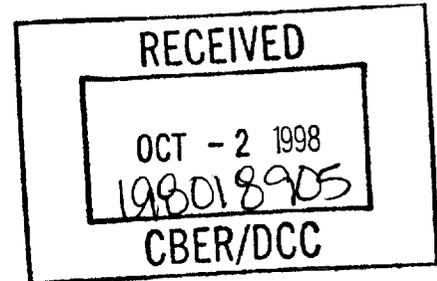


**Baxter**

2765 '98 OCT -9 A9:52

September 28, 1998

Docket Number 95S-0158  
Dockets Management Branch (HFA-305)  
Food and Drug Administration  
12420 Parklawn Dr. rm. 1-23  
Rockville, MD 20857

**RE: Investigational New Drug Application #6859**

Dear Sir/Madam:

In accordance with 21 CFR §56.109 and §312.54 concerning Baxter Healthcare Corporation's Investigational New Drug Application #6859 relating to the clinical testing of Diaspirin Crosslinked Hemoglobin (DCLHb), we are enclosing copies of information concerning ending research involving an exception to informed consent. This submission includes information that has been publicly disclosed by the IRB at the University Louisville Hospital, the IRB at Lehigh Valley Hospital in Allentown, PA, the IRB at Carolinas Medical Center in Charlotte, NC, and the IRB at East Carolina University School of Medicine in Greenville, NC. This submission also includes other miscellaneous press coverage and an update to the University of Illinois-Chicago web site related to DCLHb Traumatic Hemorrhagic Shock Research (<http://dclhb.er.uic.edu>).

The public disclosure/community consultation information from the University Louisville Hospital includes: an article in the Kentucky Emergency Physician's Interim Communique Newsletter sent to 235 members, 130 University of Louisville EM students, and 130 EM Chapter Presidents and Executive Directors, Winter 1998 edition (Attachment 1); an article in University of Louisville magazine, Winter 1998 edition sent to 100,000 faculty, students, employees and community members (Attachment 2). The site also participated in a radio program discussing the study which aired on seven (7) stations. Additional public disclosure that occurred after the study was stopped include an Article in EtUltra magazine, Summer-Fall 1997 edition distributed to 6,000 research faculty and potential funders (Attachment 3); an article in Government & Politics (Attachment 4); an article in Physicians News, Fall 1997 edition (Attachment 5); and an article in the Healthcare Quarterly supplement to Business First, December 22, 1997, circulation to 15,000 subscribers (Attachment 6).

95S-0158

SUP17

The public disclosure/community consultation information from East Carolina University School of Medicine in Greenville, NC includes an article from the University Health Systems of Eastern Carolina People magazine, January 1998 (Attachment 7).

The public disclosure information from Lehigh Valley Hospital in Allentown, PA includes three (3) articles from various local publications (Attachments 8-10).

The public disclosure information from Carolinas Medical Center in Charlotte, NC includes an advertisement placed in the Charlotte Observer, 4/01/98 (Attachment 11); and an article from the Charlotte Observer, 4/2/98 (Attachment 12).

The miscellaneous press coverage includes; an article from the Associated Press (Attachment 13); an article from International Blood/Plasma News, April 1998 (Attachment 14); an article from NewsEdge, April 9, 1998 (Attachment 15); an article from the Daily Herald, April 11, 1998 (Attachment 16); an article from the Philadelphia Business Journal, April 6, 1998 (Attachment 17); an article from the Philadelphia Inquirer 3/31/98 (Attachment 18); and an article from the Wall Street Journal, April 1, 1998 (Attachment 19).

Additionally, an update to the University of Illinois-Chicago web site related to the DCLHb Traumatic Hemorrhagic Shock Research (<http://dclhb.er.uic.edu>) is included (Attachment 20).

Outlined in Attachment 21 is the media coverage for both the March 31 and April 10 press releases announces the halt of the HemAssist trauma trial.

Additionally, an update to the University of Illinois-Chicago web site related to the DCLHb Traumatic Hemorrhagic Shock Research (<http://dclhb.er.uic.edu>) is included (Attachment 22).

In accordance with 21 CFR §312.54, this information is also being submitted to the Docket Number 95S-0158 in the Dockets Management Branch.

The submission has been organized as follows:

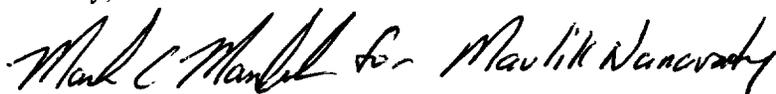
- Attachment 1: An article in the Kentucky Emergency Physician's Intern Communique Newsletter, Winter 1998 edition
- Attachment 2: An article in University of Louisville magazine, Winter 1998 edition
- Attachment 3: An Article in EtUltra magazine, Summer-Fall 1997 edition
- Attachment 4: An article in Government & Politics

- Attachment 5: An article in Physicians News, Fall 1997 edition  
Attachment 6: An article in the Healthcare Quarterly supplement to Business First, December 22, 1997  
Attachment 7: An article from the University Health Systems of Eastern Carolina People magazine, January 1998  
Attachments 8-10: Articles from local publications related to the Lehigh Valley trauma study site  
Attachments 11-12: Articles from the Charlotte Observer, 4/01/98 & 4/02/98  
Attachment 13: An article from the Associated Press  
Attachment 14: An article from International Blood/Plasma News, April 1998  
Attachment 15: An article from NewsEdge, April 9, 1998  
Attachment 16: An article from the Daily Herald, April 11, 1998  
Attachment 17: An article from the Philadelphia Business Journal, April 6, 1998  
Attachment 18: An article from the Philadelphia Inquirer 3/31/98  
Attachment 19: An article from the Wall Street Journal, April 1, 1998  
Attachment 20: An update to the University of Illinois-Chicago web site related to the DCLHb Traumatic Hemorrhagic Shock Research (<http://dclhb.er.uic.edu>)  
Attachment 21: Media Coverage Report  
Attachment 22: An update to the University of Illinois-Chicago web site related to the DCLHb Traumatic Hemorrhagic Shock Research (<http://dclhb.er.uic.edu>)

This IND (BBIND #6859) is cross-referenced to Baxter's original BBIND #4426 and subsequent amendments.

If there are any questions concerning this submission, please contact me at (847)270-5313.

Sincerely,



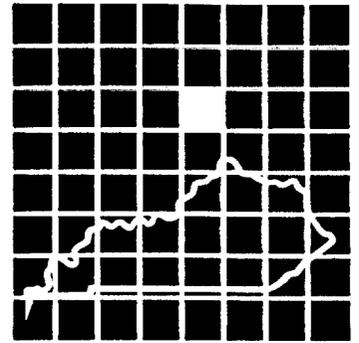
Maulik Nanavaty, Ph.D.  
Director Regulatory Affairs  
Hemoglobin Therapeutics Program

Attachment 1

THE KENTUCKY

# EPIC

EMERGENCY PHYSICIAN'S INTERIM COMMUNIQUE



WINTER 1998

## THE ORIGIN OF CARDIOPULMONARY RESUSCITATION

Tim Price, MD  
University of Louisville

Cardiopulmonary resuscitation (CPR) as we know it today has changed little during the lifetime of the speciality of Emergency Medicine. Certainly there have been changes in medical therapy of the cardiac arrest patient in the past three decades, however substantial changes in the mechanics of basic life support techniques are lacking. Most practicing physicians today are familiar with CPR but few can elaborate on the origin of this universally accepted procedure. In this article I will briefly review the development of CPR.

### Biblical Accounts

Some medical historians believe that the earliest account of CPR can be found within the Old Testament. In 1 Kings 17:17-22, one reads about a boy who became ill and stopped breathing. Elijah laid the boy on a bed.

"Then he stretched himself out on the boy three times and cried to the Lord, 'O Lord my God, let this boy's life return to him!' The Lord heard Elijah's cry, and the boy's life returned to him and he lived."

In 2 Kings 4:33-35, a similar incident is recorded in which a dead boy is brought back to life after the prophet Elishah "lay upon the boy, mouth to mouth, eyes to eyes, hands to hands" and stretched himself out on the boy two times. While some readers faithfully believe that these are accounts of miracles, some readers explain them as the first recorded examples of successful medical resuscitations.

### Pre-1800's

The first contemporary evidence of attempts at resuscitation are revealed in Renaissance writings by Vesalius (1514-1564) and Paracelsus (1493-1541) and in the 1700's in the registers of the "Humane Societies" of Amsterdam, Copenhagen, London and Massachusetts. Included in these registers were attempts at intubation by palpation, positive pressure ventilations with fireside bellows, and mouth-to-mouth ventilation on newborn infants and drowning victims.

The concept of electrical defibrillation had been reported in the register of the Royal Humane Society of London in 1774 by a man named Koenig who stated that "upon transmitting a few shocks through the thorax, I perceived a small pulsation and in a few minutes the child began to breathe with great difficulty." Actual appreciation for ventricular fibrillation did not occur until much later.

### Pre-1950's

Modern resuscitation attempts began as a matter of necessity after the discovery of general anesthesia in the 1800's. As general anesthesia was frequently complicated by apnea, airway obstruction, and pulselessness, surgeons were forced to find ways to reverse these tragic complications. Intermittent positive pressure ventilation was being used occasionally; however, exaggerated reports of barotrauma resulted in its abandonment and replacement by manual ventilation techniques. Various manual methods were described and promoted including supine chest-pressure arm-lift, prone chest-pressure only, and prone back-pressure arm-lift methods. These methods would prevail as the method of artificial respiration until the 1950's.

Endotracheal intubation by palpation was sporadically used since the late 1800's, however anesthetized patients were not typically intubated until the 1920's. By World War II, the allied forces commonly intubated utilizing direct laryngoscopy. Open-chest massage was used in the operating room for cardiac arrest associated with chloroform use, but cardiac arrest out of the operating room was considered a hopeless condition. Closed chest cardiac massage was performed on animals and human subjects in the late 1800's. However, this technique would be forgotten for another 50 years.

continued on page 5

### Inside This Issue

1998 Goals and Objectives .....	p. 3
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Research in Emergency Medicine: Waiver of Informed Consent .....	p. 5
Kentucky Board of Medical Licensure Authorized Lay Rescuer AED Programs .....	p. 6

## RESEARCH IN EMERGENCY MEDICINE: WAIVER OF INFORMED CONSENT INTRODUCED

Ashlee Miller, RN  
Mary Nan S. Mallory, MD  
University of Louisville

In October 1996, the Food and Drug Administration passed a regulation, Section 50.24(a)(7) for an exception from informed consent in emergency medicine research. The University of Louisville Department of Emergency Medicine is currently participating in the first such waiver of informed consent research project. Until this new regulation was passed, emergency physicians were very limited regarding resuscitation research.

The regulation gives additional protections of the rights and welfare of the subjects, including, at least: 1) Consultation with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn; 2) Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits; 3) Public disclosure of sufficient information following completion of the clinical investigation to appraise the community and researchers of the study, including the demographic characteristics of the research and its results. The Institutional Review Board (IRB) is responsible for the review, approval, and continuing review of the clinical investigation.

The regulation also has specific procedures in seeking informed consent. If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the clinical investigation. The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review. The IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject.

In August 1997, the University of Louisville Department of Emergency Medicine, under the direction of the IRB, completed community consultation, the initial phase of public disclosure and began the study which is designed to measure the efficacy of Diaspirin Cross-Linked Hemoglobin (DCLHb). DCLHb is an oxygen-carrying hemoglobin product which has been chemically modified, purified and pasteurized. This product is produced from expired red blood cells and does not require a crossmatch.

DCLHb is given to patients that enter with severe hemorrhage and shock. It carries oxygen to tissues with oxygenation to the heart and other vital organs. It also has a pharmacological effect of increasing blood pressure a predictable amount. The primary endpoints to this study is to decrease mortality and also decrease the endstage organ failure, that commonly happens with severe hemorrhage. The plan is to continue the study through 1998.

If you have any questions regarding waiver of informed consent or the DCLHb study being conducted at the University of Louisville Hospital, please contact us at (502) 852-5689.

## The Origin of Cardiopulmonary Resuscitation continued from page 1

### 1950's

In the middle of the twentieth century, several reports led to the development of modern CPR. In Baltimore, approximately 100 anesthetized patients and volunteers were examined under fluoroscopy. This demonstrated to observers how the epiglottis and tongue would obstruct the airway during anesthesia unless the airway was maintained using head tilt, and sometimes jaw thrust, with the mouth open. Thus the triple airway maneuver was first described.

In 1957, a crucial study compared ventilation success in mouth-to-mouth versus manual push-pull ventilation techniques in 27 adult volunteers. The non-intubated volunteers were made unconscious and paralyzed with curare. Positive pressure ventilation with mouth-to-mouth proved to be superior to ineffective manual push-pull techniques.

Finally, the generation of a pressure pulse with external chest compression was rediscovered. Kouwenhoven, a professor of electrical engineering at the Johns Hopkins Hospital, was studying external defibrillation in dogs. His research fellow, engineer Knickerbocker, was pressing the external electrodes on the dog's chest when he noticed an arterial pressure wave. A surgical resident by the name of Jude, applied this to human subjects. He documented artificial circulation by sternal compressions to patients that developed pulselessness during induction with the potent new anesthetic agent Halothane. He reported in JAMA in 1960 and 1961 that a few sternal compressions and intermittent positive pressure ventilations with oxygen promptly restored circulation in these patients. Thus modern external sternal compression was introduced. Further animal studies integrating the three components discussed above resulted in the ABC's of modern resuscitation and the recommended compression to ventilation ratio currently used.

By the latter half of the 1960's the American Heart Association had developed its recommended program for CPR and published it in the JAMA. Subsequent widespread teaching and use has resulted in universal acceptance of this process as the standard initial basic life support of the patient in cardiac arrest.

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## KACEP GOLF CHALLENGE TO BE HELD ON MAY 11TH

KACEP will be hosting a golf challenge at Marriott's Griffin Gate Resort in Lexington on Monday, May 11th. There will a continental breakfast provided, a 1 hour CME program from 8:00AM - 9:00AM, and tee-off time following the program. The cost of the entire program is \$45.00 per person for KACEP members. This will be a fundraiser for KACEP, so please help show your support and mark this date on your calendar, so that we can continue to increase our visibility and activities within the state.



Attachment 2

**Synthetic Treatment Derived from Blood Shows Promise**

U of L researchers will study a synthetic blood product that may allow emergency physicians to speed treatment of patients who have suffered severe blood loss. The product, Diasprin Cross-Linked Hemoglobin (DCLHb), is prepared from chemically modified human red blood cells. It is sterilized and pasteurized, and can be frozen for up to one year. Most importantly, DCLHb can be used on anyone, and does not require a match with the patient's own blood type. "Diasprin holds great promise for our patients with severe traumatic injury," said Mary Nan Mallory, principal investigator for the Kentucky study, who also is a physician in U of L's emergency medicine department. Even after surviving severe blood loss, Mallory explained, a patient still risks death in the first month due to the initial damage to internal organs and tissues. "We want to find out through this study," she added, "if the use of DCLHb can decrease the number of deaths that occur in that 28-day window." The U.S. Food and Drug Administration has authorized U of L to study the product in its trauma center during a two-year trial. Study criteria dictate that only the most seriously injured patients, those with severe shock and bleeding, are eligible for enrollment. These patients are at the greatest risk of death.



Emergency Medicine Instructor Mary Nan Mallory.

**Scholar Develops Grief Predictor for Miscarriage Cases**

Miscarriages happen more often than most people believe. Statistics say that 15 percent to 20 percent of all known pregnancies end in miscarriage. The rate is probably higher because sometimes women who don't know they are pregnant will pass off heavy bleeding as a strong period when, in fact, they have miscarried. Marianne Hutti, nursing professor and coordinator of U of L's nurse practitioner women's health program, has compiled 10 years of data on pregnancy loss. In her obstetrical practice, she found a need for medical providers to understand how to approach women who have experienced pregnancy loss. Her research explores factors that influence the intensity of grieving in order to help health care providers better identify men and women who need follow-up after such a loss. Says Hutti, "Understanding a client's intensity of grieving will not speed up the mental healing process but it will help care providers to give better care to grieving families." Her article, "Predicting Women's Responses to Pregnancy Loss" won an outstanding research award last summer at the national meeting of the American Academy of Nurse Practitioners.



Marianne Hutti, coordinator of U of L's women's health nurse practitioner program.

**U OF L RESEARCHERS**



Entries in this sampling include donors and recent funding amounts.

Roberto Bolli, \$292,463, National Institutes of Health, "Role of Oxygen Radicals in Postischemic Dysfunction."

Douglas Borchman, \$172,908, National Institutes of Health, "Spectroscopic and Related Studies on Lens Membrane Lipids."

Rafael Fernandez-Botran, \$99,819, National Institutes of Health, "Immunoregulation by Soluble IL-4 Receptors."

Henry Enck and Robert Taylor, \$241,450, Universidad Francisco Gavidia, San Salvador, "Contract to Provide a Master of Business Administration in San Salvador, El Salvador."

Anna Huang, \$91,000, SmithKline Beecham Biologicals, "A Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Safety of SmithKline Beecham Biologicals' Herpes Simplex Candidate Vaccine with MPL in HSV Seropositive of Seronegative Subjects without Genital Herpes Disease."

Y. James Kang, \$106,253, U.S. Department of Agriculture, "The Role of Catalase in Protection Against Copper Deficiency-Induced Heart Damage in Transgenic Mice."

Karen Lind, \$191,670, Jefferson County Public Schools, "Centers for Excellence for Research, Teaching and Learning (CERTL)."

John Van Savage, et. al., \$181,153, Alliant Community Trust Fund, "Stimulated Free Flap Myoplasty for the Acontractile Bladder."

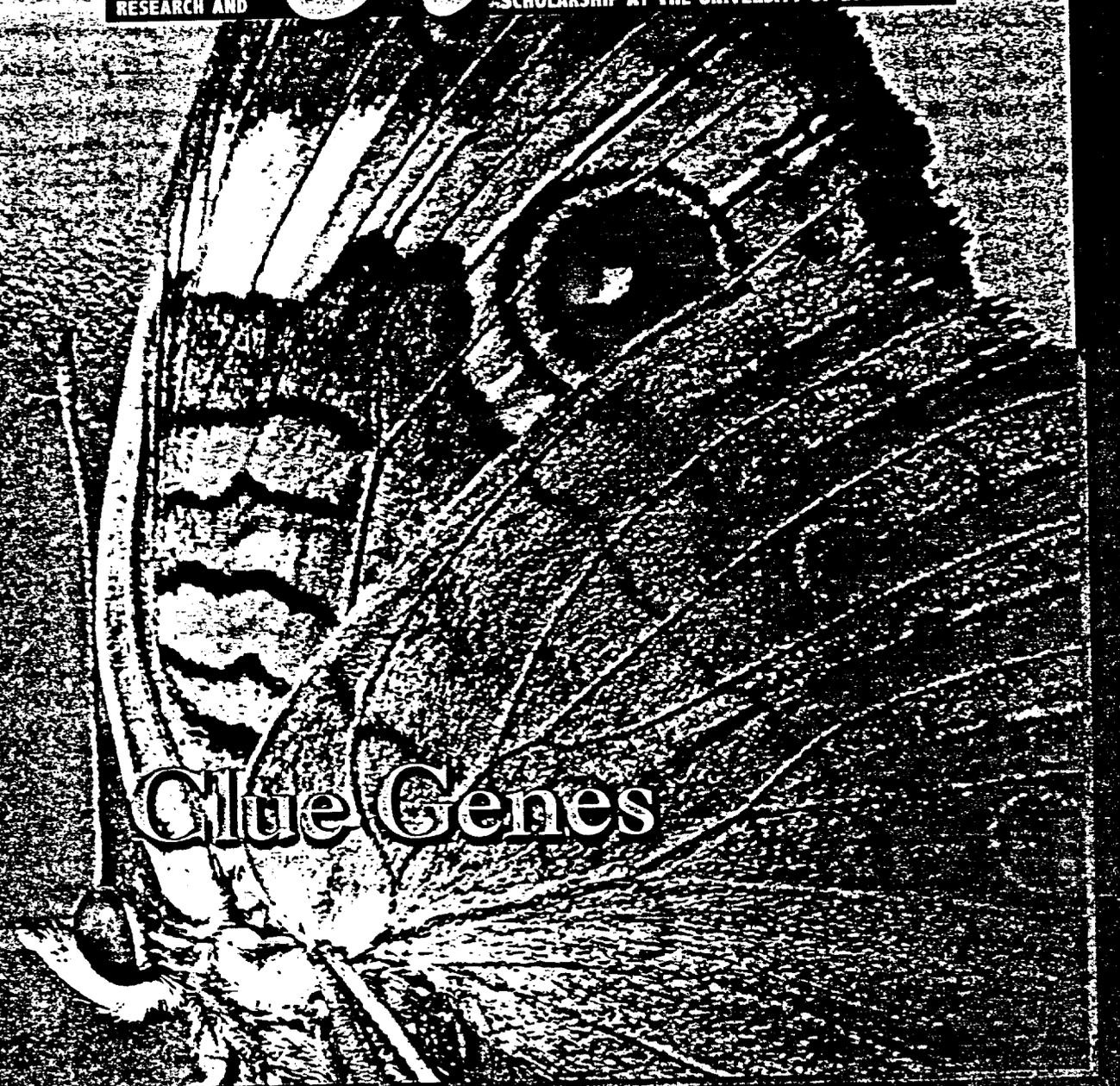
Richard Wittebort, \$174,206, National Institutes of Health, "Structural Studies of Collagen Fibrils by NMR."

Attachment 3

# LETTERA

RESEARCH AND

SCHOLARSHIP AT THE UNIVERSITY OF LOUISVILLE



## Celtic Genes

SUMMER-FALL 1997

## RESEARCH DIGEST

### Synthetic Treatment Derived from Blood Shows Promise

U of L researchers will study a synthetic blood product that may allow emergency physicians to speed treatment of patients who have suffered severe blood loss.

The product, Diasprin Cross-Linked Hemoglobin (DCLHb), is prepared from chemically modified human red blood cells. It is sterilized and pasteurized, and can be frozen for up to one year. Most importantly, DCLHb can be used on anyone, and does not require a match with the patient's own blood type.

Study criteria dictate that only the most seriously injured patients, those with severe shock and bleeding, are eligible for enrollment. These patients are at the greatest risk of death.

All patients will receive the best medical care available, stresses Dr. Mary Nan Mallory, principal investigator for the Kentucky study. The DCLHb treatment will be administered as additional therapy. The study is nationally randomized, which means of those patients at all participating centers who fit treatment parameters, approximately half will receive this additional treatment step; the other half will not.

"Diasprin holds great promise for our patients with severe traumatic injury," says Mallory, who also is a physician in U of L's emergency medicine department. Even after surviving severe blood loss, Mallory explains, a patient still risks death in the first month due to the initial damage to internal organs and tissues. "We want to find out through this study," she adds, "if the use of DCLHb can decrease the number of deaths that occur in that 28-day window."

The U.S. Food and Drug Administration has authorized U of L to study the product in its trauma center during a two-year trial. U of L and federal research protocols dictate that a patient must give informed consent before being enrolled in any clinical trial. However, patients who have suffered severe trauma and loss of blood—the type of case for which U of L's DCLHb



study was designed—sometimes are injured too seriously to give informed consent, and next of kin can't be located in time to administer treatment.

In such cases, U of L will use a waiver of informed consent recently authorized by the FDA for just such contingencies. The waiver allows researchers at U of L Hospital to administer DCLHb before informed consent can be given. The study was reviewed and approved by U of L's Human Studies Committee, which oversees the protection of human subjects in research. Patients and their families, however, have the right to withdraw from the trial at any time after they

Even when blood is replaced in patients with trauma or severe bleeding, the resulting organ and tissue damage can be fatal. U of L researcher Mary Nan Mallory will head up Kentucky's portion of a national trial to test a synthetic, blood-derived therapy that shows promise in reducing such fatalities.

have been informed.

The committee also has outlined a comprehensive "public disclosure" plan. A three-week program of advertising and publicity is under way; its aim is to inform local residents of the study and the possible use of the FDA waiver.

Attachment 4

## Debate Swirls Around New Rules for Informed Consent in Trauma Research

Scientists cite vagueness; regulators see lack of implementation

BY PAULETTE WALKER CAMPBELL

**W**HEN A MAN was admitted to the University of Louisville Hospital this month with life-threatening abdominal injuries from a car accident, he was immediately enrolled in a study to test a blood substitute called HemAssist.

Scientists believe that the product, which is made from human blood, will speed the flow of oxygen to vital organs and raise a patient's blood pressure faster than the standard treatment of blood transfusions and salt solutions.

A year ago, such an experiment could not have occurred, because the man, who was unconscious, could not give his permission to participate in the study. Federal law generally prohibits doctors from giving patients experimental treatments unless the subjects or their family members understand the risks and give their consent.

But government rules that took effect last November allow scientists to obtain waivers of that requirement so they can use experimental drugs and medical devices on patients in life-threatening situations without the patient's consent.

Federal officials and researchers are still at loggerheads, however, over how best to carry out provisions in the rule that require scientists to notify the public and to seek advice—and consent—from the local community before conducting the research.

At a meeting sponsored by the Food and Drug Administration here this month, scientists and members of panels that review research proposals told federal officials that the requirements are too vague and too costly and time-consuming to fulfill.

Mary K. Pendergast, the F.D.A.'s deputy commissioner, acknowledged that the consent requirements are the "Achilles' heel" of the new rules. But they must "be strictly adhered to," she said, "in order to protect this particularly vulnerable population of patients."

If scientists don't begin to take their obligations more seriously, she warned, "the F.D.A., if necessary, will pull the plug on this rule, or enact stricter guidelines."

### A DILEMMA FOR RESEARCHERS

Before the waiver rule was changed last November, the government's informed-consent law presented a dilemma for acute-care researchers: Most of the patients they treat are unconscious, and irreparable damage often is done within a few minutes, limiting the time available for physicians to locate relatives for consent.

Exceptions to the requirement were rarely granted. The F.D.A., which oversees research on human subjects that involves experimental drugs and devices, waived consent in some individual cases. In separate rules, the Office for Protection from

Research Risks, which monitors research supported by agencies in the Department of Health and Human Services, agreed to issue waivers if the proposed study posed no more risk than an individual would encounter in daily life—a standard met by few emergency treatments.

Because neither set of exceptions offered specific guidance for clinical trials in emergency care, institutional review boards allowed acute-care researchers to obtain "deferred consent." In such cases, physicians enrolled patients in studies without their consent, and told the patient and family members afterward.

But in 1992—following revelations that the federal government several decades previously had exposed people to radiation without their consent—the risk-protection office banned the use of deferred consent at institutions that received grants from the Health and Human Services Department, even if the study in question was not sponsored by the government.

That, in effect, stopped all acute-care research. After three years of lobbying by

**"We are talking about sacred issues here: Informed consent, autonomy, fairness, patient protection. So we can't be flippant about the amount of time it takes."**

scientific and medical societies, the F.D.A. and the Health and Human Services Department issued their joint revisions, which went into effect in November 1996.

The new rules allow doctors to test therapies in emergencies if:

- An independent physician and the local review board agree that the patient is in a life-threatening situation, requiring immediate attention.

- The other available treatments are unsatisfactory or ineffective.

- And sufficient evidence exists that the experimental treatment may help the patient.

In addition, the researchers must show that the risks of participating in the study are "reasonable, compared to those associated with the patient's medical condition at the time," and that getting the permission of the patient or a legal representative is not feasible in the brief window of time when the treatment must be provided.

### COMMUNITY CONSULTATION

The rules also require researchers to inform the population most likely to be affected by the study about its purpose, risks, and possible benefits. The researchers, the study's sponsors, and the review boards must consult with the community about the appropriateness of the research.



Mary Nan Mallory, principal investigator for a U. of Louisville hospital study: "This is a very complex rule that we are all still trying to understand."

At the study's completion, the community must be told how the experiment fared.

Federal officials at the meeting said they had expected researchers to take pains to fulfill the requirements of conducting research under the waiver. Instead, said the F.D.A.'s Ms. Pendergast, "we've seen signs that the rule is not being implemented the way we had hoped."

For example, some institutions have sought to fulfill the requirement about consulting the community merely by running local-newspaper advertisements. "An advertisement may serve as one part of a

impossible, the research may not be appropriate for that community.

Members of the review board were stumped by the question of defining target community. The regulations encourage scientists to focus their consultation and disclosure efforts only on the community most likely to be affected by the research. But Steven Peckman, associate director of human-subject research at University of California at Los Angeles, pointed out that "there are 70 different gauge groups in the L.A. unified school district—our community. How do you consult with all those groups?"

### TIME AND MONEY

Researchers also complained about time and money it takes to fulfill the requirements. Baxter Healthcare Corporation, an international pharmaceutical company, spent nearly \$7,000 to help researchers at Louisville get the word out about blood-substitute study. The sponsor supposed to bear the costs, but researchers at the meeting expressed worry about would pick up the tab for studies aren't sponsored by the government large pharmaceutical companies.

The chairman of Louisville's review panel, along with Mary Nan Mallory principal investigator, spent 40 hours a four-month period talking with local representatives about the study. "That" time spent on one study out of 1,000 the panel regulates, said Dr. Mallory. "Having said that, we are talking about sacred issues here: informed consent, autonomy, fairness, patient protection—we can't be flippant about the amount of time it takes."

Government officials at the meeting made many suggestions but few concrete answers. "These requirements will expire over time," said Robert J. Temple, associate director for medical policy in the F.D.A.'s Center for Drug Evaluation Research.

Dr. Mallory agreed. "This is a very complex rule that we are all still trying to understand. In the beginning, some of our efforts were not as broad. But the sites that interpret and apply the rule will learn more lessons we learn."



# Physician News



Fall 1997

## Physician News

As a quarterly publication highlighting events, accomplishments, and news about the University of Louisville Hospital and James Graham Brown Cancer Center medical staff. This newsletter is published by the Marketing/Public Relations Department. Information should be sent to:

Kimberlee Turner  
Public Relations  
Brown Cancer Center  
529 South Jackson St.  
Louisville, KY 40202

The University of Louisville Hospital is managed by UMC; a partnership of the University of Louisville, Jewish Hospital HealthCare Services, and Alliant Health System.

## In this Issue

- ◆ New Study for Trauma Patients
- ◆ Sentinel Lymph Node Biopsy for Breast Cancer
- ◆ National Protocol for Lung Cancer
- ◆ Managing Pain Effectively

## New Study May Improve Trauma Patients Outcome

Adult trauma patients arriving at the University of Louisville Trauma Institute/Emergency Department with severe blood loss and life-threatening shock may be enrolled in a new national study. The study is testing a blood-derived product called, Diasprin Cross-Linked Hemoglobin (DCLHb) to determine if the product effectively improves perfusion, reduces multi-system organ damage and ultimately improves mortality rates in trauma patients. The product, produced by Baxter Healthcare Corporation, is prepared from expired human banked blood that is chemically stabilized and pasteurized and does not require a cross-match before administering. "It is a hemoglobin-based oxygen carrying solution which improves perfusion when infused acutely in severe hemorrhagic shock models," says Mary Nan Mallory, M.D., Department of Emergency Medicine and principal investigator.

The randomized study, excludes severe head injuries, pregnancy, and known objections to blood products, and treats half of the patients with DCLHb and half with a saline control solution. All enrollees will receive conventional treatment



Lab Director, Jill Leonard (left) and Mary Nan Mallory, M.D. principal investigator, examine DCLHb, a blood-derived hemoglobin product from Baxter Healthcare Corporation.

including surgery and blood transfusions. Up to 10 grams of DCLHb can be administered very early during the hemorrhaging patients' resuscitation phase to enhance perfusion of vital organs in hopes of preventing subsequent multi-organ failure and possibly decreasing total transfusion requirements. "Since most trauma patients tend to die either within 24 hours or within the first 28 days, the study follows these patients over the 28-day window. The study expects to decrease the trauma patient's chance of dying by 20% from the current average of 40% based on the 28-day mortality rate seen in these very injured trauma patients," says Dr. Mallory.

One of the major challenges of the study was the waiver of informed consent for emergency research. This is the first study the FDA has approved to waive the informed consent due to the severity of the patient's injuries and difficulty of informing next of kin within the first 30 minutes of care. Patients and family members have the right to consent to continue or withdraw from the study after being informed.

Due to the waiver, the FDA required publicizing the study to the community. This involved meeting with community leaders, addressing media and placing paid advertising in

continued on page 4

Continued from page 1

newspapers. Through Dr. Mallory's direct involvement, she has been asked to present information to the FDA about publicizing the waiver of informed consent on September 29 in Bethesda, Maryland.

The University of Louisville Hospital plans to enroll 30 to 40 patients in the study over a two-year period for approximately two to three patients per month.

DCLHb has been extensively studied in earlier randomized trials involving more than 700 patients over a four-year period. Of the 350 who received the drug, few encountered temporary side effects, such as, harmless yellowing of the skin (unrelated to liver damage), temporary reddening of the urine, nausea, and back, abdominal, and muscle pain.

The national study plans to include 35 trauma centers, with the University of Louisville Hospital currently being the only one in Kentucky. The study shows promise of increasing critically low blood pressure and preventing further damage to vital organs in trauma patients that have the greatest risk of death.

For more information, contact Dr. Mary Nan Mallory, at 1-800-763-4916.

## Managing Pain Effectively

Pain is universal and is the number one reason why people seek medical attention. The person experiencing the pain is the only authority on the nature of that pain.

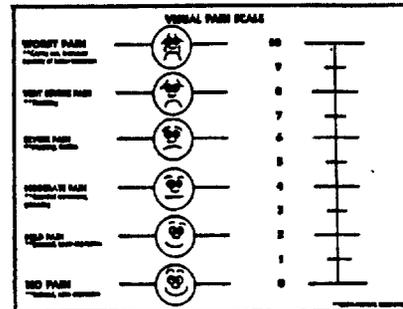
The Pain Committee, an interdisciplinary committee of the University of Louisville Hospital, meets every other month to discuss pain management. Its goal is to fully assess, intervene, document, and evaluate the effectiveness of managing pain for inpatients.

In March, new pumps were purchased for intraspinal pain management and patient controlled analgesia. Policies were written and approved to admit patients receiving intraspinal analgesia into any

unit of the hospital. Staff were given inservices on the operation of the pumps, and competency tests were distributed as well as checklists for the pumps operation.

The patient controlled analgesia pump, PCA II, allows the patient to receive a controlled dose as well as a Basal, a continuous dose, depending on the physician's order. The lockout on the pump is no longer four hours, but one hour. The pump is programmed for the patient to receive controlled pain medication for one hour.

The Visual Pain Scale



(pictured) has been reassessed from a 0-5 scale to a 0-10 scale. The 0-10 Visual Pain Scale with 0 indicating no pain and 10 meaning worst pain, was implemented on September 1 to document a patient's pain level.

For more information on the pain committee, or a copy of the AHCPA clinical practice guidelines, please contact Leslie Sanders, RN, (502) 562-3922.

## Announcements

David Seligson, M.D., Department of Orthopaedics, recently published a paper on the "Difficulty in Removal of Certain Intramedullary Nails" used in treatment of displaced diaphyseal fractures of the femur and tibia. Dr. Seligson's case reports identify a specific design problem, notably, the cross sectional design of the nail which prevents the distal, unslotted end from being extracted from the medullary cavity. The problem he sites, is preventable with a change in nail design or the development of absorbable implants.

### Osteosynthese International Annual Meeting of the Gerhard Kuntscher-Kreis and Orthopaedic Trauma Association 13th Annual Meeting

Friday, October 17 - Sunday, October 19, 1997  
Commonwealth Convention Center  
Louisville, KY

OTA is designed for traumatologist, general orthopaedic surgeons, and those interested in musculoskeletal trauma. For registration information, call the OTA staff office at (847) 698-1631.

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## In this Issue

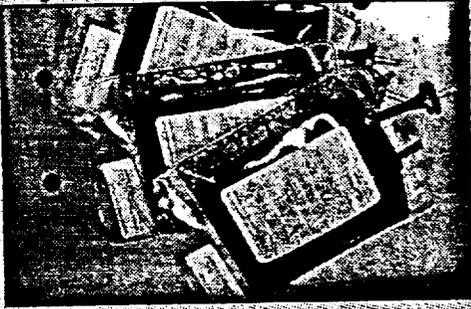
- ◆ New Study for Trauma Patients
- ◆ Sentinel Lymph Node Biopsy for Breast Cancer
- ◆ National Protocol for Lung Cancer
- ◆ Managing Pain Effectively



# HEALTH CARE

QUARTERLY





**COVER STORY**

## **In the Lab**

**Dr. Mary Nan Mallory leads  
a study on blood substitutes  
at University of Louisville Hospital**

**Page 3**

**Public/private partnership works  
to help juvenile fire setters**

**Page 6**

**Hospital foundations help boost  
public presence of their facilities**

**Page 8**

A SUPPLEMENT TO

**BUSINESS FIRST**

DECEMBER 22, 1997

# New hope for 'The Golden Hour'

*U of L Hospital participating in study of blood substitute for hemorrhaging trauma patients*

By VICTORIA DEMPSEY  
Business First Correspondent

Imagine the unimaginable. Your loved one is in a terrible automobile accident and has suffered dangerous blood loss. The precious life of your loved one will either be saved or lost during the next critical minutes.

Usually, the patient needs blood to keep the heart pumping and vital organs filled with the oxygens they need to function and not shut down. In the hospital emergency room, the clock ticks urgently as blood is typed and cross-matched. You hope that the blood bank has a ready supply for transfusion.

That strategic window of time in the treatment of trauma patients suffering severe blood loss, known to medical professionals as "The Golden Hour," is the focus of a national, multi-center study of a new product called Diasprin Cross-Linked Hemoglobin.

University of Louisville Hospital is one of 35 Level I trauma centers across the United States that have been selected to participate in the study. A Level I rating refers to quality and capability of care.

The study is designed to measure the efficacy or effectiveness of Diasprin, according to Dr. Mary Nan Mallory, assistant professor of emergency medicine at the University of Louisville School of Medicine. She is the principal investigator for the Kentucky Diasprin Cross-Linked Hemoglobin clinical trial.

Through the emergency facility of the U of L Hospital, participation began officially with the enrollment of the first patient into the study during the first week of September of this year and will continue during 18 months with a total of about 30 patients, she said.

Mallory described Diasprin as "an oxygen-carrying intravenous solution prepared from a chemically modified, purified and pasteurized hemoglobin, or red blood cells."

"Diasprin can be injected into the system immediately, carrying precious oxygens to suffering vital organs, as opposed to blood, which requires time for typing, cross-matching and locating in the blood bank," Mallory said. "In a patient who is actively bleeding and in shock, this time factor is critical."

Due to the gravity of the time element involved in administering the experimental product, Mallory said, it also is significant that she is among 20 investigators of any research project in the country to pioneer another new frontier. They are implementing the recent U.S. Food and Drug Administration allowance of a waiver of the federal regulation requiring informed consent by human subjects in research.

In other words, following very strict medical and legal criteria, Diasprin can be administered to a trauma patient in an emergency situation when that patient is in no condition to give any kind of informed permission, nor is the patient's family present to give it, for example. (See related story on page 4-B.)

"There is currently a 40-percent mortality rate nationally for severely hemorrhaging trauma patients during the first month after their injuries," Mallory said. "They often die of secondary insults, infections or organ failures. Our hope is that the mortality rate can be improved with the use of Diasprin."

"We also believe that morbidity, or the occurrence of these secondary complications, can be improved if organs



Business First photo by Ron Bath

**"Diasprin ... carries oxygen to tissue, oxygenating the heart and other vital organs and - we hope - thereby increasing chances for survival."**

Dr. Mary Nan Mallory  
University of Louisville Hospital

receive oxygen as quickly as possible after the injury."

She continued, "Diasprin is a new, or novel, class of drug. It carries oxygen to tissue, oxygenating the heart and other vital organs and - we hope - thereby increasing chances for survival. Interestingly, it also increases or restores blood pressure and increases blood volume without the actual infusion of blood."

"This is a wonderful advantage because patients of this nature are in shock and usually suffering from dangerously low blood pressure. Although there are other blood products still in the research phase that are similar, there are some that do not have this pharmaceutical effect of raising blood pressure."

Mary Thomas is director of external communications for Baxter International Inc. in Deerfield, Ill. Baxter is the developer of Diasprin, which will carry the brand name of HemAssist, she said. Thomas explained that although Diasprin and other similar products will be looked at in the long term for efficacy as a blood alternative in certain situations, at this point, the company views Diasprin as a "bridge" to transfusion.

"Following the use of Diasprin, in most cases a blood transfusion should be used when the patient is more stabilized because blood does clot and introduces white cells

into the immune system."

Mallory said the primary endpoint, or the effect to measure in the study, will be mortality, the death rate.

"We hope to see a decrease in the mortality rate in the first month for patients who have suffered dramatic blood loss from 40 percent to 30 percent with the use of Diasprin. This would reflect a 25-percent improvement," Mallory said.

"In other words, if the chances are now that four out of 10 trauma victims with severe blood loss will die, with the Diasprin we believe this will decrease to three out of 10; one-fourth of the patients having survived who wouldn't have done so without the Diasprin."

Mallory added that secondary endpoints, or measurements to report on, will be morbidity or secondary complications, including whether the use of Diasprin can decrease the necessity for blood transfusions, and whether the use of Diasprin can decrease the number of days a patient must spend in the intensive care unit.

"Theoretically, the study could fail - although we don't believe this will be the case, based on the extensive trials up to this point - to meet the primary endpoint, but could meet secondary endpoints," said Mallory.

According to Mallory, the product's side effects are minor and temporary. They are: a temporary increase in blood pressure - which she reiterates is seen as an advantage in blood-loss situations; and temporary yellowing of the skin, which dissipates after several hours.

Dr. Eddy Carrillo is chief of trauma service at U of L's School of Medicine and also is participating as an investigator in the clinical study. Carrillo said that from his vantage point, the study is particularly interesting because the trauma patients being treated with Diasprin in emergency medicine often are transferred afterward to the trauma service for surgery.

"We see close to 3,000 patients per year, including trauma patients of car wrecks, burns, shootings, stabbings and other injuries, which is an indication of how busy the service is," he said.

"From an in-house point of view, we are interested in the benefits of Diasprin as they relate to blood," Carrillo said. "First, the blood supply across the U.S. has reached critical levels on occasion. This kind of drug ultimately offers hope as a possible alternative to blood when dealing with critical patients in certain situations."

"I hope and expect that this will be the last goal of this product. So far, studies indicate that it may actually reduce the number of needed blood transfusions."

Another potential benefit, he said, is that "the possibility of using a product like Diasprin as an alternative to blood in some cases would decrease the risks to doctors and patients, alike, involving viruses such as hepatitis and HIV."

Carrillo said, "When patients arrive at the emergency room with active hemorrhaging, Diasprin can be stocked right there, with no need to type and cross. The time factor of location in the blood bank, and transportation of the blood to the trauma room, is eliminated. The product can be used immediately."

Moreover, he said, Diasprin "is a purified hemoglobin, the molecule of blood that carries oxygen. The preparation is made from human blood that has become oxidized on blood-bank shelves and is no longer usable for transfusions. It is filtered and heated to reduce the risk of blood-borne infections, including AIDS."

According to Thomas of Baxter International, the company has been developing Diasprin for about 20 years, more intensively over the last 10 years. Extensive studies

Photos and STUDY on page 4-B

**ON THE COVER**

Dr. Mary Nan Mallory works with a patient at the University of Louisville hospital emergency room. Business First photos by Ron Bath.

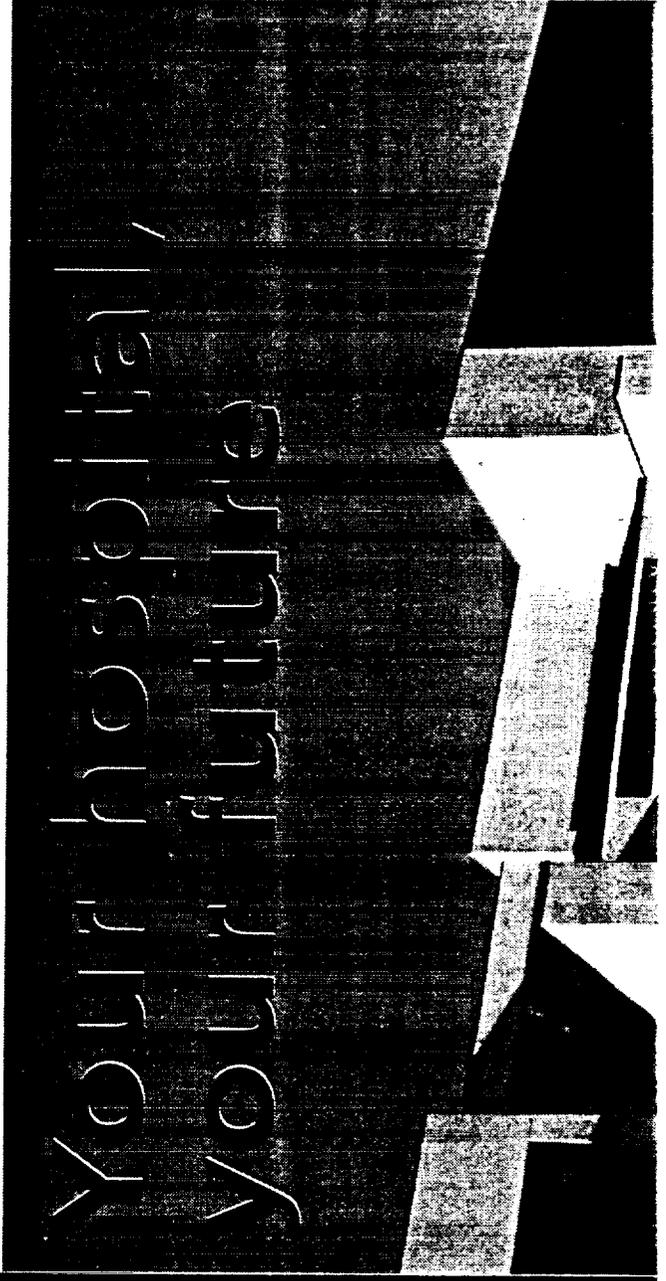
Attachment 7

# PEOPLE

UNIVERSITY HEALTH SYSTEMS  
*of Eastern Carolina*

January 1998 Volume 7, Number 1

Your hospital,  
Your future



"This is an ominous sign for the medical community and our nation, which badly needs a physician work force that is both diverse and reflective of our society as a whole," said Dr. Jordan J. Cohen, president of the AAMC, in an Associated Press news story.

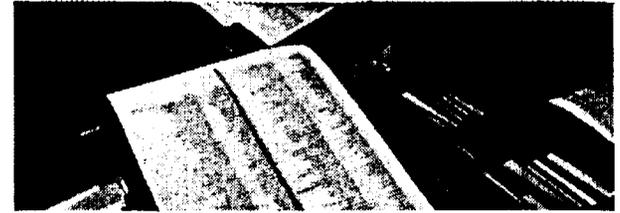
Cohen believes the decrease in applicants is clearly linked to a decision regarding the University of Texas law school and to California Proposition 209, which when passed by California voters ended affirmative action in California state universities.

In 1996, the University of Texas law school came under fire for using dual-track admission standards for

region.

In light of Broad's statement, what is the ECU School of Medicine doing? Nothing really different from before, Peden said, because the school was "ahead of the curve."

"We aren't changing anything because we feel like we're in good shape," he said. "We have been tracking this like President Broad has and, like her, we want to make sure what we are doing is fair and defensible and within the spirit and letter of the law. We have done our own review with university attorneys and the EEO officer and feel our



**B.J. Causey, ECU School of Medicine admissions representative, looks through the applications sent to the medical school for the class of 2002.** Photo by Linda Fox

## Research in brief

### New drug to be tried on some trauma patients

Led by Dr. Juan March, researchers at the East Carolina University School of Medicine and Pitt County Memorial Hospital will be performing a human drug trial using an exception to informed consent for emergency research. The research will involve the

use of a new drug administered to trauma patients with severe blood loss.

Approximately 150,000 people die each year due to trauma, according to March, an assistant professor of emergency medicine at ECU. Currently, those with severe blood loss and shock have a death rate as high as 40 percent. Diaspirin Cross-linked Hemoglobin (DCLHb) is a new experimental drug,

derived from human blood, which carries oxygen. Unlike blood, DCLHb is heated and filtered to help prevent disease transmission. It does not require cross-matching, so it can be given immediately. Initial studies on this drug have already been completed on human volunteers to determine safety and effectiveness. Some laboratory tests have been noted to change with DCLHb use, including proteins and enzymes that could indicate damage to organs such as the pancreas and liver, or to muscles, but it is believed that the benefits outweigh these risks.

The Food and Drug Administration has recently ruled that, under strict circumstances, unconscious patients whose lives are in danger (and for whom no one is available to give consent) may be given experimental treatment if there is no alternative with a good chance of success. The purpose of this trial is to determine if this new drug can prevent or treat the harmful effects of blood loss and shock.

For a detailed information booklet on this study, please call x2154.

Attachment 8

# Blood study involving LVH gets cut short

■ Trauma research halted because death rate was higher than expected.

By PETER NOAH  
Of The Morning Call

Thirteen trauma patients at Lehigh Valley Hospital were involved in an experimental blood substitute study that was halted by the product's manufacturer because more patients died than anticipated, officials said Wednesday.

At LVH, the first hospital to participate in the national study, about half received the Baxter Healthcare Corp. product HemAssist between February 1997 and February 1998. The control group received a placebo — saline solution — in addition to standard treatments.

The study was one of the country's first to test a medical product without patient consent if it wasn't immediately available.

Nationally, 100 patients with an

expected mortality rate of 40 percent were enrolled in the trauma trial, which was scheduled to include 850. Half received HemAssist.

The survival rates of the 13 patients at LVH ranged from 50 percent to 60 percent, said Dr. Robert Laskowski, chief medical officer. All received standard care.

Though specific numbers were not available, the LVH group that received the oxygen-carrying blood product matched the expected survival rate. The control group had a higher-than-expected survival rate.

"We had the anticipated results in terms of overall survival, but our numbers are really too small to conclude anything," Laskowski said. "We didn't see any adverse trends or any favorable trends, for that matter."

Though types of trauma varied, most suffered from gunshots, stab wounds and injuries from car accidents. More patients who received

Please See BLOOD Page A9 ▶

# Will warning precede 'Dearly beloved ...'?

■ It will if Lehigh County lawmaker gets his way. Some scoff at the idea.

By MEGAN O'MATZ  
Call Harrisburg Bureau

HARRISBURG — Beware: Marriage may be harmful to your health.

That's the message state Rep. Charlie Dent wants to get across to brides and grooms unaware of the dangers of domestic violence.

The Lehigh County Republican said Wednesday that he intends to introduce a bill requiring applications for marriage licenses in Penn-

sylvania to include a statement about spousal abuse.

Consider it a warning label.

The message would read, in part: "The laws of this Commonwealth affirm your right to enter into this marriage and, at the same time, to live within the marriage free from violence and abuse. Neither of you is the property of another."

The proposal has county marriage bureau clerks groaning. What's next, they asked.

"Warning: Your wife will be fat next year?" wondered Judy Moser, administrator of marriage licenses.

Please See WARNING Page A9 ▶

Special to The Morning Call

roof of his father's house on  
veve thunderstorm damaged

idents are baffled why this 192,000 people, blessed with crime rate and well-paid tech workers, suddenly has a violent and frightening

port was once known for a sto plant and middle-class using. Then came the tech-boom. Companies and s, finding neighboring Sill-ley crowded, found attrac-quarters and homes here.

wealthy flocked to the undeveloped rolling hills is city. In recent years, fueled the construction of ve custom homes, many ws of San Francisco Bay.

of those upscale neighbor-Mission Heights, where three bombs were found.

ia, a builder who emigrat-ndia more than 20 years put up several of the mul-dollar homes there.

cribed the neighborhood ionious mix of different profession, but concedes bers of his family have leaving until the bomber

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maker said four other outh Dakota, Kansas, West Virginia — include ssages on marriage li-citations.

the idea was brought to n by Kathy MacCon-er of Kathy's Place, an n based in Fogelsville es information about olence issues.

re warnings we have on olence, the closer it stopping the violence the children — break-in," said MacConnell, rrvivor of domestic

ut can I do?"

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y, 365 days a year.

# Blood study gets cut short

► Continued From Page A1

HemAssist died than those who did not, said Mary Thomas, a spokeswoman for Deerfield, Ill.-based Baxter Healthcare. "Slightly more than 40 percent" of those who received the HemAssist died, Thomas said.

There is no evidence, however, that a correlation exists between HemAssist and increased mortality, she added.

Despite Baxter Healthcare's announcement, HemAssist studies in elective surgeries will continue. Since December 1996, LVH has had 17 patients in the separate study, which administers the product in surgeries with potentially large amounts of blood loss, such as hip and knee replacements, aortic repair and abdominal pelvic procedures.

HemAssist is one of a number of experimental blood substitutes expected to save lives and ease blood shortages. The blood product does not have to be matched by type, and because of a special filtering process, is virtually virus-free.

European HemAssist trauma studies, which have been in place for about five years, will continue, Thomas said.

In Europe, HemAssist is administered at trauma sites, not at hospitals, thereby limiting the amount of time patients are in shock before they receive the prod-

uct.

Committees evaluating the study's progress decided to continue the trial because results were encouraging, Laskowski said.

The discontinued trial for trauma patients was at Phase III, usually the last before a drug is considered for approval by the U.S. Food and Drug Administration.

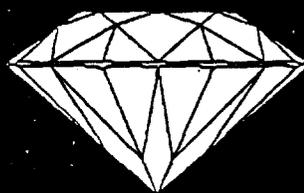
HemAssist's elective surgery study is also in Phase III.

Hospitals were able to administer the product without consent from trauma patients because the FDA and the Office of Protection of Patient Rights waived patient consent for research of emergency therapies in November 1996.

LVH spokeswoman Constance Walker said if trauma patients were not able to give consent, it was provided by family, or from the patient once his or her condition improved. Participation ceased if consent was later denied.

Thomas said results of the U.S. trauma study will be made public once the data are fully analyzed.

"We still believe that an oxygen-carrying therapy such as HemAssist can potentially benefit patients like those in the trial," she said. "However, we need to analyze the data further and determine what is the best way to safely test the product."



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Attachment 9

# Peco specifies where it will cut 70

The local distribution division, in the "pipes and wires" part of the utility, will be reduced by 20%.

By Rich Heidorn Jr.  
INQUIRER STAFF WRITER

Peco Energy officials promised yesterday that the lights would stay on and the phones would get answered despite a planned 20 percent staffing reduction at its local distribution arm.

Peco officially announced it would eliminate 700 of 3,300 jobs in its distribution company, cuts that will affect everyone from billing clerks and meter readers to technicians who respond to gas odors.

Senior vice president Kenneth G. Lawrence said Peco also would cut 150 temporary "contract" workers and consolidate its customer-service call centers and its dispatching centers for field workers. The company also will seek to cut costs

through improved purchasing and contracting procedures.

Although some layoffs will happen in the second half of this year, the entire process will take 12 to 18 months, Lawrence said.

"When the sun sets in the west, we're still the ones who make sure everybody has electricity at all times," he said in an interview.

Peco split its company in two last year in response to Pennsylvania's electric-competition law and legislation that would extend competition to retail gas customers.

The cuts, confirmed Monday and detailed yesterday, affect the "pipes and wires" portion of the business, which will remain a regulated monopoly.

The cuts do not affect Peco subsid-

aries that run the generating plants, buy and sell power in wholesale markets, and sell energy services to large commercial and industrial customers.

Both salaried and hourly employees in the distribution company will be trimmed by about 20 percent. Layoffs in the hourly ranks will be based on seniority. Managers and professional workers will not learn for up to two months whether their jobs are safe, Lawrence said.

He said that it was uncertain how many displaced workers would find a home in Peco's unregulated subsidiaries and that it would be up to Peco's board of directors whether an early-retirement plan or enhanced severance package would be offered.

Peco spokesman Neil McDermott said the cuts were necessary because the company has not raised electric rates since 1989, and won't

be able to rate cap se Peco's wor has been re third since

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## Blood-substitute study stopped as trauma deaths are checked

By Donna Shaw  
INQUIRER STAFF WRITER

A study in which some trauma patients were given an experimental blood substitute without their consent has been halted because more of them died than patients who received standard care only, the manufacturer announced yesterday.

The first U.S. hospital to participate in the study was Lehigh Valley Hospital in Allentown. Lehigh Valley began to use the product, HemAssist, in patients suffering from severe blood loss in February 1997.

The study marked what researchers said was the first time, under new government rules, that an unapproved medicine was administered to someone who was near death and unable to agree to the treatment.

The federal policy, which went into effect in November 1996, allows emergency rooms to use "promising experimental drugs and medical devices" on patients in life-threatening situations.

In making its announcement, HemAssist manufacturer Baxter Healthcare Corp. said researchers had used the product on about 100 trauma patients out of a planned total of 850 participants.

All the patients were severely injured — victims of auto accidents, knife and gunshot wounds, and the like — and had a high expected mortality, Baxter said.

Those who received HemAssist also were given standard treatment, while the placebo group received standard treatment only.

"The people who were involved in our study were pretty sick folks to start with," said Robert Laskowski, a Lehigh Valley physician who was involved in the HemAssist trial.

Although the number of Lehigh patients who participated was small, "we were right on the mark in terms of expectations," Laskowski said. "... The only surprise to us was that Baxter stopped the trial."

The Deerfield, Ill. company said it was working with clinical investiga-

tor. to determine what had happened.

Among the factors being studied are the timing of administration of HemAssist and other treatments, and the range and severity of patients' injuries, Baxter said.

Thomas Schmitz, general manager of Baxter's hemoglobin therapeutics division, said the company was confident that HemAssist "will be of critical importance for both surgeons and emergency-medicine physicians."

A European trauma study using HemAssist is continuing, as are U.S. studies using the product in surgery patients, Schmitz said. Baxter said it still expected to bring HemAssist to market in late 1999 or early 2000.

The stock price of Baxter International Inc. fell \$1.625 to \$55.125 in trading of 1.69 million shares, more than twice the three-month daily average, on the New York Stock Exchange.

## Rese firm boug

Blue Bell Inc. would million in

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A Kentucky to acquire Iba tract research million in stock nounced yester

Omnicare In provider of ph the purchase u pand its contr tions internat agreement, eac: converted into stock, a permit

Iba's Monday c Iba, which c als under contr and pharmaceu remain in Blue sees the deal a grow, said File dine A. Henwoo

"It's a terrific shareholders to our client base

## No change made in interest rates



last week's Phila. Business Journal → Editorial

## Blundering blood substitute experiments

What in heck is wrong with the people at Baxter Healthcare Corp.?

In one of the scariest headlines we've seen, it was reported this week that medical researchers have been using an experimental Baxter-produced blood substitute on trauma patients without their consent.

Oh, to be a plaintiff's lawyer.

Baxter didn't halt the research because it was suddenly struck by the patently unethical behavior in which it was engaged.

Instead, the blood-substitute study was halted because more patients who received it were dying than patients who received regular care.

Oh, to have been in the placebo group.

Baxter isn't alone in its callousness and arrogance:

The government is just as culpable.

It was the government that allowed this sort of fiddling in approving new rules that took effect in 1996 and allowed unapproved drugs to be administered to someone who is near death and unable to agree to the treatment.

Don't doctors have enough power over us?

It was the doctors at Lehigh Valley Hospital in Allentown that were the first in the nation to use the product, known as HemAssist.

There's a certain level of pioneering spirit that's needed to usher in new medicines. But there's also a measure of caution that apparently was disregarded in this case.

To be sure, HemAssist may someday save lives. But somebody at Baxter made a big blunder by allowing its use without fully understanding its efficacy or lack thereof.

Confronted with the facts today, the doctors at Lehigh don't do much to raise our confidence, either.

"The people who were involved in our study were pretty sick folks to start with," Robert Laskowski, a Lehigh Valley doctor who was involved in the trial, told a reporter.

Somebody get this guy some oxygen, stat! •

Attachment 11

...lously simple.  
 It was a question critics of alternative medicine had asked before. But only one practitioner agreed to submit to a test, said James Randi, a magician who conducted the test. Emily, however, was able to recruit 21 practitioners. Her

...practitioners should disclose these results to patients, third-party payers should question whether they should pay for this procedure, and patients should save their money unless or until additional honest experimentation demonstrates an actual effect."

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**(5478)**

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 April 3-5, 1998 Booth #1424



### Blood Replacement Research Project ends at Carolinas Medical Center

The research study at Carolinas Medical Center to evaluate a new treatment for seriously injured patients with severe loss of blood has ended.

The study, being conducted at 17 leading trauma centers across the nation, was stopped by Baxter Healthcare, Inc., developers of the patented blood substitute product involved in the study. According to officials at Baxter Healthcare, the Data Safety Monitoring committee watching over the research effort decided the study would be extremely unlikely to show the product had a beneficial effect on increasing patient survival.

This study was the first in the nation to use a new U.S. Food and Drug Administration (FDA) regulation allowing unconscious patients in danger of dying (and for whom no one was available to give consent) to receive an experimental treatment if there was no alternative treatment with a good chance of success. The FDA requires public notification of the study's outcome.

While this particular project did not prove the product to be effective, researchers at Carolinas Medical Center believe the research was worthwhile.

To communicate with us on this subject, or to receive further information from the researchers, please write us at the following address:

Blood Substitute Study c/o Cannon Research Center  
 Carolinas Medical Center  
 P.O. Box 32861  
 Charlotte, NC 28232-2861



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**99¢**

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Attachment 12

er states, but that these three are too one-sided, the Tribune reported Wednesday.

### Death rate narrows study of blood substitute

HOUSTON — A pharmaceutical company abruptly halted its study of a blood substitute in U.S. emergency room patients after discovering they were dying at a higher rate than expected.

But tests are continuing with emergency care patients in Europe and with elective surgery patients in the United States because they have shown no evidence of a higher death rate.

Baxter Healthcare Corp. ended the trauma patient study Tuesday after a review of the first 100 participants showed people given the artificial blood product, HemAssist, died at a greater rate than those who did not receive it, said Baxter spokeswoman.

Baxter had anticipated that 40 percent of the severely injured patients given HemAssist would die. The company refused to give the number of patients who died or the number of those who received HemAssist.

### Sect leaves Texas for divine event in Michigan

GARLAND, Texas — The faith still burns for the followers of the True Way, though their divine path to salvation now leads to Michigan.

The Taiwanese sect shrugged off the unrealized promises of their leader. That God would appear in person Tuesday, or on television last week on Channel 18. Seven months ago, followers moved to its suburb of Dallas — chosen because its name sounds like God's land — to wait.

Most of the 160 followers in white clothes and white cowboy hats now will move to Michigan. Here, leader Chen Hon-ming says, God will gather all worthy souls in a flying saucer and shuttle them to Gary, Ind., to save them from a nuclear holocaust.

"Teacher Chen," leader of God's Salvation Church, did not admit failure. Instead, he gave a crowd of followers, reporters, neighbors and lice five minutes to decide whether to stone him to death — they didn't.

### Stage stamp vote goes '50s drive-in memories

WASHINGTON — Tinny speakers and steamed hot dogs at the drive-in apparently are Americans' favorite memory of the 1950s.

The post office asked the public vote in February for the subjects most wanted to see on a series of stamps.

membership base, a step toward nullifying a recent U.S. Supreme Court decision that favored banks.

The court dealt a blow to credit unions in February when it ruled that they could no longer take members from outside a single group or company. That case originated in North Carolina, when several community banks sued a credit union regulator.

Many banks hailed the decision, while credit unions sought help from Congress, saying the ruling threatened their existence.

The House responded overwhelmingly to the appeal, passing legislation, 411-8, that would allow credit unions to accept outside members as long as they come from companies or groups with fewer than 3,000 people. Credit unions could also apply for exceptions to accept even larger groups.

"It stops the bleeding that would have killed the credit union industry," said Rep. Paul Kanjorski, D-Pa. "It will not unduly interfere with the banks."

Credit unions say they represent another option that individuals can tap for their financial needs. They say Congress should guarantee that all workers can join a credit union, even if their company doesn't offer one.

Bankers, however, say credit unions have a competitive advantage because they don't pay federal or state taxes, which has allowed their growth to outpace that of banks during the past decade.

"We think legislators ought to look for ways to reduce the burden on bank customers instead of asking them and the rest of the nation's taxpayers to subsidize credit unions," said Bob Denham, a spokesman for BB&T Corp., a banking company in Winston-Salem.

While the Senate may change some provisions, some version of the measure is virtually certain to be enacted.

"We obviously need a bill to correct the problem," said Senate Banking Committee Chairman Alfonso D'Amato.

Michael Beall, head of government and public affairs for the N.C. Credit Union League, said he expects support from Sen. Lauch Faircloth, R-N.C., who sits on the Senate banking committee.

A spokesman for Faircloth said the senator "basically supports the House bill, but thinks some changes are needed, in particular limiting the commercial loans and commercial deposits that credit unions can accept."

The House bill would freeze existing limits on credit unions' commercial lending power for one

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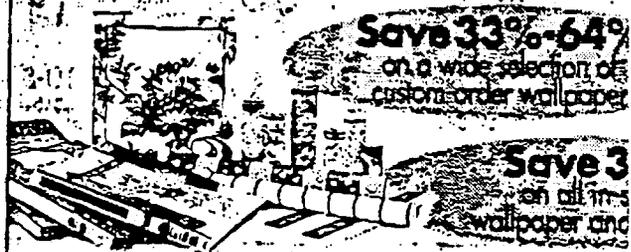


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## PAINTING TJD

To add a "cozy" feel to a den or bedroom, choose darker colors. They can bring ceilings down and walls closer to you.

Attachment 13

day's issue of the journal Cancer. Researchers have long recognized black women's higher death rate from breast cancer and have specu-

be looked at," said Dr. George Alexander of the National Cancer Institute. "How else would you explain (the disparity)?"

## Blood-substitute study stopped because of patient death rate

Associated Press

HOUSTON — A pharmaceutical company halted its study of a blood substitute in U.S. emergency room patients after discovering they were dying at a higher rate than expected.

Baxter Healthcare Corp. of Deerfield, Ill., ended the study Tuesday after a review of the first 100 participants showed people given the artificial blood product, HemAssist, died at a greater rate than those who did not receive it, said Mary Thomas, a Baxter spokeswoman.

Tests will continue with emergency care patients in Europe and with elective surgery patients in the United States because they have shown no evidence of a higher death rate.

Baxter had anticipated that 40 percent of the severely injured patients given HemAssist would die. Thomas would only say yesterday that "about half" of the 100 were given the substitute and "slightly more than 40 percent" of those died.

That means that if 50 patients got HemAssist, at least 20 died.

The company stressed that those tested were among the most gravely ill trauma patients, and that only 3 percent of the nation's emergency room patients could be eligible for

the study under federal guidelines.

The race to find a blood substitute has been intense because artificial blood could ease shortages, eliminate the need to match blood types and end the risk of contamination.

Houston's Ben Taub Hospital was to join in the trials this week.

"This was really unforeseen," said Dr. Matthew Wall of Ben Taub's trauma center. "This may simply be a statistical problem in a very select group of patients who already start with a high mortality, and the mortality may be unrelated to the drug."

The study was discontinued in Phase III testing, usually the last stage before a drug is considered for approval by the U.S. Food and Drug Administration.

No significant problems had been reported in Phase I and II trials.

Experts cannot explain the difference between the U.S. and European trauma patient studies, but speculate that the way emergency care is provided may be a factor.

"In Europe, physicians actually ride with the ambulances, and HemAssist is administered more quickly," Thomas said. "In the United States, patients are treated after they arrive at the hospital. They have been in shock longer."

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Attachment 14

- \* **A much-publicized U.S. Phase III trial of BAXTER INTERNATIONAL'S hemoglobin-based oxygen carrier product, "HemAssist," has been ended with only about 100 of a planned 850 patients enrolled, after an interim data review found that patients in the "HemAssist" group had a higher mortality rate than those in the control group.** Up to 1,000 mL of "HemAssist," a non-cellular tetrameric hemoglobin produced from screened donor red cells, or a saline control solution was administered at about nine U.S. centers to gravely injured trauma patients with persistent, severe hypoperfusion despite aggressive pre-hospital infusions of crystalloids and other therapy. The protocol stipulated, however, that all individuals enrolled in the study would receive "standard emergency care, including transfusions of blood, resuscitative fluids, and surgical intervention as required."

Baxter ended the study when it was advised by an independent data monitoring committee that there was less than a 5% chance that the excess deaths in the "HemAssist" group was due to chance alone. Investigators are studying the data to try to understand why this difference in mortality occurred. One possibility suggested by some trauma experts is that too many patients who had sustained lethal injuries might have been randomized to the "HemAssist" group; this explanation echoes concerns that the heterogeneous injuries of patients with severe hemorrhagic trauma could confound earnest attempts to scientifically assess alternative resuscitative strategies in this clinical setting.

- \* **Meanwhile, a European trauma trial, in which BAXTER'S "HemAssist" is infused at the trauma site, "is continuing on track,"** according to a Baxter official. A U.S. Phase III surgery trial is also still in progress. "We are confident that 'HemAssist' will be of critical importance for both surgeons and emergency-medicine physicians," he said. The company continues to expect to bring "HemAssist" to market in late 1999 or early 2000.

- \* **Separately, investigators at BAXTER'S Blood Substitutes Division have shown that its "HemAssist" diaspirin-crosslinked hemoglobin (DCLHb) does not appear to inhibit the true response or crossreact in the analysis of blood group, antibody screening or crossmatching.** Serum and/or red cell suspensions in which DCLHb was admixed were analyzed for their ABO and Rh blood groups, the presence of unexpected antibodies and compatibility in crossmatch testing. Additionally, it was found that the red color of DCLHb did not obscure the visual reading for agglutination testing at concentrations up to 2.22 g/dL; this corresponds to infusion of up to 1.5 liters of DCLHb into a 70 kg patient.

- \* **New findings by UK researchers strengthen the theory that fetal alloimmune anemia is caused by direct inhibition of erythroid progenitor cells by anti-Kell antibodies.** They found that human monoclonal anti-Kell antibodies and maternal serum containing anti-Kell antibodies significantly inhibited the growth of Kell-positive erythroid progenitor cells from cord blood, but had no effect on the growth of Kell-negative progenitor cells. Anti-D antibodies did not inhibit hematopoietic progenitor cell growth in either Kell-positive or Kell-negative cord blood. Their report appears in the March 19 issue of *New England Journal of Medicine*.





## **=Baxter Reports High Mortality In HemAssist Trial**

18:52:28, 09 April 1998

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Dow Jones News Service via Dow Jones

By Thomas M. Burton

CHICAGO (Dow Jones)--Twenty-four of 52 patients treated with Baxter's blood substitute in a trauma-treatment trial died, Baxter officials told Dow Jones. This compared with eight of 46 patients who died after receiving conventional trauma therapy in the same clinical trial.

Earlier this month, the Deerfield, Ill., company suspended the U.S. trauma clinical trial of HemAssist, Baxter's blood substitute product, because of the unexpectedly high mortality rate. However, Baxter has noted that it observed no such mortality rate in a surgical trial in the U.S., or in another trial of trauma patients being conducted in Europe.

Baxter officials said the death rate of 46.2% in the HemAssist group slightly exceeded the 42.6% predicted rate of death. The patients were all victims of serious accidents such as car crashes, gunshots and knife wounds, so a substantial rate of death was anticipated in any event.

By contrast, the Baxter officials said, the death rate of 17.4% in the "control" group - those treated with conventional therapy - was lower than the predicted death rate of 35.5%. The company said it had no immediate explanation for this disparity.

Baxter said it and its clinical researchers were still attempting to explain the cause of the high mortality in the HemAssist group. The product is known to cause "vasoconstriction," a tightening of blood-vessel walls that leads to higher blood pressure, and some in medicine have speculated that this could be related to the higher mortality.

The company has said, however, that the deaths do not appear to be related to this phenomenon. And some doctors even consider this tendency in HemAssist to be an advantage. Some doctors who participated in the trial have suggested that the results may simply illustrate how difficult it is to conduct a clinical trial involving severely injured patients - because the injuries are all so different from each other.

For instance, some of these doctors speculated that perhaps more patients with severe head injuries were assigned to the HemAssist group instead of the control group and that statistical accident may have led to more deaths in the HemAssist group. The company said it still is investigating the cause of the relatively higher mortality and that it will publish results on this at some point in the future.

Baxter said, though, that it still plans to market HemAssist if and when it receives regulatory approval for marketing in the U.S. or Europe. Baxter already has constructed a \$110-million production plant in Neuchatel, Switzerland, that is dedicated to making HemAssist.



# Daily Herald

Saturday, April 11, 1998

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## THE NATION

### Blood substitute not as good as predicted

HOUSTON — A pharmaceutical company said Friday that nearly half of emergency room patients given an experimental blood substitute died in a nationwide clinical trial — slightly more than the projected mortality rate. Of the 52 critically ill patients given the substitute known as HemAssist, 24 died, a 46.2 percent mortality rate, Baxter Healthcare Corp. said in a statement. The North suburban Deerfield company had projected 42.6 percent mortality for the critically ill patients in emergency rooms.

Attachment 17



# PHILADELPHIA **BUSINESS JOURNAL** GMC

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April 6, 1998

## **Blundering blood substitute experiments**

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What in heck is wrong with the people at Baxter Healthcare Corp.?

In one of the scariest headlines we've seen, it was reported this week that medical researchers have been using an experimental Baxter-produced blood substitute on trauma patients without their consent.

Oh, to be a plaintiff's lawyer.

Baxter didn't halt the research because it was suddenly struck by the patently unethical behavior in which it was engaged.

Instead, the blood-substitute study was halted because more patients who received it were dying than patients who received regular care.

Oh, to have been in the placebo group.

Baxter isn't alone in its callousness and arrogance:

The government is just as culpable.

It was the government that allowed this sort of fiddling in approving new rules that took effect in 1996 and allowed unapproved drugs to be administered to someone who is near death and unable to agree to the treatment.

Don't doctors have enough power over us?

It was the doctors at Lehigh Valley Hospital in Allentown that were the first in the nation to use the product, known as HemAssist.

There's a certain level of pioneering spirit that's needed to usher in new medicines. But there's also a measure of caution that apparently was disregarded in this case.

To be sure, HemAssist may someday save lives. But somebody at Baxter made a big blunder by allowing its use without fully understanding its efficacy or lack thereof.

Confronted with the facts today, the doctors at Lehigh don't do much to raise our confidence, either.

"The people who were involved in our study were pretty sick folks to start with," Robert Laskowski, a Lehigh Valley doctor who was involved in the trial, told a reporter.

**Somebody get this guy some oxygen, stat!**

© 1998, *Philadelphia Business Journal*

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**More Editorials**

Attachment 18

# Blood-substitute study is stopped

More patients who received the product died than of those who received standard care only.

By Donna Shaw  
INQUIRER STAFF WRITER

A study in which some trauma patients were given an experimental blood substitute without their consent has been halted because more of them died than patients who received standard care only, the manufacturer announced yesterday.

The first U.S. hospital to participate in the study was Lehigh Valley Hospital in Allentown. Lehigh Valley began to use the product, HemAssist, in patients suffering from severe blood loss in February 1997.

The study marked what researchers said was the first time, under new government rules, that an unapproved medicine was administered to someone who was near death and unable to agree to the treatment.

The federal policy, which went into effect in November 1996, allows emergency rooms to use "promising experimental drugs and medical devices" on patients in life-threatening situations.

In making its announcement, HemAssist manufacturer Baxter

Healthcare Corp. said researchers had used the product on about 100 trauma patients out of a planned total of 850 participants.

All the patients were severely injured — victims of auto accidents, knife and gunshot wounds, and the like — and had a high expected mortality, Baxter said.

Those who received HemAssist also were given standard treatment, while the placebo group received standard treatment only.

"The people who were involved in our study were pretty sick folks to start with," said Robert Laskowski, a Lehigh Valley physician who was involved in the HemAssist trial.

See TRAUMA on C2

Philadelphia

Inquirer

3-31-98

## Company halts its study of blood product

TRAUMA from C1

Although the number of Lehigh patients who participated was small, "we were right on the mark in terms of expectations," Laskowski said. "... The only surprise to us was that Baxter stopped the trial."

The Deerfield, Ill., company said it was working with clinical investigators to determine what had happened.

Among the factors being studied are the timing of administration of HemAssist and other treatments, and the range and severity of patients' injuries, Baxter said.

Thomas Schmitz, general manager of Baxter's hemoglobin therapeutics division, said the company was confident that HemAssist "will be of critical importance for both surgeons and emergency-medicine physicians."

A European trauma study using HemAssist is continuing, as are U.S. studies using the product in surgery patients, Schmitz said. Baxter said it still expected to bring HemAssist to market in late 1999 or early 2000.

The stock price of Baxter International Inc. fell \$1.625 to \$55.125 in trading of 1.69 million shares, more than twice the recent average.

Attachment 19

TECHNOLOGY & HEALTH

# Baxter Ends a U.S. Blood-Substitute Trial

By THOMAS M. BURTON

Staff Reporter of THE WALL STREET JOURNAL

Baxter International Inc. prematurely ended an advanced U.S. clinical trial of its blood substitute for severely injured patients after the company found a higher death rate among those given the product than those receiving standard therapy.

The development was a major setback to Baxter, which is further along of any company in conducting such clinical trials. The Deerfield, Ill., company has already finished building a \$110 million facility in Neuchâtel, Switzerland, to manufacture the blood substitute.

While serious, the abrupt cancelling of the study doesn't necessarily spell an end to Baxter's product, called HemAssist. That is because Baxter already has two other clinical studies under way for

HemAssist and said it hasn't encountered any safety problems in either.

The company has enrolled 100 or more patients in each of those studies, one dealing with trauma patients in Europe, the other with surgical patients in the U.S. Tom Schmitz, general manager of Baxter's hemoglobin-therapeutics division, said no safety concerns have emerged in either of those studies and that the company intends to proceed with developing HemAssist.

### Seeking Answers

The results in the U.S. trauma study left doctors at Baxter and in hospital trauma sections wondering about an explanation. Baxter didn't disclose the number of excess deaths in the HemAssist group, but said about 50 patients received HemAssist and 50 others received stan-

dard treatment for traumatic injuries like gunshots, knife wounds and car accidents. The company ended the study after an independent safety committee advised it of the increased deaths in the HemAssist group, and said there was less than a 5% likelihood that this was due to chance alone.

Baxter's product comes from outdated, donated human blood. Hemoglobin, the oxygen-carrying component of blood, is chemically altered to produce HemAssist. The idea of such blood substitutes is that they can act like human blood, but not carry the risk of infection and the need for time-consuming typing and cross-matching normally associated with donated blood.

In New York Stock Exchange composite trading yesterday, Baxter shares closed at \$55.125, down \$1.625.

It has been known for some time that HemAssist and the artificial blood products made by several competitors have an unwanted side effect called "vasoconstriction" — a narrowing of blood vessels that increases blood pressure. However, Mr. Schmitz said this tendency doesn't appear related to the deaths in the trauma study. Some doctors actually consider the effect an advantage, since the severely injured patients in the study had suffered blood loss and their blood pressure had fallen. Mr. Schmitz said Baxter is studying the medical records of patients to seek an explanation for the increased mortality.

### Problems in Creating Trials

David Gens, a surgeon at the University of Maryland's Shock-Trauma Center in Baltimore and a participant in the research, said the study's cancellation may simply illustrate how hard it is to construct a clinical trial with severely injured patients.

"The problem is, we would like the patients to be homogeneous, but trauma patients aren't," he said. "I personally believe HemAssist acts as a strong drug, and that it works." He speculated it is possible, for example, that too many patients with especially severe head injuries from car accidents or other blunt trauma might have been inadvertently assigned to HemAssist therapy, as opposed to being put into the control group.

John Barrett, director of the trauma service at Cook County Hospital in Chicago, said he was extremely surprised by the unexpectedly high death rate. "Baxter already did the safety trials, and the safety trials went fine," he said.

Baxter and several other major players continue to pursue work toward producing blood substitutes, believing there may ultimately be a multibillion-dollar market for the products both for trauma and surgical patients. Baxter said it still believes it is on track for possible marketing approval for HemAssist in late 1999 or 2000, either in Europe or the U.S.



## Press Release

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Tuesday March 31, 7:22 am Eastern Time

### Company Press Release

*SOURCE: Baxter Healthcare Corporation*

## **Baxter Ends U.S. Trauma Study of HemAssist(TM)(DCLHb)**

### **European Trauma and U.S. Surgery Trials Continue on Track**

DEERFIELD, Ill., March 31 /PRNewswire/ -- Baxter Healthcare Corporation announced today that it has ended its U.S. Phase III trauma trial investigating the efficacy of its oxygen-carrying solution, HemAssist(R)(DCLHb), for the treatment of severe traumatic hemorrhagic shock. Baxter decided to stop the trial, which had enrolled approximately 100 of its expected 850 participants, following an interim data review by the trial's independent data monitoring committee. The committee found that patients in the treatment group had an increased mortality compared to those in the control group.

Baxter and its clinical investigators are studying the data to better understand why there was a difference in mortality between the patient groups. They are assessing the impact of many factors, including the combined results of the trial's design and protocol, the timing of the administration of HemAssist(R)(DCLHb) and other medical treatments, the wide range of patient injuries and the severity of patient injuries in the two patient groups.

"We are evaluating options for trauma applications in the United States," said Thomas Schmitz, Ph.D., general manager of Baxter's Hemoglobin Therapeutics division. "We are confident that HemAssist(R)(DCLHb) will be of critical importance for both surgeons and emergency-medicine physicians.

"The European trauma trial, where physicians are administering HemAssist(R)(DCLHb) at the trauma site, is continuing on track. Our U.S. Phase III surgery trial moves forward as well."

Baxter continues to expect to bring HemAssist(R)(DCLHb) to market in late 1999 or early 2000.

### Significant Differences in Emergency Care

The ongoing European trauma trial is investigating the product's efficacy in the pre-hospital setting, where doctors administer the product as a first-line therapy at the trauma site. In contrast, U.S. doctors infused HemAssist(R)(DCLHb) in the hospital after patients had been in shock for much longer periods of time. The company noted that in light of the U.S. trauma results the European trauma study has been evaluated by its independent data monitoring committee and that committee has determined that the trial will continue on course.

The patients enrolled in the U.S. trauma trial were gravely ill -- victims of severe trauma, such as motor vehicle accidents, knife and gun shot wounds -- and had a high expected mortality. Patients involved in the HemAssist(R)(DCLHb) trial were among the most severely injured of all trauma victims, with only about 3 percent of all trauma patients eligible for trial inclusion. All individuals enrolled in the study received standard emergency care, including transfusions of blood, resuscitative fluids, and surgical intervention as required.

This U.S. trauma study was conducted under regulations issued by the U.S. Department of Health and Human Services (HHS) and the U.S. Food and Drug Administration (FDA) governing clinical-research practices in emergency medicine. These regulations are designed to protect patients' rights and well-being, while also allowing for an exception to informed consent in narrowly defined life-threatening situations. Several rigorous safety checks and patient protections are required of studies conducted under this ruling, including interim data analysis by an independent data monitoring committee. All institutions involved in the trial worked with their communities to inform them about the potential risks and benefits of the HemAssist(R)(DCLHb) trial. The results of the U.S. trauma study will be made public when the data are fully analyzed.

Baxter's Phase III U.S. surgery trial is investigating the use of HemAssist(R)(DCLHb) as an alternative to blood in patients undergoing elective surgery, such as hip and knee replacements, aortic repair and abdominal pelvic procedures.

Baxter Healthcare Corporation is the principal U.S. operating subsidiary of Baxter International Inc. (NYSE: [BAX](#) - [news](#)). Baxter International, through its subsidiaries, is a global leader in the development of products and technologies related to the blood and circulatory system. The company has market-leading positions in four areas: blood therapies, cardiovascular medicine, kidney-disease therapy and medication delivery. Through a combination of technological innovation and global expansion, Baxter is advancing medical care and improving the lives of millions of people worldwide.

This news release contains forward-looking statements that involve risks and uncertainties, including technological advances in the medical field, product approval, demand and market acceptance.

*SOURCE: Baxter Healthcare Corporation*



**[Back to Main Page](#)**

## Clinical Update

As part of Baxter's continuing commitment to provide information about its U.S. Phase III trauma trial, which was conducted under the HHS and FDA's exception to informed consent regulation, the following is a clinical update.

As previously announced, Baxter has ended its U.S. Phase III trauma trial investigating the efficacy of its oxygen-carrying solution, HemAssist (DCLHb), for the treatment of severe traumatic hemorrhagic shock. Baxter decided to stop the trial, which had enrolled approximately 100 of its expected 850 participants, following an interim data review by the trial's independent data monitoring committee. The committee found that patients in the treatment group had significantly increased mortality compared to those in the control group.

Analysis of interim patient data by the independent data monitoring committee, using a published model of predicting outcomes in trauma patients (TRISS) that combine physiologic and anatomic indicators of injury severity and age, indicate the predicted mortality in the treatment group was 42.6 percent with an observed mortality of 46.2 percent (24 of 52 patients). The predicted mortality in the control group was 35.5 percent with an observed mortality of 17.4 percent (8 of 46 patients). In addition, other indicators of injury severity were considered and although some differences were noted between the two groups, none were significant enough to indicate why the treatment group had a higher mortality rate than the control group. Further analysis of these data is ongoing.

As previously indicated, two additional advanced studies testing the efficacy of HemAssist are ongoing.

Baxter is releasing this clinical information prior to its final analysis to fulfill its responsibilities according to regulations pertaining to exception to informed consent. Additionally, Baxter intends to provide the complete clinical results in scientific forums and to distribute of the results in the communities in which the trial took place. The results also will be published on the U.S. trauma trial website at <http://dclhb.er.uic.edu/>.

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**MEDIA COVERAGE****March 31 Announcement**

<b>Daily Newspapers</b>		
<b>AP report (Houston bureau) (252)</b>		
Chicago Sun-Times	Chicago, IL	491,143
Plain Dealer	Cleveland, OH	400,593
Detroit News	Detroit, MI	370,000
St. Louis Post-Dispatch	St. Louis, MO	338,793
Atlanta Constitution	Atlanta, GA	330,885
Sun	Baltimore, MD	320,986
Milwaukee Journal Sentinel	Milwaukee, WI	320,000
Rocky Mountain News	Denver, CO	293,449
Orlando Sentinel	Orlando, FL	281,104
Times-Picayune	New Orleans, LA	265,820
Fort Worth Star-Telegram	Fort Worth, TX	263,470
Courier-Journal	Louisville, KY	244,000
Pittsburgh Post-Gazette	Pittsburgh, PA	241,798
San Antonio Express News	San Antonio, TX	235,002
St. Paul Pioneer Press	St. Paul, MN	212,648
Richmond Times-Dispatch	Richmond, VA	211,598
Virginian-Pilot	Norfolk, VA	201,236
Atlanta Journal	Atlanta, GA	189,332
Providence Journal-Bulletin	Providence, RI	188,217
Record	Hackensack, NJ	172,000
Birmingham News	Birmingham, AL	169,625
Dayton Daily News	Dayton, OH	162,105
Asbury Park Press	Neptune, NJ	160,324
News Journal	Wilmington, DE	127,678
News Tribune	Tacoma, WA	126,000
Press Telegram	Long Beach, CA	124,260
Telegram & Gazette	Worcester, MA	113,000
Times Union	Albany, NY	106,000
Gazette	Colorado Springs, CO	105,955
Daily Press	Newport News, VA	101,185
Advocate	Baton Rouge, LA	99,960
Press Democrat	Santa Rosa, CA	94,365
Vidette Times	Valparaiso, IN	92,000
Courier Post	Cherry Hill, NJ	90,393
Post-Standard	Syracuse, NY	87,900
Tribune (East Valley)	Mesa, AZ	87,590

Florida Today	Melbourne, FL	84,365
Inland Valley Daily Bulletin	Ontario, CA	83,685
Modesto Bee	Modesto, CA	83,208
Tribune-Review (Pittsburgh Edition)	Greensburg, PA	81,695
Daily Breeze	Torrance, CA	80,800
Times	Shreveport, LA	79,903
Press	Atlantic City, NJ	79,377
Ledger	Lakeland, FL	79,050
Journal Star	Peoria, IL	75,500
Corpus Christi Caller-Times	Corpus Christi, TX	71,896
Bucks County Courier Gazette	Levittown, PA	70,369
Beaumont Enterprise	Cedar Rapids, IA	68,727
Topeka Capital-Journal	Beaumont, TX	66,191
Journal Gazette	Topeka, KS	65,380
Repository	Fort Wayne, IN	62,000
Fairfax Journal	Canton, OH	62,000
Ann Arbor News	Fairfax, VA	60,000
Tallahassee Democrat	Ann Arbor, MI	58,172
Wilmington Morning Star (Local - Region - State Edition)	Tallahassee, FL	57,151
Daily Times	Wilmington, NC	57,000
Herald-Sun	Primos, PA	56,000
Quad-City Times	Durham, NC	55,000
Gainesville Sun	Davenport, IA	54,868
Observer-Dispatch	Gainesville, FL	54,041
Crain's Chicago Business	Utica, NY	50,761
Waterloo Courier	Chicago, IL	50,000
Sioux City Journal	Waterloo, IA	50,000
Times Leader	Sioux City, IA	50,000
El Paso Times	Wilkes-Barre, PA	47,920
News-Gazette	El Paso, TX	47,000
Morning Journal	Champaign, IL	46,000
Signal	Lorain, OH	46,000
Intelligencer - Record (Central Bucks Edition)	Santa Clarita, CA	46,000
Free Lance-Star	Doylestown, PA	45,976
Tyler Morning Telegraph	Fredericksburg, VA	45,014
Tyler Morning Telegraph	Tyler, TX	44,019
Lima News	Tyler, TX	44,019
Jackson Sun	Lima, OH	42,000
Burlington County Times	Jackson, TN	41,500
	Willingboro, NJ	41,000

Sun Journal	Lewiston, ME	40,276
Tuscaloosa News	Tuscaloosa, AL	40,000
San Juan Star	San Juan, PR	40,000
Alexandria Daily Town Talk	Alexandria, LA	39,000
Times Record News	Wichita Falls, TX	38,800
Grand Forks Herald	Grand Forks, ND	38,797
Star Press	Muncie, IN	38,755
Monitor	Mc Allen, TX	38,000
News Herald	Panama City, FL	37,531
Lake Charles American Press	Lake Charles, LA	37,252
Joplin Globe	Joplin, MO	36,245
Springfield News-Sun	Springfield, OH	35,000
Daily Local News	West Chester, PA	35,000
Daily Camera	Boulder, CO	35,000
Times-News	Hendersonville, NC	34,544
Morning News	Florence, SC	34,000
Longview News-Journal	Longview, TX	34,000
Telegraph Herald	Dubuque, IA	33,900
Morning News of Northwest Arkansas	Springdale, AR	33,625
Williamsport Sun-Gazette	Williamsport, PA	33,343
Chronicle-Telegram	Elyria, OH	33,000
Northwest Herald	Crystal Lake, IL	32,959
Star-Gazette	Elmira, NY	32,794
Missoulian	Missoula, MT	32,711
Norwich Bulletin	Norwich, CT	32,077
Tribune	Scranton, PA	30,213
Valley Morning Star	Harlingen, TX	30,157
Daily Texan (University of Texas)	Austin, TX	30,000
Times Herald	Norristown, PA	30,000
Elkhart Truth	Elkhart, IN	30,000
Galveston Daily News	Galveston, TX	29,854
Herald-Star	Steubenville, OH	29,218
Evansville Press	Evansville, IN	28,073
Kokomo Tribune	Kokomo, IN	28,000
Marietta Daily Journal	Marietta, GA	28,000
Bryan-College Station Eagle	Bryan, TX	28,000
Odessa American	Odessa, TX	27,840
Hattiesburg American	Hattiesburg, MS	26,706
Midland Reporter-Telegram	Midland, TX	26,500
Fort Pierce Tribune	Fort Pierce, FL	25,862

Minot Daily News	Minot, ND	25,655
Oshkosh Northwestern	Oshkosh, WI	25,174
Danville Register & Bee	Danville, VA	25,000
Intelligencer	Wheeling, WV	25,000
Temple Daily Telegram	Temple, TX	24,129
Post-Journal	Jamestown, NY	24,054
Port Arthur News	Port Arthur, TX	23,200
Santa Maria Times	Santa Maria, CA	22,500
Las Cruces Sun-News	Las Cruces, NM	22,055
Pine Bluff Commercial	Pine Bluff, AR	22,000
Rutland Daily Herald	Rutland, VT	21,921
Dominion Post	Morgantown, WV	21,500
Globe-Gazette	Mason City, IA	21,412
Daily Times Call	Longmont, CO	20,264
Holland Sentinel	Holland, MI	20,000
Muskogee Daily Phoenix & Times Democrat	Muskogee, OK	19,600
Journal Gazette	Mattoon, IL	19,500
Daily Collegian (Pennsylvania State University)	University Park, PA	19,300
Shelby Star	Shelby, NC	19,000
Daily Reveille (Louisiana State)	Baton Rouge, LA	19,000
Lawrence Journal-World	Lawrence, KS	18,683
Daily Reflector	Greenville, NC	18,660
Hawk Eye	Burlington, IA	18,500
Daily Courier	Grants Pass, OR	18,201
Facts	Clute, TX	18,100
Jefferson City Post-Tribune	Jefferson City, MO	18,026
Reporter-Herald	Loveland, CO	17,700
Crescent-News	Defiance, OH	17,500
Sun Journal	New Bern, NC	17,000
Daily News	St. Thomas, VI	17,000
News-Enterprise	Elizabethtown, KY	16,500
Coeur d'Alene Press	Coeur d'Alene, ID	16,500
Recorder	Greenfield, MA	16,000
Star Herald	Scottsbluff, NE	15,700
Middletown Press	Middletown, CT	15,323
Sentinel	Lewistown, PA	15,000
Times-Mail	Bedford, IN	14,878
Lufkin Daily News	Lufkin, TX	14,500
Sentinel-Tribune	Bowling Green, OH	14,500
Vicksburg Post	Vicksburg, MS	14,200

Athens Daily News	Athens, GA	14,000
Courier	Conroe, TX	13,777
Union Democrat	Sonora, CA	13,550
Californian (Temecula Edition)	Temecula, CA	12,600
Standard-Observer	Irwin, PA	12,500
Ashland Times-Gazette	Ashland, OH	12,222
Today's Sunbeam	Salem, NJ	12,000
Daily Republic	Mitchell, SD	12,000
Gleaner	Henderson, KY	11,658
Daily Mississippian (University of Mississippi)	University, MS	11,500
Morning Sun	Mt. Pleasant, MI	11,300
St. Croix Avis	St. Croix, VI	10,500
Journal Review	Crawfordsville, IN	10,246
Edmond Evening Sun	Edmond, OK	10,100
Garden Island	Lihue, HI	10,000
Standard Democrat	Sikeston, MO	9,900
Ledger Independent	Maysville, KY	9,600
Durango Herald	Durango, CO	9,500
Arlington Journal	Arlington, VA	9,000
Dodge City Daily Globe	Dodge City, KS	9,000
Daily Independent	Ridgecrest, CA	9,000
Olathe Daily News	Olathe, KS	8,776
Messenger	Union City, IN	8,700
Weirton Daily Times	Weirton, WV	8,200
Newton Daily News	Newton, IA	8,000
Pasadena Citizen	Pasadena, TX	8,000
Alexandria Journal	Alexandria, VA	8,000
Lompoc Record	Lompoc, CA	8,000
Delaware Gazette	Delaware, OH	7,986
Breeze-Courier	Taylorville, IL	7,565
Natchitoches Times	Natchitoches, LA	7,500
Times-Courier	Charleston, IL	7,360
Times-Bulletin	Van Wert, OH	7,058
McDowell News	Marion, NC	7,023
Antigo Daily Journal	Antigo, WI	7,000
Princeton Daily Clarion	Princeton, IN	6,700
Starkville Daily News	Starkville, MS	6,596
Laramie Daily Boomerang	Laramie, WY	6,500
Pioneer	Big Rapids, MI	6,110
Record-Herald	Wash. Court House, OH	6,000
Miami Herald (International Edition)	Miami, FL	5,994
Bluffton News-Banner	Bluffton, IN	5,600

Chesterton Tribunc	Chesterton, IN	5,400
The Dalles Chronicle	The Dalles, OR	5,284
Stephenville Empire-Tribunc	Stephenville, TX	5,200
Anadarko, Daily News	Anadarko, OK	5,100
Daily Journal	Devils Lake, ND	4,700
Hope Star	Hope, AR	4,685
Black Hills Pioneer	Spearfish, SD	4,550
Daily Republican-Register	Mt. Carmel, IL	4,300
Daily Statesman	Dexter, MO	4,200
Cape Coral Daily Breeze	Cape Coral, FL	3,500
Rensselaer Republican	Rensselaer, IN	3,463
Daily Capital News	Jefferson City, MO	3,452
Madison Daily Leader	Madison, SD	3,400
Metropolitan News-Enterprise	Los Angeles, CA	2,500
<b>The Wall Street Journal (5 editions)</b>		
The Wall Street Journal	Eastern Edition	755,153
The Wall Street Journal	Midwest Edition	489,998
The Wall Street Journal	Western Edition	386,367
The Wall Street Journal	Southwestern Edition	171,689
The Wall Street Journal	European Edition	35,379
<b>AP report (Iowa City bureau) (12)</b>		
Sunday World Herald	Omaha, NE	294,669
Gazette	Cedar Rapids, IA	68,727
Messenger	Fort Dodge, IA	21,800
Daily Nonparcil	Council Bluffs, IA	21,000
Hawk Eye	Burlington, IA	18,500
Daily Nonpareil	Council Bluffs, IA	18,500
Iowa City Press-Citizen	Iowa City, IA	16,186
Times-Republican	Marshalltown, IA	11,847
Muscatine Journal	Muscatine, IA	8,700
Fort Madison Daily Democrat	Fort Madison, IA	6,800
Atlantic News Telegram	Atlantic, IA	6,400
Creston News Advertiser	Creston, IA	5,602
<b>Daily Herald (22)</b>		
Daily Herald (Arlington Heights)	Arlington Heights, IL	12,512
Daily Herald (Hoffman Estates/ Schaumburg)	Arlington Heights, IL	11,953
Daily Herald (Elgin/ South Elgin)	Arlington Heights, IL	8,635
Daily Herald (Mount Prospect/ Prospect Hts.)	Arlington Heights, IL	8,188

Daily Herald (Palatine/ Inverness)	Arlington Heights, IL	7,446
Daily Herald (Lombard/ Oak Brook/ Villa Park)	Arlington Heights, IL	5,617
Daily Herald (Wheaton/ Glen Ellyn)	Arlington Heights, IL	4,970
Daily Herald (Bartlett/ Hanover Park/ Streamwood)	Arlington Heights, IL	4,911
Daily Herald (Lisle/ Naperville)	Arlington Heights, IL	4,589
Daily Herald (Des Plaines/ Elk Grove)	Arlington Heights, IL	4,403
Daily Herald (Algonquin/ Lake in the Hills)	Arlington Heights, IL	4,352
Daily Herald (Carpentersville Edition)	Arlington Heights, IL	3,930
Daily Herald (Buffalo Grove/ Long Grove/ Wheeling)	Arlington Heights, IL	3,657
Daily Herald (Rolling Meadows)	Arlington Heights, IL	3,620
Daily Herald (Bloomingtondale/ Itasca)	Arlington Heights, IL	3,310
Daily Herald (Warrenville/ West Chicago/ Winfield)	Arlington Heights, IL	3,235
Daily Herald (Libertyville/ Mundelein)	Arlington Heights, IL	2,716
Daily Herald (Carol Stream/ Glendale Heights)	Arlington Heights, IL	2,330
Daily Herald (Barrington)	Arlington Heights, IL	2,111
Daily Herald (Lake Zurich/ Wauconda)	Arlington Heights, IL	1,860
Daily Herald (Gurnee/ Grayslake)	Arlington Heights, IL	N/A
Daily Herald (Cary/ Fox River)	Arlington Heights, IL	N/A
<b>Daily Herald (Sunday Edition) (23)</b>		
Daily Herald (Arlington Heights)	Arlington Heights, IL	12,512

Daily Herald (Hoffman Estates/ Schaumburg)	Arlington Heights, IL	11,953
Daily Herald (Elgin/ South Elgin)	Arlington Heights, IL	8,635
Daily Herald (Mount Prospect/ Prospect Hts.)	Arlington Heights, IL	8,188
Daily Herald (Palatine/ Inverness)	Arlington Heights, IL	7,446
Daily Herald (Lombard/ Oak Brook/ Villa Park)	Arlington Heights, IL	5,617
Daily Herald (Wheaton/ Glen Ellyn)	Arlington Heights, IL	4,970
Daily Herald (Bartlett/ Hanover Park/ Streamwood)	Arlington Heights, IL	4,911
Daily Herald (Lisle/ Naperville)	Arlington Heights, IL	4,589
Daily Herald (Des Plaines/ Elk Grove)	Arlington Heights, IL	4,403
Daily Herald (Algonquin/ Lake in the Hills)	Arlington Heights, IL	4,352
Daily Herald (Carpentersville Edition)	Arlington Heights, IL	3,930
Daily Herald (Buffalo Grove/ Long Grove/ Wheeling)	Arlington Heights, IL	3,657
Daily Herald (Rolling Meadows)	Arlington Heights, IL	3,620
Daily Herald (Bloomingtondale/ Itasca)	Arlington Heights, IL	3,310
Daily Herald (Warrenville/ West Chicago/ Winfield)	Arlington Heights, IL	3,235
Daily Herald (Libertyville/ Mundelein)	Arlington Heights, IL	2,716
Daily Herald (Carol Stream/ Glendale Heights)	Arlington Heights, IL	2,330
Daily Herald (Barrington)	Arlington Heights, IL	2,111
Daily Herald (Lake Zurich/ Wauconda)	Arlington Heights, IL	1,860
Daily Herald (Gurnee/ Grayslake)	Arlington Heights, IL	N/A

Daily Herald (Cary/ Fox River)	Arlington Heights, IL	N/A
Daily Herald (Batavia)	Arlington Heights, IL	N/A
<b>Reuters report (3)</b>		
Orange County Register	Santa Ana, CA	358,010
Sunday Journal	Edmonton, AB, CN	146,208
Prince George Citizen	Prince George, BC, CN	20,200
<b>Originals (6)</b>		
Chicago Tribune	Chicago, IL	664,584
Houston Chronicle	Houston, TX	549,856
Philadelphia Inquirer	Philadelphia, PA	457,932
News-Sun	Waukegan, IL	35,000
Kenosha News	Kenosha, WI	29,300
Daily Standard	Celina, OH	10,000
<b>Business Trade (1)</b>		
Business Week	New York, NY	1,000,000
Philadelphia Business Journal	Philadelphia, PA	20,000
<b>Medical Trade (6)</b>		
General Surgery News	New York, NY	34,310
Genetic Engineering News	Larchmont, NY	26,000
FDC Reports	Chevy Chase, MD	15,000
Med Pro Month	Irvine, CA	750
Biotechnology News	Maplewood, NJ	N/A
Bio Century	San Carlos, CA	N/A

## April 10 Announcement

AP report (Houston bureau) (273)		
Atlanta Journal-Constitution	Atlanta, GA	723,016
Houston Chronicle	Houston, TX	549,856
St. Louis Post-Dispatch	St. Louis, MO	545,882
San Diego Union-Tribune	San Diego, CA	379,705
Orange County Register	Santa Ana, CA	358,010
Sunday World Herald	Omaha, NE	294,669
Rocky Mountain News	Denver, CO	293,449
Fort Worth Star-Telegram	Fort Worth, TX	263,470
El Nueva Dia	San Juan, PR	250,000
Charlotte Observer	Charlotte, NC	236,579
San Antonio Express-News	San Antonio, TX	235,002
Indianapolis Star	Indianapolis, IN	230,932
Indianapolis Star	Indianapolis, IN	230,932
Wausau Daily Herald	Wausau, WI	225,700
American Medical News	Chicago, IL	220,000
Grand Rapids Press	Grand Rapids, MI	153,061
Sunday Advocate	Baton Rouge, LA	137,368
Press-Telegram	Long Beach, CA	124,260
Lexington Herald-Leader	Lexington, KY	119,317
North County Times (Oceanside Edition)	Oceanside, CA	102,311
North County Times (Carlsbad/ La Costa Edition)	Escondido, CA	102,311
Miami Herald (El Nuevo Herald)	Miami, FL	101,389
Contra Costa Times	Walnut Creek, CA	97,500
Flint Journal	Flint, MI	96,000
Press Democrat	Santa Rosa, CA	94,365
Union Leader	Manchester, NH	89,000
Sunday Times	Scranton, PA	83,651
Sun	San Bernardino, CA	82,000
Patriot Ledger	Quincy, MA	79,688
Macon Telegraph	Macon, GA	77,665
Sunday Post-Crescent	Appleton, WI	76,200
North Jersey Herald & News	Passaic, NJ	70,000
Reading Times/ Reading Eagle	Reading, PA	67,988
Press & Sun-Bulletin	Binghamton, NY	66,506
Evansville Courier	Evansville, IN	64,500
Daily Southtown	Chicago, IL	63,764

Leader Post	Regina, SK, CN	62,356
Republican-American	Waterbury, CT	61,000
Daily Southtown	Chicago, IL	57,338
Wilmington Morning Star Local - Region - State Edition)	Wilmington, NC	57,000
Sun	Lowell, MA	55,774
Billings Gazette	Billings, MT	55,127
News Sentinel	Fort Wayne, IN	55,000
Charleston Gazette	Charleston, WV	54,500
Belleville News-Democrat	Belleville, IL	53,000
Waterloo Courier	Waterloo, IA	53,000
Sunday Signal & Saugas Enterprise	Santa Clarita, CA	50,000
Waco Tribune-Herald	Waco, TX	48,500
Sun Herald	Biloxi, MS	48,250
Sunday Herald-Times	Bloomington, IL	46,027
Citizens' Voice	Wilkes-Barre, PA	46,000
Joplin Globe	Joplin, MO	45,045
Tribune Chronicle	Warren, OH	45,000
North County Times (Escondido Edition)	Escondido, CA	45,000
Daily Review	Hayward, CA	43,740
Bradenton Herald	Bradenton, FL	43,194
Watertown Daily Times	Watertown, NY	42,485
Victoria Advocate	Victoria, TX	42,285
News-Sun	Waukegan, IL	42,000
Yakima Herald-Republic	Yakima, WA	42,000
Post-Bulletin	Rochester, MN	42,000
Jackson Sun	Jackson, TN	41,500
Gaston Gazette	Gastonia, NC	41,000
Times Herald	Port Huron, MI	41,000
North County Times (Vista Edition)	Oceanside, CA	40,316
Niagara Sunday	Niagara Falls, NY	40,000
Tri-Valley Herald (Livermore Dublin Pleasanton)	Pleasanton, CA	39,426
Tri-Valley Herald (San Ramon Valley Edition)	Danville, CA	39,426
Valley Times	Pleasanton, CA	39,077
Times Record News	Wichita Falls, TX	38,800
Valley News Dispatch	Tarentum, PA	38,200
Monitor	Mc Allen, TX	38,000
Journal Times	Racine, WI	36,433
Herald	Monterey, CA	36,000
Tribune-Star	Terre-Haute, IN	35,426

La Crosse Tribune	La Crosse, WI	34,840
Longview News-Journal	Longview, TX	34,000
Daily Commercial	Leesburg, FL	34,000
Telegraph Herald	Dubuque, IA	33,900
Williamsport Sun-Gazette	Williamsport, PA	33,343
Northwest Herald	Crystal Lake, IL	32,959
West County Times	Richmond, CA	32,721
Missoulian	Missoula, MT	32,711
Daily News-Record	Harrisonburg, VA	32,645
Eastside Journal	Bellevue, WA	32,000
South County Journal	Kent, WA	32,000
Southern Illinoisan	Carbondale, IL	32,000
Daily Progress	Charlottesville, VA	31,500
High Point Enterprise	High Point, NC	31,500
Eagle	Butler, PA	31,300
Johnson City Press	Johnson City, TN	31,031
Record-Journal	Meriden, CT	31,000
Daily Evening Item	Lynn, MA	31,000
Quincy Herald-Whig	Quincy, IL	30,307
Marietta Daily Journal	Marietta, GA	30,000
Galveston Daily News	Galveston, TX	29,854
Kenosha News	Kenosha, WI	29,300
Herald-Star	Steubenville, OH	29,218
Battle Crock Enquirer	Battle Creek, MI	28,920
Record	Troy, NY	28,222
Janesville Gazette	Janesville, WI	28,000
Bryan College Station Eagle	Bryan, TX	28,000
Marietta Daily Journal	Marietta, GA	28,000
Odessa American	Odessa, TX	27,840
North County Times (Encinitas - Solana Beach Edition)	Oceanside, CA	27,650
Hattiesburg American	Hattiesburg, MS	26,706
Midland Reporter-Telegram	Midland, TX	26,500
Sunday News Tribune	Jefferson City, MO	26,000
Citizen Tribune	Morristown, TX	25,800
Oshkosh Northwestern	Oshkosh, WI	25,174
Herald	Sharon, PA	25,123
Daily News	Longview, WA	25,000
Times Recorder	Zanesville, OH	25,000
Intelligencer	Wheeling, WV	25,000
Leaf-Chronicle	Clarksville, TN	25,000
Greeley Tribune	Greeley, CO	24,500
Post-Journal Weekender	Jamestown, NY	24,054

Standard-Speaker	Hazleton, PA	24,000
Vineland Daily Journal	Vineland, NJ	24,000
Meridian Star	Meridian, MS	23,000
Holland Sentinel	Holland, MI	23,000
Concord Monitor	Concord, NH	22,500
Mississippi Press	Pascagoula, MS	22,500
Times-Standard	Eureka, CA	22,248
Daily Park City News	Bowling Green, KY	22,013
Citrus County Chronicle	Inverness, FL	22,000
Idaho Press-Tribune	Nampa, ID	21,760
Albany Democrat-Herald	Albany, OR	21,713
Pocono Record	Stroudsburg, PA	21,600
Freeman	Waukesha, WI	21,424
Commercial-News	Danville, IL	21,000
Valdosta Daily Times	Valdosta, GA	21,000
Southeast Missourian	Cape Girardeau, MO	20,625
News-Sun (Highlands County)	Sebring, FL	20,100
Napa Valley Register	Napa, CA	20,017
Huron Daily Tribune	Bad Axe, MI	20,000
Hour	Norwalk, CT	20,000
North Hills News Record	Warrendale, PA	20,000
Spectrum	Cedar City, UT	19,618
Progress-Index	Petersburg, VA	19,200
Shelby Star	Shelby, NC	19,000
Derrick	Oil City, PA	19,000
Lawrence Journal-World	Lawrence, KS	18,683
Daily Reflector	Greenville, NC	18,660
Courier-Tribune	Asheboro, NC	18,500
Imperial Valley Press	El Centro, CA	18,500
Scottsdale Tribune	Scottsdale, AZ	18,429
Journal	Martinsburg, WV	17,931
Register-Mail	Galesburg, IL	17,733
Daily Telegram	Adrian, MI	17,500
Island Packet	Hilton Head Island, SC	17,500
Denton Record-Chronicle	Denton, TX	17,500
Goshen News	Goshen, IN	16,840
Gazette	Medina, OH	16,800
St. Augustine Record	St. Augustine, FL	16,800
Leader	Corning, NY	16,500
Henando Today	Brooksville, FL	16,500
Iowa City Press-Citizen	Iowa City, IA	16,186
Montana Standard	Butte, T	16,000
Beloit Daily News	Beloit, WI	15,370

Union	Grass Valley, CA	15,324
Middletown Press	Middletown, CT	15,323
Sunday Messenger	Canandaigua, NY	15,050
Sentinel	Lewiston, PA	15,000
Herald Journal	Logan, UT	14,665
Vicksburg Post	Vicksburg, MS	14,500
Telegraph	North Platt, NE	14,500
Sanford Herald	Sanford, NC	14,341
Helena Independent Record	Helena, MT	14,280
Free Press	Kinston, NC	14,198
Daily Times	Ottawa, IL	14,100
Courier	Conroe, TX	13,777
Saturday Daily News	Virginia, MN	13,548
Daily Mountain Eagle	Jasper, AL	13,390
Era	Bradford, PA	13,000
Hobbs News-Sun	Hobbs, NM	13,000
Alliance Review	Alliance, OH	12,750
Weekend Reformer	Brattleboro, VT	12,700
Daily Herald (Arlington Heights)	Arlington Heights, IL	12,512
News-Topic	Lenoir, NC	12,500
Daily Herald	Columbia, IN	12,500
News-Capital & Democrat	Mc Alester, OK	12,500
East Oregonian	Pendleton, OR	12,469
Daily Journal	Fergus Falls, MN	12,093
Vail Daily	Vail, CO	12,000
Daily Herald (Hoffman Estates/ Schaumburg)	Arlington Heights, IL	11,953
Express	Lock Haven, PA	11,500
Examiner	Independence, MO	11,064
Daily Democrat	Woodland, CA	11,014
Daily News	West Bend, WI	11,000
Courier	Connellsville, PA	10,957
Texas City Sun	Texas City, TX	10,700
Ada Sunday News	Ada, OK	10,500
News Messenger	Marshall, TX	10,421
Journal Review	Crawfordsville, IN	10,246
Journal	New Ulm, MN	10,000
Kent County Daily Times	West Warwick, RI	10,000
Yankton Daily Press & Dakotan	Yankton, SD	10,000
Times-Press	Streator, IL	10,000
Madison Courier	Madison, IN	9,876
Salem News	Salem, OH	9,609

Sunday Independent	Ridgecrest, CA	9,500
Mount Airy	Mt. Airy, NC	9,450
Oneida Daily Dispatch	Oneida, NY	9,400
Daily Review	Towanda, PA	9,065
Sunday News	Bogalusa, LA	9,000
Leader-Call	Laurel, MS	9,000
Rock Springs Daily Rocket-Miner	Rock Springs, WY	9,000
Daily Record	Canon City, CO	9,000
Dodge City Daily Globe	Dodge City, KS	9,000
Summit Daily News	Frisco, CO	9,000
Daily Herald (Elgin/ South Elgin)	Arlington Heights, IL	8,635
Bulletin	Latrobe, PA	8,500
Coshocton Tribune	Coshocton, OH	8,500
Union-Recorder	Milledgeville, GA	8,500
Daily Reporter	Martinsville, IN	8,441
Weirton Daily Times	Weirton, WV	8,200
Daily Herald (Mount Prospect/ Prospect Heights)	Arlington Heights, IL	8,188
Ludington Daily News	Ludington, MI	8,130
Review Times	Fostoria, OH	8,000
News Herald	Franklin, PA	8,000
Durant Daily Democrat	Durant, OK	8,000
Big Spring Herald	Big Spring, TX	7,748
Kirkville Daily Express and News	Kirkville, MO	7,600
Telegraph Forum	Bucyrus, OH	7,449
Daily Herald (Palatine/ Inverness)	Arlington Heights, IL	7,446
Parsons Sun	Parsons, KS	7,445
Urbana Daily Citizen	Urbana, OH	7,300
Antigo Daily Journal	Antigo, WI	7,000
Greensburg Daily News	Greensburg, IN	6,600
Borger News-Herald	Borger, TX	6,600
Examiner	Blue Springs, MO	6,500
Columbia Missourian	Columbia, MO	6,300
Evening Leader	St. Marys, OH	6,046
Jennings Daily News	Jennings, LA	6,000
Altus Times	Altus, OK	6,000
Westfield Evening News	Westfield, MA	5,850
Daily Herald (Lombard/ Oak Brook/ Villa Park)	Arlington Heights, IL	5,617
Record-Argus	Greenville, PA	5,600
Galion Inquirer	Galion, OH	5,500

Wapakoneta Daily News	Wapakoneta, OH	5,300
Banner News	Magnolia, AR	5,000
Daily Herald (Wheaton/ Glen Ellyn)	Arlington Heights, IL	4,970
Daily Herald (Bartlett/ Hanover Park/ Streamwood)	Arlington Heights, IL	4,911
Marion Daily Republican	Marion, IL	4,728
Daily Herald (Lisle/ Naperville)	Arlington Heights, IL	4,589
El Dorado Times	El Dorado, KS	4,500
Daily Herald (Des Plaines/ Elk Grove)	Arlington Heights, IL	4,403
Daily Herald (Algonquin/ Lake in the Hills)	Arlington Heights, IL	4,352
Daily Statesman	Dexter, MO	4,200
Marshall Democrat-News	Marshall, MO	4,150
Daily Times Leader	West Point, MS	4,136
Call-Leader	Elwood, IN	4,000
Daily Herald (Carpentersville Edition)	Arlington Heights, IL	3,930
Daily Herald (Buffalo Grove/ Long Grove/ Wheeling)	Arlington Heights, IL	3,657
Daily Herald (Rolling Meadows)	Arlington Heights, IL	3,620
Cape Coral Breeze	Cape Coral, FL	3,500
Daily Herald (Bloomingdale/ Itasca)	Arlington Heights, IL	3,310
Daily Herald (Warrenville/ West Chicago/ Winfield)	Arlington Heights, IL	3,235
Portales News-Tribune	Portales, NM	3,200
Angleton Times	Angleton, TX	3,000
Daily Herald (Libertyville/ Mundelein)	Arlington Heights, IL	2,716
Metropolitan News-Enterprise	Los Angeles, CA	2,500
Estherville Daily News	Estherville, IA	2,500
Daily Herald (Carol Stream/ Glendale Heights)	Arlington Heights, IL	2,330
Daily Herald (Barrington)	Arlington Heights, IL	2,111
Daily Herald (Lake Zurich/ Wauconda)	Arlington Heights, IL	1,860

The Dalles Chronicle	The Dalles, OR	5, 284
Daily Herald (Batavia)	Arlington Heights, IL	N/A
Daily Herald (Cary/ Fox River)	Arlington Heights, IL	N/A
Daily Herald (Gurnee/ Grayslake)	Arlington Heights, IL	N/A
Foster's Sunday Citizen	Dover, NH	N/A
Bloomberg News report (1)		
Chicago Sun-Times	Chicago, IL	491,143
Originals (5)		
Newsday (Nassau Edition)	Long Island, NY	463,406
New Era	Lancaster, PA	48,437
Intelligencer Journal	Lancaster, PA	43,263
Valley News	West Lebanon, NH	18,807

Attachment 22

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## **=Baxter Reports High Mortality In HemAssist Trial**

**18:52:28, 09 April 1998**

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Dow Jones News Service via Dow Jones

By Thomas M. Burton

**CHICAGO (Dow Jones)**--Twenty-four of 52 patients treated with Baxter's blood substitute in a trauma-treatment trial died, Baxter officials told Dow Jones. This compared with eight of 46 patients who died after receiving conventional trauma therapy in the same clinical trial.

Earlier this month, the Deerfield, Ill., company suspended the U.S. trauma clinical trial of HemAssist, Baxter's blood substitute product, because of the unexpectedly high mortality rate. However, Baxter has noted that it observed no such mortality rate in a surgical trial in the U.S., or in another trial of trauma patients being conducted in Europe.

Baxter officials said the death rate of 46.2% in the HemAssist group slightly exceeded the 42.6% predicted rate of death. The patients were all victims of serious accidents such as car crashes, gunshots and knife wounds, so a substantial rate of death was anticipated in any event.

By contrast, the Baxter officials said, the death rate of 17.4% in the "control" group - those treated with conventional therapy - was lower than the predicted death rate of 35.5%. The company said it had no immediate explanation for this disparity.

Baxter said it and its clinical researchers were still attempting to explain the cause of the high mortality in the HemAssist group. The product is known to cause "vasoconstriction," a tightening of blood-vessel walls that leads to higher blood pressure, and some in medicine have speculated that this could be related to the higher mortality.

The company has said, however, that the deaths do not appear to be related to this phenomenon. And some doctors even consider this tendency in HemAssist to be an advantage. Some doctors who participated in the trial have suggested that the results may simply illustrate how difficult it is to conduct a clinical trial involving severely injured patients - because the injuries are all so different from each other.

For instance, some of these doctors speculated that perhaps more patients with severe head injuries were assigned to the HemAssist group instead of the control group and that statistical accident may have led to more deaths in the HemAssist group. The company said it still is investigating the cause of the relatively higher mortality and that it will publish results on this at some point in the future.

Baxter said, though, that it still plans to market HemAssist if and when it receives regulatory approval for marketing in the U.S. or Europe. Baxter already has constructed a \$110-million production plant in Neuchatel, Switzerland, that is dedicated to making HemAssist.

MED-US-Artificial Blood < .0422  
Blood substitute mortality results released

HOUSTON (AP) A pharmaceutical company said that nearly half of emergency room patients given an experimental blood substitute died in a nationwide clinical trial slightly more than the projected mortality rate.

Of the 52 critically ill patients given the substitute known as HemAssist, 24 died, a 46.2 percent mortality rate, Baxter Healthcare Corp. said Friday in a statement.

The Deerfield, Illinois, company had projected 42.6 percent mortality for the critically ill patients in emergency rooms.

Baxter Healthcare halted its own clinical trial in the nation's emergency rooms on April 1 after reviewing data on the first 100 trauma patients enrolled in the study.

At the time, the company did not release the specific number of deaths in the U.S. emergency room study, only that it had anticipated about 40 percent given the substitute would die.

However, other trials involving elective-surgery and emergency-room patients in Europe continue because the death rates there are statistically unremarkable, the company said.

Baxter Healthcare spokesman Mary Thomas said the company is still trying to determine why more U.S. patients who received HemAssist died than those given the artificial blood in Europe.

It is thought that because doctors ride in European ambulances, the substitute is administered more quickly to a dying patient.

Several emergency rooms across America, including Houston's Ben Taub Hospital, had asked if they could help test the blood substitute. Some 17 other hospitals were part of the study before it was stopped.

Of the 100 patients in the halted U.S. study, 46 were in the control group that didn't receive HemAssist. Of those, 8 died, resulting in a 17.4 percent mortality rate, far below Baxter's anticipated 35.5 percent death rate.

Baxter Healthcare stressed that only 3 percent of America's emergency room trauma patients could be eligible for the study under federal guidelines. Those tested were among the most gravely ill trauma patients.

The race to find a blood substitute has been intense because artificial blood could ease the effects of whole-blood shortages, eliminate the time-consuming need to match blood types and wipe out the risk of contamination. Also, members of some religious groups refuse to accept transfusions of human blood.

(PROFILE  
(CAT:Business;)  
(CAT:Medical;)  
(SRC:AP; ST:IT;)  
)

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:SUBJECT: MED CONW  
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Received by NewsEDGE/LAN: 4/10/98 8:24 PM

NEWS

Nearly half died in artificial-blood study Firm unsure why results were worse in U.S. than in trials done in Europe

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04/11/98

The Dallas Morning News

STATE

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(Copyright 1998)

HOUSTON - Nearly half of the emergency room patients given an experimental blood substitute died in a nationwide clinical trial, statistics revealed Friday.

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The race to find a blood substitute has been intense because artificial blood could ease the effects of whole-blood shortages, eliminate the time-consuming need to match blood types and wipe out the risk of contamination. Also, members of some religious groups refuse to accept transfusions of human blood.

NEWS

Artificial blood mortality rate released / More than 46 percent died when given substitute in clinical test

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04/11/98

Houston Chronicle

3 STAR

23

(Copyright 1998)

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NEWS

Blood substitute test results: Death rate tops expectations

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04/11/98

The San Diego Union-Tribune

1 2 3 4 5 6 7

A-7

(Copyright 1998)

HOUSTON -- A pharmaceutical company said yesterday that nearly half of emergency-room patients given an experimental blood substitute died in a nationwide clinical trial -- slightly more than the projected mortality rate.

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The race to find a blood substitute has been intense because artificial blood could ease the effects of whole-blood shortages and eliminate the time-consuming need to match blood types.

Metro  
Fake blood death rate released  
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04/11/98

San Antonio Express-News

Metro

03B

(Copyright 1998)

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**ALMOST HALF THOSE ON BLOOD TRIAL DIED**

Charlotte Observer (CO) - Saturday, April 11, 1998

Edition: TWO-3

Section: MAIN NEWS

Page: 6A

Word Count: 545

MEMO:

COLUMN: NATIONAL BRIEFS

TYPE: BRIEF

TEXT:

HOUSTON

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Kingsmen to get rights, royalties to Louie, Louie'

PASADENA, Calif. - Nearly 35 years after recording the rock 'n' roll great "Louie, Louie," the Kingsmen will get back the rights to the song and their first-ever royalties.

A federal appeals court Friday upheld a Los Angeles judge's 1995 finding that the still-functioning group has the right to cancel their contract with several small record companies that haven't paid it a dime in decades.

The band that recorded the hit version of the rock standard in 1963 signed a contract in 1968 that was supposed to provide them with 9 percent of the profits or licensing fees from the record.

St. Louis Post-Dispatch, April 12, 1998

shore up Social Security. Sanford said workers could invest the money privately - in stocks or mutual funds, for example - and "earn far greater returns than today's Social Security system. They take away the ownership of retirement savings from Uncle Sam and give it back to the individual."

**Despondent teen-ager kills himself after wild car ride**

Parents in Providence, R.I., couldn't save the life of 19-year-old Jesse Frizzell, who killed himself after a wild ride in a family car with his screaming father clinging to the hood. Frizzell's father and mother, a psychologist, said they knew he was despondent after breaking up with his girlfriend. Raymond Frizzell searched for his son and found him Thursday, after the young man had bought a rifle. They tussled over the car keys and the father jumped onto the car hood when his son drove off. During the subsequent 15-minute ride, which reached speeds up to 100 mph, the teen drove through red lights, went the wrong way on one-way streets and weaved around cars, police said. The chase ended when police closed in. After stopping the car, spilling his father off onto the ground, the teen locked the doors and shot himself in the head, police said. He died Friday night, three days before his 20th birthday.

**Woman gets prison term for starving her daughter**

A judge in Rochester, N.Y., sentenced a woman to five to 15 years in prison for starving her 5-year-old retarded daughter. Supreme Court Judge William Bristol recommended Gloria Gross serve her entire sentence, rebuking the 39-year-old mother for subjecting "your own helpless daughter . . . to a long and agonizing death." By the time 5-year-old Tonya Daniels died of malnutrition last summer, she weighed 23 pounds. The girl was diagnosed with cerebral palsy during infancy. Gross was convicted of second-degree manslaughter in March after a four-day trial.

**Jury awards woman \$ 6 million in police shooting case**

A federal jury awarded \$ 6 million to a woman who sued Boynton Beach, Fla., after being shot eight times by police in an incident that triggered days of racial unrest in 1987. Jurors concluded Friday that the city and two officers violated the civil rights of Betty Willingham as she came out of her house with a knife and approached an officer who was fighting with her brother. The shooting was followed by sniper and rock-throwing attacks on police cars in a predominantly black section of Boynton Beach, 50 miles north of Miami. The jury said the city violated Willingham's civil rights by refusing to train, supervise or discipline its officers.

**Nearly half of patients who got blood substitute died \***

Nearly half of emergency room patients given an experimental blood substitute died in a nationwide clinical trial - slightly more than the projected mortality rate, a pharmaceutical company said. Of the 52 critically ill patients given the substitute known as HemAssist, 24 died - a 46.2 percent mortality rate - Baxter Healthcare Corp. said in a statement in Houston on Friday. The Deerfield, Ill., company had projected 42.6 percent mortality for the critically ill patients in emergency rooms.

GRAPHIC: PHOTO, Photo from THE ASSOCIATED PRESS - Francine Alderette, 1 1/2, cries for her mother, letting everyone know she has no desire to have her

3RD STORY of Level 1 printed in FULL format.

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Chicago Tribune

April 12, 1998 Sunday, CHICAGOLAND EDITION

SECTION: NEWS; Pg. 9; ZONE: C; Across the nation.

LENGTH: 111 words

HEADLINE: 24 OF 52 DIE IN TESTS OF BLOOD SUBSTITUTE

BYLINE: From Tribune News Services.

DATELINE: ILLINOIS

BODY:

A pharmaceutical company has reported that nearly half of emergency room patients given an experimental blood substitute died in a nationwide clinical trial--slightly more than the projected mortality rate.

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The Deerfield company had projected 42.6 percent mortality for the critically ill patients in emergency rooms.

On April 1, Baxter Healthcare had halted its own clinical trial in the nation's emergency rooms after reviewing data on the first 100 trauma patients in the study.

LANGUAGE: ENGLISH

LOAD-DATE: April 12, 1998

### **Clinical Update**

As part of Baxter's continuing commitment to provide information about its U.S. Phase III trauma trial, which was conducted under the HHS and FDA's exception to informed consent regulation, the following is a clinical update.

As previously announced, Baxter has ended its U.S. Phase III trauma trial investigating the efficacy of its oxygen-carrying solution, HemAssist (DCLHb), for the treatment of severe traumatic hemorrhagic shock. Baxter decided to stop the trial, which had enrolled approximately 100 of its expected 850 participants, following an interim data review by the trial's independent data monitoring committee. The committee found that patients in the treatment group had significantly increased mortality compared to those in the control group.

Analysis of interim patient data by the independent data monitoring committee, using a published model of predicting outcomes in trauma patients (TRISS) that combine physiologic and anatomic indicators of injury severity and age, indicate the predicted mortality in the treatment group was 42.6 percent with an observed mortality of 46.2 percent (24 of 52 patients). The predicted mortality in the control group was 35.5 percent with an observed mortality of 17.4 percent (8 of 46 patients). In addition, other indicators of injury severity were considered and although some differences were noted between the two groups, none were significant enough to indicate why the treatment group had a higher mortality rate than the control group. Further analysis of these data is ongoing.

As previously indicated, two additional advanced studies testing the efficacy of HemAssist are ongoing.

Baxter is releasing this clinical information prior to its final analysis to fulfill its responsibilities according to regulations pertaining to exception to informed consent. Additionally, Baxter intends to provide the complete clinical results in scientific forums and to distribute of the results in the communities in which the trial took place. The results also will be published on the U.S. trauma trial website at <http://dclhb.er.uic.edu/>.

4/9/98

BAXTER/HEMASSIST®(DCLHb) -- PAGE 1

**Baxter**

FOR IMMEDIATE RELEASE

Media contact: Mary Thomas, Baxter, (847) 948-2815

Investor contacts: Neville Jeharajah, Baxter, (847) 948-2875  
Mary Kay Ladone, Baxter, (847) 948-3371

**BAXTER ENDS U.S. TRAUMA STUDY OF HEMASSIST®(DCLHb)**

*European Trauma and U.S. surgery Trials Continue on Track*

DEERFIELD, Ill., March 31, 1998 - Baxter Healthcare Corporation

announced today that it has ended its U.S. Phase III trauma trial investigating the efficacy of its oxygen-carrying solution, HemAssist®(DCLHb), for the treatment of severe traumatic hemorrhagic shock. Baxter decided to stop the trial, which had enrolled approximately 100 of its expected 850 participants, following an interim data review by the trial's independent data monitoring committee. The committee found that patients in the treatment group had an increased mortality compared to those in the control group.

Baxter and its clinical investigators are studying the data to better understand why there was a difference in mortality between the patient groups. They are assessing the impact of many factors, including the combined results of the trial's design and protocol, the timing of the administration of HemAssist®(DCLHb) and

- more -

BAXTER/HEMASSIST®(DCLHb) -- PAGE 2

other medical treatments, the wide range of patient injuries and the severity of patient injuries in the two patient groups.

"We are evaluating options for trauma applications in the United States," said Thomas Schmitz, Ph.D., general manager of Baxter's Hemoglobin Therapeutics division. "We are confident that HemAssist®(DCLHb) will be of critical importance for both surgeons and emergency-medicine physicians.

"The European trauma trial, where physicians are administering HemAssist®(DCLHb) at the trauma site, is continuing on track. Our U.S. Phase III surgery trial moves forward as well."

Baxter continues to expect to bring HemAssist®(DCLHb) to market in late 1999 or early 2000.

**Significant Differences in Emergency Care**

The ongoing European trauma trial is investigating the product's efficacy in the pre-hospital setting, where doctors administer the product as a first-line therapy at the trauma site. In contrast, U.S. doctors infused HemAssist®(DCLHb) in the hospital after patients had been in shock for much longer periods of time. The company noted that in light of the U.S. trauma results the European trauma study has been evaluated by its independent data monitoring committee and that committee has determined that the trial will continue on course.

The patients enrolled in the U.S. trauma trial were gravely ill -- victims of severe trauma, such as motor vehicle accidents, knife and gun shot wounds -- and had a high expected mortality. Patients involved in the HemAssist®(DCLHb) trial were

BAXTER/HEMASSIST®(DCLHb) -- PAGE 3

among the most severely injured of all trauma victims, with only about 3 percent of all trauma patients eligible for trial inclusion. All individuals enrolled in the study received standard emergency care, including transfusions of blood, resuscitative fluids, and surgical intervention as required.

This U.S. trauma study was conducted under regulations issued by the U.S. Department of Health and Human Services (HHS) and the U.S. Food and Drug Administration (FDA) governing clinical-research practices in emergency medicine. These regulations are designed to protect patients' rights and well-being, while also allowing for an exception to informed consent in narrowly defined life-threatening situations. Several rigorous safety checks and patient protections are required of studies conducted under this ruling, including interim data analysis by an independent data monitoring committee. All institutions involved in the trial worked with their communities to inform them about the potential risks and benefits of the HemAssist®(DCLHb) trial. The results of the U.S. trauma study will be made public when the data are fully analyzed.

Baxter's Phase III U.S. surgery trial is investigating the use of HemAssist®(DCLHb) as an alternative to blood in patients undergoing elective surgery, such as hip and knee replacements, aortic repair and abdominal pelvic procedures.

Baxter Healthcare Corporation is the principal U.S. operating subsidiary of Baxter International Inc. Baxter International, through its subsidiaries, is a global leader in the development of products and technologies related to the blood and circulatory system. The company has market-leading positions in four areas: blood therapies, cardiovascular medicine, kidney-disease therapy and medication delivery.

BAXTER/HE.MASSIST@DCLHB) -- PAGE 4

Through a combination of technological innovation and global expansion, Baxter is advancing medical care and improving the lives of millions of people worldwide.

This news release contains forward-looking statements that involve risks and uncertainties, including technological advances in the medical field, product approval, demand and market acceptance.

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