

*Dr. Sawka*

ARM6.970212.015

SGRD-UE-MEP (70)

30 August 1990

MEMORANDUM THRU Director, <sup>*WSP*</sup> Military Ergonomics Division

FOR Commander, USARIEM

SUBJECT: Response to Amendment to HURC #400 Review

1. Reference memorandum, SGRD-UE-Z, 17 August 1990, subject: Report of the USARIEM Human Use Review Committee - HURC #400, and Decisions and Recommendations, dated 17 August 1990 (copy enclosed).

2. The following revisions were made as outlined in paragraph 1 of Decisions and Recommendations:

- a. Paragraph 6.b. has been modified as requested.
- b. Paragraph 6.c. has been modified as requested.
- c. The Volunteer Agreement Affidavit has been changed to reflect the preceding two modifications.

*Michael N. Sawka*

MICHAEL N. SAWKA, Ph.D.  
Chief, Physiology Branch

Encl

17 August 1990

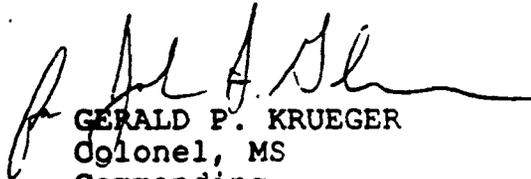
MEMORANDUM THRU Director, Military Ergonomics Division

FOR Dr. M. Sawka

SUBJECT: Report of the USARIEM Human Use Review Committee -  
Amendment to HURC #400

1. The USARIEM Human Use Review Committee has reviewed and recommended approval of subject amendment. The decisions and recommendations of the Committee are enclosed.
2. The Committee recommended approval of this study on condition that the points mentioned be appropriately modified or corrected. Following receipt of your revised protocol, I will forward it to the Human Use Office at our Headquarters for their review and determination of final disposition.

Encl



GERALD P. KRUEGER  
Colonel, MS  
Commanding

Copy to:  
Chrmn, HURC

HUMAN USE REVIEW COMMITTEE  
17 August 90  
DECISIONS AND RECOMMENDATIONS

Amendment to HURC #400, "Interaction of hydration and metabolic intensity on thermoregulatory responses during exercise-heat stress", Dr. M. N. Sawka, Principal Investigator.

1. The USARIEM Human Use Review Committee reviewed your proposed amendment at its meeting of 8 August 1990, and voted unanimously to recommend its approval pending submission to, and approval by, the Commander, USARIEM of a revised amendment and Volunteer Agreement Affidavit attending to the directives below:

a. Paragraph 6.b. should be revised to state that a separate medical monitor will individually monitor each subject whose heart rate exceeds 180/min or 90% of his measured maximum heart rate, whichever is lower. The Principal Investigator may not substitute for a medical monitor in this function.

b. Paragraph 6.c. should be revised to state that a subject will stop the exercise bout immediately if his heart rate reaches 200/min or 95% of his measured maximum heart rate, whichever is lower.

c. The Volunteer Agreement Affidavit for the parent protocol should be revised to reflect the above changes.

2. This amendment involves an exception to the safety restrictions in the USARIEM Type Protocol.

3. This amendment is judged to involve more than minimal risk to the participating subjects.



C. BRUCE WENGER, MD, PhD  
Chairman, USARIEM HURC

30 August 1990

MEMORANDUM THRU Commander, USARIEM

FOR Chairman, HURC

SUBJECT: Applicability of 180 bpm Heart Rate Criteria for Hypohydration-Heat Studies and Addendum to HURC #400

1. During April-May 1990, the undersigned conducted eight hypohydration experiments for the protocol HURC #276, "Interaction of Aerobic Fitness and the Hypohydration Response During Exercise-Heat Stress." During a preceding day, eight test subjects dehydrated by 8% of their total body water (~5% of body weight) and remained at that hydration level until the following day when they attempted a hypohydration Heat Stress Test. The Heat Stress Test (HST) consisted of treadmill walking (~50%  $\dot{V}_{O_{2max}}$ ) in a 49°C, 20% rh environment for three hours, or until the termination due to exhaustion or the achievement of physiological end-point criteria. The physiological end-point criteria were a rectal temperature of 40°C or a heart rate of 180 bpm for 10 minutes.

2. During the eight hypohydration HSTs, five subjects were stopped from exercising because of achieving the heart rate criteria. In three cases (subjects #2, #3 and #5), the subjects were asked to discontinue the HST while displaying no external signs of discomfort or strain (beyond a high heart rate). This early (at 16-21 min) discontinuation of the Heat Stress Test resulted in little or no usable scientific information being collected from these experiments. The subjects were frustrated due to having spent the previous 24 hours dehydrating and preparing for the experiment and then being told to discontinue while they experienced little or no perceived strain. The table below provides the subjects' walk times and physiological responses at the time of discontinuation of the hypohydration HSTs.

Subject #	Walk Time	Final T <sub>re</sub> (°C)	Final HR (bpm)	End Point Criteria
1.	27 min	38.5	165	Exhaustion
*2.	21 min	37.9	188	Heart Rate
*3.	16 min	37.8	188	Heart Rate
4.	40 min	39.1	185	Heart Rate
*5.	18 min	37.7	194	Heart Rate
6.	22 min	38.5	192	Heart Rate
7.	173 min	39.7	184	Exhaustion
8.	56 min	39.8	179	Exhaustion

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3. During the preceding eight years at USARIEM, I have conducted approximately 200 exercise-heat experiments on human subjects hypohydrated by 3% to 7% of their body weight. These experiments have been conducted without medical incident. During these experiments, as well as other dehydration experiments prior to my coming to USARIEM, I have always been impressed by the inability of heart rate values (by themselves) to predict an impending heat casualty.

4. For the submitted protocol (HURC #400) test subjects will hypohydrate by 3% and 6% of body weight and then attempt Heat Stress Tests in a 35°C, 20% rh environment. At each dehydration level, the test subjects will participate in separate experiments at ~30%, 50% and 70%  $\dot{V}_{O_{2max}}$ . I anticipate that the use of an end-point criteria of heart rate exceeding 180 bpm for five minutes will result in the premature termination of a majority of experiments, particularly at the 70%  $\dot{V}_{O_{2max}}$  exercise intensity.

5. I have surveyed three university laboratories that perform dehydration and exercise-heat stress experiments as to the procedures that they use to terminate their experiments. Dr. Ellsworth Buskirk, Director of Noll Laboratories at Pennsylvania State University informed me that they employ a 39.5°C core temperature criteria and the achievement of a maximal heart rate. The maximal heart rate is determined from a previously conducted maximal exercise test. In addition, consideration is given to skin pallor, ability to sweat, and subject coherence, etc. Dr. Edward Coyle, Professor, University of Texas at Austin stated that their laboratory does not employ any specific physiological criteria, and exercise-heat experiments are terminated by volitional fatigue. Dr. Ethan Nadel, Director, John B. Pierce Foundation Laboratory, Yale University, stated that their laboratory employs a 39.5°C core temperature and 180 bpm heart rate as the end-point criteria. Dr. Nadel stated that the 180 bpm end-point criteria was arbitrary, and he knew of no database to support this end-point. He stated that the 180 bpm criteria was not an institutional requirement.

6. It is requested that the undersigned be allowed to amend HURC #400 with the following heart rate end-point criteria for both the euhydration and hypohydration Heat Stress Tests:

a. At the achievement of 90% of maximal (or 180 bpm, whichever is lower) heart rate, the Medical Monitor must be on site and must make a clinical evaluation as to the subject's ability to safely continue exercise.

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The attending physician will continue to closely monitor the electrocardiogram for any signs of ischemia, conduction disturbance and dysrhythmia.

b. At the achievement of 90% of maximal (or 180 bpm, whichever is lower) heart rate, increased vigilance will be employed in monitoring the test subjects. A separate Medical Monitor will individually monitor each subject for excessive fatigue, ataxia, disorientation, or other signs of impending exhaustion. The Principal Investigator may not substitute for the medical monitor in this function.

c. When the subject achieves a heart rate of 200 bpm or 95% of his measured maximal heart rate (whichever is lower), the exercise bout will be immediately discontinued.

d. Not more than two hypohydrated subjects will be concurrently tested.

7. The intent of this amendment is to relegate the achievement of a 180 bpm heart rate from being an absolute end-point criteria (by itself) to being part of the total clinical picture for the Medical Monitor's decision-making process. This amendment will insure test subject safety, but also enable the collection of important scientific information which would otherwise not be obtained.

*Michael N. Sawka*

MICHAEL N. SAWKA, Ph.D.  
Chief, Physiology Branch

Encl

ADDENDUM

**VOLUNTEER AGREEMENT AFFIDAVIT**

For use of this form, see AR 70-25; the proponent agency is OTSG

**PRIVACY ACT OF 1974**

- Authority:** 10 USC 3013, 44 USC 3101, and 10 USC 1071-1087.
- Principle Purpose:** To document voluntary participation in the Clinical Investigation and Research Program. SSN and home address will be used for identification and locating purposes.
- Routine Uses:** The SSN and home address will be used for identification and locating purposes. Information derived from the study will be used to document the study, implementation of medical programs; adjudication of claims; and for the mandatory reporting of medical conditions as required by law. Information may be furnished to Federal, State and local agencies
- Disclosure:** The furnishing of your SSN and home address is mandatory and necessary to provide identification and to contact you if future information indicates that your health may be adversely affected. Failure to provide the information may preclude your voluntary participation in this investigational study.

**PART A(1) - VOLUNTEER AFFIDAVIT**

**Volunteer Subjects in Approved Department of the Army Research Studies**

Volunteers under the provisions of AR 40-38 and AR 70-25 are authorized all necessary medical care for injury or disease which is the proximate result of their participation in such studies.

I, \_\_\_\_\_, SSN \_\_\_\_\_,

having full capacity to consent and having attained my \_\_\_\_\_ birthday, do hereby volunteer/give consent as legal representative for \_\_\_\_\_ to participate in \_\_\_\_\_

Interaction of Hydration and Metabolic Intensity on Thermoregulatory Responses  
During Exercise-Heat Stress (Research study)

under the direction of Michael N. Sawka, Ph.D.

conducted at US Army Research Institute of Environmental Medicine, Natick, MA 01760-5007  
(Name of Institution)

The implications of my voluntary participation/consent as legal representative; duration and purpose of the research study; the methods and means by which it is to be conducted; and the inconveniences and hazards that may reasonably be expected have been explained to me by Michael N. Sawka, Ph.D.

Contact telephone(s): 508-651-5141

I have been given an opportunity to ask questions concerning this investigational study. Any such questions were answered to my full and complete satisfaction. Should any further questions arise concerning my rights/the rights of the person I represent on study-related injury, I may contact

Office of Chief Counsel

at US Army Natick Research, Development and Engineering Center (508)651-4322  
(Name, Address and Phone Number of Hospital (Include Area Code))

I understand that I may at any time during the course of the study revoke my consent and withdraw/have the person I represent withdrawn from the study without further penalty or loss of benefits; however, if the person I represent may be required (military volunteer) or requested (civilian volunteer) to undergo certain examination if, in the opinion of the attending physician, such examinations are necessary for my/the person I represent's health and well-being. My/the person I represent's refusal to participate will involve no penalty or loss of benefits to which I am/the person I represent is otherwise entitled.

**PART A (2) - ASSENT VOLUNTEER AFFIDAVIT (MINOR CHILD)**

I, \_\_\_\_\_, SSN \_\_\_\_\_ having full capacity to consent and having attained my \_\_\_\_\_ birthday, do hereby volunteer for \_\_\_\_\_ to participate in \_\_\_\_\_

(Research Study)

under the direction of \_\_\_\_\_

conducted at \_\_\_\_\_

(Name of Institution)

(Continue on Reverse)

**PART A(2) - ASSENT VOLUNTEER AFFIDAVIT (MINOR CHILD) (Cont'd.)**

The implications of my voluntary participation; the nature, duration and purpose of the research study; the methods and means by which it is to be conducted; and the inconveniences and hazards that may reasonably be expected have been explained to me by

I have been given an opportunity to ask questions concerning this investigational study. Any such questions were answered to my full and complete satisfaction. Should any further questions arise concerning my rights I may contact

at

(Name, Address, and Phone Number of Hospital (include Area Code))

I understand that I may at any time during the course of this study revoke my assent and withdraw from the study without further penalty or loss of benefits; however, I may be requested to undergo certain examination if, in the opinion of the attending physician, such examinations are necessary for my health and well-being. My refusal to participate will involve no penalty or loss of benefits to which I am otherwise entitled.

**PART B - TO BE COMPLETED BY INVESTIGATOR**

INSTRUCTIONS FOR ELEMENTS OF INFORMED CONSENT: (Provide a detailed explanation in accordance with Appendix E, AR 40-36 or AR 70-25.)

This study will examine your ability to work in the heat when you have less than normal body water (dehydrated). We wish to determine if dehydration has the same effect during light as moderate and high intensity work (treadmill walking and running). This study will be conducted at the U.S. Army Research Institute of Environmental Medicine (USARIEM) and the U.S. Army Natick Research, Development and Engineering Center (NATICK) facilities, Natick, MA, and at the Naval Blood Research Laboratory, Boston, MA.

Prior to experimental testing, your physical fitness and percent body fat will be determined as well as your energy cost to walk and run on a treadmill. You will then complete a 4 to 12 consecutive day heat acclimation program. (This could include one or two weekends). For this you will attempt daily 2-h walks in a hot-dry (104°F, 20% rh) environment. After completing the heat acclimation program, your total body water will be measured on one day, and your blood volume will be measured on another day. You will then attempt nine Heat Stress Tests during the next five weeks. You will also complete additional heat acclimation sessions between the dehydration sessions and Heat Stress Tests; no more than two Heat Stress Tests will be conducted in one week. The tests and procedures are described below.

Body Fat. To estimate your body fat, you will be weighed on a scale underwater while you hold your breath. The gas in your lungs will be measured by having you breathe oxygen through a snorkel-like apparatus. This procedure takes about 45 minutes.

I do  do not  (check one & initial) consent to the inclusion of this form in my outpatient medical treatment record.

SIGNATURE OF VOLUNTEER	DATE	SIGNATURE OF LEGAL GUARDIAN (if volunteer is a minor)	
PERMANENT ADDRESS OF VOLUNTEER	TYPED NAME OF WITNESS		
	SIGNATURE OF WITNESS		DATE

REVERSE OF DA FORM 5303-R, MAY 88

Maximal Effort Exercise. You will first practice walking (3.5 mph) and running (6 or 7 mph) on a treadmill. For the maximal effort exercise test, you will run on the treadmill and the treadmill grade will be increased (by 2 1/2%) at 1.5-minute intervals until you can no longer continue. This test takes about 30 to 90 minutes.

Total Body Water. You will be asked to drink an alcohol (190 proof) solution. The amount of alcohol will be 0.035% of your body weight (e.g., if you weigh 150 lbs., you will drink 0.84 ounces of alcohol), and it will be diluted in four times its volume of water. This would be equal to the alcohol content of two cans of beer. Venous blood samples will be obtained from your arm over the next three hours while you are seated. The total amount of blood removed will be about one ounce. This test takes about four to five hours.

Blood Volume Measurement. This test will be performed at the Naval Blood Research Laboratory in Boston. A small sample of blood (less than one ounce) will be taken from your arm vein. Radioactive material will be added, and then it will be reinjected into your arm. You will receive a very small amount of radioactive material. The total amount of radiation that you receive is less than one chest x-ray. One half of the radioactivity will be gone from your body in 30 to 60 days. Small samples of blood removed will be about one ounce. This test will take about three hours.

Heat Stress Tests. You will attempt nine Heat Stress Tests; three with normal body water levels, three when dehydrated by 3% of body weight, and three when dehydrated by 6% of body weight. For each of these hydration conditions, the exercise work intensity will be 30%, 50% and 70% of your physical fitness level. You will not complete more than three Heat Stress Tests within a given week. You will be asked to limit your food and fluid intake for about two days before the dehydration Heat Stress Tests. The day before each Heat Stress Test, you will report at 1200 h. You will first be weighed, then you will enter a Climatic Chamber, which will be 104°F (20% humidity). In the chamber, you will rest and exercise so that you sweat. If this is the day before a normal hydration Heat Stress Test, you will be given water to fully replace your sweat. If this is the day before a dehydration Heat Stress Test, you will not be given water. For a 150-lb. man to dehydrate by 3% and 6% of body weight, he would have to lose ~2 quarts and ~4 quarts of fluid, respectively. This could take 4-6 hours. Once you have lost the desired body weight, you will go to a comfortable room and remain there until the next morning. During the night and next morning, you will be allowed to eat fresh fruit, but only in the amount that your weight allows. In the morning you will enter the chamber for the Heat Stress Test. It will be 95°F (20% humidity). You will try to perform treadmill exercise (walking or running) for 50 minutes.

During all exercise tests, you will wear shorts and tennis shoes. You will have several electrodes taped to your chest so that we can monitor your heart rate. During the Heat Stress Tests, we will measure your skin, rectal and esophageal temperatures. Also, your rectal temperature will be measured during the acclimation sessions. The rectal thermometers are flexible probes which may be somewhat unpleasant to insert the first time, but are not harmful. Before each Heat Stress Test you will place a thin plastic tube through your nose and swallow it while drinking water. This tube will measure your esophageal temperature and will remain in place throughout the experiment. There may be some discomfort during the swallowing of the esophageal probe, and you may have to gag. A plastic capsule will be taped to your arm to measure sweating. During the Heat Stress Tests (and total body water measurements) you will have a sterile plastic tube (catheter) in your arm vein so that we can take blood samples. A total of ~3 ounces of blood will be obtained for each Heat Stress Test. During the exercise tests, you will be asked to periodically breathe through a mouthpiece while wearing a noseclip. In addition, you will be asked to rebreathe a carbon dioxide-oxygen mixture for 1-20 seconds for several times during each Heat Stress Test.

Potential Risks and Hazards. The primary risks of participating in this study are those associated with (a) physical exercise; (b) high body temperature; (c) dehydration; (d) obtaining venous blood samples; (e) exposure to radioactively labelled material; (f) drinking alcohol; (g) rebreathing carbon dioxide and the additional risks of the combinations of these. The stress of exercise, and especially maximal effort, increases the potential for uncovering and/or aggravating pre-existing heart problems. Therefore, the electrocardiogram will be displayed and periodically monitored. Muscle soreness, cramps, and general fatigue may also result from exercise; this pain and discomfort is temporary and not deemed harmful. Misjudgement or accident (i.e., falling on treadmill) can result in bodily injury during physical exercise. The risk of this is probably less during the supervised activities used in a study than in unsupervised exercise, free play or competitive sports. Also, breathing in water is a risk associated with the underwater-weighting procedure.

High body temperatures are expected in the acclimation sessions and Heat Stress Tests; so body temperature will be closely monitored. During passage of the esophageal probe, injury to mucus membranes could occur if due care is not taken. There is also a remote risk of shock if there is a current leak. During the Heat Stress Test, you will be provided water to maintain the desired hydration level. Testing will be discontinued, and you will be removed to a cool environment should your rectal temperature exceed 103°F, or if the rate of temperature increase exceeds 1.1°F in five minutes. Even if the above limit has not been reached, symptoms and signs of impending heat illness, such as confusion, coordination difficulties, excessive breathing and/or faintness will result in discontinuation of testing and your removal to a cool environment. When your heart rate exceeds 180 bpm or 90% of your measured maximal value (whichever is lower), a physician will individually monitor you. When your heart rate achieves 200 bpm or 95% of your measured maximal value (whichever is lower), the experiment will be terminated. During all testing, a staff member will be stationed near you to observe and assist you should the need arise. Testing will be discontinued if you show any signs of unusual distress during the work. It is recognized that overexposure to heat may lead to heat injury, "heat exhaustion", or "heat stroke". However, under this protocol safeguard tolerance limits are placed on responses to provide a margin of safety and reduce the risk to your health.

Within the past seven years, we have conducted approximately 200 exercise-heat experiments on subjects dehydrated and experienced no serious adverse physical effects. The primary risk of hypohydration is that of the subsequent high body temperature during exercise-heat stress, and these risks have been discussed.

Needle punctures and catheterization of veins in the extremities will be performed by skilled technicians with sterile techniques. These procedures involve extremely little risk of any injury beyond possible infection, bruising and temporary discomfort. Blood volume measurements with the labelled radioactive chromium and albumin methods are performed routinely in the United States, and the low level of radiation is associated with no known risks. During the course of the entire study (approximately nine weeks), you will have a total of ~30 ounces of blood removed.

There are no known health risks associated with drinking small amounts of alcohol. The alcohol has the risk of short-term intoxication; however, this feeling will subside before you are released. You will be warned against operating machinery or driving for six hours after alcohol ingestion. The risk associated with rebreathing 8 to 15% CO<sub>2</sub> (in oxygen) for 15 to 20 seconds is temporary light-headedness, and a technician will closely monitor you.

The benefits of this study to you are only indirect. You will be able to find out your percent body fat and physical fitness level. Both of these measurements are of value to individuals interested in assessing the state of their physical conditioning program. All data and medical information obtained about you as an individual will be considered privileged and held in confidence; you will not be identified in presentation of the results. Complete confidentiality cannot be promised, particularly to subjects who are military personnel, because information bearing on your health may be required to be reported to appropriate medical or command authorities, and applicable regulations note "the possibility that the U.S. Army Medical Research and Development Command officials may inspect the records."

This study requires a considerable time and energy commitment from you. You will participate in experiments that will require a significant (1-6 h) amount of time on approximately 40 days over a nine week time span. Please take your commitment seriously and plan to complete all testing if you volunteer. However, you are free at any time to withdraw from the study without prejudice.

You will receive a copy of this consent form for your personal records.