Does Dapagliflozin Provide Additional Health Benefits To Dietary Counseling For Weight Loss?

NCT03180489

Unique Protocol ID: 17-7147H

22 March 2018

Research Integrity & Compliance Review Office
Office of the Vice President for Research
321 General Services Building - Campus Delivery 2011 eprotocol
TEL: (970) 491-1553
FAX: (970) 491-2293

NOTICE OF APPROVAL FOR HUMAN RESEARCH

DATE:	March 26, 2018
TO:	Bell, Christopher, Health and Exercise Science Ackerman, Alissa, 1582 Dept Hlth & Exer Sci, Braun, Barry, Health and Exercise Science, Melby, Chris, Food Science & Human Nutrition, Biela, Laurie, Health and Exercise Science
FROM:	Felton-Noyle, Tammy, IRB Assistant Coor, CSU IRB 1
PROTOCOL TITLE:	Does Dapagliflozin Provide Additional Health Benefits To Dietary Counseling For Weight Loss? Clinical Research Protocol Title: Dapagliflozin Promotes Favorable Health Benefits That Are Independent Of Weight Loss In Overweight/Obese Adults
FUNDING SOURCE:	Funding - Grants/Contracts
PROTOCOL NUMBER:	17-7147H
APPROVAL PERIOD:	Approval Date: March 22, 2018 Expiration Date: March 21, 2019

The CSU Institutional Review Board (IRB) for the protection of human subjects has reviewed the protocol entitled: Does Dapagliflozin Provide Additional Health Benefits To Dietary Counseling For Weight Loss? Clinical Research Protocol Title: Dapagliflozin Promotes Favorable Health Benefits That Are Independent Of Weight Loss In Overweight/Obese Adults. The project has been approved for the procedures and subjects described in the protocol. This protocol must be reviewed for renewal on a yearly basis for as long as the research remains active. Should the protocol not be renewed before expiration, all activities must cease until the protocol has been re-reviewed.

Important Reminder: If you will consent your participants with a signed consent document, it is your responsibility to use the consent form that has been finalized and uploaded into the consent section of eProtocol by the IRB coordinators. Failure to use the finalized consent form available to you in eProtocol is a reportable protocol violation.

If approval did not accompany a proposal when it was submitted to a sponsor, it is the PI's responsibility to provide the sponsor with the approval notice.

This approval is issued under Colorado State University's Federal Wide Assurance 00000647 with the Office for Human Research Protections (OHRP). If you have any questions regarding your obligations under CSU's Assurance, please do not hesitate to contact us.

Please direct any questions about the IRB's actions on this project to:

IRB Office - (970) 491-1553; RICRO_IRB@mail.Colostate.edu
Evelyn Swiss, Senior IRB Coordinator - (970) 491-1381; Evelyn.Swiss@Colostate.edu
Tammy Felton-Noyle, IRB Biomedical Coordinator - (970) 491-1655; Tammy.Felton-Noyle@Colostate.edu

Felton-Noyle, Tammy

Continuing renewal has been reviewed at the convened meeting on March 22, 2018. Continuation has been approved to recruit the remaining participants with the approved recruitment and consent procedures. This renewal acknowledges an

Colorado State University
Knowledge to Go Places

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error in the initial approval letter generated by the IRB in that it should have stated approval for recruitment of 60 participants. This renewal includes two deviation reports that were assessed and two proposed amendments in response to the reports. These amendments include expanding enrollment to include participants with 10-day course of antibiotics with medical monitor support and increased enrollment a total of 200 participants. This number is to ensure participants completing the study will amount to 60 individuals. This is in response to large number of screen fails and withdrawals. Approved documents include: Consent, version dated 01March2018.

Approval Period:	March 22, 2018 through March 21, 2019
Review Type:	FULLBOARD
IRB Number:	00010468
Funding:	AstraZeneca

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Date Submitted: 03/01/2018

Approval Period: Draft

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* * * Continuing review * * *

To renew your protocol: 1. Complete this one-page form; 2. If necessary, update any sections of the protocol that need to be updated for the upcoming year (e.g., change in personnel, location); 3. Electronically "sign" the application by clicking in the check box on the bottom of the "Obligations" page; 4. Remember to click "Submit Form" and confirm your intent to submit by clicking "OK" so that the IRB administrators receive your application. You must answer each question. Input N/A to answer any questions that are not applicable. NOTE: Documents that contain much of the information required to answer the participant number questions below can be found in the "Event History" section of each protocol. The status on your homepage will be "Submitted to IRB" when your submission is successful. IMPORTANT: If the Department Head has changed since your last approval, please be sure to update the Department Head listing on the personnel Information screen of your protocol.

1. Summary: Number of Participants Associated with the Protocol:

a. Total number of participants approved to date:

We requested 60 overweight/obese adult volunteers (men and women) will be enrolled. Please see 1.e.

b. Number of participants studied since the last approval date:

80

c. Total number of participants studied since the beginning of the project:

80

d. Number of participants remaining to study (total number of participants approved LESS the total number of participants studied to date):

Please see 1.e.

e. Please explain if there is a discrepancy in participant numbers (e.g., more participants responded to a survey than had been approved):

We originally requested 60 overweight/obese adult volunteers (men and women) will be enrolled. Additionally it was stated in the protocol- “However, the number enrolled maybe higher in the event of enrollment of replacement subjects for dropout(s) that discontinued for reasons other than an adverse event due to study medication. In the event of a replacement subject being enrolled, this subject will complete all visits”.
Please also note- the approval letter states approval for 50. To clarify the above statement, as a part of this continuing review we are amending the protocol to request recruitment of a total of

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200 individuals.

2. a. **Reasons and number of withdrawals from the research (both subject and investigator initiated) since the last approval date.**

Declined participation:13
Non-compliance: 2
Screened out: 9
Moved to 14-5529H: 3

b. **Number of subjects lost to follow-up since the beginning of the study.**

14

c. **Please summarize any protocol deviations/violations or unanticipated problems (UPs)/adverse events (AEs) since the last continuing review or original approval (if this is your first continuing review). Please indicate if any of the unanticipated problems/events are being reported to the IRB for the first time. If you have or will make changes to your protocol as a result of any unanticipated problem/event or adverse event, please summarize those changes in Question #5 below.**

Please see adverse event log in the attachments.
Please see deviations: Course of antibiotics was report verbally to IRB on 1/31/2018. Wrong pill bottle 1st, Extended Invention Period, and Duration of invention are first time reports.

e. **Complaints about the research during the last year.**

none

3. **A summary of any recent findings, literature, or other relevant information (especially pertaining to risks), if applicable.**

none

4. **Description of the remainder of project:**

Y **Do you plan to recruit more subjects?**

If "No," have all subjects completed all research-related interventions? Note: Protocols must be renewed to continue recruiting participants and/or collect data from already recruited participants.

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renewed to continue recruiting participants and/or collect data from already recruited participants.

N Are you only performing data analysis? NOTE: If you are analyzing data with no identifiers (i.e., you cannot link your data to individuals), you can close your protocol by submitting a Final Report.

N Does this protocol have a Data Satety Monitoring Board (DSMB)?

If you do have a DSMB, have reports been submitted to the IRB and/or the Sponsor? Upload any DSMB reports that have not yet been submitted to the IRB since the approval or last continuing review.

5. Summarize all approved changes in the protocol since the last continuing review or since the original approval (if this is your first continuing review). For example: Have you amended your protocol during the past year? Are you requesting to make any changes for the upcoming year? Have you included any changes as a result of an unanticipated problem/event or Adverse events (AE)? Have there been any personnel changes in the past year (including a change in department head)?

Amendment 1: Minor changes to include the description of the 3-day dietary recall record and clarifications to counselling activities on visits 28 and 29 and nutritional counselor compliance documentation was uploaded.

Amendment 2: Minor update to recruitment flyer.

Request amendment: As per deviation uploaded in the attachments, to allow for a 10 day course (from 7 day course) of antibiotics.Antibiotics prescribed for any serious condition will be reviewed on case by case basis no matter the course prescribed. As a part of this continuing review we are amending the protocol to request recruitment of a total of 200 individuals.

If necessary, proceed to the appropriate section(s) of the protocol and make your requested changes. Remember that if you are requesting to revise a document that is already attached, you must delete the already attached document and upload the revised document.

6. List of Protocol Sections (and questions) that have been changed/modified.

Protocol and consent to allow for a 10 day course of antibiotics.
Added personnel- RICRO Please Add Elizabeth Thomson and Hayden Schoenberg to other key research personnel, we don't have the option to add additional personnel.
Protocol to clarify request enrollment to 200.

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* * * Personnel Information * * *

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IMPORTANT NOTE: Mandatory Personnel on a protocol are: Principal Investigator and Department Head. Only the Principal Investigator can submit the protocol; although other personnel listed on the protocol can create the protocol. Human Subjects Protection Training is mandatory for Principal Investigator, Co-Principal Investigator, and Key Personnel (as defined by NIH). Training must be updated every three (3) years.

Principal Investigator Mandatory

Name of Principal Investigator (Faculty, Staff or Postdoc)	Degree	Title
Bell, Christopher		Associate Professor
Email	**Phone**	**Fax**
Christopher.Bell@ColoState.EDU	(970) 491-7522	
Department Name	**Campus Delivery Code**	
Health and Exercise Science	1582	
Human Subjects Training Completed? PIs must complete training every three (3) years.		Y

CO-Principal Investigator

Name of Co-Principal Investigator (This could be another faculty or a Master's or Ph.D. student)	Degree	Title
Melby, Chris		Professor
Email	**Phone**	**Fax**
Chris.Melby@colostate.edu	(970) 491-6736	
Department Name	**Campus Delivery Code**	
Food Science & Human Nutrition		
Human Subjects Training Completed? Training is required for Co-PI. Training must be updated every three (3) years.		Y

No training data is available.

Additional Co-Principal Investigator

Name of Additional Co-Principal Investigator	Degree	Title
Luckasen, Gary	MD	Medical Monitor

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Email	Phone	Fax
gary.luckasen@uchealth.org		
Department Name	**Campus Delivery Code (CSU) or off-campus mailing address**	
1582 Dept Hlth & Exer Sci		
Human Subjects Training Completed? Training is required for Co-PI. Training must be updated every three (3) years.		Y

Department Head Mandatory

Name of Department Head	Degree	Title
Braun, Barry		Professor
Email	**Phone**	**Fax**
Barry.Braun@colostate.edu		
Department Name	**Campus Delivery Code**	
Health and Exercise Science		
Human Subjects Training Completed?? Training is not required for Department Head. Select "No" if you do not know if your Department Head has completed training or not.		

Administrative Contact

Name of Administrative Contact, Project Director, or Lab Coordinator	Degree:	Title
Biela, Laurie		Research Associate III
Email	**Phone**	**Fax**
Laurie.Biela@colostate.edu		
Department Name	**Campus Delivery Code**	
Health and Exercise Science		
Human Subjects Training Completed? Training is not required for Administrative Contacts		Y

No training data is available.

Other Researcher or Key Personnel

Protocol Title: Does Dapagliflozin Provide Additional Health Benefits To Dietary Counseling For Weight Loss?
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Name of Other Researcher (NOTE: Anyone listed in this role will have View Mode access only)	Degree	Title
Ackerman, Alissa		RA II - Integrative Biology Study Coordinator

Email	Phone	Fax
Alissa.Ackerman@colostate.edu		

Department Name	Campus Delivery Code (CSU) or off-campus mailing address
1582 Dept Hlth & Exer Sci	1582

Human Subjects Training Completed? Training is required for all Key Personnel on NIH grants. Training must be updated every three (3) years. Y

No training data is available.

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* * * Subject Population * * *

Subject Population(s) Checklist

Â Select All That Apply - Note that this is your Targeted Population :

- X Adult Volunteers
- Decisionally Challenged
- Elderly
- X Employees
- Fetuses
- Long-Term Patients
- Mentally Disabled
- Minors (under 18)
- Pregnant Women
- Prisoners
- Soldiers
- X Students
- Other (i.e., non-English Speaking or any population that is not specified above)

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* * * Study Location * * *

Study Location(s) Checklist

Select All That Apply - NOTE: Check "Other" and input text: 1.) If your study location is not listed, or 2.) If you would like to list details of your already-checked location (e.g., specific school within a school district)

- [ ] Aims Community College
- [ ] Colorado Department of Public Health & Environment
- [X] Colorado State University
- [ ] Colorado State University - Pueblo Campus
- [ ] Denver Public Schools
- [ ] Greeley/Evans School District
- [ ] Poudre School District
- [ ] University of Colorado Health - North (Formerly -Poudre Valley Health System - PVHS)
- [ ] Rocky Mountain National Park
- [ ] Thompson School District
- [ ] University of Colorado - Boulder
- [ ] University of Colorado - Colorado Springs
- [ ] University of Colorado - Denver
- [ ] University of Colorado Health Sciences Center
- [ ] University of Northern Colorado
- [ ] Other (In the box below, list your study location if not checked above. You may also list details of your already-checked location (e.g., specific school within a school district).

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* * * General Checklist * * *

General Checklist

Select All That Apply :

- [X] Proposed Start Date (cannot be before IRB approval): On receipt of IRB Approval

- [X] Sponsored Project (Check if you will be funded OR if you have or plan to submit a grant application in association with this protocol)
- [ ] NSF Sponsored (Please upload mandatory Data Management Plan in the Attachment section)

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X FDA or EPA-regulated research. Please contact the CSU Quality Assurance Manager, Cat Bens, at 970-491-5445 to determine if your study is under Good Laboratory, Good Clinical, or Good Manufacturing Practices (GLP, GCP, GMP).

Training Grant

X Clinical Trial. To register your trial on Clinicaltrials.gov, please contact Cat Bens, CSU Quality Assurance Manager and Clinical Trails Administrator at: 970-491-5445.

Project is associated with the Colorado School of Public Health - CSPH(faculty and/or student)

Cooperating/Collaborating Institution(s) Institution where recruitment will occur OR Institution where Collaborating PI will conduct associated research.

Interview

X Questionnaire/Survey

X Subjects will be compensated for participation

Thesis or Dissertation Project

X ÃÂ Radioisotopes/radiation-producing machines, even if standard of care. Please contact Jim Abraham, Radiation Safety Officer for questions related to use of all radiation-producing machine: 970-491-3736; james.abraham@colostate.edu. Upload your radiation-use approval (if available) or your Radiation Safety Training certificate in the attachment section.

X Human blood, cells, tissues, or body fluids. You will need to obtain IBC approval if you check this box. For information regarding IBC approval, contact Christine Johnson, IBC Coordinator: christine.johnson@colostate.edu

Tissues to be stored for future research projects

Tissues to be sent out of this institution as part of a research agreement

Human Embryos. You will need to obtain IBC approval if you check this box. For information regarding IBC approval, contact Christine Johnson, IBC Coordinator: christine.johnson@colostate.edu

Human Embryonic Cells? Provide NIH Code Number(s) or state that no federal funding will be used to support this research. You may need to obtain IBC approval if you check this box. For information regarding IBC approval, contact Christine Johnson, IBC Coordinator: christine.johnson@colostate.edu

Use of Patient-related equipment? If Yes, specify what equipment is being used.

Medical equipment used for human patients/subjects also used on animals. For questions regarding animal use approval, contact Elaine Kim, IACUC Senior Coordinator: 491-0236

Protocol involves studying potentially addicting drugs. For questions regarding approval for possession of controlled substances, contact Chris Giglio, DRC Coordinator: 491-4830; Chris.Giglio@colostate.edu.

Investigational drugs, reagents, or chemicals (IND)

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X Commercially available drugs, reagents, or other chemicals administered to subjects (even if they are not being studied)

Investigational Device (IDE)

Cancer Subjects (e.g., clinical trials, behavior/prevention) or Cancer Tissues (e.g., blood, cells, body fluids). You may need to obtain IBC approval if you check this box. For information regarding IBC approval, contact Christine Johnson, IBC Coordinator: christine.johnson@colostate.edu

Other (clarify in text box to the right)

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* * * Funding * * *

Please complete this section if: 1. This protocol will be funded, 2. You have submitted or will submit a grant application associated with this protocol. Please be sure to input your PASS/SP1 number to assist Sponsored Programs in setting up an account for your funds.

If this protocol is funded by the NIH or NSF, or will lead to the regulatory involvement of the FDA or EPA, please be certain you are cognizant of any specific regulatory requirements for data acquisition, storage, retention and sharing, as well as research expenditure allowability, with regard to this IRB protocol.

Funding Checklist

NONE

NOTE: Applicable Federal Grant Application, including competing renewals, must be attached in the Attachment Section (#16). Applicable investigator's brochure and sponsor's protocol must also be attached in section #16 for all industry-sponsored clinical trials.

Funding - Grants/Contracts

Funding Administered By	UNIVERSITY
CSU PASS #	120081
Sponsor's ID # (If known)	
Funded By	Other AstraZeneca
Principal Investigator	Bell
Grant/Contract Title if different from Protocol Title	
	For Federal projects, are contents of this protocol the same as described in Federal proposal application?

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N	Is this an Umbrella protocol?
N	Is this protocol under an Umbrella protocol?

Funding - Fellowships

Funding - Other

Gift Funding

Dept. Funding

Other Funding

*** * * Expedited Paragraphs * * ***

PLEASE READ: This online application is for projects that will be reviewed by the IRB via the expedite or full-board review process. The criteria for expedited review are listed below. Review and check what expedite criteria is/are appropriate for your project. NOTE: If your research involves or may involve greater than minimal risk, an element of deception, or is FDA-regulated research, do NOT check any of the expedited criteria listed below. Your protocol will then be reviewed by the full-board at their next regularly scheduled meeting. If your project meets the exempt criteria, please submit your exempt application via email to: RICRO_IRB@mail.colostate.edu. Information regarding exempt applications can be found here: http://ricro.colostate.edu/IRB/ExemptReview.html

Expedite Criteria:

1. **Clinical studies of drugs and medical devices only when condition (a) or (b) is met.**

   a) **Research on drugs for which an investigational new drug application (21 CFR Part 31,32) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)**

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b) Research on medical devices for which

i) An investigational device exemption application (21 CFR Part 812) is not required; or

ii) The medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

a) From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8- week period and collection may not occur more frequently than 2 times per week; or

b) From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period and collection may not occur more frequently than 2 times per week.

3. Prospective collection of biological specimens for research purposes by non-invasive means.

4. Collection of data through non-invasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

Examples:

a) Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy;

b) Weighing or testing sensory acuity;

c) Magnetic resonance imaging;

d) Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography;

e) Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

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5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this paragraph may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior(including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

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* * * Purpose,Study Procedures,Background * * *

Original Protocol Number (e.g., 07-226H)

Cloned and subsequently modified from 14-5531H

Title (Please indicate if the protocol title is different from the proposal title)

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Complete Sections 1 - 16. Specify N/A as appropriate. Do not leave any required sections blank.

1. Purpose of the study

a) Provide a brief lay summary of the project in <200 words. The lay summary should be readily understandable to the general public, and is, for example, what would be released to a newspaper if requested.

THIS PROTOCOL IS AN AMENDED/SIMPLIFIED VERSION OF IRB PROTOCOL 14-5531H.

Dapagliflozin is a medicine to treat diabetes. Its mechanism of action is via sodium-glucose co-transporter 2 (SGLT2) inhibition. In adults with diabetes, use of sodium-glucose co-transporter 2 inhibitors is associated with moderate weight (fat) loss, in addition to other health benefits, including decreased blood pressure, decreased inflammation, and decreased oxidative stress. It is unclear as to whether these health

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benefits are due to SGLT2 inhibition per se, or as a secondary effect of weight loss. We wish to compare the health benefits of dietary counseling for weight loss with and without concomitant use of an SGLT2 inhibitor.

b) **What does the Investigator(s) hope to learn from the study?**

We wish to learn if:
1. Dapagliflozin (SGLT2 inhibition) provides additional health benefits to dietary counseling for weight loss?

and if,

2. Weight loss associated with dietary counseling and the use of Dapagliflozin (SGLT2 inhibition) is characterized by normal circulating satiety signals rather than the usual diet-induced changes in circulating peptides that increase hunger and reduce satiety.

c) **Proposed Start Date (may not precede IRB approval date):**

On receipt of IRB approval.

2.

Study Procedures (If this is a student project, the methods section of the thesis or dissertation proposal must be attached in section #16 - Attachment section.)

a) **In lay language, describe all the procedures, from screening through end-of-study, that the human subject must undergo in the research project, including study visits, drug treatments, randomization and the procedures that are part of standard of care. Please note: Do NOT respond "See Attachment Section." If you would like to add tables, charts, etc., attach those files in the Attachment section (#16).**

OVERVIEW

This is a randomized, prospective, placebo-controlled, double blind, repeated measures study. 60 overweight/obese adults (body mass index > 27.5 kg/m^2) will be recruited for participation and randomly assigned to one of two 12 week treatments: (1) daily oral administration of Dapagliflozin with dietary counseling to promote weight loss; or, (2) daily oral administration of a placebo with dietary counseling to promote weight loss.

Study participants will report to the research facilities on the Colorado State University main campus on 29 separate occasions:

Visit 1: study participants will undergo screening: medical history, 12-lead electrocardiogram and blood pressure assessment at rest and during incremental exercise to volitional exhaustion, blood sampling, and measurement of body composition.

Visit 2: an oral glucose tolerance test will be performed and resting metabolic rate and blood pressure will

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Clinical Research Protocol Title: Dapagliflozin Promotes Favorable Health Benefits That Are Independent Of Weight Loss In Overweight/Obese Adults

Protocol Type: Biomedical

Date Submitted: 03/01/2018

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be measured.

Visit 3: appetite and hunger will be assessed and participants will be given a 3-dietary record form to complete.

Visits 4-27: 12 weeks of nutrition counseling/weighing (upto 2 visits per week for 12 weeks). Concurrent with these visits, research participants will ingest, on a daily basis, either Dapagliflozin or placebo.

Visit 28: an oral glucose tolerance test will be performed and resting metabolic rate and blood pressure will be measured.

Visit 29: appetite and hunger will be assessed; body composition will be measured, and participants will be given a 3-day dietary record form to complete.

DETAILED DESCRIPTION OF STUDY PROCEDURES

Visit 1: study participants will provide informed consent and undergo screening: medical history, 12-lead electrocardiogram and blood pressure assessment at rest and during incremental exercise to volitional exhaustion, blood sampling, and measurement of body composition.

These screening procedures are standard for our lab. Each of the procedures is currently active in other IRB-approved protocols (e.g. 12-3767H, 08-611H, 14-4756H).

Health History - Potential participants will complete a standardized health history questionnaire that will address past and present medication use, allergies, past and present medical conditions and physical injuries, and habitual use of alcohol and tobacco.

Body composition - Percent body-fat, fat-free mass, total and regional adipose tissue mass, and total bone mineral density will be determined using a whole-body dual energy x-ray absorptiometry scan (DEXA, Model DPX-IQ Lunar Corp., Madison, WI).

Maximal graded exercise stress testing - A 12-lead ECG, arterial blood pressure (brachial sphygmomanometer) will be obtained during quiet resting conditions in the supine and upright sitting positions, and during incremental stationary cycle ergometer or treadmill exercise until volitional fatigue. During exercise, oxygen consumption, carbon dioxide production and ventilation may be determined by indirect calorimetry. All data from these tests will be will be reviewed by a cardiologist. Only those subjects demonstrating no signs or symptoms of disease will be invited to participate in the study.

Blood sampling – Blood (~ 20 ml) will be sampled from an antecubital or hand vein for subsequent analysis of circulating factors pertinent to inclusion/exclusion criteria, including glucose, aspartate aminotransferase, alanine aminotransferase,and total bilirubin. These blood analyses will be performed in on-site (Piccolo Xpress, Abaxis, Union City, CA). Testing for Hepatitis B/C will be performed at a local, external clinical lab (e.g. University of Colorado-Health North). Per the Medical Monitor's discretion follow up blood draws maybe requested.

Visit 2: Resting Metabolic Rate (ventilated hood technique,indirect calorimetry) for 45 minutes and blood pressure will be measured. An oral glucose tolerance test will be performed.

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These procedures are standard for our lab. Each of the procedures is currently active in other IRB-approved protocols (e.g. 14-5201H).

Blood pressure will be determined three times using the left arm via standard procedures. Each assessment will be separated by 3 minutes. The mean of the three measurements will be recorded.

Participants will report to the laboratory early in the morning, following a 12-hour fast and 24-hour abstention from exercise. An intravenous catheter will be inserted into an antecubital or hand vein and kept patent with a saline drip. Following baseline blood sampling for fasting glucose and insulin, participants will ingest 75 g of dextrose dissolved in 250 ml of water over 10-minutes. Venous blood (~ 9 ml) will be sampled at time 0 (baseline) and 5, 10, 15, 20, 30, 45, 60, 75, 90 105 and 120 minutes for determination of concentration of blood glucose (2300 STAT Plus Glucose Lactate Analyzer, YSI Inc., Yellow Springs, Ohio), and insulin (commercially available assay).

Prior to the start of the oral glucose tolerance test, venous blood (~ 20 ml) will be sampled, and plasma/serum and red cells isolated and stored at -70°C for subsequent analysis of circulating markers of inflammation (High sensitive C-Reactive Protein, Tumor Necrosis Factor Alpha, and Interleukin 6) and oxidative stress (oxidized low density lipoprotein concentration, and thiobarbituric acid reactive substances).

Visit 3: Appetite and hunger will be assessed.

These procedures are standard for our lab. Each of the procedures is currently active in other IRB-approved protocols (e.g. 12-3567H).

On a day different to the oral glucose tolerance day, participants will report to the laboratory early in the morning, following a 12-hour fast and 24-hour abstention from exercise. An intravenous catheter will be inserted into an antecubital or hand vein and kept patent with a saline drip. Participants will be provided with a standardized “priming meal” comprising a commercially available, mixed-nutrient liquid meal, dosed to 1 kcal per kg body mass (Ensure, Ross Laboratories, Abbott Park, IL; 64% CHO, 22% fat, 14% protein). One hour following consumption of this priming meal, participants will be presented with a pre-weighed buffet of food from which they will have opportunity to eat ad libitum quantities over a 30 minute period. The remaining uneaten food will be reweighed and participants’ energy and macronutrient intakes will later be determined using the Food Intake Analysis System software (U Texas Health Sciences Center, Houston). Prior to the standardized primer meal, and to the buffet, and then every 60 minutes over 3 hours following the buffet, participants will be asked to rate their perceptions of hunger and satiety using a visual analog scale. At these same time points, venous blood (~ 20 ml) will be sampled, and plasma/serum isolated and stored at -70°C for subsequent determination of concentrations of hunger and satiety hormones (e.g. ghrelin, peptide YY, leptin, and insulin). At the conclusion of these tests, the study participant will give a form in which to record the amounts of food and beverage (except water) they eat and drink for three consecutive days, including 2 week days and 1 weekend day. Upon completion of the food records, the form will be returned to the research team. This information will be used to establish baseline dietary intake and will be useful information for the nutrition counselors seeking to help the participants lose weight.

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Visits 4-27: During the first 6 weeks participants will meet with a study counselor 2 times per week for dietary counseling and measurement of body weight. During the second 6-week period they will meet 1-2 times per week for dietary counseling and body weight measurement, depending on whether or not they are meeting weight loss goals. If they are losing weight as prescribed, they will meet only once per week, but if they are not meeting weight loss goals they will meet 2 times per week. Participants will need to fast for 10 hours prior to the weigh-in. On 2 random counseling occasions between weeks 4 and 10, they will be asked to recall what they ate during the previous 24 hours. If participants fail to achieve their target body weight (within 1 kg or 2.2 lbs) on three consecutive weighing sessions, they will be provided with additional counseling and instructions to aid in achieving your target body weight.

During the first two weeks of the 12 week intervention, participants will ingest one pill daily (5 mg DAPA) and for the remaining 10 weeks participants will ingest 2 pills daily (a total of 10 mg DAPA). On 3 random weigh-in occasions between weeks 4 and 10, participants will be asked to recall what they ate during the previous 24 hours.

Visit 28: Resting Metabolic Rate Test, Oral Glucose Tolerance Test, and Blood Pressure will be measured (e.g. the final week of daily ingestion of Dapagliflozin). See description of Visit 2.

Visit 29: in the HPCRL appetite and hunger will be assessed this visit will occur in week 12 (e.g. during the final week of daily ingestion of Dapagliflozin). Body composition will be measured at this visit or early the following week (e.g. week 13). The study participants will also be given the 3-day food intake record form to be completed and returned to the research team.

b) Explain why human subjects must be used for this project.

Dapagliflozin is approved for human use. Due to potential species differences it would not be appropriate to perform these studies on experimental animals.

c) Alternative Procedures. If the proposed study is a clinical trial of a drug, vaccine, device or treatment, describe alternative procedures, if any, that might be advantageous to the subject. Describe the important potential risks and benefits associated with the alternative procedure(s) or course(s) of treatment. Any standard treatment that is being withheld must be disclosed. This information must be included in the consent form.

There are no appropriate alternative procedures.

d) If the proposed study is a clinical trial of a drug, vaccine, device or treatment, will it be possible to continue the more (most) appropriate therapy for the subject(s) after the conclusion of the study?

Not applicable.

e) Study Endpoint. If the proposed study is a clinical trial of a drug, vaccine, device or treatment, what are the guidelines or end points by which you can evaluate the alternative treatments during the study? If one treatment proves to be clearly more effective than another (or others) will the study be terminated before the projected total subject population has been enrolled? When will the study end if no important

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differences are detected?

Not applicable.

f) State if deception will be used. If so, provide a rationale and describe debriefing procedures. Submit a debriefing script in the Attachment Section (#16).

There will be no deception. Subjects may receive Dapagliflozin or a placebo; they will not know which treatment (Dapagliflozin or placebo) they receive until study completion.

3. Background

a) Describe past experimental and/or clinical findings leading to the formulation of the study, if applicable.

Aside from the metabolic benefits pertaining to glucose control, inhibition of sodium-glucose co-transporter 2 (SGLT2) in patients is associated with moderate weight loss (Tahrani et al., 2011; Chen & Leung, 2013), with some studies reporting up to 4.5 kg decreases in body mass over 12 weeks (Wilding et al., 2009). Animal data are consistent with these observations (Devenny et al., 2012; Liang et al., 2012). SGLT2 inhibition is also associated with other health benefits, including decreased blood pressure (Ferrannini et al., 2010; Dobbins et al., 2012), decreased inflammation (Chen et al., 2012; Tahara et al., 2013, 2014), and decreased oxidative stress (Tahara et al., 2013, 2014)—all health benefits with very important implications for improved physiological function and decreased disease-risk. At present, it is unclear as to whether these health benefits are due to SGLT2 inhibition per se, or as a secondary effect of weight loss.

Noteworthy, the weight loss observed in patients associated with SGLT2 inhibition is not mediated by intentional dietary restriction/intervention. It is more likely to be mediated by the caloric loss associated with the decreased renal tubular reabsorption of glucose, leading to urinary glucose excretions ranging between 45 and 80 g/day (180-320 kcal/d), depending on the drug dose (Idris & Donnelly, 2009). This caloric deficit is not trivial. Typically, caloric deficits of this magnitude require either increased physical activity and/or dietary restriction.

In our original study (Protocol 14-5531H) we learned that when adults with normal, healthy glucose control use SGLT2 inhibitors, the weight loss is negligible. Nevertheless, even in healthy adults, SGLT2 inhibition leads to glucose spillage into urine that may elicit other, non-wight loss mediated health benefits. Therefore in the current project we will study the use of SGLT2 inhibitors combined with dietary counseling for weight loss.

The limitations of the use of dietary restriction for weight loss and, perhaps more importantly, sustained lower weight maintenance, are well described (MacLean et al., 2006; Strohacker et al., 2014). In response to diet-induced weight loss several biological factors, including increased appetite owing to elevation of the orexigenic hormone, ghrelin, and decreased anorexigenic hormones like peptide YY (PYY), promote increased dietary intake and subsequently weight re-gain. However, it is biologically plausible that the weight loss accompanying SGLT2 inhibition may not be accompanied by increased appetite as the unique mechanism of action allows the patient to consume/ingest calories (carbohydrates), but limits the ability for internal storage. That is, during eating, nutrient sensors within the gut release satiety factors to inhibit further dietary intake (Schaeffer et al., 2014; Strohacker et al., 2014). Ingesting calories as carbohydrates while using SGLT2 inhibitors may allow for normal satiety signaling while limiting caloric storage, thus thwarting biological impediments to long-term weight loss.

Protocol Title: Does Dapagliflozin Provide Additional Health Benefits To Dietary Counseling For Weight Loss?
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thwarting biological impediments to long-term weight loss.

Accordingly, in light of the rationale provided, we wish to determine if: 1. Dapagliflozin (SGLT2 inhibition) provides additional health benefits to dietary counseling for weight loss? 2. Weight loss associated with dietary counseling and the use of Dapagliflozin (SGLT2 inhibition) is characterized by normal circulating satiety signals rather than the usual diet-induced changes in circulating peptides that increase hunger and reduce satiety.

REFERENCES (Some of which have been provided as attachments)

Chen L, Klein T & Leung PS. (2012). Effects of combining linagliptin treatment with BI-38335, a novel SGLT2 inhibitor, on pancreatic islet function and inflammation in db/db mice. Curr Mol Med 12, 995-1004.

Chen LH & Leung PS. (2013). Inhibition of the sodium glucose co-transporter-2: its beneficial action and potential combination therapy for type 2 diabetes mellitus. Diabetes Obes Metab 15, 392-402.

Devenny JJ, Godonis HE, Harvey SJ, Rooney S, Cullen MJ & Pelleymounter MA. (2012). Weight loss induced by chronic dapagliflozin treatment is attenuated by compensatory hyperphagia in diet-induced obese (DIO) rats. Obesity (Silver Spring) 20, 1645-1652.

Dobbins RL, O'Connor-Semmes R, Kapur A, Kapitza C, Golor G, Mikoshiba I, Tao W & Hussey EK. (2012). Remogliflozin etabonate, a selective inhibitor of the sodium-dependent transporter 2 reduces serum glucose in type 2 diabetes mellitus patients. Diabetes Obes Metab 14, 15-22.

Ferrannini E, Ramos SJ, Salsali A, Tang W & List JF. (2010). Dapagliflozin monotherapy in type 2 diabetic patients with inadequate glycemic control by diet and exercise: a randomized, double-blind, placebo-controlled, phase 3 trial. Diabetes Care 33, 2217-2224.

Idris I & Donnelly R. (2009). Sodium-glucose co-transporter-2 inhibitors: an emerging new class of oral antidiabetic drug. Diabetes Obes Metab 11, 79-88.

Liang Y, Arakawa K, Ueta K, Matsushita Y, Kuriyama C, Martin T, Du F, Liu Y, Xu J, Conway B, Conway J, Polidori D, Ways K & Demarest K. (2012). Effect of canagliflozin on renal threshold for glucose, glycemia, and body weight in normal and diabetic animal models. PLoS One 7, e30555.

MacLean PS, Higgins JA, Jackman MR, Johnson GC, Fleming-Elder BK, Wyatt HR, Melanson EL & Hill JO. (2006). Peripheral metabolic responses to prolonged weight reduction that promote rapid, efficient regain in obesity-prone rats. Am J Physiol Regul Integr Comp Physiol 290, R1577-1588.

Schaeffer M, Hodson DJ & Mollard P. (2014). The blood-brain barrier as a regulator of the gut-brain axis. Front Horm Res 42, 29-49.

Strohacker K, McCaffery JM, MacLean PS & Wing RR. (2014). Adaptations of leptin, ghrelin or insulin during weight loss as predictors of weight regain: a review of current literature. Int J Obes (Lond) 38, 388-396.

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Tahara A, Kurosaki E, Yokono M, Yamajuku D, Kihara R, Hayashizaki Y, Takasu T, Imamura M, Li Q, Tomiyama H, Kobayashi Y, Noda A, Sasamata M & Shibasaki M. (2013). Effects of SGLT2 selective inhibitor ipragliflozin on hyperglycemia, hyperlipidemia, hepatic steatosis, oxidative stress, inflammation, and obesity in type 2 diabetic mice. Eur J Pharmacol 715, 246-255.

Tahara A, Kurosaki E, Yokono M, Yamajuku D, Kihara R, Hayashizaki Y, Takasu T, Imamura M, Li Q, Tomiyama H, Kobayashi Y, Noda A, Sasamata M & Shibasaki M. (2014). Effects of sodium-glucose cotransporter 2 selective inhibitor ipragliflozin on hyperglycaemia, oxidative stress, inflammation and liver injury in streptozotocin-induced type 1 diabetic rats. J Pharm Pharmacol.

Tahrani AA, Bailey CJ, Del Prato S & Barnett AH. (2011). Management of type 2 diabetes: new and future developments in treatment. Lancet 378, 182-197.

Wilding JP, Norwood P, T'Joen C, Bastien A, List JF & Fiedorek FT. (2009). A study of dapagliflozin in patients with type 2 diabetes receiving high doses of insulin plus insulin sensitizers: applicability of a novel insulin-independent treatment. Diabetes Care 32, 1656-1662.

b) **Describe any animal experimentation and findings leading to the formulation of the study, if applicable.**

See previous section (3a).

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* * * Radioisotopes or Radiation Machines * * *

You selected NO for Radioisotopes in the General Checklist. If you would like to add Radioisotopes, change the selection to YES in general Checklist.

4.

Radioisotopes or Radiation Machines Please note: For projects requiring radiation procedures, please contact the CSU Radiation Control Office (RCO). For more information see: http://www.ehs.colostate.edu/WRad/Home.aspx :

a) **If applicable, summarize in lay language the radiographic diagnostic and therapeutic procedures associated with this protocol.**

Body composition will be measured by dual energy x-ray absorptiometry (DEXA) at pre and post treament

b)

Are the radiation procedures being performed a normal part of the clinical management for the medical condition that is under study (Standard of Care) or are the procedures being performed because the research subject is participating in this project (extra CT scans, more fluoroscopy time, additional Nuclear

Protocol Title:	Does Dapagliflozin Provide Additional Health Benefits To Dietary Counseling For Weight Loss? Clinical Research Protocol Title: Dapagliflozin Promotes Favorable Health Benefits That Are Independent Of Weight Loss In Overweight/Obese Adults
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Medicine Studies, etc.,) (Not Standard of Care)? If some procedures are Standard of Care and some are Not Standard of Care, check both boxes.

NOT STANDARD OF CARE **If it is not standard of care, complete the rest of this section. Provide the CSU RCO approval information**	X	**STANDARD OF CARE** **If it is only standard of care, skip the rest of this section.**

CSU Radiation Control Office approved protocol number:

CSU Radiation Control Office protocol approval date:

For more information, see the RCO website at:http://www.ehs.colostate.edu/Wrad/home.aspx or Contact: James Abraham, Radiation Safety Officer, at 970-491-3736.

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* * * Medical Equipment for Human Subjects and Laboratory Animals; Investigatiional Devices * * *

5. Medical Equipment for Human Subjects

If medical equipment is being used for human subjects/patients, describe this equipment and indicate if the use is normal practice for the population under study. You may have already described this equipment in the Study Procedures section. If you have already listed this information in the Study Procedures Section, please do not duplicate this information here. In the space below, input N/A if not applicable, indicate if this is already listed in the Study Procedures Section, or describe the equipment.

N/A

6. Investigational Devices

Please list in the space below all Investigational Devices to be used on Subjects.

Investigational Devices

Protocol Title:	Does Dapagliflozin Provide Additional Health Benefits To Dietary Counseling For Weight Loss? Clinical Research Protocol Title: Dapagliflozin Promotes Favorable Health Benefits That Are Independent Of Weight Loss In Overweight/Obese Adults
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* * * Drugs, Reagents, or Chemicals * * *

7. Drugs, Reagents, or Chemicals

a) **Please list in the space below all investigational drugs, reagents or chemicals to be administered to subjects during this study.**

b) **Please list in the space below all commercial drugs, reagents or chemicals to be administered to subjects during this study.**

Drug Name	Dapagliflozin
Source (e.g., Pharmacy, Sponsor, etc.,)	AstraZeneca Pharmaceuticals LP
If not premixed, where will the material be mixed and by whom	Pre-mixed by Bristol-Myers Squibb Company
Manufacturer	Bristol-Myers Squibb Company
IND # (if available)	n/a
Dosage	5 mg/day of Dapagliflozin for the first 14-days, and then a dose increase to 10 mg/day of Dapagliflozin for remaining 10 weeks.
Administration Route	Oral
Y	Are these new or different uses of these commercially available drugs, reagents, or chemicals?
N	IND Regulations

Please read the IND Statements

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* * * Subject Population (a-g) * * *

Protocol Title: Does Dapagliflozin Provide Additional Health Benefits To Dietary Counseling For Weight Loss?
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8.

Subject Population - In the space below, please detail the participants that you are requesting to recruit (include requested participant number and description of each group requested). (Input N/A if not applicable)

a) Requested Participant Description (Include number of participants that you plan to study and description of each group requested, if applicable).

60 overweight/obese adult volunteers (men and women) will be studied. However, the number enrolled may be higher in the event of enrollment of replacement subjects for dropout(s) that discontinued for reasons other than an adverse event due to study medication. In the event of a replacement subject being enrolled, this subject will complete all visits. Therefore we would like to enroll 200 participants.

Participants previously enrolled in 14-5531H and withdrawn due to new information will be contacted per for future enrollment in this study. Several procedures, such as screening and DEXA, OGTT, will not be redone, but will be released for the purposes of this purpose. You can find the participant letter that went out to those participants in the attachments section.

b) What is the rationale for studying the requested group(s) of participants?

Adults who are overweight/obese are at the greatest risk of developing type 2 diabetes, thus overweight/obese adults potentially have the most to gain should the outcome of the study prove favorable. Inclusion of adults already diagnosed with diabetes might complicate the interpretation of the data; that is, as a consequence of the patho-physiology associated with diabetes, the response to our feeding treatment with or without Dapagliflozin may differ in adults with diabetes compared with adults who are diabetes free.

c) If applicable, state the rationale for involvement of potentially vulnerable subjects to be entered into the study, including minors, pregnant women, economically and educationally disadvantaged, or decisionally impaired subjects. Specify the measures being taken to minimize the risks and the chance of harm to the potentially vulnerable subjects.

Potentially vulnerable subjects will not be studied.

d) If women, minorities, or minors are not included, a clear compelling rationale must be provided. Examples for not including minors: disease does not occur in children; drug or device would interfere with normal growth and development; etc.

Women and minorities will be invited to participate. Minors will be excluded. The prevalence of type 2 diabetes is greater in adults than minors. Safety and effectiveness of Dapagliflozin in pediatric patients under 18 years of age have not been established.

e) State if any of the subjects are students, employees, or laboratory personnel. They should be presented with the same written informed consent. If compensation is allowed, they should also receive it.

If any of the subjects are students, employees, or laboratory personnel they will be presented with the

Protocol Title: Does Dapagliflozin Provide Additional Health Benefits To Dietary Counseling For Weight Loss?
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same written informed consent; compensation is allowed, they will also receive it.

f) Describe how potential subjects will be identified for recruitment (e.g., chart review, referral from individual's treating physician, those individuals answering an ad). How will potential participants learn about the research and how will they be recruited (e.g., flyer, email, web posting, telephone, etc.)? Attach recruitment materials in the Attachment Section (#16). Important to remember: potential subjects may not be contacted before IRB approval.

Please see examples of recruitment materials in the attachment section.

Potential subjects will be recruited via electronic advertisement (e.g. The Source) and email lists (e.g. CSU genfac). If necessary, potential subjects may also be recruited via newspaper advertisement (e.g. The Coloradoan), clinical trials websites (e.g. clinicaltrials.gov), and/or flyers/posters placed in public places (e.g. coffee shops) in and around the Fort Collins area. Public places includes using approved recruitment texts in social media forums.

g) If applicable, provide rationale for the inclusion of healthy volunteers in this study. Specify any risks to which these healthy volunteers may possibly be exposed. Specify the measures being taken to minimize the risks and the chance of harm to these volunteers.

Adults who are overweight/obese but otherwise healthy will be invited to participate. Inclusion of adults already diagnosed with diabetes might complicate the interpretation of the data; that is, as a consequence of the patho-physiology associated with diabetes, the response to feeding with or without Dapagliflozin may differ in adults with diabetes compared with adults who are diabetes free.

It is not possible to identify all potential risks in research procedures, but the researcher(s) have taken reasonable safeguards to minimize any known and potential (but unknown) risks. The Human Performance Clinical Research Laboratory has emergency supplies including a medicine trolley equipped with heart machines and supplemental oxygen. The research team has a great deal of experience with all of the procedures. Some of the procedures for which you are being asked to volunteer have a number of associated risks:

Body Composition
The risks associated with the DEXA are very low. The maximum radiation dose you will receive in this study is less than 1/1000th of the federal and state occupational whole body dose limit allowed to radiation workers (5,000 mrem). Put another way, the maximum dose from any scan we utilize with this DEXA ranges from 1.2 mrem (Whole body scan) to 12.2 mrem (for several of the regional scans, such as lumbar, femur, and forearm scans). The average annual background radiation you already receive is at least 620 mrem/year. The more radiation you receive over the course of your life, the more the risk increases of developing a fatal cancer or inducing changes in genes. The radiation in this scan is not expected to significantly increase these risks, but the exact increase in such risks is not known. There are no discomforts associated with this procedure. Women who are or could be pregnant should receive no unnecessary radiation and should not participate in this study.

Women will complete a pregnancy test before participating in a DEXA scan.

Exercise Tests

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There is a very small chance of an irregular heartbeat during exercise (< 1% of all subjects). Other rare risks of a stress test are heart attack (< 5 in 10,000) and death (<2 in 10,000). Wearing a mouthpiece and nose-clip can sometimes cause dryness in the mouth and mild discomfort. Difficult exercise may make you feel very tired, light headed and nauseous. Exhausting exercise will, by definition, make you feel very tired. After any exercise your muscles might ache.

ACSM guidelines pertinent to the requirement of physician supervised exercise (stress) testing will be followed.

Blood Collection
When the needle goes into a vein, it may hurt for a short period of time (a few seconds). Also there may be minor discomfort of having the needle/plastic tube taped to your arm. In about 1 in 10 cases, a small amount of bleeding will occur under the skin that will cause a bruise. The risk of forming a blood clot in the vein is about 1 in 100, and the risk of significant blood loss is 1 in 1,000. Additionally, there is a risk that you may faint while having blood collected or having the catheter inserted in your vein.

Only trained research personnel will be permitted to perform phlebotomy.

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* * * Subject Population (h-m) * * *

8. Subject Population (Input N/A if not applicable)

h) Inclusion and Exclusion Criteria (e.g., Participants must have 20/20 vision, Participants must be 30-45 years of age, etc.)

Identify inclusion criteria.

For inclusion in the study subjects should fulfill the following criteria:
1.Provision of informed consent prior to any study specific procedures.
2.Aged 18-65 years.
3.No known Type 2 Diabetes
4.Body mass index greater than or equal to 27.5 kg/m^2
5.Limited exercise participation (maximum of 3/week regularly scheduled activity sessions of < 30 minutes during the previous month).
6.Completion of a screening visit consisting of medical history, physical examination, and 12-lead electrocardiogram and blood pressure assessment at rest and during incremental exercise to volitional exhaustion (Note: Subjects with abnormal screening values may be eligible if the results are not clinically significant, as judged by the investigator or medical monitor)
7.Agree to abide by the study schedule and dietary restrictions and to return for the required assessments
8.Women of childbearing potential must have negative pregnancy test and be using acceptable contraception

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Identify exclusion criteria.

Subjects should not enter the study if any of the following exclusion criteria are fulfilled:
1.Evidence of clinically significant cardiovascular, respiratory, renal, hepatic, pulmonary, gastrointestinal, haematological, neurological, psychiatric, or other disease that may interfere with the objectives of the study or the safety of the subject, as judged by the investigator in agreement with the sponsor or medical monitor, have been hospitalized in the past 2 years as a result of these conditions, or are receiving pharmacological treatment for these conditions.
2.Use of prescription drugs (see exceptions listed below) or herbal preparations in the 2 weeks before study commencement. Prior use of medication or herbal preparations in the 4 weeks before study commencement that are intended for weight-loss and/or sold/marketed as weight-loss products or may alter metabolism.
Permitted Prescription Drugs:
•Birth Control
•Less than a 10 day short course of antibiotics. Note: Rifampicin is not permitted.Antibiotics prescribed for any serious condition will be reviewed on case by case basis no matter the course prescribed.
•Other medicines, such as those for GERD, depression, and OTC analgesics and allergy medications, may be allowed, but will be approved on a case-by-case basis.

3.Is currently enrolled in another clinical study for another investigational drug or has taken any other investigational drug within 30 days before the screening visit.
4.Habitual and/or recent use (within 2 years) of tobacco.
5.Being considered unsuitable for participation in this trial for any reason, as judged by the investigator or medical monitor.
6.History of serious hypersensitivity reaction to Dapagliflozin.
7.Severe renal impairment, end-stage renal disease, or dialysis.
8.Pregnant or breastfeeding individual.
9.Severe hepatic insufficiency and/or significant abnormal liver function defined as aspartate aminotransferase (AST) >3x upper limit of normal and/or alanine aminotransferase (ALT) >3x upper limit of normal.
10.Total bilirubin >2.0 mg/dL (34.2 umol/L).
11.Positive serologic evidence of current infectious liver disease including Hepatitis B viral antibody IGM, Hepatitis B surface antigen and Hepatitis C virus antibody.
12.Estimated Glomerular Filtration Rate <60 mL/min/1.73 m^2 (calculated by Cockcroft-Gault formula).
13.History of bladder cancer.
14.Recent cardiovascular events in a patient, including any of the following: acute coronary syndrome within 2 months prior to enrolment; hospitalization for unstable angina or acute myocardial infarction within 2 months prior to enrolment; acute stroke or trans-ischemic attack within two months prior to enrolment; less than two months post coronary artery revascularization; congestive heart failure defined as New York Heart Association class IV, unstable or acute congestive heart failure. Note: eligible patients with congestive heart failure, especially those who are on diuretic therapy, should have careful monitoring of their volume status throughout the study.
15.Blood pressure at enrolment: Systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥100 mmHg.

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16.Blood pressure at randomization: Systolic blood pressure ≥165 mmHg and/or diastolic blood pressure ≥100 mmHg
17.Individuals who, in the judgment of the medical monitor, may be at risk for dehydration.
18. Individuals with a history of fragility fracture, or bone mineral density values reflective of risk for fracture (DEXA Z-score <or= to -2 in pre-menopausal women, and men <50, and T-score <or= to -1) will not be permitted to participate.

i) Describe your screening procedures. Attach your screening document(s) (e.g., health history questionnaire) in the Attachment Section (#16).

Please see attached screening document. Subjects will be provided with the option of receiving an electronic version of the screening document in advance of visit 1.

j) Describe how you will be cognizant of other protocols in which subjects might be participating. Please explain if subjects will be participating in more than one study.

Subjects will asked if they are participating in another study or if they intend to enroll in another study. Subjects will be permitted to participate in other studies when participation does not interfere with the current study - that is, no possible interaction with Dapagliflozin or feeding, no increase risk to subject safety, etc.

k) Compensation. Explain the amount and schedule of compensation, if any, that will be paid for participation in the study. Compensation includes food, gift cards, money, tokens, etc. Include provisions for prorating payment, if applicable. Compensation should be prorated if several activities are involved for different time periods (e.g., $10 for session #1, and $10 for session #2).

Participants are provided with the following information in the consent form: "If you complete all of the visits, and all of the procedures as described for the entire study, you will receive up to $400 in total compensation. $300 will be paid in installments and prorated as follows: you will not receive compensation for visit 1 (the screening visit). You will receive $60 following completion of baseline testing (visits 2, and 3). After successfully completing 8 weeks of the intervention you will receive $60; after completing 12 weeks you will receive $60. You will receive $60 for completion of visit 28, and $60 for completion of visit 29. If you are at least 95% compliant in terms of both visits and pill ingestion, you will receive an additional $100.

Should your participation in the study end early, you will still receive feedback pertaining to your health and fitness."

l) Costs. Please explain any costs that will be charged to the subject.

Subjects are provided with the following information: "Other than transport to and from the lab, your participation should incur no costs.

m) Estimate the probable duration of the entire study. This estimate should include the total time each subject

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is to be involved and the duration the data about the subject is to be collected (e.g., This is a 2-year study. Participants will be interviewed 3 times per year; each interview will last approximately 2 hours. Total approximate time commitment for participants is 12 hours). These times should be consistent with the time commitment listed on the consent document.

The study will take place over approximately 3 years. Subjects will be involved only for approximately 4 months and will be asked to visit the Human Performance Clinical Research Laboratory and/or Nutrition and Metabolic Fitness Laboratory in the Gifford Building at CSU on 29 different occasions. Visits will last between 30 minutes and 5 hours.

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* * * Risks * * *

9. Risks (Input N/A if not applicable)

US Department of Health & Human Services (HHS) Regulations define a subject at risk as follows: "...any individual who may be exposed to the possibility of injury, including physical, psychological, or social injury, as a consequence of participation as a subject in any research, development, or related activity which departs from the application of those accepted methods necessary to meet his needs, or which increases the ordinary risks of daily life, including the recognized risks inherent in a chosen occupation or field of service."

a) PI's evaluation of the overall level of Risk. (Please check one: minimal or > minimal.)

Minimal (everyday living)
Y **> Minimal (greater than everyday living)**

b)

For the following categories include a scientific estimate of the frequency, severity, and reversibility of potential risks. Wherever possible, include statistical incidence of complications and the mortality rate of proposed procedures. Where there has been insufficient time to accumulate significant data ON risk, a statement to this effect should be included. (In describing these risks in the consent form to the subject, it is helpful to use comparisons which are meaningful to persons unfamiliar with medical terminology.) Address any risks related to:

1. **Use of investigational devices. Please include the clinical adverse events (AEs) associated with each of the devices with an indication of frequency, severity and reversibility. This information can often be found in the Investigator(s) brochure.**

N/A

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2 **Use of investigational drugs. Please include the clinical AEs associated with each of the drugs with an indication of frequency, severity and reversibility. This information can often be found in the Investigator(s) brochure.**

N/A

3 **Use of commercially available drugs, reagents or chemicals. Please include the clinical AEs associated with each of the drugs with an indication of frequency, severity and reversibility. This information can often be found in the package insert provided by the manufacturer.**

Please see the package insert provided by the manufacturer for further information.

Adverse reactions in placebo-controlled studies reported in more than 2% but less than 8.5 % of patients treated with Dapagliflozin include:

•Female genital mycotic infections, such as (listed in order of frequency reported): vulvovaginal mycotic infection, vaginal infection, vulvovaginal candidiasis, vulvovaginitis, genital infection, genital candidiasis, fungal genital infection, vulvitis, genitourinary tract infection, vulval abscess, and vaginitis bacterial.

•Nasopharyngitis (cold-like symptoms)

•Urinary tract infections, such as (listed in order of frequency reported): urinary tract infection, cystitis, Escherichia urinary tract infection, genitourinary tract infection, pyelonephritis, trigonitis, urethritis, kidney infection, and prostatitis.

•Back pain

•Increased urination

•Male genital mycotic infections, such as (listed in order of frequency reported): balanitis, fungal genital infection, balanitis candida, genital candidiasis, genital infection male, penile infection, balanoposthitis, balanoposthitis infective, genital infection, and posthitis.

•Influenza

•Nausea

•Dyslipidemia

•Constipation

•Discomfort with urination

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•Pain in extremity

In addition, use of Dapagliflozin is also associated with a risk of weight loss (up to 10 lbs over 12 weeks).

4 **When performing procedures, please include all investigational, non-investigational and non-invasive procedures (e.g., surgery, blood draws, treadmill tests).**

Subjects are provided with the following information pertaining to risks:

Body Composition
The risks associated with the DEXA are very low. The maximum radiation dose you will receive in this study is less than 1/1000th of the federal and state occupational whole body dose limit allowed to radiation workers (5,000 mrem). Put another way, the maximum dose from any scan we utilize with this DEXA ranges from 1.2 mrem (Whole body scan) to 12.2 mrem (for several of the regional scans, such as lumbar, femur, and forearm scans). The average annual background radiation you already receive is at least 620 mrem/year. The more radiation you receive over the course of your life, the more the risk increases of developing a fatal cancer or inducing changes in genes. The radiation in this scan is not expected to significantly increase these risks, but the exact increase in such risks is not known. There are no discomforts associated with this procedure. Women who are or could be pregnant should receive no unnecessary radiation and should not participate in this study.

Exercise Tests
There is a very small chance of an irregular heartbeat during exercise (< 1% of all subjects). Other rare risks of a stress test are heart attack (< 5 in 10,000) and death (<2 in 10,000). Wearing a mouthpiece and nose-clip can sometimes cause dryness in the mouth and mild discomfort. Difficult exercise may make you feel very tired, light headed and nauseous. Exhausting exercise will, by definition, make you feel very tired. After any exercise your muscles might ache.

Blood Collection
When the needle goes into a vein, it may hurt for a short period of time (a few seconds). Also there may be minor discomfort of having the needle/plastic tube taped to your arm. In about 1 in 10 cases, a small amount of bleeding will occur under the skin that will cause a bruise. The risk of forming a blood clot in the vein is about 1 in 100, and the risk of significant blood loss is 1 in 1,000. Additionally, there is a risk that you may faint while having blood collected or having the catheter inserted in your vein.

Resting Metabolic Rate
The risks associated with this measurement are very low. Some people might feel claustrophobic (fear of small places) when the bubble is placed over their head. The bubble is clear (see-through) and ventilated (room air is pumped through it). The bubble is also very, very light and easy to remove.

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5 **Radioisotopes/radiation-producing machines(e.g., X-rays, CT scans, fluoroscopy).**

Body Composition
The risks associated with the DEXA are very low. The maximum radiation dose you will receive in this study is less than 1/1000th of the federal and state occupational whole body dose limit allowed to radiation workers (5,000 mrem). Put another way, the maximum dose from any scan we utilize with this DEXA ranges from 1.2 mrem (Whole body scan) to 12.2 mrem (for several of the regional scans, such as lumbar, femur, and forearm scans). The average annual background radiation you already receive is at least 620 mrem/year. The more radiation you receive over the course of your life, the more the risk increases of developing a fatal cancer or inducing changes in genes. The radiation in this scan is not expected to significantly increase these risks, but the exact increase in such risks is not known. There are no discomforts associated with this procedure. Women who are or could be pregnant should receive no unnecessary radiation and should not participate in this study.

c)

For the following categories, include an estimate of the potential risk, if applicable.

1. **Physical well-being.**

Subjects are provided with the following information pertaining to risks to physical well-being:

Body Composition
The risks associated with the DEXA are very low. The maximum radiation dose you will receive in this study is less than 1/1000th of the federal and state occupational whole body dose limit allowed to radiation workers (5,000 mrem). Put another way, the maximum dose from any scan we utilize with this DEXA ranges from 1.2 mrem (Whole body scan) to 12.2 mrem (for several of the regional scans, such as lumbar, femur, and forearm scans). The average annual background radiation you already receive is at least 620 mrem/year. The more radiation you receive over the course of your life, the more the risk increases of developing a fatal cancer or inducing changes in genes. The radiation in this scan is not expected to significantly increase these risks, but the exact increase in such risks is not known. There are no discomforts associated with this procedure. Women who are or could be pregnant should receive no unnecessary radiation and should not participate in this study.

Exercise Tests
There is a very small chance of an irregular heartbeat during exercise (< 1% of all subjects). Other rare risks of a stress test are heart attack (< 5 in 10,000) and death (<2 in 10,000). Wearing a mouthpiece and nose-clip can sometimes cause dryness in the mouth and mild discomfort. Difficult exercise may make you feel very tired, light headed and nauseous. Exhausting exercise will, by definition, make you feel very tired. After any exercise your muscles might ache.

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Blood Collection
When the needle goes into a vein, it may hurt for a short period of time (a few seconds). Also there may be minor discomfort of having the needle/plastic tube taped to your arm. In about 1 in 10 cases, a small amount of bleeding will occur under the skin that will cause a bruise. The risk of forming a blood clot in the vein is about 1 in 100, and the risk of significant blood loss is 1 in 1,000. Additionally, there is a risk that you may faint while having blood collected or having the catheter inserted in your vein.

Resting Metabolic Rate
The risks associated with this measurement are very low. Some people might feel claustrophobic (fear of small places) when the bubble is placed over their head. The bubble is clear (see-through) and ventilated (room air is pumped through it). The bubble is also very, very light and easy to remove.

2. **Psychological well-being.**

N/A

3. **Economic well-being.**

N/A

4. **Social well-being.**

N/A

d) **In case of overseas research, or working with a specific race/ethnicity in the United States, provide background on what experience the Investigator(s) have with the proposed population. Describe qualifications/preparations that enable the Investigator(s) to evaluate cultural appropriateness and estimate/minimize risks to subjects.**

N/A

e) **Special Precautions. Describe the planned procedures for protecting against or minimizing potential risks. If appropriate, include the standards for termination of the participation of the individual subject. Discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects.**

N/A

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f)

Data Safety Monitoring

N **Is there a Data Safety Monitoring Board (DSMB)?**

If yes, describe its role and indicate who set up the Data Safety Monitoring Board (e.g., sponsor or Protocol Director).

Describe the data and safety monitoring plan developed to ensure the safety of participants and the validity and integrity of research data. Monitoring should be commensurate with risks and with the size and complexity of the trials.

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* * * Benefits, Procedures to Maintain Confidentiality * * *

10. Benefits (Input N/A if not applicable)

a) Describe the potential benefit(s) to be gained by the subjects. If there is no direct benefit to the subjects describe how the results of the study may benefit society or a particular group.

The benefits of participation in this study may include: benefits from nutrition; the patient population in general may benefit from the knowledge provided by the results of this study.

11. Procedures to Maintain Confidentiality

a) Describe the procedures that protect the privacy of the subjects and maintain the confidentiality of the data. If a linked list is used, explain when the linked list will be destroyed. Provide a sample of the code that will be used, if applicable.

Participants will be identified only on a signed consent form and initial screening form that will be kept locked and separate from other research data. Each subject will be assigned a randomly generated code (e.g. 12698afd) that will be used to identify them in association with all other research data and blood or tissue samples. Records identifying individuals will be kept in Dr. Bell's office/laboratory in a locked cabinet and will be destroyed (shredded) following completion/publication of the project. Data will only be released to regulatory/governmental entities authorized to inspect research records, such as the FDA.

b) If information derived from the study will be provided to the subject's personal physician, a government

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agency, or any other person or group (other than the research team), describe to whom the information will be given and the nature of the information, if applicable.

Unless ordered by an agent of the law, no information will be shared specific to a subject without that subject's written permission. Anonymous data will only be released to regulatory/governmental entities authorized to inspect research records, such as the FDA.

c) **Specify where and under what conditions study data will be kept, how samples will be labeled, who has access to the data, and what will be available and to whom. Federal regulations require that study data and consent documents be kept for a minimum of three (3) years after the completion of the study by the PI. For longitudinal projects and federally regulated studies, the PI may be required to keep the data and documents for a longer time period.**

Research records and data will be stored on file in locked cabinets in Dr. Bell's office/laboratory, or digitally on a password protected central server. Only members of the research team will have access to these records. The materials will be archived for a minimum of three years after completion of the project.

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* * * Potential Conflict of Interest * * *

12. Potential Conflict of Interest

Although you have already submitted CSU's official Conflict of Interest form (FCOI/COI/COC) to the University, it is the IRB's responsibility to ensure that conflicting interests related to submitted protocols do not adversely affect the protection of participants or the credibility of the human research protection program at CSU. Please answer questions a-d below. Please note that if you indicate that you have a potential financial or professional conflict of interest in relation to this protocol, your CSU FCOI/COI/COC Reporting Form must reflect this potential conflict. Link to CSU's Conflict of Interest policy: :http://www.facultycouncil.colostate.edu/files/manual/sectiond.htm#D.7.7

a)	N	**In connection with this protocol, do you or any of the protocol investigators or their immediate family members (i.e., spouse and legal dependents, as determined by the IRS) have a potential financial or professional conflict of interest?**
b)	N/A	**If you do have a potential conflict of interest, is this reported in your current FCOI/COI/COC?**
c)	N/A	**If you do have a potential conflict of interest, is there a management plan in place to manage this potential conflict?**
d)	N/A	**If you do have a potential conflict of interest, is this potential conflict of interest included in your consent document (as required in the Management Plan)?**

If you have reported a possible conflict of interest, the IRB will forward the title of this protocol to your Research Associate Dean to complete your COI file.

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For more information on CSU's policy on Conflict of Interest, please see the Colorado State University Academic Faculty and Administrative Professional Manual Sections D.7.6 & D.7.7.
:http://www.facultycouncil.colostate.edu/files/manual/sectiond.htm#D.7.7

Link to CSU's Conflict of Interest Policy: http://www.provost.colostate.edu/index.asp?url=faculty_affairs.

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* * * Informed Consent * * *

13. Informed Consent

NOTE: In order to complete this protocol, you must upload either a Consent Form or an Alteration of Consent Form (i.e., Cover Letter or Verbal Script) OR (if neither of those apply to your project) you must complete the Waiver of Consent information.

In the space below, please provide consent process background information for each Consent Form(s), Alteration of Consent Form(s), or Waiver(s).

Informed Consent

Title	17.7147H Consent Version 01March2018	
Consent Information Type	Consent	
Sponsor's Consent Version Number: (if any)		
Consent Form Template	X Attachment	17-7147H Consent.revised.01March2018

<a href='http://ricro.colostate.edu/IRB/ConsentAssentTemplates.html' target=_blank Consent Form Samples

Who is obtaining consent? The person obtaining consent must be knowledgeable about the study and authorized by the PI to consent human subjects.

How is consent being obtained?

What steps are you taking to determine that potential subjects are competent to participate in the decision-making process?

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* * * Assent Background * * *

14. Assent Background (Complete if applicable)

All minors must provide an affirmative consent to participate by signing a simplified assent form, unless the Investigator(s) provides evidence to the IRB that the minor subjects are not capable of assenting because of age, maturity, psychological state, or other factors.

See sample consent/assent forms at http://ricro.colostate.edu/IRB/ConsentAssentTemplates.html

Provide assent process background information, in the space below, for each Assent Form, Alteration Form (i.e., Cover Letter or Verbal Script), and Waiver.

Assent Background

Protocol Title:	Does Dapagliflozin Provide Additional Health Benefits To Dietary Counseling For Weight Loss? Clinical Research Protocol Title: Dapagliflozin Promotes Favorable Health Benefits That Are Independent Of Weight Loss In Overweight/Obese Adults
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* * * HIPAA * * *

15. HIPAA

Are you using PHI*? (See definition below)

N

Colorado State University is a hybrid entity and does not have a research-related HIPAA policy. If you will be working with a HIPAA covered entity (e.g., Poudre Valley Health System), you will need to follow their HIPAA guidelines. If your project will involve a HIPAA-regulated entity, in the Attachment section (#16) please attach that entity's required HIPAA consent and/or each waiver of authorization or alteration of authorization requested (e.g., waiver of authorization for access to medical records). Include HIPAA authorization language in the consent document(s) as appropriate (e.g., when enrolling subjects).

*Protected Health Information (PHI) is health information with one or more of the following identifiers. For more information see: http://www.hhs.gov/ocr/hipaa/

1. Names
2. Social Security numbers
3. Telephone numbers
4. All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code, if, according to the current publicly available data from the Bureau of the Census: (1) The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and (2) The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000
5. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older
6. Fax numbers
7. Electronic mail addresses
8. Medical record numbers
9. Health plan beneficiary numbers
10. Account numbers
11. Certificate/license numbers
12. Vehicle identifiers and serial numbers, including license plate numbers
13. Device identifiers and serial numbers
14. Web Universal Resource Locations (URLs)
15. Internet Protocol (IP) address numbers
16. Biometric identifiers, including finger and voice prints

Protocol Title:	Does Dapagliflozin Provide Additional Health Benefits To Dietary Counseling For Weight Loss? Clinical Research Protocol Title: Dapagliflozin Promotes Favorable Health Benefits That Are Independent Of Weight Loss In Overweight/Obese Adults
Protocol Type:	Biomedical
Date Submitted:	03/01/2018
Approval Period:	Draft
Important Note:	**This Print View may not reflect all comments and contingencies for approval. Please check the comments section of the online protocol. Questions that appear to not have been answered may not have been required for this submission. Please see the system application for more details.**

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17. Full face photographic images and any comparable images; and
18. Any other unique identifying number, character, or code (note this does not mean the unique code assigned by the Investigator(s) to code the research data)

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* * * Attachments * * *

16. Attachments

Attach relevant documents here. These could include: Collaborating Investigator's IRB approval and approved documents; Conflict of Interest information; Debriefing Script; Grant/Sub-contract; HIPAA Authorization Form from HIPAA-covered entity; Interview/Focus Group Questions; Investigator's Brochure; Letters of Agreement/Cooperation from organizations who will help with recruitment; Methodology section of associated Thesis or Dissertation project; Questionnaires; Radiation Control Office approval material; Recruitment Material (e.g., flyers, email text, verbal scripts); Sponsor's Protocol; Surveys; Other files associated with the protocol (you can upload most standard file formats: xls, pdf, jpg, tif, etc.) Please be sure to attach all documents associated with your protocol. Failure to attach the files associated with the protocol may result in this protocol being returned to you for completion prior to being reviewed. Students: Be sure to attach the Methods section of your thesis or dissertation proposal. If this protocol is associated with a grant proposal, please remember to attach your grant.

To update or revise any attachments, please delete the existing attachment and upload the revised document to replace it.

Document Type	**Investigator's Brochure**
Attachment	Investigator's Brochure Dapagliflozin Edition 10 (3)
Document Name	Investigator's Brochure Dapagliflozin Edition 10 (3)

Document Type	**Other Protocol Material**
Attachment	Farxiga Dapagliflozin
Document Name	Farxiga Dapagliflozin

Document Type	**Other Protocol Material**
Attachment	SGLT2 Dapagliflozin
Document Name	SGLT2 Dapagliflozin

Document Type	**Other Protocol Material**
Attachment	SGLT2 Inhibitors T2 Diabetes

Protocol Title: Does Dapagliflozin Provide Additional Health Benefits To Dietary Counseling For Weight Loss?
Clinical Research Protocol Title: Dapagliflozin Promotes Favorable Health Benefits That Are Independent Of Weight Loss In Overweight/Obese Adults

Protocol Type: Biomedical

Date Submitted: 03/01/2018

Approval Period: Draft

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Document Name SGLT2 Inhibitors T2 Diabetes

Document Type Other Protocol Material
Attachment SGLT2 Inhibitors Diabetes
Document Name SGLT2 Inhibitors Diabetes

Document Type Other Protocol Material
Attachment SGLT2 Inhibitors New Diabetes Drug
Document Name SGLT2 Inhibitors New Diabetes Drug

Document Type Other Protocol Material
Attachment Id cards for subjects
Document Name Id cards for subjects

Document Type SOP
Attachment HP-05-R1 Reporting AEs SOP
Document Name HP-05-R1 Reporting AEs SOP

Document Type Other Protocol Material
Attachment FDA safety warning 04Dec2015
Document Name FDA safety warning 04Dec2015

Document Type Other Protocol Material
Attachment CDC Hepatitis B Fact Sheet
Document Name CDC Hepatitis B Fact Sheet

Document Type Other Protocol Material
Attachment NTF Interpretation of Hep B results gjl 29 oct 2015
Document Name NTF Interpretation of Hep B results gjl 29 oct 2015

Protocol Title: Does Dapagliflozin Provide Additional Health Benefits To Dietary Counseling For Weight Loss?
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Protocol Type: Biomedical

Date Submitted: 03/01/2018

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Document Type	**Other Protocol Material**
Attachment	14-5531 H Delegation of Authority signed
Document Name	14-5531 H Delegation of Authority signed

Document Type	**Questionnaire/Survey**
Attachment	Screening Med History 08262015
Document Name	Screening Med History 08262015

Document Type	**Sponsor's Protocol**
Attachment	Bell 0009 IISR FINAL
Document Name	Bell 0009 IISR FINAL

Document Type	**Other Protocol Material**
Attachment	FDA-1572 signed
Document Name	FDA-1572 signed

Document Type	**Other Protocol Material**
Attachment	AZ amemendment concomitant meds
Document Name	AZ amemendment concomitant meds

Document Type	**Other Protocol Material**
Attachment	Nutritional counseling overview
Document Name	Nutritional counseling overview

Document Type	**Investigator's Brochure**
Attachment	Investigator's Brochure Dapagliflozin Edition 13
Document Name	Investigator's Brochure Dapagliflozin Edition 13

Protocol Title: Does Dapagliflozin Provide Additional Health Benefits To Dietary Counseling For Weight Loss?
Clinical Research Protocol Title: Dapagliflozin Promotes Favorable Health Benefits That Are Independent Of Weight Loss In Overweight/Obese Adults

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Document Type	**Investigator's Brochure**
Attachment	Investigator's Brochure Dapagliflozin Edition 12
Document Name	Investigator's Brochure Dapagliflozin Edition 12

Document Type	**Debriefing Script**
Attachment	14-5531H Participant Study Update Letter
Document Name	14-5531H Participant Study Update Letter

Document Type	**Recruitment Material (e.g., flyers, email text, verbal scripts)**
Attachment	17-7147H Example recruitment_Facebook 18Nov2016
Document Name	17-7147H Example recruitment_Facebook 18Nov2016

Document Type	**Recruitment Material (e.g., flyers, email text, verbal scripts)**
Attachment	Recruitment_Dapa_Weight Loss
Document Name	Recruitment_Dapa_Weight Loss

Document Type	**Sponsor's Protocol**
Attachment	Protocol ISSDAP0009 02202017
Document Name	Protocol ISSDAP0009 02202017

Document Type	**Questionnaire/Survey**
Attachment	17-7147H PI medical screening form 04252017
Document Name	17-7147H PI medical screening form 04252017

Document Type	**Questionnaire/Survey**
Attachment	3 day food record
Document Name	3 day food record

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Document Type	**Questionnaire/Survey**
Attachment	Hunger.Fullness.VAS
Document Name	Hunger.Fullness.VAS

Document Type	**Other Protocol Material**
Attachment	Copy of Nutritional counseling checklist
Document Name	Copy of Nutritional counseling checklist

Document Type	**Other Protocol Material**
Attachment	Copy of Nutritional counseling notes
Document Name	Copy of Nutritional counseling notes

Document Type	**Recruitment Material (e.g., flyers, email text, verbal scripts)**
Attachment	Recruitment_Dapa_Weight Loss.revisions.6-27-2017
Document Name	Recruitment_Dapa_Weight Loss.revisions.6-27-2017

Document Type	**Other Protocol Material**
Attachment	17-7147 H AE Report Log 11July2017
Document Name	17-7147 H AE Report Log 11July2017

Document Type	**Other Protocol Material**
Attachment	Protocol Deviation course of Antibiotics 26Feb2018
Document Name	Protocol Deviation course of Antibiotics 26Feb2018

Document Type	**Other Protocol Material**
Attachment	Protocol Deviation wrong pill bottle 17nov2017
Document Name	Protocol Deviation wrong pill bottle 17nov2017

Protocol Title:	Does Dapagliflozin Provide Additional Health Benefits To Dietary Counseling For Weight Loss? Clinical Research Protocol Title: Dapagliflozin Promotes Favorable Health Benefits That Are Independent Of Weight Loss In Overweight/Obese Adults
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Document Type	**Other Protocol Material**
Attachment	Protocol Deviation duration of intervention
Document Name	Protocol Deviation duration of intervention

Document Type	**Other Protocol Material**
Attachment	Protocol Deviation Extended Intervention Period 28Feb2018
Document Name	Protocol Deviation Extended Intervention Period 28Feb2018

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* * * Obligations * * *

Obligations (Researcher's Responsibilities)

The Principal Investigator is ultimately responsible for the conduct of the project. Obligations of the Principal Investigator are:

Conduct the research involving human subjects as presented in the protocol, including modifications, as approved by the Department and Institutional Review Board. Changes in any aspect of the study (for example project design, procedures, consent forms, advertising materials, additional key personnel or subject populations) will be submitted to the IRB for approval before instituting the changes (PI will submit the "Amendment/Revision" form);

Provide all subjects a copy of the signed consent form, if applicable. Investigators will be required to retain signed consent documents for three (3) years after close of the study;

Maintain an approved status for Human Subjects Protection training. Training must be updated every three (3) years (Contact RICRO to check your current approval/renewal dates). For more information: Human Subjects Training Completed?

Submit either the "Protocol Deviation Form" or the "Report Form" to report protocol Deviations/Violations, Unanticipated Problems (UPs) and/or Adverse Events (AEs) that occur in the course of the protocol. Any of these

Protocol Title: Does Dapagliflozin Provide Additional Health Benefits To Dietary Counseling For Weight Loss?
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Unanticipated Problems (UPs) and/or Adverse Events (AEs) that occur in the course of the protocol. Any of these events must be reported to the IRB as soon as possible, but not later than five (5) working days. Note that if an event resulted in life threatening injury or death OR an event resulted in substantive harm to the safety, rights or welfare to human subjects, this must be reported to the IRB within 24 hours;

Submit the "Continuing Review" Form in order to maintain active status of the approved protocol. This form must be submitted annually at least four (4) weeks prior to expiration, five (5) weeks for protocols that require full review. If the protocol is not renewed before expiration, all activities must cease until the protocol has been re-reviewed;

Notify the IRB that the study is complete by submitting the "Final Report" form.

X The Principal Investigator has read and agrees to abide by the above obligations.

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* * * Event History * * *

Event History

Date	Status	View Attachments	Letters
02/27/2017	NEW FORM PROTOCOL CLONED (14-5531H)		
03/02/2017	NEW FORM SUBMITTED	Y	
03/06/2017	NEW FORM PANEL ASSIGNED		
03/17/2017	NEW FORM REVIEWER(S) ASSIGNED		
04/05/2017	NEW FORM SUBMITTED (CYCLE 1)	Y	
04/05/2017	NEW FORM REVIEWER(S) ASSIGNED		
04/25/2017	NEW FORM SUBMITTED (CYCLE 2)	Y	
04/25/2017	NEW FORM MOVED		

Protocol Title: Does Dapagliflozin Provide Additional Health Benefits To Dietary Counseling For Weight Loss?
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04/25/2017	NEW FORM APPROVED	Y	Y
05/02/2017	AMENDMENT 1 FORM CREATED		
05/02/2017	AMENDMENT 1 FORM SUBMITTED	Y	
05/02/2017	AMENDMENT 1 FORM REVIEWER(S) ASSIGNED		
05/03/2017	AMENDMENT 1 FORM REVIEWER(S) ASSIGNED		
05/03/2017	AMENDMENT 1 FORM APPROVED	Y	Y
06/27/2017	AMENDMENT 2 FORM CREATED		
06/27/2017	AMENDMENT 2 FORM SUBMITTED	Y	
06/27/2017	AMENDMENT 2 FORM APPROVED	Y	Y
02/28/2018	CONTINUING REVIEW 1 FORM CREATED		
03/01/2018	CONTINUING REVIEW 1 FORM SUBMITTED	Y	
03/16/2018	CONTINUING REVIEW 1 FORM REVIEWER(S) ASSIGNED		
03/23/2018	CONTINUING REVIEW 1 FORM SUBMITTED (CYCLE 1)	Y	
03/25/2018	CONTINUING REVIEW 1 FORM APPROVED	Y	Y
03/26/2018	CONTINUING REVIEW 1 FORM UNDO APPROVED		
03/26/2018	CONTINUING REVIEW 1 FORM APPROVED	Y	Y
03/22/2019	PROTOCOL EXPIRED		

Statistical Analysis Plan

Baseline (pre-counselling) differences between placebo and SGLT2 inhibition groups were compared using independent Student t-Tests. Consistent with the experimental design (randomized, double-blind, parallel, repeated measures) the influence of SGLT2 inhibition on the physiological responses to dietary counselling was examined using two-way (group: placebo vs. SGLT2 inhibition x time: before vs. after dietary counselling) analysis of variance (ANOVA). The influence of SGLT2 inhibition and dietary counselling on the dynamic responses to oral glucose ingestion were examined using three-way ANOVA (placebo vs. SGLT2 inhibition x before vs. after dietary counselling x time points during the OGTT). Pairwise multiple comparison procedures were performed using the Holm-Sidak Method. Relations of interest were described using Pearson product-moment correlations. The level of statistical significance was set at $P<0.05$. Data are reported as mean and standard deviation, unless otherwise indicated. Calculations were performed using commercially available statistical software (SigmaStat 3.0, Systat Software Inc., San Jose, California, USA).

Consent to Participate in a Research Study
Colorado State University

TITLE OF STUDY:

Does Dapagliflozin Provide Additional Health Benefits To Dietary Counseling For Weight Loss?

CO-PRINCIPAL INVESTIGATORS:

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Christopher L. Melby, Dr.P.H.
Food Science & Human Nutrition
Colorado State University
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Telephone: 970-491-6736

WHY AM I BEING INVITED TO TAKE PART IN THIS RESEARCH?

You are between 18-65 years, weigh more than you prefer (body mass index is greater than or equal to 27.5 kg/m^2), free of diabetes, not pregnant, and not performing more than 30 minutes 3 times per week of moderate exercise.

WHO IS DOING THE STUDY?

Drs. Bell and Melby are running the study; local medical doctors, other researchers, and a team of trained graduate and undergraduate students are helping. AstraZeneca Pharmaceuticals LP, a company that makes medicine, is providing financial support for the study.

WHAT IS THE PURPOSE OF THIS STUDY?

Dapagliflozin (commercially available as Farxiga; pronounced: far-see-gah) is a medicine for treating type 2 diabetes. Use of Dapagliflozin causes moderate weight loss in some, but not all people. However, Dapagliflozin may have other health benefits, including decreased blood pressure, and decreased concentration of substances in the blood that are indicative of disease risk (inflammation and oxidative stress). It is unclear as to whether these health benefits are due to Dapagliflozin per se, weight loss, or a combination of the two. The purpose of the study is to determine if: 1. Dapagliflozin provides additional health benefits to dietary counseling for weight loss? 2. Use of Dapagliflozin with a calorie-restricted diet can maintain normal control of hunger and appetite.

WHERE IS THE STUDY GOING TO TAKE PLACE AND HOW LONG WILL IT LAST?

The study will take place in the Human Performance Clinical Research Laboratory (HPCRL) in the Department of Health and Exercise Science and in the Nutrition

CSU#: 17-7147H
APPROVED: 3/22/2018* EXPIRES: 3/21/2019

Laboratory in the Gifford Academic Building, Department of Food Science and Human Nutrition, on the main campus of Colorado State University (CSU), Fort Collins.

The study will take place over approximately 2 years. You will be involved for approximately 4 months and will be asked to visit the labs 1-2 times per week over 14 weeks.

WHAT WILL I BE ASKED TO DO?

Here is a brief summary of what you will be asked to do:

Visit 1: in the HPCRL, you will undergo screening: medical history, blood sampling, measurement of body composition, and 12-lead electrocardiogram (ECG) and blood pressure assessment at rest and during incremental exercise to volitional exhaustion. If your screening visits indicate that you qualify for the study, you will be eligible for enrollment.

Visit 2: in the HPCRL, your resting metabolic rate (RMR) and blood pressure will be measured, and an oral glucose tolerance test (OGTT) will be performed.

Visit 3: in the HPCRL appetite and hunger will be assessed in response to a test meal. Afterward, you will be given a form in which you will record the amounts of food and beverage you eat and drink for three days (two weekdays and one weekend day). You will return this completed food record to the research team. This information will be useful for the nutrition counselor to understand your current eating habits and to provide nutritional recommendations.

Visits 4-27: During the 12 weeks of treatment you will swallow, on a daily basis, either Dapagliflozin or placebo. During that time, you will be assigned to a nutrition counselor with whom you will meet 1-2 times per week for weigh-ins and to discuss strategies to achieve weight loss goals of approximately one pound per week (10-12 pounds at the end of 12 weeks). You will need to fast for 10 hours prior to each weigh-in, so these meetings typically take place during the morning hours. During these nutrition counseling sessions, you will be asked to participate in a variety of educational activities to help meet your assigned weight loss goal, such as how to accurately determine food portion sizes.

Visit 28: in the HPCRL, your resting metabolic rate (RMR) and blood pressure will be measured, and an oral glucose tolerance test (OGTT) will be performed. This visit will occur in week 12 (e.g. the final week of daily ingestion of Dapagliflozin or placebo).

Visit 29: in the HPCRL, appetite and hunger will be assessed. This visit will occur in week 12 (during the final week of daily ingestion of Dapagliflozin or placebo). Body composition will be measured at this visit or the start of the following week (week 13).

CSU#: 17-7147H
APPROVED: 3/22/2018* EXPIRES: 3/21/2019

Outline and timing of study visits:

Visits 1-3				Visits 4-27 (Weeks 1-12)	Visits 28-29 (Week 12)	
Screening	RMR/ OGTT	Stress test	Appetite and hunger assessment	Initiation of treatment (Placebo or Dapagliflozin daily, weigh-ins twice weekly, and nutrition counseling once weekly)	RMR/ OGTT	Appetite and hunger assessment

OGTT: Oral glucose tolerance test. RMR: Resting Metabolic Rate Test

Here is a detailed description of what you will be asked to do:

Visit 1 – Screening Visit: Medical History / Blood Test / Body Composition

The first visit to the HPCRL will be a screening visit. During this visit, we will make sure that participation in this study is right for you.

This screening visit will include the following procedures:

Medical Questionnaire
You will be asked to answer several pages of questions related to your health, any illness you may have or have had, and medications you use or have used in the past.

Blood Pressure
We will measure your blood pressure using a standard blood pressure cuff (the same as in a doctor's office). Blood pressure will be measured during all of the tests performed in the lab with the exception of body composition. There are no known risks associated with this procedure. (Duration: 5 minutes)

Pregnancy Test (Women Only)
Women who are or could be pregnant should not participate in this study. Before the body composition test(s), women will be asked to take a pregnancy test (urine test) to confirm they are not pregnant.

Body Composition
We will measure how much fat you have in your body using a test called dual energy x-ray absorptiometry (DEXA). The DEXA test requires you to lie quietly on a padded table while a small probe gives off low-level x-rays and sends them over your entire body. This test gives very accurate measurements of your body fat and bone mineral density. We will also measure the circumference of your waist and hip using a tape measure. (Duration: ~ 15 minutes)

Blood Test
During this visit, we will take approximately 20 ml (~1.5 tablespoons) from you; this is a lot less than the amount that is typically taken when a person donates blood. Your blood

CSU#: 17-7147H
APPROVED: 3/22/2018* EXPIRES: 3/21/2019

will be tested for various things to make sure you are healthy enough to consume Dapagliflozin. Your blood will be taken from veins in your arms or hands using a needle. On the advice of the medical monitor (study physician), you may be asked to have your blood tested several more times during the treatment period to make sure the study is still right for you.

Exercise Stress Test
You will be asked to perform a vigorous exercise test. This test will tell us if your heart is healthy. You will be asked to walk on a motorized treadmill or ride an exercise cycle (cycle ergometer) for approximately 10-15 minutes. The exercise will become more difficult every 2 minutes. While you are walking/riding, we will measure your heart rate with an electrocardiogram (ECG) and your blood pressure with a cuff placed around your upper arm. We will also ask you to wear a nose clip (to stop you breathing through your nose) and ask you to breathe through a mouthpiece. This will let us measure the gases you breathe. Depending on your age, a physician may supervise the test. If we do not think your heart is healthy, you will be referred to your primary care physician for further testing. There is a chance that you may not be allowed to take part in our study. (Duration: ~ 60 minutes)

The whole visit will last approximately 2 hours.

Visit 2 – Resting Metabolic Rate Test, Oral Glucose Tolerance Test, and Blood Pressure

These tests will take place early in the morning after a 12-hour fast and 24-hour abstention from alcohol, caffeine, and exercise. You will be asked to wear a T-shirt.

Resting Metabolic Rate
We will measure how your metabolism works (how many calories you burn) while you are resting. You will rest quietly on a bed for 10 minutes. After that time, we will place a clear plastic bubble (hood) over your head, through which you will be able to breath, and ask you to continue lying quietly for 45 minutes. (Duration: ~ 60 minutes)

Blood Pressure
We will measure your blood pressure using a standard blood pressure cuff (the same as in a doctor's office). We will do this three times. (Duration: 5 minutes)

Oral Glucose Tolerance Test (OGTT)
We will then perform the oral glucose tolerance test. You will be asked to drink water (300 ml or ~ 10 oz) in approximately 5 minutes. A small amount of sugar (75 g of glucose) will have been added to the water. This will make it taste sweeter and also increase your blood sugar.

After drinking the water you will sit/lie quietly for 2 hours. You will be able to read, watch TV, and/or listen to music. We will collect blood from you over the 2 hours. Your blood will be analyzed for concentrations of sugar (glucose), insulin (something that helps control blood sugar), and other things that may help control blood sugar. Your blood will

CSU#: 17-7147H
APPROVED: 3/22/2018* EXPIRES: 3/21/2019

be taken from veins in your arms or hands using needles and hollow plastic tubes called catheters.

The whole visit will last approximately 3 hours.

Visit 3 – Appetite and Hunger Assessment

This test will take place early in the morning after a 12-hour fast, and 24-hour abstention from alcohol, caffeine, and exercise. You will be asked to wear a T-shirt.

We will place a hollow plastic tube (a venous catheter) into a vein in your arm or hand. The tube will remain in your vein for approximately 5 hours. We will sample a very small amount of blood periodically throughout the duration of the visit. The total amount of blood sampled will be approximately 100 ml, or 7 tablespoons.

You will be given a liquid meal (an Energy Drink) to serve as "an appetizer" before you are given your main meal. One hour later, you will be presented with a buffet style presentation of assorted foods and beverages. You will be able to eat as much, or as little, as you like of any or all of the foods and beverages.

Throughout the visit (before the liquid meal, and before and after the main meal) you will be asked questions about your hunger and appetite.

Your blood pressure will also be measured periodically throughout the duration of the visit.

The whole visit will last approximately 5.5 hours.

Visit 4-27 – 12 Weeks of Nutritional Counseling

You will be randomly assigned to receive either the medicine Dapagliflozin or the placebo for 12 weeks and you will be given dietary counseling for weight loss. The goal of the counseling is to help you moderately reduce your calorie intake to produce weight loss of about one pound per week. You will not know if you are assigned to take Dapagliflozin or the placebo:

Condition 1) You will swallow Dapagliflozin every day.

Condition 2) You will swallow a placebo (a pill that has no effect) every day.

Regardless of the condition to which you are assigned, you will meet with your nutritional counselor 1-2 times per week for the remainder ot the study as described below.

During the first 6 weeks you will meet with your study counselor 2 times per week for dietary counseling and measurement of body weight. During the second 6-week period

CSU#: 17-7147H
APPROVED: 3/22/2018* EXPIRES: 3/21/2019

you may continue to meet 1-2 times per week for dietary counseling and body weight measurement, depending on whether or not you are achieving your weight loss goals. If you are losing weight as prescribed, you will meet only once per week, but if you are not achieving your weight loss goals you will meet 2 times per week. You will need to fast for 10 hours prior to the weigh-in. On 2 random counseling occasions between weeks 4 and 10, you will be asked to recall what you ate during the previous 24 hours. (Duration: 15-30 minutes). If you fail to achieve your target body weight (within 2 pounds) on three consecutive weighing sessions, you will be provided with additional counseling and instructions to aid in achieving your target body weight. If you fail to attend a minimum of 80% of your appointments you will be removed the study.

During the 12 weeks of your study participation, you will swallow a pill every day. The pill may be Dapagliflozin or a placebo, a pill that has no effect. You will not know which pill you are swallowing. If you are chosen to swallow Dapagliflozin, for the first 2 weeks the dose will be 5 mg/day. For the next 10 weeks, the dose will be 10 mg/day. For a description of Dapagliflozin, see below.

If you fail to ingest 90% of your medication (75 of 84 total doses), you will be removed from the study.

Visit 28 – Resting Metabolic Rate Test, Oral Glucose Tolerance Test, and Blood Pressure

You will repeat the procedures described in visit 2. This visit will occur in week 12 (e.g. the final week of daily ingestion of Dapagliflozin or placebo). (Duration: ~ 3 hours)

Visit 29 – Appetite and Hunger Assessment

You will repeat the procedures described in visit 3. You will also undergo measurement of body composition (as described in visit 1) and be asked to complete the 3-day food record again, which you will return to the research team. This visit will occur in week 12 (e.g. the final week of daily ingestion of Dapagliflozin or placebo). (Duration: ~ 5.5 hours)

WHAT IS DAPAGLIFLOZIN?

Dapagliflozin is a new medicine that is used to treat people who have type 2 diabetes (high blood sugar and/or difficulty controlling blood sugar). Dapagliflozin works by limiting the body's ability to absorb sugar from food and beverages. It does this by changing the ability of the kidneys to absorb sugar. The sugar that is not absorbed is removed from the body in urine.

ARE THERE REASONS WHY I SHOULD NOT TAKE PART IN THIS STUDY?

You will not be allowed to take part in the study for any of the following reasons:

CSU#: 17-7147H
APPROVED: 3/22/2018* EXPIRES: 3/21/2019

1. Evidence of serious (clinically significant) heart (cardiovascular), lung (respiratory), kidney (renal), liver (hepatic), stomach (gastrointestinal), blood (hematological), nerve (neurological), mental (psychiatric), or other disease, or if you have been hospitalized in the past 2 years as a result of these conditions, or are receiving medicine (pharmacological treatment) for these conditions.

2. Use of prescription drugs (see exceptions listed below) or herbal preparations in the 2 weeks before study commencement. Prior use of medication or herbal preparations in the 4 weeks before study commencement that are intended for weight-loss and/or sold/marketed as weight-loss products or may alter metabolism.

Permitted Prescription Drugs:

- Birth Control
- Less than a 10-day short course of antibiotics. Antibiotics prescribed for any serious condition will be reviewed on case by case basis no matter the course prescribed. **Note: Rifampicin is not permitted.**
- Other medicines, such as those for GERD, depression, OTC analgesics, and allergy medications may be allowed but will be approved on a case-by-case basis.

3. You are currently enrolled in another clinical study for another investigational drug or have taken any other investigational drug within 30 days before the screening visit.

4. You are a smoker: Habitual and/or recent use (within 2 years) of tobacco.

5. You are considered unsuitable for participation in this trial for any reason, as judged by the investigator or medical monitor.

6. You have a history of serious hypersensitivity reaction to Dapagliflozin.

7. You have severe kidney problems: renal impairment, end-stage renal disease, or dialysis.

8. You are pregnant or breastfeeding.

9. You have severe hepatic insufficiency and/or significant abnormal liver function based on blood tests.

10. You have a history of bladder cancer.

11. Your blood pressure during visit 1: Systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥100 mmHg.

12. Your blood pressure during visit 4: Systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥100 mmHg

CSU#: 17-7147H
APPROVED: 3/22/2018* EXPIRES: 3/21/2019

13. Patients who, in the judgment of the medical doctor, may be at risk for dehydration.

14. You have a history of bone fractures due to fragile bones and/or the results of your DEXA scan indicate results consistent with fragile/weak bones (osteopenia).

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

It is not possible to identify all potential risks in research procedures, but the researcher(s) have taken reasonable safeguards to minimize any known and potential (but unknown) risks. The Human Performance Clinical Research Laboratory has emergency supplies including a medicine trolley equipped with heart machines and supplemental oxygen. The research team has a great deal of experience with all of the procedures. Some of the procedures for which you are being asked to volunteer have a number of associated risks:

Body Composition

The risks associated with the DEXA are very low. The maximum radiation dose you will receive in this study is less than 1/1000th of the federal and state occupational whole body dose limit allowed to radiation workers (5,000 mrem). Put another way, the maximum dose from any scan we utilize with this DEXA ranges from 1.2 mrem (Whole body scan) to 12.2 mrem (for several of the regional scans, such as lumbar, femur, and forearm scans). The average annual background radiation you already receive is at least 620 mrem/year. The more radiation you receive over the course of your life, the more the risk increases of developing a fatal cancer or inducing changes in genes. The radiation in this scan is not expected to significantly increase these risks, but the exact increase in such risks is not known. There are no discomforts associated with this procedure. **Women who are or could be pregnant should receive no unnecessary radiation and should not participate in this study.**

Blood Collection

When the needle goes into a vein, it may hurt for a short period of time (a few seconds). Also, there may be minor discomfort of having the needle/plastic tube taped to your arm. In about 1 in 10 cases, a small amount of bleeding will occur under the skin that will cause a bruise. The risk of forming a blood clot in the vein is about 1 in 100, and the risk of significant blood loss is 1 in 1,000. Additionally, there is a risk that you may faint while having blood collected or having the catheter inserted in your vein.

Exercise Test

There is a very small chance of an irregular heartbeat during exercise (< 1% of all subjects). Other rare risks of a stress test are heart attack (< 5 in 10,000) and death (<2 in 10,000). Wearing a mouthpiece and nose-clip can sometimes cause dryness in the mouth and mild discomfort. Difficult exercise may make you feel very tired, light-headed, and nauseous. Exhausting exercise will, by definition, make you feel very tired. After any exercise, your muscles might ache.

Resting Metabolic Rate

CSU#: 17-7147H
APPROVED: 3/22/2018* EXPIRES: 3/21/2019

The risks associated with this measurement are very low. Some people might feel claustrophobic (fear of small places) when the bubble is placed over their head. The bubble is clear (see-through) and ventilated (room air is pumped through it). The bubble is also very, very light and easy to remove.

Dapagliflozin

Adverse reactions in placebo-controlled studies reported in more than 2% but less than 8.5% of patients treated with Dapagliflozin include:

- Vaginal yeast infections including vaginal odor, white or yellowish vaginal discharge (discharge may be lumpy or look like cottage cheese), or vaginal itching..
- Stuffy or runny nose and sore throat (nasopharyngitis)
- Urinary tract infections (UTIs), such as bladder or kidney infection.
- Low blood pressure (hypotension) which may cause you to feel dizzy, faint, lightheaded, or weak: this is particularly in persons with impaired kidney function, elderly, or persons on certain diuretics. In order to minimize this risk, we are not enrolling people who may be increased risk of hypotension.
- Impaired kidney function: this risk is increased in certain populations. In order to minimize this risk, we are not enrolling people who may be at increased risk and we are screening your kidney function prior to and during participation.
- Back pain
- Increased urination
- Yeast infection of the skin around the penis.
- Influenza (flu)
- Nausea (upset stomach)
- An Increase in bad cholesterol (LDL)
- Constipation
- Discomfort with urination
- Pain in the extremities

In a study of 5,936 patients with type 2 diabetes, one patient became ill with diabetic ketoacidosis (a metabolic sickness). If you experience any of the following

CSU#: 17-7147H
APPROVED: 3/22/2018* EXPIRES: 3/21/2019

sensations/symptoms, you should seek immediate medical help and contact the investigator: sickly or queasy (nausea), vomiting, stomach (abdominal) pain, confusion, change in breathing pattern, and unusual tiredness (fatigue) or sleepiness.

In addition, use of Dapagliflozin is also associated with modest weight loss (up to 10 lbs over 12 weeks) in some people.

ARE THERE ANY BENEFITS FROM TAKING PART IN THIS STUDY?

There are no direct benefits in participating; however, you will receive a copy of your results and information pertinent to your body composition (i.e. height and weight) and metabolic and cardiovascular risk factors. For example, in blood we will measure concentrations of glucose. You will be provided with a copy of your DEXA scan; you may wish to have this interpreted by a medically qualified professional. Finally, this study has the potential to identify an additional benefit for people who use Dapagliflozin to treat their type 2 diabetes.

DO I HAVE TO TAKE PART IN THE STUDY?

Your participation in this research is voluntary. If you decide to participate in the study, you may withdraw your consent and stop participating at any time without penalty or loss of benefits to which you are otherwise entitled.

WHAT WILL IT COST ME TO PARTICIPATE?

Other than transport to and from the campus, your participation should incur no costs.

WHO WILL SEE THE INFORMATION THAT I GIVE?

We will keep private all research records that identify you, to the extent allowed by law. For this study, we will assign a code to your data (e.g. 1234ABCD), so the only place your name will appear in our records is on the consent form and in our data spreadsheet that links you to your code. Only the research team will have access to the link between you, your code, and your data. The only exceptions to this are if we are asked to share the records of the study for audit purposes with the Food and Drug Administration, Health and Human Services, AstraZeneca, and/or the CSU Institutional Review Board ethics committee, if necessary. In addition, for funded studies, the CSU financial management team may also request an audit of research expenditures. For financial audits, only the fact that you participated would be shared, not any research data. When we write about the study to share it with other researchers, we will write about the combined information we have gathered. You will not be identified in these written materials. We may publish the results of this study; however, we will keep your name and other identifying information private.

Your identity/record of receiving compensation (NOT your data) may be made available to CSU officials for financial audits.

CSU#: 17-7147H
APPROVED: 3/22/2018* EXPIRES: 3/21/2019

CAN MY TAKING PART IN THE STUDY END EARLY?

You will be weighed twice per week in the Gifford Building. If you fail to achieve your target body weight (within 2 pounds) on three consecutive weigh-in sessions you will be provided with additional counseling and instruction to aid in achieving your target body weight. If you fail to ingest 90% of your Dapagliflozin or placebo (75 of 84 total doses), you will be removed from the study. Your participation in the study will end if you become pregnant. We ask that, in the event that you do become pregnant, you immediately notify study staff and stop taking the provided pills.

WILL I RECEIVE ANY COMPENSATION FOR TAKING PART IN THIS STUDY?

If you complete all of the visits and all of the procedures as described for the entire study, you will receive up to $400 in total compensation. $300 will be paid in installments and prorated as follows: you will not receive compensation for visit 1 (the screening visit). You will receive $60 following completion of baseline testing (visits 2 and 3). After successfully completing 8 weeks of the counseling, you will receive $60; after completing 12 weeks of counseling, you will receive $60. You will receive $60 for completion of visit 28 and $60 for completion of visit 29. If you are at least 95% compliant both in terms of visit attendance and pill ingestion, you will receive an additional $100 for a total of $400 for your participation.

Should your participation in the study end early, you will still receive feedback pertaining to your health.

WHAT HAPPENS IF I AM INJURED BECAUSE OF THE RESEARCH?

We will arrange to get you medical care if you have an injury that is caused by this research.

CSU will pay for medical expenses for the treatment of a personal injury that is a direct result of the administration of the study drug (CSU will be reimbursed by AstraZeneca). CSU will not provide compensation for lost wages or for any other damages, expenses or losses, or for medical expenses that have been covered by medical insurance.

Should you sustain an injury that is not the direct result of the study drug, you or your insurance company may have to pay for the required care. The Colorado Governmental Immunity Act determines and may limit Colorado State University, University of Colorado Denver, and University of Colorado Hospital's legal responsibility if an injury happens because of this study. Claims against the University must be filed with Colorado State University within 180 days of the injury.

WHAT IF I HAVE QUESTIONS?

CSU#: 17-7147H
APPROVED: 3/22/2018* EXPIRES: 3/21/2019

Before you decide whether to accept this invitation to take part in the study, please ask any questions that might come to mind now. Later, if you have questions about the study, you can contact the investigators via email:

Dr. Melby - chris.melby@colostate.edu
Dr. Bell - physiology@cahs.colostate.edu

If you have any questions about your rights as a volunteer in this research, contact the CSU IRB at: RICRO_IRB@mail.colostate.edu; 970-491-1553. We will give you a copy of this consent form to take with you.

WHAT ELSE DO I NEED TO KNOW?

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this website at any time.

Your signature acknowledges that you have read the information stated and willingly sign this consent form. Your signature also acknowledges that you have received, on the date signed, a copy of this document containing 12 pages.

_____ _____
Signature of person agreeing to take part in the study Date

_____ _____
Printed name of person agreeing to take part in the study Time of Day

_____ _____
Printed name of person providing information to participant Date

_____
Signature of research staff

CSU#: 17-7147H
APPROVED: 3/22/2018* EXPIRES: 3/21/2019