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Human Rights and Access to Health Care: Comparison of Domestic and International Law and Systems Implications for New Medical Technologies in Time of Crisis

Dennis McElwee

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I. INTRODUCTION

Three years prior to the American Civil War, Abraham Lincoln stated that "a house divided against itself cannot stand."[1] With the advent of international telecommunications, extensive travel and economic interdependence, the world is shrinking. As witnessed by the AIDS epidemic[2] and various strains of influenza,[3] localized health problems in third world countries quickly find their way into one's own back yard.[4] Traditional methods for differentiating domestic and international health problems have lost their meaning.[5] With regard to what is currently known about past and present health crises, the "global village" has become a global house.

This house is extremely divided. The divisions begin with basic differences in the way in which societies perceive human rights in general. Differing philosophies lead to different systems.[6] When applied to health care, present systems leave much to be desired.

The aim of this paper is to examine these differences from the perspectives of history, treaties and law. Once these differences have been

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1. Abraham Lincoln, speech at the Republican State Convention, Springfield Illinois (June 16, 1858). Lincoln borrowed this phrase from the New Testament of the Bible, Matthew 12:25, Luke 11:17.

2. Dr. Jonathan Mann, *Global AIDS into the 1990's*, WORLD HEALTH, Oct. 1989, at 6.

3. CHARLES STUART-HARRIS, INFLUENZA, THE VIRUSES AND THE DISEASE 124-31 (2d ed. 1985).

4. *Id.*

5. George A. Gellert, *The Obsolescence of Distinct Domestic and International Health Sectors*, 10 J. PUB. HEALTH POL'Y 421-22 (1989).

6. Louis Henkin, *Rights: Here and There*, 81 COLUM. L. REV. 1582, 1609 (1981).

surveyed, they are analyzed in situations where their different systems must work together. Their probable effects are examined in a potential international crisis with regard to application of an incredible array of new medical technologies. Obstructions to their use in a crisis are then explored based on present law and actual experience. Conclusions and recommendations flow directly from that analysis.

II. DIFFERING VIEWS ON BASIC HUMAN RIGHTS

The main philosophical difference in human rights perception has been described as that between "freedom from," aspiring to individual autonomy, and "having more," through more law and government.[7] These differences have also been termed "political" rights and "socio-economic" rights. The political rights are immunities or rights against invasion by the government. The socio-economic rights are rights to affirmative aid and support by one's government.[8]

"You owe me nothing; I owe you nothing. You stay out of my way and I'll stay out of yours." This expression has been described as constituting an important thread within the Anglo-American socio-moral fabric.[9] The American theory of rights is derived from individual freedom and autonomy, not claims upon society to do for the individual what he can not do for himself. The framers of the U.S. Constitution, perhaps due to their difficulties with Great Britain, saw rights as freedom from abuse by all branches of government.[10]

In the United States, programs regarding public welfare do not exist by constitutional mandate, but by the grace of Congress, subject to political and budgetary constraints.[11] There is no constitutional right to freedom from want.[12] Where some responsibility for individual welfare was finally recognized, it was seen as secondary and supplementary.[13]

Public welfare statutes are considered "entitlements" instead of rights.[14] U.S. courts have reviewed such entitlements based on the "equal protection" clause of the Fourteenth Amendment to the U.S. Constitution.[15] Their standard for review is whether or not "similarly circum-

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7. *Id.*

8. Levy, *Making Human Rights More Definite and Effective, in* HUMAN DIGNITY, THE INTERNATIONALIZATION OF HUMAN RIGHTS 249 (A. Henkin ed. 1979).

9. SANFORD H. KADISH AND STEPHEN J. SCHULHOFER, CRIMINAL LAW AND ITS PROCESSES 206 (5th ed. 1989).

10. Henkin, *supra* note 6, at 1592.

11. *Id.* at 1587.

12. *Id.*

13. *Id.* at 1590.

14. Elliot v. Ehrlich, 280 N.W.2d 637, 641 (1979); Goldberg v. Kelly, 397 U.S. 254, 262 (1970).

15. Wendy K. Mariner, *Access to Health Care and Equal Protection of the Law: The Need for a New Heightened Scrutiny*, 12 AM. J. L. & MED., 345, 347 (1986). The Fourteenth Amendment states, "No State shall . . . deny to any person within its jurisdiction the equal protection of the laws." U.S. CONST. amend. XIV, cl. 1.

stanced" individuals are treated by the government in a similar manner.[16] Consequently, the courts will review whether or not one segment of the poor is treated by the government differently from another segment of the poor. They will not decide whether the poor are being treated differently from the wealthy.[17] It does not guarantee equal treatment for all.[18] Within the U.S. several states have found that their own constitutions provide greater protection than the Fourteenth Amendment.[19]

The United States has ratified fewer human rights treaties than the vast majority of countries.[20] The U.S. is not a party to the International Covenants on Human Rights.[21] Some authors believe that treaty ratification would have little impact on American human rights because the "relevant domestic law in many respects already ensures more rights than its international counterpart."[22]

In contrast, the French concept of freedom is not freedom from the law, but through the law.[23] It includes the economic and social benefits of the welfare state as affirmative obligations of government.[24] When comparing their respective declarations of rights, due to their different historical backgrounds, the Americans declared what they had and the French declared what they desired.[25]

The French concept is in accordance with most international agreements on human rights. The Universal Declaration of Human Rights includes the right to have basic human needs satisfied - food and shelter, health care, and education.[26] The International Covenant of Economic, Social and Cultural Rights contains similar provisions.[27] The European Declaration of Fundamental Rights and Freedoms contains identical concepts providing for collective social rights, social welfare and the right to education.[28]

The Council of Europe under the European Convention on Human

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16. *Id.* at 349.

17. *Id.* at 353-54. *See also* Shapiro v. Thompson, 394 U.S. 618, 641 (1969) (rejecting state residency requirements for welfare recipients as a denial of due process for poor travelers).

18. Mariner, *supra* note 15, at 349.

19. *Id.* at 377.

20. Thomas Buergenthal, *The U.S. and International Human Rights*, 9 HUM. RTS. L.J. 141 (1988).

21. *Id.* at 142.

22. Buergenthal, *supra* note 20, at 161.

23. Henkin, *supra* note 6, at 1597.

24. *Id.*

25. *Id.* at 1592.

26. Universal Declaration of Human Rights, arts. 25 and 26, G.A. Res. 217, U.N. Doc. A/810 (1948) [hereinafter G.A. Res. 217].

27. The International Covenant on Economic, Social and Cultural Rights, G.A. Res. 2200 (annex), 21 U.N. GAOR, Supp. (No. 16) at 49, U.N. Doc. A/6316 (1967).

28. The European Parliament Declaration of Fundamental Rights and Freedoms of 12 April 1989, *reprinted in* 10 HUM. RTS. L. J. 341 (1989) [hereinafter *European Parliament Declaration*].

Rights established a Commission and Court of Human Rights which hears cases by both governments and individuals.[29] In 1975 there were approximately 2,000 cases brought before the European Commission of Human Rights. In 1987, the number had grown to 3,675.[30] About one-fifth of these lead to applications that are decided by the Commission.[31] The compliance rate by defendant governments is thought to be unusually high.[32] Finland became the twenty third Member State of the Council of Europe on May 5, 1989 and signed the European Convention on Human Rights.[33]

III. U.S. LAW REGARDING ACCESS TO HEALTH CARE AND ITS EFFECTS

There is no duty within the United States Constitution or statutes to provide medical care for the indigent.[34] The duty to provide indigent care is most often found in state statutes.[35] Nearly every state has a statutory provision which authorizes or mandates state or local governments to provide medical care for the poor.[36] Fifteen states have constitutional provisions providing for such care.[37] Laws for the benefit of the public welfare are generally construed liberally due to their remedial purpose, consequently courts tend to favor mandatory interpretation unless a statute is clearly permissive.[38] Where permissive, rather than mandatory, courts will not compel governments to provide medical assistance.[39]

In recent years, state and local indigent care budgets have been strained due to tax revenue declines, rising health care costs and changes in federal reimbursement programs.[40] Thirty-seven million patients have no health insurance.[41] The number of persons who lack health insurance has increased by 34.7% from 1977 to 1983.[42] AIDS patients now fill 9% of all hospital beds in New York City. It is estimated that 2,300 additional

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29. Levy, *supra* note 8, at 20.

30. Henry G. Schermers, *Has the European Commission of Human Rights Got Bogged Down?*, 9 HUM. RTS. L.J. 175 (1988).

31. *Id.*

32. Levy, *supra* note 8, at 20.

33. Announcement: Council of Europe Strausbourg, *Finland Joins the Council of Europe and Signs the European Human Rights Convention*, 10 HUM. RTS. L.J. 355 (1989).

34. *See* Wideman v. Shallowford Community Hospital, 826 F.2d 1030, 1032 (11th Cir. 1987).

35. M. Dowell, *State and Local Government Legal Responsibilities to Provide Medical Care for the Poor*, 3 J. HEALTH L. 1, 3 (1988-89).

36. *Id.* at 4.

37. *Id.* at 6.

38. *Id. See also* Damon v. Secretary of HEW, 557 F.2d 31, 33 (2d Cir. 1977).

39. Dowell, *supra* note 35, at 4 n. 29; *see also* Perth Amboy Gen. Hosp. v. Board of Chosen Freeholders, 386 A.2d 900 (N.J. Super. Ct. 1978).

40. *Id.* at 2.

41. Nancy Gibbs, *Emergency*, TIME, May 28, 1990, at 59.

42. *See* Dowell, *supra* note 35, *quoting* Robert Wood Johnson Foundation, *Updated Report on Access to Health Care for the American People*, Special Report No. 1 (1983).

beds will be needed in New York for the treatment of AIDS alone.[43] Government reimbursements often cover only half of the cost of treating the poor.[44] In emergency rooms the typical trauma patient bill in 1989 was $13,000; on average, hospitals take a loss of $5,000 on each.[45]

"Research indicates that if life support is used on serious heart attack victims within four minutes, and advanced life support within eight, nearly 50 percent of them survive."[46] Peoria, Illinois, saw traffic fatalities drop 50 percent within a year of setting up their trauma network.[47] Deaths among non-head-injured car accident victims dropped from an estimated 73 percent to 9 percent in Orange County, California.[48] Despite these remarkable advances in techniques and equipment, according to the National Association of Hospital Development, 40% of the nation's acute care hospitals will be closed by the year 2000.[49] Four of ten trauma centers in the City of Chicago have closed. Every hospital except one in Dade County, Florida, has closed its trauma department. That remaining hospital must service a population of two million residents.[50] "The hospitals don't just close their doors to poor people, when they're closed, they're closed to everyone."[51]

IV. EUROPEAN LAWS, INTERNATIONAL COVENANTS AND HEALTH CARE

The goal of equal access to health care is stated in a wide variety of international documents. The World Health Organization (WHO) was the first body to recognize the right to health as one of the fundamental rights possessed by every human being.[52] The World Health Assembly of WHO adopted the "Health for All" resolution in 1977 stating that "the main social target of WHO in the coming decades should be the attainment by all citizens of the world, by the year 2000, of a level of health that will permit them to lead a socially and economically productive life."[53] Article 12 of the International Covenant on Economic, Social and Cultural Rights[54] recognizes the right to the "highest attainable standard of physical and mental health," including "the creation of conditions which would assure to all medical service and medical attention in the event of sickness." Article 25 of the Universal Declaration of Human

43. Gibbs, *supra* note 41, at 65.
44. *Id.* at 59.
45. *Id.* at 63.
46. *Id.* at 59.
47. *Id.* at 63.
48. *Id.*
49. *Id.* at 64.
50. *Id.* at 59.
51. *Id.*, *quoting* Virginia Price-Hastings, Director of Los Angeles Trauma Hospital Programs.
52. Genevieve Pinet, *The WHO European Program of Health Legislation and Health for All Policy*, 12 AM. J.L. & MED. 441, 443 (1986).
53. World Health Assembly Resolution WHA 30.43 (1977).
54. *See* G.A. Res. 2200, *supra* note 27.

Rights[55] proclaims that everyone has the right to a standard of living adequate to sustain health, including medical care and necessary social services. Although not accorded the status of an international treaty,[56] the Helsinki Accords seek to bind signatories to the provisions of both the Universal Declaration of Human Rights and the International Covenant on Economic, Social and Cultural Rights.[57] Article 15(3) of the European Declaration of Fundamental Rights and Freedoms[58] declares that anyone lacking sufficient resources shall have the right to social and medical assistance.

Great Britain and Canada have had nationalized health care for an extended period of time.[59] Several West European nations have followed the principals of the international accords by enacting either socialized medicine or proactive legislation that increases the role of government in the provision of equal access to health services. Included among these nations are Finland, Italy, Greece, the Netherlands, Sweden, Iceland, Norway, Spain and Belgium.[60]

Recent statistics have indicated that "[e]quity in access to medical care has clearly failed to assure equity in health."[61] For instance, the inequity in mortality of social classes has widened since the implementation of the National Health Service in Great Britain.[62] The standard mortality ratio for semiskilled and unskilled workers has steadily increased from 1951 to 1971.[63] This indicates that proportionately far fewer semiskilled and unskilled laborers survive long enough to meet the average life expectancy. The difference between the mortality rates of these lower classes and those of the upper social classes (professional and managerial) has also grown substantially.[64] Scotland is now the nation with the highest death rate from coronary heart disease. Finland, England and Wales are not far behind.[65]

A similar pattern has developed in Canada. The difference in life expectancy between lowest and highest income levels was 4.5 years in the late 1970's. The difference was eleven years for disability-free life expectancy. "Poor people in Canada have, on the average, only 55 years of

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55. *See* G.A. Res. 217, *supra* note 26.

56. HUMAN RIGHTS, PROBLEMS, PERSPECTIVES AND TEXTS 197 (F.E. Dowrick ed., 1979).

57. Conference on Security and Cooperation in Europe: Final Act, Helsinki 1975, *reprinted in* HUMAN DIGNITY, THE INTERNATIONALIZATION OF HUMAN RIGHTS 135, 140 (Alice H. Henkin ed. 1979) [hereinafter Helsinki].

58. *See* European Parliament Declaration, *supra* note 28, at 344.

59. Editorial, *How Important is Medical Care in a National Health Program*, 9 J. PUB. HEALTH POL'Y 7, 7-8 (1988) [hereinafter *How Important*].

60. Pinet, *supra* note 52, at 447-48.

61. Editorial, *Ethical Essentials of a National Health Care Program*, 11 J. PUB. HEALTH POL'Y 5, 5 (1990) [hereinafter *Ethical Essentials*].

62. *Id.*

63. *How Important*, *supra* note 59, at 8.

64. *Id.* at 9.

65. *Id.* at 8.

healthy life, that is, life free from disability, as compared with 66 years of healthy life for rich Canadians."[66] During the 1970's Canada's death rate from lung cancer rose by 60 percent and death from cirrhosis of the liver by 25 percent.[67]

Various reasons have been offered to explain these differences, including unstable economies resulting in high unemployment.[68] Socialized medical systems have been strongly criticized for being overly bureaucratic, budget-oriented, and for only allowing support for the short-term needs of its users, while neglecting new techniques and medical innovation.[69] The lack of emphasis on preventive medicine is frequently cited as the biggest problem. It has been contended that "[e]quity in prevention is more important than equity in medical care."[70]

V. POTENTIAL INTERNATIONAL CRISIS — THE SPREAD OF RAPIDLY CHANGING VIRUSES, THEIR EFFECTS AND PREVENTION

Both capitalist and socialist health care systems have logistic and financial problems. Health complications experienced in one nation can rapidly cross borders and become worldwide complications. The changing nature of the AIDS virus and of influenza, coupled with the diminished effectiveness of vaccines, illustrates the probability of new worldwide problems that these disparate systems may have to address. This section deals with the nature of these new challenges, prior to analyzing ways to meet them and the laws that may prevent them from being met.

The WHO Global Programme on AIDs estimates that about one-tenth of one percent of the world's population is infected with the human immunodeficiency virus (HIV). About half of these people are in Africa, forty percent are in the Americas, and the remainder are scattered throughout the rest of the world.[71] It is projected that at least seventy-five percent of those infected will develop AIDS within twenty years.[72] The lifetime medical costs for a single AIDS patient is estimated to be approximately $150,000. At present, life expectancy for a newly diagnosed AIDS patient averages about one year.[73] For 210,000 additional cases, the cost would exceed thirty billion dollars.[74] A variety of nations, including the United States, have enacted legislation designed to restrict the immi-

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66. *Id.* at 9.

67. *Id.* at 8.

68. *Id.*

69. Note, *Socialized Medicine: An Analysis of Bureaucratic Inefficiency*, 8 DICK. J. INT'L L. 101, 121 (1989).

70. *How Important*, *supra* note 59, at 9.

71. Dr. Jonathan Mann, *Global AIDS into the 1990's*, WORLD HEALTH, October 1989, at 6.

72. Dr. J. Chin, *Understanding the Figures*, WORLD HEALTH, October 1989, at 9.

73. Balaji B. Singh et al., *The Impact of AIDS on Medical Disposables*, 11 MED. DEVICE AND DIAGNOSTIC INDUSTRY 61, 61, September 1989.

74. *Id.*

gration of those who might have AIDS.[75]

While the effects of AIDS and its methods of transmission have been publicized extensively, other facts about the virus have not received the same degree of exposure. For example, the rate of genetic change for portions of the AIDS virus has been found to be over a million times greater than that of most normal (eukaryotic)[76] cells.[77] The AIDS virus is capable of mutating in several different ways,[78] including the sharing of genetic material between different HTLV molecules.[79] More than one predominant viral form has been persistently found within the same individual.[80] A wider range of cellular types may be infected by HIV than was previously thought.[81] Given the extensive variation in the genes of the AIDS virus, it "clearly has the potential for drastically altering both its immunologic and biologic properties."[82] The AIDS virus of today, including its methods of transmission, may not be the AIDS virus of tomorrow.

The only other virus that approaches the rate of mutation of AIDS is Influenza Type A.[83] Although their modes of transmission and lethality are currently different, Type A flu was studied extensively, and it is a good example of the worldwide effect that an organism can have in a short period of time. In February of 1957, Type A influenza appeared in China.[84] By April, it had spread to Hong Kong and throughout Southeast Asia; by May, it had spread to India and Australia.[85] From that point, it took only three more months to spread over the rest of the earth.[86] In the United States, Type A flu caused an estimated 70,000 excess deaths, with health care and productivity losses of four billion dollars.[87] In 1968, a milder reoccurrence of the virus is estimated to have cost 34,000 lives and two to three billion dollars.[88]

In 1977, the virus again reappeared, taking approximately eight

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75. Note, *The AIDS Pandemic: International Travel and Immigration Restrictions and the World Health Organization Response*, 28 VA. J. INT'L L. 1043, 1052-55 (1988).

76. Eukaryotic cells are those with a nucleus; prokaryotic cells do not have a normal nucleus. MEDICAL TECHNOLOGY, BOARD EXAMINATION REVIEW, Vol. 1, at 397, 8th ed. (Edith Zak Helman et al. eds. 1975).

77. Bruno R. Starcich et al., *Identification and Characterization of Conserved and Variable Regions in the Envelope Gene of HTLV-III/LAV, the Retrovirus of AIDS*, 45 CELL 637, 643 (1986).

78. Starcich, *supra* note 77, at 643.

79. *Id.* at 645.

80. *Id.*

81. Robin A. Weiss and Jay A. Levy, *Virology Overview*, 2 AIDS S1, S2 (Supp. 1, 1988).

82. Starcich, *supra* note 77, at 646.

83. *Id.* at 643.

84. ARTHUR M. SILVERSTEIN, PURE POLITICS AND IMPURE SCIENCE, THE SWINE FLU AFFAIR 14 (1981).

85. *Id.* at 14-15.

86. *Id.* at 15.

87. *Id.* at 19.

88. *Id.*

months to cover the earth.[89] During this outbreak, an additional strain of the virus was isolated. The two versions occurred simultaneously in single localized areas.[90] The infection rates in children of Great Britain varied from twenty to eighty percent.[91]

Vaccines developed to fight these viruses have limited effectiveness. Despite many trials, and the use of vaccines for many years, the degree of protection for rapidly changing viruses remains in doubt.[92] One study estimates vaccine effectiveness to be only forty to sixty-six percent.[93] Another indicates only fifty to sixty-seven percent effectiveness.[94]

The World Health Organization has recognized that there are many infectious diseases for which vaccines are not yet available or are not satisfactory.[95] Effective vaccines have been developed against smallpox, yellow fever, polio, measles, mumps, German measles and others.[96] While immunization against rapidly changing viruses is still important, "no short-term experience is a reliable guide to the future pending development of other measures such as chemotherapy."[97]

VI. POTENTIAL SOLUTIONS

Given the potential for such rapidly breaking health problems, possible solutions should be reviewed prior to analyzing international legal restrictions that could prevent the use of these new remedies in a crisis. Two promising concepts are presented. The first is genetically engineered drugs, and the second is computerized medical devices.

A. *Biotechnology and Genetically Engineered Drugs*

In 1973, Paul Berg of Stanford University used a series of specialized enzymes to remove a piece of genetic material from a monkey virus. A similar process was used to open the DNA in another strain of virus. He then linked the genetic material from the first virus with that of the second. He was the first to succeed in combining the genetic code in two different organisms. In 1980, he was awarded the Nobel prize in chemistry for his efforts.[98]

Dr. Berg had founded the science of recombinant DNA. Recombinant DNA technology makes it possible to change the genetic instructions of a living cell, in order to produce desirable proteins and other large mole-

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89. STUART-HARRIS, *supra* note 3, at 131.
90. *Id.* at 130.
91. *Id.*
92. *Id.* at 192.
93. *Id.* at 192, 198.
94. *Id.* at 193.
95. *New and Activities*, 66 BULL. WORLD HEALTH ORGANIZATION 515, 519 (1988).
96. SILVERSTEIN, *supra* note 84, at 9.
97. STUART-HARRIS, *supra* note 3, at 182.
98. THE ALMANAC OF SCIENCE & TECHNOLOGY, 89 (R. Goleb ed. 1990) [hereinafter ALMANAC].

cules in large quantities. These changes are inherited by each succeeding generation of the cell.[99]

In the case of *Diamond v. Chakrabarty*, the United States Supreme Court held that a human made living organism is patentable, as a new and useful manufacture or composition of matter.[100] More than one hundred potential products for human use were estimated to be under development by biotechnology companies in 1987.[101] Sales of health care products derived through biotechnology were expected to approach 900 million dollars in 1988.[102] Over two billion dollars had been invested by 1984,[103] and 700 U.S. companies were using the technology by 1988.[104]

This technology is adaptable to a wide variety of uses. An excellent example is found in medication used to treat heart attacks. Approximately 4,000 people have a heart attack each day.[105] Chances of survival largely depend on how much permanent muscle damage the heart sustained during the time a clot blocked the normal flow of blood into the heart (myocardial infarction).[106] Tissue plasminogen activator (tPA), an enzyme which is naturally present in uterine tissue, dissolves blood clots. It is now being produced, by Genentec Inc., through genetically altered bacteria.[107]

In a European study, patients treated with the drug experienced mortality reductions of 51% at fourteen days when compared to a control group, and 36% at three months. When tPA was administered within three hours of heart attack symptoms, mortality was reduced by 82% at fourteen days post attack, and 59% at three months.[108] "Activase" (tPA) was approved by the FDA in November of 1987.[109]

Many believe that it will be the world's second billion dollar drug.[110] One dose costs about $2,200, compared to $200 to $300 for another drug, Streptokinase. Streptokinase also dissolves blood clots but is somewhat less effective than tPA.[111] Sales of tPA were estimated to be 180 million

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99. Michael Traynor, *Emerging Product Liability Issues in Biotechnology*, 3 HIGH TECH. L.J. 149, 159 (1988).

100. Diamond v. Chakrabarty, 447 U.S. 303 (1980); *see also* 35 U.S.C. § 101 (1982).

101. ALMANAC, *supra* note 98, at 98, *quoting* U.S. Cong. Off. Tech., *New Developments in Biotechnology* (1987).

102. *Id.*, *quoting* Consulting Resources Corp. of Lexington, Mass.

103. Marciniszyn, *What Has Happened Since Chakrabarty?* 2 J. L. & HEALTH 141, 141 (1987-88), *quoting Biotech Comes of Age*, BUS. WK., Jan. 23, 1984, at 84-85.

104. *Id.* at 141.

105. Editorial, *The TPA Decision*, WALL ST. J., May 28, 1987, at 30, col. 1.

106. *Id.*

107. ALMANAC, *supra* note 98, at 99.

108. Frans Van de Werf, *Lessons from the European Cooperative Recombinant Tissue-Type Plasminogen Activator (rt-PA) Verses Placebo Trial*, 12 J. AM. C. CARDIOLOGY 14a (Supp. 1988).

109. ALMANAC, *supra* note 98, at 98.

110. Marciniszyn, *supra* note 103, at 153.

111. Eric J. Topol, *Tissue Plasminogen Activator: Why the Backlash?*, 13 J. AM. C. CARDIOLOGY, 1477 (1989).

dollars in 1988.[112]

Another example of recombinant DNA technique is Erythropoietin (EPO). This is a human hormone that stimulates bone marrow cells to grow into red blood cells. Kidney failure reduces production of EPO to the extent that twenty-five percent of the 250,000 individuals worldwide who require dialysis of their blood, also require frequent blood transfusions. Using recombinant DNA techniques, EPO is now manufactured by cultured mammalian cells.[113]

In clinical trials using EPO, virtually all severely anemic patients were transfusion independent at the end of two months.[114] The market for EPO is likely to go well beyond kidney patients to other anemic patients in need of increased red blood cell production,[115] including AIDS and cancer patients.[116] The FDA released EPO for sale in June of 1989.[117]

Interferons, proteins that the body produces in small quantities in response to viral infections, provides a third example of this technique. They stimulate infected cells to manufacture substances that prevent viruses from reproducing. They also stimulate some cancer cells to make a type of protein that increases the chances that these cancer cells will be recognized and eliminated by the immune system. Genetic material for the production of interferons has now been spliced into two species of bacteria and one species of mold.[118] The FDA approved one type of interferon for treatment of a specific type of cancer (hairy-cell leukemia) in June of 1986.[119] Clinical evaluations have been underway for the use of interferons in the treatment of several other types of cancer, influenza and the common cold.[120]

Other important developments in genetically engineered products include Human Growth Hormone for the treatment of dwarfism; Interleukins which stimulate the immune system and are currently used in the treatment of kidney cancer; Factor VIII, one of the enzymes that hemophiliacs lack rendering their blood unable to form clots; and Tumor Necrosis Factor, which attacks tumors directly. More than eighty other drugs produced by genetic engineering were being tested in humans at the end of 1988.[121]

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112. ALMANAC, *supra* note 98, at 99.

113. *Id.* at 105.

114. *Epoetin Alfa Approved for Anemia Treatment*, 262 JAMA 184 (July 14, 1989).

115. Anderson, *Growing Pains for Amgen as Epoetin Wins U.S. Approval*, 339 NATURE 493 (June 15, 1989).

116. *Id.*

117. ALMANAC, *supra* note 98, at 99.

118. *Id.*

119. Marciniszyn, *supra* note 103, at 151.

120. *Id.* at 151.

121. ALMANAC, *supra* note 98, at 105.

B. *Multiple-Use Computerized Medical Devices*

Tremendous strides have also been made with electronic medical equipment. Automated Centrifugal Blood Cell Separators effectively separate whole blood into three basic components: erythrocytes (red blood cells), plasma and buffy coat (platelets and white blood cells).[122] Although initially designed to collect and transfuse large numbers of platelets and white blood cells,[123] the advantages of being able to rapidly and accurately remove specific elements from the blood were soon realized.

In an experiment involving two patients with drug resistant bronchial asthma, for example, 40% to 80% of existing plasma protein was removed from the blood stream. This fraction of the blood contains circulating immunocomplexes, auto-antibodies, toxins and metabolic products. Following treatment with this procedure, the first patient had no attacks over a period of five months. The other patient had no attacks for over a year. Prior treatment with drugs was ineffective.[124]

In 1984, the American Society of Apheresis appointed a committee to review existing experience with the technology, and develop position papers based on the best available information.[125] A listing of over fifty present and potential applications was presented. Included in that list was mysathemia gravis, rheumatoid arthritis, sickle cell disease, lupus, Guillain-Barre' syndrome, drug overdose and poisoning, hairy-cell leukemia, multiple sclerosis, burns, asthma, AIDS and solid tumors.[126] Since the compilation of that data, this equipment has also been used in the treatment of leprosy.[127]

VII. FACTORS INHIBITING THE USE OF NEW MEDICAL TECHNOLOGIES DURING AN INTERNATIONAL CRISIS

As remarkable as these new technologies in medicine may be, obstacles to their use in an international crisis are formidable. A basic comprehension of methods used to test new medical products for safety is needed to perceive the factors that may prevent their use in an international emergency. In the United States, "adequate and well controlled" studies, including human clinical investigations, are required for the presentation of the substantial evidence needed for approval of a new medical product. Effectiveness of a drug should normally be supported by more than one well controlled trial and carried out by independent investiga-

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122. *Introduction*, 1 J. CLINICAL APHERESIS 119 (1983).

123. *Id.*

124. Bamburger, *Drug-Resistant Bronchial Asthma Successfully Treated with Plasma Exchange*, 2 J. CLINICAL APHERESIS 200, 200-205 (1984).

125. *Introduction*, 3 J. CLINICAL APHERESIS v (1986).

126. *Id.* at vi.

127. D. Wallach, *Plasma Exchange in Severe Erythema Nodosum Leprosum*, 9 INT'L J. ARTIFICIAL ORGANS 183 (1986).

tors.[128] They generally require the administration of a placebo, a neutral preparation given as a medicine, as a control for comparison.[129] In some cases, this requirement may be abandoned for an "historical control where a disease has a high and predictable mortality."[130]

Data from all animal studies are required to be reported, particularly animal tests for cancer and birth defects (carcinogenicity and teratogenicity).[131] Specific analysis of numerous drug interactions must be reported using human test subjects. These effects are checked for differences with sex, race, age and size, and might include such factors as disease severity, concomitant illness, concomitant drugs, smoking and ethanol usage history and prior therapy.[132] In order to support the safety and effectiveness of each claim for the drug, each important segment of this analysis must be "statistically" significant, according to a number of methods.[133]

Biological factors for each test patient are studied. These include items such as drug absorption, distribution within the body, metabolism and excretion.[134] Dose range and dose response studies include such items as the effects of the drug on heart rate, with exercise, at different dosage levels. Other studies include effects on blood flow, kidney function, digestive system motility, gastric acid secretion, the immune system, nervous system, coagulation[135] and liver function.[136]

The aim of thoroughness is to attempt to identify all potential adverse reactions to the product. Even with the best of studies, however, this is impossible.[137] Clinical testing using up to 500 patients can be expected to turn up adverse reactions that affect ten percent or more of the population but may miss a less frequent danger. Delayed effects, unusual toxic reactions and unpredictable effects due to genetic variables are difficult to detect.[138]

A good example of the problem posed by human genetic diversity is the essential enzyme glucose-6-phosphate dehydrogenase (G6PD) in red blood cells. Over 370 genetic variants of this enzyme have been discovered.[139] About forty variants are associated with a mild deficiency, but

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128. U.S. Dept. Health Hum. Services, Public Health Service Food and Drug Admin., *Guideline for the Format and Content of the Clinical Sections of New Drug Applications*, 15 (July 1988) [hereinafter *Guideline*].

129. 21 C.F.R. § 314.126(b)(2)(i) (1989).

130. 21 C.F.R. § 314.126(b)(2)(v) (1989).

131. *Guideline*, *supra* note 128, at 42.

132. *Id.* at 32.

133. *Id.* at 69.

134. *Id.* at 12.

135. *Id.* at 12-13.

136. *Id.* at 33.

137. D. KAY, THE INTERNATIONAL REGULATION OF PHARMACEUTICAL DRUGS 48 (West 1976).

138. *Id.*

139. Beutler, *Genetic Variation of Glucose-6-Phosphate Dehydrogenase: A Catalog and Future Prospects*, 67 MEDICINE 311, 311 (1988).

individuals are normally asymptomatic. Other variants are associated with chronic hemolytic anemia. With another type of variant, the person's red blood cells split apart (hemolyze) on exposure to factors such as fava beans, infections or drugs.[140]

As can be readily seen, demonstrating the safety of a new medical product can be quite complex. This complexity produces and exposes a number of weaknesses in international cooperation. These weaknesses severely inhibit the ability to use a new medical product during an international emergency. Five general areas of weakness are discussed below.

A. *Failure to Recognize Foreign Clinical Data*

As complex and time consuming as these safety studies are, many of them are repeated needlessly. National specifications for the testing of drugs vary widely throughout the world.[141] Following the Thalidomide disaster, WHO stated that "[c]linical trials are highly time consuming, need very large numbers of patients to be observed according to generally accepted principals and would often be facilitated by international cooperation."[142] A number of countries, such as France and Mexico, requires that scientific data used for drug approval must be produced by their own scientists exclusively within their own borders.[143] One of the items intended for European harmonization is the regulation of pharmaceuticals and high technology medicines.[144]

Some progress has been made on mutual recognition of preclinical testing such as animal studies and methods of determining drug purity. Agreement to Good Laboratory Practices has been reached with Japan, the United States, the United Kingdom, Switzerland, France and West Germany in this area.[145] These agreements stipulate that each country will recognize preclinical data that meet the regulatory requirements of the other nation.[146]

Human testing is quite different. The United States accepts human test data from other nations, provided they meet the stringent requirements of "adequate and well controlled studies." Provisions for their use are made in FDA guidelines issued regarding the submission of human clinical data.[147] This appears to be a major exception to the international rule.

The Japanese, for example, do not accept most U.S. clinical data.

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140. *Id.*

141. KAY, *supra* note 137, at 59.

142. *Id.*, *quoting* WHA 15.41 (1962).

143. KAY, *supra* note 137, at 60.

144. RICHARD HURWITZ, RAF FIN. CORP. REPORT 1, 5 (1990); European Renaissance: The Economic Implications of the 1992 Internal Market, *quoting* BUS. AM., August 1, 1988.

145. Fairbain, *Japan: Drug Regulations - A United States Industrial Perspective*, 1 REGULATORY AFF. 25, 27 (1989).

146. *Id.*

147. *Guideline*, *supra* note 128, at 17, 21, 23, 25, 26, 87.

Their position is that diet and genetics can alter a drug's metabolism. Consequently, the effects of a drug may be different in Japanese as opposed to other races.[148]

Certainly there are differences. Japan has a very low rate of breast and colon cancer and a high rate of stomach cancer. In the United States, the reverse is true. However, when Japanese immigrate to the United States, within one or two generations, they show the high colon and breast cancer rates and low stomach cancer typical of Americans.[149] The low rate of cardiovascular disease in Japan changes in Japanese-Americans who switch to American diets.[150] One wonders if this is true scientific justification for requiring across-the-board duplication of American clinical data.

B. *Multinational Requirements for Animal Testing*

As discussed above, some agreements on mutual recognition of animal test data have been reached. However, as they currently stand, these procedures have a number of serious flaws. Their inherent weaknesses are another impediment to the use of new medical technologies in a crisis.

As evidenced by cigarette smoking, a twenty to thirty year period may exist between initial exposure to a carcinogen and the appearance of cancer.[151] Studies on animals, particularly for the purpose of testing for cancer or birth defects, are therefore required by most nations. Included among these are the United States;[152] India (2 species, 1 rat or mouse); Sweden (2 species, 2 dose levels); the United Kingdom (2 species, 1 small rodent or rabbit); and Venezuela (3 species, 1 a non-rodent).[153] Animal cancer tests cost about $250,000 and take about three years to complete.[154] Due to the many types of cancer and length of time required, accurate detection of a product causing cancer in only one percent of the test animals would require the use of 10,000 rats or mice.[155] Fifty animals at each of two doses are normally used. High doses are administered to animals in an attempt to overcome this limitation.[156]

The World Health Organization has considered the issue of both animal and human testing. In 1971 and 1972, WHO urged the creation of an International System of Information on Drugs. One of its purposes was to "reduce repetitive animal experimentation and unnecessary exposure

148. Fairbain, *supra* note 145, at 29.

149. Bruce N. Ames, *Identifying Environmental Chemicals Causing Mutations and Cancer*, 204 SCIENCE 587, at 587 (1979).

150. Fairbain, *supra* note 145, at 29.

151. Ames, *supra* note 149, at 587.

152. *Guideline*, *supra* note 128, at 15, 32, 42.

153. KAY, *supra* note 137, at 60.

154. Ames, *supra* note 149, at 588.

155. *Id.* at 589.

156. *Id.*

of human subjects to drugs."[157]

More serious problems exist. In a joint Finnish and Italian study a broad variety of chemical substances, known to cause birth defects in humans, was surveyed for its effects on animals.[158] Potent chemicals, such as PCBs, while producing malformations in mice, produced none in rats and rabbits. Experimental effects did not consistently reproduce the problems observed in humans, nor were they similar in different animal species. The authors of the study noted that while some of these substances did not produce malformations, they did induce some other effects. Other effects were resorption, still birth and decreased weight gain. As a result, they concluded that animal testing for birth defects seems justified.[159] However, the Advisory Subgroup in Toxicology of the European Medical Councils, who commissioned the study stated that:

> No conclusion can be drawn on the validity of the practice of testing chemicals for teratogenicity. The variations of doses and responses . . . reinforces the view . . . that only an increase in knowledge of the mechanism of action of embryotoxins will lead to sound methods for the prediction of this hazard of human exposure.[160]

In 1979, "almost all of the dozen or so organic chemicals known to cause cancer in humans also caused cancer in some laboratory animals."[161] Far more information is known today. The folly of over-reliance on animal testing is further indicated by the fact that lactose, the sugar in human breast milk, causes cancer in rats. Common table salt, in large amounts, causes birth defects in mice. Vitamin A, used by the human body to strengthen bone, is as toxic to rodents as the pesticide parathion. Thalidomide, which caused birth defects in thousands of humans, does not cause birth defects in either mice or rats.[162] Despite serious shortcomings, animal safety testing is required by most international regulatory agencies.

Alternate methods of safety testing are now being developed. The ability of a chemical to mutate or cause damage to human DNA is likely to be the major cause of cancer and birth defects.[163] In the 1970s, Dr. Bruce Ames and his colleagues developed an assay for detecting mutagens and carcinogens (the Ames test). It is based on the ability of a chemical to produce a mutation in a defective bacterial gene (i.e. a strain of Salmonella), enabling it to no longer require a previously required nutrient. The

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157. KAY, *supra* note 137, at 61, 62, *quoting* WHA 24.56 and WHA 25.61.

158. K. Hemminki and P. Vineis, *Extrapolation of the Evidence on Teratogenicity of Chemicals Between Humans and Experimental Animals; Chemicals Other Than Drugs*, 5 TERATOGENESIS, CARCINOGENESIS AND MUTAGENESIS 251-318 (1985).

159. *Id.* at 282-83.

160. *Id.* at 252.

161. Ames, *supra* note 149, at 588.

162. Richard Lipkin, *Risky Business of Assessing Danger*, INSIGHT, May 23, 1988, at 8, 12.

163. Ames, *supra* note 149, at 587.

chemical to be tested is mixed with a liver extract used to convert the chemical to forms used in the body (metabolites). This mixture is then placed on a nutrient solution that does not contain the element that the bacteria previously required in order to live. After incubation for two days, the number of bacterial colonies growing on the solution is recorded. Each of these colonies is composed of descendants of a bacteria that has been mutated from having a defective genetic instruction to having a normal one.[164]

The original validation of the test showed that about 90% of the known cancer causing substances tested were detected, other studies have confirmed this observation.[165] Some specific classes of cancer causing chemicals did not respond to the test. New strains of test bacteria are being developed for improving the accuracy of the assay.[166]

A major Japanese food additive, furylfuramide (AF-2), which tested negative in two animal cancer tests, was shown to cause cancer using the Ames Test.[167] One hundred million Japanese were ingesting this compound. Based on the Ames data, additional testing was ordered. AF-2 has now been banned.[168]

The Ames test is currently being used in over three thousand government, industrial and academic laboratories throughout the world.[169] Internationally required animal tests for carcinogenicity and birth defects have severe limitations. In addition to the lack of mutual recognition by several nations, animal testing for cancer and birth defects has been demonstrated to be inaccurate on a number of occasions. Considering these limitations, in an international health crisis, the value of short term testing, similar to the Ames test, would be immeasurable.

C. *Rules Prohibiting Transnational Cooperation*

Rules prohibiting the exportation of new treatments are another impediment to international cooperation during emergencies. The United States Drug Export Amendments Act of 1986 (DEAA),[170] was designed to help U.S. drug producers in their battles with foreign competition. It did so by allowing drugs that were not yet approved in the U.S. to be shipped to nations where they had been approved.[171] The Act requires that a domestic manufacturer, prior to exporting the drug, must be actively seek-

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164. *Id.* at 589.

165. *Id.*

166. Bruce Ames, *The Detection of Environmental Mutagens and Potential Carcinogens*, 53 CANCER 2034, at 2034-36 (May 15, 1984) [hereinafter *Detection*].

167. Bruce N. Ames and Lynne Haroun, *Letter to the Editor*, 62 MUTATION RESEARCH 393-95 (1979).

168. *Id.* at 394.

169. *Detection*, *supra* note 166.

170. 21 U.S.C. §382 (1988).

171. Note, *The Impact of the Drug Export Amendment Act of 1986 on Foreign Tort Victims*, 21 VANDER. J. TRANSNAT'L L. 809, 810 (1988).

ing approval of the drug in the United States.[172] It also requires that the drug be exported to one of only twenty-one nations.[173] The country to whom it is shipped must have already approved the product, and it must be available for sale in that country.[174] Applications must be submitted ninety days before the proposed shipment date.[175] The Secretary of Health and Human Services has thirty days to review it.[176]

These provisions are in direct contrast to those of the Helsinki Accords, which seek to expand international cooperation in the development and testing of new drugs.[177] Although the imposition of restrictions in the DEAA are probably to prevent re-importation of unimproved drugs to the United States, their inflexibility could have serious ramifications. During a crisis, the use of new medical technologies overseas would be prevented for an extended period of time. New medicines, developed within the United States, could not be used to treat a new disease in the country of origin, until it had been allowed to spread well beyond its borders.

D. *The Cost of Drug Production*

Experience has demonstrated that the distribution of production costs also inhibits international cooperation in an emergency. It has been estimated that of every 5,000 to 7,000 new substances evaluated for drug production, only 1,500 survive the initial screening. Of these, only thirty survive detailed pharmacological tests and only one of those complete the battery of tests and becomes a marketable drug.[178] On average, it takes eight years and six to seven million dollars to take that drug through the requirements of FDA approval.[179] WHO, in an attempt to provide needed drugs for underprivileged nations, established a special program on essential drugs.[180] A number of drug manufacturers agreed to provide these drugs under "financially favorable conditions."[181]

Under emergency conditions, however, experience indicates that even these minimal levels of cooperation may be difficult to maintain. In the spring of 1957, when it was first learned that a new strain of influenza had developed in Hong Kong, various scientific advisory committees urged the production and distribution of massive amounts of appropriate

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172. 21 U.S.C. §382(b)(1)(A)(i)(II) (1988).
173. 21 U.S.C. §382(b)(4)(A) (1988).
174. 21 U.S.C. §382(b)(1)(B) (1988).
175. 21 U.S.C. §382 (b)(3)(A) (1988).
176. 21 U.S.C. §382(b)(3)(C)(i) (1988).
177. Helsinki, *supra* note 57, §III(4).
178. Kay, *supra* note 137, at 22.
179. Marianne Lavelle, *Lawyers for a New Drug Must Practice Patience*, 10 NAT'L L.J., June 27, 1988, at 1, 20.
180. *Action Programme on Essential Drugs*, WHA 32.42, May 25, 1979, *quoted in* Ursula Wasserman, *WHO: Essential Drugs for Developing Countries*, 16 J. WORLD TRADE L. 444 n.2 (1982).
181. *Id.* at 446.

influenza vaccine.[182] Unfortunately, there was never enough vaccine available in the right place, at the right time to halt the spread of the virus. Manufacturers had been asked to make large investments in a vaccine with no assurance that the disease would spread. If it did not arrive, they would not be able to sell what they had produced. The disease spread quickly and producers could not keep up with the demand. After the epidemic subsided, tens of millions of doses remained unused.[183]

Conditions similar to a "black market" were created for the drug. Some groups were able to bid successfully for a vaccine that others could not afford. Large corporations were able to keep production lines going by immunizing their workers, while the poor could not obtain protection. Reports appeared in newspapers concerning the ability of a baseball club, for example, to immunize its healthy team, while high risk populations did not have access to the vaccine.[184] Market economics do not appear to respond well during a health emergency.

E. *Prior Experience of International Organizations: The Problem With International Efforts*

Current international organizations are ill-equipped to handle a fast-breaking medical emergency. Where successful programs have been conducted by international groups, they have been typified by narrowly defined circumstances. Highly technological issues are ill-suited to these groups.

The eradication of smallpox stands as a major achievement of the World Health Organization. WHO-supported national programs helped eradicate the disease through vaccinations from 1958 to its last outbreak in 1977.[185] WHO's Expanded Programmes on Immunization (EPI) are currently credited with sparing about 200,000 children from becoming paralyzed with polio. Over one million deaths from measles, neonatal tetanus and pertussis in developing countries are prevented through this program.[186] It has been postulated that these programs succeed because they are inexpensive, easily understood, easy to implement and bring immediate visible benefits.[187]

With more complex issues, however, the record is not quite as encouraging. Under pressure from developing nations, WHO attempted to pass measures designed to assure uniformity of drugs sold internationally.[188] These proposals included the creation of regional test facilities,

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182. SILVERSTEIN, *supra* note 84, at 20, 21.

183. *Id.* at 21.

184. *Id.* at 22.

185. D.A. Henderson et al., *Principals and Lessons from the Smallpox Eradication Programme*, 65 BULL. WORLD HEALTH ORGANIZATION 535-37 (1987).

186. R.H. Henderson, et al., *Immunizing the Children of the World: Progress and Prospects*, 66 BULL. WORLD HEALTH ORGANIZATION 535 (1988).

187. *Id.*

188. JOHN U. GRANGER, TECHNOLOGY AND INTERNATIONAL RELATIONS, 186-87 (1979).

upgrading national regulatory capabilities, attempts to uniformalize manufacturing controls, national certification of the quality of exported pharmaceuticals and monitoring of adverse reactions to drugs.[189]

By 1976, WHO funding of the project had been severely cut. Two reasons were seen as responsible. The first was that developing nations, who originally pressed for the measures, eventually saw the program as being irrelevant to their major needs. The second concerned the administrative, scientific and liability problems associated with reporting adverse drug reactions.[190]

When handling scientific issues, international organizations have been criticized for having serious weaknesses. A major problem is the "one nation, one vote" rule that exists in the United Nations General Assembly.[191] The bloc voting strength of underdeveloped nations has dominated debates on technical assistance to less developed countries. The selection of secretariats is not free from political influence. As a result, "sophisticated technological issues are frequently debated by politicians and foreign ministry officials who have no expertise regarding them nor any support of knowledgeable bureaucrats and private sector representatives either at the meeting or in their national capitals."[192]

In a rapidly developing international health crisis, this could be an extreme handicap. Resource allocation and major decisions must be handled by only the most well-informed individuals. The abuse of political influence could result in chaos.

VIII. WALKING A TIGHTROPE — THE POLITICAL REALITIES OF DEALING WITH A CRITICAL PRODUCT

Given their propensity for political influence and inability to deal with technical issues, it is important to understand the realities that will confront an international organization during a fast-breaking health care emergency. The decision on when to release an experimental drug for human use is highly charged politically and laden with difficult scientific issues. The perils of releasing a drug too early or too late, are both severe and numerous. Recent experiences in the United States and abroad illustrate the point.

In 1987, the FDA issued new regulations that permit the use and sale of a drug that is still under investigation (compassionate use program). These regulations permit such use provided the drug is used to treat an immediate life-threatening disease, for which there is no alternative therapy. The drug must be under investigation in an approved clinical trial, and the sponsor of the clinical trial must be actively pursuing approval of

189. *Id.* at 187-88.
190. *Id.* at 188.
191. *Id.* at 189.
192. *Id.*

the drug with "due diligence."[193] The purpose of the rule change was to give desperately ill patients the opportunity to "decide for themselves whether they would rather take an experimental drug or die of the disease untreated."[194]

The agency also created a "fast track" or expedited review process for critically needed drugs. The aim of this policy is to cut down the time required to review an application for the approval of a new drug. Alpha interferon, mentioned in Section VI(A) of this article, was approved by the FDA within six months of filing the new drug application. Even on a fast track, FDA approval normally takes two years.[195] The antiviral drug Azidothymidine (AZT), used in the treatment of AIDS, emerged from testing in two years.[196] As previously mentioned, most drug approvals take an average of eight years.[197] The perils of this program have been debated extensively in the press and in scientific periodicals.

A. *The Perils of Approving a Drug Too Slowly*

In an editorial entitled "Human Sacrifice," Wall Street Journal editors accused an FDA advisory committee of deciding to "sacrifice thousands of American lives on an altar of pedantry."[198] Advisory committees are composed of impartial experts assembled to "review and make recommendations" with respect to matters pending before the FDA.[199] Their comments are considered quite valuable but are not binding. The FDA commonly enlists the advice of such committees to obtain unbiased reviews of the evaluation of a new drug product.[200] The "human sacrifice" referred to in the editorial was that allegedly caused by the committees decision not to recommend approval of tPA, previously referred to in section VI of this article.

On the day prior to the advisory committee meeting for tPA, another Wall Street Journal editorial urged immediate approval.[201] This article stated that "bureaucratic progress must be measured against the real-world costs of keeping this substance out of the nation's emergency rooms," and emphasized that well over a thousand Americans go to their deaths each day from heart attacks.[202] After the committee's refusal to follow the Wall Street Journal editors' advice, still another editorial ap-

193. 21 C.F.R. §312.34 (1991).

194. G. Annas, *FDA's Compassion for Desperate Drug Companies*, HASTINGS CENTER REPORT, January/February 1990, at 36, *quoting* S. Jay Plager, counselor to the Undersecretary of Health and Human Services, NEW YORK TIMES, July 24, 1988, at A1.

195. Marciniszyn, *supra* note 103, at 151-52.

196. *Id.* at 154.

197. Lavelle, *supra* note 179, at 20.

198. Editorial, *Human Sacrifice*, WALL ST. J., June 2, 1987, at 30.

199. 21 C.F.R. §14.1 (1991).

200. Peter R. Kowley, et al., *The TPA Controversy and the Drug Approval Process*, 260, JAMA, Oct. 21, 1988, at 2250.

201. Editorial, *The TPA Decision*, WALL ST. J., May 28, 1987, at 30.

202. *Id.*

peared. This one, entitled "The Flat Earth Committee," cited the clinical trials used for the approval of another drug, streptokinase. The editors decided that patients who received a placebo, in order to evaluate the drug's effectiveness, "proved the drug's efficacy by going to their deaths" and that data had come to supersede the purpose of helping sick people get well.[203]

The advisory committee responded in a letter to the editor. They pointed out that without adequate and well-controlled data, one cannot distinguish between the wise early approval of a good drug, and the unwise early approval of a bad one.[204] With regard to tPA, a higher incidence of cerebral hemorrhage (bleeding in the brain) was observed at the higher dosage levels of the drug. A severe stroke or death could occur in one to four percent of the patients, at these higher dosage levels. The dose of the drug was then reduced, but relatively few patients getting the lower dose had been reported on in full. More data was needed to show safety. In addition, the drugs used in the study were produced by two different methods with one form differing from the other in several respects. These included both the time the drugs remained in the bloodstream and their peak effects.[205] The effects of the two needed greater clarification. The additional data was produced and the drug was approved six months later.

In a separate response, the committee stated that had it recommended approval, sponsors might be lead to believe that "predeliberation pressure could force approval of an incompletely evaluated compound."[206] In the advisory committee meeting regarding EPO, also referred to in section VI, an AIDS activist threatened to put thousands of AIDS activists at the doorstep of the FDA if the drug was not approved immediately.[207] EPO might correct the anemia experienced by AIDS victims as a side effect of therapy.

B. *The Perils of Approving a Critical Drug Too Quickly*

Through the FDA's compassionate use program, Dideoxyinosine (DDI) was released to a greater number of patients while still under investigation. The drug is thought to be free of the side effects associated with AIDS treatment using current drugs. A recent report from the manufacturer indicated that of 8,000 patients who had been taking the drug, 290 died. While the National Health Institute observed that the death rate was lower than that for the early trials of AZT, others labeled the death rate "a disgrace," and called for more tightly controlled clinical

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203. Editorial, *The Flat Earth Committee*, WALL ST. J., July 13, 1987, at 22.

204. Letters to the Editor, *The FDA Cardio-Renal Committee Replies*, WALL ST. J., Aug. 12, 1987, at 19.

205. *Id.*

206. Kowley, *supra* note 200, at 2251.

207. Meeting attended by author.

trials.[208]

While the "compassionate use" or "expanded access" program is fairly new and for use with critical drugs only, history contains several horror stories of non-critical drugs brought to the market too quickly. Clioquinol, an antidiarrhea medication, caused blindness, paralysis or death. In Japan alone, more than 10,000 people were injured by the drug.[209] High dose isoprenaline, administered to asthmatics, was responsible for sudden cardiac failures in England.[210] Genital malformations were found to be caused by the drug diethylstilbestrol (DES).[211] Thalidomide caused thousands of birth defects.[212] The effects of these drugs were not immediate.

In another case, the drug Azaribine (Triazure) was withdrawn from the market in the United States after being sold for one year. The drug was found to be responsible for inducing blood clots. Eight cases were reported with one death. A congressional hearing was held to determine if the FDA had not done enough to protect patients.[213]

In 1979, the United States Supreme Court considered the petition of cancer patients denied the drug laetrile.[214] The court stated that a drug is unsafe where its potential for injury may outweigh the possibility of benefit, and that the FDA has never made exception for drugs used by the terminally ill.[215] They also stated that Congress expressed concern that individuals with fatal illnesses should be shielded from fraudulent cures.[216]

The tightrope on which regulatory agencies must walk is extremely narrow. Political and media pressures increase greatly when considering a drug for the treatment of a terminal illness. In these situations, no matter what the decision, the only thing one is guaranteed is intense opposition. It is a perpetual case of damned if you do and damned if you don't.[217] Current international organizations are clearly not structured to handle these pressures.

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208. Andrew Purvis, *Case of the Unexplained Deaths*, TIME, March 26, 1990, at 53.

209. MILTON SILVERMAN, et al., PRESCRIPTIONS FOR DEATH, THE DRUGGING OF THE THIRD WORLD 45 (1987).

210. TEXTBOOK OF ADVERSE DRUG REACTIONS 210 (D.M. Davies ed. 1977).

211. PHARMACOEPIDEMIOLOGY 211 (Brian L. Strom ed. 1989).

212. Lavelle, *supra* note 179, at 22.

213. *FDA's Regulation of the Drug "Triazure": Hearings Before the Subcomm. on Intergovernmental Relations and Human Resources*, 94th Cong., 2d Sess. 1-2 (1976).

214. United States v. Rutherford, 442 U.S. 544 (1979).

215. *Id.* at 553.

216. *Id.* at 552.

217. This expression was coined by Lorenzo Dow (1777-1834), concerning his definition of Calvinism in *Reflections of the Love of God, quoted in* JOHN BARTLETT, BARTLETT'S FAMILIAR QUOTATIONS 444 (15th ed. 1980).

IX. CONCLUSIONS AND RECOMMENDATIONS

This article began with an examination of the historical and legal development of human rights philosophies, and their evolution into different systems. Each system has its unique problems. These problems become more severe when different philosophies and systems are forced to work together. Such would be the case in a sudden international emergency. Based on prior experience and current scientific knowledge, that emergency is a very real possibility.

The delivery of new, safe medical products to those in need is an important aspect of providing equal access to health care. It is ironic that so many nations that see health care as a human right, yet refuse to accept foreign clinical test data demonstrating the effectiveness of new products. The paradox is extended by the fact that a major nation that does not recognize health care as a right, the United States, has been willing to accept human test data from other nations. In the United States, however, export laws exist that bar the overseas shipment of an experimental drug. In the event of a rapidly breaking crisis, these barriers must fall. International cooperation is imperative during a global medical crisis. Until recently, animal testing was all that was available to determine the long-term side effects of drugs. A few international agreements have been reached with regard to mutual acceptance of animal test data. This is only part of the problem. Studies have clearly demonstrated the pitfalls of over-reliance on animal testing. In addition to being time-consuming and expensive, they can be inaccurate.

New methods of testing, such as the Ames test, provide a measure of hope for resolving these difficulties. With improvement in short-term tests, reliance on extensive animal testing might be reduced. This could be critical in a worldwide emergency. International cooperation and mutual recognition of test methods would again be required.

Some precedent for this concept exists. Testing drugs and devices for fever-producing substances (pyrogens) was primarily accomplished by testing rabbit colonies for temperature elevation following injection of the drug or an extract of a device.[218] As with other animal tests, the method was expensive, time-consuming and subject to variability.[219] In 1973, the FDA announced approval of a substitute that could be performed in a test tube (the LAL test).[220] It was found to be more accurate, faster and less expensive than using rabbits. Guidelines on its validation for routine use by drug and device manufacturers were issued in 1987.[221]

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218. XX U.S. PHARMACOPEIA 902 (1980).

219. U.S. Department of Health and Human Services *Sterile Medical Devices — A GMP Workshop Manual* 432 (4th ed. 1984).

220. 38 Fed. Reg. 1404 (1973).

221. U.S. Dep't Health and Hum. Services, *Guideline on the Validation of the Limulus Amebocyte Lysate Test as an End-Product Endotoxin Test for Human and Animal Parenteral Drugs, Biological Products, and Medical Devices* (Dec. 1987).

Costs and methods of reimbursement likewise inhibit the use of new medical products during an emergency. Manufacturers need some financial assurances before launching into production of a product for which a market might not be waiting. Without such assurances, both shortages and a black market in medicine may develop.

The resolution of each of these problems requires a high level of international cooperation. Current international organizations are ill-equipped to handle these issues. Political pressures associated with critical medical products are enormous. The lack of technical expertise, coupled with the politics of a "one-nation, one-vote" system, renders many current international organizations incapable of dealing effectively with challenges of this magnitude.

A new international accord is needed to formulate a world crisis strategy. Elements of that strategy should include the following:

1. The transnational recognition of human clinical test data, generated in accordance with mutually defined practices, for use in an emergency.

2. The identification of true human genetic variants and their incorporation into a worldwide system for mutually recognized clinical testing.

3. Mutual recognition of animal test data coupled with the funding, development and acceptance of alternatives.

4. The creation of an account, within the World Bank, for the purpose of funding increased production of new drugs. This account could be used by qualified manufacturers in the early stages of a potential health crisis. By doing so, manufacturers would have some assurance of expense reimbursement while the new drug might be provided earlier to help slow the spread of the disease.

5. The appointment of a highly qualified group of independent medical experts to oversee and direct these activities. This would include the oversight of qualified clinical investigators and the international use of experimental substances during emergencies.

Our recent history has demonstrated that we must at least have the capacity to respond to a worldwide medical emergency. International proclamations regarding health for all and equal access to health care are truly admirable and represent worthy goals. Without confronting the realities that divide us, however, we are blowing an uncertain trumpet.[222]

Dennis McElwee

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222. Father Theodore Hesburgh, former president of Notre Dame University, said the following: "The very essence of leadership is [that] you have to have a vision. It's got to be a vision you can articulate clearly and forcefully on every occasion. You can't blow an uncertain trumpet." TIME, May 1987, *quoted in* TOM PETERS, THRIVING ON CHAOS 399 (1987).