

UNITED STATES DISTRICT COURT  
FOR THE DISTRICT OF COLUMBIA

CAMPAIGN FOR  
RESPONSIBLE TRANSPLANTATION,

Plaintiff,

v.

UNITED STATES FOOD AND DRUG  
ADMINISTRATION,

Defendant,

Civ. No. 00-2849 (RMU)

CIRCE BIOMEDICAL, INC.,  
DIACRIN, INC., DIACRIN/GENZYME LLC,  
GENZYME CORP., NEXTRAN, INC.,  
and NOVARTIS PHARMACEUTICALS  
CORP.,

Defendant-Intervenors.

**DECLARATION OF ALIX FANO, EXECUTIVE DIRECTOR,  
CAMPAIGN FOR RESPONSIBLE TRANSPLANTATION**

1. My name is Alix Fano. I am the founder and executive director of the Campaign for Responsible Transplantation (“CRT”), the plaintiff in this lawsuit. This declaration is based on my personal knowledge, and is submitted in support of Plaintiff’s Motion for Summary Judgment.

2. I hold a Master’s Degree in public policy from Tufts University and I have been a public health advocate and writer for over a dozen years. I am the author of the book Lethal Laws (1998), a critique of federal environmental toxicology programs. I have written letters and editorials that have been printed in newspapers, magazines, and scientific journals, including Biography, British Medical Journal, Houston Chronicle, Journal of the Royal Society of

Medicine, The Lancet, New York Times, and USA Today. I have lectured around the country and served as a resource person on public health issues for television, radio, and print media.

3. CRT – a 501(c)(3) non-profit organization – was founded in January 1998 to promote a ban on xenotransplantation, which is animal-to-human organ, cell, and/or tissue transplantation, due to public health risks, and a host of medical, societal, regulatory, economic, animal welfare, and environmental concerns. CRT is dedicated to ensuring that the public is fully informed about the many issues raised by xenotransplantation. Though it began as a small group of concerned laypersons, lawyers, and scientists, CRT is now an international coalition of physicians, scientists, nurses, and public interest groups that represents over 3 million people.

4. CRT regularly disseminates information about xenotransplantation through press releases, its Internet website ([www.crt-online.org](http://www.crt-online.org)), radio and television interviews, and letters to the editors of newspapers, magazines, and journals. CRT has become an informational resource for journalists, scholars, policy-makers, advocacy groups, and concerned citizens. See Attachments 1-3.

5. On December 10, 1998 CRT filed a citizen's petition with the Department of Health and Human Services ("DHHS"), which asked the agency to initiate rulemaking proceedings to prohibit xenotransplantation, and to issue an environmental assessment of the technology as required under the National Environmental Policy Act (NEPA). See Attachment 4. The petition, which was signed by 55 scientists and concerned laypersons, was filed pursuant to the Right to Petition Government clause contained in the First Amendment of the U.S. Constitution, the Administrative Procedure Act, and the DHHS's governing statutes and implementing regulations. In the petition, CRT charged that DHHS's issuance of the Draft Public Health Service Guideline on Infectious Disease Issues in Xenotransplantation in 1996 was

arbitrary and capricious, an abuse of agency discretion, and otherwise not in accordance with law. Although CRT's rulemaking petition was formally denied on December 7, 1999 (see attached), CRT continues to collect signatures on its generic petition, which is posted on its website. See Attachment 5.

6. Xenotransplantation has been a subject of public debate for many years, in part because, as discussed more fully below, scientific evidence has shown that xenotransplantation could result in cross-species viral infections, or "xenozoonoses," in human patients and unleash a worldwide public health epidemic on the scale of the Human Immunodeficiency Virus ("HIV/AIDS"). Major newspapers and magazines – including the New York Times, Wall Street Journal, Washington Post, Scientific American, and Time magazine – have featured articles about xenotransplantation. See Attachments 6-9. In addition, several major television news programs have examined xenotransplantation, including CBS's 60 Minutes (Aug. 27, 2000, "A Pig's Heart?"), PBS's Frontline (Mar. 27, 2001, "Organ Farm"), and ABC News' Turning Point (1997, Animal Transplants: Madness or Miracle?). The Institute of Medicine and the National Academy of Sciences – two prominent organizations that examine current medical issues – have published reports or volumes about xenotransplantation. See Institute of Medicine, Xenotransplantation: Science, Ethics, and Public Policy, National Academy Press (1996) (Plaintiff's Exhibit ("Pl. Ex.") 13 In Support of its Motion for Summary Judgment); Fishman J, et al., editors, Xenotransplantation: Scientific Frontiers and Public Policy, Annals of the New York Academy of Sciences, 862: ix-251 (1998) (Attachment 10).

7. Xenotransplantation of whole organs has been therapeutically ineffective. Of the approximately 82 whole organ xenotransplants performed since 1905, all have resulted in patients dying days, hours, or sometimes minutes after surgery. See Daar A, Animal-to-Human

Organ Transplants, *Bulletin of the World Health Organization*. 77; 1: 55 (1999); Hughes J, Xenografting: Ethical Issues, *Journal of Medical Ethics* 24: 18-24 (1998) (“few patients have survived more than a few weeks and many have died in a matter of hours or less”) (Attachments 11-12). It appears that researchers have increasingly turned to cellular xenotransplantation, perhaps in the hope of finding some therapeutic potential for the technology, and because U.S. regulators have shown a willingness to approve such trials.

8. In addition to other concerns, CRT advocates in favor of a ban on xenotransplantation because of scientific evidence that demonstrates a potentially serious public health threat from the transmission of animal viruses, or “xenozoonoses,” from source animals to humans. In recent years, many reports and articles in scientific journals have demonstrated that there is a risk of transmission of animal viruses to humans in xenotransplantation. See, e.g., Patience C, et al., Infection of Human Cells by an Endogenous Retrovirus of Pigs, *Nature Medicine* 3;3: 282-6 (Mar. 1997) (Attachment 13); Murphy F, The Public Health Risk of Animal Organ and Tissue Transplantation Into Humans, *Science* 273: 746-7 (Aug. 9, 1996) (Attachment 14); Borie D, et al., Microbiological Hazards Related to Xenotransplantation of Porcine Organs Into Man, *Infection Control and Hospital Epidemiology*, 19;5: 355-65 (May 1998) (Pl. Ex. 22); Brown J, et al., Xenotransplantation and the Risk of Retroviral Zoonosis, *Trends in Microbiology* 6;10: 411-15 (October 1998) (Pl. Ex. 23); Wilson C, et al., Type C Retrovirus Released from Porcine Primary Peripheral Blood Mononuclear Cells Infects Human Cells, *Journal of Virology* 3082-7 (Apr. 1998) (Pl. Ex. 16); Allan J, Silk Purse or Sow’s Ear, *Nature Medicine* 3:275-6 (Mar. 1997) (Pl. Ex. 15); Stoye J & Coffin J, The Dangers of Xenotransplantation, *Nature Medicine* 1:1100 (Nov. 1995) (Pl. Ex. 8); Martin U, et al.,

Productive Infection of Primary Human Endothelial Cells By Pig Endogenous Retrovirus

(PERV), Xenotransplantation 7(2):138-42 (May 2000) (Attachment 15).

11. Scientific reports have shown that certain pig viruses, including at least three variants of the porcine endogenous retrovirus (“PERV”), can infect human cells in laboratory studies. See, e.g., Van der Laan L, et al., Infection by Porcine Endogenous Retrovirus After Islet Xenotransplantation in SCID Mice, Nature 407: 90 (Sept. 7, 2000); Patience C, et al., Infection of Human Cells by an Endogenous Retrovirus of Pigs, Nature Medicine 3;3: 282-6 (Mar. 1997) (Pl. Ex. 14; Martin U, et al., Expression of Pig Endogenous Retrovirus By Primary Porcine Endothelial Cells and Infection of Human Cells, The Lancet 352:692-98 (Aug. 29, 1998) (Pl. Ex. 17).

12. The likelihood that companies can breed disease free pigs is extremely slim. PERV virus is produced by cells from pig aortas, livers, lungs, kidneys, and skin – all tissues likely to be used for transplant. Reuters, Transplanted Pig Organs Could Carry Deadly Virus, (Aug. 27, 1998) (Attachment 16). Indeed, “all [pig] tissues may potentially express these viruses.” Smith D, Endogenous Retroviruses in Xenografts, The New England Journal of Medicine: 142 (Jan. 14, 1993). At least 50 copies of PERV exist in pig chromosomes so “PERV cannot be eliminated by pathogen-free, closed breeding of pigs.” Weiss R, Xenografts and Retroviruses, Science 285: 1221 (Aug. 20, 1999) (Pl. Ex. 24). Therefore, “the use of SPF [specific pathogen-free] pigs [genetically modified to reduce the risk of zoonoses] would not prevent the risk of PERV transmission to human recipients of xenografts.” Clemenceau B, et al., Porcine Endogenous Retroviral mRNAs in Pancreas And A Panel of Tissues from Specific Pathogen-Free Pigs, Diabetes Metab 25; 6: 518-25 (Dec. 1999) (Attachment 17).

13. The most significant barrier to successful xenotransplantation is the human immune system's "hyperacute rejection" of the animal cells, tissue, or organ. Weiss R, et al., Infection Hazards of Xenotransplantation, Journal of Infection 40: 21-25 (2000) (Pl. Ex. 25). Some xenotransplantation proponents claim it is possible to create genetically modified pigs, or "transgenic pigs" – the cells of which express human proteins – which could "trick" the human immune system into recognizing animal cells, tissues, or organs as "human," rather than "animal," and thereby circumvent the hyperacute rejection that would otherwise occur. Id. at 24. However, some scientists fear that this form of genetic tampering in xenotransplantation might permit PERVs to "recombine" with human retroviruses, and create new, potentially very harmful viruses that are impossible to screen in advance. Id.; see also Weiss R, Transgenic Pigs and Virus Adaptation, Nature 391: 327-8 (Jan. 22, 1998) (Attachment 18).

14. At least 50 copies of PERV exist in pig chromosomes. In one study, French researchers found the genetic material of PERV in 11 unique locations in pigs including hearts, livers, pancreases, and kidneys. Le Page M & Kaldy P, A Pig of A Problem, New Scientist p.7 (Aug. 26, 2000) (Attachment 19). Thus, PERVs are present in all pig organs and tissues likely to be used for xenotransplantation. Griffiths P, Xenotransplantation: One Trotter Forward, One Claw Back, The Lancet 356:1049-50 (Sept. 23, 2000) (Pl. Ex. 20); Reuters, Transplanted Pig Organs Could Carry Deadly Virus (Aug. 27, 1998) (Attachment 20); Weiss R, Xenografts and Retroviruses (Pl. Ex. 24) at 1221; Clemenceau B, et al. (Attachment 17) at 518-25.

15. Recent tests of patients that were treated with living pig tissue many years ago showed that 23 out of 100 still had pig DNA in their blood many years later, providing evidence of possible PERV transmission and indicating that the risk of active infectivity from PERVs or recombined viruses remains in human patients years after xenotransplantation occurs. Paradis

K., et al., Search for Cross-Species Transmission of Porcine Endogenous Retrovirus in Patients Treated With Living Pig Tissue, Science 285:1236-41 (Aug. 20, 1999) (Attachment 21);

Griffiths D, (Pl. Ex. 20) at 1049. Like HIV and AIDS, PERVs may have long incubation periods before causing disease. See Brown J, et al., (Pl. Ex. 23) at 411-412 (“a retrovirus may transmit insidiously and become well established in a population before the clinical symptoms become apparent in individuals and signal a widespread public health concern” and “more than two decades of silent human-to-human transmission occurred before HIV-1 was identified as the causative agent of AIDS in the early 1980s”).

16. PERVs are not the only infectious public health risk that is posed by xenotransplantation – source animals may harbor other, unknown “potential human pathogens.” Weiss, Infections Hazards of Xenotransplantation at 22 (Pl. Ex. 25). While “[k]nown pathogens of animals can readily be detected and . . . eliminated from . . . source animals,” “it is not possible to screen for agents that are not yet discovered” and “new microbes are coming to light all the time.” See id. (noting that several viruses have been discovered within the last [4] years,” including: “a virus related to human hepatitis E virus which may also infect humans; a torovirus; paramyxoviruses in Australia (Menangle virus); the new epidemic in Malaysia (Nipah virus), which is causing deaths in both pigs and people and has spread to abattoir workers in Singapore;” as well as PERVs). Thus, “when veterinarians give source animals such as pigs a ‘clean bill of health’, we may still not know if they might be harbouring potential human pathogens.” Id.

17. All told, from published scientific reports, CRT is aware of at least 16 patients who have died since 1992 either during or after undergoing medical procedures involving xenotransplantation. For example, in 1992, two human recipients of baboon liver transplants

died 70 and 27 days after surgery. Starzl T, et al., Baboon-to-Human Liver Transplantation, The Lancet 341:65-71 (Jan. 9, 1993) (Attachment 22). Retrospective analysis of the patients' tissues revealed the presence of baboon viruses. Allan J, et al., Amplification of Simian Retroviral Sequences from Human Recipients of Baboon Liver Transplants, AIDS Res Hum Retroviruses 14(10):821-4 (July 1, 1998) (Attachment 23). In another case, a patient died after taking part in an FDA-approved Phase I clinical trial, in which fetal pig neural cells were implanted into the patient's brain. Isacson O & Breakefield X, Benefits and Risks of Hosting Animal Cells in the Human Brain, Nature Medicine 3;9: 966 (Sept. 1997) (Attachment 24). Pig cells were observed to have survived in the patient seven months after the xenotransplantation occurred, at which point the patient died. Fink J, et al., Porcine Xenografts in Parkinson's Disease and Huntington's Disease Patients: Preliminary Results, Cell Transplant 9(2):273-8 (Mar-Apr 2000) (Attachment 25). In all cases, the xenotransplantation patients' deaths were attributed to patients' previous illnesses/medical conditions, and not to the xenotransplants themselves. However, since many of the medical details regarding the patients' deaths have never been disclosed, there is no way for CRT to verify the accuracy of these statements.

18. It might only take one infected xenotransplantation patient to start an epidemic. Currently, about 40,000 Americans are infected with AIDS annually. Lawrence K. Altman, Focusing on Prevention in Fight Against AIDS, The New York Times (Aug. 31, 1999) at F5 (Attachment 26). As one leading virologist has calculated, in xenotransplantation, "[e]ven if the risk of producing a 'new infection' were as low as one in 1000, there could be at least 10 infections each year" and "[a]ny one of these outbreaks could become a major public health problem with the potential for intercontinental spread." Collignon P, Do The Risks Outweigh The Benefits? (Attachment 27). Leading virologists, who have researched PERVs extensively,

noted that “the absence of infectious virus in, say, the first two hundred patients does not mean it will not occur in the two hundred and first.” Stoye J, et al., Endogenous Retroviruses: A Potential Problem for Xenotransplantation?, Ann. NY Acad Sci 862: 73 (1998) (Attachment 28). Xenotransplant patients could become viral time bombs, spreading new pig viruses to other humans undetected and causing an international HIV/AIDS-like epidemic. Weiss R, Xenografts and Retroviruses, Science 285:1221-2 (Aug. 20, 1999) (Pl. Ex. 24); Denner J, Immunosuppression by Retroviruses: Implications for Xenotransplantation, Ann NY Acad Sci 862:75-86 (Dec 30, 1998) (Attachment 29).

19. International public health and infectious disease experts have expressed concern that the risk of zoonoses is an international public health risk. Chastel C, The Dilemma of Xenotransplantation, Emerging Infectious Diseases, 2 2: 155 (April-June 1996) (xenotransplantation could create “a new infectious Chernobyl”) (Attachment 30); Collignon & Purdy, Xenografts: Are The Risks So Great That We Should Not Proceed? (“[t]here is a serious risk that xenotransplantation would do more harm than good”) (Attachment 31); Collignon P, Do the Risks Outweigh the Benefits?, Medical Journal of Australia, 168:516-519 (May 18, 1998) (“[t]ransplanting organs and tissues from animals to humans is one of the best experiments we could devise to ‘create’ new infectious agents”) (Attachment 32); Stoye J, et al., Endogenous Retroviruses: A Potential Problem for Xenotransplantation, (Attachment 28) (it is “imperative that we consider the threat posed by [porcine] retrovirus replication both to the individual transplant recipient as well as to society as a whole”) (Attachment 33); Borie D, et al., at 357 (“the risk of viral transmission from swine to human appears substantial”) (Pl. Ex. 22); Takeuchi Y, et al., Host Range and Interference Studies of Three Classes of Pig Endogenous Retrovirus, Journal of Virology, 72; 12 9986-91 (Dec. 1998) (Attachment 34) (“PERV infection may have

serious impact on the health of not only transplant recipients but also the human population at large, if spread of an undetected infectious agent into the community were to take place”); Allan J, Silk Purse or Sow’s Ear at 276 (in light of new data on pig viruses, “[p]ublic health officials should resist the transplant community’s clamor for animal organs”) (Pl. Ex. 15).

20. Federal agencies have also recognized the public health risk posed by xenotransplantation. For example, in a December 1999 Federal Register notice, the FDA acknowledged that “xenotransplantation may facilitate the transmission of known or as yet unrecognized agents to humans.” 64 Fed. Reg. 73562-73563 (Dec. 30, 1999) (Attachment 35). In January 2001, the FDA stated that xenotransplantation “ha[s] the potential for unique public health risks. . .” 66 Fed. Reg. 4688 (Jan. 18, 2001) (Pl. Ex. 2). The director of the FDA’s Division of Cellular and Gene Therapies has said: “[w]e recognize that [xenotransplantation products] are fraught with danger.” See Fox J, Panel Refines FDA Xenotransplant Guidelines for Protecting Blood, ASM News, 66;3:129 (2000) (Pl. Ex. 19). In addition, the Public Health Service (“PHS”), a federal agency within the Department of Health and Human Services (“DHHS”), has acknowledged that “the public health risks posed by xenotransplantation transcend national boundaries.” PHS Guideline on Infectious Disease Issues in Xenotransplantation (Jan. 19, 2001) at 3 (Pl. Ex. 1). Moreover, DHHS has stated that “infected xenograft recipients could. . . potentially transmit. . . infectious agents to their contacts and subsequently to the public at large.” Guidance for Industry: Public Health Issues Posed by the Use of Nonhuman Primate Xenografts in Humans, April 1999 (Pl. Ex. 3).

21. Despite the public health risks posed by xenotransplantation, the U.S. Food and Drug Administration (“FDA”), which oversees clinical trials, has allowed at least two dozen xenotransplantation clinical trials to proceed, involving hundreds of patients. Companies

involved in xenotransplantation have conducted hundreds of animal experiments and xenotransplantation clinical trials including procedures such as: the transplantation of baboon livers and bone marrow into patients infected with HIV and hepatitis; fetal pig brain cells into patients with neurological diseases; pig pancreas cells into diabetic patients; and the use of whole pig livers, and pig liver cells, to “filter” the blood of patients with acute liver failure.

22. Federal agencies, including the FDA – which oversees xenotransplantation clinical trials – have emphasized that, because of the public health risks that are posed by xenotransplantation, it is imperative that federal agencies’ decisionmaking be transparent and that the public be as fully informed as possible. For instance, the FDA has emphasized that the decisionmaking process through which the FDA approves biological products involving xenotransplantation should be as “transparent and as fully informed as possible” to “ensure a continued mechanism for public education and input, which FDA believes is essential to the evaluation of the public health impact of these new technologies . . .” 66 Fed. Reg. 4691-92 (Jan. 18, 2001) (Pl. Ex. 2). Thus, “disclosure is necessary to protect the public health by informing the research community and the public of the nature and the hazards of the proposed research and by permitting comment on the merits of the proposed research . . .” *Id.* Similarly, DHHS has stated that “public awareness and understanding of xenotransplantation is vital because the infectious disease risks . . . could extend beyond the individual patients to the public at large . . .” 64 Fed. Reg. 56507 (Oct. 20, 1999).

23. Through many sources of publicly available information – including articles in scientific journals and other media, statements that have been made during open sessions of federal advisory committee meetings, and information that is contained within the companies’ own press releases, Internet websites, and filings with the Securities and Exchange Commission

– CRT has learned that many companies are developing xenotransplantation products and conducting xenotransplantation clinical trials. See, e.g., Mullon C, et al., *Bioartificial Organs May Help Reduce Risk of Zoonosis in Xenotransplantation*, *Artificial Organs* 23(4): 366-376 (Nov. 4, 1999) (Attachment 35); Chen S, et al., *Treatment of Severe Liver Failure with a Bioartificial Liver*, *Annals New York Academy of Sciences* 831: 350-60 (December 31, 1997) (Attachment 36).

24. In particular, on their Internet websites, companies have been forthcoming about disclosing that they are developing xenotransplantation products, and, in many cases, have disclosed that they have submitted xenotransplantation INDs to the FDA. For example, on its publicly accessible Internet website ([www.diacrin.com](http://www.diacrin.com)), Intervenor Diacrin provides a lengthy explanation about clinical trials for its many xenotransplantation products. (Pl. Ex. 38). In addition, Diacrin posts a table on its website that discloses the regulatory status of each of its xenotransplantation products, such as whether a certain product has completed Phase I clinical trials or whether a xenotransplantation IND has cleared FDA approval and is ready to proceed into clinical trials. (Pl. Ex. 37). In addition, until recently, Intervenor Circe Biomedical described Phase II and Phase III clinical trials for its HepatAssist bioartificial liver system, which uses pig liver cells to “filter” the blood of patients suffering from liver failure, on its website. Pl. Ex. 32. Moreover, according to information on Baxter Nextran’s website, Nextran is developing transgenic pigs and has completed a Phase I clinical trial using pig livers through which to filter patients’ blood outside the body. (Pl. Ex. 34). BioTransplant – whose partnership with Intervenor Novartis recently created a new company, Immerge Biotherapeutics – is developing transgenic pigs and a technology designed to “re-educate the body’s immune system to accept transplanted cells, tissues and organs by recognizing them as ‘self’”, according to information on

BioTransplant's website. (Attachment 37). In addition to the companies that have intervened in this lawsuit, other companies have publicly disclosed that they are developing xenotransplantation products. For example, Algenix has disclosed that it is developing the LIVERX 2000 system, an external liver support system that incorporates pig liver cells.

Attachment 38.

25. In October 1997, the FDA placed a hold on all xenotransplantation clinical trials using live pig cells after a team of virologists in England reported that PERV infected human cells in laboratory test tubes, that two separate strains of the virus existed, and that the genes for both viruses appeared in a wide variety of pigs. Patience C, et al., (Pl. Ex. 14). The clinical hold was lifted once xenotransplantation companies developed tests to screen both pigs and patients for evidence of PERVs, even though the FDA said it could not guarantee the accuracy of such tests. Sheryl Gay Stolberg, Could This Pig Save Your Life?, The New York Times Magazine (Oct. 3, 1999) at p.50-51 (Attachment 39). However, the agency never adequately explained to the public why it lifted its hold on clinical trials despite the public health risks that are posed by xenotransplantation.

26. In its March 9, 2000 Freedom of Information Act request, CRT requested information about xenotransplantation clinical trials so it could ascertain whether the FDA is adequately monitoring xenotransplantation clinical trials in light of the significant public health risks that are implicated. CRT is very concerned about the many public health risks that are posed by xenotransplantation and the FDA's willingness to allow xenotransplantation to proceed into the clinical setting. For example, CRT seeks to ascertain the true number of deaths and side effects that have occurred during and after xenotransplantation clinical trials and determine informatively whether these deaths and side effects were attributable to xenotransplants or other

causes. CRT also seeks information about pig viruses that the FDA may not have yet released to the public. CRT seeks the information so it can determine objectively whether the FDA, by allowing xenotransplantation clinical trials to proceed despite scientifically proven health risks, has placed the American public and the international community at too great a risk.

27. CRT will use the requested information to educate the public about the issues surrounding xenotransplantation, particularly its risks - through press releases, radio and television interviews, letters to the editor, and the Internet. Having the information will allow CRT to judge whether its concerns are valid and its desire for a ban justified. If they prove to be so, the knowledge gained from this case will enable CRT to campaign more effectively.

Pursuant to 28 U.S.C. § 1746, I hereby declare under penalty of perjury that the foregoing is true and correct.

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Alix Fano, MA

January xx, 2002