ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS

GUIDE TO THE FINAL REPORT

The final report is written in an easily accessible style, but it is of necessity long. This guide provides a roadmap and capsule descriptions of each section of the report.

Preface

The Preface explains why the Committee was created, the President's charge, and the Committee's approach.

Introduction: The Atomic Century

The Introduction describes the intersection of several developments: the birth and remarkable growth of radiation science; the parallel changes in medicine and medical research; and the intersection of these changes with government programs that called on medical researchers to play important new roles beyond that involved in the traditional doctor-patient relationship. The introduction concludes with a section titled "The Basics of Radiation Scienc for the lay reader.

Part I. Ethics of Human Subjects Research: a Historical Perspective

Chapter 1

In chapter 1 we report what we have been able to reconstruct about government rules policies in the 1940s and 1950s regarding human experiments. We focus primarily on the Ato Energy Commission and the Department of Defense, because their history with respect to hum subjects research policy is less well known than that of the Department of Health, Education, a Welfare (now the Department of Health and Human Services). Drawing on records that were previously obscure, or only recently declassified, we reveal the perhaps surprising finding that officials and experts in the highest reaches of the AEC and DOD discussed requirements for human experiments in the first years of the Cold War. We also briefly discuss the research policies of DHEW and the Veterans Administration during these years.

Chapter 2

In chapter 2 we turn from a consideration of government standards to an exploration of the norms and practices of physicians and medical scientists who conducted research with human subjects during this period. We include here an analysis of the significance of the Nuremberg Code, which arose out of the international war crimes trial of German physicians in 1947. Using the results of our Ethics Oral History Project, and other sources, we also examine how scientists of the time viewed their moral responsibilities to human subjects as well as how this translated

into the manner in which they conducted their research. Of particular interest are the differences in professional norms and practices between research in which patients are used as subjects and research involving so-called healthy volunteers.

Chapter 3

In chapter 3 we return to the question of government standards, focusing now on the 1960s and 1970s. In the first part of this chapter, we review the well-documented developments that influenced and led up to two landmark events in the history of government policy on research involving human subjects: the promulgation by DHEW of comprehensive regulations for oversight of human subjects research and passage by Congress of the National Research Act. In the latter part of the chapter we review developments and policies governing human research in agencies other than DHEW, a history that has received comparatively little scholarly attention. We also discuss scandals in human research conducted by the DOD and the CIA that came to light in the 1970s and that influenced subsequent agency policies.

Chapter 4

With the historical context established in chapters 1 through 3, we turn in chapter 4 to the core of our charge. Here we put forward and defend three kinds of ethical standards for evaluating human radiation experiments conducted from 1944 to 1974. We embed these standards in a moral framework intended to clarify and facilitate the difficult task of making judgments about the past.

Part II. Case Studies

Chapter 5

In chapter 5, we look at the Manhattan Project plutonium-injection experiments and related experimentation. Sick patients were used in sometimes secret experimentation to develop data needed to protect the health and safety of nuclear weapons workers. The experiments raise questions of the use of sick patients for purposes that are not of benefit to them, the role of national security in permitting conduct that might not otherwise be justified, and the use of secrecy for the purpose of protecting the government from embarrassment and potential liability.

Chapter 6

In contrast to the plutonium injections, the vast majority of human radiation experiments were not conducted in secret. Indeed, the use of radioisotopes in biomedical research was

publicly and actively promoted by the Atomic Energy Commission. Among the several thousand experiments about which little information is currently available, most fall into this category. The Committee adopted a two-pronged strategy to study this phenomenon. In chapter 6, we describe the system the AEC developed for the distribution of isotopes to be used in human research. This system was the primary provider of the source material for human experimentation in the postwar period. In studying the operation of the radioisotope distribution system, and the related "human use" committees at local institutions, we sought to learn the ground rules that governed the conduct of the majority of human radiation experiments, most of which have received little or no public attention. Also in this chapter we review how research with radioisotopes has contributed to advances in medicine.

Chapter 7

The Committee then selected for particular consideration, in chapter 7, radioisotope research that used children as subjects. We determined to focus on children for several reasons. First, at low levels of radiation exposure, children are at greater risk of harm than adults. Second, children were the most appropriate group in which to pursue the Committee's mandate with respect to notification of former subjects for medical reasons. They are the group most likely to have been harmed by their participation in research, and they are more likely than other former subjects still to be alive. Third, when the Committee considered how best to study subject populations that were most likely to be exploited because of their relative dependency or powerlessness, children were the only subjects who could readily be identified in the meager documentation available. By contrast, characteristics such as gender, ethnicity, and social class were rarely noted in research reports of the day.

Chapter 8

Moving from case studies focused on the injection or ingestion of radioisotopes, chapter 8 shifts to experimentation in which sick patients were subjected to externally administered total-body irradiation (TBI). The Committee discovered that the highly publicized TBI experiments conducted at the University of Cincinnati were only the last of a series in which the government sought to use data from patients undergoing TBI treatment to gain information for nuclear weapons development and use. This experimentation spanned the period from World War II to the early 1970s, during which the ethics of experimentation became increasingly subject to public debate and government regulation. In contrast with the experiments that flowed from the AEC's radioisotope program, the use of external radiation such as TBI did not in its earlier years involve a government requirement of prior review for risk. The TBI experimentation raises basic questions about the responsibility of the government when it seeks to gather research data in conjunction with medical interventions of debatable benefit to sick patients.

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Chapter 9

In chapter 9 we examine experimentation on healthy subjects, specifically prisoners, for the purpose of learning the effects of external irradiation on the testes, such as might be experienced by astronauts in space. The prisoner experiments were studied because they received significant public attention and because a literally captive population was chosen to bear risks to which no other group of experimental subjects had been exposed or has been exposed since. This research took place during a period in which the once-commonly accepted practice of nontherapeutic experimentation on prisoners was increasingly subject to public criticism and moral outrage.

Chapter 10

Chapter 10 also explores research involving healthy subjects: human experimentation conducted in conjunction with atomic bomb tests. More than 200,000 service personnel--now known as atomic veterans--participated at atomic bomb test sites, mostly for training and test-management purposes. A small number also were used as subjects of experimentation. The Committee heard from many atomic veterans and their family members who were concerned about both the long-term health effects of these exposures and the government's conduct. In view of their concerns, the Committee undertook to reconstruct the story of human subjects research at the bomb tests, and to consider the questions raised where human experimentation was conducted in an occupational setting where risk is the norm.

Chapter 11

In chapter 11 we address the thirteen intentional releases of radiation into the environment specified in the Committee's charter, as well as additional releases identified during the life of the Committee. In contrast with biomedical experimentation, individuals and communities were not typically the subject of study in these intentional releases. Rather, the releases were to test intelligence equipment, the potential of radiological warfare, and the mechanism of the atomic bomb. While the risk posed by intentional releases was relatively small, the releases often took place in secret and remained secret for years.

Chapter 12

The final case study, in chapter 12, looks at two groups that were put at risk by nuclear weapons development and testing programs and as a consequence became the subjects of observational research: workers who mined uranium for the Atomic Energy Commission in the

western United States from the 1940s to 1960s and residents of the Marshall Islands, whose Pacific homeland was irradiated as a consequence of a hydrogen bomb test in 1954. While these observational studies do not fit the classic definition of an experiment, in which the investigator controls the variable under study (in this case radiation exposure), they are instances of research involving human subjects. The Committee elected to examine the experiences of the uranium miners and Marshallese because they raise important issues in the ethics of human research not illustrated in the previous case studies and because numerous public witnesses impressed on the Committee the significance of the lessons to be learned from their histories.

Chapter 13

Part II concludes with an exploration of an important theme common to many of the case studies--openness and secrecy in the government's conduct concerning human radiation research and intentional releases. In chapter 13 we step back and look at what rules governed what the public was told about the topics under the Committee's purview, whether these rules were publicly known, and whether they were followed.

Part III. Contemporary Projects

Chapter 14

Chapter 14 reviews the current regulatory structure for human subjects research conducted or supported by federal departments and agencies, a structure that has been in place since 1991. This "Common Rule" has its roots in the human subject protection regulations promulgated by the then-Department of Health, Education, and Welfare (DHEW) in 1974. The historical developments behind these regulations are described in chapter 3. Following a summary of the essential features of the Common Rule, chapter 14 discusses several subjects of particular relevance to the Advisory Committee's work, such as special review processes for ionizing radiation research, protection for human subjects in classified research, and audit procedures of institutions performing human subject research.

Chapter 15

Chapter 15 describes the Research Proposal Review Project (RPRP), the Advisory Committee's examination of documents from research projects conducted at institutions throughout the country, including both radiation and nonradiation proposals. Documents utilized in the RPRP were those available to the local institutional review boards (IRBs) at the institutions where the research was conducted. The goals of the RPRP were to gain an understanding of the ethics of radiation research as compared with nonradiation research; how well research proposals

address central ethical considerations such as risk, voluntariness, and subject selection; and whether informed consent procedures seem to be appropriate.

Chapter 16

The RPRP reviewed documents prepared by investigators and institutions and submitted in IRB applications. This study was complemented by a nationwide effort to learn about research from the perspective of patients themselves, including those who were and were not research subjects. The Subject Interview Study (SIS), described in chapter 16, was conducted through interviews with nearly 1,900 patients throughout the country. The SIS aimed to learn the perspectives of former, current, and prospective research subjects by asking about their attitudes and beliefs regarding the endeavor of human subject research generally and their participation specifically.

Discussion of Part III

The RPRP tried to understand the experience of human subjects research from the standpoint of the local oversight process, while the SIS tried to understand it from the standpoint of the participant. Although the two studies related to different research projects and different groups of patients and subjects, some common tensions in the human research experience emerge in both projects, and they are described in the "Discussion" section of part III. For example, it has long been recognized that the physician who engages in research with patient-subjects assumes two roles that could conflict: that of the caregiver and that of the researcher. The goals inherent in each role are different: direct benefit of the individual patient in the first case and the acquisition of general medical knowledge in the second case. The interviews with SIS participants suggest that at least some patient-subjects are not aware of this distinction or of the potential for conflict. In our review of documents in the RPRP we found that the written information provided to potential patient-subjects sometimes obscured, rather than highlighted, the differences between research and medical care and thus likely contributed to the potential for patients to confuse the two.

Part IV. Coming to Terms with the Past, Looking Ahead to the Future Findings and Recommendations

Chapter 17

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In chapter 17, our findings are presented in two parts, first for the period 1944 through 1974 and then for the contemporary period. These parts, in turn, are divided into findings regarding biomedical experiments and those regarding population exposures.

We begin our presentation of findings for the period 1944 through 1974 with a summation of what we have learned about human radiation experiments: their number and purpose, the likelihood that they produced harm, and how human radiation experimentation contributed to advances in medicine. We then summarize what we have found concerning the nature of federal rules and policies governing research involving human subjects during this period, and the implementation of these rules in the conduct of human radiation experiments. Findings about the nature and implementation of federal rules cover issues of consent, risk, the selection of subjects, and the role of national security considerations.

Our findings about government rules are followed by a finding on the norms and practices of physicians and other biomedical scientists for the use of human subjects. We then turn to the Committee's finding on the evaluation of past experiments, in which we summarize the moral framework adopted by the Committee for this purpose. Next, we present our findings for experiments conducted in conjunction with atmospheric atomic testing, intentional releases, and other population exposures. The remaining findings for the historical period address issues of government secrecy and record keeping.

Our findings for the contemporary period summarize what we have learned about the rules and practices that currently govern the conduct of radiation research involving human subjects, as well as human research generally, and about the status of government regulations regarding intentional releases.

Chapter 18

Chapter 18 presents the Committee's recommendations to the Human Radiation Interagency Working Group and to the American people. The Committee's inquiry focused on research conducted by the government to serve the public good--the promotion and protection of national security and the advancement of science and medicine. The pursuit of these ends--today, as well as yesterday--inevitably means that some individuals are put at risk for the benefit of the greater good. The past shows us that research can bear fruits of incalculable value. Unfortunately, however, the government's conduct with respect to some research performed in the past has left a legacy of distrust. Actions must be taken to ensure that, in the future, the ends of national security and the advancement of medicine will proceed only through means that safeguard the dignity, health, and safety of the individuals and groups who may be put at risk in the process.

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Many of our recommendations are directed not to the past but toward the future. The Committee calls for changes in the current federal system for the protection of the rights and interests of human subjects. These include changes in institutional review boards; in the interpretation of ethics rules and policies; in the conduct of research involving military personnel as subjects; in oversight, accountability, and sanctions for ethics violations; and in compensation for research injuries. Unlike the 1944-1974 period, in which the Committee focused primarily on research that offered subjects no prospect of medical benefit, our recommendations for the future emphasize protections for patients who are subjects of therapeutic research, as many of the contemporary issues involving research with human subjects occur in this setting. We also call for the adoption of special protections for the conduct of human research or environmental releases in secret, protections that are not currently in place.

We realize, however, that regulations and policies are no guarantee of ethical conduct. If the events of the past are not to be repeated, it is essential that the research community come to increasingly value the ethics of research involving human subjects as central to the scientific enterprise. We harbor no illusions about the Pollyanna-ish quality of a recommendation for professional education in research ethics; we call for much more. We ask that the biomedical research community, together with the government, cause a transformation in commitment to the ethics of human research. We recognize and celebrate the progress that has occurred in the past fifty years. We recognize and honor the commitment to research ethics that currently exists among many biomedical scientists and many institutional review boards. But more needs to be done. The scientists of the future must have a clear understanding of their duties to human subjects and a clear expectation that the leaders of their fields value good ethics as much as they do good science. At stake is not only the well-being of future subjects, but also, at least in part, the future of biomedical science. To the extent that that future depends on public support, it requires the public's trust. There can be no better guarantor of that trust than the ethics of the research community.

Finally, our examination of the history of the past half century has helped us understand that the revision of regulations that govern human research, the creation of new oversight mechanisms, and even a scrupulous professional ethics are necessary, but are not sufficient, means to needed reform. Of at least equal import is the development of a more common understanding *among the public* of research involving human subjects, its purposes, and its limitations. Furthermore, if the conduct of the government and of the professional community is to be improved, that conduct must be available for scrutiny by the American people so that they can make more informed decisions about the protection and promotion of their own health and that of the members of their family. It is toward that end that we close our report with recommendations for continued openness in government and in biomedical research. It is also toward that end that this report is dedicated. Some of what is regrettable about the past happened, at least in part,

because we as citizens let it happen. Let the lessons of history remind us all that the best safeguard for the future is an informed and active citizenry.