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Issues - Ricky Ray Hemophilia Act [1]

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FAX



Health Division



Office of Management and Budget
Executive Office of the President
Washington, DC 20503

To: Todd Semmes
Fax: 6-2438
From: Seferi Pashman
Number of Pages (excluding cover): 4
Subject: Ficky Ray

Voice Numbers:

Health Division (Front Office)	202/395-4922
Health & Human Services Branch	202/395-4925
Health Programs & Services Branch	202/395-4926
Health Financing Branch	202/395-4930

Fax Numbers:

Health Division (Front Office)	202/395-3910
Health Division (Room 7001)	202/395-7840
Health Division (Room 7002)	202/395-5648



EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF MANAGEMENT AND BUDGET
WASHINGTON, D.C. 20503

THE DIRECTOR

May 13, 1999

The Honorable Curt Weldon
U.S. House of Representatives
Washington, DC 20515

Dear Representative Weldon:

Thank you for your March 5, 1999, letter regarding the funding of the Ricky Ray Hemophilia Relief Fund Act of 1998. The President asked me to respond on his behalf.

The Administration certainly concurs with you that the infection of some in the hemophilia community with the AIDS virus is indeed a tragedy. As you know, President Clinton has long been committed to addressing the health issues caused by HIV and AIDS. The FY 2000 Budget includes \$1.5 billion in Federal spending for the Ryan White CARE Act. Specifically, the Budget provides a \$100 million increase in Ryan White treatment grants to help states and affected communities provide AIDS treatment, including the powerful "combination therapy" drugs that are successfully slowing the progression of the AIDS virus in many patients.

With regard to the Ricky Ray Hemophilia Relief Fund Act, the Department of Health and Human Services has issued procedures for filing petitions for payment. We support the Ricky Ray Hemophilia Relief Fund Act, but with the tight funding constraints facing us this year, we were not able to seek funding in the FY 2000 Budget.

Sincerely,

A handwritten signature in black ink, appearing to read "Jacob J. Lew".

Jacob J. Lew
Director

CURT WELDON

7TH DISTRICT, PENNSYLVANIA

2462 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-3807
(202) 225-2011

1554 GARRETT ROAD
UPPER DARBY, PA 19082
(610) 259-0700

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MIGRATORY BIRD
CONSERVATION COMMISSION
REPUBLICAN POLICY COMMITTEE
E-mail curtpa7@hr.house.gov



Congress of the United States
House of Representatives
Washington, DC 20515-3807

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GLOBE OCEAN PROTECTION TASK FORCE
CONGRESSIONAL MISSILE DEFENSE CAUCUS

March 5, 1999

President William Clinton
The White House
1600 Pennsylvania Avenue
Washington, D.C. 20500

Dear President Clinton:

I am contacting you regarding an issue of utmost importance to a large number of my constituents, the appropriation of the funds authorized under H.R. 1023, the Ricky Ray Hemophilia Relief Fund Act of 1997.

As I am sure you are aware, our nation's blood supply and blood-derived products were tainted by the AIDS virus in the early 1980's. More than 80% of people with severe hemophilia and half of all persons with hemophilia were infected with HIV, including between 10-20 percent of the spouses, children, and partners of these individuals. The average cost of hemophilia therapy alone is nearly \$100,000 each year. The cost of HIV/AIDS care is estimated to be between \$10,000 and \$50,000 annually per patient. These staggering costs are far beyond the financial capabilities of most people.

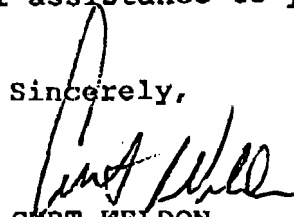
The Ricky Ray Hemophilia Relief Fund Act of 1997, which you signed into law on November 12, 1998, recognizes that the federal government has a shared responsibility for protecting the safety of the blood supply and for regulating blood products. This law authorizes \$750 million to provide \$100,000 payments to persons with hemophilia who contracted HIV through the use of contaminated blood products.

This phenomena was indeed a tragedy for which the victims deserve remuneration. \$750 million over the course of five years is indeed a considerable sum of money. I would like your thoughts as to why this money was not included in your FY2000 budget, as well as any ideas which you may have as to whether or not this money has the possibility of being allocated.

56148

Thank you for your attention to this matter. Please do not hesitate to contact me if I can be of assistance to you.

Sincerely,

A handwritten signature in dark ink, appearing to read "Curt Weldon", is written over the typed name.

CURT WELDON
Member of Congress

CW:ec

Date: 5/17/99

FAX



Health Division



Office of Management and Budget
Executive Office of the President
Washington, DC 20503

To: *Todd Summers*

Fax: *62438*

From: *Richard Turman*

Number of Pages (excluding cover): *3*

Subject:

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Health Division (Front Office)	202/395-4922
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OFFICE OF MANAGEMENT AND BUDGET
WASHINGTON, D.C. 20503

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CONSERVATION COMMISSION
REPUBLICAN POLICY COMMITTEE
E-mail: curtwa7@hr.house.gov



Congress of the United States
House of Representatives
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COMMITTEE ON NATIONAL SECURITY
RESEARCH AND DEVELOPMENT, CHAIRMAN
READINESS
MERCHANT MARINE PANEL

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BASIC RESEARCH

CO-CHAIRMAN:
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US-FBI ENERGY CAUCUS
"THE EMPOWERMENT CAUCUS"
GLOBE OCEAN PROTECTION TASK FORCE
CONGRESSIONAL MISSILE DEFENSE CAUCUS

March 5, 1999

President William Clinton
The White House
1600 Pennsylvania Avenue
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Sincerely,

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CURT WELDON
Member of Congress

CW:ec

May 18, 1998 (SENT)
(House)

STATEMENT OF ADMINISTRATION POLICY

(THIS STATEMENT HAS BEEN COORDINATED BY OMB WITH THE CONCERNED AGENCIES.)

H.R. 1023 - Ricky Ray Hemophilia Relief Fund Act of 1998

(Rep. Goss (R) FL and 270 cosponsors)

The Administration is very concerned about the individuals with hemophilia and their families who suffered because of the transmission of HIV through blood and blood products in the 1980s. Although the National Academy of Sciences' Institute of Medicine (IOM) found no negligence on the part of U.S. Government officials, the IOM did conclude that the entire public health system, including both the private and public sectors, may have missed opportunities to further reduce the risk of HIV infection from blood products.

The Administration will be pleased to work with the Congress to develop an appropriate way to assist those infected with HIV through the use of blood and blood products in the 1980s. In developing a bipartisan program, such as H.R. 1023, a number of important issues of policy as well as numerous technical and statutory issues will need to be addressed, including the ramifications of the precedent that would be set and how to pay for the assistance. We look forward to working with Congress to address these issues.

Pay-As-You-Go-Scoring

H.R. 1023 would increase direct spending; therefore it is subject to the pay-as-you-go requirement of the Omnibus Budget Reconciliation Act of 1990. OMB's preliminary estimate is that the bill would increase direct spending by \$1 million in FY 1998 and a total of \$15 million during FYs 1998-2002. The bill does not contain provisions to offset the increased direct spending. Therefore, the Administration will work with Congress to develop appropriate offsets.



EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF MANAGEMENT AND BUDGET
WASHINGTON, D.C. 20503

LEGISLATIVE REFERENCE DIVISION

1 Pages(S) Follow(s)

May 19, 1998

TO: Office of National AIDS Policy -- Todd Summers

FROM: Josie Dade

395-7362

FINAL SAP

Bill Number and Title: H.R. 1023 -- Ricky Ray Hemophilia
Relief Fund Act of 1998

**OMB HAS JUST SENT THIS STATEMENT OF
ADMINISTRATION POLICY (SAP) TO CONGRESS.**

March 13, 1998

Mr. Todd Summers
Deputy Director, White House Office of AIDS Policy
808 17th Street, NW
Suite 820
Washington, DC 20006

Re: Information to Assist in Consideration of the Ricky Ray Hemophilia Relief Fund Act.

Dear Mr. Summers:

I am supplying this additional information to assist in your consideration of issues relating to the Ricky Ray Hemophilia Relief Fund Act. To remind you of my interest in the matter, in addition to practicing law in Phoenix, I have severe hemophilia and contracted HIV from the infusion of concentrated blood clotting factor. I have spent the last three years researching and writing on the subject of FDA liability related to the infection of the U.S. hemophilia community.

This packet contains four items intended to assist in your consideration of the Ricky Ray Act. First, it contains, in the form of this letter itself, a brief summary of events giving rise to liability on the part of the FDA for the widespread HIV-infection rate of the U.S. hemophilia community. Second, it contains a copy of a letter of recommendation by Senator Kyl of Arizona concerning my efforts with regard to the Ricky Ray Act. Third, it contains a copy of an eighty page report which I authored and which appears as part of the September 19, 1996 House Judiciary Committee, Subcommittee on Immigration and Claims, Hearings Report on the Ricky Ray Act. Finally, I have included a copy of the final version of my report, with the most important 10-15% redlined to allow for expeditious review. Since I know that the time of your staff is very limited, I would greatly appreciate a staff member reading the chronology in this letter, and then portions of the redlined version of my report, as time permits. The redlined version of the document is more thorough than my earlier version appearing in the 1996 House Subcommittee Hearings Report.

I believe that these materials present public statements by the FDA which were seriously misleading as to the risk of AIDS-infection to the hemophilia community from the use of concentrated clotting factor VIII, in light of pronouncements made by the CDC at the same time. These materials, I believe, demonstrate an effort by the FDA to minimize the

Mr. Todd Summers

March 13, 1998

Page two

hemophilia community's perception of the risks of AIDS infection to a degree which justifies federal compensation for those injuries suffered. I hope you find this information helpful.

My conclusions as to these events, in brief, are as follows.

- The standard of care under the effective CFRs during the early 1980s required the FDA to demand revised labeling to include a warning as soon as there was reasonable evidence of an association of a serious hazard with clotting factor concentrate; a causal relationship need not have been proven.
- One week before the CDC issued its July 16, 1982 Morbidity and Mortality Weekly Report (MMWR) that three hemophiliacs, who had no other risk factors for AIDS and who had used different sources of factor concentrate, had contracted AIDS, the FDA had similarly warned the manufacturers of concentrated clotting factor. It did not warn consumers.
- The FDA thus was aware at that time that the agent causing AIDS was likely a blood-borne agent, based on the unique and isolated epidemiological exposures offered by the hemophilia cases.
- The FDA knew that the pharmaceuticals used a method of pooling plasma from up to 20,000 donors, and further knew, based upon its knowledge of hepatitis viral contamination of pooled plasma, that the AIDS-causing agent could potentially infect all of the approximately 100 separate hemophilia patients who received factor concentrated from each pool.
- The FDA never required any of the concentrate manufacturers to warn of the risk of AIDS from concentrate infusion at any time, and particularly did not do during the two to three year period after the July 16, 1982 MMWR until the concentrate was pasteurized and made effectively HIV-virus free.
- Instead, the FDA published articles in its FDA Consumer Magazine that appear calculated to drastically understate the risk of HIV infection to the hemophilia community, and published those articles at approximately the same time that the CDC in MMWR discussed the risks of HIV infection posed to hemophilia patients by clotting factor concentrate. One of the FDA Magazine articles most reassuring to the hemophilia community appeared during the same month that the CDC published healthcare worker safety guidelines warning against contact with the blood of hemophilia patients infusing with clotting factor concentrate.

- During that two to three year period, approximately 7,000 hemophilia patients in the United States were infected with HIV for the first time, with many receiving numerous re-infections from contaminated clotting factor. Approximately 3,500 have died at this time.

- According to an exhaustive review of the medical scientific literature available on the subject, extrapolations from stored and frozen blood samples, taken from hemophilia patients during the early 1980s, suggests that up to 3,500 hemophilia patients were still uninfected from HIV as of January 1, 1983.

- January 3, 1983 is the date of the second CDC workshop on the blood supply concerning AIDS, at the conclusion of which a number of judicial opinions and legal scholarship have found there was no reasonable scientific doubt that the AIDS-causing agent was blood borne, and that the hemophilia community was at a special risk as a result of infusing with blood products concentrated from the plasma of thousands of donors.

- A number of state and federal judicial opinions have also found that, at the conclusion of the January 3, 1983 blood workshop, the CDC and FDA were both aware that donor questionnaires concerning sexual practices should have been used, that warnings of AIDS to consumers of factor concentrate should have been issued, and that blood supply testing for the core antibody for hepatitis B would have detected 90% of the HIV circulating in the national blood supply and allowed its destruction.

- Plasma cryoprecipitate was an alternative to infusion with clotting factor concentrate in all but life-threatening circumstances, and would have exposed each patient to only ten to fifteen separate donors per infusion.

- Under the common law standards developed during the swine flu vaccine litigation, there is a rebuttable presumption that all of the intended recipients of the warnings of AIDS would have acted upon them by using cryoprecipitate instead of clotting factor concentrate in appropriate circumstances. Given that cryoprecipitate has never been associated with an HIV infection, those infections occurring after January, 1983, and other subsequent reinfections after that time, are presumed to be the responsibility of the FDA.

- Among possible funding strategies is the notion that the federal government would be paying for liability already incurred prior to the present budgetary environment, and that by waiving potential causes of action against the FDA, each fund recipient under the Ricky Ray Act would relieve the federal government of liability valued at, on average, one hundred thousand dollars per claimant. This projected value is based, in part, upon the recent settlement in the federal district court of Northern Illinois between the private pharmaceuticals

Mr. Todd Summers

March 13, 1998

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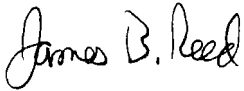
and the entire infected hemophilia community, in which each infected claimant will receive one hundred thousand dollars. Accordingly, the relief from current legal liability for those infections offered by those requisite waivers would substantially, if not entirely, offset the anticipated cost of the legislation.

For further information, please write to my home address:

Jim Reed
3232 East Hazelwood Street
Phoenix, Arizona 85018

or call (602) 468-0339 (answering machine) or work (602) 254-9844. Once again, because my co-workers, with the exception of my employer and office manager, do not know my medical condition, I would appreciate any of your staff wishing to call me at my office using discretion with regard to mentioning the nature of the call. I will promptly return any messages. Thank you for your consideration of these materials.

Very truly yours,

A handwritten signature in cursive script that reads "James B. Reed".

James B. Reed

JON KYL
ARIZONA

702 HART SENATE OFFICE BUILDING
(202) 224-4521

COMMITTEES:

JUDICIARY

INTELLIGENCE

ENERGY AND NATURAL RESOURCES

United States Senate

WASHINGTON, DC 20510-0304

October 8, 1997

STATE OFFICE:
2200 EAST CAMELBACK ROAD
SUITE 120
PHOENIX, AZ 85016
(602) 840-1891

7815 NORTH ORACLE ROAD
SUITE 220
TUCSON, AZ 85704
(520) 575-8633

Senator James Jeffords
Chairman
Senate Labor and Human Resources Committee
Dirksen Room 428
Washington, DC 20510

Dear Senator Jeffords:

I respectfully request your consideration of one of my constituents, James Reed, Esq., as a witness for the upcoming Labor Committee hearings on AIDS issues, and in particular, on the Ricky Ray Hemophilia Relief Act.

Jim has severe hemophilia and contracted HIV from the infusion of concentrated blood clotting factor to treat his medical condition. He has spent the last two years lobbying, researching, and writing on the subject of potential FDA liability related to the agency's failure to protect and later to warn hemophiliacs about the existence of tainted blood supplies. His 80-page report on this issue was printed in the September 19, 1996 House Subcommittee on Immigration Claims hearings on the Ricky Ray Act. Jim has brought, in my opinion, an in-depth and well-reasoned legal analysis to what could otherwise be an emotionally charged discussion.

I believe that Jim can offer information and analysis to the Committee that is unlikely to be presented by any other witness. I know that his oral presentation would provide a helpful synthesis of his research and add greatly to the Committee's understanding of the issue. Jim has read all the primary source materials relating to these issues, and I believe he could articulate the legal position of hemophilia sufferers in a most helpful manner.

I thank you for your consideration of this request. If you have any questions, please contact me or my staffer, Tom Alexander, at 4-4521.

Sincerely,



JON KYL
United States Senator

RICKY RAY HEMOPHILIA RELIEF FUND ACT OF 1995

HEARING BEFORE THE SUBCOMMITTEE ON IMMIGRATION AND CLAIMS OF THE COMMITTEE ON THE JUDICIARY HOUSE OF REPRESENTATIVES ONE HUNDRED FOURTH CONGRESS

SECOND SESSION

ON

H.R. 1023

RICKY RAY HEMOPHILIA RELIEF FUND ACT OF 1995

SEPTEMBER 19, 1996

Serial No. 122



Printed for the use of the Committee on the Judiciary

U.S. GOVERNMENT PRINTING OFFICE

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RICKY RAY HEMOPHILIA RELIEF FUND ACT OF 1995

THURSDAY, SEPTEMBER 19, 1996

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON IMMIGRATION AND CLAIMS,
COMMITTEE ON THE JUDICIARY,
Washington, DC.

The subcommittee met, pursuant to notice, at 9:45 a.m., in room 2226, Rayburn House Office Building, Hon. Lamar Smith (chairman of the subcommittee) presiding.

Present: Representatives Lamar Smith and Bill McCollum.

Also present: Representative Porter J. Goss.

Staff present: Cynthia Blackston, clerk; George Fishman, assistant counsel; Judy Knott, secretary; and Marie McGlone, minority counsel.

OPENING STATEMENT OF CHAIRMAN SMITH

Mr. SMITH. Before I make my opening statement and before any other member of the committee makes their opening statement, let's hear from the two Members of Congress, Congressman Porter Goss and Senator Michael DeWine. I think, for the interest of so many of you all who are here, in the interest of time and in the interest of consideration for the members who are here as well, I would like and think it would be helpful for all of us to hear from Senator DeWine and Congressman Goss. So, if there is no objection, I understand that Senator DeWine has the most pressing schedule, so we will hear from him first.

I know it will be in his testimony, but he is the Senate chief sponsor of the bill that we consider today, as is Porter Goss the House chief sponsor of the legislation.

[The bill, H.R. 1023, follows:]



The Honorable Lamar Smith
March 13, 1997
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Reference No. WASH97018

...

Mr. Chairman, the processors of plasma-derived hemophilia therapies hereby respond to your inquiry and explicitly reject any suggestion that they utilized unscreened, virus-containing "high titer plasma" which for improper, unscientific, or financial reasons was mixed with ordinary "screened plasma." Any such allegations are based on incorrect information or false assumptions. The issue you raise has involved, at best, misunderstanding and, at worst, inflammatory rhetoric and unfounded accusations. Once again, these companies appreciate the opportunity to clarify the record.

Very truly yours,

Robert W. Reilly
Executive Director

RWR/mrs

cc: Alpha Therapeutic Corporation
Baxter Healthcare Corporation
Bayer Corporation
Armour Pharmaceutical Company

**A CHRONOLOGICAL AND LEGAL ANALYSIS
OF THE
RICKY RAY HEMOPHILIA RELIEF FUND ACT¹**

James B. Reed, Esq.²

¹This document is originally copyrighted, 1996, and is intended by the author for use as part of U.S. Senate Judiciary Committee and House subcommittee hearings concerning the Ricky Ray Act.

²1989 Chair - AIDS Litigation Working Group, the National Hemophilia Foundation; Columbia Law School, JD - 1988.

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LEGAL ANALYSIS OF THE RICKY RAY HEMOPHILIA RELIEF FUND ACT

"We are carefully to preserve that life which the Author of nature has given us, for it was no idle gift." (Harvey W. Wiley, creator of the Federal Food and Drugs Act of 1906, Commencement address, Hanover College, 1867, FDA Papers, February 1972, p.1.)

"[T]he Food, Drug and Cosmetic Act is to be given a liberal construction consistent with its overriding purpose to protect the public health. . . ." United States v. An Article of Drug, Bacto-Unidisk, . . ., 394 U.S. 784, 798, 89 S.Ct. 1410, 1418, 22 L.Ed.2d 726 (1969).

INTRODUCTION

This report has three objectives: 1) to chronologize the events which give rise to liability on the part of the Food and Drug Administration ("FDA") for a significant amount of the Human Immunodeficiency Virus ("HIV") infection rate within the U.S. hemophilia community; 2) to describe the legal standards which govern the FDA and which this report concludes that the FDA failed to observe during critical periods during the period of HIV infection of the U.S. hemophilia community; and 3) to suggest a perspective of the issues designed to address the financial dimensions of the Ricky Ray Act. The conclusion of this report, that the FDA failed to observe common law standards of conduct required of it during the period of time when the hemophilia community was exposed to blood borne HIV, coupled with the unique financial problems posed by HIV infection in combination with the pre-existing medical and financial stresses imposed by hemophilia, supports the creation of a federal trust fund to assist persons infected with HIV as a result of clotting factor infusion, whether principally or through secondary spousal or perinatal infection, or their survivors.

SUMMARY

Four reasons support the conclusion that the FDA is at fault for high HIV infection rates. First, pasteurization technology was available to destroy viruses such as hepatitis and HIV, but the FDA did not require its use for concentrated blood plasma clotting factor VIII proteins ("concentrate") used by hemophilia patients.³ Second, the FDA possessed

³ Scipps Clinic & Research Foundation v. Genentech, Inc., 666 F.Supp. 1379, 1383 (N.D.Cal. 1987).

sufficient information by August 1, 1982, and at the very least, by mid-January, 1983, to require patient package inserts with the concentrate products that would have warned concentrate users of the risks of HIV transmission, but the FDA did not do so. Third, the FDA did not require that commercial blood donation centers utilize donor questionnaires that asked about sexual practices, even though the FDA was aware that the homosexual community was at a high risk for contracting, and therefore, transmitting, the AIDS virus. Fourth, the FDA did not require a procedure known as surrogate testing for HIV, which would have tested donor blood for the presence of the core antibody for hepatitis B, which frequently accompanied and therefore revealed the presence of 70-90% of the HIV present in donated blood. The National Academy of Sciences' Institute of Medicine ("IOM") and various other sources have indicated that, if the FDA had required any one of these four procedures, it probably would have prevented numerous HIV infections among hemophilia patients. This paper concludes that, if the FDA had adopted a reasonable combination of safety requirements, it would have prevented a substantial amount of the HIV infections among hemophilia patients, along with subsequent re-infections that may have accelerated the onset of AIDS. This paper will discuss the standards of FDA conduct in Section One, the pasteurization alternatives in Section Two, and the safety procedures discussed by the IOM in Section Three. Section Four discusses the availability of a treatment therapy known as cryoprecipitate that was available at the time, and which greatly reduced the risk of infection from HIV. Section Five proposes that the median midpoint of seroconversion was after January 1, 1983, and therefore, using the estimated date most favorable to the FDA, January 3, 1983, after which time no reasonable scientific uncertainty remained as to the fact that AIDS was transmitted by blood, the FDA could have prevented the seroconversion of half of the United States hemophilia population. This last point, in combination with the Ricky Ray Act requirement that fund recipients execute a waiver of a cause of action as against the FDA, provides a budgetary offset value of this legislation that is comparable to its anticipated cost, as discussed in Section Six. This paper concludes that remedial legislation such as the Ricky Ray Act is appropriate.

Blood clotting, although not fully understood, may be generally described as follows. The clotting process begins when platelets in the bloodstream adhere to the site of a wound. The platelets would be dislodged, however, unless bound in place by strands of fibrin, an insoluble polymer. The formation of a network of fibrin from its soluble precursor, fibrinogen, is critical to clotting. That formation is the result of a complex series of interactions between blood proteins. Factor VIII:C is one of the agents that activate other proteins essential to this process. A deficiency in Factor VIII C therefore prevents blood clotting.

SECTION ONE: THE MISSION OF THE FDA AND THE DUTY OF CARE IMPOSED UPON IT BY STATUTE AND COMMON LAW.

A. Statutory and Regulatory Duties of the FDA.

The Federal Food, Drug and Cosmetic Act ("FFDCA") of 1938 was originally signed into law by President Franklin Roosevelt, and has been amended numerous times since then. The Food and Drug Administration is established by the FFDCA to carry out and enforce that law. "Blood derivatives such as Factor VIII are prescription biologicals subject to federal regulation as both 'biological products' and 'drugs'" by the FDA. Walls v. Armour Pharmaceutical Co., 832 F.Supp. 1467, 1483 (M.D.Fla. 1993), citing Public Health Service Act, "Regulation of Biological Products," 42 U.S.C. § 262, and citing Food, Drug and Cosmetic Act, 21 U.S.C. §§ 301 et seq. 21 C.F.R. § 610 (1988). "Under federal law, 'labelling is broadly defined and includes not only package inserts, but also separate communications concerning the drug, such as 'Dear Doctor' letters sent by drug manufacturers to physicians to provide information about a drug.'" Walls, 832 F.Supp. at 1483.

The particular sections regarding warnings are set forth in 21 CFR Ch.2, Subpart B - Labeling Requirements for Prescription Drugs and/or Insulin, § Subsection 201.57(d) states: "Contraindications" - "Under this section heading, the labeling shall describe those situations in which the drug should not be used because the risk of use clearly outweighs any possible benefit." Subsection (e) "Warnings" states:

Under this section heading, the labeling shall describe serious adverse reactions and potential safety hazards, limitations in use imposed by them, and steps that should be taken if they occur. The labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved.

(emphasis added).

B. Common Law Standards of Liability for FDA Misconduct.

"A cause of action in tort arises out of a violation of a legal duty imposed upon an actor to avoid causing harm to others." United Blood Services v. Quintana, 827 P.2d 509, 519 (Colo. 1992). "Legal duty is defined in terms of a standard of care. The source of the duty and the corresponding standard essential to the proper discharge of the duty may originate from a judicial decision or a legislative enactment." United Blood Services, 827 P.2d at 519. Those standards are not determined by the standard of the industry at the

time, particularly where a governmental agency is invested with the powers to set that standard:

In a professional negligence case, therefore, a plaintiff should be permitted to present expert opinion testimony that the standard of care adopted by the school of practice to which the defendant adheres is unreasonably deficient by not incorporating available practices and procedures substantially more protective against the harm caused to the plaintiff than the standard of care adopted by the defendant's school of practice.

United Blood Services, 827 P.2d at 521.⁴

The FDA is governed by common law standards concerning the reasonability of its conduct. It cannot delay in carrying out its regulatory duties, once it determines that it must act. Cutler v. Hayes, 818 F.2d 879, 898 (D.C. Cir. 1987):

The deference traditionally accorded an agency to develop its own schedule is sharply reduced when injury likely will result from avoidable delay. Economic harm is clearly an important consideration and will, in some cases, justify court intervention, and "[d]elays that might be altogether reasonable in the sphere of economic regulation are less tolerable when human lives are at stake."

Public Citizen Health Research Group v. Aughtier, 226 U.S.App.D.C. 413, 702 F.2d 1150 (1983) ("in the context of the OSH Act, designed to protect workers' health . . . , the Assistant Secretary's protracted course in face of potentially grave health risks cannot be characterized as reasonable"). Therefore, an evaluation of the reasonableness of FDA response time is measured, first, by whether the FDA was reasonable in deciding whether or not it must conduct an investigation, and, second, whether the FDA was prompt in

⁴Doe v. Miles, 927 F.2d at 191.

The Maryland Court of Appeals recognized four common threads that are generally considered in most cases which conclude that blood and blood products are not unreasonably dangerous. These four common threads are: (1) the nonexistence of any scientific test capable of detecting the viral agent which contaminated the blood at the time of injury; (2) the great utility of the product; (3) the lack of any substitute for the the product; and (4) the relatively small risk of the disease being transmitted by the product. [Int: Miles Laboratories, Inc., Cutter Laboratories Div. v. Doe, 315 Md. 704, 733, 556 A.2d 1107, 1121 (1989).

investigating and otherwise responding to the problem in a substantively adequate manner. This paper concludes that the FDA response was both egregious in its delay and in its quality. Because the FDA is responsible for the safety of the nation's blood supply generally, and is responsible for clotting factor safety specifically, it is ultimately responsible for the failure by the blood banking industry to respond effectively. In so doing, this report concludes that unnecessary HIV-contamination of the blood supply occurred, as did the New Jersey Court of Appeals in Snyder v. American Association of Blood Banks, 282 N.J. Super. 23, 659 A.2d 482, 490 (N.J. Super. A.D. 1995), *aff'd* 1996 WL 290907 (N.J.):

The Report of the Presidential Commission on the Human Immunodeficiency Virus Epidemic concludes that "[t]he initial response of the nation's blood banking industry to the possibility of contamination of the nation's blood banking by a new infectious agent was unnecessarily slow." The evidence at trial supports the jury's finding that the response was not only "unnecessarily slow" but also that it was clearly imprudent and unreasonable, resulting in unnecessary contamination of the blood supply.

C. Compensation programs as a remedial device.

The Ricky Ray Act is not the first compensation program of its kind. The National Vaccine Injury Compensation Program, 42 U.S.C. §§ 300aa-10, *et seq.*,⁵ became effective October 1, 1988. Section 300aa-11(c)(1) provides the elements that a petitioner must describe in a successful petition for compensation under the Act. The NVICP provides compensation for the following: (1) medical or remedial care, and a variety of custodial and rehabilitative services;⁶ (2) award of \$250,000 in the event of death;⁷ (3) loss of earnings;⁸ (4) pain and suffering;⁹ (5) reasonable attorney fees and other costs.¹⁰ Compensation for injuries incurred before the effective date is covered by 42 U.S.C. §

⁵Previously the National Childhood Vaccine Act of 1986, as amended, by the Omnibus Budget Reconciliation Act of 1987, Public Law No. 100-203, Title IV, Dec. 22, 1987, 42 U.S.C. §§ 300aa-1 *et seq.*

⁶Section 300aa-15(a)(1).

⁷Section 300aa-15(a)(2).

⁸Section 300aa-15(a)(3).

⁹Section 300aa-15(a)(4).

¹⁰Section 300aa-15(e).

300aa-15(b), and has been interpreted to require compensation for vaccine-related injuries incurred both before and after the effective date of the statute. Brown v. Secretary of DHHS, 18 Cl.Ct. 834, 841-842 (1989). Compensation has been made under the Program for a variety of vaccines. See Brown, 18 Cl.Ct. 834 (for injuries from paralytic polio caused by administration of oral polio vaccine); Kue v. Secretary of Department of Health & Human Services, 18 Cl.Ct. 777, 778-779 (1989) (parents of infant who died as result of hypotonic-hyporesponsive collapse one day after administration of DPT vaccine entitled to recovery); Hanagan v. Secretary of the DHHS, 19 Cl.Ct. 7 (1989) (child who had seizures and resulting injuries after receipt of diphtheria-tetanus-pertussis vaccination entitled to compensation); Storrier v. U.S., 662 F.Supp. 18 (N.D. Ohio 1986) (swine flu vaccinee entitled to compensation for contraction of Guillain Barre Syndrome); Baker v. U.S., 660 F.Supp. 204 (D.Conn. 1987) (swine flu vaccinee - Guillain Barre Syndrome); Petty v. United States, 740 F.2d 1428 (8th Cir. 1984) (swine flu vaccinee - serum sickness).

The Act is separate from the National Influenza Immunization Program of 1976 (Swine Flu Act), Public Law 94-380, 42 U.S.C. 247b(j)-(l), as amended (1976). The burden of proof under the Swine Flu Act is the same as that required in a civil suit; a petitioner must prove that it is more likely than not that she has received her injuries from the vaccination. Baker v. U.S., 660 F.Supp. 204, 211.¹¹ In short, a trust fund is an available device to address similar injury in a discernable population receiving a drug under the regulation of the FDA. If the FDA is found at fault for those injuries, the only remaining issue is whether to use such a fund retrospectively as a class reimbursement device.

¹¹The Baker Court found for the plaintiff and separately held proceedings with respect to the damages issue. Baker, 660 F.Supp. at 211-212.

SECTION TWO: THE FDA FAILED TO REQUIRE PASTEURIZATION OF CONCENTRATE TO DESTROY BLOOD BORNE VIRUSES, AND, THEREFORE, FAILED TO REQUIRE THE USE OF TECHNOLOGY ALREADY DEVELOPED AND IN USE IN GERMANY THAT WOULD HAVE DESTROYED HIV AND PROTECTED ALL HEMOPHILIC USERS OF CONCENTRATE FROM CONTRACTING TRANSFUSION-ASSOCIATED AIDS.

A) A Brief History of Hepatitis and The Development of Techniques to Inactivate Blood Borne Viruses.

The procedure for heat-treating clotting factor to destroy the hepatitis B virus also destroys the AIDS virus. The technology to do so was available and in use in Germany in 1979. The FDA did not require its use, and as a result, there was no viral inactivation technique licensed in the United States until 1983. The following information serves to establish that, before HIV was widespread in the blood supply, sufficient scientific information existed to make it unreasonable for the FDA to fail to require heat-treatment of concentrate.

1) 1945 - a World War II field study (Rappaport, Capt.) found that plasma pooled and then freeze-dried by commercial manufacturers caused fourteen times as many cases of homologous serum jaundice hepatitis, now known as serum hepatitis B, a fatal form of hepatitis affecting the liver. "On the Trail of Tainted Blood," *The Philadelphia Enquirer*, April 16, 1995, p.1, p.2, col.1. It was clear that pooling the plasma of blood donors into one large plasma vat allowed the hepatitis B infection of any one donor to spread throughout the pool and infect many or most of the recipients of plasma from that pool.

2) 1950 - A study by J. Garrott Allen of the University of Chicago proved that prolonged heating at 90 degrees fahrenheit for between three and six months could kill the hepatitis B virus. *The Philadelphia Enquirer*, *supra* at p.2, cols.1,2.

3) 1962 - A study by the U.S. Office of the Surgeon General confirmed the 1945 Rappaport Study's finding that pooled plasma was the cause of numerous wartime cases of hepatitis B. Furthermore, the report concluded that the larger the plasma pool, the more likely it was to cause a hepatitis B infection. Twenty two percent of the men who received pooled plasma during the Korean War received hepatitis B infections. *The Philadelphia Enquirer*, *supra* at p.2, col.1. The cause and effect relationship between pooling plasma donations into one large vat and transmitting a virus from any one donor to many recipients was, by 1962, scientifically certain.

4) 1964 - Judith Graham Poole, M.D., reports a method of obtaining a plasma residue rich in factor VIII, known as "cryoprecipitate." Pool JG, Hershgold EJ, Pappenhagen AR, "High potency antihaemophilic factor concentrate prepared from cryoglobulin precipitate," *Nature*, 1964, 203:312.

5) 1969 - The first freeze-dried, anti-hemophilia clotting factor ("AHF") concentrates are sold on the market, and they are not heat-treated. *The Philadelphia Enquirer*, *supra*.

6) 1970 - the National Institutes of Health introduces a study published in the *Journal of the American Medical Association*, that warned that just one unit of hepatitis-contaminated plasma could contaminate an entire pool. Diluted ten million times, it was still infectious. *The Philadelphia Enquirer*, *supra* at p.2, cols. 2 and 3.

7) Mid-1970's - most American hemophilia patients were taking the freeze-dried concentrate that exposed them to thousands of plasma donors through the pooled plasma concentration system. Hepatitis B becomes the leading cause of death among American hemophiliacs. *The Philadelphia Enquirer*, *supra* at p.2, col. 3.

8) Mid-1970's - The federal government allows the continued sale of concentrate without any form of heat treatment but requires patient package inserts that warn of the risk of hepatitis B. *The Philadelphia Enquirer*, *supra*.

9) By 1974, studies had found a strong association between paid donors and hepatitis B. Paid donors were poorer and lived in particular urban areas more likely infected with disease. Goldfield, M. (1974).

10) By 1974, massive plasma pooling has begun. The plasma industry:

had devised a way to filter, concentrate, and mass produce cryoprecipitate in a freeze-dried (lyophilized) form that had a shelf life of 2 years. This product, commonly known as human antihemophilic factor concentrate or Factor VIII concentrate, was described by one manufacturer as making office treatment possible and being capable of preventing minor bleeds with prophylactic treatment.¹² The medical community and patients welcomed this convenience and eventually Factor VIII concentrates became home therapy, self-injected by the hemophiliac as needed. Thus, a new industry was born. The

¹²Citing Shanbrom, E., Fekke, T., & Tse, D. Hemophilia: Cryoprecipitate and factor IX preparation. *Modern Treatment of Hemophilia with a Potent, New AHF Concentrate*. 854-860.

commercial manufacturers eventually installed equipment in their plants to mix in excess of 20,000 liters of human plasma from approximately 20,000 paid donors who submitted to the plasmapheresis process.¹¹

Ring and Thomas, "Representing the Hemophiliac With AIDS," Courts, Health Science & the Law, Summer, 1991, vol.2, No.1, p. 175. "Thus, single-donor cryoprecipitate (collected from volunteers as a by-product of blood banks) was used less and less as the convenience products became widely available." *Id.* The difference between factor VIII concentrate and other blood components, however, was that

[u]nlike other plasma products, Factor VIII preparations were not pasteurized or treated in any manner to kill viruses present in the starting plasma. Because one donor could contaminate the entire pool [fn. omitted], the risk of viral transmission was increased in direct proportion to the number of donors represented in the starting plasma. Hepatitis transmission through use of Factor VIII concentrates became a known risk of the product.

Id.

11) 1976 - The federal government identifies problems associated with the use of clotting factor concentrates, citing the FDA's definition of safety for biologic products: "Safety means the relative freedom from harmful effect to persons affected by a product when prudently administered, taking into consideration the character of the product in relation to the condition of the recipient at the time." The Philadelphia Enquirer, *supra*.

12) 1978 - German drugmaker Behringwerke AG begins pasteurizing clotting factor concentrate to kill blood-borne viruses. The stability process is described in U.S. patent # 4,297,344 (Schwinn et al, assigned to Behringwerk dated October 27, 1981); Leonard Ring, "Representing the Hemophiliac with AIDS" Courts, Health Science and the Law, Summer 1991, vol.2, No. 1, p.175.

The [U.S. plasma] manufacturers claimed that Factor VIII concentrates could not be heated to reduce viral transmission. This is incorrect. While the Factor VIII protein is heat labile -- it loses its clotting ability when heated--a foreign manufacturer, Behringwerke of Germany, had by 1979 stabilized the Factor

¹¹referring to information "elicited from certain employees of manufacturers in deposition testimony taken in Poole v. Alpha, 86 C 7623 (N.D. Ill.) " Ring and Thomas, *supra*, at p.182, fn.14.

VIII protein so that it resisted the destructive effects of high temperatures. [fn. omitted]

Thus, technology was available. In 1981, Behringwerke was granted a patent in the United States for its pasteurization process applicable to Factor VIII concentrate [fn omitted]. (Pasteurization had long been used by the U.S. manufacturers to kill virus present in albumin, another commercially made plasma product.) This technology applicable to Factor VIII concentrates was ignored by the U.S. manufacturers. The likely reason is an economic one. Pasteurization significantly reduces the yield of concentrate obtained from starting plasma. Because economics of the plasma industry dictate that you don't waste plasma fractions, reduction of yield is undesirable from a profit perspective.

Id. at p. 176. The Ninth Circuit Court of Appeals agreed.

The technology for heat treating blood was developed in the late 1970s. The record reflects some dispute as to whether the technology was available in the early 1980s to heat treat Factor VIII specifically. However, it appears that the technology definitely was available by March 1983.

Doe v. Cutter Biological, Inc., 971 F.2d 375, 384 (9th Cir. 1992).

13) 1982 through 1983 - U.S. pharmaceuticals begin development of the first U.S. heat-treatment method.

In July 1982, when three cases of AIDS had been reported in hemophiliacs, the FDA urged the commercial manufacturers to focus on developing a heat treatment process for Factor VIII, ostensibly to reduce the risk of hepatitis B transmission. By November 1983, one manufacturer had received FDA approval for a dry heat process whereby the freeze-dried concentrate, already in its shipping vials, was placed en masse into large ovens and heated at a fixed temperature for a fixed number of hours. [footnote omitted] By February 1984, the other manufacturers had received FDA approval on similar processes, with individual variations. Also by early 1984, one of the manufacturers had not only been granted a patent [footnote omitted] but obtained FDA approval on a method of heating the

freeze-dried concentrate in a solution. Thus, when requested to act, the industry responded relatively quickly.

The pasteurization process patented by Behringwerke, however, remained unused by the U.S. manufacturers until 1986 despite clinical studies conducted in Germany showing that pasteurized concentrates had not transmitted hepatitis [footnote: Heimburger, N., Schwinn, H., & Mauler, R. (1980). Factor VIII concentrate--hepatitis safe; Progress in the treatment of hemophilia. *Die gelben Hefte*, 4, 165-174] to users. Moreover, pasteurization was known to kill hepatitis B, a hardy virus. [footnote: *Supra*, note 31] Today, the dry heat process is no longer used. [footnote: Mannucci, P.M., & Colombo, M. (Oct. 1, 1988). Virucidal treatment of clotting factor concentrates. *Lancet*, 782-785.

Ring and Thomas, *supra*, p. 181.

14) 1983 - The FDA approves the first heated clotting factor drug in March 1983. Baxter's method heated the clotting factor at 140 degrees Fahrenheit - as had been done with albumin since the 1940's - for 72 hours. Refinements in the process protected the clotting proteins from heat destruction, as had been done in Germany since 1979. *The Philadelphia Enquirer, supra*. The "dry" heat treatment process of lyophilized (dehydrated) Factor VIII clotting factor concentrate is described in U.S. Patent # 4,456,590, June 26, 1984 (Rubenstein) filed May 13, 1982. The pharmaceuticals discover from this experience with heat-treatment that HIV is even more susceptible to heat than is hepatitis.¹⁴ Goedert, *et al.* *The New England Journal of Medicine*, October 26, 1989, 321:17: "[t]he nearly complete elimination of new HIV-1 seroconversions since 1986 among persons with hemophilia demonstrates the effectiveness of these measures in preventing the transmission of HIV-1." [footnote: "Survey of non-U.S. hemophilia treatment centers for HIV seroconversions following therapy with heat-treated factor concentrates *MMWR*, 1987; 36:121-4.] *See also*, K. Schimpf, M.D., *et al.* "Absence of Anti-Human Immunodeficiency

¹⁴*New England Journal of Medicine*, Oct. 26, 1989, p. 1145:

The majority of persons with hemophilia or related disorders became infected with HIV-1 through the use of commercial clotting-factor concentrates that were manufactured before the start of self-exclusion of donors with risk factors for AIDS, HIV-1 antibody screening, and the development of viral-inactivation measures such as the heat treatment of factor concentrates. (footnote omitted). The nearly complete elimination of new HIV-1 seroconversions since 1986 among persons with hemophilia demonstrates the effectiveness of these measures in preventing the transmission of HIV-1.k:

Virus Types 1 and 2 Seroconversion After the Treatment of Hemophilia A or Von Willebrand's Disease With Pasteurized Factor VIII Concentrate," *The New England Journal of Medicine*, October 26, 1989, pp. 1148-1152. In Israel, only heat-treated factor VIII concentrate was used as of January 1984. Shlomit Orgad, *et al.* "Antibodies to HIV in Israeli Hemophiliacs: Relationship Between Serological Profile and Disease Development," *AIDS Research and Human Retroviruses*, Volume 3, Number 3, 1987, p.323. "The decline in the rate of seroconversion [in Israel] can be attributed to the replacement of NHT fac VIII concentrate with heat-inactivated factor VIII (HT fac VIII) concentrate by November 1983." *Id.*

15) 1985 - FDA approves a solvent-detergent method of purging viruses from plasma developed by Bernard Horowitz and Alfred Prince of the New York Blood Center. Today that pasteurization process is a world standard of care. Horowitz later admits that the major concern and reluctance to using heat treatment as early as the German pharmaceutical was caused by a concern over losing the potency of the clotting factors. He concluded that this later proved to be less of a problem than was expected. *The Philadelphia Enquirer, supra* at p.2, col.4.

16) February, 1987 - J. Garrott Allen, now a retired head of surgery at Stanford, testifies at a deposition that "No medical, economic or social reason could justify ever using . . . unheated, pooled plasma or its clotting products . . . [l]arge pools are highly profitable, but they are medically bankrupt." *The Philadelphia Enquirer, supra* at p.2, col.4. He also testifies later that year that he first informed the U.S. army of the benefits of heat-treating plasma in 1940. *The Philadelphia Enquirer, supra* at p.3, col.1.

Indeed, the pharmaceuticals had possessed the ability for several years to heat-treat clotting factor, but because of their perception that it was not an effective method against hepatitis, it was not used until the presence of HIV in the blood supply was recognized.

Heat-treated clotting factor concentrates were developed several years ago with the unfulfilled goal of decreasing hepatitis infectivity of factor concentrates. These products have been commercially available, but were not widely used until two studies showed that HIV is heat-sensitive (McDougal *et al.*, 1985b; Spire *et al.*, 1985). The virus was non-detectable when treated according to commercial manufacturers' various specifications (McDougal *et al.*, 1985b).

Janine M. Jason and James W. Curran, "The Epidemiology of AIDS," *Blood, Blood Products and AIDS*, edited by R. Madhok, MD, C. D. Forbes, MD (Glasgow U.), and B.L. Evatt, MD (CDC), 1987, p. 9.

17) 1993 - Charles M. Heldebrant, director of research and development for pharmaceuticals for Alpha, testifies that his company never worked on killing viruses until mid-1982. The directive to begin heat treatment came not from the medical leadership of Alpha or from the FDA, but from Alpha's marketing department, which sought to stay current with its German competitor, Behringwerke. It took Alpha only 3 to 4 months to develop the process. When asked under oath what technology he had used that could not have been developed years earlier, Heldebrant replied "Absolutely nothing." The Philadelphia Enquirer, *supra* at p.3, col.1.

The Ninth Circuit Court of Appeals concluded from similar facts that

It is possible that had the industry concentrated on applying knowledge about heat treatment to the treatment of Factor VIII, that technology could have become available at an earlier date. Heat treatment was never used by the industry during the period at issue in these cases. Since the treatment is 100% effective in destroying HIV, the process could have been an important tool in ensuring the safety of blood products.

Doe v. Cutter Biological, Inc., 971 F.2d 375, 384 (9th Cir. 1992).

18) 1993 - FDA Commissioner David Kessler testifies before a House subcommittee that his commission erred in its relationship with the blood industry, but that "those days are behind us." However, he also testified that when his own wife underwent surgery, she stored and then used her own blood instead of risking the use of the national blood supply. The Philadelphia Enquirer, *supra* at p.3, col.1.

B. Conclusion: The FDA Failed to Require a Pasteurization Process That Would Have Prevented a Substantial Amount of HIV Infection.

In sum, the technology to inactivate hepatitis, and therefore HIV, existed during the 1970s and was indeed in commercial use in Germany in 1979. Additionally, the scientific information concerning the risks of hepatitis from paid donor blood that was pooled and then sold were well known by 1974. Nevertheless, the FDA did not require heat treatment of clotting factor to destroy the hepatitis B virus, which would also have destroyed HIV and prevented all but a small percentage of infections occurring among patients, ironically, who used not cryoprecipitate instead of clotting factor concentrate. This latter group would have subjecting themselves to the same risks faced by the general population relying upon standard blood supply safety procedures.

SECTION THREE:

THE FDA FAILED TO REQUIRE THE FOLLOWING PROCEDURES RESULTED IN EXTENSIVE HIV INFECTION AMONG THE U.S. HEMOPHILIA COMMUNITY: 1) WARNINGS OF THE RISKS OF AIDS ISSUED TO USERS OF CLOTTING FACTOR CONCENTRATE; 2) SURROGATE TESTING FOR HIV BY TESTING FOR THE HEPATITIS B CORE ANTIBODY TO ELIMINATE HIV-CONTAMINATED BLOOD; AND 3) BLOOD DONOR QUESTIONNAIRES INQUIRING ABOUT SEXUAL PRACTICES.

The following information is intended to demonstrate the FDA's failure to take appropriate actions in the form of the above three categories of conduct suggested by the CDC and other organizations at pertinent times.

1) June 1981 - the Centers for Disease Control ("CDC") identify 26 homosexual men with opportunistic diseases in Morbidity and Mortality Weekly Report.

2) January 1982 - the CDC receives the first report of a hemophilia patient with Pneumocystis carinii pneumonia. Terence L. Chorba and Bruce L. Evatt, "Transfusion-associated AIDS," Blood, Blood Products and AIDS, edited by R. Madhok, MD, C. D. Forbes, MD (Glasgow U.), and B.L. Evatt, MD (CDC), 1987), p. 16.¹⁵

3) July 16, 1982 - The first case, along with the second and third cases of Pneumocystis carinii pneumonia among persons with Hemophilia A are reported in the July 16, 1982 MMWR. Patient 1 "had frequent injections of Factor VIII concentrate for severe hemophilia for many years." Patient 2, "[a]s a patient with severe hemophilia . . . had received received frequent injections of Factor VIII concentrate for several years." Patient 3 "had frequently received parenteral Factor VIII concentrate for severe hemophilia." "[T]he second and third patients were found by the CDC through routine surveillance of requests in June and July of 1982 for drugs available only from CDC to treat P. carinii pneumonia."

¹⁵The expertise of the CDC in epidemiology and the pre-eminent position of the MMWR as a pathology reporter was already well-known; its expertise in AIDS reporting also would quickly become known. Moore v. Armour Pharmaceutical Co., 927 F.2d 1194, 1196 (11th Cir. 1991).

The CDC, with the help of doctors, regularly compiles publications that represent its position on advancements in AIDS research. Input from many different physicians and researchers is printed in these publications. The publications do not necessarily represent the opinions of all the different researchers; rather, the CDC will formulate what it feels is the most accurate position, then publish it.

Terence L. Chorba and Bruce L. Evatt, "Transfusion-associated AIDS," Blood, Blood Products and AIDS, edited by R. Madhok, MD, C. D. Forbes, MD (Glasgow U.), and B.L. Evatt, MD (CDC), 1987, p. 16. Indeed, "[a]ll had been treated with large doses of commercially prepared lyophilized factor VIII concentrates as part of the treatment of their coagulation defect: Two of the three received transfusions for prophylaxis almost daily, and the third received them every four to five days." Menitove, M.D., et al. New England Journal of Medicine, January 13, 1983, 308:2, 83.

In that report, the CDC described perhaps the single most significant investigative finding in the early infection period of the hemophilia community that should have enabled the FDA to recognize and warn of the widespread contamination of the clotting factor concentrate supply:

For each patient, records of the administration of Factor VIII concentrate were reviewed to determine manufacturer and lot numbers. No two of the patients are known to have received concentrate from the same lots. (emphasis added)

MMWR, *supra*. Even that understated the extent of the varied factor VIII concentrate usage.

One patient used concentrates prepared by six different manufacturers; another, concentrates prepared by five manufacturers; and a third, concentrates prepared by three or four. None used the same lot of factor VIII concentrate.

Menitove, et al. *supra*. The CDC stated in that MMWR issue, *supra*, that:

Although the cause of the severe immune dysfunction is unknown, the occurrence among the three hemophiliac cases suggests the possible transmission of an agent through blood products.

This conclusion was based upon the fact that:

Inquiries concerning these initial patients' sexual activities, drug usage, ethnicity and travel or residence provided little evidence that the disease could have been acquired by contact with homosexuals, illicit drug abusers or Haitian immigrants. The hypothesis that AIDS developed in these patients as a result of an infectious agent transmitted by the blood products' administration seemed logical and research for the occurrence of disease in transfusion recipients intensified. Soon it became clear that AIDS was a major problem for blood banks and the plasma industry.

Terence L. Chorba and Bruce L. Evatt, "Transfusion-associated AIDS," Blood, Blood Products and AIDS, edited by R. Madhok, MD, C. D. Forbes, MD (Glasgow U.), and B.L. Evatt, MD (CDC), 1987, p. 16; *see also*, Menitove, *supra*, (the patients "were heterosexuals with no history of intravenous drug abuse"). This conclusion by the CDC, that a blood-borne agent might be at work, coupled with the fact that no two of the patients had received the same lots of concentrated clotting factor, meant that, as a result of the past experiences with hepatitis and pooled plasma, the three patients might represent several hundred infections.¹⁶ Thus, the CDC and the FDA had sufficient information to know that the entire community of severe hemophilia patients was at immediate risk of infection with the agent causing this potentially fatal immune suppression.

The Superior Court of New Jersey wrote that, following the "red flag" raised by the July 16, 1982 MMWR, "[a]t least from that time forward, the CDC and others working in the field assumed as a working hypothesis that AIDS was caused by a blood-transmissible infectious agent." Snyder v. American Association of Blood Banks, 282 N.J. Super. 23, 659 A.2d 482, 486 (N.J. Super. A.D. 1995). That the AIDS virus was blood-borne was, at this time, "a belief most experts had come to share when the hemophiliac cases were reported. . . ." Snyder, 659 A.2d at 489.

4) July 27, 1982 - the CDC, FDA, NIH, the National Hemophilia Foundation, American National Red Cross, various blood banking organizations, National Gay Task Force, New York City Health Department and the New York Inter-Hospital Study Group on the Acquired Immune Deficiency Syndrome (AIDS) and Kaposi's Sarcoma (KS) met in New York City to discuss the significance of the occurrence of opportunistic infections with *Pneumocystis carinii* pneumonia (PCP) in three patients with hemophilia. The meeting produced the "Summary Report on Open Meeting of PHS Committee on Opportunistic Infections in Patients with Hemophilia."¹⁷

¹⁶June 5, 1983 - NYT, "Blood Donor Policy Revised Over AIDS," XXII, 4:5.

Each pool of Factor VIII concentrate goes to about 100 patients. For each hemophiliac diagnosed as an AIDS victim, there are 99 who received the same lot of Factor VIII concentrate. The 99 did not contract the illness but might do so. The incubation period for AIDS appears to vary from two months to two years and could strike any one of these 99 blood recipients at any time during that span. Because of the large number of donors who contribute to each pool of plasma, it is not possible to identify the infected donor.

¹⁷The three cases were reported in the MMWR. For a discussion of lay hemophilia community access to CDC information or to the MMWR, see fn. 18, *infra*. The MMWR was a for-purchase publication whose existence and scientific importance was unknown to most hemophilia patients. Generally, little of the information that circulated among government officials was available to the lay public. The House Committee on Government Operations reported in THE FEDERAL RESPONSE TO AIDS, November 30, 1983, p. 30:

Three hemophilia patients diagnosed with AIDS are discussed, and the Summary Report concludes:

II. F. * * * Hemophilia patients use large amounts of Factor VIII (40,000 to over 65,000 factor units per year) from multiple preparations with subsequent potential exposure to material derived from thousands of donors.

G. The occurrence of PCP in three patients with hemophilia is disturbing, particularly since there is no previous evidence that this infection is common in hemophilia patients. The two patients who had immunologic studies performed demonstrated a T-cell abnormality similar to that among other patients in other high-risk groups with AIDS/KS. There is no known intrinsic immune disorder in hemophilia patients that would permit or promote such opportunistic infections.

In light of the knowledge already acquired by the U.S. medical community of the hepatitis B infection rates for hemophilia users of concentrate made from pooled plasma, it is unreasonable for the FDA at this time to have failed to realize and announce the risk of HIV infection to patients who infused with concentrate, and to have failed to take other actions described in this Section.

Indeed, the hematology community understood the risk of factor concentrate for transmitting the AIDS virus, since "[c]linically, cases occurred in persons with no other risk factors and, initially hemophiliacs who had heavy use of Factor VIII were more apt to have ARC and AIDS." Dietrich, "Epidemiology of HIV Infection," Recent Advances in Hemophilia Care, 1990, pp. 80-81. The summary report stated that "AIDS had 'characteristics which suggest an infectious etiology,' and that a 'possible mode of transmission is via blood products.'" Smith v. Cutter Biological, Inc., 823 P.2d 717, 721, fn. 4, (Hawaii 1991). At the

For the first two years of the epidemic the Department [of Health and Human Services] failed to develop a plan and budget for discharging this responsibility [for public education] in a coordinated and comprehensive way. Between 1981 and mid-1983, the public education and information dissemination effort was largely comprised of disparate meetings and conferences, occasional articles in medical journals and news releases, interviews with the press, individual phone conversations, and the publication of articles in CDC's Morbidity and Mortality Weekly Reports (MMWR). [fn. omitted] The MMWR was the most systematic dissemination vehicle used for reporting surveillance and epidemiological information, but its circulation has been severely restricted by recent budget cuts. [fn. omitted] Between August 1981 and May 1982, even the MMWR contained no information on AIDS

which suggest an infectious etiology,' and that a 'possible mode of transmission is via blood products.'" Smith v. Cutter Biological, Inc., 823 P.2d 717, 721, fn. 4, (Hawaii 1991). At the meeting's conclusion, the FDA did not require any of the previously-described safety measures, nor did the FDA require the clotting factor concentrate manufacturers to issue warnings to hemophilia patients through patient package inserts or other methods designed to effectively communicate warnings about the risk of AIDS to clotting factor concentrate users.¹⁸

5) November, 1982 - The CDC issues safety guidelines for health care workers entitled: "Acquired Immune Deficiency Syndrome (AIDS): Precautions for Clinical and Laboratory Staffs." The guidelines state:

The etiology of the underlying immune deficiencies seen in AIDS cases is unknown. One hypothesis consistent with current observations is that a transmissible agent may be involved. If so, transmission of the agent would appear most commonly to require intimate, direct contact involving mucosal surfaces, such as sexual contact among homosexual males, or through parenteral spread, such as occurs among intravenous drug abusers and possibly hemophilia patients using Factor VIII products. [. . .] These patterns resemble the distribution of disease and modes of spread of hepatitis B virus, and hepatitis B virus infections occur very frequently among AIDS cases. (emphasis added)

The CDC's guidelines clearly reflected a knowledge that AIDS was transmissible by blood. For example, those guidelines included the following:

2. Gloves should be worn when handling blood specimens, blood-soiled items, body fluids, excretions, and secretions, as well as surfaces, materials, and objects exposed to them.

* * * *

4. . . . Hands should also be washed thoroughly and immediately if they become contaminated with blood.

5. Blood and other specimens should be labeled prominently with a special warning, such as "Blood Precautions" or "AIDS

¹⁸The November 30, 1983 Committee on Government Operations Report criticized the HHS information dissemination efforts: "Until the summer of 1983, HHS did little to disseminate information about AIDS to affected communities, to health care workers, and to other occupational groups that were likely to be in contact with AIDS." THE FEDERAL RESPONSE TO AIDS, House Report, Nov. 30, 1983, p.30.

Precautions." [...] All blood specimens should be placed in a second container, such as an impervious bag, for transport. The container or bag should be examined carefully for leaks or cracks.

6. Blood spills should be cleaned up promptly with a disinfectant solution, such as sodium hypochlorite (see above).

7. Articles soiled with blood should be placed in an impervious bag prominently labeled "AIDS Precautions" or "Blood Precautions" before being sent for reprocessing or disposal. Alternatively, such contaminated items may be placed in plastic bags of a particular color designated solely for disposal of infectious wastes by the hospital.

These guidelines reflect not merely a concern that AIDS was transmissible by blood, but a conclusion by the CDC that a blood borne agent was transmitting AIDS, and that health care workers needed to be warned and protected from blood contamination.

6) November, 1982 - The FDA did not relay the CDC's concerns to the hemophilia community and provide the same information to the known users of blood products, such as hemophiliacs, that the CDC was providing to persons who only potentially were exposed to contaminated blood, such as physicians, nurses and other hospital employees. Instead the FDA published an article that same month in its November 1982 issue of FDA Consumer concerning commercial blood banks that made no mention whatsoever of AIDS. The article contained language such as the following:

Around these needs [for blood] has grown a sophisticated industry that uses whole blood and its major components efficiently, and relatively safely, to improve human health.

"Blood: A Fluid You Can Bank On," FDA Consumer, November 1982, vol.16, No.9, p.1. The only mention of blood borne viruses in the entire article was of hepatitis B, the risk of which the FDA Consumer minimized.

One problem involving blood transfusion is not yet completely solved. A viral infection of the liver called hepatitis can be transmitted in whole blood, plasma and some plasma products. The infection can be mild and virtually without symptoms, but more serious infections can lead to chronic liver disease, including cirrhosis. There also has been evidence linking at least one type of the disease, hepatitis B, with an increased risk of liver cancer.

Hepatitis B strikes an estimated 200,000 Americans, primarily young adults, each year -- with about a tenth of the cases linked to transfusions. Of the unfortunate 1 percent of hepatitis B victims whose disease is extremely severe, about half die.

Since 1972 FDA has required all blood and blood products to be tested for hepatitis B. Labels of products for transfusion must indicate whether they come from paid or volunteer donors, since blood from paid donors carries a significantly higher risk of post-transfusion hepatitis.

Id. Despite the warnings of the most prominent epidemiological research institution in the world, the CDC, the FDA ignored the CDC's warnings and published a contrary article the same month that the CDC published its blood safety guidelines concerning AIDS. The fact that the FDA acknowledged the dangers associated with paid donor blood suggests that these choices of article composition and timing of publication were intentional.

7) December 3-4, 1982 - The Blood Products Advisory Committee of the Office Of Biologics, the National Center for Drugs and Biologics, the Food and Drug Administration, meets in Bethesda, Maryland. While there were approximately fifty total participants and observers at the meeting, the official members present were: Joseph R. Bove, Chairman, Elizabeth Hasleigh, Ronald D. Miller, William V. Miller, James W. Mosley, John W. Suttle, James G. White, and Dorothea Zucker-Franklin. The summary minutes for the meeting were approved and adopted on February 7, 1983. The following minutes prove particularly relevant.

26. Dr. Jay Menitove, Blood Center of Southeast Wisconsin, Milwaukee, WI, reported on a series of studies conducted in hemophiliacs, some of whom had received AHF concentrate and others who had only received Cryoprecipitated Antihemophilic Factor. Measuring the T4/T3 cell ratio in each group, he found that the ratio was lowered in the patients receiving AHF. Similar changes had been found in patients with AIDS. His study included 42 patients, 9 in the cryoprecipitate treated group and 33 in the AHF group. One of the 9 patients in the cryoprecipitate group had an altered T4/T3 ratio as did 16 of 33 in the AHF group. Among the patients in the AHF group, no correlation was found suggesting a dose response relationship.

27. Dr Bruce Evatts, Centers for Disease Control, Atlanta, GA, briefed the committee on the current status of their investigations on AIDS. He stated that the epidemic is rising at an almost

exponential pace, with 788 domestic cases and about 50 foreign cases reported since mid-1979. The incubation period, as determined from about 35 cases where person-to-person transmission has been documented, is about 4 to 7 months with a prodrome before diagnosis of about the same period. The epidemiologic pattern seems to be similar to that of hepatitis B. Cases are now appearing among contacts of persons in the high risk groups.

Eight hemophilia patients receiving AHF have now been reported with AIDS, 3 of which are still alive. About 5 AIDS cases have been reported within the past 18 months in patients following blood transfusions. One confirmed case was a child who received an exchange transfusion at birth, was healthy following that, and then developed AIDS. One donor subsequently was diagnosed with AIDS seven months after the donation. Dr. Evatts expressed concern that transfusion associated with AIDS may follow the same increasing pattern seen with hemophilia patients.

28. The foregoing information suggests that Cryoprecipitated Antihemophilic Factor (cryo) may be preferable to AHF concentrate and that AHF requirements should be modified to include an inactivation procedure during processing. Several disadvantages with either of these alternatives were discussed. With cryo, there are problems of convenience to the patient and processing distribution difficulties among others. For AHF, most techniques to reduce infectivity will reduce the yield of Factor VIII, will increase its costs and possibly cause shortages of the product. Concerns about this latter point were expressed, noting that about 10% of the present hemophilia patients without hepatitis B markers (but all new patients) might benefit if hepatitis B infectivity were eliminated. For the new patients, there is now an effective vaccine available. Some participants preferred to leave the products as they are unless it could be shown that AIDS is absolutely related to HBV, stating that problems with HBV are not that severe now.

29. As the meeting concluded, there was a sense of urgency because of the continuing spread of AIDS and because of its long incubation time. There were suggestions for immediate steps to reduce the risk since definitive answers are not yet available. These include increasing reliance on cryo, developing less infectious Factor VIII and IX products, excluding potential high risk

donors, and adopting additional screening tests for infectious markers in donor blood. At the next meeting of the committee, closed sessions with the manufacturers will be scheduled to evaluate their efforts to prepare less infectious products. A meeting on tests to prevent transfusion transmitted hepatitis is also planned.

30. The committee did not recommend any immediate changes in the biologic regulations or regulatory activities at this time. Several investigations are being intensely pursued by the blood bank community, CDC, NIH, FDA, and the manufacturers which may lead to steps to reduce the risk to recipients of blood products. (emphasis added)

31. Although a closed meeting was scheduled for this meeting, none was held. The meeting adjourned at 3:30 p.m., December 4, 1982.

8) December 10, 1982 - The New York Times describes a report by the CDC of the fifth case of AIDS caused by a blood transfusion, including one of a hemophilia patient "who require[d] frequent transfusions of a blood clotting factor."¹⁹ The CDC report stated that "[t]his and continuing reports of AIDS among persons with hemophilia A raise serious questions about the possible transmission of AIDS through blood and blood products." What little the FDA might have failed to understand regarding the CDC's perception of the threat should have been clarified by the article. The Superior Court of New Jersey wrote that "from the point of view of CDC, the assumption that AIDS was caused by a blood-transmissible virus became a matter of high probability when it reported, in December, 1982, that an infant had died of AIDS in California after having been transfused at birth with blood from a donor who had himself subsequently died of AIDS." Snyder v. American Association of Blood Banks, 282 N.J.Super. 23, 659 A.2d 482, 486 (N.J.Super.A.D. 1995). Affirming the lower court opinion, and based on the case of that infant's seroconversion, and several others reported

¹⁹December 10, 1982 - NYT. "Infant Who Received Transfusion Dies of Immune Deficiency Illness," 1.22:3:

Altogether, the Atlanta centers have documented seven cases of the immunodeficiency disease in hemophilia patients since July. Five of the seven patients died. [...]

"These additional cases provide important perspectives on AIDS in U.S. hemophiliacs," the report said. "Two of the patients described here are 10 years of age or less and children with hemophilia must now be considered at risk for the disease. The number of cases continues to increase and the illness may pose a significant risk for patients with hemophilia," the report said.

among infants just one week later, the Supreme Court of New Jersey wrote that "by late 1982, the pattern for AIDS transmission was clear." Snyder v. American Association of Blood Banks, 1996 WL 290907 (N.J.).

9) January 1, 1983 - A retrospective of 1982 finds that

nine cases of the acquired immune deficiency syndrome (AIDS) were recognized in hemophiliacs. Eight of these individuals were previously healthy, and one had long-standing common variable hypogammaglobulinemia (1-3). All had classic hemophilia, and all had received antihemophilic (AHF) concentrates. These patients had in common severe deficiencies of their immune systems which included a persistent reduction in peripheral blood helper/inducer T-lymphocytes, with a reversal of the T-helper/inducer to T-suppressor/cytotoxic cell (H/S) ratio.

T. Vincent Shankey, PhD, et al. AIDS Research, vol. 1, No. 1 (1983), pp. 83-90.

10) January 4, 1983 - A followup meeting to the July 27, 1982 meeting is held by the CDC in Atlanta. See "Summary Report on Workgroup to Identify Opportunities for Prevention of Acquired Immune Deficiency Syndrome - January 4, 1983".²⁰ Epidemiological evidence from CDC investigations strongly suggests that blood and blood products transmitted the agent causing AIDS and that the disease could also be transmitted through intimate heterosexual contact.

²⁰The followup to both this blood advisory meeting and the July, 1982 meeting were notoriously poor. Bruce Voeller, PhD, and 1983 President of the Mariposa Education and Research Foundation, testified at the August 1 and 2, 1983 House Hearings before the Subcommittee of the Committee on Government Operations, FEDERAL RESPONSE TO AIDS, p. 173:

Dr. Bove [Yale Medical School and Yale-New Haven Blood Bank] and I both served on the two blood and AIDS panels held by the Government, as invited guests of the three governmental agencies, and neither of us has received any followup reports whatever. We have not even received the update bulletin that Secretary Heckler announced would be put out on AIDS, and indeed, I had to subscribe on my own to the MMWR published by the CDC, as was mentioned.

(See fn. 16, 18, *infra*, for a discussion of the unavailability of CDC information to the lay public.) If an invited panel member felt it necessary to complain about his inability to obtain printed summaries of information discussed there, or his need to use discretionary income to pay for a subscription to MMWR, one can imagine the difficulty of hemophilia community members to receive the same information about a meeting that generally they did not even know took place, or about a publication they generally did not know existed.

The conclusion that AIDS is blood-borne is based on two findings.²¹ First, AIDS was occurring in transfusion recipients and individuals with hemophilia who had received antihemophilic factor ("AHF") concentrate, and second, the epidemiologic pattern of AIDS is similar to hepatitis B, another blood-borne disease.

The Superior Court of New Jersey writes that, at the January 4, 1983 emergency workshop, "[t]he [CDC's AIDS] Task Force was convinced that AIDS was blood-transmissible." Snyder v. American Association of Blood Banks, 282 N.J. Super. 23, 659 A.2d 482, 486 (N.J. Super. A.D. 1995). The Snyder Court clarifies that it was not merely the CDC who believed that the AIDS virus was transmissible: "[t]he general tenor of the evidence as a whole justifies the inference that every responsible expert in the United States was convinced well before the end of 1983, and most well before the end of 1982, that AIDS was caused by an infectious, blood-transmitted agent." Snyder, 659 A.2d at 489.²² The New Jersey Court

²¹The Supreme Court of Colorado considered testimony regarding the state of knowledge of the blood borne nature of the AIDS virus at the time.

Doctor [Marcus] Conant served as co-director of the Kaposi's Sarcoma Clinic at the University of California from 1981 to 1985 and was director of the AIDS Clinical Research Center at the University of California from 1983 to 1985. Doctor Conant filed an affidavit stating that he was prepared to testify at trial to the following matters: as of January 1983 there was ample evidence available to the medical community and to national blood banks that the AIDS virus was transmissible in blood and blood products and that transfusion recipients were at risk of contracting AIDS if adequate precautions were not taken by blood banks in screening donors and performing surrogate test on donated blood; that as of January 1983 there was ample evidence that the highest risk groups for AIDS were homosexual males, intravenous drug users, Haitians, and hemophiliacs. . . .

United Blood Services v. Quintana, 827 P.2d 509, 512 (Colo. 1992).

²²Legal experts in the field, however, have placed the date at which knowledgeable and responsible parties, which would include the FDA, should have acted, much earlier, and as early as January, 1982.

The argument against foreseeability is straightforward--until the causative agent of AIDS had been identified in mid-1984, no scientific proof existed to support the hypothesis that AIDS was caused by a blood transmissible agent. Risk, by definition, however, is the possibility of injury and not its certainty. Scientific proof speaks to certainty, not risk. By January 1982, when the first report of an AIDS-related illness following concentrate injections was publicized, the risk of AIDS was not merely foreseeable but known. The legal duty to guard and warn against this specifically defined risk, therefore, came into being at this time.

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of Appeals elsewhere found that the Public Health Service Committee on Opportunistic Infections had issued a warning to the blood banking industry prior to the end of 1983 that AIDS was likely transmissible through blood products. Snyder v. Mekhjian, 244 N.J. Super. 281, 582 A.2d 307, 310 (N.J. Super. A.D. 1990). At trial in the Snyder case, Dr. Don Francis of the CDC testified as to the reaction by the blood banking industry to CDC's of blood transmissibility of the AIDS virus:

[T]he initial negativism, accepting such a thing as transfusion associated AIDS, and then the real hostility towards moving ahead and doing something, saying it was going to cost too much, it was going to cause too much trouble, was just a most unfortunate expression of AABB policy.

Snyder, 659 A.2d at 487, fn. 1. The Snyder Court found that, unfortunately, AABB policy was:

described by several of the expert witnesses as inordinately influential in setting national blood policy in the first half of the 1980's, a primary responsibility of the FDA, by reason of AABB's participation in the FDA's Blood Products Advisory Council and other agencies, councils, and committees charged with formulating national blood policy, and by reason, apparently, of its acknowledged expertise. Indeed, the Report of the Presidential Commission on the Human Immunodeficiency Virus Epidemic (June 1988) (HIV Report) concluded that one of the early obstacles to progress during the early years of the epidemic was the extent of governmental deference to industry views. The HIV Report states:

The Food and Drug Administration (FDA) has the responsibility to set the standards for the blood industry; however, it relies heavily on that industry for advice on what standards to set -- a relationship that presents a significant opportunity for conflicts of interest to arise.

Ring and Leonard, *supra*, p. 177. Warnings, such as appropriate patient package inserts, are not dependent upon scientific certainty of injury, and therefore the FDA should have required their use at this time.

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Snyder, 659 A.2d at 488-489. FDA policy was, to a large extent, AABB policy.

The afternoon of the January 4, 1983 meeting is "spent discussing the significance of the finding and the appropriate course of action." Summary Report, p. 1. At this meeting, the leading blood bank organizations are in attendance, and the blood industry vigorously opposes any required blood donor questionnaires or testing in blood samples for hepatitis B, which frequently accompanied and therefore revealed the presence of the AIDS- causing agent in the blood. The 1983 Summary Report states at page 3:

For example, if the presence of hepatitis B core antibody is used as a laboratory surrogate screening test:

1. In CDC's specimen file, 90 percent of known definite AIDS cases are positive for anti-Hbc and would be excluded as blood donors.²³

Under the lowest estimates by CDC officials since that time, surrogate testing for HIV by testing for the presence of the hepatitis B core antibody would have detected the presence of approximately seventy percent of the HIV among paid blood donors.²⁴ Nevertheless,

The FDA refused requests to perform surrogate tests on Factor VIII concentrate. [. . .] The FDA's position was that there was no data demonstrating that surrogate tests would prevent the spread of AIDS.

Gruca v. Alpha Therapeutic Corp., 51 F.3d 638, 644 (7th Cir. 1995).

²³ Ring and Thomas, *supra*, p. 182, further state:

The Hepatitis B Core Antibody test according to Thomas Spira, a member of the CDC staff in 1982, would detect 90% of high risk donors. The measurement of a donor's T-cells was also proposed as a "marker" test to screen high risk donors. This test was used by Dr. Edgar Engelman, Stanford U. Blood Center, beginning in July 1, 1983. See Report to Subcommittee on Oversight, (July 13, 1983).

²⁴ The Ninth Circuit Court of Appeals writes:

"[t]he fact that surrogate testing may not have guaranteed pure blood is not necessarily a defense to liability. There is strong indication that, at a minimum, surrogate testing would have seriously curtailed the amount of HIV infected Factor VIII. A safety measure need not be perfect before its use is considered necessary to satisfy the standard of care.

Doe v. Cutter Biological, Inc., 971 F.2d 375, 383 (9th Cir. 1992).

While it is possible that IV drug abusers might have been reluctant to disclose their IV drug history, particularly in the case of ongoing usage, the hepatitis B core antibody test was a unique opportunity to detect and destroy most of the HIV-infected blood donated by IV drug users, since the route of transmission for HIV most common among IV drug abusers also was a common route of transmission for hepatitis B. Hence, a tremendous opportunity to detect and eliminate HIV-infected plasma was missed.²⁵

The Snyder Court allowed the jury to view a 1986 "20/20" segment presenting testimony of a former FDA official who was specific in his estimation of the blood banking industry's influence over the FDA, which it was manifested in the FDA's choice not to adopt Hepatitis B core antibody testing:

JARRIEL: [voice-over]: Dr. Dennis Donohue disagrees. He was head of the FDA's division of blood and blood products from 1980 to 1986. That division regulates the blood industry.

DR. DENNIS DONOHUE, former FDA official: I thought the evidence was good that there was a correlation between anticore positive test results and those people that had been defined as being at risk for transmitting AIDS.

JARRIEL: Why couldn't you insist on that being used?

DR. DONOHUE: Well, we discussed this at an advisory committee meeting. My personal conviction was that it should be done. The committee that addressed it again said no. I thought the committee was heavily weighted, because there was no one on it who wasn't either industry or someone closely allied to industry.

JARRIEL: That sounds almost clubbish.

²⁵Smith v. Paslode Corp., 799 F.Supp. 960 (E.D.Mo. 1992).

The undisputed evidence in this case shows that no volunteer blood collector used the hepatitis B core antibody test as a surrogate marker for AIDS in 1983. [...] No federal agency or professional blood collection standard-setting entity, including the FDA and the AABB, ever required or recommended the use of a surrogate test for AIDS. Id. at par.9 ARC's testing policies and procedures in 1983 and 1984 satisfied the AABB standards, the FDA regulations and the United States Public Health Service recommendations.

DR. DONOHUE: I think it is clubbish. I think it, at times is too clubbish.

Snyder, 659 A.2d at 493-494, fn. 7. The Supreme Court of New Jersey found:

[a]s the record reflects, moreover, the AABB was a major player in both state and federal government in setting blood policy in the 1980s.

* * *

At stake for its members was a substantial financial interest in the regulation of the industry. In 1984, voluntary blood banks generated revenues of approximately one billion dollars.

Snyder v. American Association of Blood Banks, 1996 WL 290907 (N.J.) 1, 16-17. The New Jersey Supreme Court concluded that: "[n]othing other than its own self-interest and tragically bad judgment prevented the AABB from recommending surrogate testing." Snyder, 1996 WL, 1 at 18.

11) January 13, 1983 - The New England Journal of Medicine devotes several articles to the issue of AIDS and hemophilia. A study by Lederman, et al.,²⁶ concluded that "[t]he epidemiology of AIDS is suggestive of a blood-borne transmissible agent." The study also implicated concentrated clotting factor as posing a greater risk of infection than infusion with cryoprecipitate.²⁷ The same article reported that two of the cases of PCP reported in the July MMWR had resulted in fatality. The investigators found significant differences in immune system impairment in patients receiving concentrate as compared to those only receiving cryoprecipitate.

²⁶Lederman, M.D., Ratnoff, M.D., Scillian, Ph.D., Jones, Ph.D., and Schacter, Ph.D., "Impaired Cell-Mediated Immunity In Patients with Classic Hemophilia," NEJM, vol. 308, No. 2, p.79.

²⁷Lederman, M.D., et al., fn. 33, supra. The authors summarized the study results:

Our study was designed to examine the immune system of otherwise healthy patients with hemophilia who had received lyophilized antihemophilic-factor concentrates or cryoprecipitates and who might be at risk for the development of AIDS. In this study the results of both lymphocyte-subpopulation surface-marker assays and lymphocyte functional assays were found to be significantly abnormal in the group of patients receiving lyophilized preparations of antihemophilic factor.

When compared with controls, hemophiliacs treated with lyophilized antihemophilic factor had a relative decrease in helper T cells, a relative and absolute increase in suppressor T cells, and a depressed helper/suppressor T ratio. [...] Lymphocyte counts, cell-surface markers, and functions in the eight patients treated primarily with cryoprecipitate did not differ from those in controls.

Lederman, *et al.* *supra*, p. 82. The investigators conclude:

What are the possible explanations for the abnormalities in cell-mediated immunity among patients with hemophilia? Conceivably, abnormal cell-mediated immunity is part of the genetic hemophilia disorder, but this explanation is unlikely for several reasons. Until recently, hemophiliacs did not appear to be at greater risk for infections, other than those attributable to the administration of blood products. In addition, hemophiliacs treated only with cryoprecipitates had no demonstrable functional abnormalities in cell-mediated immunity. (emphasis added)

A more likely possibility is that the immune dysfunction is acquired. Active infection with hepatitis B virus is probably not responsible, since none of the 11 patients in the LYOPH group had demonstrable hepatitis B surface antigenemia. The cause of the immunosuppression in this population is not known; among patients with AIDS, however, epidemiologic evidence would implicate a blood-borne pathogen. Whether or not this putative immunosuppressive agent is responsible for the abnormalities in cell-mediated immunity that we have observed in healthy hemophiliacs and for the opportunistic infections recently described in this population remains to be determined. (emphasis added)

Lederman, *et al.* *supra*, p. 82. In the same issue of the *NEJM*, another study compared AIDS infection rates among patients using clotting factor concentrate versus those using cryoprecipitate.²⁸ The study first noted the extensive infusion histories with concentrated clotting factor for the three patients reported in the July 16, 1982 *MMWR*.

²⁸Menitove, M.D., Aster, M.D., Casper, M.D., Lauer, M.D., Gotschall, M.D., Williams, M.D., Gill, M.D., Wheeler, R.N., Piaskowski, B.S., Kirchner, B.S., and Montgomery, M.D., "T-Lymphocyte Subpopulations In Patients With Cryoprecipitate and Lyophilized Concentrates," *The New England Journal of Medicine*, vol. 308, No. 2, p. 83.

All had been treated with large doses of commercially prepared lyophilized factor VIII concentrates as part of the treatment of their coagulation defect: Two of the three received transfusions for prophylaxis almost daily, and the third received them every four to five days.

Id., p. 83. The article called further attention to the point subtly made in the *MMWR* article: the patients had all used different lots, and therefore, the AIDS-causing agent would have to be contained within not less than three different lots, potentially infecting hundreds of hemophilia patients.

One patient used concentrates prepared by six different manufacturers; another, concentrates prepared by five manufacturers; and a third, concentrates prepared by three or four. None used the same lot of factor VIII concentrate. Another case of *P. carinii* pneumonia and one of cryptosporidiosis occurring in patients with hemophilia A are currently being investigated (Evatt BL; personal communication).

Id. Once again, the difference in infection rates between users of clotting factor concentrate and cryoprecipitate was patently obvious.

The clustering of AIDS in patients with common sexual contacts and the occurrence of *P. carinii* pneumonia among users of factor VIII concentrates have led to speculation that AIDS may be transmitted to patients with hemophilia through factor VIII infusions. [footnote omitted] To evaluate this possibility we performed immunologic studies on healthy patients with hemophilia treated either with cryoprecipitate obtained from volunteer blood donors with commercially prepared, lyophilized factor VIII concentrates. Eight of 22 patients had abnormal T4/T8 ratios. None of the cryoprecipitate users and 57 per cent of the users of commercially prepared lyophilized concentrates had abnormal T4/T8 ratios ($P < 0.003$).

Id. The study concluded:

Our data are consistent with the possibility that commercially prepared lyophilized factor VIII concentrates can induce an AIDS-like picture, but a large number of patients must be studied before a definite conclusion can be drawn. . . . we urge those involved in the care of patients who use factor VIII concentrate to follow them

carefully for stigmata of AIDS and changes in immunologic status.

Id. at p.85. Hemophilia patients infusing with concentrate were actually under study for serologic conversion, without any awareness of the risks readily apparent at that time to readers of one of the most respected American medical journals.

Most astonishing in the candor of this issue of NEJM is the introductory article, summarizing the two studies contained in that issue and drawing a dramatic conclusion regarding the future of hemophilia care. First, the article made the obvious conclusion, which the interior studies nonetheless made reluctantly:

Patients receiving lyophilized commercial concentrates of factor VIII appeared more likely than those receiving cryoprecipitates to have abnormalities of T-cell subpopulations. In view of this finding, current modes of treatment must be scrutinized. Concentrates are prepared from pooled plasma from 2000 to 5000 donors, lyophilized, and packaged in vials containing 200 to 1200 IU (1 IU is equivalent to the activity in 1 ml of normal plasma) [footnote omitted]. Cryoprecipitate, on the other hand, is prepared in the blood bank from the plasma of individual donors; each bag finally contains about 100 units of factor VIII in a relatively small volume. The commercial preparation is more concentrated than the cryoprecipitate, and its unitage is more reliable, but the advantage of the cryoprecipitate is that the recipient is exposed to only one donor per bag. In the hemophiliacs studied, [footnotes omitted, referring to the interior articles] the difference between those receiving concentrate and those receiving cryoprecipitate does not seem to be explained by the fact that there was less treatment in the latter group, but one may wonder whether exposure to fewer donors is crucial.

Jane F. Desforges, M.D., "AIDS and Preventive Treatment in Hemophilia," The New England Journal of Medicine, Jan. 13, 1983, 308:2, p.95. The size of those pools was even larger, in all probability: "[i]n the case of commercially prepared products made from pooled human plasma, the donor/recipient ratio, on the average, is 20,000 to 1." Ring and Thomas, "Representing the Hemophiliac With AIDS," Courts, Health Science & the Law, Summer, 1991, vol.2, No.1, p. 174.²⁹ Desforges balanced both the convenience to the patient and the relative stress that a return to cryoprecipitate infusion therapy would place upon the nation's

²⁹ The commercial manufacturers eventually installed equipment in their plants to mix in excess of 20,000 liters of human plasma from approximately 20,000 paid donors who submitted to the plasmapheresis process. Ring and Thomas, supra, p. 175; see fn. 13, supra.

blood banks, and nonetheless concluded that a return to cryoprecipitate as the treatment of choice should be considered by patients undergoing the risk of infection.

Ease in obtaining the commercially prepared lyophilized concentrates of factor VIII has made the ambulatory program possible. The average patient requires about 40,000 units yearly, and provision of this amount of cryoprecipitate to each of the nation's 12,000 hemophiliacs would certainly stress the capacity of blood banks. It would also be difficult to design a home-infusion program with cryoprecipitate therapy, since the material must be stored in the frozen state. The present program has been extremely successful and would be given up by physicians and patients only with great reluctance. Yet it is time to consider doing so, even though we may not have enough evidence to demand such a radical change.

Id. The study concluded with an entirely new perspective upon the treatment of hemophilia.

The fact that hemophiliacs are at risk for AIDS is becoming clear. If the use of cryoprecipitate will minimize this risk, the current home-infusion program needs to be revised. The studies reported in this issue demonstrate in vitro abnormalities of immunoregulation, but the numbers are too small for definitive comparison of the risks of different modes of treatment. Unfortunately, the data are consistent with a greater potential for AIDS in the population treated with concentrate. Physicians involved in the care of hemophiliacs must now be alert to this risk. Preventing the complications of the present treatment may have to take precedence over preventing the complications of hemophilia itself. (emphasis added)

Id. This information was clearly sufficient to demand FDA action, which should have included, at a minimum, warnings to the community.³⁰

³⁰ The connection between concentrate usage and HIV was demonstrated again and again. Goedert, et al., "Antibodies Reactive With Human T Cell Leukemia Viruses in the Serum of Hemophiliacs Receiving Factor VIII Concentrate," Blood, vol. 65, No. 2, (February), 1985, pp. 492-495, described their study results:

These data demonstrate that HTLV III antibodies are detectable in the majority of hemophilia A patients, particularly those heavily treated with factor VIII concentrate. As of Oct (sic) 15, 1984, 49 hemophiliacs who did not have other risk factors have been accepted as AIDS cases by the Centers for Disease Control, including 45 patients with hemophilia A (classical

12) January, February, July and December 1983 - the FDA's Blood Products Advisory Committee meets to discuss blood collection and processing policies, including possible implementation of a surrogate test for HIV. According to the 1995 Study by the Institute of Medicine, the BPAC improperly did the following:

- a) accepted estimates that the risks of AIDS from blood transfusion was low ("one in a million"); and
- b) accepted advice that control strategies such as automatic withdrawal of AHF concentrate lots containing blood from donors suspected of having AIDS, or a switch from AHF concentrate to cryoprecipitate in mild or moderate hemophiliacs would be ineffective, too costly, or too risky.
- c) as a result, blood policy changed little in 1983.

This failure on the part of the FDA to act appears directly responsible for infection of hemophilia patients. The Institute of Medicine Report concludes:

- a) earlier implementation of either [donor screening questions about sexual preferences, particularly homosexual activities, and the use of an available surrogate test for hepatitis B core antigen (anti-HBc)] probably would have reduced the number of individuals infected with HIV through blood and blood products."

[and]

- b) when confronted with a range of options for using donor screening and deferral to reduce the probability of spreading HIV through the blood supply, blood bank officials and federal authorities consistently chose the least aggressive option that was justifiable. In adopting the limited approach, policymakers often passed over options that might have initially slowed the spread of HIV to individuals with hemophilia and other recipients of blood

hemophilia, factor VIII deficiency) and two with hemophilia B (factor IX deficiency). Estimating the hemophilia population from a 1980 Department of Health, Education, and Welfare survey, the cumulative attack rate of AIDS is six times greater for patients with hemophilia A (3.6 per 1,000 hemophiliacs). All 49 of these hemophiliacs with AIDS had been treated with lyophilized clotting factor concentrates. . . .

Id., pp. 493-494.

and products, for example, screening male donors for a history of sexual activity with other males and screening donated blood for the anti-HBc antibody. The Committee believes that it was reasonable to require blood banks to implement these two screening procedures in January 1983. The FDA's failure to require this is evidence that the agency did not adequately use its regulatory authority and therefore missed an opportunity to protect the public health." (emphasis added).

The questionnaires eventually used only went so far as to discuss high risk groups such as intravenous drug users, recent immigrants from Haiti, and those with early symptoms of AIDS or exposure to patients with AIDS; direct questions about high-risk sexual practices were not required.³¹ None of the donors were required to be directly questioned by blood bank workers.³²

13) February 6, 1983 - In the context of an article which might otherwise have alerted the hemophilia community or at least the lay press to the risks attendant the use of concentrated clotting factor, the Food and Drug Administration openly denied a linkage between blood and AIDS. *NYT*, "AIDS - A New Disease's Deadly Odyssey," VI, p.28.

In the spring of 1982, the C.D.C. received its first reports of AIDS in hemophiliacs. Some of these patients were probably exposed to the AIDS agent in a blood-clotting medication called factor VIII concentrate that is made from the blood of thousands of donors. Anywhere from 2,500 to 22,000 blood donors are used to make just one lot of this widely used product; one lot treats about

³¹Unquestionably issues of privacy entered into the decision-making process. However, "[t]o the extent that the conference participants permitted their own political and social views (however enlightened) to influence a public health decision, they acted irresponsibly." *Doc v. American National Red Cross*, 866 F.Supp. 242, 246 (D.Md. 1994).

³²These questionnaires were entirely voluntary. The U.S. District Court for the Eastern District of Missouri provided an example:

[I]n early 1983, Regional Blood Services began providing potential donors with a pamphlet entitled "What You Should Know About Giving Blood" and an insert entitled "An important message to all blood donors." *Id.* Donors were instructed to read the pamphlet and insert before donating blood. Moreover, donors were told they would be required to sign a statement indicating that they understood the information contained in the pamphlet and insert.

Smith v. Paslode Corp., 799 F.Supp. 960 (E.D.Mo. 1992).

100 patients. To date, the C.D.C. has received a total of eight confirmed reports of hemophiliacs with AIDS, six of whom have died. All used factor VIII concentrate rather than an older, less convenient blood product called cryoprecipitate, which is made from the blood of a handful of donors. In view of the AIDS threat some hemophilia experts are urging a return to cryoprecipitate, especially in mild or newly diagnosed cases.

* * *

One way to try to stop the syndrome from spreading is to keep the AIDS agent out of the nation's blood supply, if, indeed, a blood-borne virus is the culprit. Even that is still uncertain. "It's not clear at all that there's a new blood-borne virus involved," says Dr. David Aronson, director of the coagulation branch of the division of blood and blood products of the Food and Drug Administration. "I can't see anything different in the death patterns of hemophiliacs now from four years ago." As early as 1979, he says, five to 10 hemophiliacs a year were dying of unusual infections and cancers that today would be called AIDS, although the disease had not yet been identified. He theorizes that anticlotting medication itself might have an immune-suppressant effect. Dr. Aronson thinks the AIDS threat to hemophiliacs has been overstated. "It's more of a threat to change their treatment without thinking things through," he says. (emphasis added)

14) March 4, 1983 - In the March 4, 1983 edition of MMWR, the CDC writes that "Recently, 11 cases of unexplained, life-threatening opportunistic infections and cellular immune deficiency have been diagnosed in patients with hemophilia." "Prevention of Acquired Immune Deficiency Syndrome (AIDS): Report of Inter-Agency Recommendations," Morbidity and Mortality Weekly Report, March 4, 1983, 32:101-03. The CDC further concluded "Blood products or blood appear responsible for AIDS among hemophilia patients who require clotting factor replacement therapy" and that "[w]ork should continue toward development of safer blood product for use by hemophilia patients."

15) March 24, 1983 - "[T]he Food and Drug Administration issued a memorandum to 'all establishments collecting human blood for transfusion' and a separate memorandum to 'all establishments collecting source plasma.' The Food and Drug Administration at that point in time had not issued any regulations regarding AIDS, and the

March 1983 memorandum consisted of recommendations only." United Blood Services v. Quintana, 827 P.2d 509, 515 (Colo. 1992).

16) May 1, 1983 - The New York Times reports the discovery of a virus in the blood of persons with AIDS.

Evidence of an unusual virus has been found in up to one-third of blood samples from some victims of acquired immune deficiency syndrome, or AIDS, an immunological disorder that has killed about half of the 1,352 people known to have acquired it, according to the federal scientist in charge of investigating the epidemic.

Although scientists studying the disease are excited about the new research findings, they cautioned that the link between the virus and the disorder is far from certain and that they have no proof the virus causes AIDS. Other organisms are under study.

The virus is called human T-cell leukemia virus, or HTLV. It was detected in 25 to 35 percent of blood specimens of AIDS victims that were sent for testing at Harvard, according to Dr. James Curran, the epidemiologists heading the investigation at the Federal Centers for Disease Control in Atlanta. The virus was found in less than 5 percent of blood specimens from individuals who do not have AIDS and whose blood was used for purposes of scientific control, Dr. Curran said in an interview.

Lawrence K. Altman, "Rare Virus May Have Link With Immunological Illness," NYT, May 1, 1983, I, 26:1.

17) May 19, 1983 - The lay press attempts to call the attention of the government to the issue. ABC News aired a "20/20" episode which discussed AIDS, its threat to the blood supply and to hemophilia patients, and the relative nonresponsiveness of the federal government to the issue as a whole.

GERALDO RIVERA [voice-over]: Bothered by the apparently slow initial response to the AIDS epidemic, both [Representative] Waxman of California and Senator Moynihan of New York have introduced legislation requesting \$40 million a year for public health emergencies like AIDS. But Dr. Edward Brandt, the assistant secretary of health, is opposed.

DR. BRANDT: I oppose those measures because they're not needed.

RIVERA [voice-over] And Dr. Brandt is the Reagan administration official to whom all public health agencies report.

18) June, 1983 - The apparent complacency by the FDA Consumer magazine concerning AIDS continued. In contrast to these strong, but, within the hemophilia community, almost unknown, warnings by the CDC, the FDA Consumer merely noted:

The [AIDS] syndrome also has been observed in hemophilia patients who require routine injections of antihemophilic factor. The factor is produced from the pooled blood of many donors.

"Updates: Alert on AIDS", FDA Consumer, June 1983, p. 2.

19) June 5, 1983 - Despite the failure by the FDA to act, the blood banking industry was increasing certain that AIDS was blood-borne. NYT, "Blood Donor Policy Revised Over AIDS," XXII, 4:5:

Among the most vulnerable blood recipients are the thousands of hemophiliacs who rely on large amounts of plasma, processed into what is termed Factor VIII concentrate. Statistics reveal that AIDS-like illnesses were the second-leading cause of death among hemophiliacs nation-wide in the last year.

"There is little doubt that we are dealing with an infectious agent that is transmitted through the blood and through sexual contacts," said Dr. David Sencer, New York City's Health Commissioner.

20) June 17, 1983 - The epidemiological pattern of AIDS as a blood borne virus continued, still without FDA action. NYT, "AIDS Spreads Pain and Fear Among Ill and Healthy Alike," II, 4:2:

Thirteen hemophiliacs, who require regular blood transfusions, have also been infected, as well as 90 people who seem, at first glance, to fall into none of those classes of risk. In addition, 21 children, hemophiliacs or the babies of AIDS victims, have sickened, and some have died.

Cases Double in 6 Months

The figures are revised regularly, and health authorities say they lag half a month or more behind the actual caseload, in part because only a few states, including New York, require doctors to report AIDS victims. The national caseload continues to grow, roughly doubling every six months.

Dr. Harold Jaffe, investigating AIDS at the Centers for Disease Control, says the disease progressed to include a dozen people whose only apparent exposure was in receiving blood transfusions in surgery.

21) July 28, 1983 - The lay press reports on the inadequate public information telephone line, which meant that the hemophilia population did not have an adequate public information source to turn to. NYT, "AIDS Phone Line Expanding," I,12:5:

The Government's special telephone information number on acquired immune deficiency syndrome, or AIDS, has been swamped with 8,000 to 10,000 calls a day, so the system will be expanded from three to eight lines.

22) August 1, 1983 - Marcus Conant, professor of dermatology at the University of California Medical Center at San Francisco, and president of the board of directors of the National AIDS-KS Foundation, testifies before the House Subcommittee of the Committee on Government Operations, in FEDERAL RESPONSE TO AIDS, p.101, that AIDS was unquestionably blood-borne and that the federal response was overwhelmingly inadequate:

The first aspect is that we are dealing with a new sexually-transmitted blood-borne agent, probably a retrovirus, and that we have at our disposal the intellect, the abilities, the capabilities of isolating a virus, producing a vaccine and protecting a population not yet exposed who are at risk.

Dr. Conant further testified at those hearings:

The final statistic in this grim litany is that nearly 60 percent of the people who contract AIDS die from it. The disease, quite simply, is the most lethal infectious killer known to modern medicine, and it is on a rampage in this country.

In the face of this appalling specter, one would expect the government of the United States, the world's most affluent and technically advanced nation, to be sparing no resource in its fight stop AIDS. But as a physician and researcher who has worked with this problem from the beginning, I have to characterize the federal response to AIDS as bordering on the negligent.

Id. He testifies further on this point at p. 100:

As a second point, I suggested that you have been misled; that we have all been misled.

We heard a moment ago that the Government had only recently become aware of this problem.

I was invited to attend the first meeting held at Bethesda, National Institutes of Health, in the fall of 1981.

Everyone attending those meetings knew at that time what we were facing. We knew the type of disease we thought this was, a transmissible agent, probably blood-borne. (emphasis added)

Id., pp. 103-104. Dr. Conant was not alone in this estimation. The California Superior Court writes: "[a]s early as November 5, 1982, it was thought that the transmission of the agent would appear to most commonly require intimate direct contact involving . . . possibly hemophilia (sic) patients using blood clotting products." Raytheon Company v. Fair Employment and Housing Commission, 1988 WL 241125 (Cal. Superior), 1, 19.³³ One example cited by Dr. Conant was the failure of the government to demand blood screening, as compared to merely donor questionnaires.

Every American has an interest in seeing to it that the nation's blood supply is protected. Efforts must be made to develop reliable, scientific method of screening that supply for infectious agents such as AIDS. In recent months, as it has become suspected that AIDS may be transmitted through blood transfusions, the vast majority of gay men have taken themselves out of the pool of blood

³³Doc v. Cutter, 971 F.2d at 381.

Thus, although it is true that the virus was not isolated until 1984, there is evidence supporting appellants' claim that the industry strongly suspected the new disease was caused by a blood borne virus before 1984 and that means of testing the blood supply were both available and considered.

donors for the duration of this health emergency. Most blood banks have also cut back on blood drives in gay neighborhoods. But a policy of protecting the blood supply by screening donors, rather than blood, is ultimately shortsighted and ineffective. [. . .] As far as the nation's blood supply is concerned, the emphasis must therefore shift from the donor to the blood.

Id., p.113. Two conclusions emerge from this testimony; donor questionnaires for sexual practices would have been effective if adopted earlier, and the adoption of surrogate testing for the presence of HIV was so obvious based on the available scientific evidence that even those physicians not trained in hematology knew by mid-Summer, 1983, at the very latest, that surrogate testing was necessary.

23) August 5, 1983 - The New York Times reports that "[t]he number of cases of acquired immune deficiency syndrome that are reported weekly has more than doubled in the last six months," according to the CDC. The NYT article reported an increase in the number of new weekly reports of the disease to 53 a week in July, as compared to 24 a week in January and 11 per week in July 1982. The NYT article also reported the CDC's conclusion that "[o]ther groups considered high risks for the disease are people who take narcotics intravenously, recent Haitian immigrants and hemophiliacs. [. . .] researchers suspect it is spread through personal contact and by blood products."

24) August 22, 1983 - The hemophilia community held few options with regard to obtaining information from sources other than their physicians or from patient package inserts. The federal AIDS hotline, established July 1, 1983, is reported as receiving eight thousand calls per day on a total of eight lines. Only five thousand per day actually get through, with the remaining three thousand only getting busy signals. "Federal AIDS Hot Line Is Swamped by Callers," New York Times, August 22, 1983, I, 14:6. Critics said "the hot line should expand and provide workers with more training, but [Shelley Lengel of the United States Public Health Service] said there were no plans to expand the system because 'it wouldn't be cost-effective.'"

25) August 28, 1983 - The New York blood banking community, in the midst of attempting to quell what they perceive to be unwarranted concerns over AIDS, the blood supply, and particularly the risk of infection from donating blood, actually systematically attempt to deny family members the opportunity to donate blood for particular use with other family members anticipating surgery. NYT, August 28, 1983, Section 23, p.23, Col. 1.

[B]oth the American Association of Blood Banks and the American Red Cross have come out strongly against designated donations.

"We have had several people coming into the hospital for elective surgery who have said that they would like a family member to donate blood for their use," said Dr. William Schraft, director of the New Rochelle Hospital Medical Center's laboratories and blood bank. Dr. Schraft said he has tried to convince these patients that "our blood comes from the community and is good and that anyone suspected of having AIDS has been screened out."

26) August 31, 1983 - The American Red Cross recalled more than 5,500 vials of factor VIII concentrate because one donor had died of AIDS. "However, the Red Cross stressed that there is no scientific proof that AIDS can be transmitted by blood products." (emphasis added). The article did not contain any comment by the FDA.

27) September 2, 1983 - The New York Times reports the appearance of an AIDS cancer virus in the blood of hemophilia patients.

Traces of a cancer virus detected in AIDS victims have been found in hemophiliacs, researchers reported yesterday.

Doctors from the Harvard School of Public Health reported 12 percent of 172 hemophiliacs without AIDS showed antibodies against the virus, an indication they were infected with the virus at one point. Only 1 percent of a control group had it.

* * *

He said that finding the cause could help in research to fight the disease, which involves a breakdown of the body's immune system. Medical researchers believe the disease is transmitted by blood contamination and sexual contact.

UPI, "Virus Linked to AIDS is Found in Hemophiliacs," NYT, September 2, 1983, I, 13:1. Besides providing additional motivation for the FDA to reconsider its earlier estimates of the size of the HIV-infected U.S. hemophilia population, the findings also undercut the median midpoint of seroconversion estimates of September, 1982 by Eyster, Section Five, *infra*.

28) September, 1983 - The CDC and the FDA both publish information concerning hemophilia and HIV, but once again, the FDA minimizes the risk and ignores the implications of CDC recommendations to health care workers. In its September 1983 issue of FDA Consumer, the FDA fails to report the March 4, 1983 CDC conclusions that AIDS is transmissible by blood and that hemophilia patients using clotting factor concentrate were

at risk because of the method of pooling the plasma; the article instead presents the prospect of a blood borne agent as almost mere speculation:

The best evidence for transmission of AIDS through blood products is the occurrence of AIDS in a small number of hemophilia patients receiving large amounts of fact VIII, a clotting substance in blood.

"What the Experts Know About AIDS", FDA Consumer, September 1983, p.16. The article went on again to minimize the risk to concentrated clotting factor users and to emphasize the effectiveness of federal government efforts.

Factor VIII is extracted and concentrated from pooled blood plasmas donated by thousands of people, and it appears that in some rare instances the plasma has carried AIDS.

To insure the safety of plasma derivatives, FDA has collaborated with the U.S. Centers for Disease Control in examining 200 separate lots of clotting factor concentrate manufactured by the four major U.S. manufacturers and found none that contained detectable infectious viruses.

FDA Consumer, *supra* at p. 17. The latter statement is some of the best evidence of the FDA's intentional distortion of the risks to concentrate users. The statement is intended to be reassuring, but fails to mention that that was no direct test for the AIDS virus in existence at that time.³⁴ Testing for the HTLV virus was still under investigation, and could not have been among the viruses which the FDA sought to detect. The other marker for AIDS, alpha interferon, was for the first time reported as used in hemophilia patients in the August 31, 1983 NYT.

³⁴The September 8, 1983 New York Times quoted M. Elaine Eyste, M.D., of the Pennsylvania State University Medical School: "We do not have a test for AIDS." (Section I, p.20, co. 6). Doe v. Miles Laboratories, Inc., 927 F.2d 187, 190 (4th Cir. 1991) ("Not until March 2, 1985, did the Secretary of Health and Human Services license the Enzyme-Linked Immunosorbent Assay ('ELISA test') as the first test to screen blood and plasma for HIV antibodies"). Doe v. Miles, 927 F.2d at 191.

... at the time the Koyne was administered in September of 1983, there was no way to determine whether a particular unit of blood was contaminated with the HIV virus. The parties agree that an approved test to identify the presence of the HIV virus was not available until 1985 with the development of the ELISA test.

"An additional test for AIDS, called the 'Western Blot test' was licensed for use by the FDA in mid-1987. Thereafter, the Western Blot test became the standard confirmatory test." Doe v. Cutter Biological, A Div. of Miles, Inc., 852 F.Supp. 909 (D. Idaho 1994).

Further, in a devastating indictment of the FDA's timing of its articles concerning hemophilia and HIV,³⁵ Science magazine published an HTLV study, reported in the September 2, 1983 NYT, that found traces of antibodies to a rare form of leukemia in 12% of hemophilia patients, as compared to 1% of a control group. Previous studies had found 36% of men with AIDS had such viral antibodies called HTLV. Additionally, not all of the 172 hemophilia patients tested in the study had severe hemophilia. Since the severe portion of the community infused much more than the remainder of the patients, those figures frequently could have been expected to be low for severe patients. Accordingly, there was physical evidence of a statistically significant rate of infection of the hemophilia population without immediate symptoms. This justified notification of AIDS risks to concentrate users, but the FDA was silent.

In stark contrast with the FDA article, that same month the CDC issued additional health care guidelines, this time for dental workers, morticians and persons performing postmortem examinations. "Acquired Immunodeficiency Syndrome (AIDS): Precautions for Health-Care Workers and Allied Professionals," Morbidity and Mortality Weekly Report, September 2, 1983, 32:450-51. In that issue of MMWR, the CDC states that "AIDS appears to be transmitted by intimate sexual contact or by percutaneous inoculation of blood or blood products," and that

³⁵The FDA is responsible for disseminating information and for requiring warnings that are reasonable in the context of information appearing in the media concerning relevant medical information. The United States District Court for the Northern District of Iowa sought to determine whether the United States was liable for injuries from vaccination for the swine flu vaccine under a theory of strict products liability. Brazzell v. United States, 633 F.Supp. 62 (N.D. Iowa 1985). That theory of torts incurs potential liability for a manufacturer of a product regardless of the risk of foreseeability of a particular injury; the hemophilia community could pursue a separate tort theory of negligence against the FDA if exempted under the Federal Tort Claims Act, 28 U.S.C. §§ 2671, *et seq.*, since the CDC's warnings and documented cases of AIDS arguably made the risk foreseeable, and accordingly would not need to rely exclusively upon a strict liability theory. In determining whether the FDA's required warnings concerning the 1976 swine flu vaccine were inadequate, the Brazzell Court took into account the media's presentation of the issues.

Prior to her doctor's appointment to receive the swine flu shot, plaintiff read newspapers and magazines that said there was a strong possibility of a swine flu epidemic. Plaintiff also saw the President on television, supposedly getting the first shot in the government's immunization program (partial transcript of proceedings, pp. 24-25, 77-78). In light of her prior health problems, plaintiff believed that taking the flu shot was the "lesser of two evils" (partial transcript of proceedings, p. 25).

Brazzell v. United States, 633 F.Supp. 62, 66 (N.D. Iowa 1985), remanded for reconsideration on strict liability grounds. Brazzell v. United States, 788 F.2d 1352 (8th Cir. 1986); reversed and remanded on strict products liability grounds. Brazzell v. U.S., 880 F.2d 84 (8th Cir. 1989). The Brazzell holding is quite applicable in the case of the FDA's response to HIV and factor concentrate, since the FDA itself was a willing participant in the media's low estimation of the risks of HIV from blood transfusion.

Caution should be exercised in handling secretions or excretions, particularly blood and body fluids, from the following: (1) patients who meet the existing surveillance definition of AIDS [footnote omitted]; (2) patients with chronic, generalized lymphadenopathy, unexplained weight loss, and/or prolonged unexplained fever when the patient's history suggests an epidemiologic risk for AIDS [footnote omitted]; and (3) all hospitalized patients with possible AIDS.

Id.

29) September 9, 1983 - Science Magazine, "Antibodies to Human T-Cell Leukemia Virus Membrane Antigens (HTLV-MA) in Hemophiliacs," p. 1061, 1063, reports on the prevalence in asymptomatic hemophilia patients of antibodies to a virus common in AIDS patients, and concludes:

Hemophiliacs represent one of the major risk groups for development of AIDS (2, 3, 10). They may receive blood elements from tens of thousands of donors in a relatively brief period of time and they frequently receive both blood and blood products (10). The likelihood that blood from healthy HTLV-carrier individuals may be present in the donor pool thus seems high. (emphasis added)

30) September, 1983 - Armour submits a request to the FDA for the first time to change its Factor VIII labels to include an AIDS warning. Walls v. Armour Pharmaceutical Co., 832 F.Supp. 1467, 1484 (M.D.Fla. 1993). Not until January 25, 1984 did the FDA approve this labeling change. Walls, 832 F.Supp. at 1484.

31) November 2, 1983 - New York Times, II, 24:1. The FDA announces Cutter Laboratories' withdrawal of 16 lots of clotting factor containing plasma donated by a man who died of AIDS the previous month. Without describing any of the risks posed to users of clotting factor concentrate, Dennis Donohue, director of the FDA's division of blood products in the Office of Biologics, said that the man "lied" when asked by the center if he belonged to any of the high-risk groups that have been primarily identified with AIDS." Instead of providing a warning to hemophilia patients from the use of concentrated factor, the article instead provided a forum for Cutter to minimize the risk:

"We did this to assure the country's 15,000 to 20,000 hemophiliacs that we were taking every precaution even though there is no evidence that AIDS is transmitted this way," Mr. Modersbach [spokesman for Cutter] said.

32) December, 1983 - The FDA approves warnings of the risk of AIDS on the labels of Factor VIII concentrate for the first time. Gruca v. Alpha Therapeutic Corp., 51 F.3d 638, 644 (7th Cir. 1995).

33) February 1984 - Armour begins inserting warning into the Factor VIII product advising that AIDS might be transmissible by blood or blood components. Wall, 832 F.Supp. at 1484. Cutter follows in 1984 with its own labels. Ray v. Cutter Laboratories, Div. of Miles, Inc., 744 F.Supp. 1124 (M.D.Fla. 1990).

34) May, 1984 - Armour begins marketing heat-treated Factor VIII concentrate. Walls, 832 F.Supp. at 1496.

35) June, 1984 - The FDA Consumer magazine publishes an article concerning hemophilia care that clearly betrayed the FDA's bias against the CDC's conclusions and in favor of the continued use of clotting factor concentrates by hemophilia patients, as opposed to other options at less risk for transmission of the AIDS virus. J. Couric, "Hemophilia Has Outlasted The Czars," FDA Consumer, June 1984, p.18. Once again, the FDA minimized the risk of contracting AIDS through clotting factor concentrate infusions.

The bad news is that a few hemophiliacs have contracted acquired immune deficiency syndrome (AIDS) from blood plasma they received. While the number of hemophiliacs in the United States is estimated at 20,000, only a small fraction of 1 percent of those have become victims of AIDS, the notorious ailment that breaks down the body's immune system. (See "What The Experts Know About AIDS" in the September 1983 issues of FDA Consumer.)

FDA Consumer, p.19. In the Eight Circuit Court of Appeal opinion in Petty v. United States, 740 F.2d 1428, 1437 (8th Cir. 1984), *infra.*, such a warning in the context of the FDA's swine flu vaccines, had it appeared with the product, would have been legally inadequate.

The disclosure here was merely a broad, generic statement. The alleged warning here did more to dilute the seriousness of the risks at stake than it did to apprise the recipients of the existence of those risks. Indeed, it appears that assuring participation was the motivation behind the phraseology decisions rather than an effort to inform the recipients of the risks.

In short, as a matter of federal law, the FDA has previously been found to have intentionally underestimated the risks of the use of certain drugs in order to encourage their use. The FDA's practice in FDA Consumer Magazine is similar in that respect.³⁶

Regardless of the truth of the FDA's statement in that issue, the risk of infection was enormous as a result of the pooled plasma, which could spread one infection through an entire lot of clotting factor destined for hundreds of hemophilia patients. The FDA was quite familiar with these risks from pooled plasma as demonstrated by the September 1983 FDA Consumer magazine article and the general state of medical knowledge concerning the risks to the hemophilia community of hepatitis as a result of pooled plasma. The Philadelphia Enquirer, *supra* at p.2, cols. 2 and 3.

The FDA's statement as to the level of infection reveals its bias in several ways. First, the FDA was aware that half of the twenty thousand persons with bleeding disorders only required occasional clotting factor infusions, if at all. Thus, by comparing the number of AIDS cases with the entire community of hemophilia patients, the FDA statistically diluted the apparent risks of infection. Secondly, the CDC, and therefore, the FDA, was aware that there was a latency period between the date of infection and the date on which symptoms for disease would first appear.³⁷ This latency period had already led experts one year before to make their infamous predictions of an iceberg phenomenon, that the cases of AIDS occurring at that point were merely the visible tip of an iceberg of thousands more infections.³⁸ Therefore,

³⁶The language of the Eight Circuit Petty decision is similar in other respects. Although the Petty decision obviously dealt with FDA warnings accompanying the drug, and the facts regarding FDA alerts on factor concentrate were in a magazine of general distribution, the standard of what type of warning constitutes an adequate presentation of risks to the patient is similar and informative. The Petty Court wrote at pp. 1438-1439: "[t]he [swine flu vaccine] warning was inadequate in part because of the calculated ambiguity of its terms and because it was couched in terms that lulled the recipient into a false sense of security."

³⁷Even the National Hemophilia Foundation, a lay organization, knew that there was a latency period. Alan Brownstein, NHF Executive Director, testified at the August 1, 1983 House Hearings before the Subcommittee of the Committee on Government Operations, FEDERAL RESPONSE TO AIDS, that "mothers [of hemophilic children] . . . call up and say 'I infused my child last night, and I am afraid that that infusion had AIDS in it,' but we know that that is not possible to determine, knowing the incubation period. . . ." The FDA was also aware of the incubation period, and thus the fact that those few patients probably represented at least hundreds more infections.

³⁸James Lipsitt, M.D., City of Hope National Medical Center, and Executive Committee member of the Southern California Physicians for Human Rights, testified at the March 17, 1983 Senate hearings before the Committee on Labor and Human Resources, BIOMEDICAL RESEARCH, TRAINING, AND MEDICAL LIBRARY ASSISTANCE AMENDMENTS OF 1983, p.41, that "one cannot help but wonder if this new phenomenon is just the tip of the iceberg." And one year earlier, at the April 13, 1982 House hearings before the Subcommittee on Health and the Environment of the Committee on Energy and Commerce, KAPOSI'S SARCOMA AND RELATED OPPORTUNISTIC INFECTIONS, James Curran, M.D., coordinator, CDC Task Force on Kaposi's Sarcoma and Opportunistic Infections, stated that, at a time when only 300 cases of Kaposi's

36) October 26, 1984 - 52 cases of AIDS among hemophilia patients are reported in MMWR. In stark contrast to the FDA's failure to present any statistical support for potential infection rates, as opposed to cases of full blown diagnostic AIDS, the CDC pointed to a potentially serious route of transmission through concentrated clotting factor. The CDC investigated the use of clotting factor concentrate and reported:

*Update: Acquired Immunodeficiency Syndrome (AIDS) in Persons With Hemophilia." Morbidity and Mortality Weekly Report, October 26, 1984; 33:589-91. Although these publications are beyond the date when many, if not most hemophilia patients who received HIV infections were exposed for the first time, it assists in clarifying the improper behavior by the FDA with regard to information disclosure, which included: 1) failing to distinguish between potential infection rates and actual cases having progressed to AIDS; 2) continual use of language tending to minimize the apparent risk of infection through the use of clotting factor

³⁹Dr. Marcus Conant, *supra*, testified on August 1, 1983 before the House Subcommittee of the Committee on Government Operations that the incubation period for AIDS is . . . 18 months." Dr. Curran is summarized in the May 24, 1983 edition of the *New York Times*, 1, 25:1, as stating that AIDS induction period, "which can take anywhere from six months to three years after exposure before the illness shows up -- inhibits any predictions about the future course of AIDS." Curran stated that the "induction period means it's [AIDS] not going to explode across the country quickly. But is also means that the implications won't be fully known for several years, maybe a decade." Mathilde Krim, Ph.D. Sloan-Kettering Institute for Cancer Research in New York, testified, at p.139, at the same hearings that

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⁴⁰Even Joseph R. Bove, MD, Professor of Laboratory Medicine, Yale Medical School, and Director, Blood Bank, Yale-New Haven Hospital, who produced now infamously low and erroneous estimates of the risks of AIDS for patients infusing with concentrated clotting factor, acknowledged both the vital importance of CDC information and the singular importance of FDA regulatory authority:

We look to CDC for ongoing up-to-date information on which we can base future decisions about the Nation's blood supply; to NIH for research leadership and support; to FDA for whatever regulatory authority may be needed; and to the Congress, ladies and gentlemen, for financial and emotional support.

FEDERAL RESPONSE TO AIDS. August 2, 1983, p. 164. James Curran, coordinator of the CDC's task force on Kaposi's Sarcoma, also made clear at the April 13, 1982 House hearings the importance of the CDC's role in disease prevention.

Foundation without reference to more qualified sources such as the CDC.⁴¹ Under such circumstances, the U.S. District Court for Idaho found:

[t]hus, during the time period within which John Doe was likely to have been infected by contaminated Factor VIII (i.e., prior to August 1984), nothing in the record establishes that the FDA had imposed any standards, scientific procedures or techniques which would have insured the safety of Factor VIII concentrates.

⁴¹ The FDA's failure at that time even to acknowledge publicly the CDC's findings, guidelines and recommendations, must be considered unreasonable in light of the unanimous deference given the epidemiologic research expertise of the CDC. In a devastating criticism of the FDA's failure to communicate the findings and conclusions of the CDC, Bove concluded at that hearing:

I think we need an ongoing and open line of information from the CDC, which is currently the locus from which the case reporting seems to the public. I think those of us who are in the blood-collecting industry, who have responsibility for the Nation's blood-collecting systems, need to know exactly how many suspected cases there are, where they are, and at what stage the investigation is.

Do we have suspect donors? I think that information ought to be available not only to us in the blood-collecting group, but to the public. This is really public health information, and I think the people of this country need to know as quickly as possible what our CDC knows about the risks.

[Representative] Weiss. Why do you believe that information has not been forthcoming?

Dr. Bove. I can't answer that, Congressman. I think you have to ask others, but I know that there is a feeling on my part, and I suspect on the part of others, that the kind of openness about the information we think we need has not been available from CDC.

Mr. Weiss. One of you, though I don't know who, testified that the Morbidity and Mortality Weekly Report was changed from a free distribution to a paid-for distribution, and I gather from the testimony that this was done to comply with budget restraints. (emphasis added)

[d. p. 166. Although Dr. Bove stated his belief that the CDC supplied information to the National Hemophilia Foundation concerning the number of hemophilia cases of AIDS (p. 167), the conflicts of interest within the NHF described by the IOM report, and of which the FDA was clearly aware, meant that that information was not transmitted to the hemophilia community. Dr. Bove's testimony is to the effect that, absent NHF transmittal, there were no other readily accessible avenues available to the public to receive this information from the CDC. If the CDC's concerns were not reflected in FDA regulations, the public remained unaware of risks of which the CDC was fully aware.

Doe v. Cutter Biological, 852 F.Supp. at 922. The FDA failed to discharge its statutory duties, and thousands of HIV infections resulted, and countless other subsequent re-infections occurred.

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SECTION FOUR:**THE FDA FAILED TO DISCUSS OR RECOMMEND THE USE OF CRYOPRECIPITATE AS AN OPTION TO THE USE OF FACTOR VIII CONCENTRATE IN NON-LIFE-THREATENING CIRCUMSTANCES.****A. The Medical Community Was Aware That Cryoprecipitate Was An Alternative to Concentrated Clotting Factor in Most Situations.**

This section argues that the alternative methods of treatment were available in the form of cryoprecipitate, but that the FDA kept the focus of treatment choices upon concentrate usage versus no treatment. In so doing, the FDA did not timely inform the hemophilia community of the greatly reduced risk of infection from the AIDS virus through the use of cryoprecipitate.

It was in the FDA Consumer Magazine June 1984 article, probably well after the point in time when the majority of hemophilia patients who were ultimately infected had already received their first HIV exposure, that the FDA publicly first discussed the alternatives to clotting factor concentrate available to the hemophilia community. It was those alternatives discussed in the article which the hemophilia community might have utilized if possessed with full knowledge of the risks of AIDS. The FDA noted the alternatives to infusion with clotting factor concentrate:

For those with severe hemophilia, two extracts of plasma are used. One, called concentrate, is in freeze-dried form. It can be stored at room temperature for up to six months or in a refrigerator for up to 24 months. The other, cryoprecipitate, is prepared from fresh blood and must be kept in the refrigerator.

FDA Consumer, June, 1984 at p. 19, col.2. Cryoprecipitate, discovered in 1965, is a residue of blood plasma that contains a less potent concentration of clotting factor. It comes directly from a donor and is not "pooled" together with plasma concentrate from many donors in the manner in which clotting factor was concentrated after 1970 in order to mass produce the medicine. Since cryoprecipitate must be thawed before an injection and has considerably more volume, an infusion takes close to one hour, as compared to fifteen minutes for an injection of freeze-dried and rehydrated modern clotting factor concentrate. However, cryoprecipitate exposes an adult male patient weighing 150 pounds to only about twenty donors for a treatment raising his clotting factor levels to 50% or more, as compared to an exposure of up to ten thousand donors through the use of concentrated clotting factor. The level of exposures per treatment of cryoprecipitate for children is less than ten donors.

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Piet J. Hagen, former editor of the Dutch Hemophilia Journal and a world expert on blood supply systems and technology, provides an outstanding insight into the medical community's awareness of the relative risks of viral infection associated with cryoprecipitate as compared with clotting factor concentrate. Hagen's 1982 book, Blood: Gift or Merchandise, p. 15, presents a glimpse into the understanding of those relative risks maintained by experts.

Factor VIII is one of the proteins that play a part in the process of coagulation. Since 1964 factor VIII has been obtained from whole plasma by cryoprecipitation. When fresh-frozen plasma is allowed to thaw at 4C, a cold-insoluble precipitate remains that consists of the coagulation factor VIII and some fibrinogen. The remaining plasma may be used for transfusion or fractionation.

The so-called cryoprecipitate is recovered from a single donation. For clinical use preparations are made from small pools of several single donations. The advantage of this processing technique is that little factor VIII activity is lost and the risk of transmission of viral hepatitis is minimal.

Although cryoprecipitate is still in use on a large scale, more-concentrated products are available too. The advantage of intermediate or high purity concentrates of factor VIII is that they have a greater specific activity and contain relatively less fibrinogen. The volume to be injected is small that treatment of patients is less time-consuming. On the other hand, it has to be emphasized that the yield of factor VIII activity per donation processed is significantly lower. Therefore the production of these concentrates requires much more plasma and is relatively expensive. Another disadvantage is that the risk of hepatitis is greater because these concentrates are prepared from very large donor pools. This risk, however, has diminished in recent years.

It is clear that, in 1981, the hematology community, which would include the FDA and the CDC, understood both that cryoprecipitate was a practical and workable alternative to concentrated Factor VIII in all but the more advanced hemorrhages or those hemorrhages in particularly vulnerable areas, such as the cerebellum and viscera,⁴² and that the use of

⁴²Goedert, et al. "Antibodies Reactive With Human T Cell Leukemia Viruses in the Serum of Hemophiliacs Receiving Factor VIII Concentrates," Blood, Vol 65, No. 2 (February), 1985, pp. 492-495: cryoprecipitate is "difficult to use during surgery or serious hemorrhage, when high levels of clotting factors must be achieved and maintained."

cryoprecipitate would lessen the risk of viral transmission by reducing the exposure to the number of donors. This was not an unreasonable option, since Hagen reports that France used cryoprecipitate extensively: "[i]n 1981, 64% of factor VIII products was utilized in the form of cryoprecipitate and 36% in the form of concentrate." Hagen, *supra*, p.149. Information concerning the lower risks of viral transmission with cryoprecipitate, coupled with the knowledge of the presence of HIV in the blood supply, should have been made available to the hemophilia community in 1982.⁴³

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Not all hemophilia treaters embraced commercial Factor VIII concentrates. Some doctors restricted patient use to treatment of serious bleeding incidents. And some doctors continued to use cryoprecipitate, refusing to subject their patients to the known and unknown risks of transmissible disease.

For example, some doctors at University Hospitals of Cleveland Hemophilia Treatment Center continued treating patients with cryoprecipitate, the single donor transfusion obtained from volunteers. Dr. Oscar Ratnoff, University Hospitals, advocated use of cryoprecipitate; he published his successful results with this therapy. [footnote: Lederman, M.M., Ratnoff, O.D., Scillian, J.J., Jones, P.K., & Schacter, B.: Impaired. See also Ratnoff, O.D. (1984). Some complications of the therapy of classic hemophilia T. *Clinical Medicine*, 103, 653. (1983). Cell-mediated immunity in patients with classic hemophilia. *New England Journal of Medicine*, 308, 79-83. Dr. Ratnoff also reported in late 1982 that his patients did not exhibit immune system changes which were being reported in patients treated with concentrates. [footnote: Id. See also Lederman, M.M., Ratnoff, O.D., Evans, B.L., et al. (1985). Acquisition of antibody to lymphadenopathy-associated virus in patients with classic hemophilia. *Annals of Internal Medicine*, 102, 753]. These were significant data since at the time there was speculation that hemophiliacs who used Factor VIII concentrates and who were developing AIDS-defining illnesses did not have a blood transmissible disease. Rather, it was hypothesized that they were simply responding to foreign antigen overload. [footnote: Menitove, J.E., Aster, R.H., Casper, J.T., et al. (1983). T-lymphocyte subpopulations in patients with hemophilia treated with cryoprecipitate and lyophilized concentrates. *New England Journal of Medicine*, 308, 83-86. Landay, A., Poon M-C, Abo, T., et al. (1983). Immunologic studies in asymptomatic hemophilia patients. Relationship to AIDS. *Journal of Clinical Investigation*, 71, 1500] Because Dr. Ratnoff's data showed no immune abnormalities in hemophiliacs treated with cryoprecipitate, [footnote: Id.] this should have heightened suspicions that concentrates were carriers of the causative agent of AIDS. Unfortunately, Dr. Ratnoff data, along with other supporting publications, [Supra, note 35] were largely ignored.

Ring and Leonard, *supra*, p.178.

Additionally, in the very first issue of the journal *AIDS Research*, published in January, 1983, T. Vincent Shankey, PhD and M. Elaine Eyster, MD of Pennsylvania State University Medical School reported:

During the year 1982, nine cases of the acquired immune deficiency syndrome (AIDS) were recognized in hemophiliacs. Eight of these individuals were previously healthy, and one had long-standing common variable hypogammaglobulinemia (1-3). All had classic hemophilia, and all had received antihemophilic factor (AHF) concentrates.

* * * *

Recent evidence indicates that healthy hemophilia patients receiving AHF concentrates have alterations of their immune systems. These changes include decreased T-helper/suppressor ratios, and lymphadenopathy. These alterations are seen in healthy hemophiliacs treated with AHF concentrates, prepared from pools of 5,000 or more donors, but not in those treated with cryoprecipitate prepared from single donors. Furthermore, H/S ratios decrease significantly with the use of more vials of AHF, indicating that concentrate therapy is related to low H/S ratios. (emphasis added)

Shankey, et al., *supra*. As opposed to the NHF's statements, these infections resulting exclusively from concentrate usage were not due to "relative use patterns," but to the increased opportunity of infection as a result of a wider variety of "alloantigens":

In a related fashion, we propose that alloantigens in AHF concentrates could provide an important inducing event which subsequently allows a viral agent (or agents) to infect a compromised host. Thus, AHF concentrates produced from thousands of individual donors provide a very large number of different alloantigenic specificities. In contrast, hemophilia patients receiving cryoprecipitate receive substantially fewer alloantigens.

Shankey, PhD, and Eyster, MD, "The Acquired Immune Deficiency Syndrome (AIDS) In Hemophiliacs: A Hypothesis." AIDS Research, Vol. 1, 1983, p.83, 84.⁴⁴

Once again, the FDA knew the risk to the hemophilia community of AIDS infection as a result of concentrated clotting factor as compared to cryoprecipitate, but the FDA issued no warnings.

Hemophiliacs are considered prey to AIDS because they must receive blood substances, and a debate rages over whether treatment of hemophiliacs should be done with cryoprecipitate or concentrate. Cryoprecipitate is derived from the blood of a few donors [ten to fifteen], while the concentrate comes from the pooling of many [two thousand to twenty thousand], thus increasing the likelihood of possible infection.

FDA Consumer, supra at p. 19, col.3. Without a single mention of CDC warnings concerning concentrated clotting factor, the FDA article presented only the conclusions of the National Hemophilia Foundation, a non-medically-licensed, volunteer organization, which the Institute of Medicine report found had "financial and other relationships" with "the plasmas fractionation industry [which] created a conflict of interest that seriously compromised the perceived independence of NHF's recommendations." IOM Report at p.7.

The FDA Consumer magazine wrote:

Commenting on the debate of fresh versus freeze-dried blood substances, the National Hemophilia Foundation of New York says: "... there is no specific evidence indicating that there is a greater risk with concentrate than with cryoprecipitate or fresh frozen plasma. While all of the patients with hemophilia who have developed AIDS have been treated with concentrate, the

⁴⁴The Seventh Circuit explained that a related theory was advanced in 1995:

The plaintiffs presented expert scientific testimony at trial that, under the theory of antigenic stimulation, an infected person's exposure to additional HIV, other viruses, or foreign proteins, shortens this asymptomatic period, provokes increased replication of HIV, and leads to a quicker death from an AIDS-related illness. The plaintiffs asserted that, under this theory, Poole's death was hastened through his use of Factor VIII concentrate manufactured by the defendants after his initial HIV infection.

Gruca v. Alpha Therapeutic Corp., 51 F.3d 638, 641 (7th Cir. 1995).

proportion of severe hemophiliacs treated exclusively with other products is so small that this observation is expected from the relative use patterns. . . ."

FDA Consumer, supra at p. 19, col.3.

Even with this unreasonable perception in light of the scientific information concerning transmissibility and the magnification of risks from pooled plasma, the FDA Consumer noted that the National Hemophilia Foundation recommended the use of cryoprecipitate for previously untransfused patients:

The Medical and Scientific Council of the National Hemophilia Foundation has recommended that cryoprecipitate be used instead of concentrate in treating certain patients -- those under age 4, those newly diagnosed, and patients with mild hemophilia. The foundation is emphatic in its advice that the fear of contracting AIDS should not cause hemophiliacs to refuse treatment. That could cause crippling or dangerous hemorrhaging.

FDA Consumer, supra at p. 19, col.3. In placing the emphasis on choice of treatment or no treatment, instead of cryoprecipitate versus concentrate, the FDA and the NHF created a straw man argument; few hemophiliacs would have refused treatment, but certainly many would have improved their chances of avoiding AIDS by infusing with cryoprecipitate instead of clotting factor if they had only been presented with the proper information.

If one accepts the premise that commercially manufactured Factor VIII concentrate was a life-saving necessity in the life of a hemophiliac, the risk versus benefit argument is persuasive. Single-donor cryoprecipitate, however, was the life-saving, life-extending revolution in treatment. Factor VIII concentrates simply made treatment somewhat more precise since the number of Factor VIII units present in a vial are presumed to be assayed and identified on the label. The primary improvement, however, was convenience. Once this is understood, the risk versus benefit argument should receive closer scrutiny.

Ring and Thomas, "Representing the Hemophiliac With AIDS," Courts, Health Science & the Law, Summer, 1991, vol.2, No.1, p. 175. By recommending the use of cryoprecipitate for patients who had previously used little or no clotting factor concentrate, the NHF, and the FDA by reiterating and emphasizing the NHF's recommendation by failing to report countervailing CDC findings, presented a grossly self-contradictory policy. Both the FDA and the NHF implicitly acknowledged the risks of AIDS from clotting factor concentrate

usage for previously untransfused patients, while at the same time continuing to recommend its use for those already exposed to its potential viruses.

Indeed, the FDA knew that the National Hemophilia Foundation believed that clotting factor concentrate posed a special risk of AIDS transmission, because the NHF Executive Director, Alan Brownstein testified at the August 1 and 2, 1983 hearings before the House Subcommittee on Government Operations that "[t]he recognition that AIDS appears to be transmitted through clotting factor concentrates has had a profound effect on hemophiliacs and their families throughout the country." Brownstein, House Intergovernmental Relations and Human Resources Subcommittee of the Committee on Governmental Operations, FEDERAL RESPONSE TO AIDS, 98th Congress, August 1 and 2, 1983, p. 57.

If hemophilia patients had continued to treat with cryoprecipitate until the introduction into the U.S. market of heat-treated, HIV-purified clotting factor in 1984, a mere two year period from the July 1982 CDC conference, hemophiliacs would have overwhelmingly reduced their exposure to HIV. The Goedert, et al. study, reported in 65:2 Blood, p. 493, found that, while 74% of 69 hemophilia A patients who had received factor VIII concentrate but not factor IX concentrate had antibodies against HTLV III, and 90% of the 48 patients receiving factor VIII concentrate at least twice a month had HTLV III antibodies, none of the 22 hemophilia patients treated only with fresh frozen plasma or cryoprecipitate had HTLV III antibodies.⁴⁵ Every single type of internal hemorrhage could have been treated with cryoprecipitate, with the exception of cranial or visceral bleeds that required clotting factor levels of 100%, achievable only with clotting factor concentrate. Even with such occasional hemorrhages, severe hemophiliacs could have minimized their exposure by using clotting factor only during that time, and mild hemophiliacs would never have required the use of concentrate. Thus, an historically successful and viable treatment alternative to clotting factor concentrate that overwhelmingly reduced the possibility of HIV infection was available.

In short, the FDA intentionally distorted the facts concerning the risk of AIDS transmission from the use of clotting factor concentrate, and did so in a manner designed to encourage the use of concentrate as opposed to other forms of treatment such as cryoprecipitate.

⁴⁵This data is consistent with that available internationally. A study of 66 Israeli hemophilia patients for antibodies to HIV in blood samples collected between 1978 and 1985. HIV antibodies were detected in 40 patients. 38 of 45 patients treated with nonheat-treated factor VIII concentrate developed antibodies to HIV, as compared to only one seroconversion of 16 treated with cryoprecipitate and fresh plasma only. Shlomit Orgad, et al. "Antibodies to HIV in Israeli Hemophiliacs: Relationship Between Serological Profile and Disease Development," AIDS Research and Human Retroviruses, Volume 3, Number 3, 1987, p. 323.

B. A Legal Presumption Exists That the Hemophilia Community Would Have Acted Upon FDA Warnings And Utilized Cryoprecipitate In Circumstances That Were Not Life-Threatening.

Two obvious questions arise; were hemophiliacs really seeking this information at the time, and what would they have done with the correct information had they received it? Despite the relative dearth of information on those two issues, due to the absence of FDA and, accordingly, industry disclosure of risk, there is sufficient information to support the proposition the hemophilia community would have adopted cryoprecipitate as the treatment of choice until heat-treatment was available.

First, the hemophilia community sought out information relating to HIV risk, and was uninformed as a result of the absence of FDA leadership. National Hemophilia Foundation Executive Director Alan Brownstein testified at the August 1 and 2, 1983 hearings before the House Subcommittee on Government Operations that patients and family members immediately sought information concerning the risk of AIDS through concentrate usage.

Many physicians and treatment centers are deluged with calls from apprehensive patients and families seeking information and, of course, reassurance. A number of physicians themselves are concerned and disagreement exists among experts as to whether or not treatment should be modified. Some have suggested that the potential for reducing the risk of AIDS would be increased if cryoprecipitate, which is derived from smaller donor pools, was used instead of the dominant replacement therapy now in use - AHF (antihemophilic) concentrates, which are derived from much larger donor pools. Yet, there is serious question raised as to whether or not this would represent a safer alternative and, of course, the patients are caught in between as the uncertainty among physicians compounds the distress.

National Hemophilia Foundation Testimony submitted to the House of Representatives Intergovernmental Relations and Human Resources Subcommittee of the Committee on Governmental Operations, FEDERAL RESPONSE TO AIDS, 98TH Congress, August 1 and 2, 1983, p. 55.

There are two simple issues presented in that testimony: 1) hemophilia patients were seeking information about the risks of AIDS from factor concentrate infusion; and 2) physicians were becoming aware of the risks posed by the larger plasma donor pools utilized with factor VIII concentrate. The fact that most hemophilia patients were not

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informed of these risks is quite apparent from the FDA's public statements and the conclusions of the IOM report. Physicians and the FDA may have been uncertain about what the ultimate best therapy was in view of the risks present from AIDS, but this was not a reason not to inform the community about those risks and allow them to make the decisions themselves. Clearly, the hemophilia community could not have done a worse job of risk assessment than the FDA performed on their behalf.

As to the second question, whether the community would have used cryoprecipitate instead of concentrate, the evidence of a few cases indicates that a substantial portion of the population would have converted to cryoprecipitate use armed merely with the information concerning risk. Patients were understandably unaware that cryoprecipitate usage could decrease the potential risk of transfusion-associated AIDS by as much as 99.9%, the difference in risk between the largest donor pools for factor concentrate, up to 20,000 persons, and the smallest donor pools for cryoprecipitate, as low as twenty persons. In the absence of any explanation of the different risks between clotting factor concentrate and cryoprecipitate, some hemophilia patients apparently abandoned any form of plasma usage.

Some patients have abandoned appropriate use of blood products because they fear contracting AIDS. This is based on anecdotal reports from patients and physicians, particularly orthopedists, who have reported increased joint damage resulting from inadequately treated bleeding episodes. This concern is further documented by reported reductions in blood clotting factor sales from industry and reduced blood clotting factor use from treatment centers.

Brownstein, supra, p.54. If patients had been informed that they did not need to abandon treatment altogether in order to almost statistically eliminate their risk of transfusion-associated AIDS by converting their treatment choice to cryoprecipitate until heat treatment was available for factor concentrate in the U.S., those patients in all likelihood would not have abandoned the use of plasma treatment altogether. The IOM report concludes that the NHF's reaction was based upon its conflicts of interests between its commitment to the hemophilia community and its inappropriately close association, financial and otherwise, with the pharmaceutical industry.

The United States Court of Appeals for the Eighth Circuit affirmed a ruling by the U.S. District Court for the Northern District of Iowa, applying Iowa tort law, that a rebuttable presumption exists that the plaintiff drug recipient would have read and acted upon a proper warning by the Food and Drug Administration of the potential effects of the swine flu vaccine. Petty v. United States, 592 F.Supp. 687, 690-691 (N.D. Iowa 1983).

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The District Court first established that the warning was insufficient under Iowa law.⁴⁶ The Petty Court then remarked upon the context within which these insufficient notices were provided, one in which the FDA emphasized the absence of any other acceptable practice than immunization:

[T]he hardsell approach to immunization taken here had the natural effect of firmly planting within the recipient's mind the imperative need for receiving the shot. The approach taken by those charged with the administration of this program had the distinct effect of de-emphasizing the importance of making individual determinations as to the advisability of undergoing the risks of immunization.

Petty, 592 F.Supp. at 691. The similarities with the FDA's presentation of clotting factor concentrate as the only available treatment therapy are clear and apparent.

The Petty Court then adopted a rule of rebuttable presumption of the proper use of warnings:

This Court concludes that the Supreme Court of Iowa, if faced with this problem, would adopt the approach of Reyes v. Wyeth Laboratories, 498 F.2d 1264 (5th Cir. 1974), wherein the Court presumed that an adequate warning would have been read and that the recipient would have acted on the warning [ftnt 4: "See also Sterling Drug v. Cornish, 370 F.2d 82 (8th Cir.1966)"]:

Where a consumer, whose injury the manufacturer should have reasonably

⁴⁶The Petty Court writes:

In order to create the presumption that informed consent was given pursuant to this statute [Iowa informed consent law, Code of Iowa Sec. 147.137], the form must set forth in general terms the nature and purpose of the procedure, together with the known risks, if any, of death, brain damage, quadriplegia, paraplegia, the loss or loss of function of any organ or limb, . . . with the probability of each such risk if reasonably determinable, Code of Iowa Sec. 147.1347(1). The consent form given to the plaintiff failed to set forth the known risk of loss of function of any organ or limb. This symptom of serum sickness is one major element of plaintiff's damages. Thus, the Iowa informed consent law could not relieve the defendant of its liability for failure to warn of known dangers.

Petty, 592 F.Supp. at 690.

foreseen, is injured by a product sold without a required warning, a rebuttable presumption will arise that the consumer would have read any warning provided by the manufacturer, and acted so as to minimize the risks. In the absence of evidence rebutting the presumption, a jury finding that the defendant's product was the producing cause of the plaintiff's injury would be sufficient to hold him liable.

Petty, 592 F.Supp. at 691.⁴⁷ The Eighth Circuit Court of Appeals upheld the District Court's holding in its entirety, and elaborated on the inadequacy of the warning, ruling that, under Iowa law, it is not sufficient to merely contend that death may result from some causes, but the warning must describe each separate foreseeable cause.

We reject the government's contention that a reference to death satisfies its duty to warn for another reason also. Were this undifferentiated warning found to satisfy the duty to warn, which under Iowa law requires disclosure of all risks reasonably foreseeable, then the duty to warn would become very hollow indeed. Death can result from virtually any treatment. Moreover, the risk of death may be conceptually remote, whereas a more specific warning detailing the known risk of serum sickness and its symptoms would alert recipients more concretely to the risks that they actually were assuming.

⁴⁷The rule regarding product warnings is particularly important in those jurisdictions having adopted Comment K of Section 402A of the Restatement (Second) of Torts, regarding strict products liability law. Comment K states:

There are some products which, in the present state of human knowledge, are quite incapable of being made safe for their intended and ordinary use. These are especially common in the field of drugs. . . . Such a product, properly prepared, and accompanied by proper directions and warning, is not defective, nor is unreasonably dangerous. The same is true of many other drugs, vaccines, and the like, many of which for this very reason cannot legally be sold except to physicians, or under the prescription of a physician.

Petty, 592 F.Supp. at 692 (emphasis and ellipses provided by the Petty Court).

Petty v. United States, 740 F.2d 1428, 1437 (8th Cir. 1984).

The threshold for establishing foreseeability sufficient to call for warnings is not a high one. The involvement of the CDC in epidemiological studies has carried significant weight with the courts. The U.S. District Court for the Northern District of Ohio found sufficient causation of Guillain Barre Syndrome ("GBS"), a rare neurological disorder which occurred in more than a thousand swine flu vaccination recipients, where the CDC found a statistical relationship between the two.

Shortly after the initiation of the swine flu immunization program, the Center (sic) for Disease control (CDC) began a surveillance program to determine whether there was a statistical relationship between the swine flu vaccination and GBS. Preliminary data indicated that such a relationship existed and a moratorium on vaccinations was declared.

Storrier v. U.S., 662 F.Supp. 18, 22 (N.D. Ohio 1986). The difference of opinion among experts did not matter; the Storrier Court accepted the conclusions of the CDC. Storrier, 662 F.Supp. at 22.

Citing both Iowa and California law, the Eighth Circuit described the elements of proper warning under Iowa's patient standard rule:

[A]n individual must be advised of the inherent and potential hazards of the proposed treatment, any alternative methods of treatment, the risks attendant to such alternatives, and the likely results of remaining untreated.

Petty, 740 F.2d at 1436. The availability of alternative therapies, similar to the option of cryoprecipitate, was critical to the finding that the FDA failed to adequately warn of the risks of the swine flu vaccine:

There were viable alternatives for Petty, yet he received treatment without a warning apprising him of the risks and benefits and without an initial individualized balancing of the risks and benefits by a learned intermediary.

Petty, 740 F.2d at 1438. The Eighth Circuit Court succinctly concluded this issue:

Finally, we find that the vagueness of the generic warning is not mitigated by the invitation to ask questions. In some situations and for some individual idiosyncrasies, it may be necessary to

rely on recipients' questions to complete the picture of risks and benefits or to clarify issues raised. This was not such a situation. Here the warning that was given was insufficient to spark the concerns that would have engendered questions.

Petty, 740 F.2d at 1437.

The basis for the statement that hemophilia patients and family members would have made reasonable treatment decisions based on the availability of scientific information is based on the demonstrated competence of the community in managing their home care in the preceding decade. So capable were hemophilia patients and family members at diagnosing and appropriately self-infusing at home, without the assistance or advice of physicians or nurses, that in the six year period from 1975 until 1981, hemophilia patients decreased the number of annual hospital days per year from 9.4 to 1.8, decreased their unemployment rate from 36% to 12.8%, and reduced the number of days lost from work or school each year by 75%. Brownstein, *supra*. Of the approximately 9,500 severe hemophiliacs enrolled in federally subsidized treatment centers, their care dropped in cost from \$15,800 per patient per year in 1975 to \$5,932 in 1981. *Id.* While it is true that a major reason was the availability and convenience of clotting factor concentrate, the successful use of that program would not have been possible without a community educated in risk assessment, bleeding diagnosis and making appropriate treatment choices. While the episodes of bleeding, and therefore the complications from arthritis, might have been more extensive during the two year period until relatively safe, pasteurized concentrate was available in the U.S. market, that option was preferable to AIDS and widespread fatalities. It was not a choice made available to the hemophilia community, and it should have been.

SECTION FIVE:

THE MEDIAN MIDPOINT OF SEROCONVERSION OF THE HEMOPHILIA COMMUNITY WAS AFTER JANUARY 1, 1983, AND THUS, PROMPT ACTION BY THE FDA COULD HAVE PREVENTED SEVERAL THOUSAND INFECTIONS.

This section argues that the median midpoint of seroconversion of the hemophilia population occurred during 1983, and thus the FDA is responsible for at 3,500 seroconversions in the hemophilia community. This section will examine those estimates and attempt to describe the consensus of the research on the issue. This section will begin its analysis with those estimates arguing for the dates of seroconversion in 1982, and then move into estimates of 1983 median midpoints.

According to a 1987 study arguing for the earliest median midpoint of seroconversion among published studies of U.S. hemophilia patients, the 3501st hemophiliac out of approximately 7,000, became infected by September of 1982. In that investigation by Eyster, M.D., et al, *Annals of Internal Medicine*, July 1987, 107:1, p.1, the date of the median infection point of the U.S. hemophilia A population was prior to September, 1982, since 83 of the 111 patients studied had HIV antibodies in their serum at study entry in September, 1982. It should be noted that this is the earliest estimated date of the midpoint of seroconversion, and that other qualified researchers place the date several months, even as much as one year, later. Even by Eyster's estimates, greater than half of the U.S. hemophilia A community, which comprises the largest portion of hemophiliacs in the U.S. and the largest portion of infected hemophiliacs, was still uninfected at the conclusion of the July 17, 1982 CDC meeting, when it was reported that hemophiliacs were becoming infected with an AIDS-causing agent and that clotting factor concentrate exposed them to thousands of donors. Thus, prompt FDA action still could have prevented over half of the U.S. hemophilic seroconversions.

There are clear problems with the consistently early seroconversion midpoint dates predicted by Eyster, et al. In a different study, but one which advanced the same conclusion of a 1982 date of the median midpoint of seroconversion, Eyster herself admits that the high seroconversion rates for patients in the University of Pennsylvania patient pool might be the result of differences in levels of treatment sought.

It is possible that the early seroconverters were already ill during 1979 to 1982, requiring more clinic visits and providing more serum samples for HTLV-III testing, whereas the healthy

patients might have visited the clinic less often and provided fewer samples for detecting early seroconversion.⁴⁸

Eyster, et al., "Development and Early Natural History of HTLV-III Antibodies in Persons with Hemophilia," The Journal of the American Medical Association, April 19, 1985, p. 2222.

Additionally, the location of the patients in a large northeastern state affects the reliability of the study's conclusions. Many of the Pennsylvania patients reasonably could have used clotting factor manufactured from large plasma pools containing donations from New York City plasma donors. New York City demonstrated a proportionately higher incidence of AIDS in the early 1980's, and hemophilia patients in the New York City area also demonstrated an earlier median seroconversion midpoint date than other geographic locations in the United States.⁴⁹ Nebraska is a fair example of how these rates of infection, and the progression from infection to full-blown AIDS, were actually less in central, as opposed to coastal, parts of the country.⁵⁰

⁴⁸Eyster herself rejects that conclusion, arguing that "in view of the slightly higher doses of factor VIII concentrate received by the early seroconverters, it seems more likely that they visited the clinic for problems related to severe hemophilia and also had a greater probability of using one of the earliest factor VIII concentrate lots contaminated with HTLV-III." *Id.*, p. 2222. This conclusion, however, is faulty: numerous studies have linked seroconversion rates with amount of factor used, which Eyster herself admits. Therefore, the greater the amount of factor consumed, the greater the risk of seroconversion. Accordingly, the appearance of these patients in the clinic for treatment of categorically different symptoms from other patients seems more likely than their appearance merely because bleeding caused slightly elevated amounts of factor usage.

⁴⁹The FDA identified New York City, San Francisco, Los Angeles and Miami as high risk "hot spots." Cross v. Cutter Biological, 94-1477 (La. App. 4 Cir. 5/29/96), 1996 WL 293728 (La. App. 4 Cir.), at 2.

⁵⁰David J. Volzky, PhD, "HTLV-III/LAV Antibodies and Virus In Hemophilia Patients in Nebraska: Survey and Initiation of a Prospective Study," AIDS Research, vol. 2, No. 1, (1986), p. 52.

In the period of June, 1983 through May, 1984, the incidence rate of AIDS in persons with hemophilia A in selected areas of the United States was similar to that of homosexual men in New York City or San Francisco (10). Antibodies against HTLV-III/LAV were reported in 64% of hemophiliacs in Denmark (11), 72% of hemophiliacs in Georgia (12), and 85% of patients with hemophilia A in California (13).

We have recently attempted to correlate a clinical state with seropositivity to HTLV-III/LAV among hemophiliacs registered in the Nebraska Regional Hemophilia Center (14). Although 56% of patients with hemophilia A were HTLV-III/LAV-seropositive, none of them have shown signs of progression toward AIDS.

Further, under Eyster's prediction of the incubation time for the virus, a period of approximately two years, the appearance of AIDS symptoms should have occurred in 1985.

From this study, it would appear that very few if any cases of seroconversion for HTLV-III antibodies occurred in patients with hemophilia before 1979, and that the rate of seroconversion increased rapidly in 1981-1982. Thus, the interval is at least two years between the earliest seroconversion and the appearance of AIDS in hemophiliacs in late 1981 and early 1982. This interval was illustrated by our two patients who developed AIDS or AIDS-like illness. As the majority of hemophiliacs receiving factor VIII concentrate appear to have developed HTLV-III antibodies during 1981 and 1982, it is possible that the peak incidence of AIDS in hemophiliacs may not be apparent until 1985 or later.

Id., p. 2222. The evidence is obvious that the anticipated onset of AIDS-like symptoms in the community did not occur in 1985 or shortly thereafter, as predicted by Eyster. This fact is not explained by a longer latency period among hemophilia patients; the bell curve for immune suppression among asymptomatic hemophilia patients is the same in duration and shape as with homosexual men - it is merely later in time.⁵¹ Indeed, the significant infection rate among the hemophilia community of Hepatitis B, and the additional compromises of the immune systems of hemophilia patients brought on by constant

⁵¹Once again, Eyster herself admits as much:

All of the hemophiliacs who seroconverted before 1981 manifested lymphadenopathy and/or a low T-helper cell count (< 400 cells/cu mm). In contrast, the hemophiliacs in whom HTLV-III antibodies appeared after 1981 are thus far essentially normal on these two AIDS-related clinical and immunological parameters. Lymphadenopathy and/or low T-helper cell counts are present in virtually all homosexual men who were seropositive in 1982 and who lived in central New York City, where AIDS first appeared during 1979. In recent years similar findings have been noted in hemophiliacs who receive clotting factor concentrate. These findings suggest that the first one or two years after development of HTLV-III antibodies may be relatively free of AIDS-related conditions but that lymphadenopathy, a low T-helper cell count, or some other related condition such as thrombocytopenia will be found in most persons three to five years after seroconversion.

Id., p. 2222. Eyster does qualify the comparison, citing "[t]he cumulative incidence of AIDS in homosexual men with HTLV-III antibodies is only on the order of 5% to 20% (J.J. Goedert, MD, unpublished data, February 1985), and in this study of hemophiliacs with HTLV-III antibodies, the cumulative incidence of AIDS and AIDS-like illnesses, during more than three years of observation, has been lower, on the order of 2% to 4%." *Id.*

infusions with medications that were 90% foreign protein, all point to an accelerated progression to AIDS as compared to the homosexual community. Accordingly, Eyster's contentions concerning median midpoint dates of seroconversion are at odds with the dates of progression among hemophilia patients from infection to full blown AIDS.

Not only is Eyster's midpoint estimation controverted by the rate at which seropositive hemophilia patients developed symptoms for AIDS, but it is also controverted by the ultimate estimated number of seropositive hemophilia patients. There are between ten and twelve thousand severe hemophilia patients in the United States; of these, only seven to eight thousand were infected. At least ninety percent of severe hemophilia patients used clotting factor concentrate on more than one occasion between 1980 and 1987. By the beginning of 1986, pasteurization of concentrate was sufficiently standard in care to assume that few seroconversions occurred after that time among concentrate users.³² Therefore, the timeframe within which one may assume infections occurred is between the beginning of 1980 and the end of 1985. Eyster estimates that over half of the infected population possessed antibodies by October of 1982, just before the midpoint date of that six year period. However, it is clear that the amount of HIV in the blood supply (the "viral load") was progressively increasing through the end of 1983, when gay donors began self-selecting out of donor pools.^{33,34}

³²See Dateline 14, Section Two of this document, *infra*.

³³Goedert, et al. *The New England Journal of Medicine*, October 26, 1989, 321:17.

The majority of persons with hemophilia or related disorders became infected with HIV-1 through the use of commercial clotting-factor concentrates that were manufactured before the start of self-exclusion of donors with risk factors for AIDS, HIV-1 antibody screening, and the development of viral-inactivation measures such as the heat treatment of factor concentrates. [footnote omitted]

See also, K. Schimpf, M.D., et al., "Absence of Anti-Human Immunodeficiency Virus Types 1 and 2 Seroconversion After the Treatment of Hemophilia A or Von Willebrand's Disease With Pasteurized Factor VIII Concentrate," *The New England Journal of Medicine*, October 26, 1989, pp. 1148-1152.

In March 1983 the Food and Drug Administration first issued recommendations for the so-called self-deferral of blood donors who belonged to any defined risk group. In addition, medical examinations, including screening for lymph-node enlargement and unexplained loss of weight, became part of predonation medical checkups.

See also Dateline 22, Section Three of this document, testimony of Conant, MD.

The *NEJM*, October 26, 1989, 321:17, "A Prospective Study of Human Immunodeficiency Virus Type 1 Infection And the Development of AIDS in Subjects with Hemophilia," (Goedert, et al), gave the best estimate of the midpoint of seroconversion as follows:

When we studied the subjects with midpoint estimates further (Fig. 1),³⁵ we found that the first subject with severe hemophilia A seroconverted at the end of 1978, with a steadily increasing prevalence of HIV-1 antibodies during 1979 and 1980, a rapidly increasing prevalence from 1981 through mid-1983,

³⁴ There is sufficient evidence to establish that the prevalence of HIV in the blood supply was greater each month through 1984, and, accordingly, that the number of seroconversions should have been increasing each month. Indeed, a monthly, or at least quarterly increase in the number of seroconversions is consistent with the number of cases of AIDS.

The first cases were recognized less than two years ago by the epidemiologists in Atlanta who, by tracking the medical histories backward, determined that while a few cases had occurred in 1978 and 1979, the surge occurred in 1980 and the incidence has been doubling every six months since.

Sydney H. Schanberg, "A Baffling Epidemic," *NYT*, May 24, 1983, I, 25:1. See also Dateline 23, Section Three of this document.

³⁵*NEJM*, Oct. 26, 1989, p.1142, gives the method by which the midpoints of seroconversion were obtained:

For the actuarial analyses of the marker data, the dates of HIV-1 infection were estimated as the midpoint in time between the last negative and first positive specimens for subjects with previously frozen serum samples. An alternative method of estimating the seroconversion date had little effect on the calculated incidence of AIDS. (footnote omitted) Data after November 1, 1988, were censored, and standard actuarial methods were used to quantify the incidence rates of intermediate markers and AIDS. (footnote omitted) Annual incidence rates were estimated as the conditional probabilities of the development of AIDS during annual intervals after the seroconversion date. [. . .] Because of the uncertainty about the date of HIV-1 infection in the subjects who did not have stored serum samples, the evaluation of AIDS incidence rates, cofactors, and markers concentrated on HIV-1-infected subjects with midpoint seroconversion dates. Qualitatively similar results (not shown) were found in the subjects with imprecise seroconversion dates, but such data may be much less reliable in the study of time-dependent covariates. (footnote omitted).

and a leveling off by the end of 1984.⁵⁶ The first subject with a clotting disorder other than severe hemophilia A seroconverted at the end of 1979; there was a slow increase in prevalence during 1980 and 1981 and a steadier increase from 1982 through 1986 (Fig. 1). The maximum-likelihood estimate of the curve of HIV-1 incidence was very close to that of the midpoint estimate (Fig. 1), suggesting that the 319 subjects with midpoint estimates were representative of the entire cohort.

For patients with severe hemophilia A, the study placed the maximum likelihood estimate derived from all 1128 subjects whose clotting disorder, type and severity were known, as occurring in the middle of 1983. The midpoint estimate for just those subjects providing samples documented to be HIV-negative (328 subjects) was mid-1982. For those patients with other clotting disorders, the median midpoint estimate for the 231 subjects with HIV-negative study samples was the end of the first third of 1984. The median midpoint estimate for all subjects (469) regardless of HIV-negative sample availability was the middle of 1984.

Shelby Dietrich, M.D., hematologist at the Southern California Hemophilia Treatment Center, presented her conclusion of the HIV seroconversion midpoint date during the proceedings of the Symposium on Recent Advances in Hemophilia Care, held in Los Angeles, April 13-15, 1989, and published in "Epidemiology of HIV Infection," Recent Advances in Hemophilia Care, 1990, pp. 80-81.

Studies of anti-HIV seroconversion (Eyster et al, 1987, Ragni et al, 1987) reveal that seroconversion began in 1979 and by the end of 1984 70% to 85% of hemophiliacs were anti-HIV positive. The mid-point of sero-conversion is January 1, 1983. (emphasis added)

⁵⁶NEJM, Oct. 26, 1989, p. 1142.

As is typical of the gene frequencies of clotting disorders, our cohort of 1219 subjects was dominated by the 659 subjects with severe hemophilia A (factor VIII deficiency), 76.5 percent of whom had HIV-1 antibodies (Table 1). There were also important HIV-1 infection rates of 46 and 25 percent among the 249 subjects with moderate and mild hemophilia A, respectively, and of 8 to 42 percent among the 148 with hemophilia B (factor IX deficiency) (Table 1). Ten of our 72 subjects with von Willebrand's disease or other rare clotting disorders have antibodies to HIV-1 (Table 1). For each type of disorder, the prevalence of HIV-1 antibodies was directly associated with the degree of severity.

James Curran, who led the investigative effort by the CDC in the early 1980s, reflected the uncertainty of these studies and the increasing tendency by experts to identify the midpoint of seroconversion at an increasingly later date in 1983.

A large number of epidemiologic studies are currently underway to investigate the spectrum, course, and cofactors involved in HIV infection. These projects are preliminary, given the long incubation period for this disease (Lui et al., 1986) and the recency of seroconversion for most at-risk populations. For example, two independent studies suggest that over half of the factor concentrate recipients in the US acquired antibody to HIV between 1981 and the end of 1983 (Evatt et al., 1985; Eyster et al., 1985).

Janine M. Jason and James W. Curran, "The Epidemiology of AIDS," Blood, Blood Products and AIDS, edited by R. Madhok, MD, C. D. Forbes, MD (Glasgow U.), and B.L. Evatt, MD (CDC), 1987, p. 6.

Japan provides helpful data on the probable median seroconversion midpoint date for the U.S. hemophilia community. The median midpoint of Japanese hemophilia patients is reflective of the U.S. midpoint date because

[h]emodialysis patients usually receive transfusion from a limited number of Japanese donors but hemophiliacs receive infusion of commercial factor VIII concentrates prepared from pooled plasma mainly, if not exclusively, of American donors. This is likely to be the reason for the occurrence of HTLV-III/LAV infection among the Japanese hemophiliacs but not in other groups of individuals studied.

Yoshio Koyanagi, et al., "Detection of Antibodies to Human T-Lymphotropic Viruses Type I and III In Japanese Hemophiliacs," AIDS Research, 1:5 (1984), p. 353, 357. A subsequent AIDS Research article, "Clinical, Immunological, And Virological Aspects In Japanese Hemophiliacs and AIDS Patients," 2:Supplement 1 (1986), p.S141, reported that "[m]ore than 90% of antihemophilic factor concentrate has been imported from abroad, mainly from the United States."⁵⁷ In this study, sera was collected from sixty-five

⁵⁷Piet J. Hagen explains the reason for the large plasma importation need in Japan:

Green Cross [the current parent company of Alpha Therapeutic Corporation] was founded in 1950 as Japan's first (commercial) blood bank. In 1964, however, the government decided to transfer the collection of blood to the (Japanese) Red Cross because of the high incidence of hepatitis associated

hemophilia patients (58 hemophilia A, six hemophilia B and 1 with Von Willebrand's Disease), 85 hemodialysis patients and 304 healthy Japanese workers. Of the sixty-five hemophilia patients whose sera was collected during 1982 through the first half of 1984, all of whom "had received infusion of commercial factor VIII concentrate," only ten possessed antibodies to HTLV-III." *Id.*, p. 355. All eighty-five of the hemodialysis patients were negative for antibodies to HTLV-III, as were all 304 Japanese workers. *Id.* As the study reported, "[i]nterestingly, a sample obtained in 1983 from a hemophiliac was negative for anti-HTLV-III, while another sample obtained in 1984 from the same patient was positive, indicating the occurrence of seroconversion during the period." *Id.*

These variances with Eyster's early estimates cannot be explained by differences with Japan in population size or frequency of factor concentrate infusion; at the time of the study, there were an "estimated 4,000 patients with hemophilia A (15) and an annual consumption of 218,000,000 units of factor VIII concentrates." *Id.* at p.357. Further, the later midpoint of seroconversion theorists have consistently taken the position that the later conversion dates were consistent regardless of the size of the local population or its

with paid-donor blood. On the basis of this decision, the Green Cross Corporation terminated its commercial collection of blood. From that time onward it only fractionates plasma collected by the Japanese Red Cross and from foreign (commercial) sources.

Hagen, *Blood: Gift or Merchandise*, Alan R. Liss, Inc., (1982), p.122. Japan purchased Alpha Therapeutic Corporation expressly to obtain such a plasma supply:

The Alpha Therapeutic Corporation was established in the United States in 1978, when Green Cross acquired Abbott's Scientific Products Division. Green Cross paid \$24 million for Abbott's fractionation plant, which had a capacity of 300,000 liters of plasma in 1979. [...] The reason Green Cross bought Abbott's plasma division was to get a share in the American plasma supply, and to gain entry to U.S. and European markets. As mentioned before, commercial collection of blood is not allowed in Japan. Of the 193,000 liters of plasma used in Japan in 1977, 90,000 liters had to be imported. Therefore, it was attractive to Green Cross to establish a company in the United States. Through Alpha, which operated 29 plasmapheresis centers in 1980, its supply of plasma was secured.

Id. at p.122.

location, i.e., in states such as Georgia and California.⁵⁸ This evidence supports the occurrence of a midpoint of seroconversion in the United States of not earlier than 1983.

A study of Chinese patients with hemophilia also support a later date for the U.S. hemophilia median midpoint of seroconversion. Yi Zeng, et al., "Detection of Antibody To LAV/HTLV-III in Sera From Hemophiliacs in China," *AIDS Research*, 2:Supp.1, (1986), p.S147, reports that, while AIDS was first reported in China in 1981 (*Id.*), the use of ELISA, Western blots and immunofluorescence techniques revealed LAV/HTLV-III seropositivity in only 4 of 28 hemophiliacs treated with Factor VIII. Of those 28 patients, 18 had used Armour Company-produced factor VIII concentrate in the Zhejiang Province, 8 had used Alpha-produced factor VIII concentrate in Beijing, and 2 had used factor VIII product that was not clearly identified in the study as concentrate, as opposed to cryoprecipitate. All four of the seropositive patients were from the Zhejiang Province and had used Armour concentrate, and as of publication, none of them had yet demonstrated symptoms for AIDS. Once again, the low seroconversion rates for Chinese patients using American-manufactured factor VIII concentrate, along with the expectation of that symptoms of AIDS would appear within 2 years after infection for at least half of the infected patients,⁵⁹ do not support the early U.S. seroconversion midpoint predictions of Eyster.

A study of hemophilia patients in Spain support a median midpoint of seroconversion in the U.S. of not earlier than 1983. M. Ollero, et al., "Antibodies to the AIDS-Associated Retrovirus In Hemophiliacs and Other Individuals From Southern Spain: Lack of Correlation With Lymphocytes Sub-Populations," *AIDS Research*, 1:6, (1984/85), pp.439-445. The investigators studied 54 hemophilia patients, all of whom received factor VIII concentrate manufactured exclusively in the United States. *Id.*, p.439, 440. "Sera was collected from individuals with either hemophilia A or hemophilia B from March 1982 to December 1984. From 20 patients at least two or more serum samples from different years were available." *Id.* at p.440. The study reported:

⁵⁸David J. Volsky, PhD, "HTLV-III/LAV Antibodies and Virus In Hemophilia Patients in Nebraska: Survey and Initiation of a Prospective Study," *AIDS Research*, vol. 2, No. 1, (1986), p.52.

In the period of June, 1983 through May, 1984, the incidence rate of AIDS in persons with hemophilia A in selected areas of the United States was similar to that of homosexual men in New York City or San Francisco (10). Antibodies against HTLV-III/LAV were reported in 64% of hemophiliacs in Denmark (11), 72% of hemophiliacs in Georgia (12), and 85% of patients with hemophilia A in California (13).

⁵⁹Eyster, et al., "Development and Early Natural History of HTLV-III Antibodies in Persons with Hemophilia," *JAMA*, 235:15, April 19, 1985, p.2219, contends: "the latency period between exposure and appearance of AIDS ranges from five months to five years, with a mean of about two years."

When sera from different years were tested, 2/7 patients' sera collected in 1982 were antibody positive (28.5%), 14/28 (50%) in 1983, and 19/39 (48.7%) in 1984. When the multiple sera specimens from 20 patients from different years were tested, the results showed that three patients seroconverted to a positive state from 1983 to 1984 and three individuals who were initially positive for antibody to ARV became negative in the same period of time. This latter finding could indicate a reduced exposure to ARV antigens in the clotting factor preparation and a lack of infection of these individuals by the AIDS virus.

Id., p. 441. Once again, this data is consistent with a post-1983 median midpoint of seroconversion for populations using U.S.-manufactured factor VIII concentrate.

Hemophilia patients in Israel provided the most support for Eyster's predictions of early seroconversion, and yet concluded that not even half of the patients studied possessed HIV antibodies by 1983: "Of 40 seropositive [hemophilia] patients, 1 (2.5%) had antibodies by 1980, 4 (10%) by 1982, 14 (35%) by 1983, 10 (25.0%) by 1984, and 11 (27.5%) by May 1985." Shlomit Orgad, et al., "Antibodies to HIV in Israeli Hemophiliacs: Relationship Between Serological Profile and Disease Development," *AIDS Research and Human Retroviruses*, Volume 3, Number 3, 1987, p.323. The study does not indicate how much of the factor concentrate was manufactured in the U.S.; however, "only 1 of the patients who received locally prepared blood products developed antibodies to HIV." *Id.* The distinction between foreign manufactured and domestic product clearly existed, and the results indicate that most of the concentrate utilized was purchased outside of Israel.

Studies within the United States also tend to disprove a median seroconversion midpoint before 1983. A study by M. Essex, et al.,⁶⁰ which included among its authors the CDC's Evatt, collected serum samples from 45 hemophilia patients from Atlanta, Georgia,⁶¹ 41 from Birmingham, Alabama, and 39 from Los Angeles, California. The study also analyzed samples from New York City, but because they were collected between 1978 and 1982, they are not particularly helpful. The other samples were all collected in late 1982 or early 1983. *Id.* The study tested for antibodies to cell membrane antigens associated with "HTLV-MA," which antibodies had been found in 36% of a group of AIDS

⁶⁰Essex, et al. "Antibodies to Human T-Cell Leukemia Virus Membrane Antigens (HTLV-MA) in Hemophiliacs," *Science*, September 9, 1983, pp.1061-1063.

⁶¹Georgia, somewhat surprisingly, "was among the first states to report AIDS in a patient with hemophilia (1983); California did not report a case until one year later." Evatt, et al., "Coincidental Appearance of LAV/HTLV-III Antibodies In Hemophiliacs and the Onset of the AIDS Epidemic," *The New England Journal of Medicine*, vol. 312, No. 8, Feb. 21, 1985, p. 484.

patients. *Id.* The antibodies appeared among only 5-13% of the three geographic groups described. *Id.* at 221. 67% of hemophilia patients with AIDS or severe lymphadenopathy in the study possessed the antibody, and none of the 47 healthy lab or hospital workers possessed the antibody. *Id.* New York patient serum actually possessed the highest percentage of positive results at 19% (*Id.*), which continues to support the conclusion that Eyster's claims of a 1982 midpoint of seroconversion are flawed by testing serum obtained predominantly from New York and Pennsylvania patients voluntarily seeking medical treatment, presumably partly due to symptoms of suppressed immune systems.

California, by comparison, appears to have a median midpoint of seroconversion of not before mid-1983. In a study of 21 patients with hemophilia A in a California clinic, "[a]mong most of the 21 patients with hemophilia A in California, seroconversion did not occur until 1982, and then rapidly increased in 1983. By 1984, more than 85 per cent of the group had antibody to LAV [lymphadenopathy-associated virus]." Evatt, et al., "Coincidental Appearance of LAV/HTLV-III Antibodies In Hemophiliacs and the Onset of the AIDS Epidemic," *The New England Journal of Medicine*, vol. 312, No. 8, Feb. 21, 1985, p. 484.

In short, almost every seroconversion and re-infection of the U.S. hemophilia population which occurred after January, 1983, and possibly after July, 1982, was preventable by FDA acting upon the information in its possession. There appear to be over 3,500 initial HIV exposures in the U.S. hemophilia population which occurred after the January 4, 1983 CDC/FDA Workgroup meeting on AIDS. The later the date of the median point of seroconversion, the greater the direct responsibility the FDA has for the infection of the hemophilia community.

SECTION SIX: THERE EXISTS AMPLE JUSTIFICATION FOR THE HEMOPHILIA COMMUNITY'S REQUEST FOR THE CREATION OF A FEDERAL TRUST FUND FOR PERSONS INFECTED BY HIV-CONTAMINATED CLOTTING FACTOR OR THEIR INFECTED SPOUSES, CHILDREN OR OTHER SURVIVORS.

A. A Demographic Theory of Federal Disaster Relief Assistance.

The hemophilia community believes that it can overcome the economic objections to the legislation, with the first defense being that of federal disaster relief. First, this crisis among the nation's hemophilia community satisfies in all respects the requirements for federal disaster relief. It is caused by forces beyond the control of the affected community, it is devastating enough in nature to be of national concern, and it crosses state boundaries so as to require a federal effort to ensure a consistency of aid. The important issue to note is that this disaster is demographic and not geographic. Geographic disasters are those that usually receive federal funding and are easy to conceptualize, i.e., a hurricane or other natural disaster. Instead, this disaster is demographic, i.e., occurring within, but not geographically throughout, a population. It is a category of disaster much more difficult to conceptualize, but it nevertheless meets federal guidelines for relief.

Should the Congress determine that the problem was unavoidable, then by definition it was beyond the control of man and is a natural disaster. If the Congress determines that it was avoidable, then it was by definition of the type against which the FDA should have protected the hemophilia community or at least warned of its dangers. The characterization of the disaster in the latter form would justify the provision of funding under subpoint B.

B. The FDA's Misconduct Has Incurred Liability for the Federal Government, Regardless of the Availability of Funds.

1. Such misconduct does not require budgetary justifications in order to justify the enactment of the Ricky Ray Act.

For all of the reasons previously discussed, the FDA has incurred liability for the federal government by its negligence in the execution of its statutory responsibilities. The FDA misconduct is a budgetary condition precedent and thus represents a financial obligation of the government that is not optional, but has already been incurred. As such, the FDA's responsibility is not diminished by budgetary concerns.

Additionally, the Federal Tort Claims Act prevents the hemophilia community from suing the FDA for misconduct without a special legislative exemption of the FDA from the

Act's protections. Accordingly, the federal government has eliminated any alternative means for the hemophilia community to seek reimbursement from the FDA directly for their injuries.

2. Notwithstanding the absence of a philosophical need to justify a budgetary offset, the waiver provision in the Act for any claims against the federal government represents a savings to the government that substantially offsets the cost of the legislation.

The Ricky Ray Act contains a waiver of any claims as against the federal government by any person accepting payment under the Act. The value of this waiver approximately offsets the anticipated cost of this legislation. Each claim of HIV infection is certainly valued at, at least, one million dollars in damages. If the hemophilia community were granted an exemption to sue the FDA under the Federal Tort Claims Act, the FDA would be named as a defendant with approximately four defendant pharmaceuticals. Its shared liability in each suit would probably be not less than 20%, or \$200,000, for each suit. These are conservative estimates, both as to the damages level of any one suit, and as to the FDA's potential share of liability, since proper FDA action uniquely could have entirely prevented those infections where causation is established.

Given this liability level, the recent estimates of the midpoint of seroconversion as sometime during 1983, establish that the FDA could have prevented more than 3,500 infections if it had acted properly after the January, 1983 FDA/CDC meeting. Legal experts in this area have placed the date at which knowledgeable and responsible parties, which would include the FDA, should have acted as early as January, 1982. Ring and Leonard, *supra*, p.177. Accordingly, the date when the FDA should have conducted Hepatitis B core antibody testing, according to the Institute of Medicine, is not necessarily the earliest possible date when the FDA should have acted with warnings. Warnings, such as appropriate patient package inserts, are not dependent upon scientific certainty of injury, and therefore the FDA should have required their use earlier than January of 1983; instead, warnings were not first approved until January of 1984, and not at the request of the FDA, but voluntarily by a pharmaceutical.

If the FDA had done nothing more than issue warnings after the July, 1982 blood advisory meeting, it is possible it could have prevented over five thousand infections out of the approximately 7,500. Using only a median midpoint of seroconversion of January 1, 1983, as the date by which the FDA had a legal duty to begin a proper response to the evidence of HIV infection, the FDA is still responsible for at least 3,500 infections valued at, at least, \$200,000 each, representing a monetary liability by the FDA of \$700,000,000. This is sufficiently close to the projected costs of the Ricky Ray Act to justify its funding. Since the FDA is singularly responsible for the impossibility of actually establishing the median midpoint of seroconversion date with reasonable scientific certainty, the evidentiary presumption as to the number of persons who were infected as a result of the FDA's failure to act should be

construed against the FDA. However, the fact that over half of the infected population has survived to this date, and the fact that many infected hemophilia patients are not yet symptomatic, provides increasing evidence that the midpoint of seroconversion was as late as the end of 1983, which reasonably could increase the value of the statutory offset to well over one billion dollars.

3. The theory that the FDA should have required pasteurization technology not later than by 1981 solves any concerns about establishing the midpoint of seroconversion, and increases the value of the statutory waiver offset to an amount well in excess of one billion dollars.

The theory of FDA liability based upon its failure to require pasteurization eliminates the need to establish the midpoint of seroconversion. If the Congress finds that the FDA was negligent in failing to require pasteurization by 1981, the Congress must find that the FDA negligently allowed the infection of nearly the entire hemophilia community. Those several thousands of infections valued at FDA liability of \$200,000 per infection establish a statutory waiver offset of approximately one and one-half billion dollars. However, given that pasteurization would unquestionably have prevented all of the subsequent infections, the FDA's share of liability certainly would rise to at least 50% or more, with a statutory waiver offset consequently of over three billion dollars. Since it was unreasonable for the FDA to have failed to require the pasteurization of concentrated clotting factor, in light of the FDA's knowledge concerning hepatitis B, the risks of pooled plasma, and the availability of heat-treatment technology, it is reasonable to assume the existence of a budgetary offset of three billion dollars. This is clearly sufficient to justify the legislation.

- C. The FDA Should Be Deterred From Future Misconduct If the Congress Wishes to Protect Vital National Health Interests Affecting All Americans.

The national blood supply represents a vital national interest, and this legislation would deter the FDA from continuing a complacent attitude toward its safety. The problems with blood supply safety have not ended with AIDS. They have continued in the form of donor blood potentially contaminated with a possible blood borne agent causing Creutzfeldt Jacob Disease, a fatal neurological disorder. They have also continued with three new infections of hepatitis A among hemophilia patients using concentrate, as reported in the January 19, 1996 MMWR. The FDA simply is not adequately observing its responsibility to maintain the safety of the blood supply, and the requirement that the government make reparations on behalf of the FDA will create both congressional and public consternation sufficient to cause the FDA to improve its efforts.

CONCLUSION

The FDA actively obstructed the flow of information from the CDC to the hemophilia community. It reassured the public that the risk of AIDS infection from blood was low, and in order to make that reassurance consistent with evidence of AIDS among hemophilia patients, the FDA stated that the existence of AIDS among hemophilia patients was statistically minimal and not reflective of the overall risks to the hemophilia community. The FDA exclusively regulates the safety of the blood supply to the exclusion of state regulatory powers, which it expressly pre-empts to the extent that they conflict, and the FDA establishes the minimum blood supply safety levels nationally. Additionally, assurances that federal efforts are the most complete, scientifically sound and effective curtailed private efforts to monitor the safety of the blood supply. However, its actions were against the best available scientific evidence and were irresponsible in light of the purpose of the FDA and the public's reliance upon its carrying out of its public health charge. The hemophilia community was directly injured as a result to a devastating degree.

The overwhelming challenges presented to this community by the infection of patients with the most severe form of hemophilia is difficult to comprehend in an empathetic sense. As Shelby Dietrich, M.D. concluded at the 1989 Los Angeles symposium:

The spread of HIV infection among hemophiliacs via contaminated blood components and blood products has had devastating medical, social and economic effects, the dimensions of which remain unmeasurable. At least three-fourths of heavily treated classic hemophiliacs are infected with HIV [. . .] The curve of progression to AIDS is open-ended. [. . .] Infected hemophiliacs have two co-existing chronic illnesses demanding comprehensive and continuing care.

Recent Advances in Hemophilia Care, pp. 84-85. The damage caused by the FDA's inaction and misinformation is clear: over seven thousand hemophilia patients and their family members were infected with HIV, and over three thousand thus far have died. On average, one hemophilia patient or an infected family member dies every day in the United States from AIDS. In such a small community of only fifteen to twenty thousand members, it is difficult to exaggerate the negative consequences of the FDA's actions. The facts and applicable law strongly support a decision by the House Subcommittee on Immigration and Naturalization and the Senate Judiciary Committee to vote in favor of the Ricky Ray Act.