

Shock Enrollment Breakdown as of 4/30/2007									
	EMS Agencies/Hospitals	Legacy Emanuel Hospital	OHSU	Multnomah County	SW WA Med CTR	Pre-Hosp Disposition Unknown	ED unknown-no ED admit form	Total	
American Medical Response		1	0	0	0	0	1	2	
Metrowest Ambulance		0	1	0	0	0	0	1	
LifeFlight		0	0	0	0	0	0	0	
Clackamas Co. Fire Dist #1		0	0	0	0	0	0	0	
Lake Oswego Fire Dept		0	0	0	0	0	0	0	
North County Ambulance		0	0	0	0	0	0	0	
Vancouver Fire Department		0	0	0	0	0	0	0	
Camas Fire Department		0	0	0	0	0	0	0	
Clark Co. Fire Dist #6		0	0	0	0	0	0	0	
Total in Hospital		1	1	0	0	0	1	3	

TBI Enrollment Breakdown as of 4/30/2007									
	EMS Agencies/Hospitals	Legacy Emanuel Hospital	OHSU	Multnomah County	SW WA Med CTR	Pre-Hosp Disposition Unknown	ED unknown-no ED admit form	Total	
American Medical Response		2	2	0	1	2	1	8	
Metrowest Ambulance		0	0	0	0	0	0	0	
LifeFlight		0	0	0	0	0	0	0	
Clackamas Co. Fire Dist #1		0	0	0	0	0	0	0	
Lake Oswego Fire Dept		0	0	0	0	0	0	0	
North County Ambulance		0	0	0	0	0	0	0	
Vancouver Fire Department		0	0	0	0	0	0	0	
Camas Fire Department		2	0	0	1	0	0	3	
Clark Co. Fire Dist #6		0	0	0	0	0	0	0	
Total in Hospital		4	2	0	2	2	1	11	

LEGACY HEALTH SYSTEM AND INSTITUTIONAL REVIEW BOARD PROTOCOL REVISION/AMENDMENT FORM

This form is to be completed and attached to changes made to a research project. This includes any changes to the protocol, consent form or any supportive materials (as Investigator's Brochure, results from related studies or advertisements, etc.)

Principal Investigator: *Jerris Hedges, M.D. (OHSU)*
Co-Investigator Legacy Health System: *Dean Gubler, DO*

Sponsor: *NHLBI* Protocol Number: *IND 12505 & 12506*

Title: *Hypertronic Resuscitation Following Traumatic Injury*

THE PROJECT HAS BEEN CHANGED AS FOLLOWS:

- Protocol Modification *Amendment I, version 11/22/2006*
- Consent Form Modification: *Shock Consent, version 11/22/2006 12/12/06 ZW*
TBI Consent, version 11/22/2006 12/12/06 ZW
- Other (specify):
 - *Addition of Dean Gubler, DO as lead co-investigator on the study for Legacy*
 - *FDA letter, fax date 11/14/06, that states the sponsor may restart enrollment*

Does the change affect subject participation (e.g. procedures, risks, costs, etc.)?

YES
NO

If yes, do subjects previously entered need to be notified of major changes?

YES
NO *No patients are currently enrolled in the study at Legacy.*

BRIEF SUMMARY OF PROPOSED CHANGE (S) (or attach sponsor's summary):

The amendment addresses three issues:

- 1. Monitoring plan for serum sodium after study drug administration*
- 2. Study patient oversight during hospitalization*
- 3. Management of variations in hospital care*

REASONS FOR PROPOSED CHANGES:

W. J. Gubler
Investigator Signature

30 Nov 06
Date

APPROVED BY THE IRB

A. M. Muka MD, PhD
IRB Signature

29 Dec 2006
Date



Alar Mirka, M.D.
Chair, Legacy IRB
Legacy Health System
1225 NE 2nd Ave.
P.O. Box 3950
Portland, OR 97208-3950

Legacy IRB: FWA00001280

October 20, 2006

Jerris Hedges, M.D.
Oregon Health & Sciences University
Center for Policy and Research in Emergency Medicine
Mail Code: L102
3181 SW Sam Jackson Park Rd.
Portland, OR 97239-3098

RE: Hypertonic Resuscitation Following Traumatic Injury

Dear Dr. Hedges:

At its meeting of October 10, 2006, the Legacy IRB reviewed and approved the above cited study. This letter is written to clarify the IRB's disposition concerning that approval.

At that meeting the Legacy IRB approved the portion of your study that will involve Legacy patients. Specifically that involves the consent of the patient or family members of the patient to conduct follow up and the use of medical records.

In addition, by unanimous vote, the Legacy IRB respectfully disagrees that your study meets the criteria for the Exception from Informed Consent Requirements for Emergency Research as codified in 21CFR50.24. Specifically, it is the Legacy IRB's opinion that the statement in your consent form: "available treatments are unproven or unsatisfactory", which is required by 21CFR54.24 is not an accurate assessment of the current standard of care.

Please do not hesitate to contact me if you have any questions concerning this matter.

Yours truly,

Alar Mirka

Alar Mirka, M.D.
Chair, Legacy IRB

cc: C. Shupert - OHSU IRB
D. Holt - Mult. Co. IRB
S. McWilliams, SWWMC IRB

OREGON HEALTH & SCIENCE UNIVERSITY

Research Integrity Office, L106-RI
 2525 SW First Avenue, Portland, OR 97201
 Phone: (503) 494-7887

MEMO

Date: December 29, 2006

To: Jerris Hedges, MD, MD

From: Susan B. Bankowski, MS, JD, Chair, Institutional Review Board, L106-RI
 Gary T. Chiodo, DMD, FACD, Director, OHSU Research Integrity Office, L106-RI
 Charlotte Shupert, Ph.D., Associate Director, Research Integrity Office, L106-RI
 Kara Manning Drolet, Ph.D., IRB Co-Chair, Institutional Review Board, L106-RI
 Susan Hickman, Ph.D., IRB Co-Chair, Institutional Review Board, L106-RI
 Katie McClure, M.D., IRB Co-Chair, Institutional Review Board, L106-RI

Subject: IRB00001400, Hypertonic Resuscitation Following Traumatic Injury
 CR ID#: CR00002930, CR Title: 1/12/2007 ROC HS Study

<p>Continuing Study Review Protocol/Consent Form Approval</p>

This memo also serves as confirmation that the OHSU IRB (FWA00000161) is in compliance with ICH-GCP codes 3.1-3.4 which outline: Responsibilities, Composition, Functions, and Operations, Procedures, and Records of the IRB.

This study is currently approved for 250 subjects.

Your protocol (with protocol amendment #1 - October 28, 2006) is approved for one year effective 12/29/2006.

Your combined consent/authorization forms (Shock and TBI, with child assent) are approved by the IRB effective 12/29/2006.

You may use only copies of the attached approved consent/authorization form for the informed consent process.

Other items reviewed and administratively approved by the IRB include: Lay Language Protocol Summary, Grant Application, Data Collection Forms, Next of Kin Letter.

Other items reviewed and noted by the IRB include: Investigator's Brochure (ed. 2 - June 30, 2004).

This study met the criteria for EXPEDITED IRB review based on Category # 8b, where no subjects have been enrolled and no additional risks have been identified.

Subjects must receive a copy of OHSU's Notice of Privacy Practices.

Accounting for disclosures is:

Not needed because all subjects will sign a consent form and HIPAA Authorization.

This approval may be revoked if the investigators fail to conduct the research in accordance with the guidelines found in the Roles and Responsibilities document (<http://www.ohsu.edu/research/rda/rgc/randr.pdf>). Please note that any proposed changes in key personnel must be submitted to the IRB via a Modification Request and approved prior to initiating the change. If you plan to discontinue your role as PI on this study or leave OHSU, you must arrange either (a) to terminate the study by so notifying the IRB and your department head, or (b) propose to transfer the responsibility of the PI to a new faculty member using a Modification Request.

Investigators must provide subjects with a copy of the consent form, keep a copy of the signed consent form with the research records, and place a signed copy in the patient's hospital/clinical medical record (if applicable).

If this project involves the use of drugs to be dispensed to research subjects, a copy of the approved protocol must be forwarded to the Research Pharmacy Services (CR9-4).

OREGON HEALTH & SCIENCE UNIVERSITY

Research Integrity Office, L106-RI
2525 SW First Avenue, Portland, OR 97201
Phone: (503) 494-7887

MEMO

Date: December 13, 2006

To: Jerris Hedges, MD ,MD

From: Susan B. Bankowski, MS, JD, Chair, Institutional Review Board, L106-RI
Kara Manning Drolet, Ph.D., IRB Co-Chair, Institutional Review Board, L106-RI
Susan Hickman, Ph.D., IRB Co-Chair, Institutional Review Board, L106-RI
Katie McClure, M.D., IRB Co-Chair, Institutional Review Board, L106-RI

Subject: IRB00001400, Hypertonic Resuscitation Following Traumatic Injury
Modification ID#: MR00005926, Modification Title: Protocol Addendum

Modification Request Approval Communication

* This study's current IRB approval lapses on 1/12/2007 .

Your Modification Request submitted 11/21/2006 was reviewed and approved by the full board on 12/12/2006 .

Items Reviewed and Approved by the Full Board include: Protocol Addendum (October 28, 2006).

OREGON HEALTH & SCIENCE UNIVERSITY

Research Integrity Office, L106-RI
 2525 SW First Avenue, Portland, OR 97201
 Phone: (503) 494-7887

MEMO**Date:** 6/27/2006**To:** Jerris Hedges, MD

Susan B. Bankowski, MS, JD, Chair, Institutional Review Board

Kara Manning Drolet, PhD, Co-Chair, Institutional Review Board

From: Susan Hickman, PhD, Co-Chair, Institutional Review Board

Gary T. Chlodo, DMD, FACD, Director, OHSU Research Integrity Office

Charlotte Shupart, PhD, Associate Director, OHSU Research Integrity Office

Subject: IRB00001400, Hypertonic Resuscitation Following Traumatic Injury
 Modification ID#: MR00004349, Modification Title: Community Consultation
 Summation

Modification Request Approval Communication**re: Community Consultation Summation**

* This study's current IRB approval lapses on 1/12/2007.

Your protocol revision/amendment requested with your Modification Request submitted 6/27/2006 was reviewed and approved by the full board on 6/4/2006. We received your response to the IRB requirements on 7/19/2006. Your consent form/supporting materials are approved by the IRB effective 7/27/2006.

Items reviewed and approved with this modification request include:

- Revised TBI Consent and Authorization Form
- Revised Shock Consent and Authorization Form

Items reviewed and noted with this modification request include:

- 5-06 OHSU ROC Community Meetings Announcements
- 5-06 ROC ltr gov final
- 5-06 ROC ltr nghbr final
- 5-06 ROC Newsletter Article Final
- 5-06 ROC Release Final
- Calls Received regarding HS Trial
- Community Contact List
- Final Summary - ROCHSD phone results, Portland 4-18-06 v2
- HS CC Report
- Hypertonic Saline Study: Community Meetings
- Hypertonic Saline Study: Community Meetings 6-20-06
- June 23, 2006 - Pulse Check Newsletter
- Lay Brochure

- NewsBank Columbian Article
- NIH release on letterhead - March 23
- Proposed Study Seeks Article
- ROC Online Survey Comments
- ROC Presentation
- ORCHSD Prelim 2nd phone results, Portland 6-14-06
- Saline Study article
- Study Seeks OK article
- Summary of Open Community Meetings

You may use only copies of the uploaded approved consent and authorization forms for the informed consent process.

OREGON HEALTH & SCIENCE UNIVERSITY

Research Integrity Office, L106-RI (503) 494-7887

MEMO

Date: March 1, 2006

To: Jerris Hedges, MD, MD

From: Margaret Allee, RN, MS, JD, Chair, Institutional Review Board, L106-RI
Susan B. Bankowski, MS, JD, Co-Chair, Institutional Review Board, L106-RI
Gary T. Chiodo, DMD, FACD, Director, OHSU Research Integrity Office, L106-RI
Charlotte Shupert, PhD, Associate Director, Research Integrity Office, L106-RI

Subject: IRB00001400, Hypertonic Resuscitation Following Traumatic Injury

**Initial Study Review
Protocol/Consent Form Approval**

This memo also serves as confirmation that the OHSU IRB (FWA00000161) is in compliance with ICH-GCP codes 3.1-3.4 which outline: Responsibilities, Composition, Functions, and Operations, Procedures, and Records of the IRB.

This study is approved for 250 subjects.

This protocol was reviewed by the full board on 1/13/2006. The Board decided that the protocol is approvable pending the outcome of the community consultation and notification process.

Your combined consent/authorization forms (TBI and Shock with Child Assent) are approved by the IRB effective 03/01/06.

You may use only copies of the approved consent/authorization form for the informed consent process. The approved consent form can be found by logging on to the eIRB system and going to your study. Next, click on the Study Documents tab and locate your approved consent form under the Approved Documents heading.

Other items reviewed and administratively approved by the IRB include:

- Lay Language Protocol Summary
- Community Consultation Meeting Notes
- Community Consultation Notification Plan
- Grant Application
- Data Collection Forms
- Waiver of Authorization
- Next of Kin Letter

Other items reviewed and noted by the IRB include:

- Clinical Billing Schedule

DHS-Public Health Division/Multnomah County
**PUBLIC HEALTH
INSTITUTIONAL REVIEW BOARD**

800 NE Oregon Street, Suite 930

Portland, OR 97232

Phone: (971) 673-1221

Fax: (971) 673-1299

COPY

December 4, 2006

TO: Dr. Jerris Hedges
Oregon Health & Science University

FROM: David Holt, JD; Chair

SUBJECT: IRB-06-08 Hypertonic Resuscitation Following Traumatic Injury

The DHS-Public Health Division/Multnomah County Public Health IRB reviewed the protocol amendment for the above study on November 30th, 2006. The Board found the information acceptable and felt that the increased monitoring of sodium levels and enhanced oversight provide further protection for research subjects.

We understand that the FDA has also approved this protocol revision, however, is awaiting confirmation that each institution can implement the modified plan before lifting the suspension on subject enrollment. The board asks that you keep us informed on the progress of these logistics. Upon final approval by the FDA, subject enrollment may begin.

Thank you for your continued diligence in protecting the rights of human subjects in research.

cc: Denise Griffith
Charlotte Shupert

DHS-Public Health FWA# 00000520
MCHD FWA# 00004186

DHS-Public Health Division/Multnomah County
**PUBLIC HEALTH
 INSTITUTIONAL REVIEW BOARD**

800 NE Oregon Street, Suite 930

Portland, OR 97232

Phone: (971) 673-1221

Fax: (971) 673-1299

August 3, 2006

TO: Dr. Jerris Hedges
 Oregon Health & Science University

FROM: David Holt, JD; Chair 

SUBJECT: IRB-06-08 Hypertonic Resuscitation Following Traumatic Injury

We understand the purpose of this study is to determine whether giving a hypertonic saline fluid for resuscitation of patients with severe traumatic injury results in better outcomes than standard treatment. Due to the severe nature of the injuries, subjects will not be able to give consent thus you are seeking an exception from informed consent requirements as allowed by the FDA for emergency research.

The DHS-Public Health Division/Multnomah County Public Health Institutional Review Board conducted a final review of the above protocol on August 1, 2006 and the following actions have been taken:

- The board approved community consultation efforts that have taken place. Although public attendance at the meetings was less than optimal, investigators clearly made good faith efforts to seek comments from the public through multiple channels. These included outreach to minority communities.
- The board approved notification plans as outlined in the protocol. In addition, the board requests that a press conference be scheduled and investigators take an aggressive approach with the media to assure adequate coverage. The IRB wants to review media plans prior to their implementation. We also offer to participate in the media effort if it will help gain public attention.
- The board approved use of a medical-alert type bracelet so that during the notification phase, persons who wish to opt-out of study participation may do so by obtaining and wearing the bracelet.

DHS-Public Health FWA# 00000520
 MCHD FWA# 00004186

- The board approved the protocol and consent forms with the following conditions:
 - 1) Revise the consent form so subjects understand that they are not consenting to the intervention (which will already have been carried out), but are rather consenting to continued collection of information from their medical record. Specifically, under risks and discomforts, number 5, state: "Whenever personal information is collected, there is always the potential that someone who is not authorized by this consent form may see your information. However, steps have been taken to minimize this risk. Under benefits, revise to state, "You may or may not personally benefit from being in this study. However, there is a possibility you could have benefited from being in this study if the use of HSD or HS improves tissue and organ perfusion ..."
 - 2) Concern was expressed regarding statements made that investigators will continue to collect information, regardless of the subjects' willingness to do so, due to guidance by the FDA. It is this Board's expectation that the consent form be followed and that if a subject declines further participation, that subsequent data will not be collected nor used.
 - 3) The IRB wishes to be informed re: the content of actual FDA regulations relevant to obtaining patient information without patient consent. This authorization was alluded to in the Federal Register during the commentary period; however, we believe that this statement did not represent the FDA's final regulatory stance.

Please submit the revised consent form by August 31, 2006.

The Board thanks you for your on-going efforts in keeping us well informed about the project and working with us to assure that the rights of human subjects are protected.

cc: Denise Griffith
Charlotte Shupert

March 1, 2007

Jerris R. Hedges, MD
Center for Policy and Research in Emergency Medicine
Oregon Health and Science University
CRI14
3181 S.W. Sam Jackson Park Road
Portland, OR 97239-3098

RE: Resuscitation Outcomes Consortium (ROC) - Hypertonic Resuscitation Following Traumatic Injury.

Dear Dr. Hedges:

At the Institutional Review Board meeting held on February 21, 2007 the IRB conducted a continuing review for the study titled: *Resuscitation Outcomes Consortium (ROC) - Hypertonic Resuscitation Following Traumatic Injury.*

Continuing Review was approved for a period of one year 03/14/07 to 03/13/08.

Copies of the approved Continuing Review application and Informed Consent documents are enclosed for your files. Please be sure that the most recent IRB approved Informed Consent documents are used in your study.

In addition the DSMB report from the January 25, 2007 DSMB meeting and the adverse event report were presented and reviewed. Signed copies of the reporting forms are enclosed.

Please be advised that you should inform the SWMC Institutional Review Board of any changes in your protocol, if any problems emerge, or if serious or unexpected adverse patient experiences have been observed. Please note that IRB approval is granted for one year; however, the subjects' progress and your needs as principal investigator will continue to be re-evaluated on an as-needed basis.

If I can be of any further assistance, please do not hesitate to contact me through the IRB office at 360-514-6100.

Sincerely,



Sanford Plant, M.D.
SWMC Institutional Review Board

SP: sem

Cc: Lynn Wittwer MD
Denise Griffiths, Research Associate

PO Box 1600 Vancouver, WA 98668

Vancouver 360 256.2000
Portland 503 972.3000
Web www.swmedicalcenter.co

December 14, 2006

Jerris R. Hedges, MD
Center for Policy and Research in Emergency Medicine
Oregon Health and Science University
CR114
3181 S.W. Sam Jackson Park Road
Portland, OR 97239-3098

RE: Resuscitation Outcomes Consortium (ROC) - Hypertonic Resuscitation Following Traumatic Injury.

Dear Dr. Hedges:

On behalf of the Southwest Washington Medical Center Institutional Review Board on December 14, 2006 I completed an expedited review and approval of the protocol amendment #1 dated November 17, 2006. The protocol amendment addresses three issues that were recently raised by the FDA. They include: A monitoring plan for serum sodium after study drug administration; Study patient oversight during hospitalization and Management of variations in Hospital care. The revision will require that for those patients with traumatic brain injury who are receiving 3% saline infusion or mannitol boluses for management of intracranial pressure the minimum requirement will be q6hr monitoring of serum sodium for the duration of the therapy. Informed Consent revisions are not required.

In addition I have reviewed and accepted the revised FDA 1572 form and the letter notifying you of FDA approval to proceed with enrollment once all the required approvals are completed.

This information will be reported to the IRB at the January 17, 2007 meeting.

Please be advised that you should inform the SWMC Institutional Review Board of any changes in your protocol, if any problems emerge, or if serious or unexpected adverse patient experiences have been observed. Please note that IRB approval is granted for one year; however, the subjects' progress and your needs as principal investigator will continue to be re-evaluated on an as-needed basis.

If I can be of any further assistance, please do not hesitate to contact me through the IRB office at 360-514-6100.

Sincerely,

Cornelia Taylor, M.D.
Chair, SWMC Institutional Review Board

CT/sem

Cc: Lynn Wittwer MD
Denise Griffiths, Research Associate

PO Box 1600 Vancouver, WA 98668

Vancouver 360 258.2000
Portland 503 972.3000
Web www.swmedicalcenter.com

July 24, 2006

Jerris R. Hedges, MD
Center for Policy and Research in Emergency Medicine
Oregon Health and Science University
CR114
3181 S.W. Sam Jackson Park Road
Portland, OR 97239-3098

RE: Resuscitation Outcomes Consortium (ROC) - Hypertonic Resuscitation Following Traumatic Injury.

Dear Dr. Hedges:

At the Institutional Review Board meeting held on July 19, 2006 the IRB reviewed the Community Consultation Summation report dated June 22, 2006 submitted by Jerris Hedges, MD. The study protocol and Informed Consent documents were initially reviewed and approved, for a period of one year 03/15/06 to 03/14/07, on March 15, 2006, pending outcome of the community consultation.

The IRB reviewed and accepted the community consultation summation report as submitted and approved the revised informed consent forms. The study is approved to proceed. The public may wear opt-out bracelets as proposed but they are not required by the IRB for conduct of the study.

Copies of the stamped/approved Informed Consent documents are enclosed for your files. Please be sure that the most recent IRB approved Informed Consent documents are used in your study.

Please be advised that you should inform the SWMC Institutional Review Board of any changes in your protocol, if any problems emerge, or if serious or unexpected adverse patient experiences have been observed. Please note that IRB approval is granted for one year; however, the subjects' progress and your needs as principal investigator will continue to be re-evaluated on an as-needed basis.

If I can be of any further assistance, please do not hesitate to contact me through the IRB office at 360-514-6100.

Sincerely,

Cornelia Taylor M.D.
Cornelia Taylor, M.D.
Chair, SWMC Institutional Review Board

CT/sem
Cc: Lynn Wittwer MD
Denise Griffiths, Research Associate