Chronology

Genesis of the Human Genome Project

(This chronology, which runs from May 1985 through the project's "official" beginning in October 1990, lists political events, not scientific or technical accomplishments.)

1985 *May* Robert Sinsheimer convenes the first meeting on sequencing the human genome at the University of California, Santa Cruz.

October Renato Dulbecco introduces his idea of sequencing the human genome at a talk organized by the Italian embassy in Washington, DC

Charles DeLisi of the U.S. Department of Energy (DOE) has the idea of mapping and sequencing the human genome while reading a draft report on heritable mutations from the congressional Office of Technology Assessment (OTA). DeLisi and David Smith, working at DOE headquarters in Germantown, Maryland, hatch plans for a Human Genome Initiative in the days just before Christmas.

1986 *February* Sydney Brenner sends a letter to the European Commission in Brussels, urging a concerted program to map and sequence the genomes of various organisms.

March A group from Los Alamos National Laboratory, led by Mark Bitensky, convenes DOE's first meeting on sequencing the human genome, held in Santa Fe, New Mexico.

Renato Dulbecco publishes a commentary on sequencing the human genome in *Science*.

June James Watson organizes a rump session on the genome project at a Cold Spring Harbor Laboratory symposium on the molecular biology of *Homo sapiens*. Watson invites Paul Berg and Walter Gilbert to cochair the session, which reveals considerable opposition to the DOE program among molecular biologists.

July The Howard Hughes Medical Institute convenes an Informational

Forum on the Human Genome on the campus of the National Institutes of Health (NIH), the first international meeting devoted to the genome project. While there is strong opposition to a mindless sequencing project, the process of redefining the genome project to encompass mapping begins.

September The governing board of the National Research Council, National Academy of Sciences, approves a study of mapping and sequencing the human genome, which leads to a report of the same name. The study is quickly funded by the James S. McDonnell Foundation. Bruce Alberts of the University of California, San Francisco, is appointed chairman. John Burris is study director.

At the same hour of the same day, the congressional Technology Assessment Board approves an OTA project, which leads to the report "Mapping Our Genes: Genome Projects—How Big? How Fast?" LeRoy Walters of Georgetown University chairs the advisory panel. Staff includes Robert Cook-Deegan as project director.

October NIH director James Wyngaarden convenes the fifty-fourth meeting of the Director's Advisory Committee. This is the first public NIH-sponsored meeting devoted to the genome project.

1987 *February–March* House and Senate appropriations committees hold hearings on the NIH and DOE budgets for fiscal year 1988, the first year that congressionally earmarked genome research funds are set aside in the NIH and DOE budgets. DOE proposes its Human Genome Initiative. Funds for NIH come from questions put to NIH director James Wyngaarden by House subcommittee chairman Rep. William Natcher.

March Charles DeLisi and Leroy Hood testify at a hearing before a subcommittee of the House Committee on Science and Technology. Eileen Lee and other staff organize the hearing for Rep. James Scheuer, whose subcommittee authorizes funding for the DOE life sciences program. The hearing constitutes the most vulnerable moment for the DOE program, as congressional staff are uncertain whether to condone DeLisi's actions.

April DOE's Health and Environmental Research Advisory Committee releases a report recommending a DOE-led fifteen-year Human Genome Initiative, with a budget reaching $200 million per year.

May Renato Dulbecco, Paolo Vezzoni, and others launch the Italian genome program.

James Watson, David Baltimore, and Bradie Metheny, representing the Delegation for Basic Biomedical Research, meet with House and Senate Appropriations Committee members and staff (including Rep. William Natcher, chairman of the House subcommittee that funds NIH, and Senator Lowell Weicker, former chairman of the corresponding Senate subcommittee). The main purpose of the meeting is to promote more AIDS research funding, but Watson

also requests $30 million for genome research at NIH.

Senator Pete Domenici hosts a meeting on the future of DOE's national laboratories at the U.S. Capitol. Donald Fredrickson, Jack McConnell, congressional staff, and senior officials at DOE and the national laboratories attend. Fredrickson suggests genome research as a productive new direction for DOE research. McConnell and Domenici's staff draft legislation to promote technology transfer that includes a human genome component.

December Alexander Bayev and Andrei Mirzabekov first present the idea for a Soviet genome program to government officials in Moscow.

1988 *February* The National Research Council (NRC) releases its report "Mapping and Sequencing the Human Genome," which recommends a concerted genome research program with a budget to reach $200 per year.

February–March James Wyngaarden convenes the *Ad Hoc* advisory Committee on Complex Genomes in Reston, Virginia, to draft plans for a genome research program along the lines recommended by the NRC report. Wyngaarden announces his intention to form the Office of Human Genome Research at NIH and to appoint an associate director of NIH to head it. Several scientists urge Wyngaarden to appoint Watson.

April Rep. John Dingell releases the OTA report at a hearing before the House Committee on Energy and Commerce. Lesley Russell, staff biologist for Dingell, organizes the hearing, which includes testimony from OTA, Bruce Alberts, James Watson, Maynard Olson, and others.

The Human Genome Organization (HUGO) is founded at Cold Spring Harbor Laboratory. Victor McKusick, Sydney Brenner, James Watson, Leroy Hood, and others urge that scientists, rather than administrators or politicians, direct international collaboration, and suggest HUGO as the mechanism.

May First scientific meeting on human genome mapping and sequencing at Cold Spring Harbor Laboratory, organized by Maynard Olson, Charles Cantor, and Richard Roberts.

June Reps. James Scheuer and Douglas Walgren, chairmen of two subcommittees of the House Committee on Science and Technology, convene a joint hearing on NIH-DOE collaboration. The committee subsequently approves a bill similar to one already passed by the Senate that is sponsored by Senators Lawton Chiles, Pete Domenici, and Edward Kennedy. The House Energy and Commerce Committee, which shares House jurisdiction over the bill and constitutes the principal remaining congressional obstacle to passage, threatens to pass the bill also, unless NIH and DOE agree to cooperate. NIH and DOE sign a Memorandum of Understanding that fall.

September NIH director James Wyngaarden appoints James Watson NIH associate director for human genome research. Watson hires Elke Jordan and Mark Guyer as the first employees.

October Santiago Grisolia convenes the First International Workshop on Collaboration for the Human Genome Project in Valencia, Spain.

1989 *February* Sir James Cowan, secretary of the Medical Research Council, and Sir Walter Bodmer, head of the Imperial Cancer Research Fund, officially launch a genome research program in the United Kingdom. The program supports research along the lines suggested by Sydney Brenner.

April Japan's Ministry of Education, Science, and Culture (Monbusho) commences a genome research program, based on a framework drafted by Kenichi Matsubara and others.

June The European Commission's Human Genome Analysis Programme is approved in Brussels, Belgium.

August An NIH-DOE planning retreat at the Banbury Center, Cold Spring Harbor Laboratory, lays the groundwork for the first five-year plan.

September Nancy Wexler chairs the first meeting of the NIH Working Group on Ethical, Legal, and Social Issues (ELSI) at the Cloisters building, National Institutes of Health. The working group drafts a mission statement. In December, the working group becomes joint with DOE, which begins its own ELSI program under pressure from Senator Albert Gore.

October Louis Sullivan, Secretary of the Department of Health and Human Services, elevates NIH's Office of Human Genome Research to become the National Center for Human Genome Research, with spending authority. James Watson is appointed director and Elke Jordan deputy director.

1990 *February–August* Martin Rechsteiner (University of Utah) begins a letter-writing campaign opposing the genome project. Michael Syvanen (University of California, Davis) mounts a similar campaign via computer networks. Bernard Davis and colleagues from the department of microbiology at Harvard Medical School publish a letter opposing the genome project in *Science*.

April NIH and DOE release their first joint five-year plan.

June Hubert Curien, minister of science and technology, announces the French government's intention to commence a genome research program. The program is officially launched in October.

Acknowledgments

This book began in a 1987 conversation with Sandra Panem of the Alfred P. Sloan Foundation. The makings of a good story—the immensely interesting personalities already deeply engaged in supporting and opposing the genome project—gave several people the idea for a book. Sandra was interested in a book with a science policy slant, one that focused on how a highly conspicuous decision was made in the highest reaches of government. This book results from her interest. Sandra left the Sloan Foundation in 1988, but the foundation, in the person of Michael Teitlebaum, continued to support the project, despite changes in my plans too numerous to recount.

The book was delivered in draft form to W.W. Norton, where it was published in its finally revised form under the able and patient direction of editor Joseph Wisnovsky. In retrospect, as well as in prospect, this was clearly the right choice. Alan Iselin did the illustrations, and Ted Johnson did a meticulous job of copyediting. I also thank Sydney Cohen for preparing the index, which should make the book much more useful to future scholars. In addition, I must thank Joan Bossert of Oxford University Press, Howard Boyer of Harvard University Press, and Elizabeth Knoll of University of California Press for their interest and assistance. While they did not end up publishing the book, their comments and attention to the review process were greatly appreciated.

While I strive to remain objective, I was close to the action as it took place. From 1986 until 1988, I followed the genome project as the director of a team at the Office of Technology Assessment, U.S. Congress. The other members of that team were Patricia Hoben, Jacqueline Courteau, David Guston, Teresa Schwab Myers, and Gladys White. The result of the OTA project was a 1988 report, *Mapping Our Genes*.[1] Every member of the team has since proved through other accomplishments what they demonstrated on the OTA project—that they are an extraordinarily talented lot.

Our task at OTA was to report to Congress on what the genome project was, whether or not it was worth funding, and how its underlying bureaucracy should be constructed. This vantage point placed me in the midst of three

groups: scientists debating the merits of genome projects, administrators working in federal agencies responsible for funding the scientists, and members of Congress who had the constitutional authority to specify how much and in what way federal funds could be used.

Our function at OTA was to gather information, filter it, and direct it to the people who wrote laws. Congress was involved because Article 1 of the Constitution gives it sole authority to tax and spend. OTA's proximity to political power ensured ready access to the nation's best expertise; its location in the legislative branch of government insulated it from the crossfire of interagency scuffles, a particularly important advantage in this case. Gretchen Kolsrud directed OTA's Biological Applications Program while I worked there, and it was her vision of the future of biotechnology that made OTA a national center of policy-making in that field. Gary Ellis, Val Giddings, Kathi Hanna, Robyn Nishimi, Rand Snell, Kevin O'Connor, Gladys White, Nanette Newell, Susan Clymer, Geoffrey Karny, and many others created a charged atmosphere and set high standards for work on genetics and biotechnology; work of distinction was the inevitable by-product. Jack Gibbons and Roger Herdman established the institutional values that made OTA the finest place I have ever worked.

I left OTA in December 1988 to become acting executive director of the Biomedical Ethics Advisory Committee, whose mandate included an assessment of policy implications of human genetics. The venue was again Congress, but the congressional leaders associated with it were entangled in a highly charged abortion debate. The Biomedical Ethics Advisory Committee died as a result of internecine wars among its congressional patrons, closing its doors in late September 1989. It officially expired on paper a year later. I thus had the glorious task of helping to create a new federal agency, serving as acting executive director, but this happy duty later turned sour.

I then worked from December 1989 until August 1990 at the National Center for Human Genome Research, the administrative hub of the genome project within the National Institutes of Health. The center was two months old when I arrived, and I was there to watch it grow from infancy into adolescence. I have since moved on to the Institute of Medicine, National Academy of Sciences, into a field only tangentially related to genome research, although I remain involved in the debate about social, ethical, and legal issues.

The human genome debate was a passionate affair. Champions and detractors saw it as a critical battle in the history of biology; high stakes amplified differences among factions. A self-conscious historicism pervaded arguments about the project from the beginning. Proponents and antagonists argued to influence members of Congress, opinion leaders of molecular biology, and administrators of the largest life science programs in the world. While proximity to events enhanced access to information, it also distorted what I ac-

quired. I had direct contact with the principal actors, and talked with them many times even as the projects began to unfold. I attended many of the meetings and had unparalleled access to the records of various bureaucracies. I followed up with interviews of major players.

James D. Watson figures prominently in this book. In a book on the Human Genome Project, he naturally looms as a towering figure. I first met him after a lecture in Biochemistry 10, when I was a Harvard undergraduate in 1972. As a devotee of physical chemistry at the time, I did not deign to partake of biochemistry, but I did want to hear the man who wrote *The Double Helix*.[2] I had decided he was a jerk after reading the book; his lecture confirmed that impression.

It was not the last time I was wrong. I learned a great deal from Jim Watson; it was an honor to work for him. I have followed federal science policy for roughly a decade now, and have never seen a scientist so quickly adapt to the policy process. I was immensely impressed by how he took the reins of the genome project. From the time of our first interview in 1987, when he was obviously trying to learn about Congress and federal policy, I was astonished at his energy, the degree to which he was willing to learn new skills, and the facility with which he began to amble through the halls of power.

Francis Crick noted in another book supported by Sandra Panem and the Sloan Foundation: "Rather than believe that Watson and Crick made the DNA structure, I would rather stress that the structure made Watson and Crick."[3] Discovering the double helix did indeed manufacture Watson's public persona, but it was his choice how to use it. His stature was a policy tool to promote genome research that he used with zest. He did not need the genome project nearly so much as the genome project needed him.

Many other groups were generous with additional support for this book. The National Science Foundation (NSF) funded a grant to archive historically relevant documents and to create an oral history of the genome project at the National Reference Center for Bioethics Literature, Georgetown University. Most of the papers, videotapes, and other materials that I gathered are available there, along with prepublication drafts of this book deposited so that others might use them before it came out. Anita Nolen and Doris Goldstein, co-investigators on the NSF grant at Georgetown, did most of the work collecting my chaotic files into a useful archive. I dumped; they organized. Staff at NSF were remarkably free of territorial reflexes and gave me faith that committed resistance can tame a federal bureaucracy. NSF and Georgetown created a resource that should make it easier for future historians of science to correct my mistakes.

Through the efforts of Victor McKusick and Joanna Strayer Amberger, Academic Press, Inc., donated a computer to the Johns Hopkins University for my use as special features editor for the genetics journal *Genomics*. This book was largely written on that computer. I particularly thank Alan Kay,

Steve Jobs, and the software wizards at Microsoft (Word) and Niles and Associates (EndNote), who made the Macintosh computer a source of pleasure as well as power.

I owe another debt to former coworkers at the National Center for Human Genome Research, National Institutes of Health (NIH). NIH provided an unrivaled opportunity to learn how the "working" side of government operates, as opposed to the legislative side. NIH is the preeminent biomedical institution in the world, and it was a privilege to work there. I was welcomed by Elke Jordan, Mark Guyer, Jane Peterson, Pam Lokken, Anita Brooks, Linda Engel, Eric Juengst, Bettie Graham, Leslie Fink, and dozens of others. Those in the NIH genome office shared a commitment to making the genome project a success. I was offered unequaled access to the information that flowed naturally into the world's largest administrative center for genome research.

Late in 1989, Kathi Hanna, then at the Institute of Medicine (IOM), asked me to write a policy history of the genome project for an IOM committee to study decision-making. The committee used the genome project as one of several case studies of how health and science policy decisions are made.[4] I and other authors attended an extremely stimulating March 1990 meeting at the Beckman Center in Irvine, California. Paul Berg, a member of the committee, warmly recounted his own personal experience of the genesis of the genome project. Kathi Hanna's invitation to write the IOM case study forced me to commit my thoughts to paper months earlier than I would have otherwise. It also presented an unforeseen opportunity for external review, comment, and corrections. When Ted Friedmann of the University of California, San Diego, generously invited me to write a slightly longer account to open the premier issue of the book series *Molecular Genetic Medicine,* I had another such opportunity.[5] This was another connection to Academic Press, which publishes those volumes.

As I worked to complete the book, I began a new position at IOM. I thank Queta Bond, Kenneth Shine, Ruth Bulger, Gary Ellis, Jane Fullarton, Elaine Lawson, Richard Rettig, Mark Randolph, Carolyn Peters, Gail Spears, and others who saw bits and pieces of the manuscript trekked in from home. Jack Barchas and William Bunney from my board were particularly supportive, plowing through a complete draft, and Betsy Turvene from IOM's editorial office also gave invaluable advice.

Akihiro Yoshikawa identified the importance of the genome project in U.S.–Japan relations long before others. He provided initial insights about the Japanese policy process and obtained information that I could never have obtained without his help. His Russian Hill home in San Francisco was the site of more than a few late-night discussions about genome politics. Aki and Nancy also saved me many nights' hotel charges, and permitted me to sleep at the foot of Lombard Street, with a breathtaking view of one of the most beautiful cities on earth. Ken-ichi Matsubara was of inestimable help in keep-

ing me up to date about Japan, and Akiyoshi Wada was amazingly open and generous about the early workings of the Japanese genome project. Japan was not at all a closed society when it came to exchanging information about genome doings.

Academicians Andrei Mirzabekov and Alexander A. Bayev were my pipeline into the USSR, at a time of endless complexities. I must also give special thanks to Vladimir Larionov and Natalya Kouprina for permanent memories of white nights on the Neva and friendship in Maryland. Diane Hinton, first with the Howard Hughes Medical Institute and then the Human Genome Organization, knew everyone and everything. She was generous with her knowledge and, more important, her friendship. James Wyngaarden was a central figure, first at NIH, then through the Human Genome Organization, and finally at the National Academy of Sciences. He granted open access at all three sites, and provided clarifications along the way.

Several people at the Department of Energy were generous with access to their files and willing to recount stories and "soft" Washington information. David Galas, Charles DeLisi, David Smith, and Daniel Drell merit special mention among many.

Those at genome research centers, particularly the NIH-supported genome centers and Department of Energy-supported national laboratories, were also quite helpful. I attended dozens, perhaps hundreds, of site visits, meetings, and other events as the genome story unfolded, and there are far too many people to list individually, so I have made a longer list below.

And what can I say about Nancy Wexler that others have not? She is as wonderful as I make her out to be in Chapter 16.

In addition to these sources of support, I was indirectly aided by many institutions. Many paid for my travel to give lectures or to attend meetings—opportunities to keep abreast of science and politics among the various genome projects—my greatest source of information. Among the groups that helped out were:

American Association for the Advancement of Science
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Association of Academic Health Centers
Beckman Center for the History of Chemistry
Berlex Laboratories
Biomedical Ethics Advisory Committee, U.S. Congress
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Woodrow Wilson National Fellowship Foundation, Princeton, N.J.

I depended on interviews with the principal actors to reconstruct some events, particularly those for which there was little or no documentation. Most of these interviews took place informally at meetings or over the phone in the context of other work. Some, however, have been taped and transcribed for future use. Transcripts of formal interviews are available through the National Center for Bioethics Literature at Georgetown University, and through a grant from the National Science Foundation will be available on-line, subject to any restrictions imposed by those interviewed. A listing of the documents that I cited at some stage of writing this book (not all citations survived the editing process) has been deposited there as well. It is available in electronic form for scholars, in EndNote format (Niles and Associates, Berkeley, Calif.) for both PC and Macintosh computers.

The following people deserve special thanks for their contributions, either as sources of information, as means of confirming information, or for reviewing parts of the book. I have tried to be fair and comprehensive in this list, but I have no doubt inadvertently left out some individuals who helped me a great deal. I apologize for such oversights. No thanks are adequate for an undertaking so complex, when the people involved are so bright, talented, committed, and wonderfully diverse.

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Gladys White
Raymond L. White
Thomas J. White
Daniel Wikler
Benjamin Wilfond
Robert Williamson
Lois Wingerson
Robert Wood
John Wooley
Ronald G. Worton
James Wyngaarden
Kunio Yagi
Michael Yesley

Akihiro Yoshikawa Frank Young Norton Zinder.
Philip Youderian Vladimir Zharov

Every author, by reflex, notes the missed weekends, evenings, and other disruptions of family life that a book entails. As this book neared completion, our friend Marji Balzer asked how it was coming, a question posed every few months between her treks to eastern Siberia for anthropological fieldwork. It was an innocent question. I began to answer, but my wife Kathryn intervened, noting that, in our family, "book" had become a four-letter word. Like certain other four-letter words, including life and wife, this one had to be experienced to be appreciated. Through such experiences, life acquires meaning.

References and Notes

A COMPLETE SET of 1,431 references cited in this book, or in preliminary drafts of it, is available from the National Center for Bioethics Literature (NRCBL), Georgetown University, Washington, DC 20057 (1-800-MED-ETHX, or 202-687-3885). Sharon J. Durfy and Amy E. Grotevant of NRCBL also prepared a brief annotated bibliography (Scope Note 17, December 1991). Michael S. Yesley of Los Alamos National Laboratory is maintaining a bibliography of Ethical, Legal, and Social Implications of the Human Genome Project, to be periodically published by the Department of Energy. The first such bibliography was published as DOE/ER-0543T, available to DOE contractors from the Office of Scientific and Technical Information, PO Box 62, Oak Ridge, TN 37831; available to the public through the National Technical Information Service, 5285 Port Royal, Road, Springfield, VA 22161.

Accounts of early events by some of the major players can be found in:

Watson, JD. (1990). The Human Genome Project: Past, Present, and Future. *Science* **248:**44–49.

Sinsheimer, R. (1989). The Santa Cruz Workshop, May 1985. *Genomics* **5:**954–956.

DeLisi, C. (1988). The Human Genome Project. *American Scientist* **76:**488–493.

Mullis, KB. (1990). The Unusual Origin of the Polymerase Chain Reaction. *Scientific American* **262** (April):56–65.

I have previously published abbreviated descriptions of the early history in articles and book chapters, although this book corrects some inaccuracies and oversights in those accounts. The earlier accounts include:

Watson, JD, and Cook-Deegan, RM. (1991). Origins of the Human Genome Project. *FASEB Journal* **5**(January):8–11.

Cook-Deegan, RM. (1991). The Human Genome Project: Formation of Federal Policies in the United States, 1986–1990. In *Biomedical Politics*, K Hanna, Ed., pp. 99–168. National Academy Press, Washington, DC.

Cook-Deegan, RM. (1991). The Genesis of the Human Genome Project. In *Molecular Genetic Medicine*, Vol. 1, T Friedmann, Ed., pp. 1–75. Academic Press, San Diego.

French scientist Bertrand Jordan spent a year traveling around the world, visiting genome research laboratories in different countries. He wrote a series of "genome chronicles" during this experience, which were later published in book form in both French and English. This is the most useful book for capturing how scientists thought about their work and how it would be done at the time.

Jordan Bertrand. (1993). *Voyage Autour du Genome: Le Tour du Monde en 80 Labos.* John Libbey Eurotext, Montrouge, France. Also available in English as *Traveling Around the Human Genome: An In Situ Investigation,* from the same publisher.

One of the most significant early meetings predated the concept of the genome project, but brought together those involved in the technological developments that gave rise to it, summarized in:

Cook-Deegan, RM. (1989). The Alta Summit, December 1984. *Genomics* **5:**661–663.

Several other books on the genome project also review some of its historical origins:

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78. Matsubara tried to secure a ¥6.5 billion budget ($43 million) to support two five-year projects under Monbusho. The first year's budget was ¥400 million ($2.7 million) for the biology program. A second, separate but related, program focused on informatics. A new Genome Analysis Center would be established at the University of Tokyo, with a national research group and a five-year commitment (first-year budget ¥220 million, or $1.5 million). This was to be the first installment on a much larger program. The Monbusho plan laid out a strategy for genome research, urging establishment of groups in five areas: (1) physical and genetic mapping, (2) analysis of complementary DNA collections (cDNA, representing those parts of DNA transcribed to RNA and representing the expressed parts of genes), (3) pursuit of new techniques to analyze DNA, (4) informatics, and (5) science and society. The Monbusho proposal set aside funds for international scientific workshops and for training of postdoctoral fellows and other research personnel.
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91. Fujiyama, A, 1990, Interview, Englehardt Institute for Molecular Biology, Moscow, October.
92. Miyakawa, H, 1990, Dinner at author's home, Derwood, MD, 18 October.

16. A NEW SOCIAL CONTRACT

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17. BIOETHICS IN GOVERNMENT

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9. King, Patricia, 1987–1992. Conversations at meetings of the ELSI working group, Institute of Medicine activities and other events, Georgetown Law

School. King was a commissioner on both the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research and the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research; she then served on the NIH Fetal Tissue Transplantation Research Panel and the NIH-DOE Working Group on Ethical, Legal, and Social Issues, as well as on several Institute of Medicine committees and other panels.

10. Capron, Alexander Morgan, 1983–1993, Conversations connected with Office of Technology Assessment activities, Institute of Medicine activities, the Biomedical Ethics Advisory Committee, and other events, University of Southern California. Capron was consultant to the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research and the Ethics Advisory Board (Department of Health, Education and Welfare); Executive Director of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research; and chair of the Biomedical Ethics Advisory Committee.
11. Beauchamp, Tom, 1986–1991, Kennedy Institute of Ethics Tuesday seminars, electronic mail communications, and conversations, Department of Philosophy, Georgetown University. Beauchamp was on the staff of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.
12. Jonsen, Albert, 1985–1992, Conversations at Institute of Medicine activities and other events, University of California, San Francisco, and then University of Washington, Seattle. Jonsen was a commissioner on both the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research and the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research.
13. Mishkin, Barbara, 1983–1991, OTA workshop on impacts of neuroscience (1983), a meeting on prospects for a bioethics commission convened for Elizabeth McCloskey, staff to Senator Danforth (1989), and various phone and personal conversations concerning federal bioethics commissions, Hogan & Hartson, Washington, DC. Mishkin was on the staff of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, the Ethics Advisory Board (Department of Health, Education and Welfare), and the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research.
14. Stryker, Jeffrey, 1984–1993, Conversations, Office of Technology Assessment and the University of California, San Francisco. Stryker was a member of the staff for the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research and subsequently at the Office of Technology Assessment and the National Research Council.
15. Yesley, Michael S., 1988–1992, Interviews and conversations at meetings, Los Alamos National Laboratory, ELSI working group meetings, and elsewhere. Yesley was executive director of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, which operated from 1974 to 1978; he later became associated with the Department of Energy ELSI program while working in the legal office at Los Alamos National Laboratories.
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18. WIZARDS OF THE INFORMATION AGE

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3. The critical problem was to create and maintain temperatures high enough to ignite the same reactions that take place in the sun and other stars. In work with C. J. Everett, Ulam pioneered the use of the "Monte Carlo" method to model how Teller's scheme for doing this would play out. The Ulam-Everett calculations showed the reaction would fizzle before generating an explosion. The Monte Carlo technique was a way to simulate complex phenomena mathematically. It was useful in characterizing an enormous range of applications, and had vast practical implications well beyond the hydrogen bomb simulations. The Ulam-Everett calculations pre-

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"It is HUGO's position, therefore, that the US EST patent applications should not be approved. We join the American Society of Human Genetics in supporting this view.
"The Human Genome Project is a major scientific area that now depends heavily on international cooperation in order to avoid both costly competition and duplication of effort. . . . it is the entire spectrum of international scientific collaboration that may be jeopardised. HUGO therefore urges a quick resolution to the EST case.
"HUGO urges the development of a process that allows for flexible negotiation and also mediation between the potentially conflicting needs of different scientific communities. Scientists, policy-makers and administrators world-wide must work together and accept responsibility for balancing the many competing priorities."
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sidered the issues in considerably more depth. The lack of foresight was not quite as bad as alleged. OTA urged early filing of patent applications. Failure to do so could "inhibit full exploitation of an invention" and invited "foreign exploitation of research funded at US taxpayers' expense. . . . Penicillin was discovered in England, but the patent was obtained by US corporations. . . . the United Kingdom claimed the Nobel Prize, but the United States reaped most of the economic benefits." OTA also noted "there is a gray area between invention of new methods and the data that result from using them," but did not predict how DNA sequences themselves, of the sort at issue in the NIH patent application, would become the subject of patent controversy. Like scientists, public policy analysis can be humbled by the march of events.

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20. EXODUS: THE END OF THE BEGINNING

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23. Watson, JD, 1992, Interview, Cold Spring Harbor Laboratory, November.
24. Watson, JD, 1992, phone conversation, September.
25. Eckholm, E. (1992). A Tough Case for Dr. Healy. *New York Times Magazine* (1 December):67, 118, 122, 124, 126.
26. Watson sat on the scientific board of two companies (Diagnostic Products Corporation, Pall Corporation), a research institute (Roche Institute of Molecular Biology), consulted for Diagnostic Products Corp., and held stock in Genetics Institute, Oncogene Science, Amgen, Beecham, Smith-Kline, Diagnostic Products Corp., Glaxo, Eli Lilly, Merck, Pall, and other companies.
27. Watson, JD. (1988). Disqualification from Activities That Would Affect My Financial Interests. Memo to William F. Raub, Deputy Director, NIH. 31 October.
28. Watson, JD. (1989). Disqualification from Activities That Would Affect My Financial Interests. Memo to William Raub, Acting Director, NIH. 19 October.
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30. Schneider, J, 1993, Interview, Building 1; discussing a February 1991 electronic mail message from Rob Lanman, NIH Counsel, to William Raub, then acting director, NIH, and a letter from William Raub to James Watson, Office of the Director, National Institutes of Health, 5 January. The February 1991 memo did not assert a conflict of interest, but rather referred to a possible "appearance of conflict," based on stock purchases since Watson's previous disclosure statement. The argument of "appearance of conflict," while retaining surface plausibility and potential for public relations mischief, was quite different from the kind of conflict associated with a clinical trial. A clinical trial centered on a drug or device nearing market approval. The results of a trial bore directly on prospects for Food and Drug Administration approval of a new drug, and such approval for a major new drug could make the stock of even a pharmaceutical giant rise dramatically, if successful, or plummet, if unsuccessful. Genome research, in contrast, was in most cases quite distant from commercial application. There were a few exceptions, in the areas of research instrumentation or DNA diagnostics. It was nonetheless difficult to imagine how the results of a grant decision or research initiative on gene mapping could have any substantial impact on the stock of any but the smallest and most targeted genome research company. Conflict might indeed have arisen if a small instrumentation firm or DNA forensics company sought Small Business Innovation Research funding, or a similar scenario. Watson's holdings, however, were not in such companies, but in large pharmaceutical houses whose stock would be almost entirely unaffected by the fate of federal genome research decisions in the short run. They might benefit from the general knowledge emanating from NIH genome research, but this would not fall into the usual definition of conflict of interest. In retrospect, the February 1991 memo appears to be one lawyer's cautious and broad interpretation of the possibility of an "appearance" of conflict, coupled with a narrow definition of permissible behavior.
31. Watson, JD, 1992, Interview, Cold Spring Harbor Laboratory, November. Watson recalled receiving a letter from William Raub that sought information about certain stock purchases. He and Raub had then met with Jack Kress in May of 1991, after Healy had become director of NIH and before Raub left NIH to join the White House Office of Science and Technology Policy. Kress had indicated he would follow up if Watson's activities required a response.
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34. The quote from Healy comes from Hilts, PJ. (1992). Head of Gene Map Threatens to Quit. *New York Times* (9 April):A26. The quote about the waiver is taken from a letter written by Michael J. Astrue, Vice President and General Counsel of Biogen (Cambridge, MA) to the author, dated 6 July 1994.

The letter clarifies several events that took place when Astrue was chief counsel for the Department of Health and Human Services, and corrects some ambiguities in the text of the first hardback edition of this book.
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47. Roberts, L. (1992). A Standing Ovation from the Troops. *Science* **256** (15 May):957.
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EPILOGUE

1. Thompson, L. (1993). Healy and Collins Strike a Deal. *Science* **259** (1 January):22–23.
2. Botstein, D, 1988, Interview, Genentech, 19 August.
3. Healy appointed a committee to assist in the search for Watson's successor. The committee roster was included in a press packet distributed at a press conference down the hall from the NIH Director's office. The committee was co-chaired by Ruth Kirschstein, director of the National Institute of General Medical Sciences, and George Vande Woude, a former National Cancer Institute intramural researcher and current investigator at Advanced Bioscience Laboratories. The other members were Raphael Daniel Camerini-Otero, National Institute of Diabetes and Digestive and Kidney Diseases; Daryl A. Chamblee, senior policy adviser and counselor to the director, NIH; Gary Felsenfeld, National Institute of Diabetes and Digestive and Kidney Diseases; Martin Gellert, National Institute of Diabetes and Digestive and Kidney Diseases; Jay Moskowitz, associate director for science policy and legislation, NIH; Maynard Olson, Washington University; David Rodbard, Division of Computer Research and Technology, NIH; Phillip A. Sharp, Massachusetts Institute of Technology; Maxine Singer, Carnegie Institution of Washington; Shirley M. Tilghman, Princeton University; and Nancy S. Wexler, Hereditary Disease Foundation and Columbia University, National Institutes of Health, 4 May.
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ACKNOWLEDGMENTS

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Robert Cook-Deegan, M.D., is currently on the staff of the Institute of Medicine, National Academy of Sciences. From 1986 to 1988 he directed a study of the status of genome research for the Office of Technology Assessment of the U.S. Congress. He later served as an adviser to the National Center for Human Genome Research at the National Institutes of Health.

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