Performance Work Statement (PWS)
7-Day Hypobaric Hypoxia Chamber Testing

The Contractor shall provide the infrastructure, personnel, training, materials, foods, supplies, and operational support necessary to execute the objective of the hypobaric chamber testing. The objective is to investigate the physiological, cognitive, and clinical effects of mild hypobaric hypoxia to inform vehicle atmospheric conditions for NASA's Artemis Program.

Facilities are requested to perform two 7-day test protocols with continuous habitation, of which the first 2 days will be at ambient conditions for baseline data collection in the chamber and the subsequent 5 days will be at a lower atmospheric pressure. Facilities will recruit and screen 6 subjects to participate in the testing described below in two different air equivalent air altitudes in a cross-over design:

1. 7000 ft (21% O_2 at 587 mmHg [11.3 psi])
2. 9500 ft (21% O_2 at 533 mmHg [10.3 psi])

That is, each subject will complete two 7-day chamber tests, one in each condition. During these tests, the facility will collect and record data each day as outlined by NASA.

First 7-day test (n=6) at one of the two altitudes listed above

Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Ambient	Ambient	21% O_2 at 587 mmHg	21% O_2 at 587 mmHg	21% O_2 at 587 mmHg	21% O_2 at 587 mmHg	21% O_2 at 587 mmHg

At least one week washout period

Second 7-day test (same n=6) at one of the two altitudes listed above

Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Ambient	Ambient	21% O_2 at 533 mmHg	21% O_2 at 533 mmHg	21% O_2 at 533 mmHg	21% O_2 at 533 mmHg	21% O_2 at 533 mmHg

The objective of the multiple-day testing is to characterize acute responses and the time course of acclimation using clinical and physiological measurements in participants who are housed continuously for 7 days in the chamber. The data from these studies will be included in a larger data set for the development of the Aerospace Estimation Tool for Hypobaric Exposure Risk (AETHER).

Subjects

Facilities will recruit and screen applicants to participate in the two 7-day chamber test protocols as specified by NASA. Screening back-up subjects in case of subject availability issues, withdrawal, or disqualification is highly recommended. Facilities should screen subjects per their standard protocols, and the set of participants should aim to include ~50% females. Facilities will be expected to recruit an "astronaut-like" population of study participants. NASA will provide inclusion and exclusion criteria for a population demographic similar to the astronaut corps.

Target characteristics include subject's age between 30 and 60 years old and overall good health. subjects must complete a peak (or maximal) aerobic capacity (VO_2pk) test using a cycle ergometer protocol with metabolic gas analysis. NASA will provide the VO_2pk cycle ergometry test protocol, but facilities will be responsible for conducting the test. To qualify for participation, subjects must achieve VO_2pk >27.5 ml/kg/min.

Following the screening, subjects will participate in an informed consent session during which they will receive verbal and written descriptions of the test protocol, be encouraged to ask questions, and will provide written consent before proceeding to participation in the chamber study. Thereafter, subjects will be trained and familiarized with the chamber protocol and safety procedures by the facility, and the subjects will be familiarized with the scientific measurements to be implemented on each day during the test. Additionally, subjects will participate in an exercise workload verification trial to ensure the proper prescription and execution of exercise while in the chamber.

Standardized Test Plan

Facilities will implement a test protocol that includes 2 days of in-chamber baseline testing at ambient conditions, and 5 days of habitation and acclimation at the hypobaric chamber environment. On each test day in the chamber, subjects will undergo a set of measures to characterize their physiological and cognitive response to the chamber environment. The facility will provide in-chamber operators to perform physiological testing and assist with other operations but there is not a requirement for those operators to be present inside the chamber throughout the entirety of the 7-day chamber tests.

Subjects will exit the chamber upon test completion after 7 full days of data collection unless signs and symptoms that require test termination (per NASA and facility standards) occur, on request by the subject, or in the case of facility or monitoring malfunctions that preclude safe continuation of the test protocol. The test must include practices to ensure subject safety during the performance of experimental protocols to characterize health and performance during hypoxia, as well as robust hardware capabilities and procedures to ensure the ability to collect all scientific data reliably. Data collection on each day will include questionnaires, computer-based tasks, actigraphy/wearables, visual tests, cardiopulmonary function at rest and during exercise, ultrasound measurements, food records, blood and urine collection, and blood volume measurements.

Medical Monitoring

The facility will provide the appropriate medical support, to perform pre-chamber physical examinations before ingress, monitoring and assessment during the 7-day tests, and for treatment and management of subjects, as needed. Medical support also will include post-chamber physical examinations and assessments prior to release of the subjects after the chamber run is completed and follow-up with the test participants in the days after the chamber run. Responsibilities of the medical personnel include monitoring of the subject's health, including self-report, signs, and symptoms of conditions related to the hypobaric exposure.

Experimental Protocol and Multi-day Habitation

Facilities will perform standardized data collections of all measures described below on all subjects on a timeline provided by NASA. Facilities will provide for continuous habitation in the chamber, including provision of food and water, hygiene stations, sleeping stations, and management of human waste. Compliance of the subjects with the prescribed procedures should be documented, including the time for each data collection, symptoms reported by the subjects, and test operator observations.

Standardized Measures

Facilities will use a standardized set of measurements to monitor and document test subjects during their stay in the chamber. This harmonized approach enables direct comparisons of outcomes across different artificial atmospheres and supports future integration of data with NASA facilities and other external hypoxia-testing facilities. Domains relevant to astronaut health and performance to be assessed include cognition, sleep, vision, appetite and food intake, cardiopulmonary responses at rest and during exercise, blood volume and viscosity, iron metabolism, immune function, oxidative stress, and classic hypoxia-related symptoms.

The tests and schedule within the chamber test are listed below (Table 1). For tests that do not require an individual test station that has to be used by all participants, all participants should complete surveys or collect data at approximately the same time of day. For tests that must be performed sequentially across the subjects, within a subject the testing should occur at approximately the same time of day.

Assume analysis of measure below is performed by NASA.

*Table 1. Schedule and estimated duration (**minutes**) required to perform each measurement (minutes per participant per test occurrence) to characterize hypoxia responses*

Measure	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
	Site pressure baseline		**Hypoxia adaptation characterization**				
Symptomatology	15	15	15	15	15	15	15
Cognitive performance	1x60, 5x30		30	30	30	30	30
Workload	2	2	2	2	2	2	2
Sensorimotor	15	15	15	15	15	15	15
Vision	2x15	2x15	2x15	2x15	2x15	2x15	2x15
Sleep	20	20	20	20	20	10	20
Cardiopulmonary response – Rest	45	45	45	45	45	45	45
Cardiopulmonary response - Exercise	2x45 (SS, HIIT)			45 (SS)	45 (HIIT)	45 (SS)	
Blood volume quantification		45					45
Blood sampling (iron metabolism/ coagulation/oxidative damage/immune /inflammation)		5					5
Saliva sampling (immune system/ inflammation)		3	3	3	3	3	3
Food system	80	20	20	20	20	20	20
Study acceptability	5	5	5	5	5	5	5

The contractor will execute all data collection and transmittal of data to JSC for Base activities listed above. Blood and saliva biomarkers are separately included as optional work, see optional section at bottom of the page.

Assessment of Acute Mountain Sickness and Other Symptoms

To quantify hypoxia-related symptomatology, participants will complete the Lake Louise Acute Mountain Sickness (AMS) Scoring questionnaire (1) each day in the morning and evening during baseline data

collection (chamber test days 1 and 2) and during hypobaric exposure (chamber test days 3-7). The AMS score reflects the sum of 5 symptom items rated on a 0-3 scale. Consistent with standard criteria, AMS is diagnosed when a participant reports a headache plus at least 1 additional symptom – gastrointestinal symptoms, fatigue and/or weakness, dizziness and/or lightheadedness – with a total score of 3 points or greater. The Environmental Symptoms Questionnaire (ESQ) (2) will be administered on the same schedule as a more comprehensive assessment of symptomatology. In addition to these structured measures, test operators and the attending medical officer will document all symptoms reported during the study, whether elicited during scheduled assessments or spontaneously communicated by participants. This combined approach ensures comprehensive capture of both expected and unexpected manifestations of acute hypobaric hypoxia.

Cognitive Performance
Cognitive performance will be quantified using the Automated Neuropsychological Assessment Metrics (ANAM) (3) which is a suite of computer-based tests designed to measure cognitive function at a single time-point or longitudinally to detect changes in cognitive function. Subjects will perform the ANAM on a tablet device once per day at approximately same time of day for 30 minutes. If ANAM testing on a tablet device is not feasible then the computer/laptop version of ANAM will be used instead, which has been shown to have good-to-excellent reliability across a seven-day retest interval with minimal practice effects (4). To minimize practice effects, subjects will complete a familiarization and training session (60 minutes) followed by 5 baseline sessions during chamber test days 1 and 2. Cognitive performance tests will be repeated daily on chamber test days 3-7 during the hypobaric exposure.

Cognitive Workload
Cognitive workload will be assessed during baseline data collection on chamber test days 1 and 2 and each day during hypobaric exposure (chamber test days 3-7) using the NASA Task Load Index (TLX). The TLX assesses workload across several subdomains, including mental demand, physical demand, frustration, effort, and performance. The NASA-TLX is diagnostic and multi-dimensional, comprising six dimensions, and can allow for the source of workloads to be localized looking at the buildup of workload over time. The NASA TLX will be delivered via Qualtrics and takes approximately 1 minute to complete. Wireless networking capabilities in the chamber are highly desired for this application but not required.

Sleep Quality and Duration
Assessment of the impact of hypoxia on respiratory outcomes during sleep and sleep quality will be performed using the Nox T3 (Nox Medical, Alpharetta, GA), a compact FDA-cleared home sleep testing device designed to measure respiratory flow, oxygen levels, and body position. Participants will wear the Nox T3 during the two-day baseline and during test days 3-5 and 7 during hypobaric conditions to evaluate respiratory function during sleep. This will allow us to evaluate acute changes in respiratory function in response to hypoxia and the time course of adaptation to the hypobaric environment. This device is frequently used by clinicians to conduct at-home sleep apnea tests, making it easy to use compared to traditional laboratory polysomnography. The Nox T3 has been validated in clinical settings and is accurate and reliable for detecting apneas and hypopneas. The apnea-hypopnea index is calculated using a validated automated scoring algorithm. The Nox T3 does not include electroencephalography, which is the gold-standard for measuring sleep architecture, but it does include algorithms to estimate REM and non-REM sleep, providing some data to evaluate sleep architecture. Subjects also will complete the Karolinska Sleepiness Scale prior to hypobaric exposure during chamber test days 1 and 2 and in the morning and evening of each day during hypobaric exposure. The Epworth Sleepiness Scale (ESS) will be completed prior to hypobaric exposure. Participants also will wear an ActiLumus actigraph (Condor Instruments, Sao Paulo, Brazil), or equivalent, continuously before and during hypobaric exposure (all chamber test days) to compare nights when respiratory function is not measured to nights when it is measured to identify potential variations in night-to-night sleep. Also, occurrence of arousals detected in

the actigraphy data will be compared to arousals captured by the Nox T3 to determine whether actigraphy could be used to detect respiratory-related arousals during future missions.

Visual acuity and Contrast Sensitivity
The Freiburg Acuity and Contrast Test (FrACT) is a validated, tablet-based vision assessment tool designed to measure both visual acuity (VA; high-contrast spatial resolution) and contrast sensitivity (CS; ability to detect low-contrast targets) in about 5 minutes. For both VA and CS testing, individual Landolt C targets are presented randomly in 8 possible orientations. For each presentation, subjects are asked to identify the target orientation. Based on correct/incorrect subject responses, an adaptive algorithm automatically adjusts the target size (VA) or contrast (CS) in successive trials to determine the threshold at which a person can no longer reliably identify the stimulus. This approach requires minimal subject and facility training, is faster and more precise than traditional eye charts, and allows for standardized and repeatable measurements across different settings. Testing will occur binocularly under photopic visual conditions and will be completed in the morning and evening of each day prior to hypobaric exposure (chamber tests days 1 and 2) and during hypobaric exposure (chamber test days 3-7). Tablet test luminance will be standardized using a light meter; eye-to-target test distance will be set to 2 meters; and stray illumination will be minimized.

Note: The vision tests also require standardized hardware (like ANAM), to ensure consistent display brightness/resolution/etc

Color vision
The Waggoner Computerized Color Vision Test (WCCVT) is a validated, FAA/DoD-approved, tablet-based vision assessment tool designed to evaluate an individual's ability to perceive and differentiate colors. The test takes about 5 minutes. It primarily screens for congenital or acquired color vision deficiencies such as red-green (R/G) or blue-yellow (B/Y) anomalies but can also identify more severe conditions like achromatopsia. In this study, the WCCVT will be used to determine if the unique pressure and oxygen levels of the hypobaric chamber environment degrade the color perception of subjects. The test uses a series of digital images that incorporate colored patterns (numbers) embedded within a background of different colors or dots. These patterns are arranged such that individuals with normal color vision can easily identify the figures, while those with color vision deficiencies struggle or fail to see them. Testing will occur binocularly under photopic visual conditions within subject's sleep station, completed prior to depress (chamber test days 1 and 2) and in the morning and evening of each day during hypobaric exposure (chamber test days 3-7). Testing includes 25 general (red-Green) color vision plates and 12 blue-yellow plates. Tablet test luminance will be standardized using a light meter, eye-to-target test distance will be approximately 60 centimeters, and stray illumination will be minimized.

Cardiopulmonary Response at Rest
Assessment of peripheral estimates of O_2 saturation, ventilation (including tidal volume and respiratory rate), heart rate, and end-tidal PCO_2 will provide insight into the physiological responses to the hypoxic stressor. These data will be collected after at least 5 minutes of quiet rest in both the seated and supine posture. Supine posture elicits an upward shift of the diaphragm, a mild decrease in ventilation, and resulting increase in end-tidal PCO_2. Participants will be instructed to rest in supine position for 5 minutes without any activities prior to measurements. Measurements will then be taken for 5 minutes. All measurements, including SpO_2, non-invasive arterial blood pressure, heart rate and rhythm, and respiratory variables (respiratory rate, tidal volume, minute ventilation, gas exchange including end-tidal CO_2) will be measured using the COSMED Quark CPET metabolic cart (Rome, Italy) with integrated modules, or an equivalent metabolic cart. An ECG is required instead of a heart rate monitor to enable detection of dysrhythmias. Arterial pressure will be measured with automatic blood pressure cuff. Pulmonary artery systolic pressure (PASP) will be measured using Doppler ultrasound (GE Vivid IQ or

similar device), and cardiac output will be measured through assessment of left ventricular outflow tract (LVOT) velocity time integral and LVOT cross-sectional area with ultrasound, along with heart rate.

Blood Oxygenation and Heart Rate Responses to Exercise

Cardiopulmonary exercise testing (CPET) will be performed prior to hypobaric exposure at baseline and during hypobaric exposure to establish cardiorespiratory fitness (CRF) and to detect changes from baseline. A combination of two exercise prescriptions will be performed during the chamber stay that are representative of an operational exercise countermeasure profile. The steady state (SS) exercise prescription will be set at a fixed watts 50% of the way between watts at ventilatory threshold one (VT_1) and ventilatory threshold two (VT_2) (5). The high intensity interval (HIIT) prescription is set at 10% between VT_2 and adjusted watts at VO_2pk. Both the SS and HIIT prescriptions will be performed in normoxic (chamber test days 1 and 2) and hypoxic conditions (chamber test days 4-6). A load-verification trial will be performed prior to ingress to familiarize subjects with the training prescriptions and determine if modifications to the exercise prescriptions are required. All measurements, including SpO_2, non-invasive arterial blood pressure, heart rate and rhythm, and respiratory variables (respiratory rate, tidal volume, minute ventilation, gas exchange including end-tidal CO_2) will be measured using the COSMED Quark CPET metabolic cart (Rome, Italy) with integrated modules or an equivalent metabolic cart . An ECG is required instead of a heart rate monitor to enable detection of any arrythmias. Arterial pressure will be measured with automatic non-invasive blood pressure cuff. Measurements will be performed during a 5-minute resting baseline, followed by exercise on a cycle ergometer (Lode Excalibur or Corival, Groningen, Netherlands or an equivalent ergometer). Magnitude of change from resting hypoxic baseline and the rate of change back to hypoxic baseline will be recorded for each subject. The total protocol lasts about 40 minutes per subject.

Blood Volume Quantification

Intravascular volumes, including hemoglobin mass (Hbmass), red blood cell volume (RBCV), total blood volume (BV), and plasma volume (PV) will be determined using the carbon monoxide (CO) rebreathing method. This method is based on the dilution principle: inhaled CO binds strongly to circulating hemoglobin (Hb), and the resulting increase in carboxyhemoglobin is used to calculate total circulating hemoglobin mass. From Hbmass, RBCV, BV, and PV can then be derived. Measurements involve a 20-min period of supine rest to redistribute blood prior to the measurement and facilitate vascular mixing of CO in the bloodstream, followed by breathing 100% O_2 for 2 minutes to ensure full O_2 saturation immediately prior to the test, using an automated respiratory device (Carbon Monoxide Rebreather, Detalo Health, Hørsholm, Denmark). Using the same device to safely and precisely deliver CO, subjects then perform 4 minutes of CO rebreathing using a small bolus of CO of 0.8 ml/kg for females and 1.0 mL/kg for males. This amount has previously shown to prevent any notable reductions in arterial O_2 content during the rebreathing period, although a slight decrease in aerobic exercise capacity may be reported due to increases in carboxyhemoglobin (HbCO). At normal atmosphere, 12-14 h is sufficient to restore HbCO to normal levels. Measurements of CO rebreathing have been safely performed at altitudes as high as 16,700 ft (5,100 m). Venous blood sampling will be performed prior to and within 2 min following completion of CO rebreathing to determine intravascular volumes. Hemoglobin concentration ([Hb]) and hematocrit (Hct) will be obtained from a morning, fasted, venous draw to standardize pre-analytic conditions and to reduce variability from diurnal plasma-volume shifts and food/fluid intake. The CO rebreathing tests will be conducted later the same day. Because Hbmass does not meaningfully fluctuate hour-to-hour within a day, pairing a standardized morning Complete Blood Count with a same-day CO rebreathing test for determination of HbCO and Hb concentrations supports accurate calculation of intravascular volumes while limiting influence of time-of-day and feeding/hydration effects. The protocol lasts about 40 minutes per subject, and will be performed once prior to depress (chamber test day 2), and on chamber test day 7 during hypobaric exposure. A CO sensor will be placed next to the CO cylinder to minimize risk of CO poisoning from inadvertent leaks.

Blood Coagulability
Venous blood samples will be collected using a 1.8 ml and a 5.0 ml sodium citrate tube, once prior to depress on chamber test day 2 and on chamber test day 7 during hypobaric exposure. Coagulability will be measured using thromboelastography (TEG) within 60-120 min after blood draw, with samples maintained at room temperature. TEG is a noninvasive test that will detect and quantify changes in coagulation properties of blood samples during clotting. In addition, key parameters of coagulability will be determined that align with other HRP thrombosis risk studies, including fibrinogen, antithrombin, thrombin antithrombin complex, protein C, protein S, fibrin D-dimer, plasminogen, tissue plasminogen activator, plasminogen activator inhibitor type 1, platelet flow cytometry, P-selectin, V-CAM, Syndecan, Von Willebrand factor, soluble tissue factor, prothrombin fragment 1.2, heat shock protein 47.

Serum Parameters of Erythropoiesis, Iron Metabolism, and Oxidative Damage
Venous blood samples will be collected using a 4.9 ml EDTA and a 7.5 ml serum monovette blood tubes, once prior to depress on chamber test day 2 and on chamber test day 7 during hypobaric exposure. All blood collections will be fasted (8-hr fast). Key parameters of erythropoiesis and iron metabolism will be determined, CBC, including erythropoietin, iron, transferrin, TIBC, ferritin, soluble transferrin receptor, and hepcidin. Samples will also be analyzed for satiety hormones (leptin and ghrelin), antioxidant status (superoxide dismutase, catalase, glutathione peroxidase, total lipid peroxides, glutathione), C-reactive protein, Endothelin-1, GFAP, HIF-1A, HSP-70, HSP-47 folate, cortisol, and general chemistry. Blood samples will be centrifuged and serum will be collected and stored at -80°C until batch analysis.

Immunological and Inflammatory Responses
Venous blood samples will be collected using a 5.5 ml heparin monovette tube once prior to depress on chamber test day 2 and on chamber test day 7 during hypobaric exposure. Longitudinal assays include CBC, leukocyte subset phenotyping, plasma cytokine profiles (up to 38 plex analysis), and mitogen stimulated cytokine release profiles.

At least 1 ml of passive drool saliva will be collected in the morning on test day 2 and daily in the morning on chamber test days 3 to 7 during hypobaric conditions to determine the reactivation pattern of latent herpesviruses (a clinically relevant biomarker for immune dysregulation) as well as salivary stress biomarkers.

Appetite and Food Intake
To obtain the most accurate expectation of food acceptability and associated intake and health and performance outcomes, NASA will provide guidelines for dietary intake and nutrient composition per individual (see Attachment 1, **Table 2**). Measures to be implemented will characterize appetite, food intake, satiety hormones, and body composition changes to document these relationships in the hypobaric hypoxic atmosphere. Caloric requirements will be determined for each subject using the dietary reference intake predictive energy equations for active, normal weight adults. Additional calorie requirements will be determined to accommodate test operations based on VO_2max. It is expected that there will be hot water but no food warmer. Subjects will provide a weighed food and beverage record for one week prior to entering the chamber, and at least one fasted body weight on the same scale that they will use in the chamber to establish a baseline. Fasted body mass and composition will be determined by 60-min dual-energy X-ray absorptiometry (DXA) within 2 days before and after the mission to determine how much body mass loss is attributed to fat free mass. Subjects will record all foods and beverages consumed in the mission using an excel template. Subjects will provide subjective ratings for food acceptability at each meal and for appetite and nausea at various time points relative to meals both at baseline and during hypobaric exposure. Ghrelin and leptin will be measured while fasted pre- and in-mission, shared from blood draws from the oxidative damage protocol.

<u>Data Validation</u>

At the conclusion of each 7-day chamber test, the facility will deliver electronic records to NASA using a secure, NASA-approved method. The data package will include subject metadata, console and/or operator's logs (including chamber event time, data collection schedule and times), chamber pressure recordings (demonstrating depress and repress rates as well as sustained chamber pressure), chamber environmental conditions (partial pressures of O_2, CO_2, and N_2, temperature, humidity), medical monitoring logs, data recordings for each of the above measurements as applicable, in-chamber video of data collections, and case descriptions of altitude-related illness, including but not limited to symptoms and/or diagnosis of Acute Mountain Sickness (AMS), High-Altitude Pulmonary Edema (HAPE), and High-Altitude Cerebral Edema (HACE).

Test Plan Verification, Training, and Reporting

NASA will meet with each facility to discuss the test plan before submission of required documents to facility's governing IRB (and NASA, as required) to verify expectations of the chamber study and the notional schedule.

For each facility, NASA also will provide training in:

- Specific test procedures
- Exercise prescription and monitoring

NASA may monitor the chamber runs to answer any questions in real-time and recommend any changes to the procedures. At the completion of the chamber tests, NASA will coordinate a meeting with the facility to discuss results of the study and forward plans.

Equipment:

Nasa will provide Phantom plus masks for use in chamber. The facility shall provide all other equipment to conduct scientific studies outlined above.

Schedule:

Vendors will provide schedule. Work described above must be completed within 5 months of IRB approval.

Travel summary:

The facility should expect to send one representative to the Human Research Program's Investigators Workshop each Spring starting in 2027 to participate in the conference. NASA will coordinate participation in reporting for this activity, which may include contributions to a meeting abstract and presentation at the conference.

Optional work:

1. Complete data analysis and transmittal of data to JSC, including measures (i.e. hematocrit) that must be run on non-frozen blood, (blood and saliva biomarkers).

2. Additional N = 18 anticipated to be participate in both 7000 ft (21% O_2 at 587 mmHg [11.3 psi]) and 9500 ft (21% O_2 at 533 mmHg [10.3 psi]) exposures, in a cross-over design (randomized order).
3. Additional N = 6 anticipated to be participate in both 7000 ft (21% O_2 at 587 mmHg [11.3 psi]) and 9500 ft (21% O_2 at 533 mmHg [10.3 psi]) exposures, in a cross-over design (randomized order).

References

1. **Roach RC**, **Hackett PH**, **Oelz O**, **Bärtsch P**, **Luks AM**, **MacInnis MJ**, **Baillie JK**, **Lake Louise AMS Score Consensus Committee**. The 2018 Lake Louise Acute Mountain Sickness Score. *High Alt Med Biol* 19: 4–6, 2018. doi: 10.1089/ham.2017.0164.

2. **Sampson JB**, **Cymerman A**, **Burse RL**, **Maher JT**, **Rock PB**. Procedures for the measurement of acute mountain sickness. *Aviat Space Environ Med* 54: 1063–1073, 1983.

3. **Lowe M**, **Harris W**, **Kane RL**, **Banderet L**, **Levinson D**, **Reeves D**. Neuropsychological assessment in extreme environments. *Arch Clin Neuropsychol* 22 Suppl 1: S89-99, 2007. doi: 10.1016/j.acn.2006.10.010.

4. **Vincent AS**, **Fuenzalida E**, **Beneda-Bender M**, **Bryant DJ**, **Peters E**. Neurocognitive assessment on a tablet device: Test-retest reliability and practice effects of ANAM Mobile. *Appl Neuropsychol Adult* 28: 363–371, 2021. doi: 10.1080/23279095.2019.1640698.

5. **Kim KJ**, **Rivas E**, **Prejean B**, **Frisco D**, **Young M**, **Downs M**. Novel Computerized Method for Automated Determination of Ventilatory Threshold and Respiratory Compensation Point. *Front Physiol* 12: 782167, 2021. doi: 10.3389/fphys.2021.782167.

6. **Pinheiro Volp AC**, **Esteves de Oliveira FC**, **Duarte Moreira Alves R**, **Esteves EA**, **Bressan J**. Energy expenditure: components and evaluation methods. *Nutr Hosp* 26: 430–440, 2011. doi: 10.1590/S0212-16112011000300002.

Attachment 1

Total Caloric Intake

Caloric intake will be prescribed for each subject based upon age, sex, and VO_2max with adjustments for prescribed exercise (6). NASA will provide the details for these calculations.

Basic Nutrient Intake Level

The standardized nutrient intake levels should be regarded either as an adequate range, if a range is mentioned, or as a minimum intake level. For some of these nutrients (vitamins and elements), the recommended intake should be achieved on an average per week. For all other nutrients the recommended intake should be achieved every day. Subjects will consume all food items on their plate. In case of any leftovers on the subjects' plate, food items will be separated and weighed to determine the nutrient content of the unfinished food.

Dietary Restrictions Other than the Basic Nutrient Requirement

- No methylxanthine derivatives are allowed (coffee, decaffeinated coffee, black and green tea, energy drinks, chocolate, cola)
- No alcohol intake
- No flavor enhancers
- No sweat inducing spices (such as chili, hot curry)

Table 2. Standardized Nutrient Intake Levels

Nutrient	**Adequate intake**
Energy (total energy expenditure, TEE)	Basal metabolic rate (BMR) will be measured via indirect calorimetry to get individual data × 1.3 (during bed rest) or × 1.6 (ambulatory during pre- and post-bed rest)
Total fat (%TEE)	30% to 35 %
Saturated fatty acids (%TEE)	≤ 10
Monounsaturated fatty acids (%TEE)	≥ 10
Polyunsaturated fatty acids (%TEE)	≥ 7
Protein g/kgBW/d	>1.2, NTE 1.7
Carbohydrates (%TEE)	45-55
Total Fibre (g/d)	≥ 30
Electrolytes and Water	
Sodium (g/d)	1.5-2.3
Potassium (g/d)	2.6 for females; 3.4 for males
Calcium (mg/d)	1000 to 1200
Water (ml/kgBW/d) minimum intake	40-50,
Vitamins	
Biotin (µg/d)	30
Pantothenic Acid (mg/d)	5
Folate (µg/d)	400
Niacin (mg/d)	20
Riboflavin (mg/d)	1.5
Thiamin (mg/d)	1.5
Vitamin B6 (mg/d)	2
Vitamin B12 (µg/d)	2
Vitamin K (µg/d)	80
Vitamin D (ug/d RE)	5
Vitamin A (µg/d RE)	1000
Vitamin C (mg/d)	100
Vitamin E (mg/d α-TE)	15
Elements	
Copper (µg/d)	1500-3000
Fluoride (mg/d)	1.5 – 4
Iodine (µg/d)	150
Iron (mg/d)	Male: 10; Female 18
Magnesium (mg/d)	300
Phosphorus (mg/d)	700-1700
Zinc (mg/d)	12-15