Section on Protection of Human Subjects (this Human Subjects Research meets the definition of non-exempt Human Subjects Research)

PROTECTION OF HUMAN SUBJECTS

Risks to Human Subjects

a. ***Human Subjects Involvement, Characteristics, and Design***

- **Justification:** Human subject data during weight loss a requirement to validate the predictive power of the mathematical model to estimate energy intake during caloric restriction. In addition, determining what characteristics lead to larger percentages of compliance to diets requires human subject data with a broad set of markers such as demographic, psychological, and health characteristics during weight loss. In addition, many subjects cycle between positive and negative energy balance during weight loss. Data is required for accurate parameter estimation during weight cycling.
- **Characteristics of population:**

Study(Name and location)	**Male (N)**	**Female (N)**	**Age (yrs)**	**Height (cm)**	**Baseline Weight (kg)**	**Race** **W=White** **AA=African American** **L=Hispanic**
The Comprehensive Assesment of Long-Term Effects of Reducing Intake of Energy (CALERIE) PHASE I Pennington Biomedical Research Center, Baton Rouge, LA	10	13	40.2±50.1	170.9±9.3	83.3±11.8	60%W 30%AA 8%L 2%Other
Merck Placebo Arm Merck & Co, Rahway, NJ	3300 (breakdown by gender not available at this time)		≥21	Mean data not known at this time	Inclusion criteria required subjects with BMI≥27	Breakdown not available yet-database is in preparation. No race was excluded in inclusion

						criteria for this study.
Westerterp Weight Loss Data Maastrich University Medical Centre, The Netherlands	54	10	36.6±2.3	170.1±5.4	88.3±1.3	100%W
Racette University of Wisconsin-Madison		13	39.4±5.2	164.6±5.7	90.6±9.6	100%W
Levine Overfeeding Mayo Clinic	10	12	38.1±7.8	170.2±8.1	82.9±19.6	100%W
Kiel Christian-Albrechts-University, Kiel, Germany	10		25±2.0	181±0.1	74.8±8.9	100%W

- **Criteria for inclusion** We are restricting our attention to subjects who have reduced their weight through solely caloric restriction and considering only the subset database from these studies with this requirement. For the weight cycling study, we are limited to the available subjects.
- **Collaborating sites and data management** The collaborating sites are Pennington Biomedical Research Center, Mayo Clinic, Merck & Co., Maastrich University Medical Centre, The Netherlands, Christian-Albrechts University, Kiel, Germany, and University of Wisconsin. The human subject data will be obtained directly from stored spreadsheets in which all subjects are identified through a numerical code. The code does not have any identifying links that would make it possible to identify the subject. The spreadsheets will be distributed to the investigators in the proposed research electronically through secure FTP transfer and stored on the investigator's work site computer.

b. ***Sources of Materials***

- Description of research material obtained:

Study(Name and location)	**Data obtained from study**

The Comprehensive Assesment of Long-Term Effects of Reducing Intake of Energy (CALERIE) PHASE I Pennington Biomedical Research Center, Baton Rouge, LA	• Bi-weekly weights during weight loss period • Age, height, gender, and race at baseline • DXA measurements of body composition during weight loss period • DLW measurements of energy expenditures during weight loss period • Measurements of resting metabolic rate during weight loss period • Energy intake by food provided from metabolic kitchen during participant in-feeding period (first 3 months) • Target energy intake designated by study
Merck Placebo Arm Merck & Co, Rahway, NJ	• Bi-weekly weights during weight loss period • Age, height, gender, and race at baseline • DXA measurements of body composition during weight loss period • DLW measurements of energy expenditures during weight loss period • Measurements of resting metabolic rate during weight loss period • Energy intake by food provided from metabolic kitchen during participant in-feeding period (first 3 months) • Target energy intake designated by study • Mental health data (whether the subject suffers from depression) • Hormone levels during weight loss period • EKG results during weight loss period • Medical history of subjects
Westerterp Weight Loss Data Maastrich University Medical Centre, The Netherlands	• Bi-weekly weights during weight loss period • Age, height, gender, and race at baseline • DLW measurements of energy expenditures during weight loss period • Measurements of resting metabolic rate during weight loss period • Target energy intake designated by study
Racette University of Wisconsin-Madison	• Final weights at end of weight loss period • Age, height, gender, and race at baseline • DLW measurements of energy expenditures during weight loss period • Measurements of resting metabolic rate during weight loss period • Target energy intake designated by study
Levine Overfeeding	• Bi-weekly weights during weight gain period • Age, height, gender, and race at baseline • DXA measurements of body composition during weight loss period • DLW measurements of energy expenditures during weight loss

	period • Measurements of resting metabolic rate during weight gain period • Target energy intake designated by study
Christian-Albrechts-University, Kiel, Germany	• Resting metabolic rate • Physical Activity • Bi-weekly body mass • Age and height at baseline • Body composition during weight cycling

- **Researchers who have access to individually identifiable private information:** The key investigator at the study site is the only researcher with access to individually identifiable private information about the human subjects.
- **Data management on site:** All data collected at a site is managed by a office of data management and needs to be requested by the key investigator at the site.

c. ***Potential Risks***

- It is possible that when the model energy intake estimates indicate non-adherence to dietary protocols the revelation may be distressing to subjects who participated in the study and learn of the results through published material. The level of discomfort will be hard to measure unless a subject from the study contacts the site on their own.

Adequacy of Protection Against Risks

a. ***Recruitment and Informed Consent***

Informed Consent: All subjects in the studies we are examining provided informed consent which was reviewed by governing IRB except for the Westerterp studies and the Kiel study. The Westerterp studies conformed to the standards set by the Declaration of Helsinki, obtained subject written informed consent, and were approved by the University of Maastricht Ethics Committee. The Kiel study protocol was approved by the ethical committee of the Christian-Albrechts-Universitat zu Kiel.

b. ***Protections Against Risk***

- The on-site investigator will only use coded identifiers to designate subject data and the subject data will be distributed using these codes.

4.1.3 Potential Benefits of the Proposed Research to Human Subjects and Others

- **Benefits to Others**

  The potential benefits to future research participants is to relieve the burden of clinically intense measures such as DXA exams and DLW measurements by providing a non-invasive method of determining actual energy intake during weight loss.

- **Reasonable Risks**

  Weight loss research studies require knowledge of energy intake. Without this variable, the study is making assumptions about subject intake which cannot be measured. The

subject study data we are using required large amounts of participant time and effort to collect approximate measures of energy intake. The benefit of alleviating intense data collection for future weight loss subjects outweighs the risk of discomfort from knowledge of true adherence to diets.

4.1.4 Importance of the Knowledge to be Gained

- **Importance of knowledge to be gained** Weight loss studies based on the results of this research will now have a method to measure adherence that is reliable, inexpensive, and non-invasive. Moreover, non-adherent subjects can still contribute to study results since the model will be able to estimate the amount of energy intake a subject has exceeded by.

Inclusion of Women and Minorities

The CALERIE Phase I and Levine Overfeeding studies include approximately 50% representation by each gender. We do not at this time have the distribution of gender in the Merck database. We require representation by both genders to determine conclusions based on model results.

A. ***One gender:***

The Racette study, Kiel study, and portions of the Westerterp studies were collected using one gender only.

B. ***Minority groups or subgroups:***

Some minority groups or subgroups are excluded or poorly represented because the geographical location of the study has only limited numbers of these minority groups who would be eligible for the study. We compensate for the lack of diversity in a single study by pooling data from several studies which includes a broad set of minority groups. We are seeking sources of data that are diversified by race as they provide more validation for the model and more markers of possible correlations to adherence.