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As discussed earlier, you herewith receive a copy of the Executive Summary of the IOM report "HIV and the Blood Supply: An Analysis of Crisis Decisionmaking".

Best regards

GRO-C

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HIV and the Blood Supply: An Analysis of Crisis Decisionmaking

Committee to Study HIV Transmission Through Blood and Blood Products

Division of Health Promotion and Disease Prevention

INSTITUTE OF MEDICINE

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Preface

The transmission of HIV through the blood supply in the early 1980s has led to considerable concern and controversy. Many individuals with hemophilia and many recipients of blood transfusions were infected with HIV through treatment with contaminated blood and blood products before there was an HIV antibody test for screening these products. These individuals—and their families, some of whom also became infected, face considerable suffering and emotional and financial hardship as a result. They believe they were betrayed by the very people and organizations with whom they had entrusted their safety. They ask if human error, or conflicting motivations, led to this tragic course of events. These questions become even more salient in so far as threats to the safety of the blood supply persist today (e.g., because of Creutzfeld-Jakob disease, hepatitis C, and cytomegalovirus) (IOM 1992).

In April 1993, in response to concerns voiced by the hemophiliac community, Senators Edward Kennedy (D-MA) and Robert Graham (D-FL) and Representative Porter J. Goss (R-FL) requested that Secretary of Health and Human Services Donna Shalala open an investigation into the events leading to the transmission of HIV to individuals with hemophilia from contaminated blood products. The Secretary agreed that it would be useful to gain a more complete understanding of the use of blood and blood products for the treatment of individuals with hemophilia and those receiving transfusions in the early years of the AIDS epidemic. Thus, with the intention of preparing for future threats to the blood supply, the Department of Health and Human Services requested that the Institute of Medicine (IOM) establish a committee to study the transmission of HIV through the blood supply. As a result, the *Committee to Study HIV Transmission Through Blood and Blood Products* was formed. Through this historical analysis, the Department of Health and Human Services expects to improve both decision making and public health policy in meeting future challenges to the blood supply.

To carry out this yearlong study, the IOM established a committee of 14 people. The creation of an IOM committee emphasizes the importance of providing an objective and impartial review of the decision-making processes and policies that surrounded the contamination of the blood supply with HIV. The Committee was asked to examine the decisions made from 1982

through 1986 to safeguard blood and blood products, and to evaluate the actions taken to contain the AIDS epidemic. The Committee held four meetings in which members formulated explanations and discussed information that had been collected to test their hypotheses. This report, the product of the Committee's efforts, attempts to provide both a comprehensive account of the events that led to the contamination of the U.S. blood supply and a critical assessment of the difficult decisions that were made in the context of the uncertainty of this period. This report will not seek to determine liability or affix blame for any individual or collective decisions regarding HIV transmission through blood or blood products during this time period. The Committee's conclusions and recommendations are intended to provide future leaders who will have responsibility for the blood supply with lessons gained from the experiences of those who tried to slow the tide of the AIDS epidemic among recipients of blood and blood products. The Committee undertook this assignment fully aware of the benefits and risks of hindsight. Hindsight offers an opportunity to do better the next time. The risk of hindsight is unfairly finding fault with decisions made by people who had to act long before scientific knowledge became available to dispel their uncertainty. To avoid this risk, the Committee has made every effort to conduct a thorough and objective review of what was known during 1982-1986 about the transmission of HIV through the blood supply. The Committee recognized the importance of conducting an organizational analysis of the major players involved in the blood supply system and attempted, in some instances, to understand and describe their various roles, responsibilities, and responses.

To understand the views of the many organizations involved in the blood supply, the Committee's first meeting included an opportunity to hear representatives of the Office of the Assistant Secretary for Health (OASH) of the U.S. Public Health Service, Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), American Association of Blood Banks (AABB), Council of Community Blood Centers (CCBC), American Blood Resources Association (ABRA), American Red Cross (ARC), National Hemophilia Foundation (NHF), the Committee on Ten Thousand (COTT), HIV/Peer Association, and congressional staff of Senator Graham and Representative Goss. The Committee's second meeting included a public hearing in which the Committee heard presentations from interested parties. Fifty-nine speakers provided oral testimony to the Committee and an additional 50 provided written statements. A transcript of the public hearing is available through National Technical Information Services (Record Locator No. PB95142345). A list of all individuals who provided oral and written testimony appears in Appendix B. The Committee carefully considered all of this testimony as it formulated its conclusions and recommendations over the course of the following two meetings.

One of the advantages of conducting this study at this time is that many of the key participants in the 1982–1986 decision making were available to speak to the Committee and staff. The Committee believed it was critical to hear firsthand accounts of the assumptions and beliefs that influenced critical decisions about the safety of the blood supply. Fact-finding interviews were held with 76 individuals knowledgeable about all aspects of the blood supply system. These interviews included representatives of FDA, CDC, NIH, NHF, OASH, industry, and blood banks; physicians and scientists; and individuals with hemophilia. A list of all the people the Committee interviewed appears in Appendix A. The Committee also benefits from expert advice and background papers provided by consultants in plasma fractionation, blood

supply systems, anthropology, risk assessment, virology, and organizational behavior. The Committee and staff also reviewed over 700 documents provided by each of the major organizations involved and other sources. Some of the key documents not readily available elsewhere are provided in Appendix D. Other documents reviewed by the Committee are available through the archives of the National Academy of Sciences.

A special acknowledgement is extended to those people who wrote background papers for the study—Jeffrey McCullough (whose paper provided much of the information contained in Chapter 2), Salman Kashevjee, Sheri Weiser, and Arthur Kleinman—and those who helped the Committee obtain important documentation—Val Bias, Wendy Donath, Corey Dubin, Bruce Evatt, Joseph Fratantoni, William Hammes, Dana Kulin, Beth Leahy, Bruce Lesley, Jeanne Lusher, Clyde McAuley, Dick Merritt, Maria Persky, Andrea Posner, Dick Valdez, Jonathan Wadleigh, and many others. The Committee would also like to give special thanks to Lauren Leveton, Study Director, for her tireless efforts and guidance throughout the study. Thanks are also extended to the professional staff, Laura Colosi, Cynthia Abel, Kristina Becker and to summer law student intern Kathryn Astarita, for their commitment, assistance, and insight. Finally, the Committee thanks Michael Stoto, Director of the Institute of Medicine's Division of Health Promotion and Disease Prevention, for his contributions to this study.

REFERENCES

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INTRODUCTION

A nation's blood supply is a unique, life-giving resource and an expression of its sense of community. In 1993, voluntary donors gave over 14 million units of blood in the United States (Wallace, et al. 1993). However, the characteristic that makes donated blood an expression of the highest motives also makes it a threat to health. Derived from human tissue, blood and blood products can effectively transmit infections such as hepatitis, cytomegalovirus, syphilis, and malaria from person to person (IOM 1992). In the early 1980s blood became a vector for HIV infection and transmitted a fatal illness to more than half of the 16,000 hemophiliacs in the U.S. and over 12,000 blood transfusion recipients (CDC, MMWR; July 1993).

Each year, approximately four million patients in the United States receive transfusions of approximately 20 million units of whole blood and blood components. The blood for these products is collected from voluntary donors through a network of nonprofit community and hospital blood banks. Individuals with hemophilia depend upon blood coagulation products, called antihemophilic factor (AHF) concentrate, to alleviate the effect of an inherited deficiency in a protein that is necessary for normal blood clotting. The AHF concentrate is manufactured from blood plasma derived from 1,000 to 20,000 or more donors, exposing individuals with hemophilia to a high risk of infection by blood-borne viruses.

The safety of the blood supply is a shared responsibility of many organizations including the plasma fractionation industry, community blood banks, the federal government, and others. The Food and Drug Administration (FDA) has regulatory authority over plasma collection establishments, blood banks, and all blood products. Since 1973, the FDA has established standards for plasma collection and plasma product manufacture and a system for licensing those who met standards. The Centers for Disease Control and Prevention (CDC) has responsibility for surveillance, detection, and warning of potential public health risks within the blood supply. The National Institutes of Health (NIH) supports these efforts through fundamental research. During the 1950s and 1960s blood shield laws were adopted by 47 states. These laws exempt blood and blood products from strict liability or implied warranty claims on the grounds that they are a service rather than a product. The laws were developed on the premise that given the

inherently risky nature of blood and blood products, those providing them required protection if the blood system was to be a reliable resource.

As a whole, this system works effectively to supply the nation with necessary blood and blood products and its quality control mechanisms check most human safety threats. The events of the early 1980s, however, revealed an important weakness in the system—in its ability to deal with a new threat that was characterized by substantial uncertainty. With intent to prepare the guardians of the blood supply for future threats concerning blood safety, the Department of Health and Human Services commissioned the Institute of Medicine to study the transmission of HIV through the blood supply. The *Committee to Study HIV Transmission Through Blood and Blood Products* undertook this assignment fully aware of the advantages and dangers of hindsight. Hindsight offers an opportunity to gain the understanding needed to confront the next threat to the blood supply. The danger of hindsight is unfairly finding fault with decisions that were made in the context of great uncertainty.

HISTORY

The Risk of AIDS

Starting with the identification of 26 homosexual men with opportunistic diseases in June 1981, the CDC's *Morbidity and Mortality Weekly Report* became the source for reports of the epidemic. By July 1982, enough cases had occurred with common symptomatology to name the new disease "Acquired Immune Deficiency Syndrome" (AIDS). By January 1983, epidemiological evidence from CDC's investigations strongly suggested that blood and blood products transmitted the agent causing AIDS and that the disease could also be transmitted through intimate heterosexual contact. The conclusion that the AIDS agent was blood borne was based on two findings. First, AIDS was occurring in transfusion recipients and individuals with hemophilia who had received AHF concentrate; these patients did not belong to any previously defined group at risk for contracting AIDS. Second, the epidemiologic pattern of AIDS was similar to hepatitis B, another blood-borne disease.

Immediate Responses to Evidence of Blood-Borne AIDS Transmission

In the first months of 1983, the epidemiological evidence that the AIDS agent was blood-borne led to meetings and public and private decisions that set the pattern of the blood industry's response to AIDS, starting with a public meeting convened by the CDC in Atlanta on January 4, 1983. Later that month, the leading blood bank organizations, and, separately, the National Hemophilia Foundation (NHF) and the blood products industry issued statements about preventing exposure to AIDS. In March 1983, the Assistant Secretary for Health promulgated the first official PHS recommendations for preventing AIDS, and the FDA codified safe practices for blood and plasma collection.

The government and private agencies quickly identified, considered, and in some cases adopted strategies for dealing with the risk of transmitting AIDS through blood and blood

products. The recommended safety measures, however, were limited in scope. Examples include: questions to eliminate high-risk groups such as intravenous drug users, recent immigrants from Haiti, and those with early symptoms of AIDS or exposure to patients with AIDS; direct questions about high-risk sexual practices are generally not used. They reflected a lack of consensus about the magnitude of the threat, especially among physicians and public health officials, who had trouble interpreting the unique epidemiological pattern of AIDS. The recommendations also reflected uncertainty about the benefits of identifying and deferring potentially infected blood and plasma donors, treatment of blood products to inactivate viruses, recall of products derived from donors known to have or suspected of having AIDS, and changes in transfusion practices and blood product usage. The costs, risks, and benefits of these and other potential control strategies were uncertain.

Opportunities to Reformulate Policy

In the interval between the decisions of early 1983 and the availability of a blood test for HIV in 1985, public health and blood industry officials became more certain that AIDS was a blood-borne disease as the number of reported cases of AIDS among hemophiliacs and transfused patients grew. As their knowledge grew, these officials had to decide about recall of contaminated blood products and possible implementation of a surrogate test for HIV. Meetings of the FDA's Blood Product Advisory Committee in January, February, July and December 1983 offered major opportunities to discuss, consider, and reconsider the limited tenor of the policies.

Despite these opportunities and others to review new evidence and to reconsider earlier decisions, blood safety policies changed very little during 1983. Many officials of the blood banks, the plasma fractionation industry, and the FDA accepted with little question estimates that the risk of AIDS was low ("one in a million transfusions"), and they accepted advice that control strategies (such as automatic withdrawal of AHF concentrate lots containing blood from donors suspected of having AIDS, or a switch from AHF concentrate to cryoprecipitate in mild or moderate hemophiliacs) would be ineffective, too costly, or too risky. During this period, there were missed opportunities to learn from local attempts to screen potentially infected donors or implement other control strategies that had been rejected as national policy.

Research Activities

From 1983 through 1985, research on AIDS included epidemiological analysis to understand patterns of spread and etiology, the search for methods to control or eliminate the disease, and evaluation of the efficacy of potential safety measures such as surrogate tests for the infection. Related research on methods to inactivate hepatitis B virus in AHF concentrate had begun in the 1970s and came to fruition in the early 1980s.

In the early 1980s the CDC's surveillance program identified AIDS patients and rapidly characterized the disease. Scientists at NIH isolated and characterized HIV in 1984. Viral inactivation methods for AHF concentrate were developed in laboratories of the plasma

fractionators and the FDA licensed the new processes quickly. Although the pace of viral inactivation research had been slow, it accelerated in the 1980s largely in response to hepatitis, and had identified effective strategies by 1984. However, research into other potential ways to safeguard the blood supply such as the use of surrogate tests was not pursued vigorously and there was relatively little research on blood safety issues per se.

FINDINGS

The Committee framed its approach by examining four topics that are essential components of a focused strategy for ensuring the safety of the blood supply: blood product treatment; donor screening and deferral; regulation of removal of contaminated products from the market; and communication to physicians and patients.

Product Treatment

Plasma products can be treated by a variety of physical and chemical processes to inactivate viruses and thus to produce a product free from contamination and relatively safe for transfusion. Shortly after the development of the technology to manufacture AHF concentrate it was recognized that these products carried a substantial risk of transmitting hepatitis B. Although some blood derivative products had been treated with heat to destroy live viruses since the late 1940s, Factor VIII and IX concentrates in the United States were not subject to viral inactivation procedures until 1983 and 1984. If this technology had been developed and introduced before 1980 to inactivate hepatitis B virus and non-A, non-B hepatitis virus, fewer individuals with hemophilia might have been infected with HIV.

Overall, the record of the plasma fractionators and the FDA with respect to the development and implementation of heat treatment is mixed. The Committee's analysis focused on whether the basic knowledge and technology for inactivating viruses in AHF concentrate had been available before 1980 and whether industry had appropriate incentives (from FDA, NIH, NHF, or others) to develop viral inactivation procedures. In the Committee's judgment, heat treatment processes to prevent the transmission of hepatitis, an advance that would have prevented many cases of AIDS in individuals with hemophilia, might have been developed before 1980. For a variety of reasons (e.g., concern about possible development of inhibitors and higher costs), however, neither physicians caring for individuals with hemophilia nor the Public Health Service agencies actively encouraged the plasma fractionation companies to develop heat treatment measures earlier. The absence of incentives, as well as the lack of a countervailing force to advocate blood product safety, contributed to the plasma fractionation industry's slow rate of progress toward the development of heat-treated products. Once plasma fractionators developed inactivation methods, however, the FDA moved expeditiously to license them.

Donor Screening and Deferral Policies

The purpose of donor screening and deferral procedures is to minimize the possibility of transmitting an infectious agent from a unit of donated blood to the recipient of that unit, as well as to insure the welfare of the donor. Donor screening includes the identification of suitable donors; the recruitment of donors; and the exclusion of high-risk individuals through methods and procedures used at the time of donation, such as questionnaires, interviews, medical exams, blood tests, and providing donors with the opportunity to self-defer. Donor deferral is the temporary or permanent rejection of a donor based on the results of the screening measures.

By January 1983, in addition to suggesting that the agent causing AIDS was transmitted through blood and blood products and could be sexually transmitted, the epidemiological evidence also demonstrated that there were several groups who had an increased risk of developing AIDS. The highest incidence of the disease was in male homosexuals, who donated blood frequently in some geographic regions. The Committee found that organizations implemented donor screening measures in different ways at different times. Plasma collection agencies had begun screening potential donors and excluding those in any of the known risk groups as early as December 1982, and CDC scientists suggested in January 1983 that blood banks do likewise. Also in January, the blood banking organizations (AABB, ARC, and CCBC) issued a joint statement that recommended the use of donor screening questions to detect early symptoms of AIDS or exposure to AIDS patients. The statement, however, did not advocate directly questioning donors about their sexual preferences. Blood banks did institute some screening measures in early 1983, but only a few asked potential donors questions about homosexual activities. At the same time, CDC scientists also suggested that all blood and plasma collection agencies employ an available surrogate test for hepatitis B core antigen (anti-HBc). Most blood and plasma collection agencies rejected this recommendation. Although the precise impact of these two actions is not known, earlier implementation of either probably would have reduced the number of individuals infected with HIV through blood and blood products. In March 1983, the PHS issued recommendations that identified high-risk individuals for AIDS and stated that these individuals should not donate plasma or blood.

Based on its review of the evidence, the Committee found that decision makers involved with donor screening and deferral acted with good intent in some instances. In other instances, however, preference for the status quo under the prevailing conditions of uncertainty and danger led decision makers to underestimate the threat of AIDS for blood recipients. The Committee concluded that when confronted with a range of options for using donor screening and deferral to reduce the probability of spreading HIV through the blood supply, blood bank officials and federal authorities consistently chose the least aggressive option that was justifiable. In adopting this limited approach, policymakers often passed over options that might have initially slowed the spread of HIV to individuals with hemophilia and other recipients of blood and blood products, for example, screening male donors for a history of sexual activity with other males and screening donated blood for the anti-HBc antibody. The Committee believes that it was reasonable to require blood banks to implement these two screening procedures in January 1983. The FDA's failure to require this is evidence that the agency did not adequately use its regulatory authority and therefore missed opportunities to protect the public health.

Regulations and Recall

The FDA is the principal regulatory agency with authority for blood and blood products, but it exercises its authority largely through informal action. Recall—the removal of a product from the market—exemplifies the relationship between the FDA's potent formal powers and its informal modus operandi. Recall is a voluntary act undertaken by the manufacturer but overseen by the FDA, which has the authority to seize or revoke the license of a product. Regulation of blood and blood products has been generally based on establishing a scientific consensus. Because the FDA's resources are limited, it relies upon the blood industry and others for cooperation. The FDA Blood Products Advisory Committee is a venue for consensus-building about blood regulatory policy. In an industry in which firm and product reputation is critical to market success, the FDA's collegial approach is usually effective.

The Committee analyzed the FDA's exercise of its regulatory powers by examining how it acted during four critical events: (1) letters issued by the FDA in March 1983 requiring particular practices related to donor screening and the segregation of high-risk plasma supplies; (2) a July 1983 decision not to recall plasma products "automatically" whenever they could be linked to individual donors who had been identified as having or as suspected of having AIDS; (3) a decision not to recall nontreated AHF concentrate when heat-treated AHF concentrate became available in 1983; and (4) a delay of years in the FDA's formal decision to recommend tracing recipients of transfusions from a donor who was later found to have HIV. For each of these, the Committee posed a series of hypotheses to explain the FDA's actions. These focused on the reach of the agency's legal powers, the information available at the time in relation to relevant public health considerations, the agency's resources, the FDA's institutional culture, the economic costs of particular actions, and the prevailing political climate.

The analysis of these four events led the Committee to identify several weaknesses in the FDA's regulatory approach to blood safety issues. The agency's March 1983 letters may have been unclear concerning whether all of their recommendations were required to be implemented by the addressed. Handling of the case-by-case recall decision suggested that the agency lacked both the capacity to structure its advisory process adequately and to analyze independently the recommendations that were made to it. In the Committee's judgment, these and other events indicate the need for a more systematic approach to blood safety regulation when their is uncertainty and danger to the public.

Communication to Physicians and Patients

As evidence for the possibility that the blood supply was a vector for AIDS accrued, consumers of blood and blood products and their physicians found themselves in a complex dilemma about how to reduce the risk of infection. Restricting or abandoning the use of blood and blood products could lead to increased mortality and morbidity. On the other hand, continued use of these products apparently increased the risk of AIDS. The Committee investigated the processes by which physicians and patients obtained information about the epidemic and the costs, risks, and benefits of their clinical options.

A wide range of clinical options were available by late 1982 and might, in some instances, have reduced or eliminated dependence on AHF concentrate and thereby reduced the risk of HIV transmission. As often happens in times of intense scientific and medical uncertainty such as in the early 1980s, individuals with hemophilia and transfusion recipients had little information about risks, benefits, and clinical options for their use of blood and blood products.

The dramatic successes of treatment with AHF concentrate in the 1970s provided a context in which thresholds for abandoning or radically restricting the use of these products for individuals with severe hemophilia were high. Both physicians and individuals with hemophilia expressed reluctance about returning to the era of clinical treatment before the introduction of AHF concentrate. The National Hemophilia Foundation (NHF) and physicians, in their effort to find the right balance between the risks and benefits of continued use of AHF concentrate, tended to overweight the well-established benefits of AHF concentrate and underestimate the risks of AIDS, which were still uncertain.

In addition, the Committee found that prevailing assumptions about medically acceptable risks, especially regarding hepatitis, led to complacency and a failure to act upon reports of a new infectious risk with sufficient concern. Ultimately, assumptions about medical decision making practices in which patients played a relatively passive role led to failures to disclose completely the risks of using AHF concentrate and thereby did not enable individuals to make informed decisions for themselves. As the potential dimensions of the epidemic among individuals with hemophilia became clear, communication between physicians and patients was further compromised by physicians' reticence to discuss the dire implications of widespread infection with their patients and families.

Institutional barriers to patient–physician communications and relationships between relevant organizations also impeded the flow of information. If the NHF had received input from a wider group of scientific and medical experts, more explicit and systematic dissemination of a range of clinical options might well have been possible. In addition, the financial and other relationships between the NHF and the plasma fractionation industry created a conflict of interest that seriously compromised the perceived independence of NHF's recommendations.

No organization stepped forward to communicate widely the risks of blood transfusions to potential recipients. Many blood bank officials during this period publicly denied that AIDS posed any significant risk to blood recipients. In this context, and because many transfusions occurred on an emergency basis, patients were typically not apprised of the growing concerns about the contamination of the blood supply. For both individuals with hemophilia and recipients of blood transfusions, physician concern that their patients might refuse care deemed a "medical necessity" further contributed to failures to inform them of the risks.

CONCLUSIONS

Decision Making Under Uncertainty

The events and decisions that the Committee has analyzed underscore the difficulty of personal and institutional decision making when the stakes are high, when knowledge is imprecise and incomplete, and when decision makers may have personal or institutional biases.

The Committee attempted to understand the complexities of the decision-making process during this uncertain period and to develop lessons to protect the blood supply in the future. In retrospect, the system did not deal well with contemporaneous blood safety issues such as hepatitis, and was not prepared to deal with the far greater challenge of AIDS.

Although enough epidemiological evidence had emerged by January 1983 to strongly suggest that the agent causing AIDS was transmitted through blood and blood products and could be sexually transmitted to sexual partners, the magnitude of the risk for transfusion and blood product recipients was not known at this time. Policymakers quickly developed several clinical and public health options to reduce the risk of AIDS transmission. There was, however, substantial scientific uncertainty about the costs and benefits of the available options. The result was a pattern of responses which, while not in conflict with the available scientific information, were very cautious and exposed the decision makers and their organizations to a minimum of criticism.

Blood safety is a shared responsibility of many diverse organizations. They include U.S. Public Health Service agencies such as the CDC, the FDA, and the NIH, and private-sector organizations such as community blood banks and the American Red Cross, blood and plasma collection agencies, blood product manufacturers, groups like the National Hemophilia Foundation, and others. The problems the Committee found indicated a failure of leadership and inadequate institutional decision making processes in 1983 and 1984. No person or agency was able to coordinate all of the organizations sharing the public health responsibility for achieving a safe blood supply.

Bureaucratic Management of Potential Crises

Federal agencies had the primary responsibility for dealing with the national emergency posed by the AIDS epidemic. The Committee scrutinized bureaucratic function closely and came to the following conclusions about the management of potential crises.

First, unless someone from the top exerts strong leadership, legal and competitive concerns may inhibit effective action by agencies of the federal government. Similarly, when policymaking occurs against a backdrop of a great deal of scientific uncertainty, bureaucratic standard operating procedures designed for routine circumstances seem to take over unless there is a clear-cut decision-making hierarchy. An effective leader will insist upon coordinated planning and execution. Focusing efforts and responsibilities, setting timetables and agendas, and assuming accountability for expeditious action cannot be left to ordinary standard operating procedures. These actions are the responsibilities of the highest levels of the public health establishment.

Second, the FDA and other agencies in the early 1980s lacked a systematic approach to conducting advisory committee processes. These agencies should tell their advisory committees what it expects from them, keep attention focused on high priority topics, and independently evaluate their advice. Because mistakes will always be made and opportunities missed, regulatory structures must organize and manage their advisory boards to assure both the reality and the continuous appearance of propriety.

Third, agencies should not rely upon the entities they regulate for analysis of data and modeling of decision problems.

Fourth, agencies need to think far ahead. They must monitor more systematically the long-term outcomes of blood transfusion and blood product infusion to anticipate both new technologies and new threats to the safety of the blood supply. The Committee believes that the Public Health Service should plan what it will do if there is a threat to the blood supply. It should specify actions that will occur once the level of concern passes a specified threshold. The Committee favors a series of criteria or triggers for taking regulatory or other public health actions which the response is proportional to the magnitude of the risk and the quality of the information on which the risk estimate is based. Taking on small steps allows for careful reconsideration of options, particularly as information about uncertain risks unfolds. Not all triggering events need lead to drastic action; some may merely require careful reconsideration of the options or obtaining new information.

RECOMMENDATIONS

The Committee's charge was to learn from the events of the early 1980s to help the nation prepare for future threats to the blood supply. From the record assembled for this study, the Committee identified potential problems with the system in place at that time and has identified some changes that might have moderated some of the effects of the AIDS epidemic on recipients of blood and blood products. The federal and private organizations responsible for blood safety and the public health more generally will have to evaluate their current policies and procedures to see if they fully address the issues raised by these recommendations.

The Public Health Service

Several agencies necessarily play important, often differentiated, roles in managing a public health crisis such as the contamination of blood and blood products by the AIDS virus. The National Blood Policy of 1973 charged the Public Health Service (including the CDC, the FDA, and the NIH) with responsibility for protecting the nation's blood supply.

The Committee has come to believe that a failure of leadership may have delayed effective action during the period from 1982 to 1984. This failure led to less than effective donor screening, weak regulatory actions, and insufficient communication to patients about the risks of AIDS. In the event of a threat to the blood supply, the Public Health Service must, as in any public health crisis, insist upon coordinated action. The Secretary of Health and Human Services is responsible for all the agencies of the Public Health Service,[1] and therefore the Committee makes

[1] In the 1980s and now, the PHS agencies report to the Assistant Secretary of Health. As this report was being written, the Department of Health and Human Services has proposed to eliminate the office of the Assistant Secretary, so that the PHS agencies would report directly to the Secretary.

Recommendation 1: The Secretary of Health and Human Services should designate a Blood Safety Director, at the level of a deputy assistant secretary or higher, to be responsible for the federal government's efforts to maintain the safety of the nation's blood supply.

To be effective in coordinating the various agencies of the PHS, the Blood Safety Director should be at the level of a deputy assistant secretary or higher, and should not be a representative of any single PHS agency.

In considering the history of the contamination of the blood supply with HIV and the current surveillance, regulatory, and administrative structures for ensuring the safety of our nation's blood resources, the Committee became convinced that the nation needs a far more responsive and integrated process to ensure blood safety. To this end, the Committee makes

Recommendation 2: The PHS should establish a Blood Safety Council to assess current and potential future threats to the blood supply, to propose strategies for overcoming these threats, to evaluate the response of the Public Health Service to these proposals, and to monitor the implementation of these strategies. The Council should report to the Blood Safety Director (see Recommendation 1). The Council should also serve to alert scientists about the needs and opportunities for research to maximize the safety of blood and blood products. The Blood Safety Council should take the lead to ensure the education of public health officials, clinicians, and the public about the nature of threats to our nation's blood supply and the public health strategies for dealing with these threats.

The proposed Blood Safety Council would facilitate the timely transmission of information, assessment of risk, and initiation of appropriate action both during times of stability and during a crisis. The Council should report to the Blood Safety Director (see Recommendation 1). The Council would not replace the PHS agencies responsible for blood safety but would complement them by providing a forum for them to work together and with private organizations. The PHS agencies would be represented on the Council.

The Blood Safety Council should consider the following activities and issues: to deliberate the need for a system of active surveillance for adverse reactions in blood recipients; to establish a panel of experts to provide information about risks and benefits, alternative options for treatment, and recommended best practices (see Recommendation 13); and to investigate methods to make blood products safer, such as double inactivation processes and reduction of plasma pool size.

When a product or service provided for the public good has inherent risks, the common law tort system fails to protect the rightful interests of patients who suffer harms resulting from the use of those products and services. To address this deficiency, the Committee makes

Recommendation 3: The Federal government should consider establishing a no-fault compensation system for individuals who suffer adverse consequences from the use of blood or blood products.[1]

For such a no-fault system to be effective, standards and procedures would have to be determined prospectively to guide its operations. There needs to be an objective, science-based process to decide which kinds of adverse outcomes are caused by blood-borne pathogens and which individual cases of these adverse outcomes deserve compensation. As with vaccines, such a system could be financed by a tax or fee paid by all manufacturers or by the ultimate recipients of blood products. However, had there been a no-fault compensation system in the early 1980s, it could have relieved much financial hardship suffered by many who became infected with HIV through blood and blood products in the United States. The "no-fault" principles outlined in this recommendation might serve to guide policymakers as they consider whether to implement a compensation system for those infected in the 1980s.

The Centers for Disease Control and Prevention

The CDC has an indispensable role in protecting our nation's health: to detect potential public health risks and sound the alert. In order to improve CDC's efficacy in this critical role, the Committee makes

Recommendation 4: Other federal agencies must understand, support, and respond to the CDC's responsibility to serve as the nation's early warning system for threats to the health of the public.

One way to begin to implement this recommendation is for the Secretary of Health and Human Services to insist that an agency that wishes to disregard a CDC alert should support its position with evidence that meets the same standard as that used by the CDC in raising the alert.

In order to carry out its early warning responsibility effectively, the CDC needs good surveillance systems. The Committee, believing that the degree of surveillance should be proportional to the level of risk inherent in blood and blood products and should include both immediate and delayed effects, makes

Recommendation 5: The PHS should establish a surveillance system, lodged in the CDC, that will detect, monitor, and warn of adverse effects in the recipients of blood and blood products.

[1] One Committee member (Martha Derthick) abstains from this recommendation because she believes that it falls outside of the Committee's charge.

The Food and Drug Administration

The FDA has legal authority to protect the safety of the nation's blood supply, and it is the lead federal agency in regulating blood banking practice, the handling of source plasma, and the manufacture of blood products from plasma. The Committee's recommendations focus on decision making and the role of advisory committees in formulating the FDA's response to crises.

In the Committee's judgment, a more systematic approach to blood safety regulation, one that is better suited to conditions of uncertainty, is needed. In particular, the Committee recommends (see Chapter 8) that the PHS develop a series of criteria or triggers for taking regulatory or other public health actions for which the response is proportional to the magnitude of the risk and the quality of the information on which the risk estimate is based. In order that the perfect not be the enemy of the good, the Committee makes

> **Recommendation 6: Where uncertainties or countervailing public health concerns preclude completely eliminating potential risks, the FDA should encourage and where necessary require, the blood industry to implement partial solutions that have little risk of causing harm.**

In all fields, decision making under uncertainty requires an iterative process. As the knowledge base for a decision changes, the responsible agency should reexamine the facts and be prepared to change its decision. The agency should also assign specific responsibility for monitoring conditions and identifying opportunities for change. In order to implement these principles at the FDA, the Committee makes

> **Recommendation 7: The FDA should periodically review important decisions that it made when it was uncertain about the value of key decision variables.**

Although the FDA has a great deal of regulatory power over the blood products industry, the agency appears to regulate by expressing its will in subtle, understated directives. Taking this into account, the Committee makes

> **Recommendation 8: Because regulators must rely heavily on the performance of the industry to accomplish blood safety goals, the FDA must articulate its requests or requirements in forms that are understandable and implementable by regulated entities. In particular, when issuing instructions to regulated entities, the FDA should specify clearly whether it is demanding specific compliance with legal requirements or is merely providing advice for careful consideration.**

In the early 1980's, the FDA appeared too reliant upon analyses provided by industry-based members of the Blood Products Advisory Council. Thus the Committee arrived at

> Recommendation 9: The FDA should ensure that the composition of the Blood Products Advisory Committee reflects a proper balance between members who are

connected with the blood and blood products industry and members who are independent of industry.

An agency that is well-practiced in orderly decision-making procedures will be able to respond to the much greater requirements of a crisis. This consideration leads to

Recommendation 10: The FDA should tell its advisory committees what it expects from them and should independently evaluate their agendas and their performance.

Advisory committees provide scientific advice to the FDA, but they do not make regulatory decisions for the agency. The FDA's lack of independent information and an analytic capability of its own meant that it had little choice but to incorporate the advice of BPAC into its policy recommendations. To ensure the proper degree of independence between the FDA and the BPAC, the Committee makes

Recommendation 11: The PHS should develop reliable sources of the information that it needs to make decisions about the blood supply. The PHS should have its own capacity to analyze this information and to predict the effects of regulatory decisions.

Communication to Physicians and Patients

One of the crucial elements of the system for collecting blood and distributing blood products to patients is the means to convey concern about the risks inherent in blood products. In today's practice of medicine, in contrast to that of the early 1980s, patients and physicians each accept a share of responsibility for making decisions.

In instances of great uncertainty, it is crucial for patients to be fully apprised of the full range of options available and to become active participants in the consideration and evaluation of the relative risks and benefits of alternative treatments. To encourage better communication, the Committee makes

Recommendation 12: When faced with a decision in which all options carry risk, especially if the amount of risk is uncertain, physicians and patients should take extra care to discuss a wide range of options.

Given the inherent risks and uncertainties in all blood products, the public and providers of care need expert, unbiased information about the blood supply. This information includes risks and benefits, alternatives to using blood products, and recommended best practices. In order to provide the public and providers of care with information they need, the Committee makes

Recommendation 13: The Department of Health and Human Services should convene a standing expert panel to inform the providers of care and the public about

the risks associated with blood and blood products, about alternatives to using them, and about treatments that have the support of the scientific record.

One lesson of the AIDS crisis is that a well-established, orderly decision making process is important for successfully managing a crisis. This applies as much to clinical decision making as to the public health decision process addressed by earlier recommendations. As the narrative indicates, there are both public health and clinical approaches to reducing the risk of blood borne diseases. The Blood Safety Council called for in Recommendation 2 would deal primarily with risk assessment and actions in the public health domain that would reduce the chance that blood products could be vectors of infectious agents. The primary responsibility of the expert panel on best practices called for in Recommendation 13 would be to provide the clinical information that physicians and their patients need to guide their individual health care choices. To be most effective, this panel should be lodged in the Blood Safety Council (see Recommendation 2) so that both bodies can interact and coordinate their activities in order to share information about emerging risks and clinical options.

Recommendation 14: Voluntary organizations that make recommendations about using commercial products must avoid conflicts of interest, maintain independent judgment, and otherwise act so as to earn the confidence of the public and patients.

One of the difficulties with using experts to give advice is the interconnections that experts accumulate during their careers. As a result, an expert may have a history of relationships that raise concerns about whether he or she can be truly impartial when advising a course of action in a complex situation. One way to avoid these risks is to choose some panelists who are not expert in the subject of the panel's assignment but have a reputation for expertise in evaluating evidence, sound clinical judgment, and impartiality.

Financial conflicts of interest influence organizations as well as individuals. The standards for acknowledging, and in some cases avoiding, conflicts of interest are higher than they were 12 years ago. Public health officials, the medical professions, and private organizations must uphold this new, difficult standard. Failure to do so will threaten the fabric of trust that holds our society together.

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July 3, 1995
TO: Trustees
Media Contacts
FROM: Jim MacPherson
SUBJECT: FDA Purges Blood Representatives from its Advisory Committee

FDA Commissioner David Kessler today removed nearly all representatives of the blood community from the agency's Blood Products Advisory Committee. FDA officials said the action was the culmination of a nine month study on the role of "industry representatives" on the agency's advisory committees. Privately, sources admit this was a preemptive strike to deflect criticism from an Institute of Medicine (IOM) study of the agency's decisionmaking in the early 1980s on HIV and blood safety. The IOM report will be made public on July 13th. Confidential copies of the report and its recommendations were recently made available to officials of the Public Health Service, which commissioned the study, and FDA, which is part of PHS.

FDA has been criticized in recent years by Congress and hemophilia activists for the make up of BPAC and the committee members' close ties to the regulated blood community. But FDA deflected much of the criticism by stating the make up of BPAC was similar to other technical advisory committees in that it was heavily weighted toward scientists and physician-users of the regulated products. Admittedly, FDA had difficulty in applying its "industry" standard to the blood committee. For other committees industry usually means a commercial drug or device interest. But based on criticism from the IOM report, FDA apparently has extended the definition of "industry representation" to anyone who derives income from a regulated activity. Hence, the purging of the BPAC will be far deeper than any other FDA advisory committee.

We have been told that replacements for the dismissed members will be "scientists, consumers, primary care physicians, ethicists and academics." We were also told that the recent BPAC recommendations on CJD and HIV antigen testing played no part in the Commissioner's action: "It was purely coincidental."

Leaks on the purging of BPAC may stimulate media interest in the IOM report, which has been well guarded. We have been told by those that have seen the report that the blood community and commercial industry are criticized for several of the decisions made on blood safety in the early days of the AIDS epidemic. But apparently the most scathing criticism is leveled at the FDA and the National Hemophilia Foundation. The recommendations, we are told, follow closely those made by groups such as the hemophilia activist Committee of 10,000 (COTT). However, those familiar with the report said that the findings do not justify the recommendations.

The story of HIV in the blood supply is largely an old one that has been bitterly, but inconclusively, fought in the courts for nearly a decade. During the early days of the AIDS epidemic tens

of millions of lives were saved by blood transfusion. Regrettably, several thousand individuals also became infected with HIV. Those who were harmed by transfusion, understandably, want to make sure that we learn whatever lessons there are from their tragedy and make the best decisions possible for the future. It is, frankly, hard to image what additional lessons there are to be learned from the early 1980s as we now begin to approach a truly safe blood supply. Current controversies (such as CJD and HIV antigen testing) seem to revolve around theoretical risks, or those that consume high resources yet have speculative value and diminishing returns. Nevertheless, representatives of the blood community will continue to actively work with the FDA, the IOM and the public on finding the best ways to improve blood safety.

The IOM report may stimulate new media stories, increased litigation, Congressional activity and additional directives from FDA. As more new information on the report becomes available, we will make it available to you. Not knowing the specific charges or recommendations made in the report, and how the press may cover it, makes it difficult to know whether to prepare for a worst case or best case scenario. We will try to keep you informed and advise you as best we can.