IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF IOWA
CENTRAL DIVISION

JOHN & MARY DOE as Parents and John and Mary Doe as Guardians on behalf of John Doe, Jr., Plaintiffs, v. BAXTER HEALTHCARE CORPORATION, et al. Defendants. CUTTER BIOLOGICAL, a Division of Miles, Inc., et al. Intervenors-Defendants.	Civil No. 4-96-cv-10738
JOHN & MARY DOE as Parents and John and Mary Doe as Guardians on behalf of John Doe, Jr., Plaintiffs, v. CUTTER BIOLOGICAL, a Division of Miles, Inc., et al., Defendants.	Civil No. 4-96-cv-10843
JOHN DOE, II, Plaintiff, v. CUTTER BIOLOGICAL, a Division of Miles, Inc., et al. Defendants.	Civil No. 4-96-cv-10844 **EXPERT WITNESS REPORT OF WILLIAM ROBINSON, M.D. REGARDING JOHN DOE I (FED. R. CIV. P. 26)**

I, William Robinson, M.D. state and declare as follows:

1. I am a medical doctor, virologist and infectious diseases practitioner. I was a Professor of Medicine at Stanford University for 33 years and retired one year ago. I am now Emeritus Professor. My C.V. is attached hereto as Exhibit A and includes the list of my publications for the past ten years.

2. My office is located at the Stanford Medical Center, 300 Pasteur Drive, Stanford, CA 94305.

3. My compensation rate is $400/hr for deposition and trial testimony, including travel time, and $300/hr for research, preparation and review. My prior trial and deposition testimony is listed on Exhibit B hereto.

4. My opinions stated herein are based on my education, training, experience, research, medical practice, and reading in the fields of epidemiology and infectious diseases (including both viral hepatitis and HIV/AIDS), and the documents I reviewed and/or rely upon are cited and/or appended herein.

5. My entire career in medicine and research focused, in large part, in infectious diseases and viral diseases, including studies of human viruses such as viral hepatitis, HIV and other retroviruses, and their associated clinical conditions and clinical courses. Additionally, much of my research and many of my publications in peer reviewed medical literature, textbooks and treatises have been devoted to these scientific issues.

6. My opinions, as expressed herein are given within a reasonable degree of medical and scientific certainty, and are based upon information of a type reasonably relied upon by physicians and scientists in my field of expertise. I have particular knowledge and experience with respect to HIV infectivity, pathogenesis and AIDS, including reviews of data concerning the

time of infection and seroconversion. My opinions are based on my own work, as well as the works of others that have been published in the medical and scientific literature.

7. HIV is a retrovirus which has infected human populations and the hemophilia patient population in particular, at epidemic levels. The HIV epidemic in the hemophilia community resulted primarily because of infusions of HIV contaminated commercial Factor VIII and Factor IX concentrate products manufactured, distributed and/or sold by the defendants in this action.

8. Final outcomes of HIV infection vary and include, among other variations and possibilities: 1) progression to AIDS and premature death resulting from opportunistic infections and/or cancers associated with AIDS; 2) suppression of HIV infection with delayed onset of AIDS and death with antiretroviral drug therapy which has become widely used in the United States, Canada, Europe and Japan in the past decade; 3) long-term survival without treatment in a few "long-term non-progressors," whose CD4+ levels do not decline over time even in the absence of antiretroviral therapy.

9. A reliable means of assessing the progression of HIV infection is to assess the patients' CD4+ cell number counts over time, since a common finding associated with disease progression is a low CD4+ cell count. Stein, D.S., et al., 1992, "CD4+ Lymphocyte Cell Enumeration for Prediction of Clinical Course of Human Immunodeficiency Virus Disease: A Review," J. Inf. Dis. 165:352-363. While CD4+ cell numbers usually rise to near-normal levels several months after a primary HIV infection, they subsequently generally decrease steadily at an average rate of 25 to 60 cells/ul per year. Lang, W., et al., 1989, "Patterns of T Lymphocyte Changes with Human Immunodeficiency Virus Infection: From Seroconversion to the Development of Aids," J. AIDS 2:63-69. Also of assistance in assessing the progress of HIV

infection is the patient's "viral load". Pantaleo, G., et al., 1993, "Mechanisms of Disease: The Immunopathogenesis of Human Immunodeficiency Virus Infection," N. Eng. J. Med. 328:327-336.

10. I have reviewed medical and pharmacy records, and/or related excerpts and summaries, pertaining to John Doe I from the University of Iowa, Burlington Medical Clinic, Dr. Kisker, Dr. Stapleton and Dr. Clayton. I have also reviewed deposition excerpts from the November 21, 1996 deposition of John Doe I's father, the June 1, 2000 deposition of Dr. Kisker and the expert report of Dr. Roger Grimson. My opinions as they relate to John Doe I are set forth below.

11. John Doe I was born on September 24, 1978 in Iowa. He was born with a severe Factor VIII deficiency (<1% activity). He has not been found to have antibodies which inhibit factor VIII.

12. John Doe I first experienced bleeding episodes in 1979 and was treated with cryoprecipitate.

13. John Doe I first received commercial Factor VIII concentrate on May 19, 1980 and subsequently received repeated concentrate infusions each year including, approximately: 2,740 Factor VIII units in 1980; 11,870 in 1981; 12,830 in 1982; 33,000 in 1983; 17,365 in 1984 and 1,470 in 1985. Until 1983, John Doe I used a low dose of Factor VIII concentrate according to the definition of Kroner, et al 1994. In 1983, when he was first diagnosed with Hepatitis B, John Doe I used significantly more Factor VIII (moderate dose level of Kroner, et al, 1994) than he had previously. The pre-1986 Factor VIII concentrate products used by John Doe I were sold and/or made by Cutter, primarily, as well as Alpha, Miles/Cutter

and Armour. John Doe I began using exclusively heat treated products in approximately May, 1985.

14. John Doe I's medical records between birth and 1987 do not describe an illness suggestive of the acute infectious mononucleosis-like syndrome which has been reported to sometimes follow within weeks of primary HIV infection and/or seroconversion. I am aware that Dr. Kisker testified at his deposition that a September 1982 episode of "tonsillar hypertrophy" constituted, in his opinion "a seroconversion related illness." I disagree with Dr. Kisker's opinion since John Doe I suffered from recurrent tonsil problems, first observed on September 13, 1979 at 11 months of age and observed again on April 3, 1981, October 6, 1982, March 8, 1983, June 13, 1983, and December 20, 1984, since the original University of Iowa/Kisker medical records relating to the September 8, 1982 visit with Dr. Kisker fail to include any specific observation of any tonsillar enlargement in Dr. Kisker's clinical notes and follow-up report to Dr. Clayton. (UI 48, 52; Kisker 95.) In the absence of a contemporaneous record, recall of such a condition several years later is inherently unreliable. Further, tonsillitis alone in a young child is insufficient evidence by which a diagnosis of primary HIV infection can be made with a reasonable degree of medical certainty.

15. John Doe I was first diagnosed with hepatitis B in December 1983 (UI 176 - UI 177). The hepatitis B virus (HBV) infection was the direct result of John Doe I's exposure to commercial Factor VIII concentrate, a substantial portion of which was then and is now known to have been then contaminated with hepatitis B virus. He had been tested for hepatitis B surface antigen and antibody prior to 1983 with negative results. John Doe I was subsequently demonstrated to be chronically infected with hepatitis B virus by testing in 1985 and 1988 (UI 58, UI 101-UI 102). In July, 1991 a test for hepatitis C virus antibody was positive

indicating prior infection with hepatitis C virus (HCV) (UI 372) and liver function testing demonstrated chronic hepatitis indicating likely chronic hepatitis C virus infection. It is more likely than not that John Doe I contracted hepatitis C from infusion of commercial Factor VIII concentrate products contaminated with hepatitis C virus.

16. John Doe I was first informed that he was HIV positive in July 1987, following testing performed at the University of Minnesota. (Deposition of John Doe I's father, p. 63.) The 1987 HIV test results do not appear to be reflected in the available medical records, however, probably because the records of HIV infection were treated with unusually strict confidentially by the University of Minnesota, a common practice during this period. Given the absence of other risk factors for HIV in John Doe I, and the known transmission of HIV through commercial Factor VIII concentrates, it is my opinion that John Doe I contracted HIV from his infusions with commercial Factor VIII concentrate products. In my opinion it is more likely than not that John Doe I seroconverted to HIV in 1983. This opinion is based on the dose of factor VIII concentrate used in the years 1980 through 1983 and the absence of clinical evidence suggesting a time of primary infection.

17. Lymphocyte subset testing (CD4+ cells) was regularly performed upon John Doe I. See Exhibit hereto, the table of the CD4+ cell measurements over time. The pattern of CD4+ cell concentrations or counts in John Doe I demonstrate variation, as expected, and confirm a slow downward trend consistent with the progression of his disease. CD4+ Exhibit. John Doe underwent two tests which showed CD4+ levels below 200; in October 1995, he had a CD4+ count of 62 (UI 1424-25), likely partly attributable to chemotherapy (UI 1456), and on March 11, 1998 he had a CD4+ count of 171 (UI 1994). Most recent, according to John Doe I,

was a count of 500 in the Winter of 2000. (Copies of the most recent relevant medical records have been requested, but not yet received, from his treaters.)

18. Following an acute onset of illness in November, 1993, involving three weeks of lethargy, joint/muscle aches and intermittent frontal headaches, John Doe I was admitted to the University of Iowa Hospital on December 1, 1993 and discharged on December 10, 1993 with a diagnosis of non-Hodgkin's lymphoma. (UI 724-726, 922). On November 30, 1993, his CD4+ cell count was 275. Chemotherapy and related treatments were initiated upon John Doe I in the hospital, consisting of cyclophosphamide, dexamethasone, vincristine and IVIG and G-CSF support. John Doe I was subsequently hospitalized regularly for, and occasionally self-administered with, follow-up chemotherapy sessions which occurred regularly until May 2, 1995 (UI 1281), and his lymphoma has since been in remission. Non-Hodgkin's lymphoma is the most common malignancy associated with advancement of HIV infection in hemophiliacs. Ragni, M., et al., "AIDS-Associated Non-Hodgkin's Lymphomas as Primary and Secondary AIDS Diagnoses in Hemophiliacs," Journal of Acquired Immune Deficiency Syndrome, Vol. 13(1), pp. 78-86, September 1996.

19. John Doe I commenced antiretroviral therapy in September 1996 with AZT, 3TC and Indinavir/placebo (UI 1530). He apparently switched to another antiretroviral drug therapy in April, 1997 as part of the Upjohn 21 study of AZT plus 3TC versus AZT plus Dilarardine. (Stapleton letter to Kisker of 4/4/97, UI 1453.) He has since remained on combination antiretroviral drug therapy through the present time.

20. John Doe I's HIV viral load was 18,950 copies HIV per ML on April 17, 1996, 47, 825 copies/ML on August 13, 1996 (UI 1608) and, following commencement of antiretroviral therapy, dropped to 3,000 copies/ML on April 2, 1997. John Doe I himself reports

that his Winter 2000 test showed < 400 copies/ML, an undetectable level. (Again, the most recent medical records are presently unavailable and I intend to supplement the opinions in this report when these records become available).

21. Currently used anti-HIV therapy consists of a potent antiretroviral drug combinations which strongly suppress HIV replication. Survival after a diagnosis of AIDS in HIV-positive hemophiliacs has improved significantly since the widespread adoption of antiretroviral therapy and adoption of prophylaxis against opportunistic infections. Detels, R., et al., "Effectiveness of Potent Antiretroviral Therapy on Time to AIDS and Death in Men with Known HIV Infection Duration," JAMA, 11/4/98 - Vol. 280, No. 17. The antiretroviral drug therapy nevertheless has its own serious side effects in that the drugs used can deleteriously affect the patient's health by, for example, causing neuropathy, nausea and abdominal pain, bone marrow suppression, anemia, thrombocytopenia, and suppression of the immune system.

22. John Doe I is currently being maintained on multi-antiretroviral drug therapy consisting of Stavudine, Lamivudine, Indinavir, Interleuken-2 and Remune, as well as other medications, and is expected to remain on comparable therapy for the balance of his life.

23. Despite the use of antretroiviral drug therapy and drugs for prevention of certain opportunistic infections in HIV infected persons, and despite encouraging reports of the effect of antiretroviral drug combinations reducing viral load, increasing CD4+ cell counts and prolonging life for an undetermined period, patients with HIV receiving such therapy remain at significant risk of death from opportunistic infections and cancer, particularly the most common infections such as Pneumocystis carinii (PCP), CMV, toxoplasmosis, and mycobacteria including tuberculosis. Patients on prophylaxis for PCP, for example, can still develop PCP. The risks of

fatal opportunistic infection are particularly high in persons, such as John Doe 1, with a history of declining CD4+ counts and with hepatitis.

24. I am aware that Dr. Jack Stapleton's letter to Dr. Carl T. Kisker of April 25, 1996 indicates that John Doe I "certainly does appear to be a long-term non-progressor." John Doe I, however, is not a "non-progressor" in the scientific or medical sense of the term since he is, and has been on, antiretroviral medication for several years and since his CD4+ cell counts steadily decreased following his infection with HIV. Buchbinder, S.P., et al., 1994, "Long-Term HIV-1 Infection Without Immunologic Progression," AIDS 8:1123-1128. The most recent report of 500 CD4+ cells in the Winter of 2000 probably only reflects expected variation and/or responsiveness to antiretroviral therapy and cannot be expected to continue for the long term due to an absence of positive, reported long-term antiretroviral responsiveness data. Similarly, the apparent reduction in John Doe I's total HIV viral load cannot be expected to continue indefinitely in the absence of data demonstrating that virus suppression can be indefinitely maintained by such therapy.

25. It is my opinion that, based upon evidence concerning HIV, HCV, and HBV infections and John Doe I's medical history, John Doe I is more likely than not to die within the next ten to twenty years as a result of these infections. John Doe I's HIV infection and resulting illnesses and medical problems will therefore substantially shorten his normal life expectancy and cause him prolonged suffering and premature death.

26. The risk of premature death is increased for John Doe I because he has viral hepatitis resulting from his use of commercial clotting factor concentrate products. Hepatitis C virus (HCV) and HIV-1 coinfection is common in hemophiliacs. Hepatitis C is a progressive disease in more than 50% of those afflicted. A prospective study by Daar et al.

(Journal of Infectious Disease, 2001) demonstrated a negative interaction between these two viruses. Every 10- fold increase in HCV RNA resulted in a 1.66 increase in risk of progression to AIDS and a 1.54 increase in risk of AIDS-related death. The risk was the greatest for those with high titers of both viruses. Daar, E.S., et al., "Hepatitis C Virus Load is Associated with Human Immunodeficiency Virus Type 1 Disease Progression in Hemophiliacs." Journal of Infectious Disease 2001;183:589-95. Persons infected HCV as well as HIV have significantly worse prognoses than those without hepatitis virus infections. Published evidence suggests that the severity of hepatitis C is increased in HIV infected patients, and progression of HIV disease is more rapid in patients with hepatitis C.

27. Although there have been advances in medical and pharmacologic treatment, there is no cure for HIV infection and no cure for AIDS, and John Doe I's future of prolonged illness and premature death will involve painful and debilitating illnesses and medical problems certain to cause him great pain and suffering.

28. Medications necessary for John Doe I's current and future treatment include combination antiretroviral drug therapy, which are expected to be required and be taken for the balance of his life.

29. Likely future complications of John Doe I's disease and treatment include opportunistic infections and cancers usually requiring hospitalization and expensive related medications and treatments.

30. It is my opinion that the Factor VIII manufacturers acted with willful and reckless disregard for the health and safety of all hemophiliacs, including John Doe I, by failing to fully and adequately warn the hemophiliac community, by no later than July 1982 when there were three cases of AIDS in hemophiliacs, and December 1982 when there were seven or eight

cases of AIDS in hemophiliacs, of the risks of AIDS associated with Factor VIII. Had they adequately warned of those risks in December 1982, John Doe I would likely have avoided HIV infection since hemophiliacs would have ceased the use of Factor VIII (and Factor IX) except for treatment of life threatening bleeds, which John Doe I did not experience in the relevant period between December, 1982 and the adoption of heat treated products in 1985.

31. It is also my opinion that John Doe I has been harmed by his exposure to years of intermediate or crudely purified Factor VIII concentrate therapy because the use of moderately or crudely purified clotting factor concentrates (and failure to switch to cryoprecipitate or no treatment) appears to harm HIV infected patients by increasing susceptibility to HIV infection and accelerating HIV-associated immune impairment. In fact, moderately or crudely purified clotting factor concentrates even alter the immune function of hemophilia patients not infected with HIV, including causing reductions of CD4 cell counts and CD4/CD8 cell ratios. Moreover, hemophiliacs with reduced CD4 cell counts and low CD4/CD8 cell ratios appear to be more susceptible to infection with HIV than patients with normal CD4 cell counts. Beginning in 1976, only two years after licensing of factor concentrates, numerous and serious side effects were reported. These included lymphocytopenia, thrombocytopenia, splenomegaly, renal failure, elevated circulating immune complexes, diastolic hypertension, hemolytic anemia and severe liver damage. (Unsolved Problems in Comprehensive Hemophilia Treatment Therapy: National Heart, Lung, and Blood Institute, 1976). In addition, it was known that out of 1,551 hemophiliacs enrolled in the Hemophilia Study Group from 1975-1979, the prevalence of lymphocytopenia and thrombocytopenia in patients over 5 years of age on entry was found to 9.3% (94/1,012) and 5.0% (26/518), respectively. A subsequent study concluded that (a) the frequency of lymphocytopenia and thrombocytopenia was increased in multi-

transfused factor VIII deficient hemophiliacs before the advent of AIDS, and (b) persistent lymphocytopenia and thrombocytopenia appear to be strongly associated with liver disease, which was the leading cause of death in a cohort of hemophiliacs followed five or more years. Of particular interest is the follow up of 79 of these patients in the North Carolina Hemophilia Study Group with lymphocytopenia or thrombocytopenia. Eight patients (10%) developed immune system abnormalities, including idiopathic thrombocytopenic purpura, non-Hodgkins Lymphoma, generalized lymphadanopathy and oral moniliasis without obvious causes. (Long Term Follow-Up of Hemophiliacs With Lymphocytopenia or Thrombocytopenia: Eyster, Whitehurst, Catalano, Campbell et al; Blood, Vol 56, No 6 (December), 1985: pp 1317-1320).

32. Defendants are responsible not only for John Doe I's HIV infection, but also for the harmful effects of intermediate or crudely purified clotting factor concentrates since they failed to warn of the immune suppressive side effects in July 1982, when they knew of three reports of severe immunosuppression in hemophiliacs. M.M.W.R., July, 1982. The fact that long term use of intermediate purity or crudely purified factor concentrates was potentially damaging to the immune system was known to the defendants as early as 1976. The defendants, held to the standard of experts in the field, had the duty to be particularly watchful of the long term effects in patients using these products after that date and to timely warn of the risks of which they knew or should have known. Defendants failed to fulfill this duty.

33. It was known as early as the late 1970's that there was a substantial risk of transmission of certain viruses by Factor concentrates. It is my opinion with a reasonable degree of medical certainty that by the mid-1970's conditions to substantially inactivate hepatitis B virus (HBV), based in part on knowledge of the structure of HBV and other viruses, were known. These conditions would, in retrospect, have also substantially inactivated the infectivity of HIV

and the non A, non B hepatitis agent now known as hepatitis C virus (HCV). These conditions included conditions of heating, detergent treatment and lipid solvent treatment. A reasonable research effort in the 1970s using knowledge of conditions to inactivate HBV would have established methods of inactivating HBV (as well as HCV and HIV) in factor concentrates. The methodology and knowledge of HBV were available in the 1970s to accomplish this.

34. It is my opinion that any hemophilia patient who was infected with HIV from factor concentrates in the late 1970s and early 1980's was the victim of negligence because the manufacturers of commercial factor concentrates had available to them methodology that through appropriate research could have been applied to factor concentrates to substantially inactivate enveloped viruses such as HBC, HCV and HIV and render those factor concentrates non-infectious for those viruses, and they did not do so in the 1970s. Procedures developed in the 1980s to inactivate HIV infectivity in factor concentrates utilized no methodology not available in the 1970s.

I declare under penalty of perjury under the laws of the United States of America and the State of California that the foregoing is true and correct. Executed this 16th day of February, 2001 at Palo Alto, California.

By: GRO-C

William Robinson, M.D.