizio, 25 – 13900 Biella (BI), Italy
- Via Mortara 171, 44121 – Ferrara (FE), Italy

Nutrastech SRL

Via Francesco Todaro 20/22, 87036 - Rende (CS), Italy

Complife France SAS

LE QUADRILLE, 18 rue Jacqueline Auriol, 69008 – Lyon, France

Complife South Africa Pty LTD

Unit H 3, The Willows Office Park, c/o Simon Vermooten and farm Roads, The Willows – Pretoria, South Africa

Complife Iberia SLU

Calle del Capitán Arenas 3, Local 3, 08028 – Barcelona, Spain

Complife (Beijing) Testing Technology Co., Ltd

Beizhan North Street 17, Room 902, Xicheng District, 100089 – Beijing, China

Complife Romania SRL

Strada Orzari 92A, 021554 – București, Romania



ANNEX 2- Labelling

The site where the study will be conducted will label the product in the local language.

The specifications are provided below in English (Figure 1, figure 2), as well as those of the Principal study center (Figure 3, figure 4):

Figure 1. Active label

	Food supplement	
Use in accordance with the directions for use Sample for testing purposes only	Product 1 Batch No.: L2S3211025 A1 Expiry date: 10/2027 IT0008587/25 Directions for use: two capsules per day, half an hour before dinner, with a glass of water.	Study Site _____
WARNINGS:--		

Figure 2. Placebo

	Food supplement	
Use in accordance with the directions for use Sample for testing purposes only	Product 2 Batch No.: L2S3211025 A2 Expiry date: 10/2027 IT0008587/25 Directions for use: two capsules per day, half an hour before dinner, with a glass of water.	Study Site _____
WARNINGS:--		

Figure3. Active label

	Supliment alimentar	
A se utiliza conform instrucțiunilor de utilizare Mostă de destinație exclusiv testării	Produs 1 Lot Nr.: L2S3211025 A1 Data de expirare: 10/2027 IT0008587/25 Instrucțiuni de utilizare: două capsule pe zi, cu o jumătate de oră înainte de cină, cu un pahar cu apă.	Complife Romania SRL, Strada Orzan 92A, 021554 - Bucuresti, Romania
PRECAUȚII: -		

Figure 4. Placebo

	Supliment alimentar	
A se utiliza conform instrucțiunilor de utilizare Mostă de destinație exclusiv testării	Produs 2 Lot Nr.: L2S3211025 A2 Data expirare: 10/2027 IT0008587/25 Instrucțiuni de utilizare: două capsule pe zi, cu o jumătate de oră înainte de cină, cu un pahar cu apă	Complife Romania SRL, Strada Orzan 92A, 021554 - Bucuresti, Romania
PRECAUȚII: -		



ANNEX 3- Self-assessment

English Version:

1. I feel I can better control my food cravings during the day
(Completely Agree – Agree – Disagree – Completely Disagree)
2. I feel fuller for longer after meals
(Completely Agree – Agree – Disagree – Completely Disagree)
3. I experience fewer hunger sensations between meals
(Completely Agree – Agree – Disagree – Completely Disagree)
4. I am better able to stop eating a food I enjoy before feeling overly full
(Completely Agree – Agree – Disagree – Completely Disagree)
5. When I experience a strong craving for a specific food, I find it easier to resist
(Completely Agree – Agree – Disagree – Completely Disagree)
6. If I cannot eat the food I crave at a particular moment, I feel less frustrated or irritable
(Completely Agree – Agree – Disagree – Completely Disagree)
7. The sight or smell of appetizing foods triggers less urgent cravings
(Completely Agree – Agree – Disagree – Completely Disagree)
8. I feel less need to eat a snack before going to bed
(Completely Agree – Agree – Disagree – Completely Disagree)
9. I feel less bloated
(Completely Agree – Agree – Disagree – Completely Disagree)
10. I feel slimmer
(Completely Agree – Agree – Disagree – Completely Disagree)
11. I feel more comfortable with my body shape
(Completely Agree – Agree – Disagree – Completely Disagree)
12. I feel lighter overall
(Completely Agree – Agree – Disagree – Completely Disagree)
13. My clothes fit better
(Completely Agree – Agree – Disagree – Completely Disagree)
14. I feel better in general, not just in terms of weight
(Completely Agree – Agree – Disagree – Completely Disagree)



15. The product is easy to take
(Completely Agree – Agree – Disagree – Completely Disagree)
16. The product has caused fewer discomforts or adverse effects
(Completely Agree – Agree – Disagree – Completely Disagree)
17. I would be more likely to buy the product and recommend it to others
(Completely Agree – Agree – Disagree – Completely Disagree)

Romanian Version

1. **Simt că pot controla mai bine pofta de mâncare pe parcursul zilei.**
(Total de acord – De acord – Dezacord – Dezacord total)
2. Mă simt sătul(ă) pentru mai mult timp după mese.
(Total de acord – De acord – Dezacord – Dezacord total)
3. Experimentez mai puține senzații de foame între mese.
(Total de acord – De acord – Dezacord – Dezacord total)
4. Pot să mă opresc mai ușor din a mânca un aliment care îmi place înainte de a mă simți exagerat de plin(ă).
(Total de acord – De acord – Dezacord – Dezacord total)
5. Când am o poftă puternică de un anumit aliment, îmi este mai ușor să rezist.
(Total de acord – De acord – Dezacord – Dezacord total)
6. Dacă nu pot mânca alimentul la care poftesc într-un anumit moment, mă simt mai puțin frustrat(ă) sau iritat(ă).
(Total de acord – De acord – Dezacord – Dezacord total)
7. Aspectul sau mirosul alimentelor apetisante îmi provoacă pofte mai puțin urgente.
(Total de acord – De acord – Dezacord – Dezacord total)
8. Simt mai puțin nevoia de a lua o gustare înainte de culcare.
(Total de acord – De acord – Dezacord – Dezacord total)
9. Mă simt mai puțin balonat(ă).
(Total de acord – De acord – Dezacord – Dezacord total)
10. Mă simt mai slab(ă).
(Total de acord – De acord – Dezacord – Dezacord total)
11. Mă simt mai confortabil cu aspectul corpului meu.
(Total de acord – De acord – Dezacord – Dezacord total)



12. Mă simt mai ușor/ușoară în general.

(Total de acord – De acord – Dezacord – Dezacord total)

13. Hainele îmi vin mai bine.

(Total de acord – De acord – Dezacord – Dezacord total)

14. Mă simt mai bine în general, nu doar în ceea ce privește greutatea.

(Total de acord – De acord – Dezacord – Dezacord total)

15. Produsul este ușor de administrat.

(Total de acord – De acord – Dezacord – Dezacord total)

16. Produsul a cauzat mai puține neplăceri sau efecte adverse.

(Total de acord – De acord – Dezacord – Dezacord total)

17. Aș fi mai dispus(ă) să cumpăr produsul și să-l recomand altora.

(Total de acord – De acord – Dezacord – Dezacord total)

