

*BRIEFING PACKET*

*ADVISORY COMMITTEE ON HUMAN  
RADIATION EXPERIMENTS*

**Meeting**  
JULY 17 - 19, 1995

PHOTOCOPY  
PRESERVATION





**ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS**

1726 M STREET, N.W., SUITE 600  
WASHINGTON, D.C. 20036

**MEMORANDUM**

**TO:** Interagency Working Group Points of Contact for Review of ACHRE Final Report:

*Ellyn Weiss, Department of Energy*  
*Gordon Soper, Department of Defense*  
*Wendy Baldwin, Department of Health and Human Services*  
*Harry Holloway, National Aeronautics & Space Administration*  
*Nancy Tackett, Department of Veterans Affairs*  
*Brian Latell, Central Intelligence Agency*  
*Pat Glynn, Department of Justice*  
*T.J. Glauthier, Office of Management and Budget*  
*Phil Caplan, White House*

**CC:** Ruth Faden

**FROM:** Dan Guttman  
Jeff Kahn  
Steve Klaidman  
Anna Mastroianni

**DATE:** July 14, 1995

**RE:** Briefing Folder

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Enclosed are the following briefing materials for the July 17-19 meeting of the Advisory Committee at the Madison Hotel in Washington, DC:

- Federal Register notice
- Tentative agenda
- Prospective Recommendation on Compensation for Research Injuries (memorandum plus enclosures)



# **Federal Register**



# **Advisory Committee on Human Radiation Experiments**

**AGENCY:** Department of Energy.  
**ACTION:** Notice of open meeting.

**SUMMARY:** Under the provisions of the Federal Advisory Committee Act (Pub. L. 92-463, 86 Stat. 770), notice is hereby given of the following meeting:

## **DATES AND TIMES:**

July 17, 1995, 9:00 a.m.-5:00 p.m.

July 18, 1995, 9:00 a.m.-5:00 p.m.

July 19, 1995, 9:00 a.m.-3:30 p.m.

**PLACE:** The Madison, 15th and M Streets, N.W., Washington, D.C.

## **FOR FURTHER INFORMATION CONTACT:**

Steve Klaidman, Advisory Committee on Human Radiation Experiments, 1726 M Street, NW, Suite 800, Washington, DC 20036. Telephone: (202) 254-8795. Fax: (202) 254-9828.

## **SUPPLEMENTARY INFORMATION:**

### **Purpose of the Committee**

The Advisory Committee on Human Radiation Experiments was established by the President, Executive Order No. 12801, January 15, 1994, to provide advice and recommendations on the ethical and scientific standards applicable to human radiation experiments carried out or sponsored by the United States Government. The Advisory Committee on Human Radiation Experiments reports to the Human Radiation Intersagency Working Group, the members of which include the Secretary of Energy, the Secretary of Defense, the Secretary of Health and Human Services, the Secretary of Veterans Affairs, the Attorney General, the Administrator of the National Aeronautics and Space Administration, the Director of Central Intelligence, and the Director of the Office of Management and Budget.

## **Tentative Agenda**

**Monday, July 17, 1995**

9:00 a.m. Call to Order and Opening Remarks

9:05 a.m. Approval of Minutes

9:10 a.m. Public Comment

10:30 a.m. Discussion of Report Draft and Recommendations

12:00 p.m. Lunch

1:15 p.m. Discussion, Committee Strategy and Direction (continued)

5:00 p.m. Meeting Adjourned

**Tuesday, July 18, 1995**

9:00 a.m. Opening Remarks

9:10 a.m. Discussion of Report Draft and Recommendations

12:00 p.m. Lunch

1:15 p.m. Discussion of Report Draft and Recommendations (continued)

6:00 p.m. Meeting Adjourned

**Wednesday, July 19, 1995**

8:30 a.m. Opening Remarks

8:35 a.m. Discussion of Report Draft and Recommendations

12:00 p.m. Lunch

1:15 p.m. Discussion of Report Draft and Recommendations (continued)

3:30 p.m. Meeting Adjourned

A final agenda will be available at the meeting.

## **Public Participation**

The meeting is open to the public. The chairperson is empowered to conduct the meeting in a fashion that will facilitate the orderly conduct of business. Any member of the public who wishes to file a written statement with the Advisory Committee will be permitted to do so, either before or after the meeting. Members of the public who wish to make a five-minute oral statement should contact Steve Klaidman of the Advisory Committee at the address or telephone number listed above. Requests must be received at least five business days prior to the meeting and reasonable provisions will be made to include the presentation on the agenda.

## **Transcript**

Available for public review and copying at the office of the Advisory Committee at the address listed above between 9 a.m. and 4 p.m., Monday through Friday, except Federal holidays.

Issued at Washington, DC on June 28, 1995.

**Rachel Murphy Samuel,**

Acting Deputy Advisory Committee Management Officer.

(This document is not for distribution outside the DOE.)

EO 12812-2, 12812-3, 12812-4, 12812-5, 12812-6, 12812-7, 12812-8, 12812-9, 12812-10, 12812-11, 12812-12, 12812-13, 12812-14, 12812-15, 12812-16, 12812-17, 12812-18, 12812-19, 12812-20, 12812-21, 12812-22, 12812-23, 12812-24, 12812-25, 12812-26, 12812-27, 12812-28, 12812-29, 12812-30, 12812-31, 12812-32, 12812-33, 12812-34, 12812-35, 12812-36, 12812-37, 12812-38, 12812-39, 12812-40, 12812-41, 12812-42, 12812-43, 12812-44, 12812-45, 12812-46, 12812-47, 12812-48, 12812-49, 12812-50, 12812-51, 12812-52, 12812-53, 12812-54, 12812-55, 12812-56, 12812-57, 12812-58, 12812-59, 12812-60, 12812-61, 12812-62, 12812-63, 12812-64, 12812-65, 12812-66, 12812-67, 12812-68, 12812-69, 12812-70, 12812-71, 12812-72, 12812-73, 12812-74, 12812-75, 12812-76, 12812-77, 12812-78, 12812-79, 12812-80, 12812-81, 12812-82, 12812-83, 12812-84, 12812-85, 12812-86, 12812-87, 12812-88, 12812-89, 12812-90, 12812-91, 12812-92, 12812-93, 12812-94, 12812-95, 12812-96, 12812-97, 12812-98, 12812-99, 12812-100.



## **Tentative Agenda**

# ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS

## PUBLIC MEETING

JULY 17-19, 1995

Madison Hotel ❖ Executive Chambers ❖ 15th & M Street, N.W. ❖ Washington, DC

### TENTATIVE AGENDA

#### Monday, July 17, 1995

- 9:00 AM Call to Order
- Opening Remarks  
*Ruth Faden, Chair*
- 9:10 Public Comment
- 10:15 Break
- 10:30 Committee Discussion: [Part I and II chapters to be determined by the Committee]
- 12:00 Lunch
- 1:15 Committee Discussion: [Part I and II chapters to be determined by the Committee]
- 2:15 Committee Discussion: Findings (1944-74) [Part IV, Chapter 18]
- 4:00 Break
- 4:30 Committee Discussion: Recommendations for Remedies for Former Subjects [Part IV, Chapter 19]
- 6:00 Meeting Adjourned

#### Tuesday, July 18, 1995

- 9:00 AM Committee Discussion: Recommendations for the Remedies of Former Subjects [Part IV, Chapter 19]
- 10:45 Break
- 11:00 Committee Discussion: Research Proposal Review Project [Part III, Chapter 15]
- 11:45 Committee Discussion: Subject Interview Study [Part III, Chapter 16]
- 12:30 PM Lunch



1:45 Committee Discussion: Contemporary Projects--An Ethical Analysis [Part III, Chapter 17] Findings for the Contemporary Period [Part IV, Chapter 19]

3:30 Committee Discussion: Recommendations for the Protection of the Rights and Interests of Human Subjects [Part IV, Chapter 19]

4:00 Break

4:30 Committee Discussion: Recommendations for the Protection of the Rights and Interests of Human Subjects [Part IV, Chapter 19] (continued)

6:00 Meeting Adjourned

**Wednesday, July 19, 1995**

8:30 AM Approval of Minutes of June 21-23, 1995 Meeting

8:35 Committee Discussion: Strategy and Direction and Sign off of Final Report

9:30 Committee Discussion: Findings--Contemporary Intentional Releases [Part IV, Chapter 18]

Committee Discussion: Recommendations for Balancing National Security Interests and the Rights of the Public [Part IV, Chapter 19]

10:45 Break

11:00 Committee Discussion: Recommendations on Openness [Part IV, Chapter 19]

12:15 PM Lunch

1:30 Committee Discussion: Executive Summary

3:30 Meeting Adjourned

**Prospective Recommendation on  
Compensation for Research Injuries  
(memorandum plus enclosures)**



## MEMORANDUM

**TO:** Members of the Advisory Committee on Human Radiation Experiments

**FROM:** Advisory Committee Staff

**DATE:** July 6, 1995

**RE:** Prospective Recommendation on Compensation for Research Injuries

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At the June meeting, some Committee members suggested that the Committee provide additional support for its recommendation that the federal government review the area of compensation for research injuries of future research subjects (Recommendation 13a, chapter 19, draft date June 9). It was suggested that the Committee indicate that some or all of its members are in agreement with the recommendations and conclusions of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, a group that studied this issue in detail in 1982. Many of you are familiar with the President's Commission two-volume report, Compensating for Research Injuries: The Ethical and Legal Implications of Programs to Redress Injured Subjects. To refresh your memory, and to provide those who are not familiar with it with an opportunity to review it, we have enclosed volume one of the report, which includes a summary. (A table of contents for volume two is also attached. Please contact Tracy Smith if you would like a copy of the 509 page appendix as well.)

We recommend that you review this report and then indicate on the attached "ballot" whether you agree with Commission's conclusions and recommendations. Depending on the response, a sentence will be added either to the body of the recommendation or to the explanatory note, e.g., the Committee is [or some or a substantial number of Committee members are] in agreement with the conclusions and recommendations of the President's Commission supporting the review and evaluation of various alternative compensation schemes by the federal government.

For additional background reading, we have provided you with a relevant excerpt from a recent report of an Institute of Medicine committee titled Women and Health Research (National Academy Press, 1994). As noted in a footnote to the Advisory Committee draft recommendation, the Institute of Medicine recommended that the National Institutes of Health review the area of compensation for research injury.

We have attached a "ballot" for you to return by the first day of the meeting (July 17) indicating whether you are willing to indicate your support of the President's Commission conclusions and recommendations.

If you have any questions about any of this material, please contact Anna Mastroianni.

### Enclosures:

"Ballot" for faxing

President's Commission for the Study of Ethical Problems in Medicine and Biomedical Research, Compensating for Research Injuries: The Ethical and Legal Implications of Programs to Redress Injured Subjects, June 1982, Volume I; and Table of Contents, Volume II, Appendices.

Women and Health Research, National Academy Press, 1994, p. 169 and Appendix D.

**"Ballot" for faxing**



## **Compensation Recommendation**

Please fax (202/254-9827) or return to Tracy Smith and Anna Mastroianni by July 17. (Please check one.)

Name: \_\_\_\_\_

☐

I would like to be noted as agreeing with the conclusions and recommendations of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical Research, Compensating for Research Injuries: The Ethical and Legal Implications of Programs to Redress Injured Subjects, June 1982.

☐

I would not like to be noted as agreeing with the conclusions and recommendations of the President's Commission.

**President's Commission for the Study of  
Ethical Problems in Medicine and  
Biomedical Research, Compensating for  
Research Injuries: The Ethical and Legal  
Implications of Programs to Redress Injured  
Subjects, June 1982, Volume I**



FB83-236794

**Compensating for Research Injuries  
The Ethical and Legal Implications of  
Programs to Redress Injured Subjects  
Volume 1. Report**

**(U.S.) President's Commission for the Study of  
Ethical Problems in Medicine and Biomedical and  
Behavioral Research, Washington, DC**

**Jun 82**



**U.S. Department of Commerce  
National Technical Information Service  
NTIS**

## BIBLIOGRAPHIC INFORMATION

PB83-236794

Compensating for Research Injuries: The Ethical and Legal Implications of Programs to Redress Injured Subjects. Volume 1. Report.

Jun 82

PERFORMER: President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, Washington, DC.

See also Volume 2, PB83-236802. Also available in set of 2 reports PC\$16.00, PB83-236786 and in set of 15 reports PC\$115.00, PB83-236695.

The suggestion of compensation for research injuries has been a mainstay of ethical and public-policy discussions of research with human subjects for many years. The failure to resolve the issue exposes the entire research enterprise to the public recriminations that could follow from one or a series of serious, uncompensated injuries to subjects. The importance of biomedical and behavioral research for this country is manifested in the many billions of dollars that such research receives each year in an attempt to conquer disease and to relieve human suffering. The formal ethical standards and individual consciences of investigators, as well as Federal rules and guidelines developed in the past two decades, have done much to protect research subjects and to reduce the risk of injury to them. Some risk remains nevertheless--risk that though statistically small may manifest itself in serious ways for individuals. A social policy experiment is needed to see whether compensation programs might provide a feasible means further to reduce the risk of unremedied injury to, ....

KEYWORDS: \*Workmens compensation, \*Injuries, \*Research projects.

Available from the National Technical Information Service, Springfield, Va. 22161

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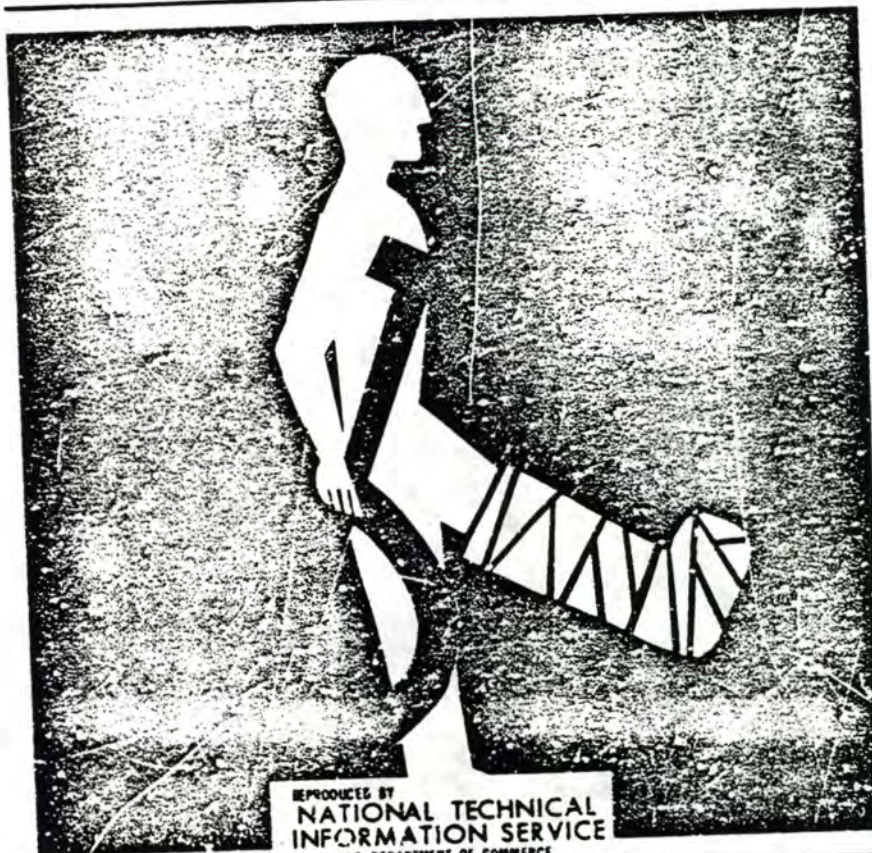


PB33-236794

# Compensating for Research Injuries

The Ethical and  
Legal Implications of  
Programs to Redress  
Injured Subjects

Volume One: Report



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President's Commission for the Study of  
Ethical Problems in Medicine and  
Biomedical and Behavioral Research

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# **Compensating for Research Injuries**

**A Report on the Ethical  
and Legal Implications  
of Programs to Redress  
Injuries Caused by  
Biomedical and Behavioral  
Research**

**Volume One: Report**

**June 1982**

**President's Commission for the Study of  
Ethical Problems in Medicine and  
Biomedical and Behavioral Research**



# President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research

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\*Sworn in February 11, 1982.  
†Sworn in March 12, 1982.

†Term expired February 11, 1982.

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President's Commission for the Study of Ethical Problems  
in Medicine and Biomedical and Behavioral Research  
Room 555, 2000 K Street, N.W., Washington, D.C. 20006 (202) 693-6031

June 11, 1987

The President  
The White House  
Washington, D.C. 20500

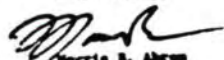
Dear Mr. President:

On behalf of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, I am pleased to transmit our Report on Compensating for Research Injuries. This study was undertaken at the request of the Department of Health and Human Services (HHS), although the concern that it addresses extends to agencies throughout the Federal government which conduct or support research with human subjects. In light of the Commission's earlier recommendation (conveyed in December 1981 in our first Biennial Report on Protecting Human Subjects) that HHS officially assume the role of lead agency in this field, we believe that HHS should be responsible for acting on the recommendations presented in the enclosed report. Other Federal entities can then benefit from the experience of HHS.

Several Federal panels have previously recommended the establishment of a governmental program of compensation for injured research subjects. Although the Commission concludes that redress should be made for many such injuries, it recommends that no program be instituted at this time. Instead it would seem advisable for HHS to conduct a small, controlled experiment to determine whether a formal program is needed and, if so, the most fair and efficient means of providing compensation.

The Commission is pleased to have had an opportunity to assist in the resolution of this important topic.

Respectfully,

  
Morris S. Abram  
Chairman

Copies to: Honorable George Bush  
Honorable Thomas F. O'Neill, Jr.



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**How Did This  
Issue Arise?**

**I**

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## Introduction to the Social and Cultural Setting

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The power of medicine to cure and to prevent illnesses has increased enormously during the present century. All those having access to medical care have been the beneficiaries. Advancements in preventive measures and therapeutic techniques have reduced the threat of early death and crippling disability. The result has been a significant improvement in the quality as well as the quantity of life.

An outstanding feature of contemporary medicine is its commitment to research and to the scientific application of research findings. Exploration and experimentation distinguish the new, more effective therapeutics from the old more than any other factor. Indeed, one of modern science's most visible and humanly significant contributions is the progress of medicine in the past half century. The social benefits of medical research have been enormous, and its value is reaffirmed with each successful act of treatment or prevention.

The ratio of benefits to costs in medical experimentation has been remarkably favorable. This has been true not only of the dollar costs of laboratories and the like but also of the human costs sustained as research-related injuries. At the same time, however, these human costs must not be disregarded. New techniques, unless they are adopted blindly, must be tested, and testing in turn requires not only laboratory and animal studies but also the use with human subjects of uncertain methods whose range of effects cannot be predicted precisely in advance. Risk is thus inherent in medical research, no matter how conscientious the investigator and careful the research. Quite obviously not all experimental drugs and techniques prove to be more successful than other existing treatments; and many experiments are performed on healthy volunteers who need no treatment in the first place. Even when a new treatment proves to be a relative success, the initial

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experiments may reveal that certain patients cannot benefit or may be especially susceptible to toxic side effects.

These untoward results of medical experimentation occur far less frequently than do the benefits, but to those who are affected they can be real and serious. Research-related injuries are harms<sup>1</sup> that occur as a nearly unavoidable result of an enterprise undertaken for social benefit. Those who receive the benefits—and this includes nearly all members of society—recognize a responsibility for collective support if the research enterprise is to be successful, as is attested by the magnitude of funding for biomedical research from governmental bodies and charitable contributions. Naturally, that responsibility would seem to extend to the human costs of the research enterprise. The chapters which follow address the question: What is a fair system of fulfilling that responsibility? The issue is approached through consideration of the need for a program, the ethical arguments for and against, and the formulation of possible proposals and recommendation of a social policy experiment to test out alternative policies.

The balance of this chapter attempts to sketch the social and cultural setting of the problem of research-related injuries. The cultural ethos colors one's appreciation of the facts specifically relevant to the issue. Furthermore, the problem of research injuries is not *sui generis*. It is but one instance of a much larger set of issues with which American society is presently grappling, that of the risks imposed by technological progress. For example, large-scale enterprises such as energy production and mass immunization, while conducted largely for the social good, put certain individuals at special risk. The plight of those, relatively few in number, who actually sustain injury is made vivid by the communications media and presents the nation with questions of conscience: Who is responsible for the welfare of these people? What are they owed, and by whom? Why were they put at risk, and should steps be taken to ensure that there will be no more victims? Our policy on research injuries will inevitably reflect the development of any public consensus on these wider problems of risk. In turn, the policy on research injuries could conceivably influence the course of the larger debate and raises questions of "horizontal equity" in redressing injuries of one type but not of others.

<sup>1</sup> The terms *injury* and *harm* have distinct meaning in the law; the former connotes wrongfulness or the occurrence of something for which a plaintiff can seek redress. Ordinary discourse does not make so clear a distinction, however. In this Report, the terms are used synonymously to mean damage regardless of wrongfulness, fault, or responsibility. Since, in common parlance, the concern of the Report is with *injured research subjects*, *injury* will be the term used in most instances.

To explore the wider context in which the problem of compensation of injured research subjects arises, this chapter first considers the place of the research enterprise in society, that of the volunteer subject, and differing conceptions of the relationship between them. The varied, often inchoate, images of research and its subjects greatly complicate the task at hand. In the next section, the Commission examines another factor that complicates thinking about compensation—social attitudes toward risk and toward spreading the risks beyond those whom they touch directly. The chapter concludes by considering a number of basic social issues that underlie the debate over research injury.

### **Roles and Relationships in Human Experimentation**

**The Role of Biomedical and Behavioral Research.** Since World War II, the magnitude of biomedical and behavioral research in the United States has increased tremendously, as has the Federal government's participation. By 1960, health research had become an \$8-billion-a-year enterprise, with over half the funding coming from the Federal government,<sup>2</sup> through the National Institutes of Health and over twenty other agencies; furthermore, a large proportion of the privately sponsored research on drugs, medical devices, other consumer products and pesticides is conducted pursuant to extensive Federal regulation, although not supported by public funds.

The centrality of research in medicine, particularly in American society in recent decades, makes it easy to forget that the role of the professional clinical investigator and the institutionalization of clinical research are historically recent, 20th century developments. Nevertheless, over the past fifty years and particularly since World War II, certain changes are discernible in the settings and modes of organization of biomedical and behavioral research. A progressive shift has occurred from the type of small, collegial, personally directed units such as those depicted in the 1950s by Means and Fox<sup>3</sup> to massive, sprawling institutions which often dominate the academic environments they inhabit or which are conducted under industrial and governmental control.

Americans generally share the benefits of enhanced understanding of human physiology and advances in therapy. Similarly, although contributions to the public purse are not strictly proportionate, it is the citizenry as a whole that sponsors publicly supported research. Research, then, is an

<sup>2</sup> National Institutes of Health, BASIC DATA RELATING TO THE NATIONAL INSTITUTES OF HEALTH - 1960, U.S. Government Printing Office, Washington (1960), Figures 1 and 2, Tables 1-3.

<sup>3</sup> J.H. Means, *WARD 4*, Harvard University Press, Cambridge, Mass. (1958); René C. Fox, *EXPERIMENT PERILOUS*, The Free Press, Glencoe, Ill. (1959).



enterprise that is collectively sponsored and responsive to the collective good.

The widespread enthusiasm shown in recent decades for medical research can be at least partly explained by one single fact: all of us are threatened by disease and disability. The risks of nature affect everyone, rich or poor, black or white, male or female (though some risks are higher for less-advantaged groups). Research offers the promise of reducing some of these risks. Research can also help to reduce some of the risks imposed by health care itself, for a significant amount of clinical research is designed to test the safety and efficacy of currently accepted medical practices. For example, two clinical trials which spawned widely publicized litigation by injured subjects—the University of Chicago study of the use of diethylstilbestrol (DES) during pregnancy to prevent miscarriage, and the multi-center clinical trial with premature infants examining the relationship of oxygen therapy to the incidence of blindness resulting from retrolental fibroplasia—provided the scientific basis for rejecting or modifying those therapies. Were such research never conducted, these therapies might still be employed in general medical practice.<sup>4</sup> Thus, acceptance of controlled risks in clinical research can, and regularly does, result in knowledge which reduces the “risks of everyday life,” including those risks associated with standard medical care, for all members of the society.<sup>5</sup>

Increased freedom from risks is, then, one promise of research. But there is no easy path toward this goal. Scientists must test out hypotheses, and they must sometimes use human beings—meaning their own bodies or others’—as a laboratory to understand normal physiology as well as abnormal conditions, and to fill in important gaps in knowledge about the efficacy and safety of new medical interventions. Thus, in its pursuit of preventive, diagnostic, and therapeutic interventions which are intended to *reduce* the risks caused both by nature and by human activities, research *imposes* other risks. These

<sup>4</sup> Some of the most important evidence about the effects of DES come from a controlled experiment at the University of Chicago in the early 1950s. Three of the women involved in this experiment are now suing the university for having put them at the risk. The university and others will be more careful in the future, thus increasing the risk that new cancer sources will go undetected. Meanwhile the fear of lawsuits is making doctors and hospitals reluctant to help track down DES daughters, thus increasing the risks that some of them will get cancer that isn't caught in time.

Michael Kinaley, *Fate and Lawsuits*, 182 THE NEW REPUBLIC 20, 25 (June 14, 1970).

<sup>5</sup> In *novum*, these facts, the Commission expresses no judgments on the ethical or legal questions, including those of informed consent, raised in ongoing or recently concluded litigation.

risks of research are borne by only a tiny fraction of the number of persons who face the risks of disease and disability that research is designed to combat. More importantly, the manifestation of these research risks as actual injuries is *not* spread evenly over the entire population; they occur for an unfortunate few among those who serve as subjects.

**The Role of the Research Subject.** One's thinking on the question of compensation for research injuries is directly affected by the way in which one conceives of the subject's role. Two experts on these matters contend that "[p]art of the difficulties that have surrounded legal and policy efforts to deal with the issue of compensating persons for research-related injuries...reside in our lack of understanding about the development, social roles and attributes of clinical research and its participants."<sup>6</sup>

Research subjects may be popularly clothed with certain images—for example, those of *hero*, of *victim*, and of *employee* or *contractor*—and each of these images colors our conclusions about the character, moral status, and claims of the research subject. The appropriateness of providing compensation for research-related injury varies with the definition of the subject's role. For the hero, the wellsprings of public gratitude are overflowing; witness the donation of funds to provide \$800,000 of accident insurance for the astronauts on the space shuttle. The claim of the victim is different, but also powerful: disclosure of the Tuskegee abuses resulted, finally, in the provision of compensation by the Federal government.<sup>7</sup> And for an employee or contractor, compensation may be a matter regarded as a proper subject of negotiation.

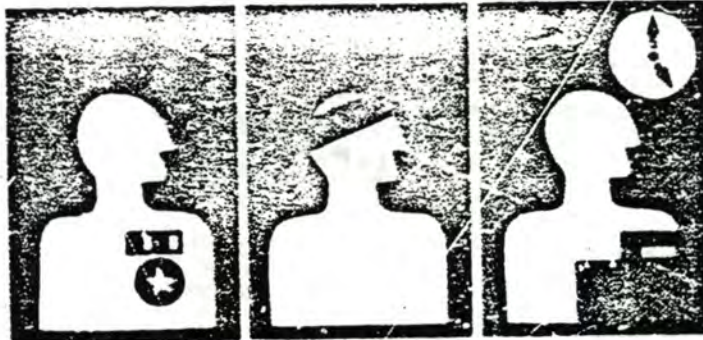
The category into which research subjects are placed also has a bearing on the importance and significance attached to the research subject's informed consent. The consent of a hero is not an issue; heroism results from spontaneous action or deliberate "volunteering." The notion of victim, however, has quite different resonances; the victim is often passive, and formal consent—if any has even been obtained—may be viewed as uninformed or the result of duress. Consent is most compatible with the image of research subject as employee or

<sup>6</sup> Judith P. Swazey and Leonard H. Glantz, *A Social Perspective on Compensation for Injured Research Subjects* (1981); see Appendix A to this Report. Major portions of this chapter are based upon this paper, which develops themes which emerged at a meeting of consultants with several members of the Commission's staff on November 25, 1981. In addition to Dr. Swazey of Medicine in the Public Interest and Professor Glantz of Boston University the participants included Commissioner Renée C. Fox, and Professors Roy Lubove of the University of Pittsburgh, Barbara Rosenkrantz of Harvard University, and Stephen Toulmin of the University of Chicago.

<sup>7</sup> James H. Jones, *BAD BLOOD*, Free Press, New York (1981) at 217-19.



contractor. Although questions may arise about the relative freedom and negotiating power of an employee compared with



those of the person or firm offering employment, voluntary agreement of all parties is the essence of the relationship.

Finally, the different images of the research subject connote quite different views of intent and of moral status. To the hero is ascribed the intention to help; his or her intent is seen as beyond the ordinary call of duty and thus the appropriate object of praise and respect. The victim, on the other hand, does not merit moral esteem but rather is seen as an object of others' sympathy (and, perhaps, of guilt). The case of the employee or contractor tends toward moral neutrality, with attention being directed more toward the fairness of the bargaining process than to any particular outcome.

Societal views of research subjects appear to be ambivalent and shifting. It is notable that in the period through the 1940s, the most common image in the press and in literature was that of the research subject as hero or as selfless societal benefactor. Patients who also served as subjects, the physician-investigators who carried on medicine's long tradition of self-experimentation, and the normal (healthy) persons who volunteered to contract malaria, inhale new nerve gases, be injected with curare, and so forth, were recognized, valued and often celebrated for giving of themselves to advance medical knowledge and technique. The Walter Reed Society, composed of some 500 persons who had volunteered for high-risk experiments, embodied a view of research subjects as identifiable, often heroic societal benefactors.\*

Beginning with the revelations at Nuremberg of barbaric medical "experiments" by the Nazis and increasingly over the following decades, a second image—that of the victim—came to influence the way research subjects were perceived. Public

\* B. Davidson, *So He Took the Cobra Venom and Shot It Into His Arm*, *COLLIER'S*, 52-55 (Nov. 1, 1952).

revelations about the research projects associated with the names Tuskegee,<sup>9</sup> Willowbrook,<sup>10</sup> and the Brooklyn Jewish Chronic Disease Hospital,<sup>11</sup> focused renewed public attention on the possible abuses of the rights and welfare of subjects in the name of research. The importance of research, and the necessity and value of the research subject, continued to be affirmed. The horror stories were generally felt to be the unusual instances rather than the tip of an iceberg of "mal-research." Nonetheless, new protections for research subjects were put in place, designed to ensure that subjects participated voluntarily and that no unnecessary risks were imposed—in short, to prevent future research subjects from becoming "victims."<sup>12</sup>

The growth of the clinical research enterprise during the 1960s and 1970s helped to shape another image of the research subject, one that seems to have increasing prominence today. As research increased in volume, especially with the growth of large controlled clinical trials, the role of the research subject became more routinized and less visible. For many in the society, research subjects became less readily identifiable, either as heroes or victims. A few research institutions now hire people as subjects quite in the manner of an ordinary job,<sup>13</sup> complete with negotiations over salary and benefits, and coverage under an insurance plan similar to workers' compensation. Moreover, a "consent form" is often viewed as a contract between a subject and an investigator.

The question of how subjects ought to be viewed may have no satisfactory answer, simply because none of the images sketched here fit all subjects or fit any subjects uniquely. Indeed, the difficulty of choosing between these and other images probably accounts for some of the difficulty encountered by this Commission and by other groups in deciding whether the prospective subject's informed consent should be taken as relieving researchers and their sponsors of responsibility for the injuries which may result. The arguments and programs set forth in this Report try to take into account the several images of research subjects and the probability that there may be some truth in each.

**The Relationship of Subjects to the Research Enterprise.**  
The relationship of the various parties to the research enter-

<sup>9</sup> Tuskegee Syphilis Study Ad Hoc Advisory Panel, FINAL REPORT, U.S. Department of Health, Education, and Welfare, Washington (1973).

<sup>10</sup> Jay Katz, with assistance of A.M. Capron and E.S. Glass, EXPERIMENTATION WITH HUMAN BEINGS, Russell Sage Foundation, New York (1972) at 1007-1010.

<sup>11</sup> *Id.* at 9-65; Hyman v. Jewish Chronic Disease Hospital 15 N.Y. 2d 317, 205 N.E. 2d 338 (1965).

<sup>12</sup> John A. Robertson, *The Law of Institutional Review Boards*, 28 U.C.L.A. L. Rev. 434 (1978).

<sup>13</sup> See, e.g., pp. 53-56 *infra*.



prise may also be viewed in different ways. For example, the relationship of investigator to subject may be assimilated, perhaps unconsciously, into the physician-patient relationship. Indeed, many investigators are physicians, and many subjects are patients—although many also are not. Physicians, in any case, are thought to have important obligations to their patients including, significantly, "*primum non nocere*." Seen in this light, a physician could have violated the patient-subject's rights if injury occurred without the expectation of a sufficient therapeutic benefit; compensation could conceivably then be in order simply as a form of reparation.

These obligations and rights do not obtain, however, if the investigator is instead conceived of as one party who wishes to contract for the services of another (or the use of that person's body). But if the relationship is to be understood in the latter way, it becomes essential to take into account differences in power between subjects and research institutions. Research subjects may be sick or poor and are not organized into unions or lobby groups. Subjects tend to be engaged in their "work" for relatively short periods of time. They are simply not situated to form a cohesive constituency to demand protection on a collective basis, the way other groups of workers have during the past century. Research facilities are usually large, imposing, and staffed by professionals of high social status. Indeed, research subjects at the National Institutes of Health or military hospitals face the power and authority of the government itself. Because of the inherent inequality of such relationships, the various parties to the research enterprise are not necessarily free and equal agents involved in a situation equivalent to ordinary negotiations for mutual benefit.

**The Relationship of Subjects to the Beneficiaries of Research.** The relation of research subject to investigator and to research institution is not, however, the only one requiring attention. Also of importance is the relationship between subjects and the beneficiaries of research. Once again, the significance of this relationship may be understood in several very different ways. It has been suggested, for example, that the use of human subjects in research be viewed as an instance of "gift exchange," characterized by three norms: to give, to receive and to repay.<sup>14</sup> On this view, the subject *gives* by participating in research and, especially, by accepting the risk of injury; and a social disequilibrium results if injury occurs unless that gift is *repaid* in the form of compensation by the government, acting as agent of the beneficiaries in society. A contrasting view, however, would regard compensation as a means of limiting the size of the gift bestowed by the research subject; but this might violate an obligation of society to

<sup>14</sup> M. Mauss, *THE GIFT: FORMS AND FUNCTIONS OF EXCHANGES IN ARCHAIC SOCIETIES*, L. Cunnison (trans.), The Free Press, Glencoe, Ill. (1954).



receive the gifts that the volunteer subject wishes to bestow. That an obligation to provide at least emergency medical care for injured subjects is felt is evident from the fact that such care is generally provided.<sup>15</sup> A feeling of gratitude toward those who have bestowed gifts may be part of the explanation for this ad hoc compensation.

### Risk (and Risk-Spreading) as a Social Problem

The manifestation of risk in the form of injury, disability and death is a part not only of research but also of life itself. At times we seem to face risk head on and even welcome the challenge it represents; at other times it threatens to overwhelm us with its seemingly uncontrollable manifestations. The means used to prevent and to spread risk have developed piece by piece and are not wholly consistent; they are evolving today under increasingly close scrutiny.

At one time in history, injuries could be clearly divided into two groups, those caused by a human agency and those attributed to "fate." For the former, redress could be sought through the law (criminal as well as tort law), provided that the person responsible could be identified, as was usually the case. For the latter, the expected response was uncomplaining acceptance of this personal working out of the grand scheme of things—or, perhaps, a search for the personal fault that might explain an "act of God." The world then may not have been a better place to live, but it was surely simpler.

Neither the old paradigms of injury nor the responses they engendered seem to work well today. In particular, tort litigation is in many ways ill suited to assigning responsibility for a large portion of modern injuries. The individual nature of tort cases—often employing a jury—works well when a determination of personal wrongdoing is needed, both to

<sup>15</sup> See Chapter 3 *infra*.



assess the amount the defendant must pay to make the plaintiff whole and also to declare the community's standard of conduct as a warning to individuals in the future. But many injuries arise today which do not seem to have been caused directly by a single individual: numerous separate actions, some by institutions rather than individuals, often widely separated in time and space from the injury, must coincide for an injury to occur. The instrumentalities of harm are like the boy in the rhyme who "shot an arrow in the air, it fell to earth [he] knew not where." The chain of causation and responsibility may become so tangled as to preclude anything other than an arbitrary assignment of liability on the parties seen as best able to bear the costs. Although the growth of nonfault liability in several areas (most notably, for injuries caused by consumer products) has removed the additional burden of trying the issue of negligence, the complex problems of causation still remain.

The collapse of the second part of the ancient paradigm of risk—the uncomplaining acceptance of a divinely ordained fate—is well illustrated in the recent litigation over risks of cancer allegedly imposed by use of DES. It is well nigh impossible for an individual plaintiff in a DES case to prove that *her* vaginal cancer resulted biologically from her mother's having been given DES while the plaintiff was *in utero*. Instead, causation is established as a statistical matter, by showing that it is more probable than not that the injury came from the administration of DES.

To women with other forms of cancer, the compensation of the DES daughters, rather than seeming a great triumph, may appear instead a failure of science and society to establish the cause of *their own* grievous harm and to provide compensation. It does not matter that for many (perhaps even for most), there is no single "cause," in the legal sense of the word as employed in the DES litigation, but rather a coincidence of factors from genes to workplace environment, from health care to personal habits. What matters is that redress is available to some, while others are told that it is just fate. Yet, as a commentator recently pointed out, it is nonsensical to rule that cancer is a matter of fate only insofar as its cause is unknown.<sup>18</sup>

Any attempt to spread *some* risks has the danger of seeming unfair for failing to spread *all* risks. Risks in the biomedical sphere have posed special problems of late for the existing means of cost-allocation. Although partiality is, thus, always a danger, there may be reasons for special attention to providing compensation for research injuries. While one must take care not to oversentimentalize the investigator-subject relationship, one need not reject legitimate opportunities to

<sup>18</sup> Michael Kinsley, *Fate and Lawsuits*, 182 THE NEW REPUBLIC 20 (June 14, 1980).

support its positive, moral attributes. From this perspective, a compensation program based on human need rather than fault, and enlisting investigators as proponents of the claims of injured subjects rather than as adversaries in a courtroom battle, takes on an additional social meaning, a meaning specially suited to the nature of the investigator-subject relationship and their joint venture into the unknown. In this respect, a program for nonfault compensation diverges sharply from the existing medical malpractice framework, with its insidious effects on the doctor-patient relationship.

The Commission notes that policymakers in the United States are not alone in considering this problem. In Sweden, insurance coverage has been available since 1975 to provide compensation to subjects injured as a result of participation in biomedical research.<sup>17</sup> Similarly, accident insurance has been available at the University of Leiden (The Netherlands) since 1976 for medical research projects determined by the Committee on Medical Ethics to warrant such coverage.<sup>18</sup> In March 1978, a Royal Commission (the "Pearson Commission") reported to the British Parliament its recommendation that "any volunteer for medical research or clinical trials who suffers severe damage as a result should have a cause of action, on the basis of strict liability, against the authority to whom he has consented to make himself available."<sup>19</sup> Finally, in 1980, a World Health Organization working group to develop international guidelines for human experimentation concluded that "natural justice demands that every subject participating in medical research should have automatic entitlement to reasonable and expeditious compensation for any injury sustained as a result of participation."<sup>20</sup> Proposed guidelines reflecting that conclusion are under consideration by the World Health Organization and the Council for International Organizations of Medical Sciences.

### Research Injuries and the Larger Social Context

Concerns about compensating injured research subjects reflect an ambivalence in individual and social views regarding research and risk. On the one hand, there is a general understanding and acceptance in this society that research is a

<sup>17</sup> Harry Boström, *On the Compensation for Injured Research Subjects in Sweden* (1980); see Appendix K to this Report.

<sup>18</sup> E.L. Nouch, *Materials Concerning Compensation of Subjects Injured in Research at the University of Leiden, The Netherlands* (1980); see Appendix L to this Report.

<sup>19</sup> Royal Commission on Civil Liability and Compensation for Personal Injury, *REPORT*, Her Majesty's Stationery Office, London (1978), Vol. 1 at 286.

<sup>20</sup> John F. Dunne, *Proposed International Ethical Guidelines for Human Experimentation*, XIVth CIOMS Round Table Conference, Session 1 (Medical Ethics and Medical Education), Mexico City (1980).



social good which provides us with beneficial knowledge and techniques. On the other hand, investigations by Executive and Congressional bodies and the advent of public regulations for protection of human subjects manifest the increasingly widespread concern about the motives of researchers, the consequences of research, and the use of human beings as experimental objects.

Compensation of injured research subjects is but one of several interrelated social responses to these tensions. In recent decades, much emphasis has been placed on the informed consent of research subjects and on the regulation, and limitation, of risks incurred in research. Compensation provides a third element, complementing these first two when injuries occur in even well-designed, carefully conducted research on informed and consenting subjects. (These themes are explored more fully in the next chapter.)

But just as compensation is only one facet of the social, ethical, and legal concerns about the conduct of research with human subjects, so the concern with the protection of human subjects, in turn, has been generated and responded to in relationship to broader societal concerns. Human experimentation has both reflected these broader concerns and helped to foster them. This linkage is particularly evident with respect to three closely related aspects of contemporary American society. First, one finds today an enhanced concern with victims—real, imagined, or potential—of all kinds.<sup>21</sup> Second, there is a new awareness of the inequality of some groups' bargaining power.<sup>22</sup> Third, populist doubt and suspicion about "big" and "powerful" institutions such as government, medicine, and science has been renewed and extended to the authority and power vested in "experts" of all kinds.<sup>23</sup>

These social trends, coupled with a new assertiveness by members of groups who have suffered from unequal and unfair treatment in the past and who now insist that their rights be recognized, have forced Americans to reexamine, and to act upon, their standards of personal, institutional, and governmental responsibilities. The social movements of recent years have clearly had an impact on thinking about the rights of

<sup>21</sup> See, e.g., Marshall S. Shapo, *A NATION OF GUINEA PIGS: THE UNKNOWN RISKS OF CHEMICAL TECHNOLOGY*, Free Press, New York (1979); *Proposed Amendments to Title 28 of the U.S. Code: Hearings on Radiation Compensation (S.1483) Before the Senate Committee on Labor and Human Resources*, 97th Cong., 1st Sess. (Oct. 27, 1981); Joe Hurlson and Burt Galaway (eds.), *CONSIDERING THE VICTIM*, Charles C. Thomas, Springfield, Mass. (1975).

<sup>22</sup> See Swazey & Glantz, *supra* note 6 at 10; 15 U.S.C. §57 a(b), 1975 Magnuson-Moss FTC Improvement Act (expense reimbursement to permit public participation in rulemaking).

<sup>23</sup> Loren R. Graham, *Concerns about Science and Attempts to Regulate Inquiry* 107 *DAEDALUS* 1 (1978).

research subjects; they cause one to rethink the treatment of, and responsibilities toward, members of this class of persons.

Correlatively, abuses suffered by a few research subjects have themselves contributed to this wider social questioning. The confluence of concerns with victims, unequal bargaining power, and powerful institutions is strikingly illustrated by apprehensions about the ways researchers and research agencies, including the Federal government, can mislead, exploit, or injure subjects in the name of patient welfare, scientific progress, or public good. To the earlier reports of projects at Willowbrook and Tuskegee have recently been added revelations of the experiments with psychotropic drugs sponsored by the CIA and the Defense Department's biological warfare testing accidents at the Dugway Proving Ground.<sup>24</sup> All have been lightning rods for attracting attention to problems in governing research and in testing human subjects with fairness and due concern.

The research injuries with which this Report is concerned are not primarily those that result from unethical practices on the part of investigators. Most of the examples receiving current attention are actually old experiments, recently come to light or the subject of contemporary reexamination.<sup>25</sup> The focus of this Report is on harms resulting from risks of relatively low frequency and severity, visited on subjects of well-planned, carefully conducted, ethical research. It must be recognized, however, that social attitudes toward the compensation of those harmed in ethical research will be colored by public perception of the plight of those injured through abuse. Risk and injury are common to both kinds of research, and these will likely be the chief subject of moral concern. The centrality of risk in the conduct of research is testified to by the development of a new lexicon—necessary risk, acceptable risk, risk acceptance, danger-of-danger, risk-of-risk, uncertainty-of-uncertainty—and in the emergence of a new occupational category of institutional "risk managers."

<sup>24</sup> *Biomedical and Behavioral Research: Human-Use Experimentation Programs of the Department of Defense and Central Intelligence Agency: Hearings on S. 2515 Before the Subcommittee on Health of the Senate Committee on Labor and Public Welfare and the Subcommittee on Administrative Practice and Procedure of the Senate Judiciary Committee, 94th Congress, 1st Session (1975).*

<sup>25</sup> See, e.g., Jones, *supra* note 7; Robert Gomer, John W. Powell and Bert V.A. Roling, *Japan's Biological Weapons: 1930-1945*, 37 *BULL. OF THE ATOMIC SCIENTISTS* 43 (1961). This article is based in part on documents released under the Freedom of Information Act which reveal that in World War II the Japanese had used prisoners of war as subjects of research at biological warfare experimental stations. The records of these experiments had been turned over to representatives of the United States in exchange for immunity from war crimes prosecution.



The Commission's study of compensation for research injuries represents an attempt to explore how much inequality and risk are required by the research enterprise, and to examine the justice of the existing distribution of risks (to subjects) and benefits (to the wider society). In the course of this inquiry, three sets of issues have been identified: they set the framework for this Report.

**The Basis for Public Policy.** Existing data reviewed in Chapter Four suggest that the number of research injuries, and particularly of uncared-for injuries, is not large. Further, the creation of a compensation system would entail both economic costs and administrative burdens. Thus, the creation of a compensation program is potentially susceptible to attack on narrow cost-benefit grounds, particularly when viewed against other social programs and priorities. The ultimate persuasiveness of this attack cannot, however, be determined on the basis of existing data.

On the other hand, commentators often criticize the inability of our governmental system to respond to problems in advance of a crisis or a catastrophe. Scientific research entails risks, and the laws of probability decree that such risks will, someday, result in harms. Here the government has the opportunity to anticipate, rather than react to, headlines-in-the-making—headlines which may breed lasting public mistrust of science. Further, how the government responds to the problem of victims of research injuries will both reflect and help to determine the kind of society we wish to be, and to become. Thus, the question looms: Is policy to be determined solely by cost-benefit calculations, or is there room in the policymaking process for an additional dimension of social values and responsibility?

**Social Responsibility and Individual Consent.** As manifested in judicial opinions, ethical codes and Federal regulations, this country has determined both that informed consent is a prerequisite to participation in biomedical and behavioral research and that research posing unjustifiable or otherwise unacceptable risks may not go forward. But what of risks which cannot, or ought not, be avoided? If competent individuals knowingly consent to run the risk of participation in research without the expectation of compensation in the event of injury, ought not that altruistic gift be respected? Or is such a gift more than society should request or even accept? Does there come a time when to rely on "informed consent" is to exploit the goodness—or the weakness—of those who deserve society's respect and gratitude instead?

**Administrative Feasibility and the Plight of the Helpless.** A compensation program which excludes therapeutic research (or more generally, sick patients) is markedly simpler and less costly to administer than a more comprehensive program. Yet it is precisely in cases of therapeutic research

involving sick patients that the subjects may be most in need and that the quality of consent given is most likely to diverge from the ideal. Three options present themselves:

- to exclude such classes of research or research subjects from coverage entirely;
- to experiment with novel methods of determining causation, extent of injury, and other factors in a fashion designed to reconcile need, "deservingness," and administrative feasibility; or
- to abandon the requirement linking the injury to the research and instead provide medical care and financial assistance solely on the basis of human need.

Is our society prepared to accept the notion of social responsibility embodied in this last option—a notion consistent with broadened social responsibility not merely for research injuries, but for all the vicissitudes of modern life? If not, where should the line be drawn?

Fortunately, the Commission was not charged with resolving these large questions in the abstract, and it has not sought to do so. Rather, the Commission has grappled with these themes as they apply to the concrete and immediate issue of compensation for research injuries. In recognizing that some questions are, finally, unanswerable, the Commission also recognizes that in a dynamic society, the quest for perfect and eternal answers may invite paralysis.



In the history of biomedical ethics, discussion of compensation for research-related injuries has taken place against a background of shifting emphasis on two other mechanisms for the protection of human subjects: informed consent and limitation of risks. In the period immediately following the Nuremberg trials, concern focused primarily on the need for voluntary, informed consent through which potential subjects could either agree or decline to accept the risks inherent in a particular research activity. It was thought that a research institution could discharge its obligations to research subjects primarily by assuring that they were fully and fairly informed of the risks involved. Later it became apparent that informed consent was not always sufficient protection: subjects had been recruited for projects that seemed (at least to outsiders) to have entailed unreasonable risks. Therefore, procedures were adopted by the Federal government requiring prior review of research protocols to control or limit the amount of risk to which subjects might be exposed.

This chapter describes the development of arguments for compensation against a backdrop of the formal implementation of other protective mechanisms for informed consent and risk limitation. The complexity of the relationships among these three themes (informed consent, limitation of risk, and compensation) and the shifts of emphasis over time best lend themselves to analysis through a division of the recent past into two periods: 1945-1966, and 1966 to the present.

### **Reliance on Codes and Consent (1945-1966)**

**Outside Encouragement for Self-Regulation.** In the wake of the Nuremberg trials of Nazi war criminals after World War II, concern about voluntary informed consent was the central focus of biomedical research ethics. Because of the horror that greeted revelations about the abusive and unethical experi-

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ments that had been performed on unconsenting prisoners by the Nazi physicians on trial, the first principle of the Nuremberg Code states that "[t]he voluntary consent of the human subject is absolutely essential."<sup>1</sup>

Subsequent codes adopted by individual countries and medical associations were derivative of the Nuremberg judgment. They too placed primary emphasis on assuring that the consent of research subjects is truly voluntary and based upon a full understanding of the risks involved.<sup>2</sup> Disclosure of the risk was deemed of primary importance; limitation (if any) on the amount of risk that might be voluntarily assumed by subjects was secondary and generally took the form of exhortations to researchers to satisfy themselves that the risks of the research are justified by the anticipated benefits (to the subject or to general knowledge) and not to inflict death or disabling injury. These limitations derive from principles five and six of the Nuremberg judgment prohibiting experiments "where there is an *a priori* reason to believe that death or disabling injury will occur" and caution that risk should never exceed "the humanitarian importance of the problem to be solved by the experiment."

Hence, in the mid-1950s when the first suggestions for provision of compensation for injured research subjects appeared in print, there were no regulations or review procedures to limit the risk that might be presented in research. In fact, Irving Ladimer reported in 1955 that there had been two recent deaths associated with biomedical research: a laboratory technician, following an overdose of an experimental drug, and a prisoner, following an injection of hepatitis virus.<sup>3</sup> Commenting on the general problem of research-related injuries, Ladimer noted that "commercial insurance coverage and provision of medical care for consequences directly related to the [research] project are methods observed by responsible organizations."<sup>4</sup> No references or examples were cited, however.

In an unpublished doctoral thesis, Ladimer subsequently examined the liability to which research investigators were

<sup>1</sup> *United States v. Brandt*, 2 TRIALS OF WAR CRIMINALS BEFORE THE NUREMBERG MILITARY TRIBUNALS (The Medical Case) 181 (Military Tribunal I, 1947).

<sup>2</sup> See, e.g., *Principles for Those in Research and Experimentation* adopted by the General Assembly of the World Medical Association in 1954; *Report on Human Experimentation*, Public Health Council of the Netherlands (1955); *Ethical and Religious Directives for Catholic Hospitals*, adopted by the Catholic Hospital Association of the United States and Canada (1965); *Responsibility in Investigations on Human Subjects*, Medical Research Council, Great Britain (1963). All are reprinted in Henry K. Beecher, *RESEARCH AND THE INDIVIDUAL*, Little Brown and Co., Boston (1970), Appendix A.

<sup>3</sup> Irving Ladimer, *Law and Medicine: A Symposium*, 3 J. PUB. L. 467, 473 (1955).

<sup>4</sup> *Id.* at 509.



exposed and concluded that "a doctrine of liability without fault may be imposed, on the theory of a social cost of medical research, resembling the concepts supporting programs such as workmen's compensation."<sup>6</sup> He further observed that in fashioning a remedy for injured subjects, "public attitude as well as precedent law will be decisive."<sup>6</sup>

The idea of providing compensation for injured research subjects was proposed more formally in a 1960 article in the *Duke Law Journal*, in which Donald P. Dietrich discussed the possible application of a nonfault compensation scheme to subjects of psychological research.<sup>7</sup> Although he acknowledged that measuring the harm and establishing the amount of damages would be more difficult in the case of psychological injuries, Dietrich claimed (citing a half dozen articles on tort liability for psychic injuries) that the difficulties of proof would not be insurmountable.<sup>8</sup>

A problem that would come to have more significance in philosophic debates on the subject a decade later also emerged in Dietrich's article: the effect that a subject's knowing acceptance of the risk should have on the experimenter's responsibility to compensate for any injuries. Dietrich pointed out that although a subject may have known and consented to what the experimenter intended to do, still, he may not have fully realized the risks involved. "Mere knowledge of the facts which create the risk of harm is not enough unless there is a true appreciation of the nature and extent of the risk...."<sup>9</sup> Dietrich's skepticism regarding potential subjects' ability to appreciate risks foreshadowed adoption of other protective devices based, in part, on studies that provided empirical verification of his concern.<sup>10</sup>

<sup>6</sup> Irving Ladimer, *LEGAL AND ETHICAL IMPLICATIONS OF MEDICAL RESEARCH ON HUMAN BEINGS*, unpublished dissertation submitted to the George Washington University School of Law, at 153 (1958) (on file in the Law School Library).

<sup>7</sup> *Id.* at 154.

<sup>8</sup> Donald P. Dietrich, *Legal Implications of Psychological Research with Human Subjects*, 1960 *DUKE L. J.* 265-274.

<sup>9</sup> *Id.* at 273, citing: Smith, *Relation of Emotions to Injury and Disease: Legal Liability for Psychic Stimuli*, 30 *VA. L. REV.* 193-252 (1944); McNiece, *Psychic Injury and Tort Liability in New York*, 24 *ST. JOHN'S L. REV.* 1 (1949); Smith, *Medical Evidence in Industrial Injury Cases with Special Reference to Neuropsychiatric Claims*, in *Workmen's Compensation Problems*, 167 *U.S. DEPARTMENT OF LABOR BULL.* 11, 49 (1953); Smith & Bradford, *Medicolegal Aspects of Craniocerebral Injuries*, 3 *J. PUB. L.* 663 (1954); Worden, *Some Neglected Aspects of Injury, Mental Anguish and the Concept of Psychic Damage*, 3 *J. PUB. L.* 377 (1954); Report of the New York State Law Revision Commission, *STUDY RELATING TO INJURIES RESULTING FROM FRIGHT OR SHOCK*, Leg. Doc. No. 65(E) (1936).

<sup>10</sup> Dietrich, *supra* note 7, at 272.

<sup>11</sup> See, e.g., Chauncey Starr and Chris Whipple, *Risks of Risk Decisions*, 206 *SCIENCE* 1114 (1980); Vincent T. Covello and Joshua

After analyzing the possible theories and probable outcome of a suit for damages that might be brought by someone injured as a result of participating in psychological research, Dietrich then described the broad outlines of a nonfault compensation scheme. Because his discussion so closely resembles subsequent discussions appearing over the next twenty years, it is worth repeating in its entirety:<sup>11</sup>

Within an analytical framework such as this, then, the first human experimentation case may be decided, and a hitherto unaccounted-for element of the true cost of such experimentation distributed. Such an extension of the law, however, will not resolve the dilemma of society's needing research while at the same time requiring due legal protection for both experimenter and subject.

The resolution of this dilemma can be premised upon the recognition that society is more than the ultimate beneficiary of research; through governmental action, society is the initiator of most research. This condition alone, it would seem, should justify the following:

- (1) A policy of liability without fault should be evolved for harm resulting from psychological experimentation.
- (2) Where the government undertakes or participates in the research program, it should also assume the burden of making injured subjects whole, through treatment and rehabilitation and by the payment of monetary compensation.
- (3) The government should consider such an underwriting program as would be required to assume costs to subjects taking part in private research programs conducted under modern, controlled conditions.

Among the effects of such developments on the whole environment of psychological experimentation would be compensation of the injured subject without regard to the doubtful questions of liability and proof of injury, thereby encouraging the participation of a sufficient number of subjects of varying levels of personality integration.

Further, there would also be legal protection for the experimenter who is part of an approved modern, controlled research program, thus encouraging research conducted on high planes. On the other hand, experimenters not of this class—those who are not associated with approved modern, controlled research programs—would be strictly liable for any harm which results from their inducing others to serve as subjects of their

Menkes, *Issues in Risk Analysis*, paper presented at AAAS meeting, San Francisco (January 1990), to be published in AAAS Symposium Volume: *RISK IN THE TECHNOLOGICAL SOCIETY*.

<sup>11</sup> Dietrich, *supra* note 7, at 273-274, original citations omitted.



"research." Admittedly, the effect may be to discourage to some extent research which is not specifically socially sanctioned.

Finally, national research effort in this area would become more ordered in the sense and to the extent that the essentiality of each research program, as balanced against the program's total cost, would be the basis for go-ahead decisions by agencies having in view the entire research picture.

It is not surprising that Dietrich, writing at a time when there were few other formal controls in research, saw a compensation program not merely as a means of redressing injuries but also of social control and resource allocation.

Meanwhile, requirements for informed consent were added to Federal law as part of the 1962 Kefauver-Harris amendments to the Federal Food, Drug and Cosmetic Act.<sup>12</sup> The legislation—passed following the birth of a number of severely deformed children to women who had taken the sedative thalidomide during pregnancy—was intended to increase Federal control of drug testing in general and to require that prescription drugs be proven effective, as well as safe, prior to marketing.<sup>13</sup> As part of the conditions imposed for testing new drugs, Congress required that sponsors of such investigations assure that they would (a) inform any human beings involved in the tests that the drugs were being used for investigational purposes, and (b) obtain the consent of the subjects or their representatives (unless it is infeasible to do so or, according to professional judgment, contrary to the best interest of a particular patient/subject).<sup>14</sup> One apparent result of the Kefauver-Harris amendments was an increase in the amount of research with human subjects conducted in this country and abroad to provide the data needed to support new drug applications.

Emphasis on informed consent culminated in the Declaration of Helsinki, adopted by the World Medical Association in 1964. The Declaration distinguished (as had the Medical Research Council of Great Britain, a year earlier) between "clinical research combined with patient care" and "nontherapeutic clinical research." For the former, the Declaration urged that informed consent be obtained "if at all possible, consistent with patient psychology." For nontherapeutic research, consent of the subject was urged in all cases with the exception that if the subject was legally incompetent, consent of a legal guardian should be procured. The Declaration also established the basic principle that the inherent risks of research should be "in proportion to" the anticipated benefits to the subject or to others.

<sup>12</sup> 76 Stat. 780, 87th Cong., 2d Sess.; Oct. 10, 1962. See 21 U.S.C. § 355.

<sup>13</sup> 21 U.S.C. § 358(i).

<sup>14</sup> *Id.*

Apparent Problems in a Mighty Enterprise. Between 1945 and 1955, the annual research expenditures of the National Institutes of Health had increased many hundredfold from \$701,800 to \$458,600,000.<sup>16</sup> This was a reflection of vast public support of biomedical and behavioral research in the aftermath of World War II based upon an appreciation of the benefits to be derived from scientific progress.

Throughout this period, great attention was also paid to the ethical issues surrounding the conduct of research with human subjects. In 1960, the Law-Medicine Institute of Boston University received a large grant from the Public Health Service to investigate the legal and ethical aspects of research with human subjects.<sup>17</sup> In 1963, the Institute published a major anthology on *Clinical Investigation in Medicine: Legal, Ethical and Moral Aspects*. Although major emphasis continued to be on problems of informed consent, suggestions for "group consideration" or prior review of research began to appear as well.<sup>18</sup>

Experience during the period 1955-65 moved the discussion from an academic to a public arena as it became apparent that some research subjects were truly being exposed to risk for the benefit of others. In some cases, the subjects assumed the risks unknowingly; in other cases, although the subjects may have consented, it was questionable whether they should have been asked—or permitted—to do so. Although such cases were few, compared to the amount of clearly acceptable research being conducted, the publicity attending questionable cases heightened public awareness and concern.

One of the first incidents to alarm the general public took place at the Jewish Chronic Disease Hospital in Brooklyn, N.Y. The widely publicized case involved two physician-investigators who injected cultured cancer cells into debilitated, elderly patients under their care, without informing the patients or gaining their consent. The research was funded, in part, by the Public Health Service.<sup>19</sup> In 1965, after a series of hearings and recommendations of the appropriate grievance committees, the New York Board on Medical Licensure and Discipline accepted a determination of the Medical Grievance Committee that the

<sup>16</sup> Data supplied by Dr. John Sherman, of NIH, reported by Henry K. Beecher in *Ethics and Clinical Research*, 274 NEW ENG. J. MED. 1354, 1355 (1966).

<sup>17</sup> Irving Ladimer and Roger W. Newman (eds.), *CLINICAL INVESTIGATIONS IN MEDICINE: LEGAL, ETHICAL AND MORAL ASPECTS*, Law-Medicine Research Institute, Boston University (1963) at iv.

<sup>18</sup> *Id.* at 208-210.

<sup>19</sup> Jay Katz, with the assistance of A.M. Capron and E.S. Glass, *EXPERIMENTATION WITH HUMAN BEINGS*, Russell Sage Foundation, New York (1972) at 19.



two principal investigators had been "guilty of fraud or deceit in the practice of medicine and of unprofessional conduct."<sup>19</sup> Both physicians were placed on one year's probation, but the recommended suspension of their licenses to practice medicine was stayed.<sup>20</sup>

In 1966, Dr. Henry K. Beecher of the Harvard Medical School published a landmark article in the *New England Journal of Medicine* describing a number of research projects he viewed as unethical largely because of the risks to which the subjects had been exposed.<sup>21</sup> Some of the experiments he described involved withholding treatment from control groups without their knowledge or consent. Others, however, involved the use of medical or surgical procedures of considerable risk (cardiac catheterization, liver biopsy) for research purposes. In one case, reported Beecher, an investigator had transplanted a melanoma (cancerous tumor) from a dying patient to her mother; although the tumor was excised shortly thereafter, the mother died a little over a year later from diffuse melanoma that had spread from the small piece of transplanted tumor.<sup>22</sup>

Beecher's article drew national attention both because it appeared in the prestigious *New England Journal* and because it was written by a highly respected physician. Moreover, the examples were drawn from reports published in a leading (unnamed) biomedical journal.<sup>23</sup> Noting that Englishman M. H. Pappworth was then in the process of assembling over 500 papers based upon unethical experiments, Beecher concluded that "unethical or questionably ethical procedures are not uncommon."<sup>24</sup> In his introduction to the article, he had said:<sup>25</sup>

I believe the type of activities to be mentioned will do great harm to medicine unless soon corrected. It will certainly be charged that any mention of these matters does a disservice to medicine, but not one so great, I believe, as a continuation of the practices to be cited.

An ethical approach to research with human beings required, in Beecher's view, that "the gain anticipated from an experiment must be commensurate with the risk involved. An experiment is ethical or not at its inception."<sup>26</sup> He concluded that assuring this ethical approach rests primarily upon two factors: informed consent of the subject, and "the presence of

<sup>19</sup> *Id.* at 63.

<sup>20</sup> *Id.*

<sup>21</sup> Henry K. Beecher, *Ethics and Clinical Research*, 274 *NEW ENG. J. MED.* 1354 (1966).

<sup>22</sup> *Id.* at 1356.

<sup>23</sup> *Id.* at 1335.

<sup>24</sup> *Id.*

<sup>25</sup> *Id.* at 1354.

<sup>26</sup> *Id.* at 1330.

an intelligent, informed, conscientious, compassionate, responsible investigator."<sup>27</sup>



A year later, Pappworth published *Human Guinea Pigs*, a detailed recitation of experiments reported in reputable journals in which subjects were exposed to a variety of risky procedures not intended to benefit them.<sup>28</sup> In chapter after chapter, he described the insertion of catheters and biopsy needles into important organs of the body (bladder, kidney, heart, liver) and resulting meningitis, shock, liver damage and cardiac arrest. The subjects of these procedures were newborns, infants and children (both healthy and diseased), pregnant women, prisoners, patients undergoing surgery, the mentally disabled, the aged, the critically ill, and the dying.

The published articles revealed little concern on the part of investigators for their subjects. One reported on a research project that involved leaving a catheter in the liver of subjects for periods ranging from two to nineteen days:

The authors somewhat surprisingly record that "There were no serious complications. Several unexpected findings were encountered!" They mention, however, that in three patients the needle accidentally pierced the bowel; in two instances it punctured a main artery; another patient had his gall bladder punctured; one patient had syncope (shock); and three had large haemorrhages.<sup>29</sup>

Pappworth concluded that "the voluntary system of safeguarding patients' rights has failed and new legislative procedures are absolutely necessary."<sup>30</sup> He recommended prior review of all proposed research by Medical Research Committees and, in the case of research sanctioned by those committees, compulsory reporting of: the purpose of the research, the initial condition of the subjects, evidence of free and comprehending consent, outcome of the experiment (including an account of any injury or accident), "mention of all and every

<sup>27</sup> *Id.*

<sup>28</sup> M.H. Pappworth, *HUMAN GUINEA PIGS*, Beacon Press, Boston (1967) at 70-71.

<sup>29</sup> *Id.* at 70.

<sup>30</sup> *Id.* at 200.



complication, even if considered minor," and confirmation that the coroner was notified in the case of any death resulting directly or indirectly from the experiment.<sup>31</sup>

### Prior Review and Limitations on Risk (1966-Present)

In 1966, the Surgeon General of the United States directed that all research proposals submitted for financial support from the Public Health Service must undergo prior review by an investigator's institutional associates "to assure an independent determination of the protection of the rights and welfare of the individual or individuals involved, of the appropriateness of the methods used to secure informed consent, and of the risks and potential medical benefits of the investigation."<sup>32</sup> Prior review of research by a medical committee composed of medical staff had been an established procedure in the United States at the Clinical Center of the National Institutes of Health since its opening in 1953.<sup>33</sup>

In April, 1971, another controversial research project received major public attention when the British medical journal, *Lancet*, published a sharp criticism of experiments which involved injecting hepatitis virus into mentally retarded children at the Willowbrook State School in New York.<sup>34</sup> The investigators justified their research by reference to the circumstances of their subjects:

- (1) they were bound to be exposed to the same strains under the natural conditions existing in the institutions;
- (2) they would be admitted to a special, well-equipped and well-staffed unit where they would be isolated from exposure to other infectious diseases which were prevalent in the institution...;
- (3) they were likely to have a subclinical infection followed by immunity to the particular hepatitis virus; and
- (4) only children with parents who gave informed consent would be included.<sup>35</sup>

The Willowbrook studies had been extensively criticized by theologian Paul Ramsey, in 1970, for exposing institutionalized children to unknown and unjustified risks.<sup>36</sup> Others now

<sup>31</sup> *Id.* at 209-210.

<sup>32</sup> Surgeon General, *Memo to Heads of Institutions Conducting Research with Public Health Service Grants* (February 8, 1966).

<sup>33</sup> Stuart M. Sessoms, *Guiding Principles in Medical Research Involving Humans*, *National Institutes of Health*, 32 *HOSPITALS* 44 (1958).

<sup>34</sup> Stephen Goldby, *Experiments at the Willowbrook State School*, 1 *LANCET* 749 (1971).

<sup>35</sup> Saul Krugman, *Experiments at the Willowbrook State School*, 1 *LANCET* 966, 967 (1971).

<sup>36</sup> Paul Ramsey, *THE PATIENT AS PERSON*, Yale University Press, New Haven, Conn. (1970) at 47-55.

quickly joined in the debate.<sup>27</sup>

At the same time that attention was being focused on the need to limit the risks to which subjects might be exposed, some authors continued to press for a nonfault compensation program for injured research subjects, either as a mechanism for controlling risks or as a matter of societal obligation.<sup>28</sup>

In a 1967 article in the *Journal of the American Medical Association*, Richard Bergen proposed that injuries arising from participation in clinical research be included in malpractice insurance coverage already held by sponsoring institutions.<sup>29</sup> He viewed such coverage as the "ideal solution" to the problem because the sponsoring organizations would be able to provide insurance for physicians working under their auspices at less cost than if the physicians were to purchase the insurance individually; moreover, paying for such coverage is an "appropriate cost for the sponsoring institution to pay."<sup>30</sup>

Several months later, Delford L. Stickel, M.D., approached the matter from the perspective of a physician interested in organ transplantation but also concerned about normal volunteers in biomedical research. Writing in *Law and Contemporary Problems*, Stickel adopted and forcefully supported Bergen's suggestions, recommending that the insurance be of a nonfault variety and adding two observations: (1) that the premiums set for the insurance coverage "would provide useful checks on overly dangerous research" and (2) that regulations

<sup>27</sup> PROCEEDINGS OF THE SYMPOSIUM ON ETHICAL ISSUES IN HUMAN EXPERIMENTATION: THE CASE OF WILLOWBROOK STATE HOSPITAL (May 4, 1972), published by the Urban Health Affairs Program, New York University Medical Center.

<sup>28</sup> The call for compensation had begun again shortly before the dramatic events of 1966:

[S]ince the benefits of research redound to society, society should accept the responsibility for assuring that the investigator who proceeds with care and caution should not be inhibited in his research because of any inherent hazard. Likewise, the partner-subject—the "clinical material" for the investigator—should not be placed at disadvantage, if injury should result directly from his participation. The cost of protection should therefore be considered a proper charge to the business of doing research, to be assumed by the sponsor, in much the same way as other administrative costs are borne by government or industry in production and service operation.

Irving Ladimer, *Clinical Research Insurance* (editorial), 16 J. CHRON. DIS. 1229, 1233 (1963).

<sup>29</sup> Richard P. Bergen, *Insurance Coverage for Clinical Investigation*, 201 J.A.M.A. 305-306 (1967).

<sup>30</sup> *Id.*



or legislation establishing a duty to provide such insurance might be necessary.<sup>41</sup>

The arguments in favor of a compensation mechanism as a means to control research were elaborated but ultimately doubted by Yale Law Professor Guido Calabresi.<sup>42</sup> Writing in a special issue of *Daedalus* in 1969, devoted to "Ethical Aspects of Experimentation with Human Subjects," Calabresi examined issues of risk-taking and methods for protecting human lives through indirect controls such as those operating in accident law. His support for a system of compensation rested on the perceived need to impose better controls on the research enterprise. Calabresi argued that having to compensate for research injuries would stimulate better analysis of the possible risks and benefits of a given research proposal. He saw the indemnification of injured subjects as a secondary, although desirable, result.<sup>43</sup>

In the end, however, Calabresi concluded that he did not believe a compensation fund would be the best method of controlling the research enterprise; instead, he recommended review committees at the research institution (with diversity of membership as subsequently required by HEW). His discussion of a compensation fund, he emphasized, was "primarily to indicate that very little work has gone into the search for complex control devices that would balance present against future lives and still put no one in the position of clearly deciding against individual lives."<sup>44</sup>

Complex control devices in the form of local review committees were, even then, being developed by HEW (now HHS), and were soon to be implemented. The development of DHEW policy for protection of human subjects and its conversion to Federal regulation is part of the final phase of this story.

**Strengthening Regulations.** The decade of the 1970s was one of extraordinary Federal activity in the review and regulation of research ethics, both in Congress and in the administrative agencies.

In response to rising concern about the need to protect human subjects, the Public Health Service in 1971 extended the 1966 Surgeon General's memorandum into a formal *Institutional Guide to DHEW Policy on Protection of Human Subjects* to explain HEW's grant administration policy. It contained an

<sup>41</sup> Delford L. Stickel, *Organ Transplantation in Medical and Legal Perspectives*, 32 LAW AND CONTEMPORARY PROBLEMS 597, 609 n. 32 (1967).

<sup>42</sup> Guido Calabresi, *Reflections on Medical Experimentation in Humans*, in EXPERIMENTATION WITH HUMAN SUBJECTS (ed. by Paul Freund), George Braziller, New York (1970).

<sup>43</sup> *Id.* at 395.

<sup>44</sup> *Id.* at 396-399.

important modification of the Surgeon General's requirement that research supported by HEW grants and contracts undergo "peer review" at the investigator's institution.<sup>46</sup>

The committee must be composed of sufficient members with varying backgrounds to assure complete and adequate review of projects. ... No member of an institutional committee shall be involved in either the initial or continuing review of an activity in which he has a professional responsibility. ... The committee should be able to determine acceptability of the proposal in terms of institutional commitments and regulations, applicable law, standards of professional conduct and practice, and community attitudes.

Similar review requirements had already been incorporated in FDA regulations governing investigational new drug studies.<sup>47</sup> The HEW policy explicitly required that the risks of any research project be justified either by the potential benefits to the subjects or by the importance of the knowledge to be gained, and cautioned review committees to "be alert to the possibility that investigators, program directors, or contractors may, quite unintentionally, introduce unnecessary or unacceptable hazards, or fail to provide adequate safeguards."<sup>48</sup> Committees were also advised to determine that proper precautions would be taken to deal with emergencies that might develop and, of course, to assure that the informed consent of subjects would be obtained by adequate and appropriate methods.<sup>49</sup>

The Institutional Guide to DHEW Policy was issued in December of 1971. Several months later, Jay Katz's substantial casebook, *Experimentation with Human Beings*, was published.<sup>50</sup> It presented the most complete collection of materials on this subject ever compiled, together with commentary and provocative questions about the proper allocation of authority and responsibility for protecting human subjects among those who conduct research, those who fund it, those who review it, those who run the research institutions, the Federal government, professional societies, and the subjects themselves or (in some cases) their parents or legal guardians.

Coincident with the renewed regulatory and scholarly interest, an instance of unethical experimentation again became front-page news through articles describing a Public

<sup>46</sup> U.S. Department of Health, Education, and Welfare, THE INSTITUTIONAL GUIDE TO DHEW POLICY ON PROTECTION OF HUMAN SUBJECTS, DHEW Publication No. (NIH) 72-102, U.S. Government Printing Office, Washington (1971) at 4.

<sup>47</sup> *Id.*, citing 21 CFR 130.

<sup>48</sup> *Id.* at 5.

<sup>49</sup> *Id.* at 5-7.

<sup>50</sup> Jay Katz, with assistance of A. M. Capron and E. S. Glass, *EXPERIMENTATION WITH HUMAN BEINGS*, Russell Sage Foundation, New York (1972).



Health Services study in which black males in Tuskegee, Alabama, suffering from syphilis had—by study design—gone untreated for forty years.<sup>20</sup> Although the study had been initiated in 1932, it had continued long after penicillin was demonstrated to be an effective treatment for the disease. Moreover, a review committee (composed of physicians and PHS staff) had reviewed the project in 1969 and decided that the study should be continued.<sup>21</sup> In 1972, after the research program was revealed in the national press, the Assistant Secretary for Health and Scientific Affairs (HEW) established an ad hoc panel to examine the Tuskegee Syphilis Study in particular and HEW policies and procedures for the protection of human subjects in general.

The final report of the advisory panel contained disturbing conclusions regarding excessive risk to subjects and lack of consent, as well as recommendations for improvement. Specifically, the panel concluded that the Tuskegee Syphilis Study was "ethically unjustified at its inception in 1932" because no provisions were made for informing the subjects about their participation or for obtaining their consent, and that "its results are disproportionately meager compared with known risks to human subjects involved."<sup>22</sup> The panel further concluded that the study should have been terminated and the participants treated "especially as of 1953 when penicillin became generally available"<sup>23</sup> and finally, that the Public Health Service should terminate the study immediately and arrange for the immediate treatment of surviving participants.<sup>24</sup>

The panel praised the existing HEW review committee system but expressed concern about the dominance of biomedical professionals in the regulatory process, the vagueness of the guidelines, "critical loopholes" in the consent procedures, insufficient attention to vulnerable subject populations, neglect of the require-



<sup>20</sup> Fred Gray, *Statement before Subcommittee on Health, Committee on Labor and Public Welfare, U.S. Senate*, March 8, 1973, at 1334.

<sup>21</sup> *Tuskegee Syphilis Study Ad Hoc Advisory Panel, FINAL REPORT*, U.S. Department of Health, Education, and Welfare, Washington (1973) at 10-11.

<sup>22</sup> *Id.* at 7-8.

<sup>23</sup> *Id.* at 11.

<sup>24</sup> *Id.* at 18-19.

ments for continuing review, and absence of effective enforcement procedures.<sup>24</sup> Moreover, the panel noted:<sup>25</sup>

No policy for the compensation of research subjects harmed as a consequence of their participation in research has been formulated, despite the fact that no matter how careful investigators may be, unavoidable injury to a few is the price society must pay for the privilege of engaging in research which ultimately benefits the many. Remitting injured subjects to the uncertainties of the law court is not a solution.

The panel recommended (among other things) the development of a "no fault" clinical research insurance plan to assure compensation for subjects harmed as a result of their participation in research."<sup>26</sup>

From February through July, 1973, the Subcommittee on Health of the Senate Committee on Labor and Public Welfare, chaired by Senator Edward Kennedy, held a series of hearings on human experimentation. Testimony was received regarding a number of incidents (including Willowbrook and Tuskegee) that had heightened public concern about research with human subjects. Bernard Barber reported on a sociological study of biomedical research institutions which showed that the ethical sensitivity of principal investigators was far from adequate and that prior review of experiments was far from universal. Dr. Katz repeated the criticisms and recommendations of the advisory panel's report on the Tuskegee Syphilis Study and raised questions of administration and authority highlighted in his casebook.<sup>27</sup> His colleague, Alexander M. Capron, raised similar concerns and specifically suggested an indemnification program for all research subjects "to cover all consequences of their participation, including those arising unforeseeably and without negligence."<sup>28</sup>

As a result of the hearings, Congress included provisions on the protection of human subjects in the National Research Act, adopted in 1974. The Act not only directed the Secretary of HEW to require establishment of Institutional Review Boards (IRBs) at all grantee institutions, it also created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Commission was charged with investigating and reporting to the President, the

<sup>24</sup> *Id.* at 23.

<sup>25</sup> *Id.*

<sup>26</sup> *Id.* at 23-24.

<sup>27</sup> *Hearings before the Subcommittee on Health of the Committee on Labor and Public Welfare, United States Senate, Quality of Health Care-Human Experimentation*, Part 3, March 7-8, 1973, at 1048.

<sup>28</sup> *Id.* at 845.



Congress, and the Secretary, HEW, on many aspects of research with human subjects.<sup>28</sup>

At the same time that Congress was creating the National Commission, HEW was in the process of converting its grants administration policy to formal regulations governing the conduct of research with human subjects. Proposed regulations were published in 1973,<sup>29</sup> and final rules were issued in 1974.<sup>30</sup> For the most part, the regulations codified the policies set forth in the *Institutional Guide*. One important change, however, was in the applicability of the regulations. Under the old HEW policy, local committee review was required only for research involving risk to human subjects; whether or not the proposed research presented any risk was a matter determined by the principal investigator. Under the new regulations, *all* research involving human subjects had to undergo review by a local Institutional Review Board (IRB), and it was the IRB that determined whether or not risk was involved, and what the consent requirements should be.

Throughout the early 1970s, a number of other Federal agencies adopted the HEW policies and procedures for the protection of human subjects. By 1977, a review conducted by the staff of the National Commission revealed that of the 20 separate Federal entities (other than HEW) that conduct or support research with human subjects, 19 had formal policies or regulations governing such research. Of those, 17 adopted the HEW standards and procedures to a substantial degree.<sup>31</sup>

**Continuing Reservations.** Despite all the improvements in regulating the conduct of research, however, concern persisted. No matter how well a project is reviewed, no matter how carefully it is conducted, a chance always remains that someone might be injured. If that should occur, there was still no mechanism to provide compensation.

Beginning in 1970, the National Institutes of Health (NIH) submitted a series of compensation proposals to the Secretary, HEW.<sup>32</sup> Each of the three programs proposed would have

<sup>28</sup> Pub. L. No. 93-348, 96 Stat. 342 (1974). An early version of the bill contained a provision that the Commission "develop a mechanism for the compensation of individuals and their families for injuries or death proximately caused by the participation of such individuals in a biomedical or behavioral research program." (S. 2072, 93rd Cong., 1st Sess., June 26, 1973).

<sup>29</sup> 38 FEDERAL REGISTER 27882 (Oct. 9, 1973).

<sup>30</sup> 39 FEDERAL REGISTER 18914 (May 30, 1974).

<sup>31</sup> National Commission for the Protection of Human Subjects, REPORT AND RECOMMENDATIONS: INSTITUTIONAL REVIEW BOARDS, U.S. Government Printing Office, Washington (1978) at 93 *et seq.*

<sup>32</sup> HEW Secretary's Task Force on the Compensation of Injured Research Subjects, REPORT, U.S. Department of Health, Education, and Welfare, Washington (1977) (hereinafter cited as TASK FORCE REPORT) at III-2.

provided compensation (without proof of negligence) for subjects injured as a result of participation in research activities supported in whole or in part by Federal funds. All three, however, failed to gain Departmental backing, reportedly because of one or more of the following reasons:

- (1) The social and fiscal implications of the proposals had not been assessed;
- (2) Alternatives to a Federally administered program had not been explored; and
- (3) The problem was not adequately defined.<sup>63</sup>

The next step was taken by the HEW Medical Malpractice Commission which forwarded its report to Secretary Elliot Richardson in January 1973. Although it had not been charged with the responsibility of reviewing human research, the Malpractice Commission included in its report a recommendation that "whenever a grant or other funding is provided by the Federal government for medical research involving human subjects, the grant should include a sum sufficient to provide either insurance or a self-insurance fund in order to provide compensation to any human subject who may be injured in the course of the research."<sup>64</sup> The Commission added that the same should apply to research that the Federal government itself conducts and to research conducted in the private sector.<sup>65</sup>

In September 1974, prompted by a request by HEW Secretary Cesar Weinberger, the Acting Assistant Secretary for Health (Dr. Theodore Cooper) suggested seven possible approaches for further action on the compensation question. The option selected by the Secretary was the creation of a Task Force (composed of HEW staff) to conduct "a detailed study of whether and how to compensate subjects injured in the course of research."<sup>66</sup> One of the reasons for selecting that option was that it had not yet been determined "whether a problem exists which is serious enough to justify the resources needed to develop a compensation mechanism."<sup>67</sup>

The Task Force met 24 times over a period of 18 months, and reviewed: (1) a series of reports prepared by experts in law, ethics, and insurance; (2) results of a telephone survey of adverse effects reported (by principal investigators) to have occurred over a three-year period; (3) an analysis of current Federal compensation programs, and (4) responses from the insurance industry to inquiries posed by the Assistant Secretary for Health.<sup>68</sup>

<sup>63</sup> *Id.*

<sup>64</sup> REPORT OF THE SECRETARY'S COMMISSION ON MEDICAL MALPRACTICE, U.S. Department of Health, Education, and Welfare (11/78) at 79.

<sup>65</sup> *Id.*

<sup>66</sup> TASK FORCE REPORT, *supra* note 64, at III-2.

<sup>67</sup> *Id.* Appendix A, at 9.

<sup>68</sup> *Id.* at II-1.



In January 1977, the Task Force published the following recommendations:

- (1) Human subjects who suffer physical, psychological, or social injury in the course of research conducted or supported by the PHS should be compensated if (1) the injury is proximately caused by such research, and (2) the injury on balance exceeds that reasonably associated with such illness from which the subject may be suffering, as well as with treatment usually associated with such illness at the time the subject began participation in the research.
- (2) The amount of compensation should be commensurate with the "excess" injury as defined above.
- (3) Subjects participating in PHS-*conducted* (intramural) research should be included (and should be informed of such inclusion) in the definition of employees within the F.E.C.A., and if injured, should receive such compensation as provided by the Act.
- (4) Subjects participating in PHS-*sponsored* (i.e. extramural not PHS-*conducted*) research should be supplied assurance of compensation (and should be informed of such assurance) by the institution conducting the research. Such compensation should be equal to that provided subjects under the F.E.C.A.
- (5) A Notice of Intent to Issue Regulations should be published as a first step toward implementing recommendation four above and to explore the availability of compensatory assurance.
- (6) If the provision of such assurance should prove to be infeasible these subjects should be assured protection under the F.E.C.A. as would be the participants of PHS-*conducted* research detailed in recommendation three above.
- (7) Research which is PHS-regulated, but not PHS-supported or PHS-conducted, should not be included in the above recommendations. However, we do recommend that the FDA consider legislation which would enable them to require that compensation mechanisms be made available to subjects injured in the course of PHS-regulated research.<sup>71</sup>

The Task Force Report was reviewed by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, which transmitted a general endorsement of the recommendations to HEW Secretary Joseph A. Califano, Jr.,<sup>72</sup> in June 1977. The Commission subsequently recommended (in its report on Institutional

<sup>71</sup> *Id.* at II-2.

<sup>72</sup> Letter from Kenneth J. Ryan, Chairman, to Joseph A. Califano, Jr. (June 9, 1977).

Review Boards) that prospective subjects be told whether treatment or compensation would be available if harm occurs as well as whom to contact in such an event.<sup>75</sup> That recommendation was implemented by DHEW in an "Interim Final Regulation" which took effect January 2, 1979.<sup>76</sup> In issuing the regulation, the Acting Assistant Secretary for Health noted that: "[S]ince the amendment is being adopted prior to public comment, its scope will be limited to treatment and compensation for physical injury and only to those physical injuries arising from biomedical or behavioral research."<sup>77</sup>

Nevertheless, the research establishment was uneasy.<sup>78</sup> At least one major university challenged the adoption of a new regulation without opportunity for public review and comment as required by the Administrative Procedures Act.<sup>79</sup> The Association of American Medical Colleges (AAMC), responding to what it called "great confusion and consternation within the Nation's universities, medical schools and teaching hospitals," convened an ad hoc study group to "examine the feasibility of acquiring appropriate insurance coverage and to develop positive suggestions regarding the character of a compensation scheme."<sup>80</sup>

The AAMC study group concluded that, although the Task Force had provided a good conceptual framework, it had not resolved the practical problems involved in the development of a compensation scheme. Therefore, the group recommended that HEW ask its Ethics Advisory Board to study the economic aspects of various possible systems in hopes that it could "resolve the issues in a fashion which takes cognizance of the dynamics of the private insurance system, the needs of academic institutions and the nature of the clinical research enterprise."<sup>81</sup> Finally, the AAMC asked about the ethical acceptability of a number of limitations it believed insurance companies would impose on any coverage for research-related injuries.

The AAMC letter, addressed to Joseph A. Califano, Jr., was received at HEW on June 28, 1979, just a few weeks before Califano was replaced as Secretary of HEW by Patricia R. Harris. In the first week of October, 1979, Secretary Harris sent a memorandum to the Chairman of the Ethics Advisory Board

<sup>75</sup> National Commission for the Protection of Human Subjects, *supra* note 63, Recommendation 4(f) (iv) and (v), at 21.

<sup>76</sup> 43 FEDERAL REGISTER 51569 (November 3, 1978).

<sup>77</sup> *Id.*

<sup>78</sup> William J. Curran, *Compensation for Injured Research Subjects: Regulation by Informed Consent*, 301 NEW ENG. J. MED. 646 (1979).

<sup>79</sup> Letter from Estelle A. Fishbein, General Counsel, to Robert Beckus (January 17, 1979).

<sup>80</sup> Letter from John A. Cooper, M.D., President, AAMC, to Joseph A. Califano, Jr. (June 28, 1979).

<sup>81</sup> *Id.* at 6.



formally requesting that the Board consider whether or not there is an ethical obligation to compensate injured subjects. If so, the Board was then asked to consider whether it would be ethical to impose the limitations that the AAMC suggested might be necessary.<sup>30</sup>

Before the Board could formally agree to consider the compensation question, word came that the Board would be terminated at the end of the 1980 fiscal year. Since it was still in the process of completing two other reports, the Board's Chairman and Vice Chairman decided that it would be infeasible to attempt a study of the compensation problem in the time remaining, and so advised the Department.<sup>31</sup>

Instead, the Ethics Advisory Board recommended that the President's Commission take up the subject. David Hamburg, Vice Chairman of the Ethics Advisory Board, conveyed this recommendation to the Commission at its first meeting in January 1980 as part of his report on the history and activities of the Board. He explained that the Board had found the compensation issue important, but would be unable to undertake the study in the time remaining to it. Before adjourning its first meeting, the Commission voted to undertake a study of the problems surrounding compensation for research injuries.

#### **The Study Undertaken by the President's Commission**

The Commission undertook an investigation of the problems relating to the feasibility of compensating for research injuries that underlay the questions posed by Secretary Harris to the Ethics Advisory Board. Attempts were made to obtain data from various sources on the nature and incidence of research injuries experienced (or likely to be experienced) in the varied kinds of research conducted in the United States. In addition, a series of discussions were held with officials of the insurance industry to determine the likelihood that private insurance of appropriate coverage would be available to research institutions. Finally, position papers and scholarly reports were also solicited on a number of relevant topics.

In an effort to collect data on the nature and incidence of research-related injuries, the Commission requested detailed descriptions and analyses of the experience of two research institutions that have had compensation programs in effect for a period of years. Under contract with the Commission, such reports were prepared by administrators at the University of Washington at Seattle and the Quincy Research Center in

<sup>30</sup> Memorandum from Patricia Roberts Harris to the Chairman of the Ethics Advisory Board. (October 4, 1979).

<sup>31</sup> Memorandum from the Staff Director, Ethics Advisory Board, to the Under Secretary HEW regarding reassignment of the Board's duties (December 21, 1979).

Kansas City, Missouri. A similar report describing the insurance program covering biomedical research in Sweden was prepared for the Commission by the physician responsible for assigning a risk factor to each research project (from which premium rates are established). A discussion of their findings and conclusions appear in Chapter Four of this Report; the papers are reproduced in the Appendix. The Commission also sought information on the nature and frequency of adverse effects experienced by subjects in research supported, conducted or otherwise regulated by various Federal agencies. Officials of the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) testified on this subject at the Commission's meeting in May 1980. Information was solicited by mail from approximately twenty other Federal agencies known to conduct or support research with human subjects.

Because the Swedish insurance program relies upon a procedure of assigning a risk factor to each research project, the Commission also requested a review of existing literature on adverse effects of twenty selected invasive procedures used in biomedical research (e.g., liver biopsy, bone biopsy, urinary bladder catheterization, lumbar puncture, angiography). The purpose was to determine the extent to which the risk presented to human subjects could reliably be determined in advance and thus to assess the feasibility of setting insurance premiums according to the risk involved in the research projects conducted at a given institution. The findings of that study are also discussed in Chapter Four.

Members of the Commission staff held a series of discussions with senior officials of major insurance companies, brokers and trade associations to solicit their cooperation in determining the extent to which private insurance coverage might be available or, alternatively, the advisability of providing for self-insurance through collective insurance pools. The results of those discussions were presented by representatives of the insurance industry in testimony before the Commission and are reflected in Chapter Five and in Appendices P and Q to this Report.

The Commission requested further exploration of the ethical arguments for and against the proposition that the Federal government has an obligation to provide compensation for research-related injuries. Of particular concern was the extent of the government's obligation (if any) to persons whose participation in research involved testing a new therapy from which they expected to benefit. At public hearings, the Commission heard testimony from the Association of American Medical Colleges, the American Society of Clinical Oncology, the Association of American Cancer Institutes and others urging that the Commission not recommend that compensation be provided to patients who participate in research to test new



therapeutic interventions from which the subjects expected to benefit.

A contrary position was urged by a representative of the DES Registry who, in several appearances before the Commission, described the difficulties of "DES daughters" in obtaining and paying for medical care necessary to identify early signs of cancer or other abnormal conditions associated with their mothers' ingestion of DES during pregnancy. Although most of the women who took DES in the 1940s and 1950s did so on the advice of their physicians, several hundred women participated in research designed to test the effectiveness of the drug after it was already in general use for the prevention of miscarriage. Those who were research subjects believe they or their daughters should be compensated for the unanticipated effects of the drug. Other organizations also urged that injured subjects receive compensation.<sup>22</sup> The Commission noted repeatedly that its task was not to resolve the merits of making payments for past injuries but rather to recommend policy for the future.

The Commission also requested reports on legal mechanisms for compensating for personal injury and the extent to which such remedies would be available in the case of research injuries. In addition, health policy analysts were asked to prepare a critical analysis of Federal programs that currently provide compensation or health benefits for certain classes of people (e.g., Federal employees, mine workers suffering from black lung disease, persons with end-stage kidney failure). The latter report examined the difficulties encountered in administering such programs and in containing their cost. Chapter Five contains a review of these materials.

Finally, a former Federal Insurance Administrator and others urged the Commission to consider carefully whether available data on nature and incidence of research injuries justify implementation of a program that might well be associated with high administrative expenses and substantial induced costs. The Commission's concern in this regard is reflected in Chapter Six.

In summary, the Commission received testimony from Federal officials, expert consultants, professional organizations, insurance industry officials and members of the general public at public hearings in January, May and September of 1980 and in January 1981. Commissioners deliberated during those meetings as well as in May and September 1981, while reviewing preliminary drafts of this document. Thus, major portions of six Commission meetings were devoted to review-

<sup>22</sup> See e.g., Testimony of Phyllis Wetherill, on behalf of the DES Registry, transcript of the 4th meeting of the President's Commission (September 15, 1980) at 212; Letter from Bennett Stark, founder National Committee for Victims of Human Research to Morris R. Abram (January 17, 1980); see Appendix T to this Report.

ing the materials, discussing the issues, and developing the recommendations contained in this Report.



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**Do Deserving Subjects  
Not Receive  
Compensation?**

**II**

## The Ethical Basis for Compensation

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Any policy on the possible compensation of injured research subjects must take into account many practical factors: the cost of such a program the program's vulnerability to abuse, technical difficulties in administration, and the political influence of those who would benefit and those whose budgets might be adversely affected. Behind these practical concerns, however, loom some basic ethical questions: Is there a moral responsibility to compensate research subjects for medical bills, lost wages, and other out-of-pocket costs that are a direct result of injuries sustained in research conducted or sponsored by the Federal government? Is the investigator's obligation limited to informing subjects of the risks? Or is the subject's consent insufficient to guarantee that no wrong is done? Is compensation for injury required as a matter of justice? If not, might it be morally important because of beneficial effects on society, or because it provides the opportunity to realize an ethical ideal other than justice?

Persons of good will differ in their beliefs concerning the moral importance of compensation of injured research subjects, and this division of opinion over the ethical issues explains some of the lack of consensus as to the need for and value of a compensation program. This chapter addresses the logic of the major distinctly ethical arguments voiced in favor of, and in opposition to, compensation for injured research subjects. The arguments are not definitive and thus will not overcome all doubts raised about research injury compensation. Rather, this exposition is intended to indicate the range of opinion reviewed by the Commission and to provide the reasoning behind the Commission's conclusions.

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### A Question of Justice

The basic case for a program of compensation for injured subjects can be stated briefly: Medical and scientific experimentation, even if carefully and cautiously conducted, carries certain inherent dangers. Experimentation has its victims, people who would not have suffered injury and disability were it not for society's desire for the fruits of research. Society does not have the privilege of asking whether this price should be paid; it is being paid. In the absence of a program of compensation of subjects, those who are injured bear both the physical burdens and the associated financial costs. The question of justice is why it should be these persons, rather than others, who are to be expected to absorb the financial, as well as the unavoidable human costs of the societal research enterprise which benefits everyone.

The argument in favor of compensating injured subjects proceeds from a simple rule of thumb for determining the justice of the distribution of burdens and benefits in contexts like that of medical research: those who receive the benefits should be those who undertake the risks. In some medical research, the subjects are patients who volunteer precisely because the experiment offers the greatest chance of cure; prospective benefits outweigh prospective risks and distributive justice is not a major concern. When, however, as is often the case in research with human subjects, those who bear the risks are not the direct beneficiaries of the research, it is felt that the scales of justice are out of balance. Institutional Review Boards and other protective mechanisms have been designed to ensure that the balance is thrown off-center as little as possible, consistent with the goal of permitting promising research to continue. Compensation may be regarded as a means of restoring the balance after the fact, when the residuum of risk not eliminated by the protective devices has eventuated in injury. Like the protective devices, compensation is a further means of limiting the burdens borne by individual subjects in research.

**The Argument from Fairness.** The ethical norms underlying most of the literature favoring a program of compensation is that of fairness, a key element in the concept of justice. One formulation of a principle of fairness was provided to the Commission, following the philosophers Hart and Rawls:

If there is a "mutually beneficial scheme of social cooperation," then "a person who has accepted the benefits of the scheme is bound by a duty of fair play to

do his part and not to take advantage of the free benefits by not cooperating."<sup>1</sup>

Stated as such, this is a principle of distributive justice: it dictates an assignment of benefits and burdens that is held to be just. This principle is invoked, for example, by moral and political theorists to justify the extraction of taxes from those who may never have signed an actual agreement to contribute to the state's budget. The idea is simply that if one benefits while others take their turns, then one too must take his or her turn. This notion of fairness appeals to an ideal of reciprocity in social relations, is discussed in Chapter One of this Report. In the research context, it is the government, representing the society, which must "take its turn." The research subject has contributed by exposing himself to risks, and the government must do its part.

Professor James Childress formulated for the HEW Task Force a related principle which called for compensation if:

- (1) The injured party accepts or is compelled to accept a position of risk...
- (2) The activity is for the benefit of society...
- (3) Society, through the government or its agencies, conducts, sponsors, or mandates the practice in question.<sup>2</sup>

If these features are present, then whether or not the injured party was a volunteer,

[t]he moral principle of fairness creates a societal obligation to this participant, who can claim as his *right not merely* consideration of damages but compensation at least for major injuries. The obligation is *voluntarily incurred* by the society, through its establishment, endorsement, or mandate of the practice in question, and its acceptance of the individual's participation, whether it drafts, encourages, or merely accepts him. This obligation is based on the *relationship* between the parties in question, not on the fact that society through biomedical research wrongfully injured the participant (which would have been a matter of reparative justice). It reflects the moral principle of fairness.<sup>3</sup>

Professor Childress's contribution seems to have been incorporated into the Task Force's official view, as expressed in the ethics chapter of its final Report:

[B]ecause society is both the beneficiary and the sponsor of research, compensatory justice (that form of

<sup>1</sup> Bernard Boxill, *Consent and Compensation*, (1980), Appendix C to this Report at 16 quoting John Rawls, *Legal Obligation and the Duty of Fair Play*, in Sidney Hook, ed., *LAW AND PHILOSOPHY*, New York University Press, New York (1964) at 9-10.

<sup>2</sup> James Childress, *Compensating Injured Research Subjects: I. The Moral Argument*, 6 HASTINGS CTR. REP. 21, 24 (December 1976).

<sup>3</sup> *Id.* (emphasis in the original; footnote omitted).



justice which seeks to redress injury even when no fault or blame is associated with the injury<sup>4</sup> may come into play for the redress of injuries suffered by persons in connection with biomedical or behavioral research conducted, supported, or regulated by the Federal Government.<sup>4</sup>

Another important precedent is the Veterans' Compensation for Service-Connected Disability or Death Program. The obligation here is toward those

who have entered into a special relationship of service to the American society, and who are, therefore, entitled to special compensation in the event of a service-connected disability. In short, the American society has recognized a special obligation to compensate veterans for injuries sustained in connection with their service since society is both sponsor and beneficiary of their services.<sup>5</sup>

Further, soldiers

...could sustain compensable injury—even serious injury or death—without anyone being guilty of negligence or any other tort. [S]ociety, through its governmental agents, has intervened in the lives of the injured individuals, and therefore society may be said to have an obligation to repair (so far as possible) injury done to individuals, whether they are volunteers or draftees, in connection with their service to society.<sup>6</sup>

The Task Force cautioned that "the analogy... is by no means perfect," but reported being "impressed by the obligation on the part of society to provide compensation..."<sup>7</sup>

The Task Force's desire to base its recommendation on an appeal to fairness has evident appropriateness and appeal. Though these principles of fairness do not command universal assent among contemporary moral or political theorists, they have received considerable support in leading theories of distributive justice. They provide a moral basis for government mechanisms necessary for the harmonious functioning of large and complex societies, which must proceed in the absence of an actual contract and which would be crippled if denied the means for dealing with the problems of "free riders" who would take advantage of others' contributions to the public good.

<sup>4</sup> HEW Secretary's Task Force on the Compensation of Injured Research Subjects, REPORT, U.S. Department of Health, Education, and Welfare, Washington (1977) (hereinafter cited as TASK FORCE REPORT) at VI-4.

<sup>5</sup> *Id.* at VI-2-3.

<sup>6</sup> *Id.* at VI-3.

<sup>7</sup> *Id.*

The point of the argument from fairness, then, is that the potential beneficiaries of medical research—which includes the entire citizenry—ought not have a “free ride” at the expense of injured research subjects. If the human costs of research are low—say, a matter of a little time and inconvenience—then the allocation of costs is not a serious ethical issue. When, however, higher costs are occasionally imposed, as in the case of injured subjects, the question “Who pays?” becomes important. Research subjects are already doing more than their share, merely by the fact of having volunteered. Those who are injured bear the greatest burden of all. According to this view, certainly, they are the *pari passu* appropriate parties to have to bear the financial costs of injury. Let those costs be shouldered by the potential beneficiaries who have contributed neither time nor health to the research effort. The society ought to meet this expense, through government action if necessary, in order to compensate the injured subjects.

The *CUA* of *Subject* Consenting Subjects as Free Agents. There is, however, another view which holds that a failure to compensate injured research subjects is necessarily an injustice. This view attempts to rebut the argument from fairness by stressing the possibility of informed consent to the risk of injury. Professor H. Tristram Engelhardt, who in his capacity for the Task Force argued in favor of compensation, stated that

[F]ree and informed consent would seem in most cases equivalent to waiver of any moral basis for a claim to recover for damages. Respect for freedom of the individual would include, as this argument would go, respect for that individual's freedom to choose to risk and suffer for others' benefit. When a human subject, who is sufficiently informed and who is free to choose, chooses in the absence of coercion to participate in an experiment, it would appear that the subject has given up any strict moral claim to compensation for damages and lost to being a subject in an experiment.<sup>2</sup>

Similarly, Callahan admits that

[i]t shows that an injured party voluntarily assumed a risk is owed a defense against that party's claim for reparation or compensatory justice.<sup>3</sup>

The moral principle underlying these statements is often given in its Latin formulation: *volenti non fit injuria*—there is no injury (for which another party is responsible) to one who consents. Its application in the research context appears

<sup>2</sup> H. Tristram Engelhardt, Jr., *A Study of the Federal Government's Ethical Obligations to Provide Compensation for Persons Injured in the Course of Their Participation in Research Supported by Funds Administered by the Secretary, HHS, TASK FORCE REPORT*, *supra* note 4, Appendix A at 48.

<sup>3</sup> Callahan, *supra* note 2, at 24.



straightforward: the subject is told of the risks; he consents to joining the experiment even though those risks are present, and he has not been promised any compensation. Why, then, would society be obligated to compensate in the case of injury?

The Task Force, after much debate, took a strong stand on this question:

Informed consent in the research setting functions as a recognition of and a protection for a person's integrity and autonomy, but does not imply a waiver of the right of the person to compensation in the event of injury.... Even if a subject perfectly understands a research procedure and agrees to participate in that procedure, the subject's consent does not, in and of itself, include, explicitly or implicitly, a waiver of compensation. [V]olunteers may give informed consent to participation in biomedical and behavioral research without thereby surrendering the right to be compensated should injury occur.<sup>20</sup>

But if, as the Task Force stated, one ought to respect the autonomy of the potential subject, it is at least initially difficult to understand why there is a moral requirement to compensate a subject who consents to participation without the expectation of compensation in case of injury. If respect for autonomy requires the subject's consent to be secured before using him or her as a research subject, why would that same respect not also require that the subject be permitted to agree to shoulder the risk of injury without the possibility of compensation?

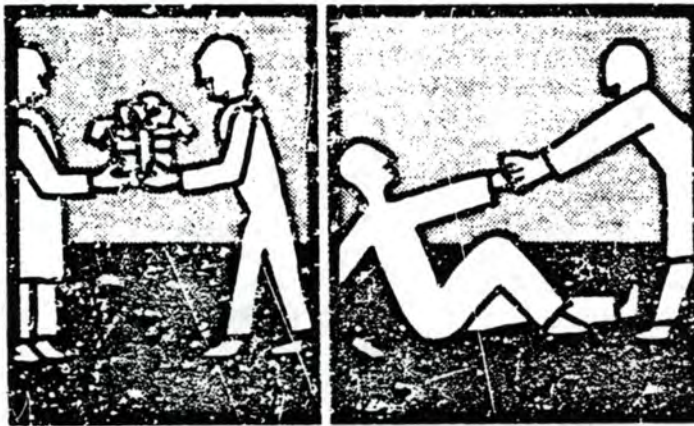
The Task Force, it must be recalled, was speaking of a consent form (and process) that merely listed the risks and benefits of procedures, together with a statement of certain rights of the patient having nothing to do with compensation. Perhaps it could be said of that consent form, and of the process of obtaining consent which the form records, that the signing and consenting did not amount to an assumption of responsibility for risk. Shortly after the Task Force's report, however, institutions receiving Federal funds for research were told to include an explicit statement on their policy of providing or not providing medical care and other compensation.<sup>21</sup> Thus the consent form became something closer to an explicit assumption of risk. And the forms could be made even clearer on this score—for example, with the addition of a sentence such as: "In signing this form I knowingly and freely assume all risks attendant to the nonnegligent conduct of this experiment and do not expect, and will not seek to hold others liable for, compensation in case of injury not resulting from negligence." In this latter instance, if not at present, it is

<sup>20</sup> TASK FORCE REPORT, *supra* note 4, at VI-5d.

<sup>21</sup> 43 FEDERAL REGISTER 51559 (November 2, 1978), now codified at 45 CFR §46.116(a)(3)(1981).

difficult to understand a contention that the subject's consent did not entail an assumption of risk.

Thus, there would seem to be an inconsistency in a position that would allow a subject of medical research to volunteer his or her time and comfort but not to assume the risk of possible injury. When the subject agrees to participate in an experiment, he or she voluntarily makes a gift to society of the time and inconvenience involved in participation, and agrees to bear any discomfort, which may be quite substantial. In some cases, subjects are paid for their time and trouble, but often they are not. One does not think that unless they are paid a sum proportional to their contribution, they have been treated unjustly. Indeed, subjects who are not paid may be especially admired. Their participation in the research is simply accepted as a gift.



A subject is, moreover, in a position to give still another gift. This is the gift of security, the assumption of the risk of injury without guarantee of compensation. Some potential subjects might be willing to give only the gift of their time and trouble, but others are willing to give not only that gift but also the gift of security. Why should it be considered unjust to accept the second gift if it is perfectly ethical to accept the first?

Whereas the Task Force asked whether volunteers must be compensated, the "free agent" view asks whether the government should be considered unjust if it refuses to accept volunteers who are unwilling to make the additional gift of their security. The government, that view holds, is under no obligation to accept as research subjects those who will not or cannot waive all rights to compensation if injured. As long as the government's needs can be met by accepting as volunteers only those who can pledge to forswear compensation if injured,



there is no injustice done to anyone by failing to compensate injured subjects.<sup>12</sup>

**Fairness vs. Consent.** These two perspectives on the question of whether failure to compensate injured subjects of medical research is unjust thus lead to quite different conclusions. The argument from fairness holds it to be unfair to impose the financial costs of injury upon those physically injured in the course of altruistic service to the community as research subjects. The second perspective stresses the freedom of citizens to volunteer their security as well as their convenience. As long as subjects make their choices freely, no injustice is done if only those subjects are accepted who assume responsibility for the cost of injuries.

Which of these two perspectives ought to be adopted in the case of research-related injuries? The Commission recognizes that each is worthy of serious consideration, and further recognizes that the divergence of views on the matter of compensation of subjects is but one instance of a divergence in thinking about social justice generally.

The fairness argument, stated in isolation, seems particularly convincing. It is, intuitively, quite unfitting that persons already injured should be saddled with the attendant costs; and it is equally unfitting that potential subjects be asked to agree to assume those costs as a condition of being enrolled in research. This view of justice prevails in many other contexts. Soldiers and other Federal employees, for example, are not asked to waive rights to compensation if injured on the job, even though it might be possible to recruit persons for these positions even were such a waiver required. Indeed, even private employers are not permitted to ask employees to waive coverage under Workmen's Compensation programs. The question of what would constitute a just distribution of burdens and benefits is decided in these other contexts before it is asked whether a waiver could be obtained; what matters is less whether an employee would agree to be denied compensation than whether this should even be asked.

When one fails to compensate injured subjects, though fiscal resources are available, one does not display the virtue of charity. Indeed, since the need arises because these subjects have displayed their concern for others by becoming subjects, a failure to compensate is distinctly uncharitable. The core question, however, is whether failure to compensate is not only uncharitable but unjust. A definitive answer would, it seems require the Commission to choose between the rival views of

<sup>12</sup> This is not to argue that compensation would violate any right of prospective patients to take chances. The regulations governing use of human subjects are in many respects protective of subjects regardless of their willingness to accept risks. The argument here is, rather, that the government is not being unjust in being unprotective.



justice: one emphasizing the achievement of an equitable pattern of distribution of the benefits and costs of research, the other stressing the transactions of free agents, whatever the resulting distribution. On the former view, the government has a strict obligation to compensate injured subjects, and its present failure to do so constitutes an injustice. On the latter view, uncompensated, injured subjects suffer no injustice so long as they freely and knowingly assumed responsibility for these costs before joining the experiment in which they were injured. Failure to compensate would then at most constitute a deficit in charity or benevolence.

Several serious reservations about the consent that is obtained from subjects make the latter view less convincing to the Commission. First, the consent argument's appeal to the notion of a gift freely offered would be strongest if the research subject were offered at the time he or she agreed to participate the alternatives of either having or not having compensation available should injury result.<sup>13</sup> If subjects then reject the promise of compensation, they would appear to wish to donate

<sup>13</sup> A contrary-to-fact hypothetical might help to clarify this point. Suppose that a private insurance company were willing to sell insurance policies to individuals for individual research projects and found a means to do so which did not involve large transaction costs. The policies would compensate the subjects in case of injury, just as the program recommended by the Task Force would do. Imagine that a given subject is first asked to volunteer for a medium-risk study, and at the same time asked to buy his own insurance policy. The terms of the request, then, are that the subject donate his time and trouble, and that in addition he pay out the (say) additional \$1.50 that the insurance company charges for insuring him. The researcher accepts no volunteers who are unwilling to donate the \$1.50 along with the time and trouble. One may suppose further that the researcher has no problem in finding enough people of good will and adequate pocket money for the experiment.

The terms of the subject's agreement in this hypothetical would be perfectly and obviously just, in the view of those who construe consent as involving assumption of risk. Perhaps not everyone would be willing to volunteer for experiments if they had to buy an individual insurance policy as a condition for joining. But if they did, they will not have been treated unjustly. Again, if it is morally acceptable for them to volunteer their time and trouble, it must be morally acceptable for them to volunteer the extra \$1.50. And if they were insured by a private insurer, there would be no apparent need for any government compensation program, even though the subjects may be injured in an experiment designed to benefit society generally and conducted or sponsored by the government.

The contrariness-to-fact of this hypothetical deserves emphasis. The Commission has investigated the possibility of providing subjects with the chance to purchase individual insurance policies at the time of enrollment in research projects. The Commission's consultants have reported that such a scheme would be utterly impractical. Thus, if no compensation program is undertaken by research institutions or



both their time and their security. But in the absence of such an offer of future compensation, one cannot conclude that the consent of subjects who wish to aid research indicates their desire to make the additional gift of their security. Moreover, if injured subjects would accept compensation were it offered, then it would appear that they did not wish to make the gift of their security. This is not to say that consent could not be valid without an offer of compensation, but it does suggest that an element of capitalizing on subjects' desire to help science may sometimes occur.

Many subjects will have an altruistic desire to aid research by offering their time, together with a personal desire not to put their security at risk. If the research investigator and the government can afford to offer compensation for injury, but refuse to do so knowing that they will still obtain volunteers, they thereby exploit the altruistic motivation of volunteers: when a subject gives the willing gift of his or her time, the unwilling gift of his or her security is extracted as well. If exploitation is a form of unfair taking advantage of another, then the government or researcher may act unfairly in asking for volunteers while refusing them the possibility of compensation for injury.

In particular cases, there may be no ground for concern over the moral sufficiency of consent—for example, when an intelligent, financially secure, educated adult agrees to undertake a small, accurately estimated risk of a minor harm of known character. But rules concerning compensation of subjects will not, as a practical matter, be able to distinguish these simple cases from the more difficult ones and the conditions of less-than-ideal consent are present often enough that the difficulties should be taken into account in formulating policy.

In many experiments, the risks are not well known. A treatment may be so new that the pattern of adverse reactions or side effects has not been established, nor will it be possible to determine whether a given subject is at especially high risk for these harms. Remote risks of serious harms are especially likely to attend experimental procedures. Consent in such cases is necessarily somewhat blind, and true appreciation of risk is doubtful, even for ideally competent subjects. Further, there is accumulating evidence that people do not perform well in calculating the expected utilities of events with small probabilities of occurrence.<sup>14</sup> Events of different orders of magnitude of probability may be given the single rating of "unlikely." Assigning full responsibility to the subject for

by the government, subjects will continue to be uninsured for lost wages, and, for those having inadequate health insurance, for medical bills resulting from research injuries.

<sup>14</sup> Amos Tversky and Daniel Kahneman, *The Framing of Decision and the Psychology of Choice*, 211 *SCIENCE* 453 (1981).

assumption of remote, but serious, risks of research thus takes on the air of exploitation of known weaknesses.

In the case of remote risks, when subjects agree to participate without compensation for injury, their gift of security is a small one because the substantial harm that might ensue is discounted for its low probability. For the unfortunate few subjects for whom the harm later materializes, however, an uncompensated injury dramatically increases the size of their gift to the research enterprise. While they agreed at the outset to bear the injury without compensation should it occur, one may reasonably conclude that they did not expect it to occur and did not truly intend to make this larger gift.<sup>15</sup> Viewing the exchange in this light helps to account for some lingering sense that even allowing for the subject's valid consent to participate without compensation for injury, it is unfair for them to have to bear such a substantial burden. It may also help explain the strong obligation felt by many people (including many researchers) to provide compensation in order to "repay" this gift (as noted in the discussion of the gift relationship in Chapter One), since the gift is not only large but probably more than the subjects initially intended to make.

To these difficulties may be added a host of standard complaints about the consent process. Patients who are subjects are sometimes, despite recitations of subjects' rights, in fear of displeasing their care-givers and hence in a dependent and unfree relationship. Patients are often agitated and distraught because of the very medical condition that qualifies them for an experiment. Moreover, a significant number of subjects, including children, the severely retarded, and the senile, are simply incompetent. The propriety of altruism-by-proxy which may be asked of these subjects is not established, even for the small risks permitted by the HHS regulations.

It can be presumed that under the current regulatory system, consent to treatment in most research involving human subjects meets the standards upon which society insists for valid transactions in other contexts, such as commerce. Indeed, the knowledge, competence, and independence of the contracting parties in society generally are seldom scrutinized as closely as are those qualities of potential subjects in biomedical

<sup>15</sup> Thus, injuries that arise because of unanticipated risks would seem to be more deserving of redress than those that arise from risks the subject knew about. One might wish, therefore, to experiment with a program in which eligibility depends on the type of risk manifested, but such a division would appear to be too complicated. Instead, it seems more sensible simply to regard all serious injuries to be, in some very real sense, "unanticipated" by those who suffer them. Like many other factors, the issue of unanticipated risks serves as a reminder of the ethical problems with placing too heavy reliance on the notion of "voluntary, informed consent" in the sense of a forced waiver of any claim for recompense for research injuries.



cal research. Nevertheless, it is fitting to use a higher moral standard in the research context. The goals of human health and well-being that motivate research ought to be reflected as well in a higher moral standard than the *caveat emptor* of the marketplace.

### Additional Reasons for Compensation

In addition to arguments based upon justice, there are at least two other moral grounds for a program of compensation.

**Appropriate Regard for Patient-Subjects' Well-Being.** Justice is not the only standard of morality. There are acts, or failures to act, that are surely wrong even though they violate no one's rights and are not instances of injustice. Acts can be mean-spirited, selfish, cheap, irresponsible, though they comply with the rules of conduct required by justice.

Ordinary English does not provide a precise vocabulary in which to distinguish these sorts of wrongs, nor does moral theory itself speak with one voice—in part because the classifications are matters of substance as well as semantics. Still, it is worthwhile to make a rough distinction between considerations of justice and other, still important, moral considerations. As regards the present subject, the most important such consideration would be the distress of anyone injured in the course of research who was faced with large medical bills and loss of income due to research-related disability. Such instances of need suggest the simplest of all arguments for a program of compensation: the serious need of those few injured in research can be met without untoward expense or difficulty by a program administered through research institutions. If, as Henry Beecher wrote, medical experimentation must be "ethical in its inception,"<sup>16</sup> then, one may add, it must also be ethical in its consequences. A program of compensation for research-related injuries would help to ensure that the consequences of research would be good ones rather than bad. In this view, not to adopt such a program would be a selfish and cheap or even irresponsible disregard of patient-subjects' well-being.

Of course, this argument is unduly simple. The claim advanced is not in itself sufficient to establish the rightness of enacting a compensation program, although it *may* lend support to a decision that rests on a stronger moral claim. But it depends on showing that a serious need of injured subjects can be met without imposing disproportionate burdens on others. One is, after all, not considered irresponsible for failing to do something heroic, only for failing to meet a great need without great cost to oneself.

<sup>16</sup> Henry K. Beecher, *Ethics and Clinical Research*, 274 *NEW ENG. J. MED.* 1354, 1360 (1966).

**Public Conceptions of Justice.** Although the moral sensibilities of the public on this issue are not known, there are certain indirect indications that lack of compensation of injured subjects is, or would be, seen as wrong. A television documentary on injured subjects, for example, stressed the lack of compensation as one of the wrongs perpetrated.<sup>17</sup> And the government gave considerable publicity to its efforts to locate and compensate the victims in certain widely reported cases of research-related injury.<sup>18</sup> Finally, many individual researchers provide the immediate medical care needed by injured subjects, presumably because they feel some sort of moral obligation, even though they are (as a matter of their "contract" with the subjects) under no legal obligation to provide such free treatment.

Thus, whether or not the moral argument in favor of an obligation to compensate is compelling, many members of the public subscribe to it. Even those who are not themselves convinced that failing to compensate injured subjects is a true injustice may not wish to see their government involved in an action that has even the appearance of an injustice.

If, then, research injuries come to public attention yet remain uncompensated, public support for research with human subjects might be reduced. Failure to redress injuries, particularly if they are large, could be taken as evidence that those who direct the research enterprise do not have as strong an interest in the well-being of their research subjects as they do for their scientific endeavors. The resulting erosion of confidence that scientists and the public share an identity of goals could result in a climate of opinion inimical to research and, indeed, to all risk-taking for public benefit. This result might satisfy those whose sole agenda is the protection of subjects from risks, but it would work to the detriment of society as a whole.

Research on human subjects, if done as part of a broad attack on disease, is of necessity risk-laden. The public, if it is to support this enterprise, must find the human costs tolerable. It will be more likely to do so if the costs are widely shared through a program of compensation of subjects who are injured in research. The moral importance of medical research—a value worthy of respect and protection—thus adds weight to a conclusion in favor of compensation for research injuries.

### **Obligations to Subjects in Therapeutic Research**

A crucial issue is whether compensation is owed to all subjects whose medical condition worsens in some respect in

<sup>17</sup> *Mission: Mind Control*, produced by Paul Attmeyer, American Broadcasting Company, January 30, 1979.

<sup>18</sup> See, e.g., James H. Jones, *BAD BLOOD*, Free Press, New York (1981) at 217-12.



the course of research. The ethical arguments already developed are premised upon some notion of sacrifice, of giving a benefit to the whole. This situation is met most clearly by subjects in "nontherapeutic research" who undergo procedures unconnected with their own condition (indeed, they are often "normal volunteers").

At first sight, "therapeutic research"—that is, an experiment designed to gain generalizable knowledge about a medical intervention by employing it under controlled conditions with a group of patient-subjects—would appear to be disqualified ethically because participating subjects may be seeking benefit for themselves as patients rather than being solely vessels through which knowledge can flow to others. This view would treat therapeutic research as an example of ordinary (albeit innovative) therapy for purposes of compensation; patients who become subjects are seen as taking no greater risk than they would otherwise face in dealing with their illness.

The distinction between therapeutic research and innovative therapy is a narrow one. In innovative therapy, a physician is simply trying something new to benefit the patient often because existing remedies have failed. In therapeutic research, a physician-investigator follows a research protocol in order to produce generalizable knowledge through testing out a medical intervention that, it is hoped, may be of benefit. This goal creates at least a potential conflict of interest on the part of the physician-investigator, over and above any hazards inherent in the particular study design. Each patient who is also a research subject is exposed to the possibility that the procedures most conducive to his recovery will be altered so that the research program can best be carried out (for example, that random assignment will remove the possibility of access to certain procedures).<sup>19</sup> The patient could avoid this jeopardy by seeking the innovative therapy outside of the research context, where this is available. Where the patient instead decides to become

<sup>19</sup> The considerations set forth here do not require compensation of the subjects who experience poorer outcomes in randomized trials in cases in which all arms had equal chances of therapeutic success. This will be true even if most or all of the enrollees in one of the arms do much less well than those in the other arms, and even if those who do less well would have done better had they received standard therapy outside of the experiment. The reason is that the subjects, at the time of entry into the study, did not take positions of added risk: as far as could be ascertained, each arm was as likely as were the others to turn out to be the best one. (Where the arms of the randomized trial are not of equal expected therapeutic value, of course, the arguments in favor of compensating might apply.) Hence there would be no sacrifice imposed on the subjects by the study, nor would there be an act of altruism involved in enrolling, unless there were added dangers from any incidental procedures, added to the patients' treatment solely for research reasons.

the subject of therapeutic research, he or she makes a gift (however slight) of some of his or her security to the larger society.

Moreover, some therapeutic research will not offer a patient his or her best chance for recovery. It is, furthermore, quite common for therapeutic experiments to involve procedures, especially tests, that are performed only for scientific reasons. In all of these cases, the medical intervention being studied may be intended to be "therapeutic" for the patient-subject, but compensation for injuries would rest on the same footing as for nontherapeutic research: the patient is making a contribution to society.

### Conclusions

A program of compensating for research injuries will help to equalize the burdens of progress in this field that would otherwise fall very unevenly on people. Competing conceptions of justice lead to contrary conclusions about whether justice requires that such a program be adopted. Fairness argues for compensation, but the alternative argument from the consent of free agents denies this. Although, for both philosophical and practical reasons, it is not persuaded by the latter argument, the Commission does not hold that compensation is a basic right (such as the right to a fair trial), to be provided regardless of cost, practicality, or other policy considerations. The arguments for compensation of injured subjects on fairness grounds simply do not establish so strict an obligation.

Several additional considerations add weight to the arguments for compensation beyond the notion of fairness, both in ethical theory and in the public perception of the government's stance. First, the moral claims of charity and generosity ought not to be ignored—although the obligations they create have inherent limits, for one is not judged wrong in failing to be heroic. Second, the frailties of the consent process, especially with regard to small risks of serious harm, weigh heavily as a reason for added "protection" in the form of after-the-fact recompense at least for any serious harms experienced by subjects.<sup>20</sup>

<sup>20</sup> A further benefit of a general program of compensation would be a partial amelioration of certain harms visited by unethical research practices. The overwhelming majority of research subjects are recruited under honorable conditions. Research scientists, while having a research agenda in addition to any therapeutic relationship with a potential subject, have generally been as solicitous of patient welfare as they would be for their own. The current review process is in place, however, because there have been exceptions. Only a few cases have come to light, but there does not exist a means of monitoring the actual consent process closely enough to deter a scientist determined to break the rules. Further, studies of the incidence of injury have relied heavily on reporting by those who would have caused the



The Commission concludes that compensation of injured subjects is appropriate to the research enterprise. A program to assure compensation is thus a desirable policy goal for a just and compassionate government, both as the sponsor of most biomedical and behavioral research and as the means through which society acts on matters of common interest, such as the search for new biomedical discoveries. Whether a program should be adopted depends on the need for it (Chapter Four) and the alternative means (Chapter Five), and upon whether the program's transaction costs, vulnerability to abuse, or difficulty of administration would be disproportionate to the ethical problems at which the program would be aimed (Chapter Six). Moreover, a full evaluation of the ethical arguments for and against compensation for research injuries must take these practical considerations into account. Such practicalities are in themselves ethical matters because they turn on questions of the fair allocation of resources, the potential impact of a program on the rights of other parties, and horizontal equity with persons suffering from other misfortunes.

injuries. Thus there is some cause for concern over injury due to participation in research under fraudulent conditions, as when potential benefits are exaggerated or risks are undisclosed.

There are existing legal remedies for harms visited upon subjects through deception and fraud, and it would be convenient for the Commission to be able to formulate its recommendations without having to consider these cases. It is reasonable, however, to ask whether the existing legal protection is adequate, and, if not, to suggest policies which might help to protect subjects. A general program of compensation of subjects injured in research would provide a partial remedy for the problem of injuries to subjects recruited through deception, and the Commission counts this as a point in favor of a compensation program.

## The Nature and Extent of Research-Related Injuries

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In pursuit of an answer to the underlying question at issue—should there be a compensation program for research injuries?—the preceding chapter established that some subjects may “deserve” such compensation if injured. In this chapter the Commission turns to the next part of the overall question and examines how many subjects are injured and how severely. Given the extent of Federal involvement in the research enterprise, surprisingly little is known about either the magnitude of the problem of injury to subjects or the nature of the injuries. The Commission sponsored two studies of the incidence of injuries at research institutions with existing compensation programs. These studies do not provide definitive answers at the national level, but are suggestive of the nature and scope of the problem. Taken together with data from other sources, they provide a basis for several modest, but important, conclusions:

- (1) the incidence of serious injury and the absolute numbers of people seriously injured are small;
- (2) most injuries are trivial in nature and require no medical intervention;
- (3) of those injuries that require intervention, most are only temporarily disabling;
- (4) most serious injuries and fatalities associated with research are more likely to result from underlying disease than from the research *per se*;
- (5) patient-subjects in therapeutic research are more likely than normal subjects in nontherapeutic research to suffer injury; and
- (6) the existence of compensation programs does not stimulate excessive or unmerited claims of injury.



Before examining the data on research-related injury, it is important to note that there is no agreed-upon use of the term "research injury." No attempt is made in this chapter to specify the term definitively. Rather, in reviewing previous studies, the definitions used in each will be noted in order to avoid spurious comparisons. Many quite disparate definitions have been employed for various purposes. In different contexts, "injury" has been used to denote (or, in some instances, has merely not been clearly distinguished from) "adverse effect," "clinical event," "significant medical event," "complication," and "unanticipated consequence."<sup>1</sup>

Many studies employ some scale of seriousness to distinguish among the consequences of research. Such distinctions tend to be made along a dimension of disability (*i.e.*, trivial, temporarily disabling, permanently disabling or fatal) or to be operationalized in terms of the amount of medical care needed as measured either by the extent of the intervention (no treatment, physician intervention, referral, hospitalizations) or by the "cost" of that intervention (which may or may not include lost earnings as well as medical care costs).<sup>2</sup>

The lack of a uniform definition of injury makes it difficult to compare reports on the consequences of research. Keeping this potentially serious limitation in mind, the Commission analyzed data from many sources in order to try to determine whether injuries of any significance (either in terms of frequency or seriousness) are occurring in research with human beings in such a way that a general compensation program for such research would appear to be needed. Correlatively, are the injuries that occur of such an extent that compensation could be paid without overburdening the research enterprise?

It would seem that the most relevant data to answer these questions would come from institutions with compensation programs already in place. Since no published information was available from these programs, the Commission solicited reports from the University of Washington in Seattle and the Quincy Research Center in Kansas City, Missouri. Data from

<sup>1</sup> In Phase 1 drug trials, for example, it may be appropriate and necessary to note all "events," including consequences of the drugs and intercurrent illness, but such "events" are not the same as research-related injuries. Furthermore, some of the terms used to connote injury actually precede injury in time. That is, a "complication" may, if it is not handled correctly, become an injury and therefore be only an indirect consequence of the research. Although it is important for informed consent and IRB clearance to indicate what are considered to be possible (hence anticipated) consequences of the research, and it is important for scientific purposes to take account of unanticipated consequences of research, these are not the same as research-related injuries. For discussions of injury it is the seriousness of the consequence, not its predictability, which is important.

<sup>2</sup> Office of Technology Assessment, U.S. Congress, *COMPENSATION FOR VACCINE-RELATED INJURIES* (1980).

these reports were compared with existing data from other sources, including a previously published longitudinal study of a drug testing facility in Michigan, and broad-based data from multiple institutions.

### Longitudinal Institutional Studies

The University of Washington in Seattle and the Quincy Research Center in Kansas City, Missouri, reported their data regarding numbers of subjects covered and the kinds of research in which they were involved, the nature and incidence of injury, the number of claims made (and paid) for medical care or compensation, and the cost of the insurance program. Data from the two programs are not fully comparable because the University of Washington is a general research facility while Quincy is a drug testing facility and because of different definitions of injury. Nonetheless the programs are large enough to generate data that are suggestive of the extent and nature of research-related injury and these data seem to be corroborated by other reports.

**General Research Program: University of Washington, Seattle.** Diana McCann and John Pettit, of the University of Washington at Seattle, analyzed records for the years 1972-1981 during which an estimated 356,000 subjects on more than 5300 protocols for biomedical research were covered by the university's compensation program.<sup>3</sup> During that period, investigators were required to submit detailed reports to the Human Subjects Review Office on the subjects involved in their research and any adverse effects experienced by those subjects that were possibly related to their participation in the research.<sup>4</sup>

McCann and Pettit reported that for the year prior to the establishment of the insurance program, survey data indicate adverse effects in 4.6% of the studies (5 out of 110) involving 0.07% of the subjects (10 out of 14,942). None of the subjects were partially or permanently disabled and no deaths were reported.

This exceptionally low rate of injury could be accurate or may be partly an artifact of the retrospective survey. Since the insurance program began, the university has had two means of reporting adverse effects internally. An "Adverse Effect Report" is used when there is a likelihood of a claim against the

<sup>3</sup> Diana McCann and John R. Pettit, *A Report on Adverse Effects Insurance for Human Subjects* (1980); see Appendix H to this Report. The data were updated by Ms. McCann in February 1982.

<sup>4</sup> It is noteworthy that even where a compensation program exists at a single institution, the precise number of research subjects is not known. It should also be noted that subjects participating in behavioral research have been excluded from the compensation program since the second year of the program.



university, while a "Status Report" is required on an annual basis for all adverse effects. The former has been used and are summarized for nine years; the latter have been in effect for only four years. Although the reports provide details about the nature of the adverse effects, they are often vague with respect to the numbers of subjects who experienced particular adverse effects, making it very difficult to calculate incidence rates. Fortunately, for purposes of this Report, most of these imprecisions appear in reports of effects that were merely transient and trivial.

A further difficulty in interpreting the data reported by McCann and Pettit arises from the ambiguous use of the phrase "adverse effect." Whether an adverse effect means both "anticipated" and "unanticipated" consequences or just unanticipated consequences has not been resolved by the institution. At present, current policy allows individual investigators to report whichever they prefer. In the adverse effects and status reports, therefore, the term is apparently used in both ways.

The Commission staff reviewed the descriptive information accompanying the data for each of the status reports; the incidents listed there as "adverse effects" were more numerous than those reported separately on "adverse effects" forms. Omitting "trivial" injuries (such as headache, nausea, dizziness, soreness and other transitory symptoms not requiring medical intervention) the staff calculated that in the first eight years 144 subjects (or 0.04% of the estimated total of 358,000) experienced temporary disability; none were permanently disabled and two patient-subjects died. Most of those who experienced injury were patient-subjects with existing disease.

Reports on 34 "adverse effects" of research (involving 42 subjects) were filed with the university's Human Subjects Office in the first nine and one-half years of the compensation program, but only 18 claims for compensation were submitted. The small size of this figure is probably due to a combination of factors. First, although subjects are told that medical care is available in case of injury, they are not specifically informed of the existence of the formal compensation program; second, claims are normally initiated by investigators; and finally, there are informal mechanisms for handling some injuries. About the final point, McCann and Pettit report:

It is known that some medical care and other professional services are provided to subjects who experience both anticipated and unanticipated adverse effects for which no claim is made against the adverse effects compensation program.... How such care is financed or accounted for is not reported to a central office, therefore this information is not available. The following means are likely: time donated by the health professional; costs absorbed by a grant or contract, as appropriate,

e.g., the Clinical Research Center, and reciprocal services provided within the health professions.<sup>5</sup>

It has taken some time for the program to become well established at the university, and the rate of claims has picked up in the last several years.

In all cases in which an injury is found to have been related to the research procedure, some payment has been made. Most have been very modest (from \$2 to \$249 for expenses); until recently, the largest payment made was \$1550. A claim for an injury that resulted from contamination of the equipment used in an experiment has now been settled for \$10,000. Six of the 42 injuries were reported as "not related" to the research project; only in one case did the subject file a claim, which is the only claim of the 13 in which payment has not been made.

**Nontherapeutic and Therapeutic Drug Testing: Quincy Research Center.** A second report was prepared by John Arnold, M.D., Director of the Quincy Research Center in Kansas City, Missouri, a drug testing facility whose subjects have been covered by a workers' compensation program since 1975.<sup>6</sup> Because much of the research at Quincy is performed to support applications for new drug licenses, careful reports are kept of the number of subjects involved in each protocol, the duration of their participation in each research project and all "clinical events" (including intercurrent illnesses such as colds, flu, appendicitis, drunkenness, toothache, eye surgery, etc.)

Data reported by Dr. Arnold are from 151 Phase 1 (nontherapeutic) projects involving 2596 normal volunteers, and 78 Phase 2-4 (therapeutic) projects involving 2478 patient volunteers.<sup>7</sup> Simple frequency counts of undifferentiated "clinical events" as well as "significant clinical events with sequelae" are reported for both study types and subject categories. Both the total number of clinical events and the number of serious events are greater in Phase 2-4 studies with patient-subjects than in Phase 1 studies with normal volunteers. Patient-subjects are more likely than normal subjects to withdraw from protocols because of significant clinical events and, although the incidence rates are very low, patients are

<sup>5</sup> McCann and Pettit, *supra* note 3, at 27.

<sup>6</sup> John D. Arnold, *Incidence of Injury During Clinical Pharmacology Research and Indemnification of Injured Research Subjects at the Quincy Research Center* (1980); see Appendix I to this Report.

<sup>7</sup> Phase 1 studies are used to determine toxic dosage and pharmacological actions of drugs such as metabolism, absorption and elimination. Phase 2 trials are conducted on a limited number of patients to evaluate specific disease treatment or prevention. Phase 3 and 4 studies involve extensive clinical trials to assess safety, effectiveness and optimal dosage levels for treating specific diseases. The phases proceed sequentially.



more likely to be hospitalized (1.43% vs. 0.2%) and to die (0.24% vs. 0).

It appears that most of the clinically significant side effects occurred because of preexisting disease in patient-subjects rather than as a direct consequence of the experimental drugs or participation in the research. None of the six deaths and only seven of the 38 hospitalizations could conceivably have been research-related, whereas three of the five hospitalizations for normal volunteers could have been as a consequence of the research. From these data Dr. Arnold concluded that the conduct of Phase 2 through 4 protocols is "inherently beset by greater incidences of primary disease states in outpatient participants" for three reasons. First, the testing of drugs and devices for "efficacy" requires preexisting disease states in selected participants; second, testing under these protocols involves research participation of greater than average duration; and third, the subjects tend to be of more advanced age.

A second conclusion from the data from the Quincy Center derives from the fact that normal volunteers are more likely than patient volunteers to be referred for medical care as a result of significant clinical events. In addition, protocol termination and alteration of protocol designs are more likely in Phase 2 studies than in Phase 3-4 studies.

The available data on significant clinical events with participant and protocol sequelae support the conclusion that the incidence of drug- and participation-related events is higher in Phase 1 protocols employing normal participants by reason of heretofore undiscovered drug effects that are toxic to a greater or lesser extent to human subjects. By employing normal adult male subjects for the conduct of Phase 1 protocols, these events were more easily and immediately resolved via therapeutic intervention and additional physician consultation and resulted in a minimization of the amount of actual risk to participants and additional sequelae such as early termination from protocol and/or hospitalization. Thus, Phase 2 data indicate that normal male participants were able to tolerate the ultimate hazards of early Phase 1 drug testing without serious sequelae, as evidenced by findings of no deaths and few hospitalizations but increases in participant referrals for additional medical care and physician consultations. We believe the same drug-related complications would have been fatal or very serious in ill outpatients.<sup>9</sup>

A third suggestion from Dr. Arnold's data is that the number of clinical events is directly proportional to the length of exposure. The average number of days on protocols was

<sup>9</sup> Arnold, *supra* note 8 at 12.

<sup>10</sup> *Id.* at 30.

almost twice as great for patients than for normal subjects (25 vs. 14 days) and on the average, patients had 35% more clinical events per participant.<sup>10</sup> Obviously, existing illness is a confounding variable in trying to ascertain the relationship between risk exposure and injury; the illness itself can worsen over time thereby leading to its own effects and rendering the patient-subject more susceptible to injury. When injury occurs, it may be difficult to differentiate whether it is due to the preexisting illness or to the intervention.

**Nontherapeutic Drug Testing: Michigan State Prison.** A previously published study of research injuries was conducted by Dr. Chris Zarafonitis and other members of the Protocol Review Protection Committee for the State of Michigan Department of Corrections.<sup>11</sup> They examined clinically significant adverse effects in a Phase 1 drug testing program involving normal prison volunteers during a twelve-year period from 1964-1976. Records were reviewed for 805 protocols involving 29,162 participants over 614,534 subject days.

The authors reported 58 adverse drug reactions and six additional "complications" temporally related to the drug study, forming a total of 64 subjects (.2%) who experienced "significant medical events" (i.e., "the associated appearance of objective clinical signs or laboratory abnormalities; and sufficient discomfort, hazard, or potential hazard to require physical intervention, e.g., to stop test drug, initiate appropriate therapy, and follow-up to recovery or other outcome"). None of the adverse reactions and only one of the complications were permanently disabling; one subject, on placebo, died of cerebrovascular hemorrhage while asleep. Thus, a clinically significant medical event occurred once every 9602 days of subject exposure or about once every 26.3 years of individual subject participation.

Although the data from the three institutional studies are quite consistent, it is important to compare these with data from a broader base in order to determine how representative these particular institutions are of the research universe.

### Broadly Based Sources of Data

Since American society has been providing extensive governmental support for research for many years, a logical source of data to answer questions about the overall incidence

<sup>10</sup> McCann and Pettit also reported longer average risk duration for patients than for normal volunteers although it was found to be highly variable (3 to 20 times greater) depending on the particular mix of research projects in any one year.

<sup>11</sup> Chris J. D. Zarafonitis, Philip A. Riley, Park W. Willis, Lawrence H. Power, Judson Werbelow, Leo Farhat, Wendall Beckwith and Bernard H. Marks. *Clinically Significant Adverse Effects in a Phase 1 Testing Program*. 24 CLIN. PHARM. & THER. 127 (1978).



of injuries would be the Federal agencies that conduct, support or regulate research. Unfortunately, very little retrospective data is available from Federal sources.

An alternative method would be to follow a prospective approach. Rather than count up the number of injuries that have occurred in a particular period in the past, one could estimate the number that can be expected to occur in the future. To do this, one would have to know the total number of human subjects participating in research, the portion involved in various types of research, and the probability and severity (collectively termed "risk") of injury associated with each type of research. Again, the facts needed to carry out this approach appear to be lacking.

**Government-Reported Incidence of Harm.** The Commission has found that data on research-related injuries and on research subjects generally are extremely limited in terms of both the amount of information available and its generalizability.<sup>12</sup> Despite the very major role of the government in research, there is no comprehensive Federal mechanism for collecting data on injuries. In response to direct inquiries, officials from FDA and NIH testified that neither agency compiles such information. In addition, of the more than twenty other Federal agencies that conduct or support research with human subjects, only one (the National Bureau of Standards) was able to provide the Commission with information on either the nature or the incidence of injuries experienced by subjects in research conducted under its auspices.<sup>13</sup> Neither the government as a whole nor the individual agencies have data on the number or kind of injuries sustained by subjects of Federally conducted, supported, or regulated research.

The only Federal attempt to collect and analyze data on research injuries was a special study conducted in 1976 by Philippe Cardon and his associates for the HEW Secretary's Task Force on the Compensation of Injured Research Subjects.<sup>14</sup> In a telephone survey, investigators were asked to report the number of subjects involved in therapeutic and in nontherapeutic studies, the nature and incidence of injuries "that could be attributed to the conduct of the experimental regimen," and whether those injuries were experienced by

<sup>12</sup> See the Commission's Biennial Report on PROTECTING HUMAN SUBJECTS, Government Printing Office, Washington (1981), for findings and recommendations on data on research participation and injuries.

<sup>13</sup> The agency reported two injuries since 1975: one subject who fell while testing emergency egress from mobile homes and one who allegedly injured his back during research to establish portability guidelines for the FTC.

<sup>14</sup> Philippe V. Cardon, F. William Dommel, Jr. and Robert R. Trumble, *Injuries to Research Subjects: A Survey of Investigators*, 295 NEW ENG. J. MED. 650 (1976) (report prepared for the HEW Secretary's Task Force on the Compensation of Injured Research Subjects).

subjects of therapeutic or nontherapeutic research. Injuries were classified as: trivial, temporarily disabling, permanently disabling, and fatal.

Investigators reported on a total of 132,615 subjects. Overall, 3.0% of the subjects experienced trivial adverse effects, 0.7% experienced temporarily disabling injuries, less than 0.1% were permanently disabled and 0.03% died. (All of the fatalities occurred in patient-subjects in therapeutic research.) Of the more than 39,000 subjects participating in therapeutic research studies, 10.8% experienced adverse effects or injuries most of which were trivial in nature. Only 2.4% of subjects were temporarily disabled, less than 0.1% were permanently disabled and approximately 0.1% died. Most of the 43 fatalities were not clearly related to the research. In fact, 37 (86%) of the reported deaths were in cancer chemotherapy trials. In the other categories as well, many of the "injured" were cancer patients who experienced familiar side effects of standard treatment. The incidence of injury for subjects participating in nontherapeutic research was even lower. Of 93,399 subjects, only 8.8% experienced injuries, most of which were trivial. Thirty-seven people (0.1%) were temporarily disabled, one person was permanently disabled and there were no fatalities. The authors correctly point out: "the data are a gross summation of the many interactions and perceptions of patients and subjects, principal investigators and probably others involved in the conduct of their research, the authors of the questionnaire and the telephone interviewers. Other approaches and assumptions might give different results."<sup>18</sup>

Furthermore, it is likely that in a retrospective telephone interview there will be some underreporting of injuries because of incomplete records, problems of recall, and unwillingness to disclose such information. How large a bias this introduces into the data is not known. These data are not, however, inconsistent with those reported by McCann and Pettit for the University of Washington.

**Prospective Approach.** An alternative method for determining the incidence and seriousness of research injuries would be to look forward rather than backward. Each research project entails certain steps or procedures. Some of those carry known risks. If one added to those risks an appropriate factor for the risks of any new and untested procedures—and for the risk, if any, of the particular and perhaps novel use of the known procedures in combination—it should be theoretically possible to project a risk for each type of research. When multiplied by the number of subjects in each research activity, the result would be an estimate of the injuries expected. Again,

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<sup>18</sup> *Id.* at 653.



unfortunately, neither basic data on numbers of subjects nor the more sophisticated numbers needed for risk estimates are available.

*Number of subjects.* Very little information is available about the numbers of people serving as research subjects at any given time who are at risk of injury. Neither the funding agencies nor the recipient institutions are required to collect such information. Thus, although it is known, for example, that the Public Health Service (PHS) supports approximately 80% of the Federally funded biomedical research that is conducted throughout the country, the number of subjects involved in such studies is not known. This is also true of other Federal agencies supporting research.

In the 1977 HEW Task Force Report it was estimated that approximately 600,000 subjects are involved annually in PHS-supported clinical trials (i.e., controlled studies of new therapies).<sup>16</sup> Such trials are only a part of the research supported by the Public Health Service; a large amount of research involves studies of basic physiology, normal growth and development, and a variety of other inquiries utilizing normal volunteers.

Other partial estimates include the Food and Drug Administration's figure of 375,000 subjects per year participating in research designed to test new drugs and medical devices; this figure is expected to increase as a result of the recent promulgation of regulations governing the testing of medical devices.<sup>17</sup>

It seems unlikely that a firm estimate of the number of subjects at risk for injury at a given time could be prepared from figures currently available; any such conclusions would be based on too many levels of approximations, extrapolations and assumptions to be reliable. Thus, without either the numerator or the denominator with which to determine the incidence of research-related injuries, neither the absolute magnitude of the problem nor the size of the universe from which it emanates can be known with certainty.

*Subject characteristics.* Although the PHS and FDA have not provided direct assessments of the characteristics of subjects and of the projects in which they are involved, some data were collected by the University of Michigan's Survey Research Center in the study of IRBs it performed for the National Commission for the Protection of Human Subjects in 1975.<sup>18</sup> These data provide the best available description of the

<sup>16</sup> HEW Secretary's Task Force on the Compensation of Injured Research Subjects, REPORT, U.S. Department of Health, Education and Welfare, Washington (1977) at VIII-2.

<sup>17</sup> Information provided by personal communication with John C. Petricciani, M.D., Director, Bioresearch Monitoring Program, FDA (1980).

<sup>18</sup> Robert A. Cooke and Arnold S. Tannenbaum, *A Survey of Institutional Review Boards and Research Involving Human Subjects*.

characteristics of subjects participating in biomedical and behavioral research. Principal investigators were asked to estimate the age, sex, racial and income distributions of their experimental subjects. Projects were then weighted, based on the number of subjects, to produce overall estimates of demographic characteristics of research subjects.

**Table 1. Demographic Characteristics of Biomedical and Behavioral Research Subjects**

|        |                  |       |
|--------|------------------|-------|
| SEX    | Female           | 51.0% |
|        | Male             | 48.0% |
| RACE   | White            | 71.2% |
|        | Black            | 20.7% |
|        | Other            | 7.1%  |
| INCOME | Higher           | 11.7% |
|        | Middle           | 51.3% |
|        | Lower            | 31.5% |
| AGE    | Newborn          | 5.8%  |
|        | 3 months-6 years | 9.2%  |
|        | 7-12 years       | 5.3%  |
|        | 13-18 years      | 7.6%  |
|        | 19-40 years      | 42.0% |
|        | 41-64 years      | 20.8% |
|        | 65+ years        | 7.4%  |

Additional figures on subjects' characteristics are divided according to percent of projects rather than percent of subjects. Figure 1 shows the subjects participating in therapeutic and nontherapeutic research and their source (by percent of project). Note that both patients and nonpatients are involved in therapeutic as well as nontherapeutic research. This apparent inconsistency is easily explained. First, research in preventive medicine is usually conducted on normal volunteers yet is considered therapeutic (e.g., vaccines, controlled diet to prevent heart disease, fluoride in toothpaste to prevent cavities). On the other hand, some studies are undertaken to understand a disease process; although the subjects must necessarily be patients suffering from the disease, since the research provides them with no treatment, these studies are considered nontherapeutic.

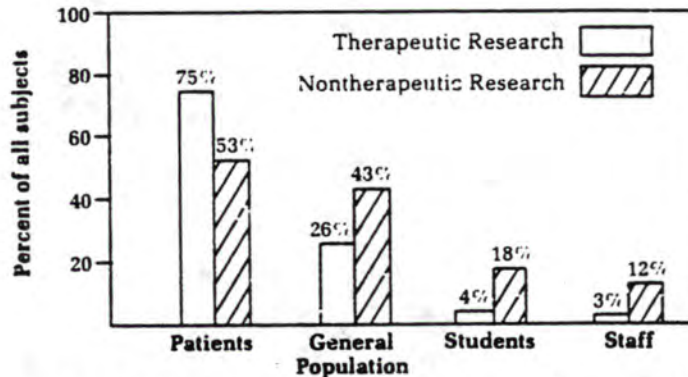
These data do not indicate the numbers of subjects involved in each kind of project. Although one might assume



that the number of subjects in therapeutic and nontherapeutic research, for example, are equal.<sup>19</sup> the actual data on this

**Figure 1. Subjects Participating In Research  
(By Percent of Projects)\***

Source: Survey Research Center, 1977, Table XV.4



\*Totals may add up to more than 100% since respondents could check more than one kind of subject.

question are fragmentary and contradictory. Cardon found in his review of 132,615 subjects in 538 projects supported by NIH and ADAMHA that the subjects in nontherapeutic research outnumbered those in therapeutic research by more than two to one.<sup>20</sup> Arnold in his examination of more than 5000 subjects participating in pharmacology research found they were evenly divided between therapeutic and nontherapeutic.<sup>21</sup> Generalizations to the universe of research subjects cannot be made from either study.

Although the proportion of subjects participating in therapeutic and nontherapeutic research is not known, the relative proportions of types of studies are known, as shown in Figure 2. The Survey Research Center found in its survey of IRBs that 43% of the projects reviewed by IRBs were therapeutic research, designed (or likely) to provide some therapeutic, diagnostic or prophylactic benefit for the subjects.<sup>22</sup> The remaining studies were nontherapeutic in that they were not likely to provide a health benefit to the participants, but rather

<sup>19</sup> Cooke and Tannenbaum, *supra* note 18, assume that since the proportions of therapeutic and nontherapeutic protocols are approximately equal so are the numbers of subjects in each kind of study.

<sup>20</sup> Cardon, *et al.*, *supra* note 14.

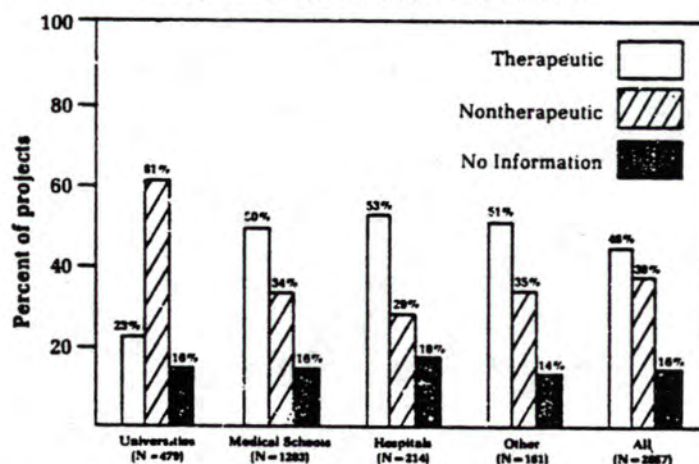
<sup>21</sup> Arnold, *supra* note 6.

<sup>22</sup> Cooke and Tannenbaum, *supra* note 18.

were expected to benefit society at large (in the form of new knowledge) or to benefit other persons suffering from, or at risk of, certain disorders.

**Figure 2. Distribution of Therapeutic/Nontherapeutic Projects (By Type of Institution)**

Source: Survey Research Center, 1977, Table XV.4



NOTE: Therapeutic research is that designed (or highly likely) to provide participating subjects with a diagnostic, preventive or therapeutic benefit.

Nontherapeutic research, while providing no anticipated benefit to subjects, is expected to provide benefits to society generally or to future patients.

That same study found that 65% of projects involved biomedical interventions such as clinical evaluations of bodily issues or fluids, administration of drugs or other agents and use of diagnostic and/or therapeutic devices. Only 7% of the studies involved "behavioral interventions" which were defined to include educational intervention, modification of an organization or service delivery system, social psychological therapy and behavior modification. The remaining 28% of the projects were other kinds of behavioral studies principally involving interviews and questionnaires, psychological and educational testing and behavioral observation.

**Risks of research.** Clearly, not all research carries potential risks of physical injury. In fact, subsequent analysis of the Survey Research Center's data revealed that the four most prevalent research procedures are non-invasive: use of data from existing records (53.8% of subjects), obtaining a medical

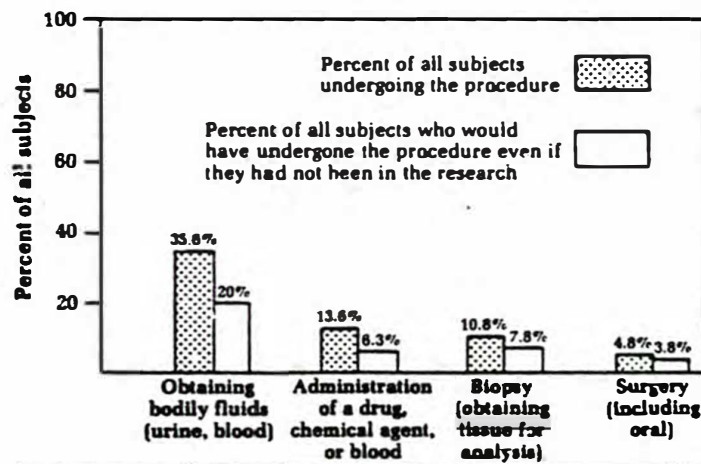


history (50.1%), self-administered questionnaires (45.3%), and interviews (37%).<sup>23</sup>

Figure 3 shows the percent of all research subjects exposed to the four invasive procedures most frequently used in research. It is important to note that the majority of subjects would have undergone each of these procedures as a routine part of their treatment or diagnosis even if they had not been participants in research. Furthermore, although the procedures are labelled "invasive," many carry no risk of physical injury. Cooke's examination of research procedures suggests that most subjects participating in Federally sponsored or regulated research are exposed to no discernible risk. The remainder of subjects may be submitting to procedures involving some risk of physical harm, but in most cases apparently would have undergone those procedures anyway for diagnostic or therapeutic purposes.

**Figure 3. Percent of All Subjects Exposed to Four Invasive Procedures Most Frequently Used In Research**

Source: Robert A. Cooke, Survey Research Center, 1980. Tables 1-5



In a study prepared for the Commission, Drs. Mary Harvey and Robert Levine evaluated the literature on risk of injury associated with twenty invasive procedures used in human experimentation and also evaluated the reliability of the risk estimates themselves.<sup>24</sup> Risk of injury was defined as "the

<sup>23</sup> Robert A. Cooke, *Some Notes on the Subjects of Biomedical and Behavioral Research* (1980); see Appendix D to this Report.

<sup>24</sup> Mary Harvey and Robert J. Levine, *Risk of Injury Associated with*

probability of injury occurring when a specific procedure is performed repeatedly under similar circumstances. "[I]njury occurs as a result of one or more complications associated with the performance of an invasive medical or surgical procedure."

Most published reports of research projects in which these procedures were used either did not discuss complications and injuries at all, or did so only in descriptive terms. Reports that did exist were incomplete and inconsistent thereby making it impossible to establish meaningful estimates of research risks. An attempt to extrapolate from the clinical literature to the research literature revealed further difficulties. Not surprisingly, retrospective reports of injury tended to be lower than prospective reports for the same procedures because of underreporting, low response rates, and insufficient data in existing medical records. Prospective studies tended to give a wide range of estimates.

Finally, the circumstances under which procedures are performed affect the amount of risk involved. The skill of the investigators, familiarity with the procedures, equipment availability, institutional policies and the existing disease state of the patients are just some of the variables which influence the occurrence not only of the initial complications, but also their subsequent resolution.

For example, it has been suggested that at least some procedures requiring sophisticated technology are best performed in hospitals that do many such procedures each year.<sup>28</sup> Conversely, at least one study has raised the question "whether access to the latest obstetrical savvy and gear may lead to overmuch intervention, possibly boosting the risk as well as the cost of having a baby."<sup>29</sup> Thus although some procedures are inherently more dangerous than others, how much more depends on circumstances. Hence, injury can only be predicted in terms of estimated ranges of probable events.

## Conclusions

It is evident from the preceding discussion that full data do not exist with which to answer the questions posed initially. One has neither broad-based retrospective data on overall incidence of injury nor adequate data with which to calculate the extent of expected injury in the research universe because

*Twenty Invasive Procedures Used in Human Experimentation and Assessment of Reliability of Risk Estimates* (1980); see Appendix E to this Report.

<sup>28</sup> Harold S. Luft, John P. Bunker and Alain C. Enthoven, *Should Operations be Regionalized?*, 301 NEW ENG. J. MED. 1364 (1979).

<sup>29</sup> *Small Hospitals Found Better for Normal Births*, 22 MEDICAL WORLD NEWS 25 (December 7, 1981).



none of the components is known with precision. Federal agencies do not know how many subjects there are nor how they are distributed across the different kinds of research endeavors.

What studies there are do show that most research involves minimal or no risk of physical harm. Yet it is also apparent that risk is a composite of many factors, such that for those procedures which do entail risk its magnitude cannot be specified.

Although the evidence consistently suggests that the incidence of serious injury is small, nonetheless, it is clear that at least some subjects sustain injuries as a result of their participation in Federally funded or regulated research. For them, as for those who invite them to undertake risks on behalf of society, the question of compensation is real and of immediate importance. Furthermore, the studies of the Quincy and University of Washington programs demonstrated that compensation was paid at those institutions without overburdening the research enterprise. Finally, it is likely that only when there are functioning compensation programs—even on a limited, pilot basis—will the lack of data be remedied.

## Existing Remedies and Their Limitations

5

Although injuries in the course of IRB-approved biomedical or behavioral research appear to be neither frequent nor severe, they do occur. When subjects are injured, what remedies are currently available to them? Do existing judicial or administrative remedies assure adequate compensation?

The Commission has found that to a certain degree, some of the claims by injured subjects can be and are being met outside any formal legal structure. Many investigators and research institutions apparently provide emergency and short-term medical care to subjects injured in research.<sup>1</sup> Such care is provided, often without charge to the subjects (or their health care insurers), as a matter of professional and institutional responsibility. For subjects with minor, short-lived injuries (who constitute a large proportion of injured subjects), the provision of free, on-the-spot medical care dispenses with any need for formal "compensation" for research injuries.

This informal means of resolution is, however, neither universal nor comprehensive. On occasion, research injuries could have severe consequences for the subject's physical well-being and ability to earn a livelihood or perform family responsibilities; further, they could require continuing medical care or supervision over an extended period. In such circumstances, the injured subject may not be able to count on the largess of the research institution. Moreover, the research institution and investigator may find that the financial demands exceed the capacity of their research budgets or the discretionary funds available to them.

This chapter examines several issues which arise when serious injuries do occur: What factors currently govern the

<sup>1</sup> Testimony of Edward Holmes, M.D., on behalf of the Association of American Medical Colleges, transcript of 4th meeting of the President's Commission (September 15, 1990) at 169-74.



ability of injured research subjects to secure medical care and financial redress for injuries sustained as a result of participation in research? To what degree are these factors, particularly as reflected in the legal rights of injured subjects, in accordance with the ethical claims of the subject and the moral obligations and responsibilities of the investigator and the wider society? What changes are necessary to give legal effect to the underlying ethical claims?<sup>2</sup>

<sup>2</sup> These issues are addressed, at least in part, by a growing legal literature on compensation of injured research subjects. Many of the seminal early treatments are discussed in Chapter Two of this Report, including articles by Ladimer, Dietrich, Bergen, Stickle, and Calabresi. Other articles noteworthy include: Bernard R. Adams and Marilyn Shea-Stonum, *Toward a Theory of Control of Medical Experimentation with Human Subjects: The Role of Compensation*, 25 CASE W. RES. L. REV. 604 (1975); Nancy E. Cahill, *Compensation of Subjects Injured in Experimental Medicine Programs: The Ethical and Legal Considerations*, 1 J. LEGAL MED. 110 (1979); Ciba Foundation Study Group, *MEDICAL RESEARCH: CIVIL LIABILITY AND COMPENSATION FOR PERSONAL INJURY: A DISCUSSION PAPER*, The Ciba Foundation, London (1980); Patricia J. Cooper, *Compensation for Human Research Subjects: Reform Ahead of Its Time?*, 2 J. LEGAL MED. 1 (1980); Bernard M. Dickens, *Contractual Aspects of Human Medical Experimentation*, 25 U. OF TORONTO L. J. 406 (Fall 1975); J.E. Harmon, *Compensation of Research Subjects for Adverse Effects*, in U.S. Department of Health, Education and Welfare, *ISSUES IN RESEARCH WITH HUMAN SUBJECTS*, DHEW Publication No. 80-1858, U.S. Government Printing Office, Washington (1980); Seymour Perry, *Compensation of Research Subjects for Adverse Effects*, in *ISSUES IN RESEARCH WITH HUMAN SUBJECTS*; John A. Robertson, *Compensating Injured Research Subjects: II. The Law*, 6 HASTINGS CTR. REP. 29 (1976); Arthur Jay Silverstein, *Compensating Those Injured Through Experimentation*, 33 FED. BAR J. 322 (1974).

See also the discussions of compensation for research injuries in Charles Fried, *MEDICAL EXPERIMENTATION: PERSONAL INTEGRITY AND SOCIAL POLICY*, American Elsevier Publishing Co., Inc., New York (1974) at 13-43, 165-72; George J. Annas, Leonard H. Glantz and Barbara F. Katz, *Compensation for Harm: An Additional Protection for Human Subjects*, in *INFORMED CONSENT TO HUMAN EXPERIMENTATION: THE SUBJECT'S DILEMMA*, Baulinger Publishing Co., Cambridge, Mass. (1977) at 257-277.

Two additional bodies of legal literature address questions similar to those arising in the research context. For pioneering discussions of nonfault insurance for adverse effects resulting from standard medical practice, see Clark C. Havighurst and Laurence R. Tancredi, *Medical Adversity Insurance - A No-Fault Approach to Medical Malpractice and Quality Assurance*, 51 MILBANK MEMORIAL FUND Q. 125 (1973); Robert E. Keeton, *Compensation for Medical Accidents*, 121 U. PA. L. REV. 590 (1973).

Articles discussing compensation for injuries associated with vaccine or immunization programs include Marc A. Franklin and Joseph E. Mais, Jr., *Tort Law and Mass Immunization Programs: Lessons from the Polio and Flu Episodes*, 65 CALIF. L. REV. 754 (1977);

## Negligence

Customarily, redress for personal injuries is provided in the legal system by the law of torts. For a subject to receive compensation through the courts for a research-related injury, the subject would have to establish legal liability for the injury on the part of one or more named defendants—typically, the investigator or the research institution. At present, such legal liability must be predicated on a showing of negligence.<sup>3</sup> That

Irving Ladimer, *Legal and Regulatory Perspectives in Mass Immunization Programs*, 643 INSURANCE LAW JOURNAL 459 (1976); Leslie C. Ohta, *Immunization Injuries: Proposed Compensatory Mechanisms - An Analysis*, 11 CONN. L. REV. 147 (1978); Bonnie L. Siber, *Apportioning Liability in Mass Inoculations: A Comparison of Two Views and a Look at the Future*, 6 N.Y.U. REV. OF LAW AND SOCIAL CHANGE 231 (1977). For comprehensive recent discussions of compensation issues in broader contexts, see Eli P. Bernzweig, *BY ACCIDENT NOT DESIGN: THE CASE FOR COMPREHENSIVE INJURY REPARATIONS*, Praeger Publishers, New York (1981); Jeffrey O'Connell, *ENDING INSULT TO INJURY: NO-FAULT INSURANCE FOR PRODUCTS AND SERVICES*, Univ. of Illinois Press, Urbana, Ill. (1975).

<sup>3</sup> Cases based solely on "mal-research" have not been reported. Virtually all decisions resulting in the award of damages to injured research subjects appear to be based, in whole or part, upon proof that injuries resulted from participation in research to which the plaintiff (or individuals authorized to act on his or her behalf) did not grant legally effective informed consent. Such cases might be litigated on the basis of negligence or, in some jurisdictions, on the legal theories of trespass or battery. Alexander M. Capron, *Informed Consent in Catastrophic Disease Research and Treatment*, 123 U. PA. L. REV. 340, 403-423 (1974).

Thus far, there has been only a single reported appellate decision in a North American jurisdiction sustaining a damage award for a research injury. *Halushka v. University of Saskatchewan*, 52 W.W.R. 608 (Sask. Ct. App. 1965) (upholding jury verdict of \$22,500 based on lack of adequate informed consent). In a second case, decided as this Report was in preparation, a New York jury awarded \$2.9 million in damages to an individual blinded by retrolental fibroplasia. The jury found that following his premature birth, the plaintiff had been enrolled in a randomized clinical trial of oxygen therapy without the consent of his parents. The jury awarded damages on the basis of both malpractice and lack of informed consent. *Burton v. New York Hospital*. An appeal is now pending.

Informed consent issues have also been raised in ongoing litigation growing out of research on DES conducted at the University of Chicago in the early 1950s. *Minx v. University of Chicago*, 460 F. Supp. 713 (N.D. Ill. 1978). The first human use of an artificial heart, while perhaps not constituting "research with human subjects" in the technical sense of that term, also resulted in litigation over the adequacy of informed consent; in that case, plaintiff's challenge was rejected by the courts. *Karp v. Cooley*, 493 F.2d 408 (5th Cir. 1974). Thus, when subjects are enrolled in research protocols without proper consent, and their participation results in injury, the injured subjects



is, unless the plaintiff-subject can prove the defendant was "at fault," he or she cannot legally recover for the injuries.

**Requirements for, and Obstacles to, Recovery.** The traditional formula for the elements necessary to state a cause of action for negligence includes:

- (a) A duty or obligation, recognized by the law, that a person conform to a certain standard of conduct ("due care") for the protection of others against unreasonable risks.
- (b) A failure to conform to the standard required.
- (c) A reasonably close causal connection between the conduct and the resulting injury ("proximate cause").
- (d) Actual loss or damage resulting to the interests of another.<sup>4</sup>

The standard of "due care" in human research conducted by a professionally qualified investigator would be that established by his or her peers. Thus, in order to prevail in a lawsuit against an investigator (or the research institution for which the investigator works and which is legally responsible for the investigator's acts), a subject must prove that the investigator departed from those standards (i.e., was "negligent") and as a result caused the subject's injury. Needless to say, it is often difficult to establish a "standard" of care for interventions that are (or contain components that are) by definition innovations from existing standards. (The accepted norms for researchers, including consultation with peers and proper institutional approval of protocols, would provide *some* standards for judging the due care of a researcher on procedural matters.) In addition, the injured subject would probably be barred from recovery if negligent conduct on his own part contributed to the injury or if he "assumed the risk" of injury in consenting to participate in the research.

The obstacles in the way of recovery posed for any plaintiff by the requirements of tort law loom especially large in the research context. Some—though not all—of these special difficulties arise because it is often hard to prove negligence in the setting of advanced scientific research. Of course, research scientists, like biomedical and behavioral scientists in standard practice (and like all other human beings), are not immune from simple carelessness. The lack of due care in such instances may be palpable and easy to prove. The very ethos of scientific investigation, however, requires that research be conducted precisely, and the available data on incidence of

may seek relief in the courts on the basis of lack of informed consent. The remainder of this chapter places primary emphasis on means of redress available to injured subjects who would not be in a position to complain that their informed consent was totally absent.

<sup>4</sup> William L. Prosser, *HANDBOOK OF THE LAW OF TORTS*, (4th ed.) West Publishing Co., St. Paul, Minn. (1971) at §30, p. 143.

research injuries (and the virtual absence of court decisions awarding damages for negligently conducted research) suggest that errors careless enough to result in serious injury are very rare in biomedical and behavioral research.

Considerably more subtle questions may be posed in particular cases regarding the decision to move from animal experimentation to research with human subjects, the design of the research protocol, and technical aspects of the actual conduct of the protocol. Scientific judgments must be made at many points along the way. When are such judgments negligent? Under traditional tort principles, the burden is on the injured subject to prove, by expert testimony, the "standard of care" owed by the investigator (and any reviewing bodies) to the research subjects. Marshalling such expert evidence may be an exceedingly difficult undertaking for the research subject. In addition to the highly technical nature of the issues involved, the subject may encounter difficulties in finding other investigators willing to testify on his behalf—a phenomenon parallel to the so-called "conspiracy of silence" in medical malpractice litigation.<sup>5</sup>

The difficulties of establishing negligence in the research setting are further complicated by the legal requirement of "foreseeability." As stated by the late Dean William Prosser:

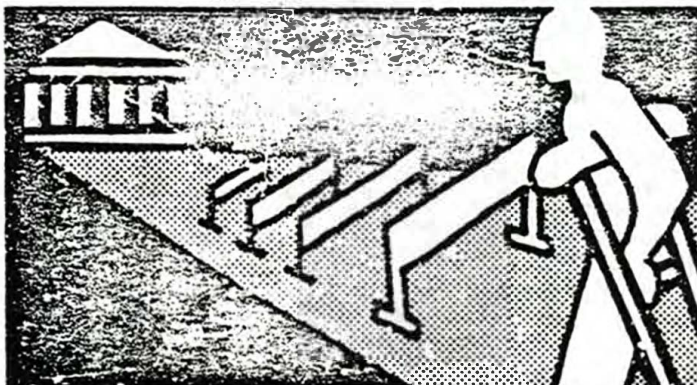
Negligence...is conduct which falls below the standard established by law for the protection of others against unreasonable risk. It necessarily involves a foreseeable risk...If the defendant could not reasonably foresee any injury as the result of his act, or if his conduct was reasonable in the light of what he could anticipate, there is no negligence, and no liability.<sup>6</sup>

The application of this legal requirement of foreseeability to particular factual situations is often controversial, and legal scholars disagree even as to the guiding principles. Given the very nature of scientific research as a venture into the unknown, the foreseeability doctrine introduces an unpredictable and confounding factor into any litigation concerning the conduct of research. Research is often carried out precisely because the range of consequences of a particular intervention and the probability of each outcome are unknown. The research is conducted in order to find out more about them. In these circumstances, what are the "foreseeable" risks, and what are the steps reasonably required to protect against them? Can that be known prior to carrying out the research? The intrinsic difficulty of such questions suggests the magni-

<sup>5</sup> See, e.g., Melvin M. Belli, *An Ancient Therapy Still Applied: The Silent Medical Treatment*, 1 VILLANOVA L. REV. 250 (1956); Richard M. Markus, *Conspiracy of Silence*, 14 CLEV.-MAH. L. REV. 520 (1965); Note, *Overcoming the 'Conspiracy of Silence': Statutory and Common Law Innovations*, 45 MINN. L. REV. 1918 (1961).

<sup>6</sup> Prosser, *supra* note 4, at § 43, p. 250.





tude of the burden placed on an injured subject who, in order to prevail, must establish the appropriate standard of care and prove it to have been breached in his or her particular case.

A further set of obstacles to recovery, legally characterized as "defenses," focuses on the conduct of the injured subject in agreeing to participate in the research and in complying with the requirements of the research protocol. A subject whose unreasonable behavior contributes to his or her injury may be barred from recovery entirely on grounds of contributory negligence, or be limited to a reduced damage award under the newer doctrine of comparative negligence. An injured subject may also be required to overcome the claim that he or she assumed the risk of injury in agreeing to participate in the research.

The "assumption of risk" label has been loosely used by courts and commentators to describe a variety of circumstances in which an individual confronts a known danger, is injured, and is then denied recovery by the courts. As noted by Prosser, the doctrine "has been a subject of much controversy and has been surrounded by much confusion..."<sup>7</sup> Expressing a view consistent with much recent scholarship, Professors John Fleming and Stephen Sugarman argue that in many situations in which the law imposes the entire loss on the victim rather than permitting recovery, the result is "perhaps best explained, not on the ground of 'assumption of risk,' but rather because the defendant was not negligent. Often in these cases the injurer has offered to provide a benefit to the victim which can practically only come with a risk attached; and the well-warned victim has quite reasonably chosen to confront the risk."<sup>8</sup>

<sup>7</sup> *Id.* at §68, p. 439.

<sup>8</sup> John G. Fleming and Stephen D. Sugarman, *Perspectives on Compensating Accident Victims* (1980), see Appendix F to this Report.

Applying this analysis to the situation of the injured research subject, Professors Fleming and Sugarman find it "unnecessary to use the doctrine 'assumption of risk' to explain why well warned research subjects whose misfortune it is to suffer from a carefully run experiment will fail to recover damages in a suit based on negligence."<sup>9</sup> In such circumstances, there has simply been no negligence, and hence no basis for a recovery.

A closely related question is whether a subject waives his legal rights to recovery in granting informed consent to participation in research, particularly since, in compliance with 45 C.F.R. §46.116(a)(6), subjects participating in research involving more than minimal risk must be provided "an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs ...." The answer to this question is clear. Federal regulations explicitly preclude "any exculpatory language through which the subject is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence."<sup>10</sup> Even in the absence of such explicit regulatory language, the courts disfavor exculpatory clauses in medical contexts,<sup>11</sup> and there are substantial policy arguments supporting this position.<sup>12</sup>

Other difficulties encountered by injured research subjects seeking relief in the courts are common to all tort litigation. Foremost among these is the problem of causation. Proof of causation may be particularly difficult in the research setting, requiring sophisticated analysis of often subtle statistical variations in risks and outcomes. In negligence and other tort litigation, the burden is on the injured party both to come

<sup>9</sup> *Id.* at 23.

<sup>10</sup> 45 C.F.R. §46.116 (1981).

<sup>11</sup> See, e.g., *Tunkl v. Regents of the University of California*, 32 CAL. RPT. 33, 383 P. 2d 441 (1963).

<sup>12</sup> See, e.g., Comment, *Legal Implications of Psychological Research with Human Subjects*, 1980 DUKK L. J. 265, 272.

Although the subject may have known what the experimenter intended to do and may have been willing to have this done to him, still, the subject may not have fully realized the risks involved. Mere knowledge of the facts which create the risk of harm is not enough unless there is a true appreciation of the nature and extent of the risks: only then is the subject's assent given under circumstances which make it legally effective. The important point here, however, is that, in ascertaining whether the subject truly appreciated the risk of harm involved, it is inevitable that considerations of policy, depending on the result desired, will consciously or unconsciously influence the court's decision.

See also *Annas et al.*, *supra* note 2 at 257-58, and Fleming and Sugarman, *supra* note 8, at 22-24.



forward with evidence suggesting causation and ultimately to persuade the trier of fact that his or her injury was "proximately caused" by the defendant's breach of a standard of care.<sup>13</sup>

A plaintiff claiming negligence must also surmount hurdles posed in some situations and in some jurisdictions by doctrines of charitable immunity (when the research is conducted by a charitable institution) and sovereign immunity (when the research is conducted or, perhaps, supported by a governmental agency), and by statutes of limitations which, in some jurisdictions, effectively preclude recoveries for certain latent injuries. With the exception of the latent injury problem (which is discussed in the Appendix to this Report<sup>14</sup>), these doctrines are not peculiar to the research context and do not require detailed discussion here.

**Critique of Negligence as a Remedial Mechanism.** Quite apart from the considerable difficulties of prevailing in a negligence action, a more fundamental question remains: as a matter of moral responsibility and public policy, ought proof of negligence to be required as a prerequisite to recovery for research injuries? This question lies near the heart of the Commission's discussion of ethical issues in Chapter Three: a few points are reiterated here to contrast the ethical arguments with the current state of the law.

First, and most obvious, the negligence system is structured to preclude recovery for injuries not resulting from negligent conduct. It is widely recognized that "despite the exercise of the highest degree of care and skill by the medical investigator concerned, death or a personal injury which was quite unforeseen and indeed quite unforeseeable might be suffered"<sup>15</sup> by a research subject. In many settings, the obstacles to recovery may be—indeed, probably are—quite appropriate. There ought, after all, to be good reasons for the legal system to shift the costs of an activity from A to B. The difficulties in the way of such a shifting of costs simply reflect the protections established by society against the misapplication of this legal power. But if research subjects *should*, on ethical grounds, be compensated for their injuries, despite the lack of negligence by an investigator, the rules of negligence law will be patently inappropriate.

Second, as pointed out in a recent article critical of the tort system's handling of the DES litigation, "[t]he doctrines of tort law were devised for straightforward moral situations—some-

<sup>13</sup> See pp. 138-139 *infra*.

<sup>14</sup> See pp. 140-141 *infra*; see also Appendix S to this Report.

<sup>15</sup> Royal Commission on Civil Liability and Compensation for Personal Injury, REPORT, Her Majesty's Stationery Office, London (1978), Vol. 1 at §1339 (hereinafter cited as ROYAL COMMISSION).

body's misbehavior causes harm to somebody else—and for narratives that observe the three unities of classical drama: time, place, and action."<sup>16</sup> The focus of traditional (negligence) tort doctrine on the immediate parties to an accident—the victim and the allegedly negligent defendant—fits the moral equation of research injuries only imperfectly. The immediate parties—subject and investigator—encompass only one aspect of the wider society's interest in biomedical and behavioral research. Much research is conducted with the encouragement or, indeed, financial support of the government itself. The fruits of research accrue to the society at large, in a form economists term "positive externalities." Thus, society as a whole has a direct stake in the conduct of scientific research. Even on the theories supportive of a "fault" component in tort litigation, the presence of strong societal externalities suggests a modification in the usual calculus of fault, so that society will share in the financial burdens, as well as the benefits, of research activity. Thus, the traditional emphasis of negligence law on the "moral drama" of the defendant's behavior fails to capture (in economists' terms, to "internalize") the societal interest in the conduct of research. Other approaches, not founded on negligence, could do so more successfully.

A final point, different in character although carrying similar implications, derives from the nature of the relationship between investigator and subject in the conduct of research. Ideally, the relationship is a collaborative one in which the subject knowingly accepts certain risks of physical injury on behalf of society and participates, together with the investigator, in the ongoing research.<sup>17</sup> The bond between investigator and subject may, however, be rent asunder by the adversary system characteristic of tort litigation, most particularly when judgment in favor of a subject is dependent on proof of an investigator's wrongdoing. While the negligence system is often applauded for creating incentives for acting with care, the knowledge that an injury could result in a courtroom battle may also create incentives less worthy of support: a certain distance, lack of candor, and perhaps even reluctance to provide necessary immediate care when the provision of such care might alert a possibly litigious subject that something had gone amiss. Such incentives may be physically harmful to the subject; they are certainly destructive of the collaborative ideal held out for the relationship between investigator and subject. It is often argued that the existing system of recoveries for

<sup>16</sup> Michael Kinsley, *Fate and Lawsuits*, 102 THE NEW REPUBLIC 20, 21 (June 14, 1980).

<sup>17</sup> See, e.g., Talcott Parsons, *Research with Human Subjects and the Professional Complex*, 38 DAEDALUS 325-360 (1969); Renée C. Fox, *EXPERIMENT PERILUS*, The Free Press, Glencoe, Ill. (1959).



medical malpractice has poisoned relationships between doctors and patients.<sup>18</sup> The Commission believes that the malpractice system should not serve as the model for remedying injuries that arise in ethically conducted biomedical and behavioral research.

### Strict Liability

Britain's Royal Commission on Civil Liability and Compensation for Personal Injury (the "Pearson Commission") recently recommended the doctrine of strict liability in tort as an alternative to the negligence system for providing compensation to subjects injured in research.<sup>19</sup> In the Commission's words, "any volunteer for medical research or clinical trials who suffers severe damage as a result should have a cause of action, on the basis of strict liability, against the authority to whom he has consented to make himself available."<sup>20</sup> Strict liability has also been characterized by some commentators as an "appealing solution" to the problem of research injuries.<sup>21</sup>

An inquiry into whether strict liability provides an answer for subjects injured in research has two components. First, is strict liability a remedy *now* available to injured research subjects? Second, if it is not, ought it to be?

**Roots in History and Policy.** The doctrine of strict liability, which permits recovery without proof of negligence, has ancient roots in Anglo-American law. Indeed, in the early common law development of the law of torts, the focus was on causation; no inquiry was made into "fault" as that term is now employed. As the doctrine of negligence developed, largely replacing the earlier concepts, several pockets of strict liability remained. In more recent times, strict liability has reemerged as an increasingly prevalent theory of tort liability. Today, its principal applications are to activities viewed as "ultrahazardous" or "abnormally dangerous" and to defective products (including, but not limited to, those products posing extraordinary danger). A variant of strict liability theory applies to pharmaceuticals and certain medical devices which are viewed as "unavoidably dangerous."<sup>22</sup>

Contemporary courts and scholarly commentators have sought to justify the expanding scope of applicability of strict liability on explicit policy grounds. In one landmark decision, the Chief Justice of the California Supreme Court explained:

<sup>18</sup> See, e.g., David Mechanic, *Some Social Aspects of the Medical Malpractice Dilemma*, 8 DUKE L. J., 1179 (1975).

<sup>19</sup> ROYAL COMMISSION, *supra* note 15, at §1341.

<sup>20</sup> *Id.*

<sup>21</sup> Note, *Medical Experiment Insurance*, 70 COLUM. L. REV. 965, 968 (1970).

<sup>22</sup> *Escola v. Coca Cola Bottling Co.*, 24 Cal. 2d 453, 150 P.2d 436, 440-41 (1944).

Even if there is no negligence, however, public policy demands that responsibility be fixed wherever it will most effectively reduce the hazards to life and health inherent in defective products that reach the market. It is evident that the manufacturer can anticipate some hazards and guard against the recurrence of others, as the public cannot.

Dean Prosser summarized the views of many contemporary scholars, stating that the courts, in applying strict liability to abnormally dangerous conditions or activities, have in effect recognized a new doctrine

that the defendant's enterprise, while it will be tolerated by the law, must pay its way. There is "a strong and growing tendency, where there is blame on neither side, to ask, in view of the exigencies of social justice, who can best bear the loss and hence to shift the loss by creating liability where there has been no fault."<sup>22</sup>

**Applicability to Research Injuries.** Whether strict liability doctrine applies to research with human subjects is, at present, an open question. No court has explicitly ruled on the issue in the context of contemporary, scientifically designed and peer-reviewed research. The factors which govern the applicability of strict liability to new areas provide no unequivocal guidance.<sup>24</sup> Three factors have been recognized as favoring application of the doctrine. Research activity is clearly valuable to the community.<sup>25</sup> Risks of injury cannot be entirely eliminated by the exercise of reasonable care.<sup>26</sup> In some sense, research is not a matter of "common usage," although this conclusion might be disputed.<sup>27</sup> On the other hand, research is typically not conducted in inappropriate settings.<sup>28</sup>

Probably the critical factors in determining the applicability of strict liability doctrine to research are whether research involves "a high degree of risk of some harm"<sup>29</sup> and whether the "gravity" of the harm which may result is likely to be "great."<sup>30</sup> While the popular imagination might be tempted to answer these questions affirmatively, the evidence marshalled by the Commission strongly suggests that research conducted with IRB approval does not involve high risks of serious injury and, on empirical grounds, probably should not be viewed as an "abnormally dangerous activity."<sup>31</sup>

<sup>22</sup> Prosser, *supra* note 4, at §75, p. 494 original citations omitted.

<sup>24</sup> American Law Institute, *RESTATEMENT (SECOND) OF TORTS*, §519 ff (1970).

<sup>25</sup> *Id.* at §520 (f).

<sup>26</sup> *Id.* at §520 (c).

<sup>27</sup> *Id.* at §520 (d).

<sup>28</sup> *Id.* at §520 (e).

<sup>29</sup> *Id.* at §520 (a).

<sup>30</sup> *Id.* at §520 (b).

<sup>31</sup> See Chapter 4, *infra*.



In addition to these factors specified by the *Second Restatement of Torts*, courts considering the applicability of strict liability to research with human subjects would be guided by existing legal precedents. An initially plausible argument can be constructed, on the basis of several early English and American cases, that physicians experiment "at their peril." Closer examination of these cases, however, indicates that they do not concern research in its modern sense and should not be viewed as governing precedents for the application of strict liability to contemporary research.

The earliest such case, *Slater v. Baker and Stapleton*, C.B.,<sup>22</sup> was decided by an English court in 1767, prior to the advent of the legal doctrine of negligence. The decision upheld a judgment against an eminent surgeon who employed a novel means of treating a broken leg, with unfortunate results. The court noted that "many men very skillful in their profession have frequently acted out of the common way for the sake of trying experiments" and held that such behavior opened the way to liability in the event of injury:

[T]his was the first experiment made with this new instrument; and if it was, it was a rash action, and he who acts rashly acts ignorantly....<sup>23</sup>

*Slater* was followed, a century later, by an American case, *Carpenter v. Blake*.<sup>24</sup> There the court said:

[W]hen the case is one as to which a system of treatment has been followed for a long time, there should be no departure from it, unless the surgeon who does it is prepared to take the risk of establishing, by his success, the propriety and safety of his experiment.<sup>25</sup>

Taken together, the *Slater* and *Carpenter* cases appeared to establish the proposition that physicians depart from established modes of treatment at their peril, and that injuries resulting from experimental treatment would be actionable without further proof of negligence.

Yet for several reasons it would probably be mistaken to apply this proposition to contemporary research. First, the conduct at issue in *Slater* and *Carpenter* was not scientifically designed research in the modern sense, but the "trying out" of an "innovative therapy" or "nonvalidated medical procedure," for which different norms may be appropriate. Second, contemporary requirements that Federally supported research pass scientific and IRB muster suggest that the gap between "human experimentation" and professional norms of practice is narrower today than was true of the conduct condemned in the

<sup>22</sup> 95 Eng. Rep. 660 (1767).

<sup>23</sup> *Id.* at 662-63.

<sup>24</sup> *Carpenter v. Blake*, 60 Barb. 488 (N.Y. Sup. Ct. 1871), *rev'd on other grounds*, 50 N.Y. 606 (1872).

<sup>25</sup> 60 Barb. at 524.

early legal cases. Third, and most important, the law itself has changed over the past century, pointing toward a more nuanced evaluation of the facts and circumstances surrounding the decision to employ innovative or experimental treatments.

The beginnings of this change were already discernible in the nineteenth century. In an 1895 case, *Jackson v. Burnham*,<sup>38</sup> the court, while repeating the rule that "if a physician sees fit to experiment...he should do so at his peril,"<sup>39</sup> construed the rule to require only that the physician "must be able, in the case of deleterious results, to satisfy the jury that he had reason for the faith that was in him, and justify his experiment by some reasonable theory."<sup>40</sup> By 1935, when the Michigan Supreme Court decided *Fortner v. Koch*,<sup>41</sup> the courts recognized explicitly that "if the general practice of medicine and surgery is to progress, there must be a certain amount of experimentation carried on."<sup>42</sup> The legal requirements were, essentially, those of consent and reasonableness: "such experiments must be done with the knowledge and consent of the patient or those responsible for him, and must not vary too radically from the accepted method of procedure."<sup>43</sup>

The transition in legal standards, from "the physician experiments at his peril" standard of *Slater and Carpenter*, to the reasonableness criterion of *Fortner v. Koch*, paralleled a more general tendency in tort law during the nineteenth and early twentieth centuries: the emergence and solidification of negligence as the touchstone of tort liability. This development was particularly evident in the field of medical malpractice litigation, which has steadfastly adhered to a standard of liability based upon professional negligence,<sup>44</sup> and which today

<sup>38</sup> 20 Colo. 332, 39 P. 577 (Colo. 1895).

<sup>39</sup> *Id.*, 39 P. at 580.

<sup>40</sup> *Id.* at 580.

<sup>41</sup> 272 Mich. 273, 261 N.W. 762 (Mich. 1935).

<sup>42</sup> *Id.* at 765.

<sup>43</sup> *Id.*

<sup>44</sup> One possible exception may be *Helling v. Carey*, 83 Wash.2d 514, 519 P.2d 981 (1974), in which the Washington Supreme Court found the defendant ophthalmologists negligent as a matter of law for failing to conduct a pressure test for glaucoma on a young patient, despite undisputed testimony that such testing was not heretofore required by the "standards of the profession." The court concluded that, in the circumstances presented, medical professionals should be held to a higher standard. Another justice concurred in this result but argued that the court was in fact imposing a standard of liability which "approached that of strict liability" (Concurring opinion of Utter, J.). Justice Utter urged that the court should explicitly recognize the applicability of strict liability doctrine to medical malpractice, in part in the belief that awarding compensation on the basis of strict liability rather than negligence would avoid unfairly "imposing a stigma of moral blame upon doctors who...used all the precautions commonly prescribed by their profession in diagnosis and treatment." *Id.* at 984. See also *Gates v. Jensen*, 595 P.2d 919 (Washington, 1979).



provides perhaps the closest analogue to research "malpractice."

Thus, the proposition that research with human subjects is an "abnormally dangerous activity" subject to strict liability standards finds no clear support in the empirical evidence or in legal precedent. While the possibility cannot be excluded that an innovative court might seek to apply strict liability to research injuries should a sympathetic case come before it (particularly in light of the steadily expanding scope of strict liability in recent decades), on the current state of the law the Commission concludes that injured subjects contemplating legal action would find little encouragement in the doctrine of strict liability.<sup>43</sup>

<sup>43</sup> A second branch of strict liability doctrine, that applicable to defective products, requires brief mention here. Under the doctrine of products liability, as formulated in §402A of the SECOND RESTATEMENT OF THE LAW OF TORTS, one who sells a "product in a defective condition unreasonably dangerous to the user or customer" may be strictly liable for physical harms caused thereby, without regard to whether the seller "has exercised all possible care in the preparation and sale of his product." The applicability of this doctrine to products which may be employed in research, particularly pharmaceuticals and certain medical devices, is a matter of controversy. Comment k to §402A of the SECOND RESTATEMENT recognizes a category of "unavoidably dangerous products," including drugs, "which, in the present state of human knowledge, are quite incapable of being made safe for their intended and ordinary use." Such products are not viewed as defective, and hence are outside the scope of §402A products liability, if they are "properly prepared, and accompanied by proper directions and warning." Nonetheless, particularly through their interpretation of the warning requirement, the courts have imposed rather expansive liability on drug manufacturers, often basing their decisions on policy grounds arguably applicable to biomedical research as well. In one much discussed case, concerning liability for a polio case arguably induced by a vaccine, the Fifth Circuit Court of Appeals analyzed the issue this way:

"Until Americans have a comprehensive scheme of social insurance, courts must resolve by a balancing process the head-on collision between the need for adequate recovery and viable enterprises.... This balancing task should be approached with a realization that the basic consideration involves a determination of the most just allocation of the risk of loss between the members of the marketing chain.' ...Statistically predictable as are these rare cases of vaccine-induced polio, a strong argument can be advanced that the loss ought not lie where it falls (on the victim), but should be borne by the manufacturer as a foreseeable cost of doing business, and passed on to the public in the form of price increases to his customers.

*Reyes v. Wyeth Laboratories, Inc.*, 498 F.2d 1284, 1294 (5th Cir. 1974) (quoting *Helene Curtis Industries v. Pruitt*, 385 F. 2nd 841, 862 (5th Cir. 1967)). The Court thereby imposed liability for failure to warn of a less-than one-in-one-million risk of contracting polio from a live virus vaccine. A similar analysis might be employed in a research



Outside the main body of strict liability law which arose and expanded in scope primarily as a matter of judge-made law, instances have arisen in which the doctrine's scope has been expanded, or limited, by legislative action. Indeed, the very uncertainties about the doctrine's applicability to biomedical research also arose with respect to legal liability associated with accidents at nuclear power installations, and this uncertainty (and the possibility that courts in different states might resolve the issues differently) played a major role in prompting Congressional action on the Price-Anderson legislation, which in practical effect imposed a nationwide strict liability policy for major nuclear accidents.<sup>44</sup> The Pearson Commission, which favored strict liability as a basis for compensating subjects injured in research in the United Kingdom, similarly recommended that strict liability be imposed by legislative enactment. Thus, the proper question becomes whether existing strict liability doctrine should be extended to encompass research with human subjects.

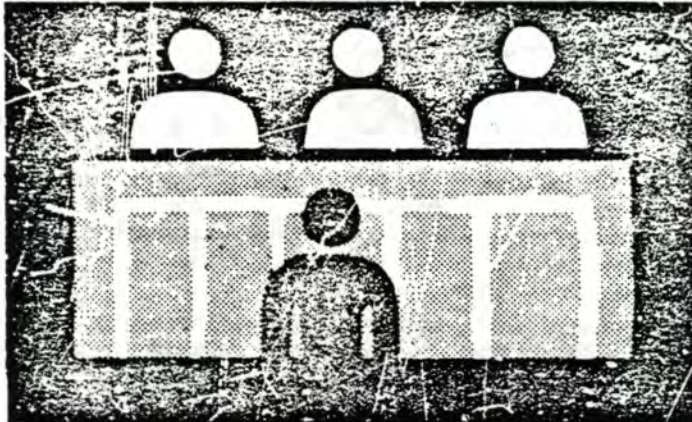
**Critique of Strict Liability.** The question of extending strict liability to cover research with human subjects poses substantial policy issues, whose resolution depends in part on the alternatives to which strict liability is being compared. To be sure, the availability of a cause of action for strict liability would enhance the position of injured research subjects unable to prevail on negligence theories, a result many would consider more just than the existing system. On the other hand, a strict liability system would perpetuate many characteristics of courtroom tort litigation which have been widely criticized, not least by those in the medical profession. Litigation based on strict liability principles would retain the adversary character of all tort litigation, pitting the interests of the injured subject against those of the investigator (even if not directly calling the conduct or competence of the investigator into question). Financial recoveries would likely be sought, in the first instance, against the investigator or the research institution, although the principles justifying recovery point to the beneficiaries of research (*i.e.*, the entire society) as the more appropriate source of redress. Like any courtroom litigation,

setting, suggesting that standards of liability might differ as between research employing drugs or medical devices and other modes of research. See also Fleming and Sugarman, *supra* note 8, at 29.

<sup>44</sup> Pub. L. No. 85-258, 71 Stat. 578, as amended, 42 U.S.C. § 2110. In fact, the technique employed in the Price-Anderson Act to accomplish this result was not a straightforward declaration of a "strict liability" standard, but a complex waiver of certain defenses (including the absence of negligence) which might be available under state law. The reason for this rather roundabout approach was a Congressional hesitancy to "Federalize" the standard of tort liability, an area traditionally reserved to the states. See generally, Legislative Drafting Research Fund, Columbia University, *ISSUES OF FINANCIAL PROTECTION IN NUCLEAR ACTIVITIES* (1973), at 2-7 to 2-9.



the process would likely be long, costly, and uncertain. The injured subject's ability to recover would depend, in substantial part, on his or her ability to secure skilled legal counsel—often a problem in cases not involving large potential awards. In the event of ultimate victory, a significant proportion of the award would be diverted to legal fees. Administrative burdens and costs (in time and money) to the defendant investigator or research institution would also be high.



In addition to all of these oft-criticized features of courtroom litigation in general, the application of strict liability doctrines to research injuries would not resolve several of the dilemmas that are especially acute in the research setting. Strict liability, like negligence, requires the subject to prove that his or her injury was caused by participation in the research. This often complex and scientifically demanding task typically must be performed to the satisfaction of a lay jury; there is no provision for fact-finding by a scientific board. Similarly complex determinations may be required by the doctrine of foreseeability, which remains applicable to strict liability cases in many jurisdictions. Further, the doctrine of assumption of risk, as it applies to strict liability cases, is, if anything, still more confused than it is in the negligence setting. Assumption of risk is most likely to provide a defense against strict liability when the subject has unreasonably, or voluntarily with full knowledge and appreciation, encountered a recognized danger;<sup>18</sup> however, the doctrine's precise contours are likely to vary considerably among jurisdictions, injecting a further element of uncertainty into the litigation.

Thus, while in many respects an improvement over the currently applicable negligence approach, the adoption of strict

<sup>18</sup> Prosser, *supra* note 4, at § 79, pp. 522-24.



liability as a legal remedy for research injuries is in no sense a panacea.

### Nonfault Approaches

A number of administrative or insurance compensation mechanisms are already in place in the United States. While only a few small-scale, nongovernmental programs are specifically directed toward compensating subjects injured in research, several more broadly based social welfare programs provide incidental benefits to such persons.<sup>54</sup>

**Government Compensation Programs.** A multitude of Federal, state, and local government programs provide compensation of various types to the injured, medical care to the ill, and financial assistance to the needy. None of these programs is universal in coverage or comprehensive in scope. Nor do initiatives for comprehensive national health care or guaranteed minimum incomes currently appear in prospect. Thus, injured research subjects are eligible for government assistance only insofar as they qualify under categories other than their status as research subjects.

For some injured subjects, assistance available under existing governmental programs may be perfectly adequate. For Federal civilian employees participating in research "while in the performance of [their] duty,"<sup>55</sup> compensation is available in the event of injury through the Federal Employees' Compensation Act (F.E.C.A.). For elderly retirees injured in research, Social Security and Medicare may relieve much of the financial burden. For others, the only recourse may be to Federal and state welfare systems, for which they may or may not be eligible. As regards injured research subjects, the "social safety net" is highly permeable: many injured subjects may simply fall through.

As part of its study of compensation for research injuries, the Commission examined the structure and operation of a number of currently functioning governmental compensation programs. One of the Commission's objectives was to determine the degree to which existing programs meet the needs of injured research subjects. In this regard, the Commission corresponded with over twenty Federal agencies and departments, and members of the Commission staff met with representatives of the Departments of Labor and of Health and Human Services, the Food and Drug Administration, the Social Security Administration, and the Veterans Administration, to discuss the availability of retrospective data and the feasibility of collecting prospective data reflecting the incidence of claims

<sup>54</sup> Existing programs are discussed briefly *infra* at pp. 114-122 and are described more fully in papers prepared for the Commission. See Chapter 7 *infra*.

<sup>55</sup> F.E.C.A., 5 U.S.C. § 8102(a).



by injured research subjects and the benefits provided to them. None of the agencies contacted maintained records in a form amenable to such analysis, and considerations of time and cost ruled out prospective studies by the Commission. Thus, deficiencies in data limited this portion of the Commission's study to the qualitative conclusions indicated above.

**Insurance Mechanisms.** It is clear that existing insurance-in-force does provide some protection for subjects injured in research. The primary source of protection is general health insurance that may be carried by individual research subjects. Although such individual health insurance is neither universal nor comprehensive, it does provide a source of benefits to insured individuals for health costs associated with research injuries.<sup>48</sup> Such insurance does not, however, cover lost wages or other non-health-care related costs associated with serious injuries.

While general health care coverage for persons participating in research offers at least a partial answer for medical costs associated with research injuries, industry representatives were deeply skeptical of the practicability of marketing to potential research subjects policies specifically designed to cover the risks associated with participation in particular research projects. This skepticism was founded, in part, on the extraordinary difficulties and expense involved in efforts to secure private insurance to cover risks in a much-discussed bone marrow transplant case.<sup>49</sup> More generally, the transaction costs and administrative burdens of writing coverage for individual participants in research were considered to pose insuperable problems in marketing such insurance.

<sup>48</sup> While there have been occasional suggestions that injuries resulting from voluntary participation in research activity might be excluded from coverage under terms of existing health insurance policies, see John Robertson, *Compensating Injured Research Subjects: II. The Law*, 6 HASTINGS CT. REP. 29 (1976), it appears that such statements result from a confusion between the use of insurance proceeds to support the research itself, which is typically precluded by insurance contracts, and the use of insurance proceeds to pay for standard medical care necessitated by an injury associated with participation in research. The Commission has been unable to document instances of insurance company exclusions of the latter type, and the Commission's insurance expert, George Bernstein, testified that on the basis of his extensive inquiries within the insurance industry, no such exclusions currently exist or are contemplated. Transcript of the 6th meeting of the President's Commission (January 9, 1981) at 187-88.

<sup>49</sup> Letter from Albert L. Broseghini, Ph.D. (Director, Research Administration, The Children's Hospital Medical Center, Boston, Mass.) to Senator Edward M. Kennedy (December 2, 1974), reprinted in the HEW Secretary's Task Force on the Compensation of Injured Research Subjects, REPORT, U.S. Department of Health, Education, and Welfare, Washington (1977) (hereinafter cited as TASK FORCE REPORT) Appendix B at 123.

Insurance industry representatives were considerably more favorably disposed to a system which would provide blanket coverage for all research subjects at a particular institution during a given period of time. A substantial consensus emerged that such blanket policies could be written and premiums set on the basis of the overall research mix and past claims experience of a given institution, although specific, high-risk protocols might require individualized underwriting examination. An institution-wide approach would entail substantially lower transaction and administrative costs. (For example, the private insurance company that provided coverage for research injuries at the University of Washington as an "add-on" to the university's liability policy initially set the premium at 50¢ per subject.<sup>29</sup>) Furthermore, rate-setting on an institution-wide basis was felt to provide sufficient grounding for underwriting decisions, with an initial break-in period during which insurers would be allowed some recovery of their costs in the event of excessive loss experience.

Alternatively, insurance might be written separately for each research protocol. Theoretically, this would lead to individualized assessment of each project, thereby providing a means for the "market" in research to adjust the amount of research in light of an economic quantification of risk. The Commission is skeptical that such "fine tuning" has an adequate basis in scientific fact,<sup>30</sup> or that the additional costs and administrative burdens involved would be outweighed by

<sup>29</sup> The University of Washington has for several years been a self-insurer. The total amount paid in claims to injured subjects in the nearly 10 years it has had a formal compensation program averages less than 5¢ per subject. This amount does not include the value of free medical services provided to subjects. See Chapter 7 *infra*.

<sup>30</sup> Such a "market control" approach has been discussed by Guido Calabresi, *Reflections on Medical Experimentation in Humans*, in *EXPERIMENTATION WITH HUMAN SUBJECTS* (ed. by Paul Freund), George Braziller, New York (1970), and Clark C. Havighurst, *Mechanisms for Compensating Persons Injured in Human Experimentation*, TASK FORCE REPORT, *supra* note 49, Appendix A, at 81-108, among others. Professor Harry Boström of the University of Uppsala in Sweden testified to the Commission that an analogous system is currently in effect in Sweden. Boström, *On the Compensation for Injured Research Subjects in Sweden* (1980); see Appendix K to this Report. However, the volume of research in Sweden is such that a single individual (Professor Boström) is able to review *all* insured protocols and to determine insurance premiums on the basis of comparative evaluation of risks associated with them. The vastly greater scope of research conducted in the United States would, in the view of the Commission (and of representatives of the insurance industry), render such a "ratings bureau" approach to American research totally impractical. Further, on the basis of a careful analysis of risk literature conducted for the Commission, a minutely graded ranking of risks would be impossible or grossly misleading. See Mary Harvey and Robert J. Levine, *Risk of Injury Associated with Twenty Invasive Procedures*



any ability of the "market" to reduce the amount of truly risky research beyond the existing system of IRB review. Further, industry representatives were dubious that such an approach would be administratively feasible.

The series of discussions between Commission staff and industry representatives culminated in testimony before the Commission by insurance industry representatives in September of 1980. In that testimony, the representatives stated "that we would like to participate with you in seeing that a reasonable compensation program for human subjects is developed."<sup>22</sup> Stressing that the program should not be "unlimited and open-ended," and that the development of a new insurance mechanism must proceed with moderation, the insurers reiterated their support for "the development of pilot programs and assessment of experience under those programs" as "the best route to develop an actual program for the compensation of human subjects."

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*Used in Human Experimentation and Assessment of Reliability of Risk Estimates* (1980), Appendix E to this Report.

<sup>22</sup> Testimony of Dennis R. Connolly, Senior Counsel to the American Insurance Council, transcript of 4th meeting of the President's Commission (September 15, 1980) at 1.

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## What Should Be Done?

## III

In this study, the President's Commission has, in effect, explored the widely held hypothesis that a program of compensating for research injuries is needed because subjects who deserve compensation are not receiving it. This appears to be at least partially true; providing compensation to injured subjects (even when research projects are conducted with due care) is ethically desirable—indeed, some would claim that a moral obligation to compensate exists. Yet, though it emerged in Chapter Five that any subjects who are injured may find it difficult to obtain recompense under existing tort or administrative remedies, the Commission found (in Chapter Four) that the frequency with which this occurs is not firmly established. Thus, more data are needed to provide a sound basis for policy on this subject. Furthermore, the strength of the ethical requirement to provide compensation for research-related injuries depends in the view of some people, as discussed in Chapter Three, upon the practicability of doing so. Thus, it is imperative to obtain reliable information on the extent of the need for compensation as well as the horizontal inequities, transaction costs, vulnerability to abuse, and difficulties of administration that providing compensation might entail. In other words, it must be determined, first, whether the incidence of injuries to research subjects is great enough to warrant institution of a formal compensation program, and, second, whether the costs of compensating those injured in research can be prevented from escalating uncontrollably and consuming an inordinate portion of the overall research budget. In this Part, the Commission explores, first, the manner in which data could be developed (Chapter Six), and, second, the basic features of any compensation program (Chapter Seven).



The paucity of reliable data was described in Chapter Four. No definitive national data on the incidence or severity of injuries in Federally conducted or supported research exist. The costs of acquiring comprehensive data through a methodologically valid *retrospective* survey would be very high—in the Commission's view, too high to be justified. Further, the results of any such survey would be criticized because retrospective data cannot disclose the extent of those costs that are "induced" by the existence of a compensation program. Consequently, such data might understate both the number of potential claims and the associated costs that would arise were the existence of a compensation program made known to subjects.

Some witnesses urged the Commission to conclude that no further exploration of compensation programs should occur in the absence of proof of a crying need. But an absence of data on injuries should not be equated with data on an absence of injuries. Other groups and individuals possessing great familiarity with biomedical research suggested that the inadequacies of the data be remedied. The Association of American Medical Colleges, for example, argued for "instituting such a compensation system on a pilot basis, limited by time, by number of institutions or geography, to permit the gathering of relevant data on the basis of real experience."<sup>1</sup>

Although wishing to avoid the term "pilot" program which might be misunderstood as a commitment to moving to a full-scale program, the Commission agrees with the thrust of the AAMC's argument. It has concluded that the problem of research injuries should not be shelved once again, to be passed on from commission to commission for further review, with each inquiry being stymied by the lack of data. Therefore,

<sup>1</sup> Letter from John F. Sherman, Vice President, Association of American Medical Colleges, to Chairman Morris B. Alram (May 7, 1980).

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the Commission urges that steps be taken to acquire data prospectively on the nature and incidence of research-related injuries through a test of one or more approaches to compensating for research injuries.<sup>2</sup>

As a baseline for comparison, data are needed on the incidence of research injuries nationally. To this end, the President's Commission, in its first *Biennial Report*, recommended that the regulations governing all research conducted or supported by Federal agencies be amended to require annual reporting of the number of research subjects as well as data about their injuries.<sup>3</sup> Although this is a procedural suggestion and was made in the context of a review of the Federal rules on research, it is at its heart a matter of ethical concern. (The Commission was disappointed to find that most research sponsors have not regularly compiled data on the occurrence of injuries in the research projects they support.)

The proposed solution thus addresses both ethical and practical problems and should not be difficult to implement. Principal investigators receiving government funds are already required by Federal grant and contract rules to submit annual progress reports as well as final reports on their research. Although data about the numbers of research subjects, injuries and consequences may well be included in the narratives of such reports, they are not easily retrievable. The Commission was informed that with few exceptions, such data are not routinely collected and collated by any one office within the various departments. An expeditious and inexpensive way to collect data on the universe of research subjects and research-related injuries would be to develop a form to be completed annually by all principal investigators as part of their progress and final reports on each project. Completed forms should be sent to the office within the Department of Health and Human Services that has "lead" responsibility in the field. The data would then be collated so that information about the number of subjects and incidence of injury would be readily available. Indeed, the Veterans Administration has already implemented just such a requirement for all research it sponsors.

<sup>2</sup> The Commission took on a request to provide advice about the development of a means for compensating research subjects for injuries that occur in the future. It lacks the authority for the investigation that would be needed to determine whether *retrospective* compensation should be made to subjects who may have been injured in past research projects. A number of such subjects are pursuing claims in the courts already, as described in Chapter 5.

<sup>3</sup> President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, *PROTECTING HUMAN SUBJECTS: FIRST BIENNIAL REPORT ON THE ADEQUACY AND UNIFORMITY OF FEDERAL RULES AND POLICIES, AND THEIR IMPLEMENTATION, FOR THE PROTECTION OF HUMAN SUBJECTS IN BIOMEDICAL AND BEHAVIORAL RESEARCH*, U.S. Government Printing Office, Washington (1981) at 73.



Although this system should provide basic information about risks and injuries in research, it will not reveal the costs and benefits of having a compensation program. Therefore, the Commission recommends that a modest social policy experiment be conducted to determine the need for, and feasibility of, comprehensive or partial programs to compensate injured subjects.

During the past two decades the Federal government has conducted a series of experiments in which new social policies have been implemented under reasonably controlled conditions and evaluated in order to see how specific aspects of the policies work in practice. Such experimentation has been used to test the effects of instituting a negative income tax, housing allowances, and various types of health insurance plans.<sup>4</sup> The use of social policy experimentation has been encouraged by a broad range of scholars and policy analysts as a "rational" approach to policy innovation.<sup>5</sup> The great advantage of such experimentation is that it allows innovative programs to be tested and proven useful or deleterious before a decision is made about instituting them on a comprehensive basis. The government can then modify or abandon those programs before public expectations are created or constituencies formed that force the government to remain committed to ineffective programs. Given the importance of empirical data in evaluating the need for, and feasibility of, a compensation program, a limited experimental trial seems particularly appropriate.

The Commission recommends that the compensation experiment be designed and administered by the Department of Health and Human Services with appropriate consultation with other governmental bodies which sponsor or conduct research. The relevant office within the Department would develop (or contract to have developed) the detailed plans for the experiment, including its administration and evaluation.<sup>6</sup>

<sup>4</sup> U.S. Office of Economic Opportunity, PRELIMINARY RESULTS OF THE NEW JERSEY GRADUATED WORK INCENTIVE EXPERIMENT CONDUCTED BY THE OFFICE OF ECONOMIC OPPORTUNITY (February 18, 1970); see also Alice Rivlin, SYSTEMATIC THINKING FOR SOCIAL ACTION, Brookings Institution, Washington (1971) at 94-106.

<sup>5</sup> Henry W. Riecken and Robert F. Boruch, eds., SOCIAL EXPERIMENTATION: A METHOD FOR PLANNING AND EVALUATING SOCIAL INTERVENTION, Academic Press, New York (1974) at 1-39; Rivlin, *supra* note 4; Campbell, *Reforms as Experiments*, 24 AM. PSYCH. 419 (1969).

<sup>6</sup> The office within HHS that is most familiar with research involving human subjects is the Office for Protection from Research Risks at NIH. That office does not, however, have extensive experience with design or evaluation of social experiments. Thus, the Department may wish to turn to the Office of the Assistant Secretary for Planning and Evaluation and perhaps to other bodies with expertise in this field in assigning responsibility for the design and conduct of the research compensation experiments recommended here.

### Specific Aims of the Experiment

The experiment with formats for compensation should be designed to answer the following questions:

- (1) How great is the need for a program to compensate for research injuries?
  - (a) How many research subjects are exposed to risk of injury?
  - (b) How many research injuries occur?
  - (c) How serious are the injuries?
  - (d) For what proportion of these injuries is medical assistance currently provided by formal or informal procedures (*i.e.*, how effective are such procedures in meeting existing medical needs)?
  - (e) For what proportion of these injuries are payments currently made for loss of wages and other expenses (*i.e.*, how effective are existing means in meeting economic needs)?
  - (f) To what extent does failure to provide adequate compensation create serious problems for injured subjects or for the research enterprise?
- (2) What effects result from introduction of a compensation program?
  - (a) Does the institution of a formal compensation program undermine current, informal methods of providing for the immediate medical needs of injured subjects?
  - (b) Would the availability of compensation bring more research injuries to light (*i.e.*, encourage the reporting of injuries which would otherwise not be known to persons other than those immediately involved)?
  - (c) Does the availability of compensation lead to large numbers of specious claims?
  - (d) Does the availability of compensation make it easier for researchers to recruit subjects?
  - (e) Does the assurance that injured subjects will be compensated produce an environment that is more conducive to research, and how does it affect the nature and amount of research?
- (3) What costs and benefits are entailed in a compensation program?
  - (a) How many subjects would be anticipated to be eligible to receive funds under a compensation program?
  - (b) Can those administering a compensation program distinguish specious from valid claims? What are the administrative costs of making such determinations?
  - (c) How difficult is it in practice to discern a causal connection between research interventions and subse-



quent adverse effects? What approaches to the determination of causation seem most effective and just?

(d) What are the costs, both in claims paid and in administrative expenses, of a compensation program?

(e) How would the costs be affected by the inclusion of Federally supported as well as Federally conducted research?

(f) How would the costs be affected by covering those injuries caused by procedures undertaken solely as an aid to the research design and not for a patient-subject's welfare, when in the absence of such "nonbeneficial procedures" therapeutic research would be excluded from the compensation program? Can such injuries be reliably identified?

(g) What approaches to compensation provide the most favorable balance of benefits against administrative burdens and costs?

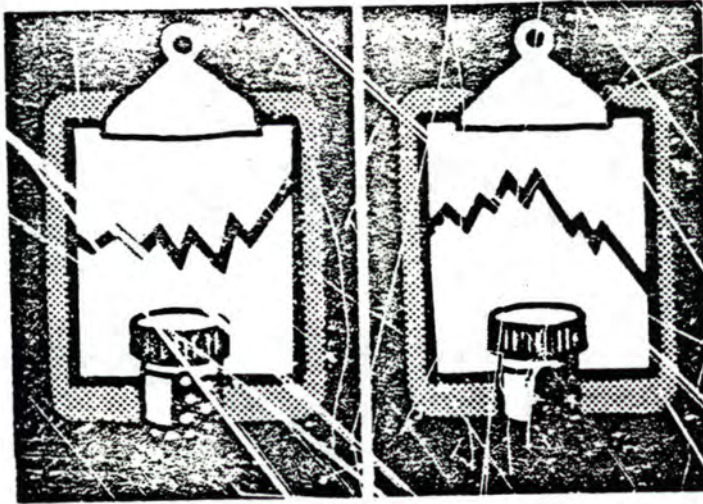
### Research Plan

Although the actual design of the experiment is left to the office within HHS that conducts it, the remainder of this chapter is intended to indicate the type of research the Commission views as desirable and to provide general guidance concerning the scope and nature of such research. Particular features of possible compensation programs are discussed in Chapter Seven.

The Commission proposes that the three sets of questions listed above be answered by experimental compensation programs established at a small number of institutions and by ongoing collection and analysis of data from these institutions and matching institutions without compensation programs. Questions concerning the costs and problems of administering a compensation program would be answered by establishing and monitoring experimental compensation programs at institutions willing to participate in the experiment. Uniform data should be collected on the number of subjects participating in research, number of injuries, seriousness of injuries, and so forth. Additionally, all injuries resulting in claims for compensation should be documented, including the amount of money paid out in compensation, administrative costs, number of claims honored and denied, and the details of each incident. During the experiment, the Commission recommends that compensation be restricted to nontherapeutic experiments and perhaps to injuries caused by procedures undertaken as an aid to the research and not with the intent of providing possible therapeutic benefit to patient-subjects.

In addition to providing information about the general feasibility of a compensation plan, the experiment should provide a basis for determining whether any type of compensa-

tion program should be recommended or adopted on a more permanent basis.



The effects of introducing a compensation program on existing mechanisms for dealing with injuries resulting from research could be partially assessed through the use of historical controls at the compensating institutions; however, sufficient data do not appear to exist. Consequently, a number of institutions without compensating programs should be selected as "matched controls" and monitored according to the data-gathering protocol established for institutions at which the experimental compensation programs are being tested. For such a comparison to be meaningful, of course, there must be no systematic differences between the two groups of institutions (other than presence or absence of a formal compensation program). The noncompensating institutions that are monitored will serve a dual purpose. Besides being the "control" group for the compensating institutions, they will provide data against which to check the annual reports submitted by principal investigators (*i.e.*, how many injuries occur, how serious they are, etc.).

### Methodological Issues

The Commission encourages those designing the research to give careful consideration to the following methodological issues:

**Sample Selection.** As with all survey research, the validity of the conclusions that can be drawn from this study will depend, at least in part, on the representativeness of the sample being studied. Obtaining a representative sample may be particularly difficult, however, given the wide variety of



institutions in which research is conducted. Institutional settings for research range from the Clinical Center at the NIH, to universities, medical schools and hospitals, to small independent research facilities. One approach that might be used is known as "quota sampling." Institutions involved in Federally conducted or supported research would be grouped in appropriate categories. A sample containing a certain number (quota) of institutions from each category would then be drawn. Within each category of institutions in the sample, half would initiate an experimental compensation program; the other half would be monitored in a similar manner but would not have a compensation program. Under ideal circumstances, the selection of institutions from each category in the sample would be random, as would be the assignment of institutions within each category to have or not have a compensation program.

The Commission believes this basic approach can and should be applied to Federally conducted and Federally supported research. However, the Commission believes that the NIH Clinical Center, because of its centrality in Federal biomedical and behavioral research and its traditional leadership role in the scientific community, should not be randomly assigned but should participate in the experiment as a compensating institution. If a successful compensation program cannot be established at the NIH Clinical Center, the Commission is skeptical that any such program should be imposed by the Federal government on other research institutions.

With respect to Federally supported research conducted at non-Federal research institutions, the major issue in considering sample selection is whether participation should be mandatory (i.e., tied to federal funding) or voluntary. Scientifically, mandatory participation is preferable since it reduces the likelihood of biased sampling that would occur if the "self-selected" institutions that volunteered to participate differed as a group from those that do not. The Commission sees several advantages in voluntary participation, however, and on balance believes that, if possible, participation should be on a voluntary basis. The assistance of groups such as the AAMC which support a limited, experimental evaluation of research injury compensation should be sought in persuading institutions to participate in the experiment.

Two approaches might be used to reconcile the desirability of participation on a voluntary basis with the need for random selection and random assignment to compensating or noncompensating categories. One approach would be to select the sample and assign the chosen institutions to compensating or noncompensating status on a random basis, but to allow institutions to "opt out" of the experiment if they were unwilling to participate in their assigned role. An alternative approach would be to solicit institutions to volunteer to

participate in the experiment on the understanding that they would then be assigned randomly either to the experimental (compensating) or control group. Under either approach it would be possible for the government to offer institutions incentives in order to assure that a sufficient number of institutions would be willing to participate. For institutions that agreed to participate in the experimental compensation program, the government might, for example, offer to cover the costs of compensating for injuries that occurred on non-Federally funded as well as Federally funded research (provided, of course, that the former as well as the latter passed through IRB review).

**Sample Size.** In determining the number of institutions that will compose the sample for this study, the implementing agency will need to balance the need for reliable data with the need to minimize the costs of conducting the experiment. The following considerations are relevant to this decision:

(1) The degree of variation among research institutions imposes certain requirements. If institutions are divided into categories for quota sampling, at least two institutions from each category should be included in the sample (one to initiate a compensation program, the other not). Thus, the number of categories determined to be necessary to reflect institutional diversity will have a direct bearing on the sample size.

(2) Given that institutions are the unit of analysis, a sufficient number of institutions must be studied to obtain adequate statistical sensitivity (*i.e.*, an adequate ability to detect differences) when comparing compensating and non-compensating institutions. Otherwise, substantial real-world differences between compensating and noncompensating institutions would fail to show up as "statistically significant effects" in the experimental data.

**Duration of Study.** Three considerations argue for conducting the study over a period of several years. First, the incidence of research injuries is expected to be quite low. Unless the study continues long enough to allow a fairly large "sample" of injuries to occur, there is a danger that the particular experience with injuries observed in a limited period may, by chance, be unrepresentative of research injuries in general. Second, because research injuries may not become known immediately, a study of short duration may underestimate the rate of injuries. Finally, because initial reactions to a novel program may be unrepresentative of later reactions, a valid evaluation of a compensation program may not be possible until it operates long enough to become established and known.

### **Costs**

Until the parameters of the recommended experimental evaluation of compensation approaches are more fully delineated—a task which the Commission believes can only be



carried out by those with final responsibility for designing the experiment—it is impossible to estimate the costs of the experiment. Rough yardsticks are provided by the experience of the University of Washington, where commercial premium costs were less than \$1.00 per covered subject (and actual payments were less than 5¢ per subject), and by the Quincy Research Center, where costs were less than those associated with workers' compensation premiums for professional employees. In addition to premium costs, of course, the experiment will incur certain administrative costs and the costs of design and evaluation.

The Commission notes that under existing Public Health Service policy, reasonable insurance costs incurred by contractors and grantees are already allowable expenses. Thus, the implementation of a compensation experiment would not create a new category of expense insofar as insurance premium costs are concerned. By statute, funds are available to HHS for research and development experiments on programs. The Commission believes that such funds might usefully be applied to the compensation experiment, and that a satisfactory experiment could be conducted for a very small fraction of 1% of current Federal expenditures on biomedical research grants and contracts.

### **Standards for Evaluating the Desirability of Instituting a Compensation Program**

The ethical desirability of compensating victims of research injuries is strong, but the decision whether to adopt a compensation system must in the Commission's view be made by balancing the seriousness of the problem against the costs and practical difficulties of the solution. A finding of substantial need would argue strongly in favor of a compensation program even if significant costs and practical difficulties might be entailed. If the need for a compensation program is shown to be small, however, the cost and difficulty of administering make a permanent program seem much less necessary or desirable.

A finding that relatively few serious injuries occur to subjects in research should not in itself be taken to indicate that no compensation program is needed. Few serious injuries resulting from properly conducted research have been reported or documented. The examples of research injuries most frequently recited (*i.e.*, the Tuskegee syphilis experiment, the CIA-sponsored psychoactive drug research, and so forth) occurred prior to the existence of the review processes required by current Federal regulations. Nonetheless, it is undeniable that human research involves some risks. In the long run, it may well be more protective of the field of biomedical and behavioral research for it to be prepared to meet any human disaster which may result from its activities.

The alternative—a knowing decision to do nothing to provide a fair and simple avenue of relief in the event of serious injury—carries serious danger for public confidence in science and scientific research. Moreover, any program adopted in the wake of such an event would almost certainly be less well-designed than one adopted in light of the results of a well-conducted social policy experiment.<sup>7</sup>

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<sup>7</sup> For a fuller discussion of the issue of compensating for injuries arising from certain causes in therapeutic research, see pp. 132-135. The terms are defined and their practical interrelationships are shown in Appendix S.



## Consider Various Features of Nonfault Insurance Programs

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What features might be tried out as part of the social policy experiment proposed by the Commission? One alternative, rejected by the Commission, would be to create a remedy through the judicial system. It does not seem wise to remit injured subjects "to the uncertainties of the law court"<sup>1</sup> or to require them to hurdle the formidable barriers to recovery that exist even in strict tort liability.

The Commission also examined various governmental health and compensation programs and private insurance plans to determine whether they might serve as models for further study and experimental evaluation regarding compensation for research injuries. While the existing programs also appear to be inadequate, they point to the possibility of a non-judicial, nonfault system of compensating for research injuries. The factors favoring this approach are nicely summed up in a report prepared by the Ciba Foundation study group established in response to the Pearson Commission's recommendation favoring strict liability:

Compared with litigation a no-fault compensation scheme would have the advantage of administrative simplicity. Claims can generally be handled quickly and, since the claimant would not be seeking redress from the researcher, his employer or the funding agency, it would be proper for the researcher to assist the claimant in the preparation of his claim. The researcher and the participant in the research would, therefore, not be adversaries as would be inevitable in any scheme based

<sup>1</sup> Tuskegee Syphilis Study Ad Hoc Advisory Panel, FINAL REPORT, U.S. Department of Health, Education and Welfare, Washington (1973) at 23.

upon litigation. It is in the public interest that all participants in medical research should appreciate that their well-being, and the public interests, are overriding considerations in the mind of the investigator.<sup>2</sup>

This chapter first reviews the governmental and private insurance models and presents the reasons for their rejection. The rest of the chapter discusses the varying features that might be considered for nonfault insurance programs to compensate for research injuries.

### Existing Governmental Programs as Models

The Commission began its study of existing Federal models by reviewing the materials prepared for the HEW Secretary's Task Force on the Compensation of Injured Research Subjects in 1975. Those materials included detailed descriptions of four major Federal compensation programs: the Federal Employees' Compensation Act (F.E.C.A.), the Black Lung Benefits Act, the National Flood Insurance Act, and the Veterans Administration service-connected disability program. The report prepared for the Task Force on these programs appeared in an appendix to the Task Force's final report and is reprinted, for convenience, in the appendix volume accompanying this Report.<sup>3</sup>

The Commission then undertook to update these materials and to explore certain programs and issues in greater depth. Some of this work was carried out by a health policy analyst who reviewed in some detail the suitability of F.E.C.A. and the Veterans Administration program as models for compensation for research injuries, brought prior work on the black lung program up to date, and provided information on Social Security disability programs, Medicare, and state workers' compensation programs.<sup>4</sup>

Members of the Commission staff also canvassed the literature and reviewed administrative and legislative proposals regarding compensation for injuries associated with vaccine and immunization programs, radiation from nuclear weapons testing, toxic substances in the environment, and medical accidents, as well as proposals for modifications in product liability law. These inquiries took advantage of ongoing studies concerning compensation programs in other

<sup>2</sup> Ciba Foundation Study Group, *MEDICAL RESEARCH: CIVIL LIABILITY AND COMPENSATION FOR PERSONAL INJURY*, Ciba Foundation, London (1980) at 9.

<sup>3</sup> Frederick G.G. Barber, *Report on Federal Models*, HEW Secretary's Task Force on the Compensation of Injured Research Subjects, REPORT, U.S. Department of Health, Education, and Welfare, Washington (1977) (hereinafter cited as TASK FORCE REPORT) Appendix A at 167-198.

<sup>4</sup> Stanley B. Jones, *Existing Federal Programs as Models for Compensation of Human Subjects* (1980); see Appendix M to this Report.



Federal agencies and in interagency working groups. Particular attention was paid to the lessons of the swine flu vaccine program, including the continuing litigation associated with it, and to contemporaneous studies by the Congressional Office of Technology Assessment of compensation for vaccine-related injuries.

**F.E.C.A. and Other Workers' Compensation Programs.** F.E.C.A. is the workers' compensation plan applicable to approximately three million civilian Federal employees, and to certain other persons as well.<sup>5</sup> The plan is generally similar in structure to most state workers' compensation plans, although benefits are paid directly by the government and tend to be more comprehensive in scope and more generous in amounts (particularly for highly paid employees) than state plans. The program is administered by the Office of Workers' Compensation Programs within the Department of Labor.<sup>6</sup>

F.E.C.A. provides benefits to covered employees both for injuries resulting from accidents and for diseases proximately caused by their employment. Benefits are provided through an administrative mechanism without regard to fault (except for willful misconduct or intoxication by the injured employee) and include compensation for loss of wages, dollar awards for bodily impairment or disfigurement, medical care for an injury or disease, rehabilitation services, and compensation to survivors in the event of an employee's death. Compensation levels are established on the basis of a percentage of an employee's pay level. Awards are subject to administrative review but are not subject to challenge in the courts.

F.E.C.A. has been extended, by statute, to apply to a number of "non-typical" types of Federal employees and, indeed, non-employees. Among the persons currently covered by F.E.C.A. are Peace Corps and VISTA volunteers, members of the Civil Air Patrol and National Teacher Corps, Job Corps enrollees, certain student-trainees, and non-Federal law enforcement officers injured in the course of enforcing Federal law.<sup>7</sup> Methods have been devised to accommodate the special compensation requirements of such individuals.

F.E.C.A. is not the only Federal legislation providing workers' compensation benefits. The Federal Longshoremen's and Harbor Workers' Compensation Act (the "Longshoremen's

<sup>5</sup> 5 U.S.C. Ch. 81, §§8101 *et seq.* See generally Comptroller General's Report to the Congress, COMPENSATION FOR FEDERAL EMPLOYEE INJURIES: IT'S TIME TO RETHINK THE RULES, HRD-79-78 (August 22, 1979) (hereinafter cited as Comptroller General's Report on Compensation).

<sup>6</sup> Comptroller General's Report on Compensation, *supra* note 5.

<sup>7</sup> See 5 U.S.C. §§8101(1), 8141-8143, 8143a, 8144, 8191.

Act") governs workers' compensation for privately employed persons engaged in maritime employment.<sup>8</sup> The Longshoremen's Act has been extended, by statute, to provide coverage for several additional classes of workers, including persons employed at military, air, and naval bases outside the United States; employees of "nonappropriated fund instrumentalities" (e.g., military base post exchanges); employees working on the outer continental shelf under United States jurisdiction; and, until recently, employees in the District of Columbia.<sup>9</sup>

Benefits under the Longshoremen's Act are generally similar to, but somewhat less generous than, those available under F.E.C.A. Unlike the situation under F.E.C.A., awards under the Longshoremen's Act are paid by private employers and may be appealed in the Federal courts. This administrative mechanism is thus subject to several of the criticisms leveled against common law tort remedies which entail resort to the courts. The Longshoremen's Act does, however, provide a Federally recognized alternative to F.E.C.A. with benefit levels closer to those provided under state workers' compensation laws.

In addition to these Federal programs, all fifty states have their own workers' compensation acts requiring employers to provide benefits to workers who suffer work-related injuries and diseases. To be eligible for benefits, normally an employee must experience a "personal injury by accident arising out of and in the course of employment."<sup>10</sup> Beyond this common framework, eligibility criteria and benefit levels vary widely among the states. Many state plans are criticized as inadequate, particularly with respect to coverage of work-related illnesses and diseases. A Federally mandated National Commission on State Workmen's Compensation Laws made numerous recommendations for improvements in its 1972 report;<sup>11</sup> many of these recommendations have yet to be implemented.

What, then, are the lessons of Federal and state workers' compensation programs, and to what degree do existing programs, particularly F.E.C.A., provide useful models for a compensation system for research injuries? The problem of injured research subjects seeking compensation is similar in several respects to the position of the injured industrial worker, suggesting the plausibility of the workers' compensa-

<sup>8</sup> 33 U.S.C. Ch. 18, §§901 *et seq.* Other workers' compensation plans embodied in Federal legislation include the Jones Act, covering merchant seamen, and the Federal Employers' Liability Act, covering railroad employees.

<sup>9</sup> See 42 U.S.C. Ch. 11, §§1351-1654; 5 U.S.C. §§6171-6173; 43 U.S.C. §§1335-1343; D.C. Code §§501-504, repealed by District of Columbia Workers' Compensation Act of 1979, D.C. Law 3-77.

<sup>10</sup> *Report of the National Commission on State Workmen's Compensation Laws*, U.S. Government Printing Office, Washington (1972) at 32.

<sup>11</sup> *Id.*



tion approach as a model for research injuries. The history and rationale for workers' compensation laws underline some of these similarities, as well as a few significant differences.

Workers' compensation programs were established in the early part of this century in response to growing dissatisfaction with the tort system as a vehicle for resolving claims arising from work-related injuries. The new approach abandoned several requirements under the tort system viewed as unfair or unduly burdensome to injured workers, and permitted workers to recover if their injurer arose in the course of their employment, without proof of fault by the employer. In this respect, workers' compensation laws recognized industrial accidents as an inevitable hazard of modern industry. The new approach also recognized that the human costs of injury, like the costs of repairing machinery, were part of the costs of the enterprise and should be borne by those who benefit from the enterprise, not by the injured workers. This philosophy found expression in a slogan of the time: "the price of the product should bear the blood of the workingman." Scholars of the period believe the adoption of workers' compensation laws contributed to industrial harmony and social peace.<sup>12</sup>

At present injured research subjects enjoy no benefits comparable to workers' compensation, although there are notable structural similarities with the situation of ordinary American workers. Injured subjects, like workers a century ago, face special obstacles in securing relief through the tort system. Because of the special character of the research enterprise as a venture into the unknown, research injuries are an inevitable hazard of the enterprise. Further, the human costs of injury incurred in research are truly costs of the research enterprise to society—costs necessarily incurred to obtain the benefits of scientific progress.

It may be argued that research subjects *volunteer* to participate in research, while workers effectively have little choice about incurring workplace hazards to earn their livelihoods. To the extent that subjects participate in research purely out of altruistic motives, this observation may be correct. To that extent, the analogy between workers' compensation and compensation for research injuries is imperfect. Yet, on the ethical plane, that difference adds weight to the injured subject's claim against society, since the volunteer has acted altruistically. And to the degree that some subjects participate in nontherapeutic research as a convenient means of casual employment-for-pay (a not uncommon practice among university and medical school students), parity of treatment suggest

<sup>12</sup> Comptroller General's Report on Compensation, *supra* note 5, Appendix II, and see generally Roy Lubove, *THE STRUGGLE FOR SOCIAL SECURITY, 1900-1935*, Harvard University Press, Cambridge, Mass. (1968) at 45-65.



that subjects should be entitled to workers' compensation benefits much as are other employees-for-pay.

The workers' compensation analogy does tend to break down with respect to one class of subjects: patients who participate as subjects in therapeutic research with the expectation of securing personal health benefits. Such subjects may seem more akin to patients receiving standard medical care (who are not entitled to compensation on a nonfault basis) than to workers eligible for workers' compensation. Further, such patient-subjects pose many of the administrative difficulties which workers' compensation programs have been least successful in answering: determining causation of diseases that are not arguably work-related; measuring the degree of "excess injury," or the exacerbation of preexisting health conditions; and calculating the benefits owed to persons not currently in the work force. For these reasons, the Commission believes that the uncritical application of workers' compensation models to therapeutic research involving already sick patient-subjects is fraught with potential hazards. However, with respect to nontherapeutic research (especially that involving healthy subjects), the Commission concludes that workers' compensation, and F.E.C.A. in particular, offers a potential model for compensating injured research subjects.

**Veterans Benefits.** A second approach carefully examined by the Commission is the compensation system administered by the Veterans Administration for service-connected disability or death. Under this program, benefits are provided to veterans for disabilities incurred in, or aggravated by, a period of military service though not necessarily "caused" by the service. Benefits include health care and rehabilitation, typically provided in VA facilities, and financial compensation for lost earning capacity due to the disability. These benefit programs make no distinction between men and women who volunteered for service and those who were conscripted.

In marked contrast to workers' compensation approaches, VA service-connected disability benefits are payable without regard to the beneficiary's employment status. Rather, benefits are determined according to an "average man" concept. Disabilities are rated and compensated according to a comprehensive schedule of injuries and diseases, under which varying percentage ratings are assigned, depending on the degree of severity of any given disability. These percentage ratings represent, as nearly as possible, the "average impairment in earning capacity" resulting from a particular disability in civilian occupations. In applying the "average man concept," there is an assumption that all young people who entered military service at an early age would have the potential for attaining an "average civilian occupation income" at the time of their discharge. These disability payment levels are adjusted yearly by Congress, to correspond to cost-of-living increases



provided in other Federal benefit programs. This "income loss compensation" can be reduced if it can be demonstrated that the individual was already disabled before entering service, in a way definable in the schedule for rating injuries and diseases. In that event, only the "additional disability" is compensable.<sup>13</sup> research can be prevented from escalating uncontrollably administrative cost. Claim decisions are subject to administrative review, but because of the relatively simple administrative structure of the program (and the existence of other VA programs providing for the needs of the veteran), few appeals are taken. No appeals to the courts are permitted.

The Commission believes a number of features of the VA service-connected disability program bear close examination in the structuring and experimental evaluation of alternative compensation plans for injured research subjects. In particular, the "average man" concept may have promise in determining benefit levels for injured subjects whose current income, if any, may not accurately reflect their true earnings capacity.

The Commission's health policy consultant noted that "if participation in research experiments were deemed by law to be equivalent to service in the military, research subjects might be covered" by the VA service-connected disability program.<sup>14</sup> The Commission believes this suggestion bears further exploration, but notes that VA benefits, unlike those afforded under F.E.C.A. or the Longshoremen's Act, have not historically been extended to new groups of beneficiaries.

**Vaccine and Immunization Programs.** Many of the issues involved in recent Congressional and Executive Branch efforts to formulate a national policy on compensation for injuries in vaccine and immunization programs bear a close relationship to questions arising in the context of research injuries. The Commission notes that the approaches under consideration for vaccine injuries are closely analogous to those examined here.<sup>15</sup>

The Commission agrees, for example, with the conclusion of the Office of Technology Assessment that "the swine flu program is widely regarded as exemplifying the problems inherent in compensating for vaccine related injuries via the tort law system."<sup>16</sup> The preference of the President's Commis-

<sup>13</sup> Letter from Dorothy C. Rasinski, M.D., J.D., Associate Director, Medical-Legal Affairs, Veterans Administration, to Alan J. Weisbard (1980).

<sup>14</sup> Jones, *Existing Federal Programs as Models for Compensation of Human Subjects*, *supra* note 4, at 33-34.

<sup>15</sup> Office of Technology Assessment, U.S. Congress, *A REVIEW OF SELECTED FEDERAL VACCINE AND IMMUNIZATION POLICIES* (1979); Office of Technology Assessment, U.S. Congress, *COMPENSATION FOR VACCINE-RELATED INJURIES* (1980); Reports and Recommendations of the National Immunization Work Groups (1977).

<sup>16</sup> *COMPENSATION FOR VACCINE-RELATED INJURIES*, *supra* note 15 at 13.

sion that nonfault administrative and insurance mechanisms be explored as a means to compensate for research injuries, rather than pursuing remedies through the tort law system (including strict liability), is based in part on the swine flu experience.<sup>17</sup>

**Evaluation of Governmental Alternatives.** The Commission has noted the tendency of governmental compensation programs, once enacted, to expand beyond their originally contemplated scope, placing ever greater demands on the Federal treasury. One significant factor underlying the escalation in costs of many Federal compensation programs has been the general rate of price inflation throughout the economy, and

<sup>17</sup> The Federal government's ill-fated 1976 effort to immunize the public against swine flu nearly ended before it began, when vaccine manufacturers refused to transfer their vaccines from bulk to bottles for distribution, because the manufacturers were unable to secure insurance coverage against potential liability for vaccine-related injuries. Emergency legislation was rushed through Congress, providing that any claims arising from the swine flu program should be filed against the Federal government, while preserving the government's right to sue manufacturers for indemnification in the event of negligence in the production of the vaccines. Public Law 94-380. See R. E. Neustadt and Harvey V. Fineberg, *THE SWINE FLU AFFAIR: DECISION-MAKING ON A SLIPPERY DISEASE*, U.S. Department of Health, Education and Welfare, Washington (1978). Under this legislation, the government assumed the "duty to warn" potential vaccine recipients of any known adverse reactions to the vaccine, and undertook to defend against any claims brought for vaccine injuries.

The results are well known. Although the feared swine flu epidemic never materialized, there quickly developed a mini-epidemic of claims against the Federal government, many related to the onset of Guillain-Barre Syndrome (GBS). As of August 12, 1981, some 4039 claims for a total of over \$2.89 billion in damages had been filed. Of these claims, 1523 had progressed to lawsuits, requiring extraordinary efforts on the part of lawyers at the Justice Department, as well as imposing considerable expense on the government and burden on the Federal court system. Perhaps the major potential advantage of this system to the Federal government, the possibility that the government might have prevailed on the merits in many cases (on the basis that the government should not be held accountable for a failure to warn of risks that were unknown at the time) was put in question when then HEW Secretary Califano issued a statement accepting the government's responsibility for GBS claims. See *Compensation for Vaccine-Related Injuries* *supra* note 15, at 13-17. While the legal effect of this statement is open to question, the Justice Department subsequently took the position that it would not require proof of a theory of liability in cases in which GBS was established (although proof of liability is required in all other cases). As a result, the government incurred both the substantial costs of courtroom litigation and liability for the large damage awards associated with such litigation. It is difficult to imagine how an administrative mechanism for nonfault compensation could do worse.



the still higher inflation in medical costs. The Commission sees little in the design of a compensation program for research subjects which could significantly affect this overriding fact.

A second factor responsible for escalating costs is the power of particular political constituencies to expand the scope and benefit levels of compensation programs. To some degree, such expansions may serve legitimate policy interests; often it is merely a matter of politics. One of the most striking features of the research injury question is the near absence of any active constituency group of research subjects. If the Commission's data on the incidence of research injuries is correct, it is exceedingly unlikely that any large or powerful constituency group representing injured research subjects will arise.

The presence or absence of a powerful constituency group does not affect the moral claim to compensation of those subjects who are injured in research. The lack of such a group does, however, diminish the likelihood that overwhelming political pressures will force an initially modest compensation program to expand beyond its appropriate contours.

Nonetheless, the Commission has paid special attention, in articulating its several alternative approaches toward compensation, to those aspects of a compensation program which might expand the scope and expense of a program beyond those initially contemplated. Perhaps most significant among these are the questions whether a program should encompass nonphysical injuries; injuries sustained in therapeutic research; and injuries sustained in research not conducted or supported by the Federal government. Careful study of benefits and costs should precede any decision to include these categories in a compensation program.

A third reason why the scope of compensation programs has expanded and their costs have escalated is the tendency, particularly in the courts, to accord more liberal interpretations to eligibility and benefit criteria. Therefore, the Commission recommends that court review be precluded initially and dollar ceilings be set on awards as features of any program being tested out; reexamination of these features ought to await several years experience with an actual program in place.

A fourth basis for escalating costs is greater awareness by potential beneficiaries of the compensability of injuries. To the degree such awareness leads persons to make claims who are legitimately entitled to compensation, any "escalation" in costs is a sign that the program is doing its job and reaching the persons intended to receive benefits. However, greater awareness of the availability of compensation may also lead to specious claims by persons not legally entitled to relief. Costs associated with such claims include both any benefits erroneously paid out to undeserving claimants and the administrative expense of processing invalid claims. This problem of poten-

tially excessive "induced costs" was a significant concern of several witnesses who questioned the wisdom of a compensation program and is seriously regarded by the Commission.<sup>18</sup> The Commission's recommendation that any compensation program be tested first through a small experiment is based on the conclusion that the potential for induced costs must be carefully evaluated before Federal policymakers consider instituting a comprehensive plan or promulgating a requirement that research institutions adopt such plans.

### Insurance Mechanisms as Models

Members of the Commission staff conducted extensive and fruitful discussions with representatives of the insurance industry—including company officials, insurance brokers, trade association officers, and institutional risk managers—to determine what role insurance mechanisms could usefully play in assuring medical care and financial redress for injured subjects. Several conclusions emerged from these discussions.

The insurers (and other interested parties) made a number of specific suggestions concerning the terms of a compensation program. Their submissions are published in the appendix volume accompanying this Report.<sup>19</sup> The focus here is not on these specific suggestions, but broader structural approaches to incorporating insurance mechanisms as part of a compensation system. At least three distinct models (as well as combinations of these models) may be envisioned: institutional private insurance, institutional self-insurance, and pooled or collective insurance.

**Institutional Private Insurance.** Institutional private insurance is perhaps the most familiar model. Under this approach, each research institution would purchase, from commercial insurance companies, nonfault coverage for all subjects participating in covered research at that institution. Terms of coverage would be negotiated by the relevant institution and the insurance carrier, subject to minimum requirements. Premiums would be set according to normal underwriting standards, reflecting the type of institution, the mix of research conducted, and any prior claims experience. Coverage could be marketed either as a separate insurance product or, more likely, as part of the overall insurance package provided for the institution.

This is the approach successfully employed at the University of Washington (Seattle) for a number of years, originally in conjunction with the Argonaut Insurance Company and subse-

<sup>18</sup> Testimony of George Bernstein, Esq., transcript of 6th meeting of the President's Commission (January 8, 1981) at 189-93.

<sup>19</sup> See Appendices O, P, Q, R, T to this Report.



quently, between 1973 and 1979, with the Aetna Casualty and Surety Company.<sup>20</sup> The insurance carriers in that instance wrote coverage through a special endorsement to the university's comprehensive general liability insurance policy. Coverage was originally provided following a survey of adverse effects associated with research at the university during a one-year base period, at a premium cost of 50¢ per subject, or \$17,500. In subsequent years, the cost of insurance coverage was a fixed charge of \$35,000, without regard to the number of subjects covered. The university's human subjects officer and risk manager reported that the insurance program "relieved concerns within the university for the economic protection of human subjects" and that "there have been no complications in the insurance program."<sup>21</sup>

The major drawbacks of this private insurance approach are, first, that the terms of coverage must be sufficiently attractive to induce participation by the private insurance industry (which implies significant limitations on the extent of coverage) and, second, that some research institutions may have difficulty in securing coverage. As noted by representatives of the private insurers, "the larger and more respected institutions will obtain coverage more easily," while other institutions "may be unable to obtain such coverage because their projects are too risky or because it is impossible to assess the degree of risk in the program. This will be particularly troublesome with respect to research in smaller institutions engaged in high risk, even if potentially beneficial, research."<sup>22</sup>

**Institutional Self-Insurance.** The second model is that of institutional self-insurance. Here the institution itself defines the terms of coverage and establishes an actuarially sound sinking or reserve fund to cover future claims. No private insurance carrier is involved. As a result, the terms of coverage are potentially quite flexible, and many institutions find self-insurance less expensive and more satisfactory for their needs than insurance procured on private insurance markets. An increasing number of universities and hospitals have switched from commercial to self-insurance in recent years. For example, the University of Washington has for three years provided its own liability coverage, including insurance for adverse effects associated with research, through a program of self-insurance.

<sup>20</sup> Diana McCann and John R. Pettit, *A Report on Adverse Effects Insurance for Human Subjects* (1980); see Appendix H to this Report at 1.

<sup>21</sup> *Id.* at 3. The University of Washington has for several years been a self-insurer. The total amount paid in claims to injured subjects in the nearly 10 years it has had a formal compensation program averages less than 5¢ per subject. This amount does not include the value of free medical services provided to subjects.

<sup>22</sup> See note 18 *supra*.

There are several drawbacks to institutional self-insurance, however, particularly for smaller research institutions. Since each institution establishes a fund to cover its own claims, risks are not spread as widely as with commercial insurance. Thus, in the event of an unusual string of losses (or even a single catastrophic loss), the reserve fund may be endangered, requiring claims to be paid out of general funds. Further, many states have laws limiting the ability of state instrumentalities or nonprofit institutions to self-insure. In the state of Washington, a legislative change was required before the state university could self-insure.

The compensation program for research injuries at the Quincy Research Center, a drug testing facility in Kansas City, Missouri, combines elements of self-insurance and private insurance.<sup>25</sup> The research center has provided medical care under a self-insurance approach for all research participants since 1975. In addition, the research center provides financial compensation in the event of injury through a workers' compensation-type insurance arrangement. The director of the research center reports that standard rates for research subjects as employees are approximately twice as great as those for physicians and consultants, approximately five times as great as those for clerical office employees, slightly less than one-third as great as those for chauffeurs and drivers, and approximately equal to those for analytical chemists.<sup>26</sup>

**Collective or Pooled Insurance.** A third model for insurance coverage for research injuries is collective or pooled insurance. Under this system, a group of research institutions could band together, perhaps with government assistance, to establish a collective insurance pool. Such an arrangement would retain many of the advantages of self-insurance, notably including flexibility in the terms of coverage and the ability to move forward with a program even in the absence of interest by the private insurance industry in providing appropriate coverage. But the collective approach would permit greater spreading of risks among institutions than would institutional self-insurance, and could be expected to result in lower administrative costs. Collective insurance pools might be especially important for smaller research institutions which face difficulties in securing coverage for research injuries in the private insurance market or in establishing their own self-insurance programs.

The Commission is not aware of any collective insurance pools for research injuries now operating in the United States. However, many such pools have been established for other

<sup>25</sup> John D. Arnold, *Incidence of Injury During Clinical Pharmacology Research and Indemnification of Injured Research Subjects at the Quincy Research Center* (1980); see Appendix I to this Report.

<sup>26</sup> *Id.* at 34-35.



analogous purposes. In many states, such insurance collectives are the primary source for medical malpractice insurance. A number of universities and hospitals have also participated in such plans to cover other insurance needs. These arrangements could be modified to provide coverage on a nonfault basis, for research injuries. While state laws and regulations pose obstacles in certain jurisdictions, it seems clear that many institutions could provide protection to research subjects through such collective insurance pools.

**Evaluation of Insurance Alternatives.** The Commission does not believe that any one of these insurance models is fully satisfactory for all research institutions in all circumstances. The Commission concluded however, that if compensation for research injuries were desired virtually all research institutions desiring (or mandated) to develop a reasonable insurance program providing minimally adequate coverage for subjects injured in research conducted at that institution could do so through one or more of these models. The necessary arrangements would take a certain amount of time, as well as cooperation and coordination among research institutions, risk managers, insurance brokers, and insurance companies, but nonfault insurance coverage for research injuries appears to be feasible. Moreover, if implemented in sensible fashion, it offers a better basis for providing compensation to injured research subjects at reasonable cost to research institutions and the Federal government than any alternatives, such as tort litigation.



The Commission notes that under the existing policy of the Department of Health and Human Services, institutions conducting research pursuant to Federal grants and contracts may procure insurance coverage providing protection for research subjects on a nonfault basis, and may recover associated (reasonable) expenses under their grants and contracts as indirect costs or, in certain instances, as direct costs.<sup>22</sup> Thus,

<sup>22</sup> The Public Health Service Grants Policy Statement provides (at p. 19) that:

Insurance is usually treated and reimbursed as an indirect cost. In certain situations, however, where special insurance is required because of risks peculiar to the project, the premium

for institutions wishing to do so, insurance protection for subjects may now be provided, at government expense, without the need for changes in Federal statutes or regulations. The logic of the Commission's reasoning would point toward regarding the costs of a compensation program as direct costs like other identifiable items (including appropriate remuneration of subjects for their time and trouble in participating).

Having determined that a nonfault insurance system should be the basis of the "compensation programs" being tested, the Commission proposes a number of variables that should be considered in designing the experimental compensation programs. Before discussing those variables, however, the Commission's intent with respect to certain basic elements that the experimental compensation programs should embody should be made clear.

### Objectives of a Compensation Program

From what has already been said it can be seen that a major objective of any "compensation plan" is to ensure that necessary medical care and financial indemnities are provided, in a fair and just fashion, to protect research subjects (and others who are dependent upon them for support) from the remediable harm that occurs as a result of injuries suffered in research. "Easing the plight of the victim"<sup>28</sup> is not, however, the sole consequence—and need not be the sole objective—of a compensation program. A compensation program might also serve as a means of social control over the funding and conduct of biomedical and behavioral research.

First, the funds spent in compensating injured subjects could help to identify, and perhaps even to quantify with some precision, a cost of doing research that had previously been overlooked in decisions regarding the number or type of experiments to undertake. Specifically, it has been suggested

may be charged as a direct cost if consistent with institutional policy. Such premiums may include those on hazard, malpractice, and other liability insurance to cover grant-supported personnel and activities.

See also the provisions governing recovery of allowable insurance costs at 45 CFR Part 74, Subpart Q, Appendix E (hospitals); and OMB Circulars A-87 (state and local governments); A-21 (educational institutions); and A-122 (other nonprofit organizations).

<sup>28</sup> The idea of a compensation fund is in no sense original. It has, however, usually been suggested as a device for easing the plight of the victim. I am not here suggesting it for that purpose (worthy though it might be), but rather as a way of introducing an additional control element over when a medical experiment is considered worthwhile.

Guido Calabresi, *Reflections on Medical Experimentation in Humans*, in *EXPERIMENTATION WITH HUMAN SUBJECTS* (ed. by Paul Freund), George Braziller, New York (1970) at 196, n. 2.



that a compensation program could discourage overly risky research<sup>27</sup> and encourage economically "efficient" allocation of research funds.<sup>28</sup> To the extent that specific funding decisions take account of the injuries associated with the research, an appropriate incentive is provided to researchers to exercise additional care in their work.<sup>29</sup>

As laudable as such objectives may be, the difficulties in risk-estimation discussed in Chapter Four suggest that a system capable of producing actuarial estimates of risk exact enough to make superior decisions about allocation of research funds is, at best, an elusive ideal. Even were such estimates feasible, they would involve an expenditure of time and resources far in excess of that needed to establish a fair system of compensation—and probably far in excess of any benefits that might be gained from "wiser" decisions about the amount and kind of research that ought to be undertaken. Consequently, the Commission concluded that reliance in achieving control over research is better placed on other means (such as prior review by an IRB) rather than on the compensation system.

Within its own sphere, any program for providing compensation ought to be fair and efficient. That is, it should (a) treat like cases alike, (b) involve fair payment for the harm sought to be remedied, and (c) disburse payments with maximum efficiency and minimum administrative cost.

Finally, the existence of a compensation program may have indirect consequences for the research enterprise or for society generally. By indicating society's concerns for individuals serving the interests of the collectivity, a compensation program not only avoids a potentially unattractive societal image for research but may also permit research that is otherwise seen as "too risky" (because of the possible consequences for its subjects) to go forward. Indeed, the existence of compensation may make people more willing to serve in research projects generally. The experience gained through experimental compensation programs for research injuries may also provide instructive information for other forms of Federally sponsored activities.<sup>30</sup>

Any compensation system necessarily entails some balancing of competing objectives. A design feature that advances one objective (e.g., providing comprehensive compensation) may undercut other objectives (e.g., promotion of the most

<sup>27</sup> Clark C. Havighurst, *Mechanisms for Compensating Persons Injured in Human Experimentation*, in TASK FORCE REPORT, *supra* note 3, Appendix A at 81, 83.

<sup>28</sup> Richard Zeckhauser, *An Analysis of Mechanisms for the Compensation of Injured Research Subjects*, in TASK FORCE REPORT, *supra* note 3, Appendix A at 155, 156.

<sup>29</sup> See Havighurst, *supra* note 27, and Zeckhauser, *supra* note 28.

<sup>30</sup> See Zeckhauser, *supra* note 28; see also, Calabresi, *supra* note 28.



cost-effective research]. The ultimate choice of objectives will be for the policymakers who choose among (or modify) the options set forth below. As noted earlier, the Commission, in considering compensation programs, has had in mind solely the objectives *internal* to the compensation system (*i.e.*, fair and efficient provision of relief to the victims of research in a manner that can be administered easily and at a cost that imposes the minimum burden on the research sector), rather than the broader goal of enhancing the regulatory process.

### Basic Elements of a Compensation Program

(1) Definition of "compensation." The term "compensation for research injuries" has been variously defined, often leading to misunderstanding. As employed here, the term encompasses two aspects:

- (a) assurance that necessary medical care and related services are provided to subjects injured in research, and
- (b) financial indemnification of an injured subject, or the subject's family, for economic losses sustained (including both out-of-pocket costs and lost wages) as a direct consequence of research injury.

A recurrent source of confusion as to the intended scope of a compensation program results from the fact that medical care for subjects injured in research is often provided directly by the investigator or by the research institution, without charge to the subject and often without any formalized accounting for the cost of the services rendered. As a conceptual matter, "compensation" encompasses the provision of such care, whether or not the financial value of the care is ever billed to the subject or even calculated as a bookkeeping entry. Sometimes, medical care for an injured subject may be provided for a fee by care-givers entirely unrelated to the research or the research institution, or may otherwise be accompanied by a bill for services rendered. Here, of course, "compensation" includes payment of the bill as well as provision of the care itself.

In both cases, what is *ethically* relevant is that necessary care is provided and that the costs of that care do not fall upon the injured subject. The questions of where the costs of the care ultimately fall (other than upon the injured subject), and how those costs are accounted for, are financially important and must be considered in the design of the financing side of any compensation program. Experience gained through the operation of the compensation experiment will provide valuable clues as to the most efficacious financing structure. In this regard, however, the Commission recognizes the desirability of permitting flexibility as to how medical care is provided and financially accounted for, particularly in cases of trivial injuries or other injuries not requiring long-term medical care. Where "flexibility" should not be permitted is in the basic



requirement that necessary care be provided in appropriate circumstances, and that the injured subject not be financially burdened by the cost of the care.

(2) Research covered. Coverage should be limited to biomedical research and specified behavioral research (*i.e.*, only such behavioral research as is affirmatively determined in advance to impose more than minimal risk of bodily injury to research subjects) which is reviewed and approved in accordance with Federal regulations for the protection of human subjects.

(3) Nature of Injuries. Benefits should be provided on a nonfault basis to subjects sustaining nontrivial bodily injuries or death as a result of their participation in covered research.

(4) Benefits. Benefits should include short-term, emergency medical care, longer-term medical care (including rehabilitation) and related services, death benefits, and economic costs. (More limited benefits might be available to seriously ill subjects participating in covered research.)

(5) Other payments. Benefits should be provided only to the extent that they are not paid by other sources (*e.g.*, health or disability insurance, liability insurance, social security, court judgments or private settlements).

(6) Unreasonable conduct. Benefits should be reduced or eliminated when injury results from the failure of the subject reasonably to conform to the provisions of the research (*e.g.*, intentional falsification of medical history, failure to comply with investigator's directions on avoiding alcohol, drugs, etc.).

(7) Fact-finding. The use of expert fact-finding panels and arbitration for the resolution of disputes should be encouraged.

(8) Funding. The experimental compensation program should be funded by the Federal government. Reasonable costs of private, group, or self-insurance incurred by non-Federal research institutions should be recognized as allowable direct costs under Federal grants and contracts.

### **Variables to be Included in the Experimental Design**

The Commission believes that those with final responsibility for designing and implementing the compensation experiment should have freedom to establish the configuration of the compensation plans that will be evaluated. The following discussion of the variables to be considered is offered as an aid to those making the decisions.

#### **Scope of Covered Research**

**Government involvement.** The ethical arguments favoring a compensation program for research injuries are strongest where the nexus between the research and the Federal government is closest. That is, the greater the role of the Federal government in the design, funding, and conduct of the

research, and in the encouragement of subjects to participate, the greater the obligation of the Federal government to provide, or to assure the provision of medical care and financial assistance to subjects injured in the research. Thus, a program might cover any or all of the following: (i) research conducted intramurally by Federal agencies; (ii) research supported by Federal grants and contracts; and (iii) research submitted to Federal agencies in fulfillment of regulatory requirements (e.g., for licensing of new drugs, medical devices, pesticides, etc.).

With respect to research supported by Federal agencies, several sponsoring agencies (including the Public Health Service) currently permit research institutions to include reasonable expenditures for insurance procured to protect subjects of research as part of the costs of grants and contracts;<sup>21</sup> the practice is not widespread, however.

The creation on an experimental basis of compensation programs for Federally funded research should encourage the sponsors of private research submitted to FDA and other regulatory agencies to establish parallel nonfault compensation plans and to share their data with the agency overseeing the Federal experimental program. Indeed, some private sponsors of research have already implemented such plans. Until the results of the experimental evaluation are available, it is not possible to evaluate the desirability of requiring all sponsors of research that is privately funded but Federally regulated to provide nonfault compensation.

Finally, it has been argued that since the ethical considerations underlying compensation do not vary according to the source of the funds to conduct the research, any compensation program should apply to all institutional research, not just to Federally funded research.<sup>22</sup> "In addition to a question of simple equity among subjects, there are practical difficulties in having a compensation program that only applies to some studies even though the risk to the subject may be the same."<sup>23</sup> Although this position is highly persuasive, it does not follow, that "the cost of any such compensation program should be fully borne by the Federal government."<sup>24</sup> Intra-institutional equity could be achieved by voluntary action of each institution or by a governmental mandate. But such a requirement would at the moment be out of keeping with the entire theory of the data-gathering experiment. Nevertheless, the Federal government might offer to cover the costs of compensation in non-Federally as well as Federally supported research as an inducement to institutions to participate in the experiment.

<sup>21</sup> Public Health Service Grants Policy Statement at 19.

<sup>22</sup> John R. Pettit, Chair, University Risk Management and Insurance Association (URMIA) Human Subjects committee, letter to Alan J. Weisbard (August 20, 1981); see Appendix R to this Report.

<sup>23</sup> *Id.*

<sup>24</sup> *Id.*



*Type of research and IRB review.* Under well-established regulations, codified for the Department of Health and Human Services at 45 CFR Part 46, all Federally conducted or supported research with human subjects must undergo prior review. For most of the studies that could produce claims for compensation, the process required includes prior review and approval by a properly constituted Institutional Review Board (IRB) established by the body conducting the research.

The requirement of proper institutional review would exclude from coverage research which has not been fully screened and which may pose special risks of injury. Such a requirement may be necessary to safeguard the financial integrity of the compensation fund and to encourage investigators to cooperate with the IRB process. (Investigators who improperly short-circuit the review process may be liable to injured subjects in the courts under the legal theory of negligence per se; in some situations, however, potential defendants may escape liability under the defenses of sovereign or charitable immunity.)

Under recent revisions to the regulations on IRBs, certain research, in which risk is believed to be minimal or nonexistent, need not undergo full review by the IRB. Some such research, primarily that involving surveys, questionnaires, and educational tests or the study of existing pathological and diagnostic specimens, poses no risk of bodily injury and is formally "exempt" from IRB review. Such research might well be left outside the scope of the compensation plans to be tested, since the primary concern is with redressing the harms that accompany bodily injury.

Other research, believed to pose only minimal risks of harm, is permitted by the new regulations to be reviewed and approved on an expedited basis. Biomedical research falling within this "expedited review" category may result in bodily injury to research subjects (e.g., a chipped tooth suffered by a subject who faints and falls following a "blood draw"). Therefore, bodily injuries resulting from biomedical research subject to expedited review probably should be included within the coverage of the experimental compensation plan.

A large proportion of behavioral research poses no risk whatever to subjects. Further, many though not all of the risks posed by behavioral research are risks of purely psychological or social injury. Inclusion of all behavioral research in a compensation program would impose economic costs and administrative burdens unwarranted by any possible benefits.

It is undeniable, however, that some research characterized as "behavioral" poses risks of bodily injury to research subjects. Such risks may flow from physical interventions similar to those employed in biomedical research, from subjecting subjects to unusual or unexpected stress, or from other causes. Bodily injuries resulting from such research should be

compensable, both as a matter of fairness and to avoid imposing administratively difficult requirements for line-drawing between biomedical research and physically risky behavioral research. The regulatory distinction between behavioral research eligible for expedited review and that requiring full IRB review could form the basis for distinguishing between behavioral research that is included in the compensation program and that which is not.

*The problem of therapeutic research.* The question of whether "therapeutic research" should be excluded from a compensation program for research injuries has been among the most vexing and contentious arising in the course of the Commission's study of compensation for research injuries.<sup>35</sup> The view that *all* research, whether "therapeutic" or "nontherapeutic," must be covered by a compensation program was not found to be persuasive. There is much to be said as an analytical matter, of course, for the conclusion of the Secretary's Task Force that "the distinction between therapeutic and nontherapeutic research ... is not a valid criterion on which to make a determination as to which injured subjects are to be compensated."<sup>36</sup> But, as the Task Force acknowledged, it would be inordinately expensive to "compensate" all patient-subjects for all illness or injury they experience after participating in research.<sup>37</sup> Even setting aside the difficulties of

<sup>35</sup> A closely related question involves the applicability of a compensation plan for research injuries to injuries incurred in the development of vaccines and in immunization programs. Compensation for vaccine-related injuries has received extensive attention elsewhere, notably in reports issued by the Office of Technology Assessment. See A REVIEW OF SELECTED FEDERAL VACCINE AND IMMUNIZATION POLICIES *supra* note 15 and COMPENSATION FOR VACCINE-RELATED INJURIES, *supra* note 15. While vaccine injuries share certain characteristics with research injuries in that they are often incurred in governmentally encouraged (or sometimes required) activities on behalf of the public good, vaccine injuries also possess distinctive characteristics. Insofar as vaccines, virtually by definition, offer some promise of preventive health benefits to the subjects on whom they are tested, vaccine trials would be classified as "therapeutic" and thus excluded from the scope of compensable injuries under Plans I and III as well as under Plan II, unless the injuries were caused by additional research procedures classified as "nonbeneficial." It is recognized, however, that subjects in vaccine research are typically "normal volunteers," a status that might justify classifying the research as "nontherapeutic." The Commission concludes on balance that all vaccine-related injuries, both from the research and development phase and from routine administration, would probably best be handled by a single compensation system specifically addressed to vaccine injuries.

<sup>36</sup> TASK FORCE REPORT, *supra* note 3, at VI-9.

<sup>37</sup> A distinction between "normal" and "sick" subjects is also sometimes advanced as a means of limiting the costs of a compensation program. This basis for excluding therapeutic research from coverage under a compensation system — that therapeutic research involves



separating injuries that were caused by the research from those that were not, measuring the *extent* of the injury is conceptually as well as practically extremely difficult. Many patients participate in highly risky experiments precisely because their condition is already so desperate that they have, in common parlance, "nothing left to lose" and they hope that something new will help them. The Task Force's proposed means of dealing with this difficulty, the so-called "on-balance test," was found by the Commission to pose enormous burdens of administration which could not be justified in light of the relatively weaker moral claim for compensating patients who participate in research with the hope of deriving personal health benefits.

Furthermore, providing compensation to subjects of therapeutic research on any more favorable basis than that applicable to injuries resulting from ordinary medical practice (including innovative therapy) accords research injuries preferential treatment. For reasons discussed more fully below, such a preference might not be ethically inappropriate. But it would generate a serious question in need of an empirical answer: Would inclusion of therapeutic research within a program's coverage create unfortunate (and expensive) incentives for patients to enroll in research protocols or for their physician to include them to make them eligible to have any "adverse effects" paid for, as they would not be if the patient's condition worsened during ordinary medical care?

Many researchers and commentators feel a moral debt toward patient-subjects who are injured in therapeutic research. Such research is intended, at least in part, to benefit society

"sick" subjects—was not persuasive to the Commission. The proposed distinction would exclude from coverage those subjects for whom "injuries" are most likely to occur and to be of greatest severity, and those cases in which separating causes (underlying illness vs. research interventions) will be most problematic. The Commission finds the distinction between sick and well subjects to be unsupportable as a basis for policy because it might encourage researchers to recruit their subjects from amongst sick patients. Sick patients are sometimes recruited to *nontherapeutic* research on matters unrelated to their illness. The sick and dependent are already a vulnerable population, in need of compassion and protection. If a sick person is injured in a research project in a way that would entitle a normal subject to compensation, under one of the alternative programs set forth here, then the sick subject's claim to compensation stands on the same ethical ground as any other subject's. Special considerations about the measurement of the resulting injuries may, however, need to be taken into account. For example, the death benefit for a marginal decrease in life-expectancy of a terminally ill patient-subject participating in nontherapeutic research may be subject to a dollar ceiling not applicable in the case of a research-induced death of a normal volunteer.

and to advance knowledge. And the subjects are seldom in a position to insist on receiving the experimental treatment outside a research protocol. For reasons of science, it is usually appropriate (and sometimes required under Federal regulations) to confine the procedure being tested to persons enrolled in a formal experiment. Moreover, the number of care-givers able to employ any significant new procedure will typically be small, and they will probably all be providing it in research settings, either individually or in collaborative projects. Thus though no evil or self-serving motivation is at work, a classic contract of adhesion may nonetheless result. For the patient-subject the choice to enroll in the experiment is a choice *à prendre ou à laisser*.

Some patient-subjects may thus be made to contribute to the general welfare in a way they otherwise might not. Yet society is not necessarily under a strong obligation to compensate those who are injured. This is particularly true if the "contribution" required of patient-subjects does not in fact impose any additional burden on them. The Commission found no conclusive data either to support or to contradict a conclusion that, when viewed as a whole on a retrospective basis, therapeutic research produces worse results than those experienced by comparable patients in standard (or innovative) therapy in settings not formally designated as "research."

Patients enrolled in experiments, however, are sometimes exposed to additional procedures that are undertaken for reasons of the research design rather than strictly for the benefits they provide.<sup>38</sup> As regards these "nonbeneficial" procedures, patient-subjects in therapeutic research are in the same position as are other subjects enrolled in experiments not intended to be therapeutic. Thus, it may be worthwhile to evaluate the practicability of permitting recovery for a limited class of injuries associated with therapeutic research: those arising from research that employs certain procedures that are "nonbeneficial" from the subjects' viewpoint.

All research projects coming within a compensation program should undergo prior review. As part of this review, under existing regulations (see, e.g., 45 CFR §46.118(A)(6) & (7)), the IRB or other responsible officials must assure that approved consent forms disclose whether compensation will be provided in the event of injury. Accordingly, an IRB will

<sup>38</sup> For example, in some therapeutic research, fluid samples are taken more frequently or in greater volume than necessary for proper patient care, in order to gather additional data or to better document the research. Other times, an additional procedure may be performed (e.g., a spinal tap) to learn more about the metabolic effects of a drug under study. If information derived from examination of the spinal fluid, while useful for a research objective, is neither necessary for, nor related to, the care of the patient, then the tap would be a "nonbeneficial" procedure.



have to determine whether or not research is "therapeutic"; if it is, the fact that compensation is unavailable would have to be disclosed as part of the consent process. The HHS officials responsible for the proposed social policy experiment may, however, also wish to explore whether any harm caused by "nonbeneficial" research procedures can be separated from that caused by the research intervention as a whole and whether compensating for such harm is feasible and desirable. If so, the IRBs at a few institutions will need to undertake the additional task of determining whether each therapeutic research protocol involves any "nonbeneficial" procedures. If it does, subjects would be told of the compensation program for any injuries caused by the specified "nonbeneficial" procedures (but not injuries resulting from their underlying disease or from the therapy being tested). At a like number of institutions matched for relevant characteristics, the IRBs would perform the same analysis of the protocols, but compensation would not be promised or paid. Instead, the people conducting the social policy experiment would simply monitor the outcome of the therapeutic research to see how many injuries are reported to have been caused by procedures identified in advance by the IRB as "nonbeneficial." In this fashion it should be possible not only to test the feasibility of identifying "nonbeneficial" procedures in protocols and of separating injuries caused by such procedures from those with other causes, but also to have some idea whether the existence of a compensation program at an institution leads to a higher rate of reported injuries from nonbeneficial procedures. This issue can be further examined when the people conducting the social policy experiment examine the records in each case and review the basis on which a researcher determined that an injury was caused by a "nonbeneficial" procedure in therapeutic research.

**Eligibility for Benefits.** The eligibility criteria must specify which persons may receive benefits, for what types of injury, and on the basis of what proof.

**Subjects of covered research.** Benefits could be limited to persons injured in their capacity as research subjects or could be extended to investigators or to certain third parties injured as a result of research activities. In his testimony before the Commission, Dr. John Arnold of the Quincy Research Center suggested a number of possibilities of third party injury, notably including motor vehicle accidents caused by research subjects unfit to drive, or injuries resulting from aggressive behavior by subjects under the influence of investigational drugs. The Commission suggests that existing legal remedies provide appropriate recourse for third parties injured in such circumstances, and that extension of nonfault liability for injuries of this sort under the compensation system would not be advisable.

In this respect, the Commission departs from the recommendation of the Secretary's Task Force that injured third parties should be compensated where "it is established by a preponderance of evidence that the injury is a *direct* consequence of the research."<sup>39</sup> (Emphasis in original.) The Task Force did not elaborate on what is meant by "direct," and representatives of the insurance industry have expressed considerable skepticism as to the practicability of this distinction. Further, there is serious doubt as to the availability of private insurance to cover third party injuries associated with research. While recognizing that injuries to third parties resulting from research—even indirectly—may be regarded as part of the true social cost of the research enterprise, the Commission believes that such injuries may be excluded from a nonfault compensation system as tangential to the main concerns of the system and as better handled by other means.

One remaining issue is the proper characterization of fetuses *in utero* of women who participate in research during the course of their pregnancies. Existing legal mechanisms may or may not provide appropriate relief in such situations. If a fetus whose mother is a research subject is directly exposed to bodily injury by actions of the investigators, such a fetus could be made eligible for compensation in the event that it is born with an injury indisputably caused by the research. It should be noted that injuries to fetuses, like injuries to other research subjects, may be affected by provisions governing compensation for latent injuries (see below).

**Nontrivial bodily injuries.** The Secretary's Task Force recommended in 1977 that compensation should be provided for "physical, psychological, or social injury" resulting from research. The "interim final regulation" published by the Department on November 3, 1978, required disclosure to subjects, as part of the informed consent process, of the availability of "compensation and medical treatment ... if physical injury occurs."<sup>40</sup> The recently promulgated HHS regulations governing protection of human research subjects eliminate this limitation to "physical" injury, on the basis that "the Department sees no reason to limit such disclosure to only one kind of injury."<sup>41</sup> The question of whether compensation should be provided for psychological or "social" injury (however defined) has been a controversial one, and has received careful consideration by the Commission.

Although the courts have increasingly recognized claims for emotional or psychological damages in defined circumstances (e.g., a mother's claim of emotional anguish on seeing her child injured or killed in a motor vehicle accident, even in

<sup>39</sup> TASK FORCE REPORT, *supra* note 3, at VI-12.

<sup>40</sup> 43 FEDERAL REGISTER 51559 (November 3, 1978), now codified at 45 CFR §46.116(a) (3) (1981).

<sup>41</sup> 46 FEDERAL REGISTER 9383 (January 28, 1981).



the absence of actual or threatened physical injury to the mother herself), many commentators have expressed concern measuring its degree, and computing appropriate monetary damages.<sup>42</sup> All of these concerns have been expressed in letters or presentations to the Commission from representatives of the insurance industry, university risk managers, the Association of American Medical Colleges, researchers, and other independent experts.<sup>43</sup>

Similar objections have been raised regarding the provision of compensation for "social injuries," a term left undefined by the Task Force which has resulted in considerable confusion and misunderstanding. The Commission understands the term "social injury" to refer to injuries to reputation, personal relationships, or legal status resulting from the disclosure of identifiable personal information gathered in the course of research. The Commission believes that the most serious problems likely to arise in this area (e.g., unauthorized disclosures of sensitive private information) are better handled by a combination of careful prior review of the design of research projects posing such risks and, where necessary, pursuit of legal remedies through the courts.

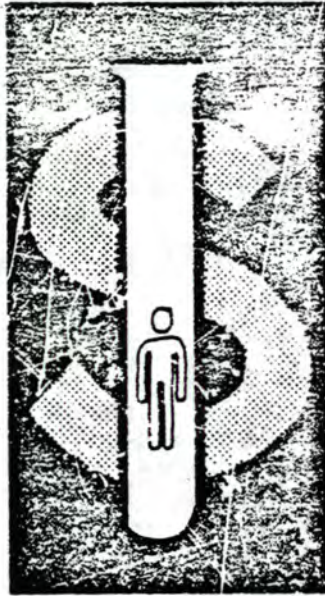
Nevertheless, as revealed in testimony before the Commission, the insurance industry appears willing to provide coverage for "social and emotional injuries" having "some relationship to an actual physical injury" and "directly related" to participation in research.<sup>44</sup> It may eventually prove possible, in addition, to provide compensation for objectively measurable damages, including lost wages and out-of-pocket costs, associated with verifiable manifestations of psychological injuries. The Commission suggests that the feasibility of such coverage be among the variables tested in the compensation experiment.

With respect to trivial bodily injuries, which constitute a large proportion of the adverse effects associated with partici-

<sup>42</sup> See Havighurst, *supra* note 27, at 89-90; see generally, *supra* notes 7-8 in Chapter 2 *infra*.

<sup>43</sup> American Insurance Association, *Statement Before the President's Commission*, see Appendix Q to this Report; University Risk Management and Insurance Association, *Position Paper Regarding a Compensation Program for Adverse Effects of Human Subjects Research* (1980), see Appendix R-1 to this Report at 16; Letter from John F. Sherman, Ph.D. (Vice-President, Association of American Medical Colleges) to Morris Abram (May 7, 1980) see Appendix T-13 to this Report at 6; John D. Arnold, *Incidence of Injury During Clinical Pharmacology Research and Indemnification of Injured Research Subjects at the Quincy Research Center*, see Appendix I to this Report at 19-27; Letter from Philippe V. Cardon, M.D. to Barbara Mishkin (July 3, 1980), see Appendix T-2 to this Report.

<sup>44</sup> Testimony of Dennis R. Connelly, James D. Morrow and John R. Pettit, transcript of 4th meeting of the President's Commission (September 15, 1980) at 150-58.



pation in research, the Commission believes that the administrative burdens and costs of including such injuries in a formal compensation scheme are likely to be unacceptably high relative to the compensation paid out and to the need (measured by degree of injury) of the injured subjects. Further, it appears that minor research injuries are being—and can continue to be—handled adequately by informal means, principally first aid and other medical care provided immediately by the research team and their institutional associates. A threshold level of bodily injury thus appears to be an acceptable prerequisite for coverage under the compensation system.

The Commission's reasoning with respect to dignitary harms is somewhat different, although the result is the same. Subjects improperly denied the opportunity for fully informed consent have suffered injury to their dignity and autonomy, even in the absence of bodily harm from participating in research. The question is whether a compensation system for research injuries should serve as a supplemental policing mechanism, in addition to the IRB and the possibility of legal action, to assure fully informed consent. The dangers of such an approach include the possibility of a heavy burden of claims and administrative paperwork, significant potential for meritorious claims, and a diversion of financial and administrative resources from other uses in the absence of serious physical or economic injury. Absent bodily injury, a nonfault compensation program is probably not an appropriate mechanism for redress in cases of failure by the investigator or the research institution to comply with existing laws and regulations requiring informed consent as a prerequisite to participation in research.

**Causation.** Determining the cause of injuries experienced by research subjects will be difficult at best, especially in the context of therapeutic research or research (whether therapeutic or nontherapeutic) involving seriously ill patients. Even where theoretically satisfactory criteria for delineating causation can be established, the application of these criteria to actual cases by a large-scale, bureaucratic claims-resolution process can be deeply problematic. For example, compensation systems for occupational diseases have been less than



notably successful in discerning the etiology of diseases, and administrative decisions often result in appeals and protracted litigation. These difficulties are probably inescapable given the current state of the art of medical science.

Some compensation systems have sought to avoid these difficulties by creating legal presumptions (e.g., designating specific injuries for which causation need not be proved) or by the simple (but sometimes expensive) expedient of providing compensation for all injuries that occur "in the course of specified activities. Such systems exchange a measure of certainty as to causation for a more streamlined and less costly means of resolving claims. Whether this "tradeoff" is desirable depends on the characteristics of the problem the compensation system is designed to address.

With respect to nontherapeutic research, the Commission believes that problems of causation can be adequately managed through the familiar legal standard of proximate cause, coupled with a mild presumption of causation, through a shifting of the burden of "disproving" causation to the research sponsor.

More difficult questions of causation are likely to arise in the provision of compensation in the event of injuries resulting from nonbeneficial procedures employed in therapeutic research. The Commission encourages the use of expert review bodies and experimentation with different presumptions and standards and burdens of proof for the resolution of difficult questions of causation, and, closely related, of the degree of "excess injury."<sup>4</sup>

**Standards of Conduct.** The extent to which a subject's own improper conduct should exclude that subject from receiving compensation in the event of injury attributable, at least in part, to that conduct must be determined.

Two types of misconduct require special mention in this regard. First is behavior by a subject which is knowingly and deliberately self-destructive. Injuries resulting from willful intention to injure oneself or others are frequently excluded from coverage under workers' compensation and similar programs, and the Commission believes that such injuries should be excluded here.

Conduct which might be characterized as reckless or negligent, though short of willful self-destruction, poses a more difficult problem. Subjects may fail, for example, to provide complete and truthful responses to questions concerning their

<sup>4</sup> To illustrate one possibility: If a subject can demonstrate a "reasonable likelihood" that his injury resulted from a particular research procedure, a presumption of causation could be created. This presumption could then be overcome by clear and convincing scientific evidence that the injury resulted from causes extrinsic to the research.

medical history. Similarly, subjects may fail to heed an investigator's directions with respect to diet, ingestion of alcohol or drugs, or other limitations on behavior during the course of research. Such failures may be either deliberate or inadvertent, and in many cases are likely to proceed from an incomplete awareness of the gravity of possible consequences. The Commission believes that such behavior, not amounting to willful self-destruction, should reduce, but not necessarily eliminate (except in extreme cases) a subject's entitlement to compensation.

**Time for Making a Claim.** The problem of latent effects—adverse effects which are not manifested as injuries for a substantial period of years following exposure to the causative agent—will pose enormous difficulties in structuring a program of private insurance to provide compensation for research injuries. For a variety of technical reasons related to the accounting and financing reserve procedures utilized by the insurance industry, the insurers will almost certainly insist on a so-called "outside limitation" on their period of potential liability. This time limitation would be measured from the date of a subject's last participation in the research procedure, and would impose an absolute cutoff on claims brought after a fixed period. While the insurers have been willing to discuss an outside limitation period as long as ten to fifteen years, such a limitation would nevertheless preclude the award of compensation (through a private insurance mechanism) for injuries resulting from exposure to carcinogenic or other agents with latency periods measured in decades. The insurers candidly acknowledge that under such a provision, "there may well be instances where persons may be viewed as worthy of receiving compensation. Nevertheless, they will not receive it."<sup>46</sup>

The resistance to providing relief for latent effects is not universal. In particular, several Federal workers' compensation programs impose no outside limitation period, and require only that a claim be brought in timely fashion after the injury has manifested itself and the claimant can reasonably be expected to be aware of the causal relationship between the injury and his employment.<sup>47</sup>

<sup>46</sup> Connolly, Morrow, and Pettit, *supra* note 44.

<sup>47</sup> Section 8122 of F.E.C.A. provides, in pertinent part, that:

- (a) An original claim for compensation for disability or death must be filed within 3 years after the injury or death....
- (b) In a case of latent disability, the time for filing claim does not begin to run until the [subject] has a compensable disability and is aware, or by the exercise of reasonable diligence should have been aware, of the causal relationship of the compensable disability to his [participation in covered research]. In such a case, the time for giving notice of injury begins to run when the [subject] is aware, or by the exercise of reasonable diligence



The Commission discerns no ethical rationale for setting any particular cutoff for victims of research-related latent injuries from a compensation program, but does recognize the practical problems involved in providing coverage for such injuries.

The Commission noted in addition that if any compensation plan is tested during an experimental period and later terminated, arrangements must be made either to inform potential research subjects, prior to their participation, that compensation for latent injuries will not be available after a specified period of time, or to establish a fund to cover liabilities for injuries that arise later.

**Nature and Extent of Benefits.** The primary component of "compensation" in the vast majority of cases of research injury will be the provision of medical care required as a result of the injury. The immediate concern is that necessary medical care be available to the injured subject; the second is that the financial burden of such care not fall upon the injured research subjects.<sup>66</sup>

should have been aware, that his condition is causally related to his [participation in covered research], whether or not there is a compensable disability....

(d) The time limitations in subsections (a) and (b) of this section do not--

- (1) begin to run against a minor until he reaches 21 years of age or has had a legal representative appointed; or
- (2) run against an incompetent individual while he is incompetent and has no duly appointed legal representative; or
- (3) run against any individual whose failure to comply is excused by the Secretary on the ground that such notice could not be given because of exceptional circumstances.

<sup>66</sup> For example, F.E.C.A. provides:

§103(a): The United States shall furnish to [a subject] who is injured in the [course of research], the services, appliances, and supplies prescribed or recommended by a qualified physician, which the Secretary of Labor considers likely to cure, give relief, reduce the degree or the period of disability, or aid in lessening the amount of the monthly compensation. These services, appliances, and supplies shall be furnished--

(1) whether or not disability has arisen--

(3) by or on the order of United States medical officers and hospitals, or, at the employee's option, by or on order of physicians and hospitals designated or approved by the Secretary.

The employee may initially select a physician to provide medical services, appliances, and supplies, in accordance with such regulations and instructions as the Secretary considers necessary, and may be furnished necessary and reasonable transportation and expenses incident to the securing of such services, appliances, and supplies....

§103(b): The Secretary, under such limitations or conditions as he considers necessary, may authorize the employing agencies

The Commission heard testimony that short-term medical care is routinely provided by investigators or research institutions in the event of injury to research subjects, usually without charge to the subject. Yet, apart from information provided by the University of Washington and the Quincy Research Center, both of which have formal compensation programs, no systematic empirical evidence to support that claim was advanced, and the Commission's efforts to secure such evidence have been unsuccessful. Furthermore, examination of consent forms gathered from a number of research institutions suggests that the availability of free medical care in the event of injury, if that does constitute institutional policy, is not always brought to the attention of research subjects. Nevertheless, there appears to be no empirical basis for rejecting the claim that much short-term emergency care, and some related services, is provided in the event of research-related injuries although not announced to subjects in advance.

The situation with respect to longer-term medical care and related social and rehabilitative services, as well as long-term medical surveillance, is more difficult but also more clear. Available evidence suggests that few research institutions have made provision for supplying or financing such care. There is little basis for confidence that such care is now generally available, without cost to the subject, in the event of serious injury.

There appears to be little opposition to the notion that a compensation system, if one is to exist, should assure the provision of necessary medical care and closely allied services, both short- and long-term, without cost to a research subject with more than trivial injuries. (The experimental period should allow exploration of the related question: ought such medical care be paid for by the "compensation fund" if it is minor and not expensive? This is a question more of bookkeeping and institutional efficiency rather than one of ethics. It serves as a reminder, however, that the experiment is intended to provide information of practical as well as ethical import.)

Those planning the compensation experiment must also determine the extent to which death benefits should be provided to a subject's survivors. How, if at all, should such benefits be limited in cases of a preexisting condition—particularly a terminal illness? Death benefits might be provided

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to provide for the initial furnishing of medical and other benefits under this section....

8104(a): The Secretary of Labor may direct a permanently disabled individual whose disability is compensable under this subchapter to undergo vocational rehabilitation. The Secretary shall provide for furnishing the vocational rehabilitation services....



either according to a periodic schedule or as a lump-sum payment.

A certain number of research-related injuries result in functional impairments disabling subjects from participating in some or all of the activities of everyday life, whether permanently or for some period of time. Sometimes this entails loss of time from paid employment, possibly resulting in loss of wages. Disability may also entail out-of-pocket costs for housekeeping services, child care, and other activities normally performed by the injured research subject. In other instances, disability may entail losses which are very real, but are harder to measure in monetary terms, e.g., loss of time from school, or worsened conditions for already hospitalized patients. There appears to be little objection, in principle, to the provision of some level of financial compensation for actual loss of wages and out-of-pocket costs directly resulting from research-induced injuries.

While some provision of compensation for financial losses is an accepted objective, questions have been raised about the means for implementing this principle and about its extension to nonmonetary losses. These concerns result, in large part, from fears of abuse and consequent unjustified costs. Experience with other compensation programs now in operation suggests these fears are not without basis.

The issue of benefit levels for disability is relatively straightforward in most compensation systems. In workers' compensation programs, for example, the injured worker is paid a fixed percentage of lost wages, perhaps with some adjustment if there are a dependent spouse and children. In contrast, many subjects of biomedical and behavioral research have no meaningful wage level to provide a basis for this computation. Research subjects include, among others, persons with no current earnings (institutionalized persons, the unemployed, the elderly), and persons whose current wages do not reflect their potential earning capacities (medical students, interns). The small sums provided to some research subjects are remuneration for their time and inconvenience and are unlikely to provide a satisfactory basis for calculating compensation levels in the event of disabling injury. Thus, an alternative approach must be identified if benefits are to be provided in such cases.

Among the several possible approaches outlined for the Commission, one borrows the "average man" concept employed by the Veterans Administration, which determines benefit levels on the basis of a percentage (reflecting the degree of disability) of the earnings of the average worker in the nation, rather than on the basis of the earnings history or potential of the particular person injured.<sup>4</sup> A distinct but

<sup>4</sup> Jones, *supra* note 4.

related approach is embodied in the Federal Employees' Compensation Act, which provides benefits to disabled volunteers in the Peace Corps, VISTA, the Jobs Corps, and similar programs at levels pegged to the Federal GS scale (GS-7 to GS-11 for Peace Corps,<sup>20</sup> GS-2 for the Job Corps<sup>21</sup>). Central to both these approaches is a determination that persons with similar disabilities should receive similar benefits. In addition to the administrative simplicity of this approach, it carries an ethical appeal as well.

This approach is not without its drawbacks however, particularly with respect to incentives that might be created in the recruitment of research subjects. A fixed scale of disability payments might tend to discourage potential subjects with higher current or potential earnings while inducing participation by the poor. If this effect is substantial, it would violate the ethical norms of a just distribution of risks and benefits across the society.

On the other hand, concern has been expressed that the provision of "generous" financial benefits, particularly to persons not currently in the labor force, would induce abusive claims and provide little incentive for the affected individuals to return to normal activities as quickly as feasible. One possible remedy, endorsed by the insurers, the medical colleges, and the university risk managers, would be to impose waiting periods during which disability payments would not be made. Differing waiting periods may be considered for current wage earners and for non-wage earners.

Finally, the Commission notes that a serious problem with many compensation systems, particularly those providing relief for long-term disabilities, is that they include no provision for adjusting benefit levels in response to inflation. As a result, periodic payments which were adequate at the time of award become, over the years, completely inadequate to meet the needs of the disabled party. This problem could be avoided if provision is made to index benefit levels to changes in the cost of living.

#### Limitations on Benefits

*Pain and suffering.* The award of damages for "pain and suffering," in traditional tort litigation, is to restore the injured party, as nearly as possible, to the position he would have been in absent the wrongful injury. In addition to repaying actual dollar losses, an attempt is made to compensate in dollars for intangible losses, including pain and suffering. The calculation of damages for pain and suffering is recognized, however, as very inexact, and some legal scholars argue that awards for pain and suffering constitute, in effect, a way for jurors to

<sup>20</sup> Currently \$15,922 - \$23,586.

<sup>21</sup> Currently \$9,381.



"punish the wrongdoer" and to provide funds for the injured party to pay legal fees.

In nonfault systems, the tacit element of "punishing the wrongdoer" is reduced or eliminated, several barriers to recovery for the injured party are removed, and greater stress is placed both on providing compensation in a manner more precisely tied to measurable losses and on controlling the overall costs of the system. Accordingly, the Commission concludes that recovery for pain and suffering, which is generally excluded from recovery under nonfault systems, should also be excluded here.

For that class of research involving already hospitalized, critically or terminally ill patients, however, a compensation system limited to lost wages and out-of-pocket costs—that is, one which does not cover pain and suffering—may amount to an empty promise. Patients in such research may offer true altruistic service to the society and may suffer grievously from the toxic and painful effects of powerful drugs. The Swedish compensation programs provide a precedent for the award of scheduled benefits, tied to objective criteria, which might be followed in this regard. The Commission suggests that such a feature might be tested during the compensation experiment.

**Punitive damages.** Punitive damages, expressly reserved in tort law for conduct which is intentional, deliberate, and outrageous, are virtually always excluded from nonfault compensation systems. Were such egregious conduct to occur in a research context and result in injury, it is likely that the injured subject could pursue a legal remedy through the tort system. There appears little need to encumber a nonfault compensation system for research injuries with a concept so rooted in the negligence system, and the Commission recommends that punitive damages be excluded.

**Legal fees.** Historically, the introduction of nonfault compensation systems has often been accompanied by hopeful rhetoric about reducing or limiting the role of lawyers. This has rarely, if ever, proved to be the case, and the Commission hesitates to suggest that this system will prove the exception.

In recent years, a number of environmental and civil rights laws have provided for the award of attorneys' fees to the prevailing party in order to encourage attorneys to assist in the vindication of especially prized rights. Such laws remain the exception rather than the rule, however, and few compensation systems now provide for the payment of attorneys' fees to a prevailing claimant. The Commission recommends that fees for attorneys and expert witnesses be excluded from coverage.

**Ceiling on Benefits.** In addition to limitations on compensation built into the definitions of injury and of specific indemnities, the Commission believes that overall ceilings on monetary benefits should be imposed to control costs and preserve the fiscal integrity of the compensation program(s).

during the course of the compensation experiment. For example, overall limitations of \$100,000 and \$10,000 per subject might be tried. Were a compensation program eventually to be adopted, a Federal backup program to provide compensation in excess of this ceiling for claims that arise in Federally supported research might be advisable.

**Offset for Recoveries from Collateral Sources.** While one important justification for the enactment of a nonfault compensation program for research injuries is the inadequacy of existing remedies for injured subjects, the Commission recognizes that many injured subjects are eligible for certain benefits from a variety of sources external to the compensation plan itself.

The traditional approach in tort litigation and in some government programs, including benefits under the Veterans Administration programs, is *not* to reduce benefits to offset recoveries from most other sources. This policy avoids penalizing people for their foresight in securing health and life insurance. Further, this approach is consistent with the theoretical argument that to the extent research (or any other activity) results in injuries, the costs of those injuries are part of the underlying social costs of pursuing the activity. On this view, such injury-related costs should be taken into account by those who make decisions about pursuing (or funding) the activity, whether or not the injured party also happens to have another source of payment for his or her injury. This rationale is expounded by those who analyze the objectives of a compensation system from an economic standpoint, and similar rationales have sometimes been discussed by courts in cases involving drug or vaccine injuries.<sup>22</sup> This approach would regard the compensation program as "primary" in the cost-bearing sense.

On the other hand, a provision allowing offsets for recoveries from at least some collateral sources might significantly reduce the budgetary costs of a compensation program, and is strongly urged by the insurers, the medical colleges, and some, but not all, participants in the university risk managers study. Under this approach, the compensation system would be "secondary" to other sources.

The basic justification of a compensation system for research injuries is to avoid leaving unpredictable, unfair or unbearable economic burdens on the backs of those who have agreed to serve as subjects. To the extent that the costs created by research injuries have already been paid by other sources, this critical function of a compensation system has been met. Since the Commission does not believe that the compensation program would be a good way of "controlling" what research

<sup>22</sup> See Calabresi, *supra* note 26; Havighurst, *supra* note 27; Zeckhauser, *supra* note 28.



gets undertaken, it does not regard it as necessary to attempt to quantify *all* costs to society of the "research enterprise." In particular, the Commission is concerned that the costs of a compensation program not be permitted to escalate in a fashion that would endanger the integrity and continued existence of the program itself, much less endanger biomedical and behavioral research. Accordingly, the Commission suggests that benefits under the experimental program be "secondary" to other sources of benefits, so as to allow limited funds to be used where they are most needed.<sup>22</sup>

**Relation to Alternative Legal Remedies.** As previously noted, much of the impetus for a nonfault compensation system for research injuries derives from the inadequacies of existing legal remedies in providing fair and expeditious relief for such injuries. Nonetheless, in some cases, an injured subject may perceive the possibility of a large recovery through the tort system, as well as a smaller (and more certain) recovery through the nonfault compensation program. The question is whether a subject should be permitted to pursue both remedies, either simultaneously or sequentially.

Most workers' compensation systems were designed to be exclusive remedies, doing away with preexisting legal remedies against the employer and fellow-employees. Over the years, as workers' compensation awards have (by statute) remained low while tort awards have increased dramatically, the courts have allowed that original exclusivity to be eroded. In the present legal environment, there is room for substantial doubt

<sup>22</sup> The Commission suggests that those conducting the compensation experiment not employ compensation programs that would specifically provide for subrogation of the compensation fund to any claim an injured subject may have against any person, other than the investigators or the research sponsor, nor provide for a retroactive adjustment in the amount of compensation after recovery from such a third party. It would seem proper to protect the funds available for compensation payments if the subject's injury has been caused by a third party's wrongdoings; moreover, once a tort claim against a third party has been adjudicated in a subject's favor, the subject would be receiving "double recovery," once from the fund and again from the tort action. The experience with subrogation rights under other governmental compensation schemes, however, is that they are seldom invoked; the United States Attorneys to whom they are assigned do not make them matters of high priority because the amounts involved rarely justify the costs and other burdens of prosecuting the claims. Under Plan I, the F.E.C.A. provisions (§8131 on subrogation and §8132 on adjustment after recovery from a third party) could be applied; a choice will have to be made under Plans II and III whether to provide for subrogation and other aspects of potential excessive compensation (see, for example, §8129 of F.E.C.A., which authorizes regulations to recover over-payments) or to allow experience with these issues to accumulate during the experimental period in order to determine if the cost savings justify the administrative burdens.

that a compensation program for research injuries that purported to provide an exclusive remedy for such injuries would be acceptable to the courts, particularly if the program imposes significant limitations on the size and nature of potential recoveries and requires binding arbitration of disputes. It is also doubtful social policy to deny a subject, severely injured as a result of *negligent* conduct, his right to pursue a substantial damage award in the courts.

On the other hand, one may question the desirability of affording an injured subject two bites at the apple: a quick and relatively certain recovery through the compensation program plus the chance of a large recovery in the courts. These are questions that deserve consideration in designing the "variables" to be tested in the experiment with compensation programs. Among the alternatives a compromise resolution, which is likely to be acceptable to the courts, seems attractive: requiring an injured subject to make a binding election within a reasonable time following injury as to which avenue to pursue. A subject would thereby waive any legal rights to alternate routes of recovery. This is essentially the system now in effect at the University of Washington, and it appears to be acceptable in principle to the insurers.

**Resolution of Disputes.** Any system involving the acceptance and rejection of claims and the determination of benefit levels is likely to result in occasional disputes. To the extent a compensation system for research injuries involves difficult questions of causation or of the extent of injury or may require individualized determinations of benefit levels for subjects with no wage history, those disputes will probably be complex. Recognizing this fact, the Task Force recommended that "the compensable injury criteria should be applied only after a group of competent individuals has reviewed each case and reached a determination whether and to what extent compensation should be given."<sup>24</sup>

One vehicle for the resolution of disputes in this context is arbitration. Arbitration is frequently employed in insurance contexts, and its use as part of a research-injury compensation program appears acceptable to the insurers, as well as to other commentators.<sup>25</sup> The one objection sometimes expressed is that arbitration may tend to provide "something for everyone," rather than clear, principled decisions. This objection could be explored through the compensation experiment.<sup>26</sup>

<sup>24</sup> TASK FORCE REPORT, *supra* note 3, at VI. 2.

<sup>25</sup> Irving Ladimer, *Arbitral Processes For a Program to Compensate Injured Research Subjects* (1980); see Appendix N to this Report.

<sup>26</sup> For example, §8149 of F.E.C.A. provides for administrative review, and §8128(b) of F.E.C.A. provides that final administrative action be

(1) final and conclusive for all purposes and with respect to all



**Financing Mechanisms.** Assuming that compensation should be provided to subjects injured in research, who should pay the costs? Insofar as the ethical basis for providing compensation to subjects injured in research is founded on service rendered to society in general, including future generations, the society at large, acting through the Federal government, would appear to be the appropriate source of funding for a compensation program.

With respect to research conducted by the government—e.g., intramural research at the National Institutes of Health—direct government funding of a compensation program is relatively straightforward. With respect to other classes of research, however, additional factors may be relevant.

One possible function of a compensation program is to provide incentives to researchers and research institutions to conduct research safely. To the degree that these costs of compensation are shared by researchers and research institutions, incentives are created to enhance the safety of their research and to consider carefully the advisability of high-risk research. These incentives are thought to operate even in the context of a nonfault system, where negligence as such is not at issue.

The Commission believes, however, that adequate incentives for the careful conduct of research are provided by existing scientific norms and the consciences of those who place their fellow human beings at risk in experiments; these internal standards are buttressed by requirements for prior IRB approval and by the possibility of tort action in the event of negligence resulting in injury. The Commission is doubtful that imposing the financial and administrative burdens of cost-sharing on research institutions would produce added safety for subjects. Again this is a matter that might be tested; alternatively it might be decided as a matter of policy that the costs of a nonfault compensation system should be borne exclusively by sponsors of the research—and, during the proposed social policy experiment, these costs ought probably be borne solely by the Federal government.

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questions of law and fact; and

(2) not subject to review by another official of the United States or by a court by mandamus or otherwise.



RENEWED

DATE

9-12-83

NTIS



**President's Commission for the Study of  
Ethical Problems in Medicine and  
Biomedical Research, Compensating for  
Research Injuries: The Ethical and Legal  
Implications of Programs to Redress Injured  
Subjects, June 1982, Table of Contents  
Volume II, Appendices**

## President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research

Morris B. Abram, M.A., J.D., LL.D., *Chairman*,  
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**Social and  
Philosophical  
Perspectives**

**I**



President's Commission for the Study of Ethical Problems  
in Medicine and Biomedical and Behavioral Research  
Room 405, 2000 K Street, N.W., Washington, DC 20006 (202) 692-8201

June 11, 1982

The Honorable Richard Schweiker  
Secretary  
Department of Health and  
Human Services  
Washington, D.C. 20201

Dear Mr. Schweiker:

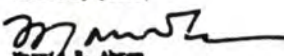
On behalf of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, I am pleased to transmit our report on Compensation for Research Injuries. As you know, this study was not within the Commission's statutory mandate. We embarked upon it at the urging of your Department's Ethics Advisory Board and with the support of your predecessor, Patricia Roberts Harris, in hopes that we could resolve a problem of considerable complexity that has been a matter of concern within the Department, and the Federal government generally, for some years.

Other individuals and groups who have examined this issue, including the HHS Secretary's Task Force in 1977, have recognized the justice of providing compensation to subjects injured in research. The Commission finds, however, that present data do not provide an adequate basis to decide whether the ethical obligation toward subjects should be met through a Federally sponsored or mandated program or can be left to individual initiative and *ad hoc* arrangements. To determine the need for, and practical feasibility of, a compensation program, the Commission recommends that a small experiment be undertaken over a three to five year period.

Compensation plans with varied features could be tried out at several research institutions, including the Clinical Center of the National Institutes of Health, while data were also being gathered at other institutions without compensation programs. Through this two-part effort to gather data, it should be possible both to measure the apparent overall magnitude of research injuries and to determine the effect of a program's existence on the frequency and severity of the injuries reported. The objectives of the experiment and details about the programs that could be tested are set forth in this Report and its separate Appendix volume, which contains additional supporting material.

Although we have not been able to write the last word on this subject, we hope to have advanced the discussion. Final decisions on this matter, we believe, are best left to your Department as part of its statutory authority for the administration of Federal support for biomedical and behavioral research. Other Federal research agencies, as well as the private sponsors of research with human subjects, will doubtless be guided by your experience in assessing possible formats for compensation programs.

Sincerely yours,

  
Morris S. Abram  
Chairman



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Volume Two: Appendices, which contains studies prepared for  
the Commission, material submitted for its consideration, and  
possible compensation plans;



## Summary and Conclusions

The origin of this study by the President's Commission was a suggestion conveyed by Dr. David Hamburg, the Vice-Chairman of the Ethics Advisory Board in the Department of Health, Education and Welfare (HEW), when he testified at the Commission's first meeting in January 1960. Dr. Hamburg explained that the Board would be unable, prior to its demise in September 1980, to offer the Secretary the advice she had requested concerning the advisability of the recommendations for a program to compensate subjects injured in research that had been submitted to the Secretary by an HEW Task Force in 1977. Like virtually all committees and individuals who had studied the subject, the HEW Task Force had concluded that people who are harmed as a result of participating in research ought to receive some compensation for their injuries. The Secretary informed the Commission that she would be pleased to have it take up the inquiry and would provide support for necessary studies.

The more deeply the Commission looked into the subject, the more difficult it became to provide a simple reply to the questions originally posed by the Secretary. The Commission has concluded that it would be ethically desirable to remedy as a matter of course any harm suffered by subjects as a direct consequence of the added risks of participating in research. Yet even if it is ethically desirable for compensation to be provided, it does not follow that the Federal government has an ethical obligation to establish or to require a formal compensation program in all research projects supported or regulated by the government. For the latter, it is necessary to demonstrate the existence of unmet need and to weigh that need against other needs in the public arena.

### The Question at Issue

In this Report the Commission seeks the answer for the following question: Are subjects who deserve compensation for research injuries not receiving it?<sup>1</sup> In light of the many earlier examinations of the subject of research compensation, the Commission began with the hypothesis that the answer to this question was "yes." If the answer to the question were in the affirmative, the Commission understood its further task to be the design of a compensation plan that would respond to the needs uncovered in its study.

It is apparent that the hypothesis that the Commission set out to test actually encompasses issues of both an empirical and a philosophical nature. Specifically, the original question reflects several underlying questions: (1) What does one mean by "deserve compensation"? (2) How many such subjects are injured each year in research, and how severely? and (3) Which of these subjects receive no compensation at present, and why? The Commission has found itself more able to answer some of these questions than others. The question of what ought to be encompassed within "compensation for research injuries" and the question of who deserves such compensation are fully addressed in this report. In investigating the empirical issues, however, the Commission was able to expand upon the existing knowledge but unable to find data sufficient to resolve fully the questions of the extent of present injuries and of present redress. The absence of data on injuries is not, needless to say, the same as data on the absence of injuries.

### Alternative Responses to Inconclusive Data

From this outcome several conclusions might be drawn. One might conclude that what is needed is further data gathering about the existence of research injuries. Indeed, in its First Biennial Report on *Protecting Human Subjects*, submitted to the President and Congress in December 1981, the Commission recommended that investigators conducting Federally funded research routinely submit data on the number of subjects involved in such research and the number and extent of injuries suffered, on an annual basis. From such data, as well as supplementary inquiries, it ought to be possible to provide a better answer to the empirical questions addressed in this report.

<sup>1</sup> In other contexts the term "compensation" connotes payment for services rendered. In this Report the term is used solely to indicate payments made to redress an injury after the fact; payment for the time and trouble of participating in research is termed "remuneration."



There are, however, reasons to doubt that this approach will provide sufficient data. In the absence of a formal compensation mechanism there is good reason to doubt that subjects or investigators will adequately report the occurrence and extent of injuries suffered by subjects in research. Furthermore, it is only through experience with compensation programs that two of the most difficult questions that are always raised in opposition to such programs can be answered: first, what are the administrative costs of the programs, including the costs of distinguishing between injuries deserving compensation and those claims that do not deserve to be compensated (and that, it is assumed, would not be asserted in the absence of a compensation program)? Second, do feasible means exist to differentiate harm to subjects in therapeutic research that results from research procedures from harm that flows from the medical intervention being tested?<sup>2</sup>

Clearly, an experimental trial of one or more compensation programs is more likely than simply collecting data in the absence of such programs to provide the necessary information for the formulation of appropriate public policy. Yet that approach would entail greater costs, since an experiment to gather the data would involve the expenditure of time and money in design and execution. At a time when the Federal funds available for biomedical and behavioral research are not keeping up with the rate of inflation, there are more than the usual reasons to question any suggested expenditures in new areas. It may well be, therefore, that those with responsibility for the decision in the Department of Health and Human Services (HHS) will conclude that an experiment of the sort set forth in this Report is not justified at this time. On balance, however, the Commission recommends that such an experiment be undertaken, because in the absence of such an investigation of the need for, and feasibility of, compensation programs, it believes that policymakers will be in no better position to answer the questions addressed by this Report in five years than they are today.

<sup>2</sup> The term "therapeutic research" is used loosely to describe any experimental or innovative steps taken as part of an attempt to treat subjects suffering from disease (in comparison with "nontherapeutic research," which employs subjects not affected by the disease being studied). The Commission uses the term to mean research to evaluate practices or procedures that are intended to provide, or that have some reasonable possibility of providing, therapeutic, diagnostic or preventive health benefits to subjects. Such research therefore involves two parts: (1) the practice or procedure that is being evaluated and (2) any nonbeneficial research procedure that is unnecessary for a subject's own welfare and is performed solely as an aid to the research process.

### The Recommended Experiment

The suggestion of compensation for research injuries has been a mainstay of ethical and public-policy discussions of research with human subjects for many years. The time has come to determine the wisdom of those suggestions. The failure to resolve the issue not only exposes subjects of research to a possible wrong—it exposes the entire research enterprise to the public recriminations that could follow from one or a series of serious, uncompensated injuries to subjects. The importance of biomedical and behavioral research for this country is manifested in the many billions of dollars that such research receives each year in an attempt to conquer disease and to relieve human suffering. The formal ethical standards and individual consciences of investigators, as well as Federal rules and guidelines developed in the past two decades, have done much to protect research subjects and to reduce the risk of injury to them. Some risk remains nevertheless—risk that though statistically small may manifest itself in serious ways for individuals. A social policy experiment is needed to see whether compensation programs might provide a feasible means further to reduce the risk of unremedied injury to subjects and to avoid the occurrence of events that might needlessly tarnish the reputation of research.

Accordingly, the Commission recommends that the Secretary of Health and Human Services conduct a small-scale experiment in which several institutions would receive Federal support over three to five years for the administrative and insurance costs of providing compensation on a nonfault basis to injured research subjects. At different institutions the features of the compensation plan could be varied (*i.e.*, the level of benefits provided; means of determining causation, whether nonphysical injuries would be covered; whether certain injuries arising in therapeutic as well as nontherapeutic research would be covered; etc.). Information derived from such variations, as well as from the experience of comparable institutions without research compensation programs, should permit HHS to determine not only the need for a full-scale program, if any, but also the format and auspices that appear best suited to achieve the desired results.

### The Format of the Report

The first part of this Report explores the origin and context of the issue of compensating for research injuries. The first chapter introduces such social and cultural factors as the relationship of subjects to the research enterprise and concerns about cost-spreading in a risk-conscious society. Chapter Two places the present study into the setting of research regulation since World War II. During this period, proposals for injured subjects' compensation were made in many contexts but



seldom were accompanied by more than a rough sketch of the details of a plan of implementation.

Part Two delves into the several parts of the basic question: Are injured subjects who might deserve compensation not receiving it? Chapter Three examines the ethical theories—sometimes competing and sometimes complementary—that shed light on the question of subjects' deserts. In the case of injuries to voluntary, informed subjects, a strong moral claim for recompense does not emerge. Whether such ideal subjects actually exist is a serious ethical issue, and one that cannot be ignored in policy formulation. It would, moreover, appear to be morally preferable, on grounds both of fairness and of gratitude, not to insist that subjects waive all claims for redress as part of consenting to research, particularly nontherapeutic research.

Chapter Four analyzes the existing data on the incidence and severity of research injuries. While data from existing programs suggest that nonfault insurance is an efficient and inexpensive means of providing recompense for research injuries, there also appear to have been few injuries at the handful of institutions that already have formal compensation programs. Why are other injured subjects not guaranteed recompense? In Chapter Five, existing legal rights and remedies are examined. The limitations of negligence and strict liability as bases for recovery at law arise from the restricted nature of the legal duties owed to subjects, the waiver of rights implied by consent, and the difficulty of proving causation. Under nonfault systems, some although not all of these barriers to recovery are removed.

Through this examination, the Commission arrives at a partially affirmative answer to the question of whether or not there is an unmet obligation to injured research subjects. Available information does not, however, provide the definitive basis for a recommendation to undertake a compensation program, through Federal sponsorship or under the mandate of Federal regulations. Instead, in Part Three of this Report, the Commission sets forth the issues that could be resolved through a "social policy experiment." Since the request for this study came from what is now the Department of Health and Human Services (HHS), which is the major Federal sponsor of biomedical and behavioral research with human beings, and since the Commission has previously recommended that the Department become the lead agency in overseeing regulations on the protection of research subjects, the Commission believes that the experimental compensation programs should be conducted under the aegis of HHS.

**Selected text from Women and Health Research, National Academy Press, 1994,  
p. 169 and Appendix D.**



With regard to the latter, the new federal policies calling for inclusion of women in clinical studies will help establish new standards that will be relevant to legal actions.

Many of the concerns voiced about liability in the context of research including women are the same as those with regard to the tort system in general. For example, expert scientific testimony is necessary to establish that a particular drug caused an injury. There are inherent difficulties in assuring the unbiased nature of such testimony in what are often highly technical cases.

**The committee recommends that current and future initiatives toward general tort reform include attention to issues of research-related injury, including issues of proof of causation.**

The question of whether there should be a special compensation scheme for injuries sustained by children as a result of a parent's participation in a clinical study is similar to that raised in the context of research subjects in general. The committee does not recommend adoption—at this time—of a special compensation scheme limited to coverage of children injured prenatally or preconceptually. Any new compensation scheme focusing only on such injuries poses especially difficult problems with regard to establishing causation and averting large numbers of questionable recoveries. Appendix D discusses several existing compensation schemes dealing with children and illustrates these and other difficulties.

**The committee recommends that NIH thoroughly review the area of compensation for research injury in general and that consideration of implementation of any compensation scheme include attention to prenatal and preconceptual injuries to children resulting from a parent's participation in a clinical study.**

Our current health care reimbursement system does not include coverage for medical care resulting from injuries sustained during research. This could be accomplished through a system of universal access with adequate coverage.

**The committee recommends that health care reform efforts include considerations of medical care for research-related injury.**

The committee recognizes that, regardless of their basis or justification, fears about liability are real. On balance, however, the committee concludes that liability concerns should not represent an impediment to implementation of public policies that favor the broader inclusion of women in clinical studies.

## D

# Compensation Systems for Research Injuries

This appendix provides information about compensation systems for research injuries, including: (1) an account of existing compensation systems; (2) the history of past efforts to enact a national system; (3) the issues to be considered when setting up such a system; and (4) lessons to be learned from the experiences of existing compensation systems in the area of medical malpractice.

### EXISTING COMPENSATION SYSTEMS

There is no comprehensive compensation program to cover injuries resulting from privately and publicly funded research. Current federal policy, which applies to federally funded research with "more than minimal risk" to participants, requires that institutions that maintain a compensation system must inform participants of its existence as part of the informed consent process (45 C.F.R. 46.116(a)(6)).

Some institutions have set up their own compensation systems, but many others lack formal policies on compensation but provide acute care for research injuries as a matter of practice. No agency within DHHS, including NIH, currently has a formal compensation policy for injuries resulting from extramural or intramural research. For intramural research, acute care for injuries is routinely provided.

Beyond acute care, however, an injured research participant's only recourse is legal action under the Federal Tort Claims Act (FTCA) (F.W.



Dommel, Office for Protection from Research Risks, personal communication, July 1993). For extramural research, the institutions conducting the research may formulate their own policies regarding compensation, including the option to offer none at all. Most provide acute care for research injuries, but the Office of Protection from Research Risks at NIH knows of no institutions that offer long-term care (F.W. Dommel, Office for Protection from Research Risks, personal communication, July 1993).

Despite the lack of federal guidance in this area, some institutions and pharmaceutical manufacturers have set up compensation systems for research injuries. For example, the University of Washington, the public institution receiving the largest amount of federal biomedical research dollars, has had a liability insurance program that would extend to research injuries in place since 1976.<sup>1</sup> But the University of Washington's program appears to be unique. Most research institutions require participants, as part of the informed consent process, to attest to private insurance coverage of medical costs resulting from research injuries (Kolberg, 1993).

Pharmaceutical manufacturers typically have in-house compensation schemes that pay for medical expenses of injuries directly resulting from drug trials. Pharmaceutical companies also carry liability insurance that would probably reimburse them for loss if a participant brings a successful tort action against them.

#### EFFORTS TO DEVELOP A NATIONAL SYSTEM

There has been an ongoing debate since the 1970s about the merits of establishing a compensation system for all participants injured in research (Mariner, 1994). The Public Health Service (PHS) has examined the issue of establishing a compensation system for research injuries over a number of years. In the 1970s, NIH submitted three proposals to the secretary of the Department of Health, Education, and Welfare (HEW)<sup>2</sup> that would have authorized the federal government to indemnify participants in research sponsored in whole or in part by federal funds for any medical and other expenses resulting from research injuries. None of the proposals was accepted.<sup>3</sup> In 1973 an ad hoc panel of the assistant secretary for health (HEW), reviewing the Tuskegee Syphilis Study, recommended a no-fault compensation system (Mariner, 1994). Although no such system was established, HEW reached settlement agreements with all survivors and with some heirs of participants in the Tuskegee study.

In 1975 HEW created a task force to look at compensation for research injuries resulting from federally funded, conducted, and regulated research. The task force recommended that human subjects who suffer physical, psychological, or social injury in the course of research supported by PHS should be compensated if the injury was caused by the research and "the

injury on balance exceeds that reasonably associated with such illness from which the subject may be suffering, as well as with treatment usually associated with such illness at the time the subject began participation in research" (HEW, 1977:II-2).

The task force recommended that participants in intramural research be covered by expanding the Federal Employee's Compensation Act (FECA)<sup>4</sup> to include research participants. For extramural research directly supported by PHS, the task force proposed that institutions be required to offer assurance of compensation to each participant, with the compensation to be no less than that provided under FECA. If upon further inquiry the secretary found that it would not be possible for institutions to assure compensation for injured research participants, the task force suggested that FECA be expanded to cover compensation for these participants as well. For research that was regulated but not financially supported by PHS, the task force recommended that the FDA consider legislation that would enable them to require that compensation be made available to injured research participants (HEW, 1977). Drafts of legislation to amend FECA to include participants in research were sent to HEW Secretary Joseph Califano, and proposed regulations to implement the task force's recommendations were also prepared. The same week in August 1979 that Califano was scheduled to sign the proposed rules and forward legislation to the Congress, he was fired by President Carter (Kolberg, 1993). The issue was not picked up by his successor.

After the task force released its report in 1977, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research endorsed the recommendations but, without further study, recommended only that subjects be told in the informed consent process whether or not compensation was available (Mariner, 1994).<sup>5</sup>

The secretary of HEW then asked the department's Ethics Advisory Board to look into the recommendations, but the board was dissolved before it could complete the task. Before its termination, the board requested that the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research continue to consider the issue of compensation. The commission concluded in 1982 that compensation for research injuries was ethically desirable, and suggested that HEW (by now, DHHS) conduct a trial of different forms of compensation systems. Several institutions were to receive federal money over a period of 3-5 years to cover the costs of providing some form of no-fault compensation to injured research subjects (President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, 1982). Although DHHS considered such experiments, it concluded that they were not feasible and decided not to initiate the trials (C. McCarthy, former director of OPRR, personal communication, July 1993).



Recently there have been more efforts to investigate the possibility of compensation for injured research participants. In January 1993, the Recombinant DNA Advisory Committee (RAC) sent a letter to NIH Director Bernadine Healy, asking her to form a panel to look at covering medical costs of research-related, nonnegligent injuries. The letter stated that it was "unfair to expect individuals, their families, or their insurers to absorb unpredictable and potentially substantial medical costs arising out of these individuals' participation as research subjects" (Walters, 1993a). In a subsequent letter, the RAC appealed to Dr. Healy to ask the health care reform task force to address the issue of providing health care coverage for persons who are injured as a result of participating in clinical research (Walters, 1993b).

The effort to investigate compensation for research injuries is not limited to the United States. Although countries with national health care systems generally do not face the same pressures to create a separate compensation system for research injuries (President's Commission, 1982), nevertheless two major international health organizations developed compensation recommendations. The same year the commission released its report, the World Health Organization (WHO) and the Council for International Organizations of Medical Sciences (CIOMS) issued their guidelines for human subjects research, which declared that volunteer subjects are entitled to full compensation for temporary or permanent disability or death.

These guidelines also recommended that pharmaceutical manufacturers assume responsibility for injuries resulting from research they sponsor. A recently revised version of these guidelines (1993) states that every subject is entitled to equitable compensation, except for expected adverse reactions from investigational interventions to diagnose or prevent disease (Mariner, 1994).

#### ISSUES IN DEVELOPING A NATIONAL COMPENSATION SYSTEM

Professor Mariner, in her paper published in Volume 2 of this report, discusses a variety of compensation systems for research injuries and their advantages and disadvantages. Advantages of a federal compensation program include the ability of injured parties to get benefits more easily, because they are not required to go into court and prove fault; usually, they need only show plausible evidence that their injuries were research-related. Other advantages include a higher percentage of injured participants and offspring receiving compensation, as well as a higher percentage of each compensation award going directly to the injured party.

In addition, the costs to administer the system are far less than those of litigation. These costs may be spread over all who benefit from the research

enterprise, particularly if the program is funded through general tax revenues (Mariner, 1994).

Disadvantages to a compensation system include the difficulty that some claimants may have showing the causal relationship between their injuries and the research. This would be particularly relevant in the case of offspring injuries, where causation is often nearly impossible to prove. In addition, the existence of a compensation system may result in more people making claims under the system than would have otherwise pursued recovery through the courts. This may indicate a real need for the program; but it may also result in an unjustifiable rise in program costs, because people can misjudge the cause of their injuries (Mariner, 1994).

The issues to be considered in developing a compensation system are numerous and complex. One crucial issue that must be resolved is determining *who* and *what* gets compensated (Mariner, 1994). For example, should the compensation system be available to all research participants, or only those participating in research for which they receive no health benefits? The issues are arguably more complex if offspring injured by a parent's participation in a clinical trial are to be included in the system. For example, if the parent consented to research after being adequately informed, is an offspring injury still eligible for compensation? Would the system cover injuries to offspring in protocols where the parent agreed to use contraception, and subsequently used inadequate contraception or none at all?

Once it is determined *who* is to be compensated, the next question is: *what* injuries will be eligible for compensation? The resolution of this issue is particularly important for offspring injuries, because their injuries are often discovered many years after the research protocol is complete. The section below discusses three specific examples of compensation systems set up to alleviate medical malpractice concerns, and it demonstrates the relative advantages and disadvantages between setting up a system with a broad base of compensable events and restricting the system to specific types of injuries.

Another important feature of any compensation system is the extent of the benefits available to eligible participants. The current tort system provides the most generous compensation available, with benefits ranging from recompense for physical injuries and lost wages to pain and suffering and, occasionally, punitive damages (Abraham, 1988). But since a compensation system offers some benefit to the participant in the rapid recovery of damages with administratively easy procedures, the participant is in turn asked to forego full recovery. The resolution of the question of benefits requires a compromise between the desire to be fair to the participant and the need to create a system that will remain fiscally solvent over time. Any compensation system necessarily limits recovery relative to what a plaintiff could gain pursuing a claim through the tort system, which creates some question



of horizontal justice: persons suffering injury from other causes can recover full tort damages, whereas those injured through research are entitled to limited recovery (Abraham, 1988). This concern would be alleviated, however, by allowing injured research participants to elect the system in which to pursue recovery. In addition, a decision must be made about whether the system will be applied retroactively or only to prospective participants (Mariner, 1994).

A related issue to the scope of benefits is the payment mechanism. Built into any compensation system is a structure for paying out benefits. Under a third-party insurance scheme, groups and individuals involved in the conduct of research would be required to obtain private insurance to cover research injuries. If a system requires first-party insurance, the participant is required to purchase insurance before entering a clinical study. Under a social insurance system, the government would insure or reinsure individuals or groups conducting research against the costs of research injuries. Finally, patient compensation funds could serve as the available pool of money for compensating research injuries, for which contributions may be exacted from the various groups involved in the conduct of research (Abraham, 1988).

How the system would be administered is also a critical consideration. To some extent it will be governed by the payment mechanism selected. For example, a third- or first-party insurance-based system will likely be administered by an insurance company. If the system is government-sponsored, an agency will need to be set up to handle the claims. Within issues of administration are concerns about the participants' right to appeal any decisions not to compensate (Mariner, 1994).

Although in theory the creation of a compensation system for research injuries appears to be a worthwhile endeavor, it is by no means an uncomplicated solution. As demonstrated above, the complexities involved in setting up a compensation system are numerous, and decisions made in structuring the system have direct implications for how fairly the compensation system will meet the burden of research injuries.

#### EXAMPLES OF COMPENSATION SYSTEMS IN THE AREA OF MEDICAL MALPRACTICE

The debate about tort reform in the area of medical malpractice has been an active one for more than a decade. Given the similarity in legal issues between medical malpractice and liability for research injuries, examples of medical malpractice reform efforts may be particularly instructive to any consideration of a compensation system for research injuries. This section discusses the advantages and disadvantages of three examples:

the birth injury compensation systems in Virginia and Florida, and the National Vaccine Injury Compensation Act.

### Virginia and Florida

During the late 1980s, legislatures in Virginia and Florida enacted narrowly circumscribed no-fault compensation schemes to alleviate insurer concern about particularly high damage awards in cases where infants sustained severe, disabling neurological injury during the delivery process.

Under the Virginia Birth-Related Neurological Injury Compensation Act (Va. Code §§ 38.2-5000 et seq. [1990 Real. Vol.]), an infant sustaining "birth-related neurological injury," as defined in the act, is entitled to payment for medical, rehabilitative, and residential expenses not recoverable from any governmental program or private insurance. The infant also receives reasonable expenses of filing a claim and a scheduled amount for loss of earnings between ages 18 and 65. Eligibility for compensation also depends on whether a child was delivered by a "participating physician" or in a "participating hospital." Damages are not recoverable for pain and suffering. In circumstances where the act applies, the remedies it provides are exclusive, supplanting the tort system.

One distinguishing element to Virginia's system is its very limited applicability. Even after an amendment that broadened the act's original definition of "birth-related neurological injury," it remains very limited in scope. In addition, the act requires that the disability must cause the infant to be "permanently in need of assistance in all activities of daily living." As a result of the narrow scope of coverage, by mid-1993 only four claims had been paid under the Virginia Act.

The Virginia scheme is financed through annually assessing physicians and hospitals, with possible surcharges against insurers should that become necessary. Currently *every* physician in the state is assessed \$250 annually.<sup>6</sup> "Participating physicians" pay \$5,000 and "participating hospitals" pay according to the number of live births in their facility during the previous year.

Florida's no-fault compensation scheme was modeled largely on the Virginia law. Its definition of "injury" is different, however, and far more claims have been paid under Florida's act, even though it has been in operation for less time. This may well be not only because of the somewhat less restrictive definition but also because Florida provides for a lump-sum payment of as much as \$100,000. All hospitals are required participants under the Florida act.



### National Childhood Vaccine Injury Act

The National Childhood Vaccine Injury Act (42 U.S.C.A. § 300aa-1 to -33 [1989]) was enacted by Congress to provide payments to children suffering harm through vaccine-related accidents on a "no-fault" basis. The ostensible purpose was to assure that vaccine production would continue. Before passage of the act, the costs of liability for vaccine-related injuries were grossly out of proportion to the profits manufacturers derived from the sale of vaccines. Under the act, an injured party must first file a claim with the Department of Health and Human Services. The injuries eligible for compensation are strictly prescribed, and the likelihood of receiving compensation depends on whether the injury appears in the Vaccine Injury Table.

The major advantage of the act is that once a claimant demonstrates an injury from the Vaccine Injury Table, he or she is eligible to receive compensation for damages; there is no need to show that anyone was negligent. The damages are limited, however, including only actual costs of treatment not covered by public or private insurance and attorneys' fees, with caps on damages for pain and suffering (Clayton and Hickson, 1990). Children whose injuries do not appear in the table must show that the vaccine actually caused their injuries, which can be difficult to prove. If a compensation award is offered and the family accepts it, they may not pursue a legal action in tort against the vaccine manufacturer or the physician. If the family chooses not to accept the award (or if the claim is rejected as ineligible for compensation), the family may pursue recovery through the tort system (Clayton and Hickson, 1990).

The advantages of the act include the guarantee of some measure of recovery for eligible children, without the delays and often prohibitive requirements of the tort system—for example, the need to prove negligence. Because of the choice to limit the compensable injuries, however, there may be injured children who receive no compensation. In addition, the Congressional Budget Office estimates that 220 vaccine-related injuries occur each year (Clayton and Hickson, 1990, citing H. Rep. No. 100-391, 100th Cong., 1st Sess. 693-4 [1987]). But there is a limit of 150 awards a year, which means that the act will lapse unless Congress steps in to provide more funds (Clayton and Hickson, 1990). Thus, there is reason to be concerned that the system could collapse under the weight of eligible claims.

### NOTES

1. The coverage, provided on a no-fault basis, has an upper limit of \$10,000, is limited to expenses from physical injuries, and applies only to injuries to healthy, normal participants (H. McGough, Human Subjects Di-

vision. University of Washington, personal communication, June 1993). As a condition of accepting reimbursement for physical injuries, the participant waives the right to seek legal action in tort against the university. In the past five years there have only been three or four claims for compensation, and the university has paid less than \$2,000 in compensation for injuries (E. Cherry, Risk Management Office, University of Washington, personal communication, June 1993).

2. The health and welfare components of HEW are now the Department of Health and Human Services (DHHS).

3. The proposals were rejected for one or more of the following reasons: the social and fiscal implications of the proposal had not been adequately investigated, alternatives to a federal compensation program had not been examined, and the extent of the problem had not been fully defined (HEW, 1977).

4. FECA is the statute that specifies limited levels of compensation for federal employees who are injured in the course of their work.

5. This recommendation was incorporated into the federal regulations governing human subjects research (45 C.F.R. section 46.116(a)(6)).

6. There are exceptions for retired physicians and others working in free clinics. See Va. Code section 38.2-5020.D (Cum. Sup. 1992).

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- 42 USCA §300aa-1 to -33 (1989)
- 45 C.F.R. 46.116(a)(b)
- Va. Code Sections 38.2-5000 et seq. [1990 Real. Vol.]