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:	June 19, 2017
TO:	Rudroff, Thorsten, Health and Exercise Science
	Braun, Barry, Health and Exercise Science, Kindred, John, Health and Exercise Science, Biela, Laurie
FROM:	Swiss, Evelyn, CSU IRB 1
PROTOCOL TITLE:	Medical marijuana and its effects on motor function in people with Multiple Sclerosis: An observational case-control study.
FUNDING SOURCE:	Other Funding
PROTOCOL NUMBER:	16-6685HH
APPROVAL PERIOD:	Approval Date: June 15, 2017 Expiration Date: June 14, 2018

The CSU Institutional Review Board (IRB) for the protection of human subjects has reviewed the protocol entitled: Medical marijuana and its effects on motor function in people with Multiple Sclerosis: An observational case-control study.. 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, Assistant IRB Coordinator - (970) 491-1655; Tammy.Felton-Noyle@Colostate.edu

Swiss, Evelyn

Continuing renewal has been reviewed at the convened meeting on June 15, 2017. Continuation has been approved to recruit the remaining 34 (14 active user; 20 non user) participants with the approved recruitment and consent procedures. Approved documents include: Control Consent, version

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12 May 2017; MMJ Consent, version 12 May 2017.

Approval Period:	June 15, 2017 through June 14, 2018
Review Type:	FULLBOARD
IRB Number:	00010468
Funding:	CSU Crowdfunding Charge

PROTOCOL
Biomedical
Colorado State
University

Protocol # 16-6685HH
Date Printed: 07/18/2018

Protocol Title: Medical marijuana and its effects on motor function in people with Multiple Sclerosis: An observational case-control study.

Protocol Type: Biomedical

Date Submitted: 06/06/2017

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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* * * 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:
   40 (20 MS users; 20 MS non users)

   b. Number of participants studied since the last approval date:
   6 (all MS users)

   c. Total number of participants studied since the beginning of the project:
   6

   d. Number of participants remaining to study (total number of participants approved LESS the total number of participants studied to date):
   34
   (14 MS users; 20 MS non users)

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

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

2 - participants never showed up for scheduled visits and never returned communications, no procedures were performed on these participants

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

N/A

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.**

none

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.**

N/A

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.

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)?**

balance test changed - legged test to two legged test (mCTSIB)
No Rate of Force Development tests performed
Order tests in each visit changed

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.

N/A

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* * * Personnel Information * * *

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
Rudroff, Thorsten		Assistant Professor
Email	**Phone**	**Fax**
Thorsten.Rudroff@colostate.edu	(970) 491-8655	
Department Name	**Campus Delivery Code**	
Health and Exercise Science		
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
Kindred, John		Graduate Assistant
Email	**Phone**	**Fax**
John.Kindred@colostate.edu		
Department Name	**Campus Delivery Code**	
Health and Exercise Science		
Human Subjects Training Completed? Training is required for Co-PI. Training must be updated every three (3) years.		Y

No training data is available.

Department Head Mandatory

Name of Department Head	Degree	Title
Braun, Barry		Professor
Email	**Phone**	**Fax**
Barry.Braun@colostate.edu	(970) 491-7875	
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.		Y

Administrative Contact

Name of Administrative Contact, Project Director, or Lab Coordinator	Degree:	Title
Biela, Laurie		
Email	**Phone**	**Fax**
Laurie.Biela@colostate.edu		
Department Name	**Campus Delivery Code**	
244		
Human Subjects Training Completed? Training is not required for Administrative Contacts		N

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
Employees
Fetuses
X Long-Term Patients
Mentally Disabled
Minors (under 18)
Pregnant Women
Prisoners
Soldiers
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): August 2016

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)

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

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

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)

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 - Fellowships

Funding - Other

Gift Funding

Dept. Funding

Other Funding

Other Fund Name	CSU Crowdfunding Charge
Account #, if known	72153

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* * * 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.)

    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.

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)

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

Medical marijuana and its effects on motor function in people with Multiple Sclerosis: An observational case-control study.

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.

Medical marijuana is commonly prescribed people with Multiple Sclerosis (MS) for symptom, e.g. spasticity and pain, management. Unfortunately not much is known about its effects outside the treatment for these 2 symptoms. Several previous studies have suggested people with MS using medical marijuana have lower levels of physical disability and improved walking abilities. A major limitation of these previous studies is that the investigators used subjective measures of motor function. In this proposed observational case-control study we plan to objectively measure multiple domains of motor function, such as: fatigue, strength, and walking ability in people with MS who are smoking medical marijuana.. No marijuana will be brought on to campus or given to participants. After an online screening and initial phone interview cases (medical marijuana users (smokers)) and controls (non-users) will perform a battery of clinical testing over the course of 3 sessions spread across a 3 week period. Participants will use a log to track their medical marijuana use, which was identified as an area that needed more investigation during the NIH's symposium on marijuana and cannabinoids held at the NIH campus 22 and 23 March, 2016.

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

We expect to identify alterations in motor performance between medical marijuana users (smokers) and non-user who have MS. This line of inquiry will open up future research avenues into the long term benefits and consequences of chronic medical marijuana usage for the treatment of physical impairments in people with MS. We also hope to begin the formation of preliminary usage guidelines for people with MS contemplating using medical marijuana for symptom management.

We hope to determine how regular cannabis use alters resting brain activity in people with MS.

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

August 2016

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).**

Prospective participants will be recruited from the Integrative Neurophysiology Laboratory's (INPL) participant database, the clinical practice of Dr. William Shaffer, Banner Health, Greeley CO, and through advertisements in the Colorado and Wyoming Chapter of the National MS Society newsletters. All experimental procedures will be performed in the INPL (Director: Thorsten Rudroff, PhD, FACSM). Interested individuals will perform an initial screening via an online questionnaire, hosted by Qualtrics, which has a contract with the College of Health and Human Sciences. Contact information for the prospective participants' information will be accessible only to the research staff according to HIPPA regulations. After completion of the online screening form, INPL personal will contact eligible participants via phone and establish 20 case/control matched pairs, 40 total participants. After the pair has been identified INPL staff will schedule the participants' first visit. Eligibility requirements for this study are: medically diagnosed with MS, 30-75 years of age, Moderate disability (Patient Determined Disease Steps score 2-6). Cases will verbally confirm their usage of medical marijuana before matching is conducted. We will only recruit people with MS who smoke medical marijuana. Exclusion criteria include: relapse with the last 60 days; high risk for cardiovascular disease (American College of Sports Medicine risk classification); changes in disease modifying medications within the last 45 days; concurrent neurological/neuromuscular disease, concurrent conditions unrelated to MS that would exacerbate fatigue (anemia, hypothyroidism, shiftwork-related fatigue, B12 deficiency, major sleep disorder, or major depressive disorder); history of traumatic brain injury, seizure disorders, hydrocephalus, traumatic brain injury; diabetes; hospitalization within the last 90 days; alcohol dependence (>2 drinks per day); present history (last six months) of drug abuse; and inability to understand/sign informed consent. Additional participants may be screened and recruited if problems arise within a matched pair, e.g. participants drop out or are unable to meet time commitments.
Medical Marijuana users will be asked to refrain from using cannabis for 8 hours prior to all testing and training to prevent any behavioral/physiological effects of acute intoxication which result from THC.

The experimental protocol for this study consists of three testing sessions.

Session 1
Upon arrival to the Integrative Neurophysiology Lab (INPL) at CSU the investigators will explain the protocol procedures and receive signed informed consent from the participants. After consent a urinalysis assessment for Δ9-tetrahydrocannabinol (THC) will be performed to confirm case/control status. Next participants will complete several questionnaires: Activities-specific Balance Confidence (ABC) Scale, Fatigue Severity Scale (FSS), Beck's Depression Inventory (BDI), the MS Quality of Life (MSQOL)-54 Instrument, the MOS Pain Effects Scale (PES), and the Numeric Rating Scale of Spasticity (NRS). After the questionnaires are complete the participants will undergo a resting metabolic rate (RMR) test. For the RMR participants will be in a supine position for approximately 50 minutes while their expired air is captured and analyzed. Hand grip strength will be assessed using a hydraulic handgrip dynamometer. Participants will perform the hand grip assessment in a seated position with the arms next to the torso and the elbow flexed at 90 degrees with a neutral wrist position. Prior to the conclusion of the first session participants will be introduced to the ActiGraph accelerometer. Participants will be asked to wear the monitor for 7 days in between the first and second visits during the waking hours. During non-wear times, participants will be asked to write any activities performed in a log. Participants will also be given a log to track their medical marijuana usage and they will be asked to bring in any medical labels, labels only no marijuana will be brought onto the CSU campus, so that THC content can be recorded by the investigators. It is expected that the first visit will last between 2-3 hours.

Session 2
At least 7 full days after Session 1 participants will return to the INPL. During this visit participants will perform the MS Functional Composite (MSFC), which consists of a 25 foot walk test (25FWT), the 9 hole peg test (9HPT), and the Paced Auditory Serial Addition Test (PASAT). For the 25FWT participants will be asked to walk 25 feet as quickly, but as safely as possible. This will be performed in a cordoned off hallway with the length clearly marked off. Participants will begin after a short countdown and the time it takes to complete will be measured with a handheld stop watch. Two trials of the 25FWT will be performed and

INPL staff will walk alongside the participants to minimize the risk of falling. Next the 9HPT will be performed. Participants will begin w/ their dominant hand and quickly move 9 cylindrical plastic pegs from a concave dish into 9 holes. Pegs will be placed in the holes 1 at a time and once all pegs are in a hole the participants will remove the pegs and return them to the dish. Each hand will be tested twice and the time of completion will be recorded with a handheld stop watch. The PASAT will be performed after the 9HPT. This test consists of the playback of a series of pre-recorded numbers spoken on a computer. The participants are asked to add the last two spoken numbers which occur every three seconds for a 2 minute period of time. The number of correct answers is recorded by the test moderator. (Previously performed in IRB# 14-5152H)

After the MSFC is concluded participants will rest for at least 5 min before balance testing is performed. To test balance participants will perform the modified clinical test of sensory interaction on balance (mCTSIB). For this test participants will be asked to stand with their feet together with no shoes on. They will stand quietly in this position for 30 sec under 4 conditions: eyes open, eyes closed, eyes open on a foam pad, and eyes closed on a foam pad. At the conclusion of balance testing participants will rest in a seated position for at least 5 min and the instruction for the next test will be given/demonstrated.

After balance assessment strength testing of the right and left legs will be performed. Participants will perform strength testing in a seated position with their knee and hip joints at 90 degrees of flexion. A linear force transducer will be attached to the participant's ankle. Once the participant is in the proper position they will be instructed to perform a series of isometric maximal voluntary contractions (MVC). Participants will be instructed to increase the force of the knee extensors over a period of 3 sec, hold their maximum force output for 3 seconds, and then relax. Participants will perform subsequent trials after at least 1 min of rest. Once the participants' MVC no longer increases in force the investigators will unstrap the person's leg and test the other side. (Previously performed in IRB# 14-5152H)

The next procedure to be performed will be the 6 minute walk test (6MWT). For this test participants will be asked to walk as far as they can in 6 minutes. The test will be performed in a cordoned off hallway with 2 cones placed 30 meters apart. Once the participants begin walking, a timer will be started and the distance covered every min will be recorded. Participants are allowed to stop and rest during the test if required. Every minute during the walk test participants will be asked their rating of perceived exertion (RPE, 0-10 scale).

Session 2 will last approximately 2-3 hours.

Session 3
Force steadiness will be tested during the third visit for both the left and right quadriceps. Three MVC will be performed to verify strength tested during visit 2. Participants will perform 2 trials at 3 different force levels (5, 25, and 50% MVC), in a randomized order, holding each force level for 20 seconds. At least 1 minute rest will be given between each trial. Tests will be performed on the right and left legs. Surface electromyography will be performed on the muscles of the quadriceps femoris and hamstrings (vastus lateralis, vastus medialis, rectus femoris, and biceps femoris). Visual feedback will be provided to the participants on a computer monitor positioned at eye level approximately 1 meter away.

The last test performed will be the timed-up-and-go (TUG), which consists of rising from a chair, walking 3 meters, returning to the starting point, and sitting down. During this test INPL staff will walk near the participants to provide support if needed. The participants are instructed to complete the task as quickly as possible. The time it takes them to complete the task will be measured with a handheld stopwatch.

Session 3 will last approximately 2 hours

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

The goal of this project is to determine how medical marijuana affects aspects of motor performance in people with MS. Therefore all clinical testing needs to be performed in the patient population that is being studied.

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.

N/A

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?

N/A

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 differences are detected?

N/A

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).

N/A

3. Background

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

Several participants in our previous study investigating the predictors of physical activity in patients with MS were using cannabis products. When these individuals were compared to matched individuals they seemed to perform better on the tests measuring motor function. From this initial data, only 4 cannabis users, we became interested in determining if medical marijuana would improve physical function and fatigue in people with MS. Currently we are performing an anonymous online survey hosted through the Qualtrics website investigating cannabis use in people with neurological disorders (CSU IRB# 126-16H). To date, over 450 peoples have taken this survey, with approximately 40% stating they currently use cannabis based products for symptom management.

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

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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.

N/A

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 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

STANDARD OF CARE

If it is only standard of care, skip the rest of this section.

this section. Provide the CSU RCO approval information section.

CSU Radiation Control Office approved protocol number:

CSU Radiation Control Office protocol approval date:

For more information, see the RCO website at:<a href='http://www.ehs.colostate.edu/Wrad/home.aspx' target=_blank >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

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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.

Please read the IND Statements

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

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).**

We plan on recruiting 40 people with MS: 20 are regular cannabis users (smokers), 20 are not users, with an estimate that approximately 5 from each group will not complete the study (i.e. drop out).

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

To investigate the effects of medical marijuana usage on physical function we will employ an observational case-control design. Cases (MS medical marijuana users) will be compared to age, sex, and disease duration matched controls (MS non-cannabis users). The research team has experience with all the methods involved.

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.**

N/A

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.**

N/A

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.**

N/A

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.**

Prospective participants will be recruited from the Integrative Neurophysiology Laboratory's (INPL) participant database, the clinical practice of Dr. William Shaffer, Banner Health, Greeley CO, and through advertisements in the Colorado and Wyoming Chapter of the National MS Society newsletters. All experimental procedures will be performed in the INPL (Director: Thorsten Rudroff, PhD, FACSM). Interested individuals will perform an initial screening via an online questionnaire, hosted by Qualtrics, which has a contract with the College of Health and Human Sciences. Contact information for the prospective participants' information will be accessible only to the research staff according to HIPPA regulations. After completion of the online screening form, INPL personal will contact eligible participants via phone and establish 20 case/control matched pairs, 40 total participants. After the pair has been identified INPL staff will schedule the participants' first visit.

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.**

N/A

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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.

Medically diagnosed with MS, 30-60 years of age, Moderate disability (Patient Determined Disease Steps score 2-6). Cases will verbally confirm their usage of medical marijuana (smokers) before matching is conducted.

Identify exclusion criteria.

Relapse with the last 60 days, high risk for cardiovascular disease (American College of Sports Medicine risk classification), changes in disease modifying medications within the last 45 days, concurrent neurological/neuromuscular disease, hospitalization within the last 90 days, and inability to understand/sign informed consent. Additional participants may be screened and recruited if problems arise within a matched pair, e.g. participants drop out or are unable to meet time commitments.
•A condition unrelated to MS that would exacerbate fatigue, such as anemia, hypothyroidism, shiftwork-related fatigue, B12 deficiency, major sleep disorder, or major depressive disorder
•Medical diagnosis or condition that makes participating in exercise training dangerous, such as major renal, pulmonary, hepatic, cardiac, gastrointestinal, HIV, cancer (other than treated basal cell cancer), other neurological disorders, or pregnancy
•History of heart attack or current diagnosis of cardiovascular disease
•History of seizure disorders (or on medications known to lower seizure threshold), hydrocephalus (buildup of fluid in the brain), or diabetes
•Alcohol dependence or abuse (>2 drinks/day), or present history (last six months) of drug abuse
•History of significant traumatic brain injury or hydrocephalus
•Pregnancy
•Recent hospitalization (within the last 3 months) or enforced bed rest/sedentary state.

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

Prospective participants will be recruited from the Integrative Neurophysiology Laboratory's (INPL) participant database, the clinical practice of Dr. William Shaffer, Banner Health, Greeley CO, and through advertisements in the Colorado and Wyoming Chapter of the National MS Society newsletters. All experimental procedures will be performed in the INPL (Director: Thorsten Rudroff, PhD, FACSM). Interested individuals will perform an initial screening via an online questionnaire, hosted by Qualtrics, which has a contract with the College of Health and Human Sciences. Contact information for the prospective participants' information will be accessible only to the research staff according to HIPPA regulations. After completion of the online screening form, INPL personal will contact eligible participants via phone and establish 20 case/control matched pairs, 40 total participants. After the pair has been identified INPL staff will schedule the participants' first visit.

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.**

We will ask participants whether they are involved in other studies. If they are, we make sure that there are no interference.

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 will receive compensation for their time in the lab totaling $75.00. Participants will receive a $20, $25, and $30 prepaid Visa gift card at the conclusion of the 1st, 2nd, and 3rd session respectively.

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

No costs for participants.

m) **Estimate the probable duration of the entire study. This estimate should include the total time each subject 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 probable duration of the study will be 12 months.

1. Visit: 2-3 hours
2. Visit 2-3 hours
3. Visit 2 hours

*** * * 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.)**

Y **Minimal (everyday living)**
> 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

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.**

N/A

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

Motor Tasks
The most likely adverse event to happen during this protocol is a fall. During the performance of all tests research personnel will be within an arms distance of the participants to provide support if needed. The hallway in which the 6 minute walk test will be performed also has hand rails that can be used at any time if needed. During the step test a hand rail will also be available. All research staff of certified in CPR, AED, and First Aid by the American Red Cross. All participants will be low or moderate risk for an adverse cardiac event as classified by the American College of Sports Medicine. In the case of such an event emergency personal will be notified using standard Human Performance and Clinical Research Laboratory procedures.

Minor muscle pain/stiffness/cramps can occur during the performance of the different strength measurements. If this occurs, the participant will be allowed to move/stretch/massage the muscle. If pain is increased or participant is uncomfortable completing the strength testing those assessments will be skipped. Minor skin irritation can also occur from the surface electromyography electrodes. After and area is properly prepped, if the participant has a skin reaction the electrodes will not be utilized and the task will be performed sans electromyography.

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

N/A

c)

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

1. **Physical well-being.**

Motor tasks
The most likely adverse event to happen during this protocol is a fall. During the performance of all tests research personnel will be within an arms distance of the participants to provide support if needed. The hallway in which the 6 minute walk test will be performed also has hand rails that can be used at any time if needed. During the step test a hand rail will also be available. All research staff of certified in CPR, AED, and First Aid by the American Red Cross. All participants will be low or moderate risk for an adverse cardiac event as classified by the American College of Sports Medicine. In the case of such an event emergency personal will be notified using standard Human Performance and Clinical Research Laboratory procedures.

Minor muscle pain/stiffness/cramps can occur during the performance of the different strength measurements. If this occurs, the participant will be allowed to move/stretch/massage the muscle. If pain is increased or participant is uncomfortable completing the strength testing those assessments will be skipped. Minor skin irritation can also occur from the surface electromyography electrodes. After and area is properly prepped, if the participant has a skin reaction the electrodes will not be utilized and the task will be performed sans electromyography.

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

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.

There is no direct benefit from participating in this research study to the individual research participants. The knowledge derived from this study will allow people with Multiple Sclerosis the ability to make a more informed decision regarding medical marijuana use for disease symptom management. Currently there are no scientifically based guidelines for the use of medical marijuana for this population. This research protocol will provide the groundwork to establish these guidelines allowing medical practitioners and patients to make informed decisions about the possible benefits and consequences of medical marijuana use.

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.

Personal identification is limited to the initial online screening. After eligibility has been determined,

prospective participants will be assigned a unique study ID, example: MSMMJ-###. Subsequent to the assignment of the study ID, all data collected will be collected under the individual's study ID only. A list corresponding personal data to study ID will be kept in a locked filing cabinet within theINPL where access is restricted to authorized key holders. All data will be kept for a minimum of 3 years according to University / State / Federal regulations. All hard copy data will be destroyed via burning at the time that study data is no longer needed/required.

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

N/A

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.**

Electronic data will be stored on the university computer network with access restricted to research personnel. Computers are password protected and require direct on-campus to connections for access. Hard copy information will be stored in a locked filing cabinet in the Integrative Neurophysiology Laboratory. Access to the room is restricted to authorized key holders (Director: Thorsten Rudroff, Students: John Kindred, Nathan Ketelhut). Afterhours access to the building and the department space is restricted to authorized personnel (Department faculty and staff) between the hours of 1700-0700. All data will be kept on hand for at least 3 years. After which hard copies will be destroyed and electronic data deleted from the University's computer system via system administrators. Any backups containing data will be cleaned and sanitized using University approved procedures by the College of Health and Human Sciences IT staff.

Urine samples will be collected for confirmation of participant's group status (case versus control). After immediate confirmation with testing strips the biological samples will be disposed in approved biological sample containers per University / State / Federal regulations.

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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.

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	Control Consent Am 4 12May2017	
Consent Information Type	Consent	
Sponsor's Consent Version Number: (if any)		
Consent Form Template	X Attachment	Consent_Control_Group_20170512 (2)

<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?

Title	MMJ Consent Am 4 12May2017	
Consent Information Type	Consent	
Sponsor's Consent Version Number: (if any)		
Consent Form Template	X Attachment	Consent_MMJ_Group_20170512 (1)

<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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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 <a href=http://ricro.colostate.edu/IRB/ConsentAssentTemplates.html target=_blank > 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

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* * * HIPAA * * *

15. HIPAA

Are you using PHI*? (See definition below)

Y

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

Document Type	**Other Protocol Material**
Attachment	MSQOL54_995
Document Name	MSQOL54_995

Document Type	**Other Protocol Material**
Attachment	MSFC_Manual_and_Forms
Document Name	MSFC_Manual_and_Forms

Document Type	**Other Protocol Material**
Attachment	MMJ_use_log
Document Name	MMJ_use_log

Document Type	**Other Protocol Material**
Attachment	FSS
Document Name	FSS

Document Type	**Other Protocol Material**
Attachment	Beck_Depression_Inventory
Document Name	Beck_Depression_Inventory

Document Type	**Other Protocol Material**
Attachment	Activity LOG
Document Name	Activity LOG

Document Type	**Other Protocol Material**
Attachment	activities_specific_balance_scale_nov_5_2012
Document Name	activities_specific_balance_scale_nov_5_2012

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

Document Type	**Letters of Agreement.Cooperation**
Attachment	Letter_Dr. Shaffer
Document Name	Letter_Dr. Shaffer

Document Type	**HIPAA Authorization Form**
Attachment	HIPAA Release generic
Document Name	HIPAA Release generic

Document Type	**Other Protocol Material**
Attachment	MOS Pain Effects Scale (PES)
Document Name	MOS Pain Effects Scale (PES)

Document Type	**Other Protocol Material**
Attachment	NRS_Spasticity_Figure 1
Document Name	NRS_Spasticity_Figure 1

Document Type	**Letters of Agreement.Cooperation**
Attachment	Letter of Support Dr. Ross, IMPACT Network
Document Name	Letter of Support Dr. Ross, IMPACT Network

Document Type	**Letters of Agreement.Cooperation**
Attachment	IMPACT 2016 Report Public Final
Document Name	IMPACT 2016 Report Public Final

Document Type	**Recruitment Material (e.g., flyers, email text, verbal scripts)**
Attachment	Rudroff_Recruitment_flyer_MMJ (2) Qaualtric web address
Document Name	Rudroff_Recruitment_flyer_MMJ (2) Qaualtric web address

Document Type	**Other Protocol Material**
Attachment	Rehab Measures - Modified Clinical Test of Sensory Interaction...[3726]
Document Name	Rehab Measures - Modified Clinical Test of Sensory Interaction...[3726]

Document Type	**Collaborating Investigator's IRB approval and associated documents**
Attachment	Rudroff NTF 16.6685HH
Document Name	Rudroff NTF 16.6685HH

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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 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
05/26/2016	NEW FORM CREATED		
06/28/2016	NEW FORM SUBMITTED	Y	
07/05/2016	NEW FORM PANEL ASSIGNED		
07/14/2016	NEW FORM REVIEWER(S) ASSIGNED		
07/18/2016	NEW FORM REVIEWER(S) ASSIGNED		

08/01/2016	NEW FORM REVIEWER(S) ASSIGNED		
08/17/2016	NEW FORM MOVED		
08/17/2016	NEW FORM APPROVED	Y	Y
10/03/2016	AMENDMENT 1 FORM CREATED		
10/04/2016	AMENDMENT 1 FORM SUBMITTED	Y	
10/14/2016	AMENDMENT 1 FORM REVIEWER(S) ASSIGNED		
11/04/2016	AMENDMENT 1 FORM REVIEWER(S) ASSIGNED		
11/11/2016	AMENDMENT 1 FORM MOVED		
11/11/2016	AMENDMENT 1 FORM APPROVED	Y	Y
11/11/2016	AMENDMENT 2 FORM CREATED		
11/11/2016	AMENDMENT 2 FORM SUBMITTED	Y	
11/11/2016	AMENDMENT 2 FORM APPROVED	Y	Y
02/22/2017	AMENDMENT 3 FORM CREATED		
02/22/2017	AMENDMENT 3 FORM SUBMITTED	Y	
02/23/2017	AMENDMENT 3 FORM REVIEWER(S) ASSIGNED		
03/07/2017	AMENDMENT 3 FORM APPROVED	Y	Y
05/12/2017	AMENDMENT 4 FORM CREATED		
05/15/2017	AMENDMENT 4 FORM SUBMITTED	Y	
05/16/2017	AMENDMENT 4 FORM REVIEWER(S) ASSIGNED		
05/18/2017	AMENDMENT 4 FORM MOVED		
05/18/2017	AMENDMENT 4 FORM APPROVED	Y	Y
06/06/2017	CONTINUING REVIEW 1 FORM CREATED		
06/06/2017	CONTINUING REVIEW 1 FORM SUBMITTED	Y	
06/09/2017	CONTINUING REVIEW 1 FORM REVIEWER(S) ASSIGNED		
06/19/2017	CONTINUING REVIEW 1 FORM APPROVED	Y	Y
05/30/2018	FINAL FORM CREATED		
05/30/2018	FINAL FORM SUBMITTED	Y	
05/30/2018	FINAL FORM APPROVED	Y	N
05/30/2018	CLOSED		

Consent to Participate in a Research Study
Colorado State University

TITLE OF STUDY: Medical marijuana and its effects on motor function in people with Multiple Sclerosis: An observational case-control study.

PRINCIPAL INVESTIGATORS:
The principal investigator is a researcher in the Department of Health and Exercise Science at Colorado State University:

Thorsten Rudroff, Ph.D., FACSM
Thorsten.Rudroff@ColoState.EDU
970-491-8655

WHY AM I BEING INVITED TO TAKE PART IN THIS RESEARCH?
You are an adult aged between 30 and 60 years of age, and you were diagnosed with Multiple Sclerosis.

WHO IS DOING THE STUDY?
Dr. Rudroff and the Integrative Neurophysiology Laboratory students/research staff.

WHAT IS THE PURPOSE OF THIS STUDY?
The purpose of this study is to determine possible benefits and consequences associated with medical marijuana use for the management of symptoms related to a diagnosis of Multiple Sclerosis.

WHERE IS THE STUDY GOING TO TAKE PLACE AND HOW LONG WILL IT LAST?
The study will take place in the Integrative Neurophysiology Laboratory in the Department of Health and Exercise Science, on the Colorado State University campus. The study will run for approximately 12 months. You will take part in the study for approximately a total of 8 hours over the span of three weeks.

WHAT WILL I BE ASKED TO DO?
You will be asked to participate in two sessions on two different days:

Visit 1
Your first visit will include the following procedures and tests:

- *Urinalysis*: We will ask you to provide a urine sample for the confirmation of your research group assignment.
- *Questionnaires:* You will be asked to complete a series of questionnaires to determine your fatigue levels, perceived risk of falling, mood, and quality of life.
- *Resting Metabolic Rate*: You will lay comfortably on a bed while we capture the air you are breathing out. Will analysis this air to determine how many calories

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you typically burn throughout the day and whether the carbs, proteins, or fats are your primary sources for energy generation.

- *Handgrip Strength:* We will measure your maximal handgrip strength using a device which you have to squeeze alternately with your left and right hand up to five times.
- *Physical Activity:* At the end of the first session, you will be introduced to the ActiGraph device, which will measure physical activity. You will be asked to wear this device on your waist for a period of seven days (five week days and two weekend days). You can remove the ActiGraph at night. You will be asked to return the ActiGraph at your second experimental session, which will be at least seven days after the first session. Furthermore, you will receive a log to track their wear time.

This visit will last approximately 120-180 minutes.

Visit 2

Your second visit will consist of the following tests:

- *MS Functional Composite*: This is a series of 3 tests. The first test consists of you walking 25 feet as quickly and safely as possible, 2 times. The next test involves you placing 9 plastic pegs into a square grid of holes and removing them. The last test will have you add (+) a series of numbers spoken on a computer.
- *Balance test:* In this test you will stand on a platform with your feet next to each other. You will stand quietly for 30 seconds in 4 different conditions: eyes open, eyes closed, eyes open on a foam pad, and eyes closed on a foam pad.
- *Leg Strength:* The maximal strength of each leg will be measured by having you perform a series of maximal effort knee extension, knee flexion, plantar/dorsi-flexion trials. This will be performed one leg at a time up to five times.
- *6 minute walk test:* The object of this test is to walk as far as possible for 6 minutes. You will walk back and forth in a hallway around cones, and are permitted to slow down, to stop, and to rest as necessary. You may lean against the wall while resting, but resume walking as soon as you are able.

This second visit will last approximately 120-180 minutes.

Visit 3

Your third visit will consist of the following tests:

- *Force Steadiness*: For this test you will produce a submaximal force, 5%, 25% and 50% of your maximum strength, of your thigh muscles and hold for a period of 20 seconds. During this time we will place 4 stickers on your muscles designed to measure the electrical activity of your muscles while they are contracting.
- *Timed-Up-and-Go*: For this test we will record the time it takes you to rise from a chair, walk 3 meters, and return to the position you started in.

This third visit will last approximately 120-180 minutes.

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ARE THERE REASONS WHY I SHOULD NOT TAKE PART IN THIS STUDY?
You should not take part in this study if:

- A relapse of disease symptoms in the last 60 days
- A condition unrelated to MS that would exacerbate fatigue, such as anemia, hypothyroidism, shiftwork-related fatigue, B12 deficiency, major sleep disorder, or major depressive disorder
- Medical diagnosis or condition that makes participating in exercise training dangerous, such as major renal, pulmonary, hepatic, cardiac, gastrointestinal, HIV, cancer (other than treated basal cell cancer), other neurological disorders, or pregnancy
- History of heart attack or current diagnosis of cardiovascular disease
- History of seizure disorders (or on medications known to lower seizure threshold), hydrocephalus (buildup of fluid in the brain), or diabetes
- Alcohol dependence or abuse (>2 drinks/day), or present history (last six months) of drug abuse
- History of significant traumatic brain injury or hydrocephalus
- Pregnancy
- Recent hospitalization (within the last 3 months) or enforced bed rest/sedentary state.

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.

Risks of Performing Motor Tasks

Generally, the procedures outlined for measuring force and muscle activity during the motor tasks are safe. Nevertheless, there is potential for injury (muscle strain), resulting from the maximal contractions. There is a 0.01% chance of death (in people who have heart problems), a 0.02% risk of cardiac arrhythmias that would require you to go the hospital (in people with heart problems), and a risk of an increase or decrease in blood pressure.

All contractions are voluntary and you can stop immediately if they experience any slight pain or discomfort. Following participation, you may experience some muscle soreness. Muscle soreness tends to be more common for individuals who have not exercised recently. Other risk factors may include increased feelings of anxiety and/or stress induced by the experiment, which can lead to an increase in heart rate and blood pressure. The electrodes that will be used to measure muscle activity could potentially

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cause skin irritation after removal. Furthermore, your skin will need to be shaved prior to placing the electrodes, which can also cause irritation.

General Risk

Even though the risk is minimal, there is a risk for breach of confidentiality. Your data will be coded to prevent any link to your identity, and any identifying material will be locked in a secure filing cabinet. Furthermore, the potential physical risks of participating in the proposed experiments are reasonably small. The motor performance tasks have been used previously by the members of the investigative team without complication.

ARE THERE ANY BENEFITS FROM TAKING PART IN THIS STUDY?
There may be no direct benefit to you associated with this research. This study is designed for the researcher to learn more about the effects of medical marijuana use for symptom management related to your diagnosis of Multiple Sclerosis. This study is not designed to treat any illness or to improve your health specifically.

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.

WHAT WILL IT COST ME TO PARTICIPATE?
Other than transport to and from the lab, 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. Your information will be combined with information from other people taking part in the study. When we write about the study to share 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.

We will make every effort to prevent anyone who is not on the research team from knowing that you gave us information, or what that information is. For example, your name will be kept separate from your research records and these two things will be stored in different places under lock and key. You should know, however, that there are some circumstances in which we may have to show your information to other people. We may be asked to share the research files with the CSU Institutional Review Board ethics committee for auditing purposes, if necessary.

CAN MY TAKING PART IN THE STUDY END EARLY?
If you fail to show up to your visits you may be removed from the study.

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

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Yes, you will receive $20, $25, and $30 pre-paid Visa gift cards after the 1st, 2nd, and 3rd visits, respectively.

WHAT HAPPENS IF I AM INJURED BECAUSE OF THE RESEARCH?
The Colorado Governmental Immunity Act determines and may limit Colorado State University's legal responsibility if an injury happens because of this study. Claims against the University must be filed within 180 days of the injury. The research team will not cover any injury resulting in this study. You and/or your health insurance will be responsible for paying for any study-related injury.

FUTURE STUDIES:
Would you like to be contacted for future studies that you may be eligible for? Please initial: _____Yes _____No

WHAT IF I HAVE QUESTIONS?
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 investigator, Dr. Thorsten Rudroff, via phone 970-491-8655 or email: Thorsten.rudroff@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.ClinicialTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at anytime.

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 5 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

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Name of person providing information to participant Date

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- *Handgrip Strength:* We will measure your maximal handgrip strength using a device which you have to squeeze alternately with your left and right hand up to five times.
- *Medical Marijuana Use*: We will give you a log to track your medical marijuana usage over the next 7 days.
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Signature of person agreeing to take part in the study Date

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

_____ _____
Name of person providing information to participant Date

_____
Signature of Research Staff

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Statistical Analysis

All data are reported as Mean (Standard Deviation) unless otherwise noted. Pearson's correlations were calculated between demographic variables (age, height, weight, BMI, disease duration) and whole brain SUV to identify possible covariates for the SPM analysis. Significant factors were individually tested as covariates during SPM analysis.

Demographic, clinical, and extracted regional SUV variables were compared between the two groups using unpaired student's t-tests. If a clinical variable differed between the two groups a Pearson's correlation was performed with it and regional SUVs. Cohen's D measures of effect size were calculated for the regional SUVs. Analysis was performed using IBM SPSS Statistics for Windows version 24 (IBM Corp., NY, USA) with alpha set to 0.05.