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## Research Lecture

### Government Grant Writing & the PHS 398 Form

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## Global Objectives

- Conduct successful research
- Improve EM patient care
- Live a fulfilled life with a great career
- Make the world a better place

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## Specific Objectives

- Learn how to find, obtain federal grants
- Be a successful federal grant writer
- Obtain federal grants
- Complete the work outlined in the grant
- Be able to utilize the resources well
- Enjoy the process
- Repeat

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## Session Plan

- Identify sources of federal grant funds
- Consider an example: TBI
- Look at grants.gov and the Internet
- Discuss how the PHS 398 is filled out
- Examine specific sections of PHS398 using a manuscript of published research
- Look at a biographical sketch

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## Government Grant Sources: Some Considerations

- Huge numbers of grants and resources
- All agencies need successful researchers, grant writers, and work completers
- Get global, think across the board
- Think about the many agencies that overlap and create opportunities and synergies

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## Government Grants, Contracts: Necessary Perspective

- You are getting paid to deliver a service
  - Salt and pepper shakers
  - Portable GPS systems
  - Study of motorcycle helmet use and effects on spine and CNS outcomes following TBI
- Contracts even more specific in required deliverables

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## Government Grant Sources: TBI

- CDC: epidemiology, use of guidelines
- NINDS: Effect of new acute therapies
- DoD: Field (EMS) stabilization, Rx
- DHS: Mass casualty management
- CMS: Cost of initial evaluation and use of advanced neuroimaging
- United Healthcare: ditto

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www.grants.gov  
CRISP

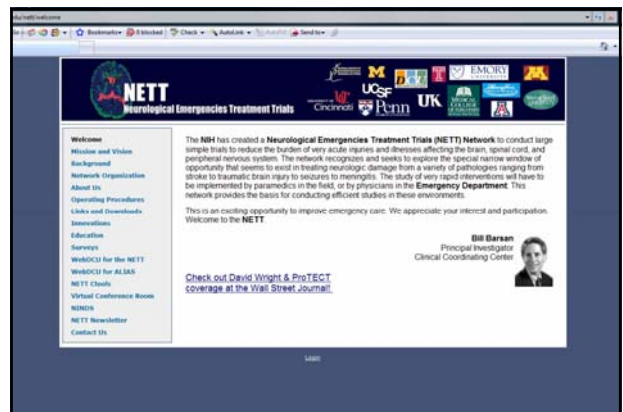
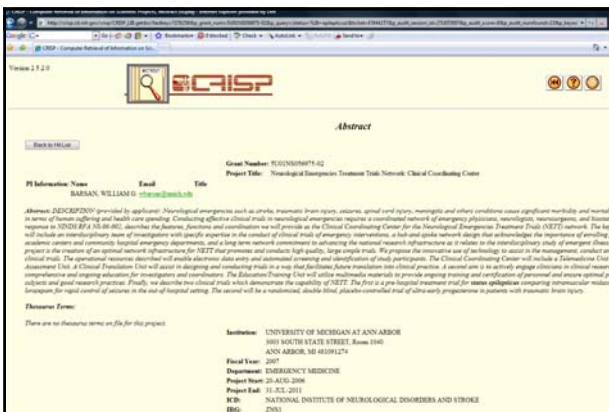
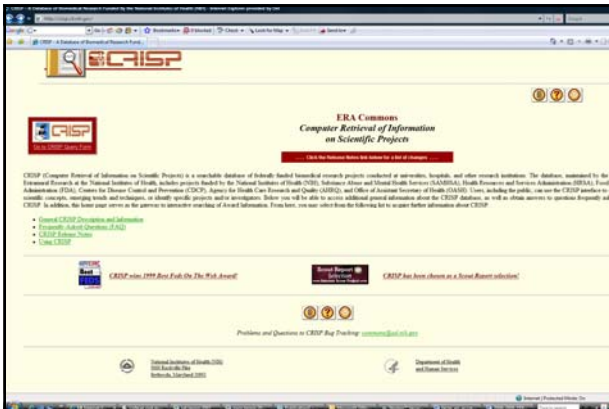
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# 2007 Emergency Medicine Research Workshop

## Government Grants and the PHS 398 Form

### Edward P. Sloan, MD, MPH, FACEP



## PHS 398 Form: The Procedure

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# 2007 Emergency Medicine Research Workshop Government Grants and the PHS 398 Form Edward P. Sloan, MD, MPH, FACEP

Applications for  
**Public Health Service Grant**  
PHS 398

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
**PUBLIC HEALTH SERVICE**

**Grant Application**  
**PHS 398 (Revised 9/2004, Interim Revision 4/2006)**

See the [4/7/2006 NIH Guide Notice NOT-05-08-056](#) for important changes to this version.

All notable changes made to PHS 398 form pages are listed at the bottom of this page (Updated 6/19/2007).

**DOWNLOADABLE INSTRUCTIONS AND FORM FILES**

Some of the MS Word and PDF files are large and may take a few minutes to download.

**PHS 398 Instructions - 4/2006 Revision**

**PHS 398 Instructions - 4/2006 Revision**

These instructions are to be used for all PHS 398 applications submitted for administrative review on or after May 10, 2006. See [NIH Guide Notice NOT-05-08-056](#).

The outline of the PHS 398 has been organized into three distinct parts, each of which is available as a separate file in the MS Word and PDF versions. Please investigators and institutions will need to use all three parts on the instructions to prepare a complete and complete application.

PHS 398 Instructions Files	MS Word	PDF	Large
Part 1: Introduction	MS Word	PDF	Large
Part 2: Research Support Requirements	MS Word	PDF	Large
Part 3: Policy, Assessment, Definitions	MS Word	PDF	Large

If the data below the three parts do not function properly when using the MS Word and PDF versions of these instructions, save the three files to your hard disk (see [Saving Files Locally](#)) rather than opening them in your browser. See the [three files](#) are saved to the same directory.

**PHS 398 Form Files - 4/2006 Revision**

These are a number of the form pages have been revised. Not all form and form pages have been revised. The form provided below include a list of forms with the file #, date and version #. For the full list of forms visit the [PHS 398 Form Files](#) page.

PHS 398 Form Files	MS Word	PDF
Form Page 1: Cover Page	MS Word	PDF
Form Page 2: Introduction	MS Word	PDF
Form Page 3: Research Support Requirements	MS Word	PDF
Form Page 4: Research Support Requirements	MS Word	PDF
Form Page 5: Research Support Requirements	MS Word	PDF
Form Page 6: Research Support Requirements	MS Word	PDF
Form Page 7: Budget to Total Project Period of Support	MS Word	PDF
Form Page 8: Budget to Total Project Period of Support	MS Word	PDF
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**For Questions Related To:**

- Application Procedures/Forms Submission Contact Information: [application@phs.gov](#) or 301-452-5174
- Publication Policies: Visit the PHS 398 Form Help Desk: [PHS 398 Form Help Desk](#)

**NOTE:** Other software packages for completing these applications may be available from other sources. However, it is essential that the type size and format specifications are met. Otherwise, application processing may be delayed or the application may be returned to the applicant without review.

**Disclaimer:** References to these without package number conditions should be interpreted to be an endorsement or recommendation of any product, service, or enterprise by the National Institutes of Health, any other agency of the United States Government, or any changes of the United States Government, nor warranties are stated or implied.

**NOTABLE CHANGES TO PHS 398**

- The PHS 398 instructions have been revised to reflect the following changes:
  - The new budgeting information has been revised to reflect current NIH policy.
  - Changes to instructions have been made to clarify applicability rules that the grant is complete and to form instructions have been revised to reflect the following changes:
    - Changes to the budgeting information have been revised to reflect current NIH policy.
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    - Changes to the budgeting information have been revised to reflect current NIH policy.
  - Changes to the budgeting information have been revised to reflect current NIH policy.
  - Changes to the budgeting information have been revised to reflect current NIH policy.

**Current Research Plan**

The PHS 398 recommends the following format and page structure: Organize **Section 2** of the Research Plan to answer these questions: **What is the problem? Why is it important? What are the goals? How will you solve it? What are the expected outcomes? How will you measure success? How will you disseminate the results? How will you ensure the long-term impact of the research?**

**A. Specific Aims**  
The PHS 398 requires you to state the specific aims of your research project. It is a good idea to state the specific aims in a separate section, creating a new design theme to separate this section, including an outline page and a table of contents.

**B. Background and Significance**  
Provide the background leading to the present application. Identify existing studies, and specifically identify the gaps that the project is intended to fill. State the importance and health relevance of the research, the specific aims of the project, and the long-term impact of the project. If the project is intended to fill a gap in the knowledge, state the scientific rationale for the project. Describe the specific aims of the project and the long-term impact of the project. Describe the specific aims of the project and the long-term impact of the project.

**C. Preliminary Studies/Progress Report**  
For new applications, use this section to provide an account of the previous investigator/professor's preliminary studies performed to date. This section should include the following information:

- Background and Significance
- Specific Aims
- Background and Significance
- Specific Aims
- Background and Significance
- Specific Aims

**Progress Report for Continuing Applications/Supplemental Applications.** A Progress Report must be provided for continuing applications and supplemental applications. The Progress Report should include the following information:

- Background and Significance
- Specific Aims
- Background and Significance
- Specific Aims
- Background and Significance
- Specific Aims

**Research Design and Methods**

Describe the research design, including the study design, procedures, and analysis to be used to accomplish the specific aims of the project. Describe the administrative capabilities in detail. Include the data to be collected, analyzed, and interpreted as well as the data management plan. Describe any new technology, including any new software, equipment, techniques, or technology for the proposed research. Describe the planned efforts to address the aims of the project. Provide a timeline for the project. Provide a timeline for the project. Provide a timeline for the project.

**B. Sample Selection/Recruitment**  
Describe the process of identifying and recruiting subjects for the study. Describe the process of identifying and recruiting subjects for the study. Describe the process of identifying and recruiting subjects for the study.

**C. Data Management/Analysis**  
Describe the process of collecting, managing, and analyzing data. Describe the process of collecting, managing, and analyzing data. Describe the process of collecting, managing, and analyzing data.

**Item 14. Applicant Organization Certification and Acceptance**

**STOP Read this section carefully.**

An original signature, in ink, is required. If you are unable to sign, you may have another individual sign for you. The signature must be in ink. The signature must be in ink. The signature must be in ink.

The applicant organization is responsible for verifying its eligibility and for ensuring, verbally and in writing, that the most current institutional guidelines of all administrative, fiscal, and scientific affairs are followed. The applicant organization is responsible for verifying its eligibility and for ensuring, verbally and in writing, that the most current institutional guidelines of all administrative, fiscal, and scientific affairs are followed.

**Authorizations and Certifications**  
Each application to the PHS requires that the following policies, assurances and certifications be verified by the signature of the Official Signing for Applicant Organization on the Face Page of the application. The policies, assurances and certifications listed below may or may not be applicable to your project, program, or type of applicant organization.

- Human Subjects Research
- Research Involving Human Subjects
- Research Involving Human Subjects
- Research Involving Human Subjects
- Research Involving Human Subjects

## Compelling Grant Writing: *Specifics*

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## Problem Statement

- What is the problem, and why do we care?
- Is there an opportunity to solve the problem and make a positive impact?

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## Needs Assessment

- Answer the question: what do we need to do? Why?

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## Global Objective

- What are we trying to do?

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## Specific Objective

- What specifically are we trying to do in order to meet the global objective?

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## Project Plan

- How are we going to meet the specific objectives?

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## Assessment

- How are we going to measure the success in meeting our global objectives?

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## PHS 398 Form: *The Procedure*

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## Abstract

- Tell the whole story in 250 words or less:
  - What is the problem?
  - What is the study question?
  - What will you do to answer it?
  - What will be the implications?
  - Do you have the means to get it done?

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## Specific Aims

- Specific aims are not global aims
- Specific aims relate to the study question, the research, and the deliverables
- Specific aims are designed to answer specific questions

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## Background and Significance

- Why should we care?
- What is the issue?
- Where are the treatment and outcome problems?
- How can this work address those issues?
- What prior research gaps exist?

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## Preliminary Studies or Progress Report

- Have you done any work that matters in this research area?
- Did the preliminary work lead to the methods of this proposed project?
- Does this work suggest that you will succeed in this work?

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## Research Design & Methods

- What question are you asking?
- What are the baseline assumptions?
- How do these assumptions lead to the design and methods proposed?

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## Framework for Achieving Aims

- How will you deliver on answering the specific questions identified in the Specific Aims section?
- What is the overall structure of the work?

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## Data Collection and Analysis

- What data, what statistics, what questions answered with the data?
- Include sample size calculation here based on initial assumptions

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## Novel Methods or Technologies

- Are you going to use a noteworthy method or testing technology?
- What are the implications that would enhance the likelihood that funding will take place?
- Does this make success more or less likely? Why?

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## Potential Limitations

- Acknowledge that all work has limitations and strengths
- Identify briefly 2-3 limitations that could impact the ability to answer the question or the generalizability of the results

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## Potential Hazards or Risks

- Be realistic, identify all patient risks
- Confirm IRB approval and patient safeguards
- Address all human subject issues completely
- HIPAA issues addressed here

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## Human Subject Issues

- Linked to potential hazards and risks

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## Study Sequence or Timeline

- What will take place in what order, over what period of time? Why?
- What will take place in series or parallel?
- What happens if one step cannot be completed?
- What stopgap measures might be used?

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## Budget

- Tie the budget to people costs, other direct costs, and specific activities that will lead to the ability to provide the deliverables
- Include all of the costs needed to deliver on the obligations
- If you wouldn't pay for it, don't put it in!

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## Budget

- Cost per patient
- Cost of doing the business
- Who do you have to hire to get the job done?
- Think of building a home. You are the general contractor.

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## Budget

- What are the IRB costs?
- What will tests cost?
- What will it cost to collect the data?
- What will it cost to analyze the data?
- What will it cost to present and publish the data?
- What are space and storage costs?

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## Personnel, Bio Sketch

- Only put people on the grant who can deliver on their role in providing deliverables
- Use the Bio sketch to promote who you and other are, and why you will succeed
- Venture capitalist: what matter most?
- Not the idea or the process, but the people who will pull it off!

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## Institutional Support

- Are the institutional pieces in place to allow the deliverables to be produced?
- Have all collaborators stated support?

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## Assurances & Certifications

- Boilerplate materials available from grants and contracts office
- Be aware of what you are certifying and assuring to be true

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## PHS 398 Form: An Example

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**Diapsirin Cross-Linked Hemoglobin (DCLHb) in the Treatment of Severe Traumatic Hemorrhagic Shock**  
 A Randomized Controlled Efficacy Trial

Edward P. Sloan, MD, MPH  
 Max Koenigsberg, MD  
 David Gens, MD  
 Mark Cipolle, MD, PhD  
 Jeffrey Runge, MD  
 Mary Nan Maloney, MD  
 and George Rodman, Jr, MD  
 for the DCLHb Traumatic Hemorrhagic Shock Study Group

**Context** Severe, uncompensated, traumatic hemorrhagic shock causes significant morbidity and mortality, but resuscitation with an oxygen-carrying fluid might improve patient outcomes.

**Objective** To determine if the infusion of up to 1000 mL of diapsirin cross-linked hemoglobin (DCLHb) during the initial hospital resuscitation could reduce 28-day mortality in traumatic hemorrhagic shock patients.

**Design and Setting** Multicenter, randomized, controlled, single-blinded efficacy trial conducted between February 1997 and January 1998 at 18 US trauma centers selected for their high volume of critically injured trauma patients, but 1 did not enroll patients.

**Patients** A total of 112 patients with traumatic hemorrhagic shock and unstable vital signs or a critical base deficit, who had a mean (SD) patient age of 39 (20) years. Of the infused patients, 79% were male and 56% were white. An exception to informed consent was used when necessary.

**Intervention** All patients were to be infused with 500 mL of DCLHb or saline solution. Critically ill patients who still met entry criteria could have received up to an additional 500 mL during the 1-hour infusion period.

**Main Outcome Measures** Twenty-eight day mortality, 28-day morbidity, 48-hour mortality, and 24-hour lactate levels.

## Abstract

- Tell the whole story in 250 words or less:
  - What is the problem?
  - What is the study question?
  - What will you do to answer it?
  - What will be the implications?
  - Do you have the means to get it done?

Edward P. Sloan, MD, MPH, FACEP



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**Intervention** All patients were to be infused with 500 mL of DCLHb or saline solution. Critically ill patients who still met entry criteria could have received up to an additional 500 mL during the 1-hour infusion period.

**Main Outcome Measures** Twenty-eight day mortality, 28-day morbidity, 48-hour mortality, and 24-hour lactate levels.

**Results** Of the 112 patients, 98 (88%) were infused with DCLHb or saline solution. At 28 days, 24 (46%) of the 52 patients infused with DCLHb died, and 8 (17%) of the 46 patients infused with the saline solution died ( $P = .003$ ). At 48 hours, 20 (38%) of the 52 patients infused with DCLHb died and 7 (15%) of the 46 patients infused with the saline solution died ( $P = .01$ ). The 28-day morbidity rate, as measured by the multiple organ dysfunction score, was 72% higher in the DCLHb group ( $P = .03$ ). There was no difference in adverse event rates or the 24-hour lactate levels.

**Conclusions** Mortality was higher for patients treated with DCLHb. Although further analysis should investigate whether the mortality difference was solely due to a direct treatment effect or to other factors, DCLHb does not appear to be an effective resuscitation fluid.

## Specific Aims

- Specific aims are not global aims
- Specific aims relate to the study question, the research, and the deliverables
- Specific aims are designed to answer specific questions

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be easily stored in the emergency department and immediately infused in trauma patients without the need for cross-matching.

The primary objective of this efficacy trial was to reduce 28-day mortality of traumatic hemorrhagic shock patients by 25%, from 40% to 30%, through the additional infusion of 500 to 1000 mL of DCLHb during the initial hospital resuscitation period. The study also attempted to demonstrate a significant reduction in 28-day morbidity, 48-hour mortality rates, and 24-hour lactate levels.

**METHODS**  
**Study Design**  
 This was a multicenter, randomized, single-blinded, normal saline procedure-controlled, efficacy and safety study of DCLHb in severe traumatic hemorrhagic shock (FIGURE 1). This clinical trial was conducted in compliance with the regulations governing good clinical trials and good clinical practice. Study

rollment in this study.

Patients with significant traumatic brain injury, as determined by clinical criteria (ie, posturing, blown pupil) that suggest a space-occupying lesion, were excluded. Patients whose death was thought to be imminent, suggesting a futile resuscitation effort, were also excluded, as were patients whose injury occurred more than 4 hours prior to infusion. Also excluded from the protocol were minors, pregnant women, and patients who opposed to study participation or the use of blood or blood products. Although there was an attempt to enroll all eligible patients into this study, the data do not reflect a consecutive patient series. Outcome data for patients who either refused participation or were missed as potential study participants were not collected.

Randomization was stratified by clinical site, using permuted blocks of 4 or 6 patients.<sup>21</sup> The investigators were informed of this randomization scheme in the study protocol. Each site was provided with a sequential set of sealed en-

man red blood cells from volunteers whose blood had been found to have negative results for hepatitis B surface antigen, human immunodeficiency virus 1 and 2, and cytomegalovirus. The 500- to 1000-g (50 to 100 g of hemoglobin) study provided 714 to 1428 mg of DCLHb to a 70-kg person. Patients were less likely to become ineligible to be infused for other clinical reasons. Trauma patients who arrived at the hospital within 60 minutes of hospital arrival received up to 1000 mL of either the 10% DCLHb or normal saline through a distal or peripheral intravenous infusion was to begin no later than 60 minutes after the patient first arrived at the hospital. The entire dosing of the study was to be completed within 2 hours of its onset, such that it received study solution after hospital for more than 2 h

## Background and Significance

- Why should we care?
- What is the issue?
- Where are the treatment and outcome problems?
- How can this work address those issues?
- What prior research gaps exist?

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DEATH FROM TRAUMA frequently results from hemorrhagic shock that is refractory to optimal resuscitation efforts.<sup>1</sup> Patients with uncompensated hemorrhagic shock, especially those with large base deficits, are at the greatest risk of multisystem organ failure and death.<sup>2,3</sup> Standard therapies, including the rapid infusion of large volumes of crystalline solutions of blood, may exacerbate the morbidity caused by severe trauma.<sup>4-6</sup> Studies suggest that small-volume resuscitation, slow resuscitation, delayed resuscitation, or the use of an oxygen-carrying resuscitation fluid might improve outcome in hemorrhagic shock.<sup>7-9</sup>

This clinical trial was conducted to determine if dextran cross-linked hemoglobin (DCLHb), a purified and chemically modified human hemoglobin solution, could improve cellular perfusion and reduce mortality and morbidity when used as an adjunct to standard therapy in severely injured hemorrhagic shock patients. It was studied for use in trauma because it can

tal signs of a critical base deficit, who had a mean (SD) patient age of 39 (20) years. Of the infused patients, 79% were male and 56% were white. An exception to informed consent was used when necessary.

**Intervention** All patients were to be infused with 500 mL of DCLHb or saline solution. Critically ill patients who still met entry criteria could have received up to an additional 500 mL during the 1-hour infusion period.

**Main Outcome Measures** Twenty-eight day mortality, 28-day morbidity, 48-hour mortality, and 24-hour lactate levels.

**Results** Of the 112 patients, 98 (88%) were infused with DCLHb or saline solution. At 28 days, 24 (46%) of the 52 patients infused with DCLHb died, and 8 (17%) of the 46 patients infused with the saline solution died ( $P = .003$ ). At 48 hours, 20 (38%) of the 52 patients infused with DCLHb died and 7 (15%) of the 46 patients infused with the saline solution died ( $P = .01$ ). The 28-day morbidity rate, as measured by the multiple organ dysfunction score, was 72% higher in the DCLHb group ( $P = .03$ ). There was no difference in adverse event rates or the 24-hour lactate levels.

**Conclusions** Mortality was higher for patients treated with DCLHb. Although further analysis should investigate whether the mortality difference was solely due to a direct treatment effect or to other factors, DCLHb does not appear to be an effective resuscitation fluid.

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JAMA, November 17, 1999—Vol 282, No 19 1857

## Preliminary Studies or Progress Report

- Have you done any work that matters in this research area?
- Did the preliminary work lead to the methods of this proposed project?
- Does this work suggest that you will succeed in this work?

Edward P. Sloan, MD, MPH, FACEP



DEATH FROM TRAUMA frequently results from hemorrhagic shock that is refractory to optimal resuscitation efforts.<sup>1</sup> Patients with uncompensated hemorrhagic shock, especially those with large base deficits, are at the greatest risk of multisystem organ failure and death.<sup>2,3</sup> Standard therapies, including the rapid infusion of large volumes of crystalline solutions of blood, may exacerbate the morbidity caused by severe trauma.<sup>4-6</sup> Studies suggest that small-volume resuscitation, slow resuscitation, delayed resuscitation, or the use of an oxygen-carrying resuscitation fluid might improve outcome in hemorrhagic shock.<sup>7-9</sup>

This clinical trial was conducted to determine if dextran cross-linked hemoglobin (DCLHb), a purified and chemically modified human hemoglobin solution, could improve cellular perfusion and reduce mortality and morbidity when used as an adjunct to standard therapy in severely injured hemorrhagic shock patients. It was studied for use in trauma because it can

tal signs of a critical base deficit, who had a mean (SD) patient age of 39 (20) years. Of the infused patients, 79% were male and 56% were white. An exception to informed consent was used when necessary.

**Intervention** All patients were to be infused with 500 mL of DCLHb or saline solution. Critically ill patients who still met entry criteria could have received up to an additional 500 mL during the 1-hour infusion period.

**Main Outcome Measures** Twenty-eight day mortality, 28-day morbidity, 48-hour mortality, and 24-hour lactate levels.

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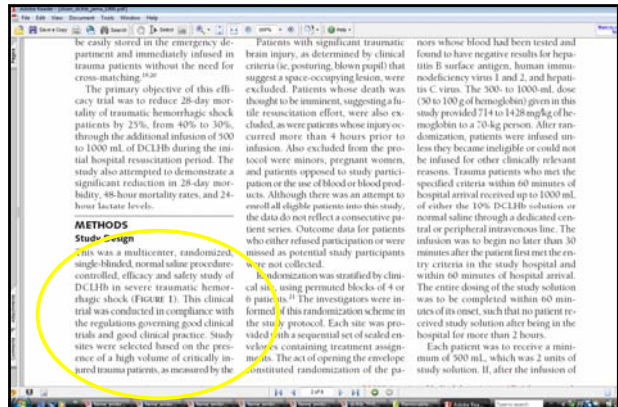
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## Research Design & Methods

- What question are you asking?
- What are the baseline assumptions?
- How do these assumptions lead to the design and methods proposed?

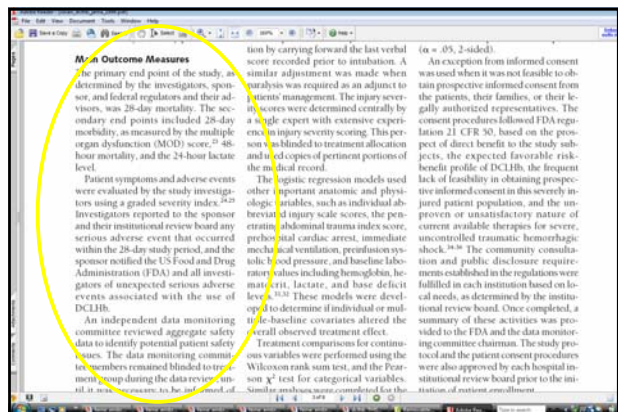
Edward P. Sloan, MD, MPH, FACEP



## Framework for Achieving Aims

- How will you deliver on answering the specific questions identified in the Specific Aims section?
- What is the overall structure of the work?

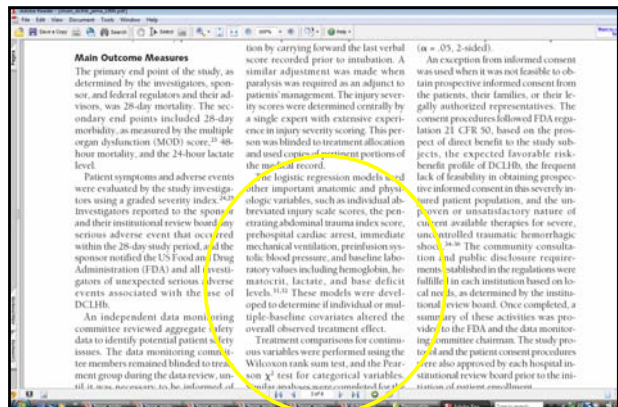
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## Data Collection and Analysis

- What data, what statistics, what questions answered with the data?
- Include sample size calculation here based on initial assumptions

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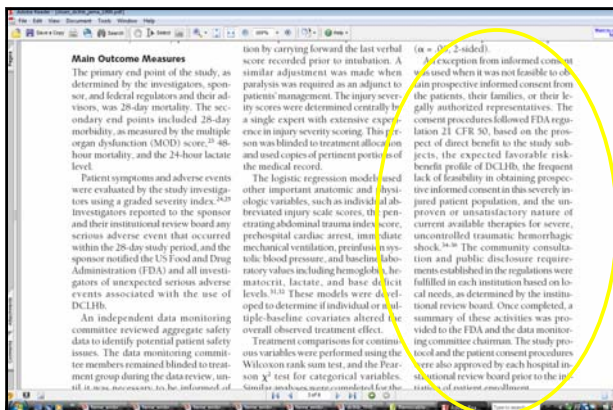




# 2007 Emergency Medicine Research Workshop

## Government Grants and the PHS 398 Form

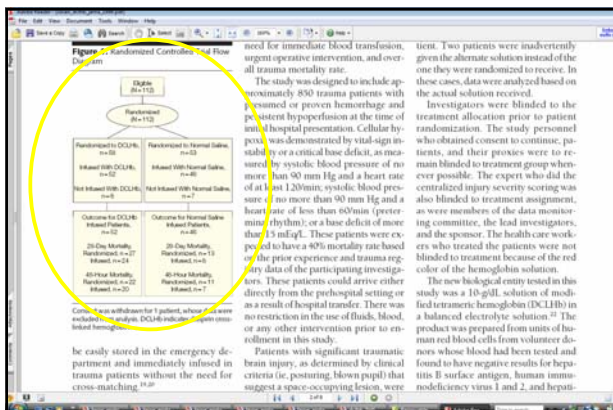
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## Study Sequence or Timeline

- What will take place in what order, over what period of time? Why?
- What will take place in series or parallel?
- What happens if one step cannot be completed?
- What stopgap measures might be used?

Edward P. Sloan, MD, MPH, FACEP



## Conclusions

- Government grants are abundant
- PHS 398 form allows for systematic application process
- Need to provide a detailed report of the work and the deliverables
- Websites such as grants.gov assist in the process

Edward P. Sloan, MD, MPH

## Recommendations

- Become facile at doing government grant writing
- Know what is out there, and think global
- Consider how multiple federal grants can be obtained and utilized, promoting success in the research enterprise
- Be able to complete the PHS 398 form

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## Thank you.

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