Congressional Quarterly

Ralph M. Hall (D) Texas - 4th District
Of Rockwall - Elected 1980

BIOGRAPHICAL DATA
(Prepared: July 1989)

Born: May 3, 1923, Rockwall County, Texas.
Education: Attended Texas Christian U., 1943; U. of Texas, 1946-47; Southern Methodist U., LL.B. 1951.
Military Career: Navy, 1942-45.
Occupation: Lawyer; businessman.
Family: Wife, Mary Ellen Murphy; three children.
Religion: Methodist.
Political Career: Rockwall County judge, 1950-62; Texas Senate, 1963-73; sought Democratic nomination for lieutenant governor, 1972.
Capitol Office: 236 Cannon Bldg. 20515; 225-6673.

IN WASHINGTON
(Prepared: July 1989)

Hall's conservative voting record is not the kind the Democratic leadership generally appreciates. But on Energy and Commerce, he is a favorite of Chairman John D. Dingell, even though the two do not always see eye-to-eye. Hall's folksy sense of humor and encyclopedic supply of rural Texas stories can defuse tense confrontations, and his political acumen gives him considerable influence when he decides to weigh in on an issue.

That is not to say that Hall is one of the committee's more active members. He makes no pretense of being a workaholic, but when issues important to the energy industry come up, Hall makes his presence felt.

When the committee debated nuclear-accident liability legislation in 1987, Hall offered an amendment to allow utility lawyers to get paid before victims if damage claims exceed the compensation fund. Success required the panel to reverse an earlier decision, but working with industry lobbyists, Hall chalked up a 22-20 win.

Hall also played a role in the committee's 1988 approval of a product liability bill, a longtime industry priority. One of Hall's pro-business amendments - to prohibit states from classifying as "environmental" any injuries that might otherwise fall under product liability - was backed by chemical manufacturers and condemned by consumer activists. Another, more popular, amendment aimed to limit "frivolous" lawsuits by plaintiffs and delaying tactics by defendants. Both proposals passed, though the bill died at the end of the 100th Congress.

Hall's prime interest, however, is oil and gas, and he is known as a shrewd advocate for decontrol. After years of bitter stalemate, Energy and Commerce passed a decontrol bill by voice vote in early 1989. "I wouldn't be more surprised to see my old dog Red sharing his food with the cats," he said of the

unanimity, "or the mockingbird not flying down to peck at the squirrels."

On the whole, Hall more often than not is at odds with his party. He tested the limits of his independence in 1985, when he voted "present" rather than support Thomas P. O'Neill Jr. for Speaker. He viewed with equanimity the possibility that the leadership might retaliate by removing him from Energy and Commerce. "I wouldn't blame them if they did," he said cheerfully. "I do what I have to do, and they do what they have to do."

AT HOME
(Prepared: July 1989)

An early starter in politics, Hall was elected judge in his home county while still in law school. After 12 years, he moved up to the state Senate and spent a decade there, rising to become president pro tem.

In 1972 Hall entered statewide politics, running for lieutenant governor on a conservative platform. But he finished fourth in the Democratic primary, retired from politics and concentrated on business.

When 4th District Democratic Rep. Ray Roberts announced his retirement in 1980, Hall decided to re-enter politics. His opponent in the primary was Jerdy Gary, the son of a former Oklahoma governor. Hall contrasted his Texas upbringing with Gary's Oklahoma roots, and won nomination with 57 percent.

Because of Ronald Reagan's popularity among the 4th's voters, Hall's November contest with Republican John H. Wright turned out to be closer than expected. Though Wright, a Tyler business manager, was well-known only in the eastern part of the district, Reagan's strong showing helped Wright pull 48 percent. But Republicans have not mounted a comparable challenge since. In 1988, he had his best presidential-year showing yet, winning two-thirds of the vote.

One way Hall heads off opposition is to make his feelings about national Democratic politics unmistakably clear; chosen as an uncommitted delegate to the Democratic convention in 1984, he opted not to go, commenting acerbically that he "didn't want to elbow some gay guy out of the way to get to a committee meeting."

Congressional Quarterly

Robert G. Torricelli (D) New Jersey - 9th District
Of Englewood - Elected 1982

BIOGRAPHICAL DATA
(Prepared: July 1989)

Born: Aug. 26, 1951, Paterson, N.J.
Education: Rutgers U., A.B. 1974, J.D. 1977;
Harvard U., M.P.A. 1980.
Occupation: Lawyer.
Family: Wife, Susan Holloway.
Religion: Methodist.
Political Career: No previous office.
Capitol Office: 317 Cannon Bldg. 20515; 225-5061.

IN WASHINGTON
(Prepared: July 1989)

Torricelli is bright and cocksure, a young man in a hurry who so far has left a trail in the House marked more by the compelling, made-for-TV quote or deed than by legislative substance.

In part, that is because he has chosen to make his mark mainly on the Foreign Affairs Committee, which is less a bill mill than a policy oversight board. Also, as a man with acknowledged ambitions for higher office, Torricelli aims for a larger audience than the House, where his brash and self-assertive style rubs some colleagues the wrong way. Having dropped long-held plans to run for governor in 1989, it remains to be seen whether he will devote more time in the House to the sustained and largely unseen work of legislating.

Even among his media-oriented contemporaries, Torricelli has shown a flare for garnering the kind of news coverage once reserved for senior members. In his first month in office, at 31, national TV followed his trip to El Salvador, where he arranged for the return of the body of a journalist, a New Jersey native, who had been murdered there. He also drew publicity for obtaining a papal audience for a 97-year-old constituent - "Great television," he said.

But Torricelli took his most notable step to date in 1989, when he became a surprise addition to the legal team defending Speaker Jim Wright. Torricelli said he did so after reviewing the ethics committee's report against the Speaker, at Wright's request, and concluding that Wright was getting a raw deal. Still, colleagues had trouble seeing what was in it for Torricelli beyond national publicity.

Torricelli had not been a close associate of Wright before, and he joined the Speaker's defense when Wright's political demise was imminent. For a man with statewide ambitions in New Jersey, he seemingly had nothing to gain by becoming linked to the Texan's ethics case. And he subsequently ruffled other members by his arguments that all lawmakers, like Wright, have

friends at home who ingratiate themselves with the local congressman while asking nothing in return, appearances to the contrary.

Torricelli's brief role in the Speaker's behalf was a departure for a man who until then concentrated on Foreign Affairs. Widely traveled since joining the panel, he seems to have formed opinions on just about every area of policy. "I'd like to be more of a deep thinker on national and foreign affairs . . . an architect of national policy," he said after his first term. From the start he was an outspoken liberal critic of Reagan's policies, with a sharply cynical view of the president's stewardship.

After his El Salvador trip, Torricelli blasted U.S. support for its government. Also in 1983, he endorsed a nuclear weapons freeze, saying, "I want Ronald Reagan to hear a desperate voice from the American people. No more phony arms control negotiations; no more talk of limited nuclear war or winnable nuclear war."

When the scandal over arms sales to Iran broke in 1986, Torricelli twitted Reagan by recalling the president's frequent accusation that Democrats are weak toward hostile nations: "We now discover that the emperor has no clothes." He supported sanctions against South Africa, contrasting Congress' initiative with Reagan's opposition: "We're not talking about apartheid. We're not studying it. We don't want to have anything to do with it."

In 1987, Torricelli bitingly objected to Reagan's policy of providing Navy escorts for Kuwaiti tankers in the Persian Gulf, and not only because Congress was not consulted. "We cannot assume," he said, "that contingencies have been considered, options have been explored, the military have been consulted - in short, that competent people are making intelligent judgments about the policies."

The next year he was out front again after the United States downed an Iranian civilian airliner, killing 290 people. Torricelli proposed a measure opposing Reagan administration moves to compensate the victims' families, arguing, "It is going to be an American admission of error that will divert attention from the fact that Iran was grossly negligent in its operations." Neither the administration's negotiations with Iran nor Torricelli's proposal went any further.

During the downfall of Philippine President Ferdinand E. Marcos, he was in the national spotlight supporting Corazon Aquino and strongly opposing Marcos' admission to the United States. With many Jews among his constituents, Torricelli is quick to oppose any suggested cuts in aid to Israel.

He also has used his Foreign Affairs seat to promote the interests of the maritime industry and unions. In 1987, the House adopted his amendment to the foreign aid bill requiring countries that receive cash aid to buy U.S. goods and ship them on U.S. ships. The bill died in the Senate. In 1988, he amended the House defense bill to direct the Navy to encourage U.S. construction of diesel-powered submarines for allies; the Navy had ordered shipyards not to build such subs for Israel,

reportedly out of fear that the Navy then would be pressured to buy some diesel models in lieu of nuclear-powered subs.

Torricelli also is an active member of the Science, Space and Technology Committee. As such, he attracted wide attention after the 1986 explosion of the space shuttle Challenger for quickly proposing legislation to build a new vehicle and for bluntly criticizing both the National Aeronautics and Space Administration and Congress. "Congress just didn't support NASA, it believed in it," he said. "We still believe in it, but NASA will no longer be left to its own devices."

He subsequently took up the cause of Hercules Inc., an aerospace company that wanted to break Morton Thiokol's monopoly on booster rockets; two years later, his efforts paid off when NASA decided to pursue a new generation of rockets, and threw the competition wide open. From his seat on Science, in 1986 Torricelli was able to include provisions for research and development projects in the law that reauthorized the "superfund" toxic-waste cleanup program.

AT HOME
(Prepared: July 1989)

Torricelli's political resume re-flects the same drive and intensity that have marked his career in Washington. He began his political apprenticeship as a teenager by working for the Bergen County Democratic organ-ization. In college, he was an active campus politician who ran three successful campaigns for class president using a sound truck to attract voters. He went on to become an aide to Democratic Gov. Brendan T. Byrne.

After a brief stint as executive director of the New Jersey Democratic Party, Torricelli joined the staff of Vice President Walter F. Mondale. That connection got him the important job of running the 1980 Illinois primary for President Carter, whose lopsided victory over Sen. Edward M. Kennedy proved he did well.

In 1982, redistricting made the 9th District attractive to Democrats, so Torricelli moved there from his original home in northern Bergen County and began preparing a campaign against GOP Rep. Harold Hollenbeck. A moderate Republican who enjoyed labor support, Hollenbeck had survived three terms in his blue-collar constituency, but had never before faced strong opposition.

Hollenbeck played down his partisan affiliation, but he had backed President Reagan's economic plan in 1981, something Torricelli emphasized. The incumbent also suffered from his lackadaisical manner, staying in Washington while Torricelli campaigned door-to-door. Hollenbeck returned home during the October recess, but even his own staff sometimes did not know where to find him. Torricelli ended up winning only 12 of the district's 38 towns, but nearly all were among the larger ones; he won 53 percent of the overall vote.

Aided by a redistricting plan that gave him a somewhat more Democratic constituency, Torricelli did not meet much GOP opposition in 1984. In 1986, district Republicans hoped that a

hot contest down the ballot, for Bergen County executive, would spur turnout and give county legislator Arthur F. Jones a chance against Torricelli. But the reverse occurred: Torricelli won with 69 percent of the vote, his biggest margin ever. He took two-thirds of the vote in 1988.

Torricelli's big winning margins sparked speculation about his potential as a future statewide candidate, which the Democrat fueled by testing the waters for a 1989 campaign to succeed retiring GOP Gov. Thomas H. Kean. But by early 1989, his Democratic House colleague James J. Florio - the party's gubernatorial nominee and a narrow loser to Kean in 1981 - had established himself as the front-runner. Torricelli took himself out of the competition and strongly endorsed Florio - even writing a letter to other potential Florio foes, suggesting they stay out of the race to avoid a divisive primary.

Congressional Quarterly

Lee H. Hamilton (D) Indiana - 9th District
Of Nashville - Elected 1964

BIOGRAPHICAL DATA
(Prepared: July 1989)

Born: April 20, 1931, Daytona Beach, Fla.
Education: DePauw U., B.A. 1952; attended Goethe U., Frankfurt, West Germany, 1952-53; Indiana U., J.D. 1956.
Occupation: Lawyer.
Family: Wife, Nancy Nelson; three children.
Religion: Methodist.
Political Career: No previous office.
Capitol Office: 2187 Rayburn Bldg. 20515; 225-5315.

IN WASHINGTON
(Prepared: July 1989)

For House Democrats, Hamilton's is the quiet voice that resounds. During a quarter-century in Congress, the professorial Hoosier has built a reservoir of respect few members can match, thanks to his intellectual power and his unquestioned personal integrity.

Colleagues' one complaint is that he so rarely taps that reservoir, that he shies from the bold steps that might antagonize one faction or another. Judicious caution, the key to Hamilton's influence and credibility, can also be his handicap. Never was that more clear than in the evolution of the Iran-contra scandal.

In the 100th Congress, Hamilton did a much-commended job as House chairman of the special committee that investigated the Reagan administration's 1985-86 arms sales to Iran and the diversion of profits to the Nicaraguan rebels in violation of a ban on contra aid. Yet the facts of the affair might have emerged sooner if Hamilton, as Intelligence Committee chairman in 1985 and 1986, had not held back from probing early reports of illegal White House activity in his reluctance to engage in partisan warfare.

Hamilton's hesitation was all the more crucial since he is one of Congress' most respected foreign policy voices, a longtime member of the Foreign Affairs Committee besides being a former Intelligence chairman. "One of the emerging lessons from these events," Hamilton said as the scandal unfolded, "is that we did not have sufficient oversight." The committees involved, he added, including his own, "did not do as good a job as we should have done."

But, as he was to ask over and over, what can Congress do - what can he do - if questions are met with administration lies? The initial lie was told to Hamilton directly. In September 1985, he had called then-national security adviser Robert C. McFarlane before Intelligence; McFarlane assured Hamilton that

National Security Council aide Lt. Col. Oliver L. North had not "in any way been involved with funds for the contras." "I for one am willing to take you at your word," Hamilton replied, and the matter was dropped.

That incident, and the subsequent revelations during the Iran-contra hearings, seemed to leave this minister's son with both a sense of betrayal and a penitence about his own role. How that might affect his lawyerly style is unclear, particularly given the change of administrations and President Bush's pledge to cooperate with Congress. But when the affair followed Hamilton into the 101st Congress, he was quick to respond.

Documents disclosed in North's 1989 criminal trial provided new evidence to contradict Reagan's and then-Vice President Bush's denials of their involvement, and raised questions about why the Iran-contra committee did not get the documents. Hamilton in April asked Bush for explanations and urged Intelligence, of which he is no longer a member, to investigate.

House Democratic leaders' selection of Hamilton to chair the Iran-contra hearings - jointly with a Senate team, as it turned out - was a reflection of their confidence that the Indianan, with his straight, crew-cut appearance and low-key, articulate style, would set a fair and non-prosecutorial tone for a national television audience. He asked few questions through the summer hearings, but gave lengthy summations following key figures' testimony that laid calm emphasis on their evidence of lies and subversion of foreign policy.

That occasionally irritated House Republican members of the panel; one accused Hamilton of "pontificating," of sounding "like a judge passing judgment on a witness." Generally, however, Republicans gave Hamilton high marks for his fairness in conducting the proceedings.

To State Department aide Elliott Abrams, who testified that his past responses to Congress had been misleading but literally correct, Hamilton replied, "The object here is not to avoid a perjury indictment. . . . The object is to make the Constitution of the United States work. Congress is a partner, not an adversary." In impassioned remarks to North, Hamilton said, "I don't have any doubt at all, Colonel North, that you are a patriot. . . . But there is another form of patriotism that is unique to democracy. It resides in those who have a deep respect for the rule of law and faith in America's democratic traditions."

Hamilton accepted the testimony of Vice Adm. John M. Poindexter, McFarlane's successor as national security adviser, that he did not inform Reagan about the diversion of funds to the contras; Hamilton's co-chairman, Sen. Daniel K. Inouye, was more skeptical. Ultimately, the committee's majority concluded that Reagan was responsible for the mistakes and illegalities of his "cabal of zealots." But Hamilton had to admit again that Congress did not get to the bottom of the affair.

Hamilton's two years heading Intelligence in the 99th Congress marked perhaps the first time in his career that did not evoke universal praise. But overall, he handled the panel's

work with his customary fairness and grace, maintaining the independent approach to the CIA that had established the committee's reputation.

His style and policy views have formed during his long service on Foreign Affairs, which he joined as a freshman in 1965. He is chairman of its Europe and Middle East Subcommittee, and one of a handful of members who have made the once-passive Foreign Affairs equal in stature to its traditionally dominant Senate counterpart. He is now the committee's No. 2 Democrat, and is 14 years younger than current Chairman Dante B. Fascell of Florida.

Despite his evenhandedness, Hamilton does have strongly held views. He was a leader of the opposition to Reagan's contra aid policy from the time it was disclosed in the early 1980s; he said diplomacy involving Central American leaders would have a better chance of success than trying to force Nicaragua to negotiate democratic changes "with a gun to its head."

He drafted a compromise proposal in 1985 designed to aid Nicaraguan refugees and promote a regional peace treaty - "tough-minded diplomacy" he called it. But the House voted for contra aid, which Hamilton opposed even though it was limited to "humanitarian" assistance. A year later, he again was on the losing side as the House gave the contras an additional $100 million, mostly military aid.

Behind Hamilton's stance is a basic discomfort with an American military presence in Central America. "The problems there are fundamentally economic and social, and we're responding with military might," he once said. However, in 1988 the pragmatic Hamilton broke ranks with Democratic anti-contra purists to support a humanitarian aid proposal that House Democratic leaders put forward to block Reagan's military aid request. And in 1989 Hamilton voted for a humanitarian aid compromise drafted by congressional leaders and Secretary of State James A. Baker III.

Hamilton believes emphatically that Congress should be consulted as an equal partner in foreign policy. In 1986, he unsuccessfully opposed Reagan's covert aid to guerrillas in Angola, saying it amounted to a major policy shift that should be publicly debated. The president, he said, "cannot expect sustained support for foreign policy initiatives, including covert action operations, that are generally unpopular or where a covert action mechanism can be viewed as having been chosen to avoid public debate or a congressional vote on the matter."

Lawmakers' suspicion of the Reagan administration's failure to inform them, or to carry out Congress' mandates, only led them to add more such strings to foreign aid bills. Against his instincts, Hamilton was a leader in the effort. With Central America in mind, in 1987 he sponsored provisions limiting the president's flexibility to decide which countries get aid, how much and what type. With the end of the Reagan administration, however, Hamilton headed a bipartisan Foreign Affairs task force that in early 1989 recommended dropping many such limitations in return for the administration's cooperation.

On his subcommittee, Hamilton has sought to steer a middle

course between the panel's dominant pro-Israel faction and those who want to strike some balance toward friendly Arab states. Unlike many in Congress, he is not reflexively opposed to arms sales to Arab nations, but instead considers requests case by case. It is the kind of controversial issue Hamilton likes to avoid, yet his position makes that impossible. Underlying his approach is a sense that U.S. arms do not much advance Mideast peace, but that realpolitik requires the United States to accommodate moderate Arab states and to help secure them against their radical neighbors - as long as any military aid is not a direct threat to Israel.

Hamilton does maintain good relations with the formidable Israel lobby; to do otherwise would threaten his standing and influence among his colleagues. But he sharply criticized Israeli raids on Palestinian camps in Lebanon and, in the 98th Congress, was one of only four committee members who voted against a House resolution seeking to move the U.S. Embassy in Israel from Tel Aviv to Jerusalem - a high priority for many supporters of Israel. In 1988 he was one of 37 signatories to a letter protesting Israel's deportation of a Palestinian-American advocate of non-violent resistance in the occupied territories.

From the start of his House career, Hamilton has enjoyed his colleagues' high regard. He was president of the huge freshman Democratic class elected in 1964. In 1965, he received widespread attention with a letter to President Johnson saying it was "time to pause" in action on Great Society social programs.

In 1972, Hamilton sponsored the first measure that Foreign Affairs adopted to stop the Vietnam War. The proposal, which called for a U.S. withdrawal contingent on release of all prisoners of war and on a cease-fire plan with North Vietnam, later was killed on the House floor, but it helped set the stage for later congressional actions to end the war.

In the post-Watergate period of public concern for government integrity, Hamilton was one of the members to whom the House turned for guidance on ethics issues. In 1977 he chaired a task force that recommended new House rules limiting members' outside income and honoraria. In 1979-80, amid a rash of scandals, Hamilton was the dominant Democrat on the House ethics committee rather than its mercurial chairman, Charles E. Bennett of Florida.

He worked on the committee's recommendation of censure for Michigan Democrat Charles C. Diggs Jr., convicted in a kickback scheme, and on the Abscam bribery investigations. On Abscam, Hamilton broke with the committee when it recommended that Pennsylvania Democrat Michael "Ozzie" Myers be expelled following his bribery conviction. The matter came to the floor the day the House was to recess for the 1980 elections, and Hamilton said the rushed atmosphere denied Myers due process. But the House voted to expel Myers, making him the first member in history ousted for corruption.

In 1988, Hamilton was among those considered as a running mate for Democratic presidential nominee Michael S. Dukakis. By the next year, the ethics spotlight was on the House again, with

the resignations under fire of Speaker Jim Wright and Democratic Whip Tony Coelho. Hamilton was briefly discussed - privately among House Democrats and publicly in the press - as a potential leadership draftee who could help restore the image of the party and the House. But even his admirers predicted Hamilton's caution would dissuade him. "I really had a large number of contacts suggesting that I do (run)," he said. "But I am not pursuing them."

AT HOME
(Prepared: July 1989)

In the early months of 1989, Hamilton was contemplating an unexpected and momentous question in Indiana. Party leaders were urging him to challenge junior GOP Sen. Daniel R. Coats in the 1990 special election to fill the remainder of Vice President Dan Quayle's Senate term.

Despite the limits of his base in the state's rural southeast, Indiana political observers considered him the party's most promising candidate against Coats. So great was the respect for Hamilton in both the state and national party structures that the nomination was almost literally his to refuse.

But refuse it he did. The special Senate election will coincide with the regular congressional election, so Hamilton would have been forced to sacrifice his seat and 13 terms of House seniority to take on Coats. Even if he won, he would have faced another campaign just two years later, when the Quayle term expired. For a cautious man like Hamilton, that was a venture worth walking away from.

The son and brother of ministers, Hamilton has a devotion to work that comes out of his traditional Methodist family. From his days in Evansville High School in 1948, when he helped propel the basketball team to the state finals, to his race for Congress in 1964, he displayed a quiet, consistent determination.

When he graduated from DePauw University in 1952, he received an award as the outstanding senior. He accepted a scholarship to Goethe University in Germany for further study.

Hamilton practiced law for a while in Chicago, but soon decided to settle in Columbus, Ind., where his interest in politics led him into the local Democratic Party. In 1960 he was chairman of the Bartholomew County (Columbus) Citizens for Kennedy. Two years later he managed Birch Bayh's Senate campaign in Columbus.

He was the consensus choice of the local Democratic organization for the 9th District House nomination in 1964, and won the primary with 46 percent of the vote in a field of five candidates. He went on to defeat longtime Republican Rep. Earl Wilson, a crusty fiscal watchdog who had represented the district for almost a quarter of a century.

Hamilton has been re-elected easily ever since. After a few years, Republicans gave up on defeating him and added Democrats to his district to give GOP candidates a better chance elsewhere

in the state. In 1976, for the first time in the history of the district, the Republicans put up no candidate at all. In 1980 and 1984, Reagan's popularity in Indiana caused Hamilton no trouble.

Conceding that Hamilton was unbeatable, the GOP Legislature made no effort to weaken him in 1981 redistricting, although they removed Hamilton's hometown of Columbus from the district. He moved to the next county, was re-elected with 67 percent and has won since by similar margins.

Congressional Quarterly

George E. Brown Jr. (D) California - 36th District
Of Riverside - Elected 1962
Did not serve 1971-73.

BIOGRAPHICAL DATA
(Updated: July 1989)

Born: March 6, 1920, Holtville, Calif.
Education: Graduated from El Centro Jr. College, 1938;
U.C.L.A., B.A. 1946.
Military Career: Army, 1942-46.
Occupation: Physicist, management consultant.
Family: Widowed; four children.
Religion: Methodist.
Political Career: Monterey Park City Council, 1954-55;
mayor 1955-58; Calif. Assembly, 1959-63;
sought Democratic nomination for U.S.
Senate, 1970.
Capitol Office: 2188 Rayburn Bldg. 20515; 225-6161.

IN WASHINGTON
(Prepared: July 1989)

Watching Brown today, as he listens patiently to committee testimony on the science budget or shuffles from the House floor to enjoy another cigar in the solitude of the members' lobby, it is hard to recall the spirited anti-war crusader of the 1960s. But he is the same man; Brown has simply mellowed with the times, and perhaps grown weary with the years of political battle.

The impression of a divergence is underscored by fact: Brown has had, in effect, two separate House careers in which to pursue his liberal causes, broken by a one-term absence after his 1970 Senate defeat. Two issues - environmentalism and opposition to nuclear war - are the link between them.

When Brown returned to the House in 1973, the Vietnam War was ending. He settled quietly into the Science and Agriculture committees and followed his issues, thoughtful but detached. Though a senior member of Agriculture now, he only seems engaged when the discussion turns from farm policy to the subject of pesticide regulation. On Science, he is an avid defender of the Environmental Protection Agency, and the leading opponent of military uses of space.

The old peace advocate re-emerges in debates on space-based military programs. Brown has succeeded in at least slowing the development of anti-satellite (ASAT) weapons; for several years before 1988, he sponsored the amendments to annual defense bills that imposed one-year bans on testing ASAT weapons against targets in space, contingent on Soviet abstention.

In 1988, however, he and cosponsor Lawrence Coughlin of Pennsylvania, a Republican moderate, gambled for the kill and lost. They proposed a permanent ban. Though still contingent on

mutual Soviet restraint, the proposal caused some members to feel "squeamish," by one's description. It was defeated 197-205.

Brown is one of the more outspoken foes of the strategic defense initiative (SDI). He has supported efforts to cut its funding, and to commit the United States to continued observance of the 1972 anti-ballistic missile treaty - a document he says SDI would violate.

He fights against the Pentagon's growing role in space not only on defense bills, but also on legislation for the National Aeronautics and Space Administration (NASA), over which Science has jurisdiction. A strong believer in civilian exploration, Brown complains about the hefty fraction of NASA's pinched budget that goes for defense-related work. "That's about all NASA is at the present time - an appendage to the Pentagon," he said in 1986.

Brown's anti-military approach to space policy may have cost him a couple of key committee seats. In November 1987 he announced his resignation from the Intelligence Committee, calling it "a protest to the administration's use of the classification system to prevent members of Congress from engaging in vital national debates." However, Brown had come under pressure to resign from conservative Democrats, who agreed with the Reagan administration that Brown had divulged classified information about U.S. military satellite capabilities. He insisted he relied only on published accounts.

Earlier, in 1985 and 1987, the chairmanship of the important Science Subcommittee on Space Science went to a colleague with far less seniority, Bill Nelson of Florida. Nelson's 1985 victory over Brown was explained in part in regional and generational terms: Nelson, whose district includes the Kennedy Space Center, drew support from junior members and the panel's Floridians. But also, Brown's strong opinions about the use of space funds probably alienated some members who believe virtually any space expenditure is a good one. He considered reasserting his seniority claim to the chair again in the 100th Congress, but was dissuaded by a lack of support.

Having lost the Science Subcommittee in 1985, Brown could have retained the chairmanship of the Agriculture Subcommittee on Department Operations and Research that he had held for four years. He chose not to.

That assignment had been frustrating because it involved managing the contentious and unsuccessful legislative effort to renew the Federal Insecticide, Fungicide and Rodenticide Act. The FIFRA debate pitted pesticide manufacturers against environmentalists demanding more industry regulation. Brown was the referee, and not a happy one. "If this ever comes up again while I am on the committee," he said at one point, "I hope you will refer it to another subcommittee."

Nevertheless, in the 100th Congress, Brown not only regained the Agriculture subcommittee (after conceding the Science panel to Nelson), he also took responsibility for the FIFRA bill and helped steer a stripped-down version into law. He and other leaders of the House and Senate Agriculture committees broke the

stalemate only by agreeing to drop the bill's most controversial provisions. The final measure required chemical companies to determine the health risks of their products under a mandatory timetable, and charged them fees to help finance EPA reviews of their research. But gone were provisions to allow stronger state laws, excuse farmers from liability and protect groundwater.

On other farm issues, Brown has never been an activist. He ranks third among the 27 Agriculture Democrats, but rarely speaks out and was not a major participant in work on the five-year farm bill in the 99th Congress.

On other issues, Brown casts liberal votes much as he did during the 1960s. Occasionally, however, he has cast pragmatic pro-defense votes he might have denounced two decades ago.

Early in the 101st Congress, he and Republican Jerry Lewis, from the neighboring 35th District, led the futile opposition to a package of proposed military base closures. The package, compiled by a blue-ribbon commission, had widespread support in Congress since most members' home-state bases escaped inclusion. But among the targets was Norton Air Force Base in Brown's district, employer of 4,520 military personnel and 2,133 civilians.

In 1980 he began voting for a California product, the B-1 bomber. "If the B-1 was being built in some other state," he once explained, "and I didn't have two Air Force bases and a lot of retired military people who feel strongly about the B-1, I'd probably have voted the other way."

This is the man, after all, who became a peace advocate as a scientist, and argued his cause from the start of his first term, in 1963. That year, he opposed extension of the draft as it passed the House 388-3. He voted against civil defense money, saying it "created a climate in which nuclear war becomes more credible."

By the spring of 1965, he had already begun speaking out against the Vietnam War, accusing President Johnson of pretending "that the peace of mankind can be won by the slaughter of peasants in Vietnam." For the next five years he kept up such protests, refusing to vote for any military spending while the war continued; in 1966 his was the only House vote against the $58 billion defense bill.

Brown acquired a national reputation for his anti-war work during those years, but even then much of his legislative time was devoted to environmental issues. He supported a ban on offshore oil drilling along the California coast, backed federal land-use planning and proposed to outlaw production of internal combustion engines.

One intriguing legacy from the 1960s is Brown's relationship with President Bush, who served with him in the House late in the decade. Despite his liberalism, Brown was one of a number of Democrats whom Bush befriended. Both had to leave the House after 1970 Senate defeats, and Bush subsequently wrote to his former gym partner that he regretted the loss of "the paddleball earnings that you have made possible for me, my wife and my children."

AT HOME
(Prepared: July 1989)

Before his 1970 Senate campaign, Brown's political career revolved around the heavily Hispanic community of Monterey Park. His recent phase has focused on middle-class politics in San Bernardino, 50 miles east.

Born in a small town in California's Imperial Valley, Brown attended college in Los Angeles, then settled in Monterey Park after getting his physics degree. While working for the Los Angeles city government, he began dabbling in Monterey Park politics. After four years on the City Council and in the mayor's office, he was elected to the state Assembly, where he focused on housing issues.

In 1962 the new 29th District was created on Brown's home turf. He easily defeated two strong primary opponents and Republican H. L. "Bill" Richardson in the general election.

Once he developed his reputation as an anti-war leader, Brown attracted a series of opponents - Democrats and Republicans - who challenged him on the Vietnam issue. His closest call came in 1966 against Republican Bill Orozco, who capitalized on his Mexican-American heritage. Brown won by 3,000 votes; it was clear he would have tough future races.

Rather than run again for what had become a marginal seat, Brown decided in 1970 to take on GOP Sen. George Murphy. But to do that he had to wage a primary against U.S. Rep. John V. Tunney, son of former boxing champion Gene Tunney. After American troops invaded Cambodia that spring, polls began to show Brown edging in front of Tunney, who had been much less outspoken against the war. Brown called for the impeachment of President Nixon because of the invasion. Tunney then turned his aim on Brown, accusing him of being a radical and advocating student violence. Brown attempted to deflect what he termed Tunney's "dirty" tactics, but failed and lost by a 9-percentage-point margin.

However, Brown exacted a revenge of sorts. His description of Tunney as the "lightweight son of the heavyweight champ" became part of California political folklore and helped end Tunney's career in 1976.

Brown's political resurrection came just two years after his failed Senate bid, in a newly created district in the San Bernardino-Riverside area. There it was middle-class white conservatives, not Mexican-Americans, who caused problems for Brown.

The 1972 Democratic primary in the new district was a fierce battle. Brown was attacked as an extreme liberal, but he prevailed in the eight-candidate field by finishing second in all three parts of the district. While not impressive, his 28 percent of the vote was enough to get him on the fall ballot as the Democratic candidate in a district over 60 percent Democratic in registration. He won comfortably in November.

Brown topped 60 percent in three consecutive elections, even though 1974 redistricting put more of fast-growing and conservative Riverside County into the district, forcing Brown

to rely more on San Bernardino County votes to carry him. But in 1980, Brown's tally plunged to 53 percent. He got some help in 1981 from a partisan Democratic remap that patched together the most Democratic district possible for him from portions of Riverside and San Bernardino. Still, changing demographics have brought young, conservative-minded voters into the area, and in recent years Brown has been a focus of GOP attention.

In the 1980 election, Republican John Paul Stark, a conservative whose organization came largely from the Campus Crusade for Christ, held Brown below a majority in Riverside for the first time. Brown survived because of his comfortable margin in San Bernardino County.

Brown increased his margin over Stark in a second campaign in 1982, but the challenger returned in 1984 with what Republicans - and many Democrats - believed would be his strongest effort yet. This time, he had the advantage of President Reagan's name on the top of the GOP ballot. But Brown had prepared carefully for the second rematch. His attention to the Stringfellow Acid Pits, a toxic-waste dump near Riverside, played well among middle-class voters susceptible to Stark's appeal.

In addition, Brown took his campaign onto Stark's home ground. He made the rounds of local churches - mainstream and fundamentalist - delivering his own arguments on the importance of extending "pro-life" views to take in nuclear-weapons issues and humanitarian concerns. He wound up taking 57 percent.

In 1986, Brown faced Bob Henley, a San Bernardino businessman. Henley's more moderate politics gave Republicans hope that he could appeal to a broader coalition than Stark. As it turned out, however, Henley had trouble even getting the business community to warm up to him, and he had great difficulty raising money until late in the campaign. As in 1984, Brown addressed his areas of weakness head-on, using a program of coffees around the district to meet new voters, and working hard to line up endorsements from law enforcement groups and local businessmen. He again took 57 percent.

Stark was back a fourth time in 1988, heartened by the district's declining Democratic registration. He may be right about the demographic trend, but he has yet to broaden his own base. Brown was held to 54 percent, but Stark mustered just 42 percent.

Congressional Quarterly

James H. Scheuer (D) New York - 8th District
Of Queens - Elected 1964
Did not serve 1973-75.

BIOGRAPHICAL DATA
(Prepared: July 1989)

Born: Feb. 6, 1920, New York, N.Y.
Education: Swarthmore College, A.B. 1942;
Harvard Business School, M.A. 1943;
Columbia U. Law School, LL.B. 1948.
Military Career: Army, 1943-45.
Occupation: Lawyer.
Family: Wife, Emily Malino; four children.
Religion: Jewish.
Political Career: Sought Democratic nomination for mayor of N.Y.C., 1969; defeated for renomination to U.S. House, 1972; returned to House, 1974.
Capitol Office: 2466 Rayburn Bldg. 20515; 225-5471.

IN WASHINGTON
(Prepared: July 1989)

In the House, Scheuer is scarred forever by his defeat in battle with John D. Dingell, the autocratic chairman of the Energy and Commerce Committee. At the start of the 97th Congress in 1981, the business-oriented Dingell fended off Scheuer, an irascible liberal, for the committee chair. He proceeded to strip his rival of power: Though second in seniority on Energy and Commerce, Scheuer holds no subcommittee chairmanship.

Scheuer - who electorally has endured some extreme permutations of redistricting - has shown a good deal of resilience. On consumer and environmental issues, the ornery survivor remains a crusader, often acting as a front man for California Democrat Henry A. Waxman, the committee's leading liberal, who prefers to play the inside game. Scheuer has also found a niche in the chairmanship of the lower-profile Science Subcommittee on Natural Resources, Agriculture Research, and Environment.

Scheuer's most notable characteristic, though, remains the gruff and belligerent manner that hindered him in his fights with Dingell. No one ever accused Dingell of disarming opponents with charm, but he expertly charted the deal-cutting route to institutional power. Scheuer, on the other hand, was the angry activist, firing off bromides against injustices done to consumers and the environment. While Scheuer was making caustic statements, Dingell was making political allies.

The chairmanship battle grew out of an animosity that developed between the two men over several years. Dingell's main legislative role on Energy and Commerce had been to protect the automakers based in or near his Detroit-area district; Scheuer

was a leading proponent of requiring air bags, a safety device, in cars, an idea Dingell vehemently opposed. Dingell also was irked by Scheuer's persistent calls for stringent anti-pollution standards under the Clean Air Act, and his defense - while serving in the 1970s as chairman of the Energy and Commerce Subcommittee on Consumer Protection - of the Federal Trade Commission, which had become an irritant to many members by seeking to regulate business activity.

For years, the two rarely spoke to each other. And after Dingell defeated Scheuer to take over the full committee in 1981, he "decided" Energy and Commerce had too many subcommittees. There was little doubt which one had to go: Scheuer's cherished Consumer Protection panel.

The deed was done over the furious objections of Scheuer, who said he was being punished for his air-bag crusade. But the 14-7 vote stripping him of his subcommittee also reflected his standing among colleagues. The abrasive Scheuer had not impressed many with his abilities as chairman, and had not made up for that in personal terms.

In the years since, Scheuer has continued in his role as an outspoken activist. But his limited legislative clout is illustrated by the history of the legislation to ban smoking on passenger-airline flights. For years, Scheuer had submitted anti-smoking proposals that went nowhere. But in the 100th Congress, Illinois Democrat Richard J. Durbin, a fast-rising junior member of Appropriations, took up the cause, built a constituency for it, and pushed to passage a smoking ban on flights of two hours or less.

Scheuer has had some success in using his knowledge of House procedures to put obstacles in Dingell's legislative path. In 1987, Dingell was pushing a product-liability bill; it was favored by business interests, who preferred a single federal standard in place of the patchwork of state liability laws, but opposed by consumer advocates, who said injured parties would have a harder time recovering damages. When Dingell tried to force committee markup on the bill that November, Scheuer invoked a rule barring committee action while the full House was considering certain business. Though Dingell eventually forged ahead, the bill ultimately stalled in committee.

Earlier, Scheuer lost a legislative battle with Dingell and other pro-auto industry members, but was vindicated by the Supreme Court. In 1982, Congress exercised its "legislative veto" power for the first time, overturning a proposed rule requiring car dealers to disclose defects in used cars that they sold. Scheuer strongly opposed the veto action, calling it "violently and flagrantly anti-consumer, and in my opinion, grossly against the wishes of the American people." In 1983, the Supreme Court issued a sweeping decision that declared most uses of the legislative veto unconstitutional.

The blow of his 1981 chairmanship defeat was cushioned somewhat by the fact that his Science Subcommittee has jurisdiction over the Environmental Protection Agency (EPA). Scheuer went to war with the Reagan administration over what he viewed as its efforts to eviscerate the EPA's regulatory

functions, and rushed to the forefront of the investigation into misconduct at that agency in 1982.

It was Scheuer who charged that former EPA official Rita M. Lavelle might have perjured herself in denying that she sought the dismissal of an employee who criticized management of hazardous-waste programs. That charge was one of several that led to Lavelle's dismissal in early 1983; she was later convicted and sentenced to time in federal prison. Scheuer also charged that EPA kept a "hit list" on which staff scientists and scientific advisers were rated for political acceptability during the Reagan transition.

In the 100th Congress, Scheuer promoted his proposal to create an executive branch advisory board on issues affecting biotechnology, the field in which scientists perform genetics research into improved strains of agricultural plants and animals, and cures for diseases such as cancer and AIDS. Scheuer's bill was approved by the Science Committee in August 1988, despite the Reagan administration's opinion that it would create an unnecessary layer of bureaucracy. But the bill was blocked in Energy and Commerce by Dingell.

When Scheuer first came to Congress in 1965, he was a strong advocate of President Lyndon B. Johnson's "War on Poverty," and he remains supportive of those programs that have survived the years. He describes Head Start, the preschool program for children of low-income families, as "the jewel in the crown of the poverty program . . . and it has had an unblemished record of success."

AT HOME
(Prepared: July 1989)

Scheuer has had one of the most peripatetic political careers of any House member in recent years. He has challenged three incumbent members of his own party for renomination and beaten two of them. He has run in five different districts and won in four.

The son of a wealthy real-estate man, Scheuer had a highly successful career himself in home building and construction, specializing in urban renewal. He entered politics in 1964 as part of the reform wave that swept over the Bronx that year, winning a seat in Congress by defeating Rep. James Healey, a Democrat allied with the traditional party organization.

He mounted a disastrous campaign for mayor of New York City in 1969, finishing last in a field of five candidates despite an expenditure of $550,000.

In 1970, when a new Hispanic district was created in the South Bronx, much of it from Scheuer's territory, he moved into a neighboring district and defeated Rep. Jacob Gilbert, another Democratic organization loyalist, for renomination. Two years later, the Bronx lost a district and Scheuer was thrown in with Democratic Rep. Jonathan B. Bingham. This time he was not successful, and he had to retire from the House.

But Scheuer did not give up on a congressional career. Political developments in Brooklyn opened another opportunity

for him. Democratic Rep. Frank J. Brasco of the 11th District got into legal trouble and retired in 1974. Scheuer decided to run in that district and won the primary over the candidate backed by the Brooklyn organization. After that, his electoral career quieted down for the balance of the decade. The organization did not challenge him, and he did not bother the organization.

This peaceful arrangement served Scheuer well in 1982, when the Legislature merged his district with that of Queens Democrat Joseph P. Addabbo. Scheuer moved one more time, to the new 8th, and Queens Borough President Donald Manes, who was also the county Democratic chairman, persuaded local party figures not to run against him. He has not had any trouble since then. In 1988, Scheuer drew no Republican opposition.

Congressional Quarterly

F. James Sensenbrenner Jr. (R) Wisconsin - 9th District
Of Menominee Falls - Elected 1978

BIOGRAPHICAL DATA
(Prepared: July 1989)

Born: June 14, 1943, Chicago, Ill.
Education: Stanford U., A.B. 1965;
U. of Wisconsin Law School, J.D. 1968.
Occupation: Lawyer.
Family: Wife, Cheryl Warren; two children.
Religion: Episcopalian.
Political Career: Wis. Assembly, 1969-75;
Wis. Senate, 1975-79.
Capitol Office: 2444 Rayburn Bldg. 20515; 225-5101.

IN WASHINGTON
(Prepared: July 1989)

The adjectives that colleagues use to describe Sensenbrenner's personality - pompous, brusque, nitpicking - make it clear that this conservative Republican would never win a House popularity contest.

But if he is held in icy regard, Sensenbrenner also is recognized as a diligent conservative on the liberal-dominated Judiciary Committee, someone who can go beyond the role of mere objector to package his views into workable legislation.

There is a partisan quotient to the criticisms of Sensenbrenner's personality: Through the years, Judiciary Democrats have been put out by his strongly worded statements against abortion, the Equal Rights Amendment and the Legal Services Corporation, and for capital punishment.

However, even a number of Republican colleagues have found the opinionated Sensenbrenner tough to take. At one meeting of the Judiciary Committee in the 98th Congress, Sensenbrenner became angry because Florida Republican Bill McCollum offered an amendment similar to one he had prepared. His long public outburst bothered McCollum so much that for weeks he refused even to sit next to Sensenbrenner.

But if Sensenbrenner's personality sometimes makes it difficult for him to find allies on either side of the aisle, he clearly is willing to cooperate with anyone, even a Democrat, when he believes strongly in something.

In the 97th Congress, Sensenbrenner played a major role in crafting a compromise with committee Democrats on the extension of the Voting Rights Act. In doing so, he angered Illinois Republican Henry J. Hyde, who had strong objections to the bill and had been trying to stall it. But Sensenbrenner's persistence was vindicated when the Reagan administration, which initially balked at the bill, hailed its passage as one of President Reagan's major civil rights accomplishments.

In another example of his strong-minded independence,

Sensenbrenner, who had not been a gun-control advocate, supported a 1988 amendment to the omnibus drug bill mandating a seven-day waiting period prior to the purchase of a handgun. When the National Rifle Association sent a letter into his district criticizing the measure as "back-door registration of American firearms owners," Sensenbrenner turned his fire on the gun lobby, holding a news conference to denounce the mailing as "misleading and inflammatory."

Still, his overall thrust on Judiciary is solidly conservative. The ranking Republican on the Civil and Constitutional Rights Subcommittee, he carried the Republicans' banner in their attempts to modify a pair of civil rights-oriented bills in the 100th Congress.

In 1988, Sensenbrenner led the battle in committee against the provision in a fair-housing bill that would have set up a system of administrative-law judges, empowered to rule on housing discrimination cases and impose financial damages and fines. Taking a position supported by Reagan and the National Association of Realtors, Sensenbrenner argued that the system, under which a violator would be forced to pay fines without the benefit of a jury trial, might be unconstitutional.

His amendment, replacing the administrative law system with an expedited federal court trial procedure, was defeated by a 14-20 Judiciary vote. However, the final bill enacted later that year contained a compromise that met Sensenbrenner's concerns halfway: It set up an administrative-judge process, but gave any party in a discrimination suit the right to request a jury trial.

Sensenbrenner had less success in 1988 when trying to reshape the Civil Rights Restoration Act - a bill so named because it aimed at overriding the Supreme Court's 1984 Grove City College v. Bell decision, which said that only the "program or activity" of an institution receiving federal assistance, and not the entire institution, was required to comply with federal anti-discrimination laws. His alternative to the Democrat-backed bill was defeated by the House on a 146-266 vote.

Though Republicans had many objections to the Grove City bill, Sensenbrenner's proposal centered on the "religious tenets" clause, which provided exemptions from the law to "any operation of an entity which is controlled by a religious organization." Sensenbrenner's amendment included a provision to broaden the clause to cover entities controlled by or "closely identified with the tenets" of a religious organization.

But most Democrats and some Republicans, including ranking Judiciary member Hamilton Fish Jr. of New York, objected. Fish denounced the measure as "unwise and unnecessary," and noted that the language was intended to cover seminaries and not colleges with broader enrollments.

Sensenbrenner was not happy with his setback on the bill. When some Science Committee Democrats opposed a bill, written by Pennsylvania Republican Robert S. Walker, mandating sanctions against federal contractors who do not maintain drug-free work places, Sensenbrenner lashed out. "If you object to using the string of federal funds," he said, "then you should not have

supported Grove City."

At the start of the 101st Congress, Sensenbrenner took over as ranking Republican on the Science Subcommittee on Space. In that spot, he seems likely to be a leader of the panel's bipartisan consensus in favor of U.S. space programs. In a speech supporting the National Aeronautics and Space Administration's budget priorities for fiscal 1990, Sensenbrenner warned those looking for budget savings in those programs that "it's easy to be 'penny-wise' and 'pound-foolish.' "

In the 100th Congress, Sensenbrenner was ranking member on the Science Subcommittee on International Scientific Cooperation, where he argued that the concept of cooperation was not appreciated by America's major trade competitor, Japan. He stated that Japan had taken advantage of the United States by developing and marketing products based on expensive U.S.-financed basic research, and he called on Reagan to be tougher in demanding that the Japanese contribute more to the basic research effort.

Japan's proposal for a limited economic contribution to allied efforts to protect Persian Gulf shipping lanes in 1987 enraged Sensenbrenner. "American servicemen have died far away from home protecting the oil that drives Japanese industry, an industry that takes jobs away from United States workers . . . ," he said in October of that year. "This time the international community should band together to let Japan know its freeloading days are over."

AT HOME
(Prepared: July 1989)

Sensenbrenner has held public office ever since his graduation from law school. Despite his reputation for pomposity, his personal resources and conservative views have earned him an undefeated record at the polls.

Sensenbrenner is heir to a paper and cellulose manufacturing fortune, much of which stems from his great-grandfather's invention of the sanitary napkin shortly after World War I. Marketing it under the brand name Kotex, Sensenbrenner's ancestor went on to become chairman of the board of Kimberly-Clark.

To reach Congress in 1978, Sensenbrenner had to dip into family wealth to overcome an unexpectedly strong GOP primary challenge. With Republican Bob Kasten leaving the 9th District to run for governor, Sensenbrenner was viewed as the obvious successor. He had been elected to four terms in the state Assembly before moving in 1975 to the state Senate, where he quickly rose to be assistant minority leader. He had a solid political base in the older, more affluent lakeside suburbs, and his conservative stance reminded voters of the popular Kasten.

But his opponent was Susan Shannon Engeleiter, a state legislator who would later become state Senate GOP leader, the party nominee for the U.S. Senate in 1988 and then director of the Small Business Administration. Just 26 when she challenged

Sensenbrenner, Engeleiter put on a strong campaign in the western, more middle-class part of the district, which she represented in the state Assembly. More gregarious than Sensenbrenner, she outpolled him by 5,600 votes in the 9th's four western counties. Only Sensenbrenner's familiarity in the areas along Lake Michigan - Ozaukee and the most Republican part of Milwaukee - allowed him to win the primary by 589 votes.

The 1978 Democratic nominee, Milwaukee lawyer Matthew J. Flynn, was also on his way to higher visibility in statewide politics as party chairman and a candidate for the U.S. Senate. But he could not raise enough money to compete with Sensenbrenner on an equal footing. Sensenbrenner campaigned on his support for cutting taxes and defeated Flynn by a solid margin.

Congressional Quarterly

Harris W. Fawell (R) Illinois - 13th District
Of Naperville - Elected 1984

BIOGRAPHICAL DATA
(Prepared: July 1989)

Born: March 25, 1929, West Chicago, Ill.
Education: Attended North Central College, 1947-49;
Chicago-Kent College of Law, J.D. 1952.
Occupation: Lawyer.
Family: Wife, Ruth Johnson; three children.
Religion: Methodist.
Political Career: Ill. Senate, 1963-77; candidate for Ill.
Supreme Court, 1976.
Capitol Office: 318 Cannon Bldg. 20515; 225-3515.

IN WASHINGTON
(Prepared: July 1989)

Fawell brings to his legislative work the same attention to detail that made him a successful attorney. By the time a bill comes before one of his committees, Fawell not only has read it line by line, he is likely to have underlined and highlighted the document and scribbled notes in the margins about questions he wants to raise.

This precision makes Fawell something of a bug on esoteric funding issues that most House members overlook. But a couple of these matters turned into unexpected victories for the Illinois Republican during the 100th Congress.

In early 1988, Fawell led the effort to overturn an $8 million appropriation to build schools in Paris for Jewish refugees from North Africa. The funding had been a pet project of Democratic Sen. Daniel K. Inouye of Hawaii, who attached it to a 1987 catchall appropriations bill at the behest of a U.S. refugee-assistance group. But Fawell, who regarded the measure as a boondoggle, submitted a bill to rescind the money, and organized more than two dozen House members to protest it. After the issue attracted media attention, a chastened Inouye asked that the funding be dropped.

That August, Fawell also opposed a bill to allow Boston College to write off $12 million on a loan it obtained to build a library named after former House Speaker Thomas P. O'Neill Jr. Fawell said the write-off would constitute an inappropriate grant for a private college's general-purpose library, since the facility was not dedicated to O'Neill's House career. Though Fawell was one of only two members to speak against the bill on the House floor, it was defeated, 158-239.

On the broader issues that come before Education and Labor, his major committee assignment, Fawell reflects the conservative business orientation of his suburban district. He is averse to any federal mandate that would raise the cost of doing business.

An opponent of measures to require business owners to provide health insurance to employees, Fawell says, "Many small business firms simply cannot pay the $1,800 to $3,600 per-employee, per-year cost." In 1988, he described a proposed minimum-wage increase as a "maximum job-loss bill."

But while Fawell supported most Reagan administration economic and defense policies, his voting record did not place him in the ranks of House hard-liners: He opposed Reagan's position on just over a third of House legislation in the 100th Congress. Most notably, Fawell advocated strengthening the Clean Air Act, a stand that earned him a "Clean Air Champion" award from the environmentalist Sierra Club.

AT HOME
(Prepared: July 1989)

Fawell can afford to talk about the need to assess issues from a "businessman's point of view." The political mainstream in the 13th ranges from the moderate to far right within the Republican Party. Fawell's only electoral worries would arise within his own party, and those are unlikely; he has rolled over his Democratic opponents.

As the campaign treasurer for his longtime friend, veteran Rep. John N. Erlenborn, Fawell was perfectly positioned in 1984 when Erlenborn announced his surprise resignation after 20 years of service. He picked up most of Erlenborn's old political network, and Erlenborn's veteran chief aide became his campaign manager.

That help proved invaluable in winning the GOP primary. Fawell, who as a state legislator had promoted measures to aid the handicapped, faced two conservative opponents - state Sen. George Ray Hudson and former state Sen. Mark Rhoads - who tried to portray him as a liberal. But Hudson and Rhoads were waging their own dogfight, complete with name-calling over who was the more genuine ideologue.

With backing from the formal Du Page and Cook County GOP organizations as well as conservative contacts, Hudson seemed at least an even bet to defeat Fawell as the campaign entered the last few weeks. But he lost some support because of his age (64), and he was further weakened when he fell off a stage and broke his leg during the campaign. Fawell took the nomination over Hudson by more than 3,000 votes, and coasted through November.

Committee on Budget (SD–621), 4–0642—CONTINUED

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Senior Analyst for—
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Income Security.—Jim Ricciuti (SD–627), 4–0564.
Energy and Natural Resources.—Austin Smythe (SD–625), 4–0539.
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Agriculture.—Bruce Blanton (SD–635), 4–6588.
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Commerce, Science, and Transportation

(Suite SD–508, phone 4–5115, meets first and third Tuesdays of each month)

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Wendell H. Ford, of Kentucky.
J. James Exon, of Nebraska.
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John D. Rockefeller IV, of West Virginia.
Lloyd Bentsen, of Texas.
John F. Kerry, of Massachusetts.
John Breaux, of Louisiana.
Richard H. Bryan, of Nevada.
Charles S. Robb, of Virginia.

John C. Danforth, of Missouri.
Bob Packwood, of Oregon.
Larry Pressler, of South Dakota.
Ted Stevens, of Alaska.
Robert W. Kasten, Jr., of Wisconsin.
John McCain, of Arizona.
Conrad Burns, of Montana.
Slade Gorton, of Washington.
Trent Lott, of Mississippi.

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John Breaux, of Louisiana.
Charles S. Robb, of Virginia.

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Larry Pressler, of South Dakota.
Conrad Burns, of Montana.
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Lloyd Bentsen, of Texas.
John Breaux, of Louisiana.
Charles S. Robb, of Virginia.

Ted Stevens, of Alaska.
John C. Danforth, of Missouri.
Bob Packwood, of Oregon.
Robert W. Kasten, Jr., of Wisconsin.
Larry Pressler, of South Dakota.
Slade Gorton, of Washington.
Trent Lott, of Mississippi.

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General Counsel.—Linda J. Morgan.
Minority Chief Counsel and Staff Director.—Walter B. McCormick, Jr.
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Robert E. Palmer
Staff Director
Subcommittee on International Scientific Cooperation

Committee on Science, Space and Technology 822 HOB Annex 1
U.S. House of Representatives Washington, D.C. 20515

Richard Getzinger - science attaché Tokyo
Very competent

Questions for NIH

1. What international efforts are currently underway to map the human genome (i.e., France, U.K., Japan, U.S.S.R., etc.)?

2. What are the current plans to divide up the mapping effort internationally?

3. Will all countries involved in the mapping effort be contributing equitably in basic research?

4. Will all countries be sharing mapping results equally?

5. Are there competitive concerns in sharing mapping database information?

6. Are there competitive concerns in sharing sequencing technology?

7. Are there any other competitive concerns which need to be addressed as the genome is mapped?

8. How are social and ethical concerns being addressed as the genome is mapped? Are there any international guidelines?

9. How is NIH's role being coordinated with other agencies and international efforts?

10. Is there any legislative role in increasing the amount of international cooperation, competitive or ethical issues?

MEMORANDUM

Date: September 15, 1989

From: Pam Lokken

Subject: Briefing for House Subcommittee on International Scientific Cooperation, Committee on Science, Space, and Technology

To: Dr. Jordan, Director
Office of Human Genome Research

Here is some background information concerning current international cooperative efforts on human genome research that I have pulled from our files and the minutes of our Program Advisory Committee meetings.

We will be meeting at 3:00 pm on Monday, September 18, 1989 with two staff members from the Subcommittee on International Scientific Cooperation: Dr. Robert Palmer, Staff Director of the Subcommittee and Mr. Chuck McElyea. The NIH delegation will include both of us and Ms. Kris Kiser of DLA.

Mr. McElyea indicated in telephone conversations with Ms. Kiser that the Subcommittee is interested in an informal briefing on international cooperation in the genome project. This briefing is in anticipation of a Subcommittee hearing scheduled for October 19, 1989 in which Dr. Watson will be one of the witnesses.

The hearing is to focus on the current status of the genome project internationally and future plans to divide the work of the genome project. They are interested in ethical issues surrounding the genome initiative as well. Mr. McElyea stressed that this is to be an information gathering hearing and that no legislation has been introduced on this topic. He said that they would appreciate our recommendations for any other hearing witnesses.

DRAFT
9/18/89

INTERNATIONAL EFFORTS

During the first Program Advisory Committee Meeting on the Human Genome, in an attempt to define the extent of interfacing activities that would be appropriate between the human genome program in the U.S. and similar programs in other countries, Dr. McKusick stated that the most important aspect of this interface will be exchange of data and biological resources. Such exchange would enable investigators to work more efficiently and would help to minimize duplication of effort.

Europe: Commission of the European Communities (CGC)

The CGC proposed to use the techniques of molecular genetics to analyze the structure of the human genome. It is a basic scientific program directed toward understanding the human genetic function rather than its interpretation. The program is to be implemented through genetic and physical mapping of the genome, as well as technology developments. The primary aim is the creation of a set of tools for use in studying the human genetic function.

An Ad Hoc Working Party On Human Genome Analysis, chaired by Professor Peter Pearson of the Netherlands, exists to advise the CGC on specific programmatic matters. Two representatives from each of the EEC's member states comprise the membership of the Working Party. The Working Party has six Study Groups encompassing the following areas:

1) Human Genetic Mapping
2) Ordered Clone Libraries
3) Advanced Genetic Technologies
4) Training/Fellowships
5) Datahandling and Databases
6) Ethical, Social and Legal Aspects

The Working Party's recommendations envisage scientific coordination among numerous networks of European laboratories. Proposed financial support over three years for undertaking the program breaks down this way:

Improvement of the genetic map	3.3
Physical mapping	3.4
Datahandling and databases	2.2
Advanced genetic technologies	2.2
Training	1.9
Ethical, social and legal aspects	1.0
Scientific management	1.0
Total (European Currency Units)	15.0 (mioECU)
(approximately $15 million U.S. dollars)	

The Working Party recommended that scientific links be established with the U.S. and Japanese human genome programs as well as with other organizations, such as the Human Genome Organization (HUGO). Dr. Pearson stated that the EEC's human genome program plans to offer training fellowships that will allow less technologically advanced European countries to participate in and benefit from the program. Dr. Pearson also supports multigovernmental funding for programs involving Japanese or U.S. investigators working in conjunction with European teams. The EC's genome program contains an ethics study group and Dr. Nancy Wexler, chairperson of the NIH Program Advisory Committee's ethics working group, will attend the next meeting of the European counterpart.

United Kingdom

The Office of Human Genome Research proposed that a formal interchange take place among representatives of the UK and U.S. Human Genome Programs. A UK representative (Dr. Michael Kemp) attended the last meeting of the OHGR Program Advisory Committee. Dr. D A Rees, Secretary of the Medical Research Council (London), indicated in a letter to Dr. Jordan that they are very interested in establishing close ties between the two programs.

During the first Program Advisory Committee Meeting of the Human Genome, Dr. Mark Pearson reported that British scientists have developed new techniques for the detection of sequence polymorphisms. In addition, they have developed microsequencing methods for determining sequences at the end of restriction fragments, making it possible to generate large amounts of information that can facilitate the ordered overlapping of DNA sequences. Dr. Pearson also discussed the U.K.'s large-scale mapping and sequencing projects, which have focused on the human genes CF, NF, and HD; viral genomes, including cytomegalovirus; plants, including Arabidopsis; and bacteria. Dr. Watson noted that the UK plans to spend approximately $12.5 million over a three year period for research on Arabidopsis.

During the second Program Advisory Committee Meeting of the Human Genome, Dr. Watson informed the Committee of an opportunity to join British investigators working on sequencing the C. elegans genome. The project is to involve sequencing 15,000,000 base pairs per year and will take approximately 6 years to complete. He estimated that a 3-year grant of approximately $600,000 per year would be needed to explore the feasibility of the project, provided an equal sum is contributed by the U.K. The Program Advisory Committee unanimously endorsed the concept of joint funding of such an effort.

West Germany

Dr. Jordan met with Mr. Friedrich-Adolf Jahn, Deputy Minister of Justice, in July 1989 to talk about the human genome project. The West German Cabinet is drafting regulations regarding human genome sequencing and mapping. Human genome analysis is a highly controversial issue in the FRG, possibly due to the legacy of the Nazi movement and its eugenic principles. The Research and Technology Committee of the Bundestag has objected to the genome initiative of the European Community on the grounds that knowledge of inheritable diseases gained from genome research may persuade, or in some countries, conceivably compel individuals with potential genetic disorders not to reproduce. The Bundestag argues that such developments would constitute a version of eugenic justification. West German research organizations are proceeding independently to coordinate genome research in the FRG.

Belgium

Dr. Jordan met with a delegation of Belgian officials in May 1989 to discuss human genome research.

Denmark

Dr. Jordan met with Dr. Peder Olesen Larsen, Director of the Danish Research Administration, in May 1989 to discuss the human genome project.

Spain

Several Spanish laboratories are working on the molecular diagnosis of some hereditary diseases with DNA probes. The National Research Program on Health is undertaking a program called "Analysis of the Human Genome: Medicine Predictive".

Japan

The Japanese Council for Aeronautics, Electronics and other Advanced Technologies established the Subcommittee on Human Genome Analysis as a part of their Biotechnology Committee. A document was published in June 1988 by the Science and Technology Agency entitled "Comprehensive Strategy for Promoting R&D on Human Genome Analysis". The document supports the idea of international cooperation for such a huge undertaking and suggests that an international symposium be held in Japan. It also states that Japanese researchers should participate in HUGO conferences.

The Japanese government initiated an international program called Human Frontier Science Program (HFSP) which aims to promote international cooperation in basic research. The HFSP issued its first Invitation for Applications in August 1989. Grants for basic research (including the potential for a large program in human DNA sequencing), fellowships, and international conferences will be awarded to researchers in Canada, U.S., Japan and the European Community. The organization plans to establish offices in Strasbourg France and will have a budget of $24 million in Japan's FY90.

The current genome mapping project in Japan is located at the Life Science Center of the Institute for Physical and Chemical Research (RIKEN) under the Science and Technology Agency (STA). It is under the direction of Dr. Ikawa who spent two years at NIH laboratories and is internationally known for his work on molecular biology.

During the first Program Advisory Committee Meeting on the Human Genome, Dr. Maynard Olson discussed Japan's endeavors in the area of human genome research. He reported that the Japanese have focused heavily on sequencing projects, in contrast to the approach generally taken in the U.S., which is to concentrate on linkage and physical mapping, with a phase-in of sequencing as technological improvements materialize. Specifically, Japanese researchers have completed the sequence of chloroplast DNA and are currently coordinating a major effort to sequence the E. coli genome. There is also a Japanese demonstration project geared toward streamlining the sequencing process by using the polymerase chain reaction (PCR) for the preparation of sequencing templates. The project is relatively small but contacts with industry will be the next step if scaleup is warranted.

Dr. Olson noted that the interagency coordination situation in Japan is very complex, with various ministries, including the agricultural, education, and technology ministries, involved in mapping and sequencing projects. The existence of an advanced, monolithic plan is a misperception in the U.S. Basic research in biomedical science has been severely underfunded in Japan, so diversion of scarce resources is a major concern there. Nevertheless, Japan's hierarchal system lends itself to concentration on programmatic goals. He suggested that observation of Japan's coordination strategies may provide insights relevant to management of the human genome program in the U.S. It was also noted that Japan's management strategy has been successful coordination between academia and industrial laboratories, particularly with regard to data base management and software development.

HUGO

HUGO was established in 1988 to facilitate international collaboration in the mapping and sequencing of the human genome.

HUGO will also coordinate the efforts of investigators involved in mapping and those who work on sequencing and cloning. In addition, HUGO will coordinate research among investigators working on different species. HUGO receives partial funding from the Howard Hughes Medical Institute but hopes to obtain multigovernmental as well as private funding. The organization is incorporated in Geneva and has established three continental offices: one in London, one in Bethesda, and one in Osaka.

Dr. McKusick has indicated that HUGO is planning a wide variety of activities, ranging from international training programs to development of guidelines on ethical, social legal, and commercial issues surrounding the human genome project. It will arrange for the exchange of data, samples, and technology relevant to genomic research and will assist in the organization and funding of the Human Gene Mapping Workshops.

INTERNATIONAL CONFERENCES

Spain

In October 1988 an international workshop on "Present Status at Several National Levels and Proposal for International Cooperation on the Human Genome Project" was held in Valencia Spain. The purposes of the meeting were to define the present state of the art in sequencing and gene mapping in Europe, the U.S., and in Japan, and to stimulate international cooperation in the genome project.

At the conference, a proposal was presented to the Workshop on International Cooperation for the Human Genome Project by a representative of the Latin American Network of Biological Sciences. The proposal presented ideas for how Latin America could participate in the human genome project.

Japan

In March 1989, an international meeting was held in Japan to discuss molecular approaches to the human genome. There was extensive discussion of model organisms, mapping and sequencing technology, human diseases, and general molecular genetics.

The Council for International Organizations of Medical Sciences (CIOMS), established under the auspices of the World Health Organization and UNESCO, is planning a conference entitled "Genetics, Ethics and Human Values: Human Genome Mapping, Genetic Screening and Genetic Therapy". The conference is to be held in July 1990 in Japan. Dr. Wyngaarden and Dr. Watson have been asked to speak at the conference.

France

The United Nations Educational, Scientific and Cultural Organization (UNESCO) organized a conference in Paris in February 1989 to address international cooperative efforts on the human genome. UNESCO hopes to establish and develop collaboration with existing intergovernmental and non-governmental bodies, facilitate the access of developing countries to research efforts on the human genome, promote international and collaborative genome research projects, and encourage the international exchange of information.

USSR

UNESCO held a second conference on international cooperative efforts on the human genome in Moscow in June 1989. The conference was hosted by the Academy of Sciences of the USSR. Dr. Watson attended the conference.

Human Genome Mapping Workshops

The workshop was originally designed to provide an international forum within which new data could be organized into a coherent human genome map. Data from individual laboratories are compared and combined to provide an up-to-date and accurate account of the human gene map. A common nomenclature is devised so that the map can be reported without ambiguity and with precision. The workshops provide a means for the scientific community to organize itself to deal with the task of analysing a large, complex genome. The Human Gene Mapping Workshop has reorganized itself and now is projecting meetings in the United Kingdom (1991) and in Japan (1993). The Tenth International Workshop on Human Gene Mapping was in New Haven, Connecticut this past June.

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FOR RELEASE ON DELIVERY

Testimony by

Dr. James D. Watson, Director
National Center for Human Genome Research

National Institutes of Health
Public Health Service
Department of Health and Human Services

On International Scientific Cooperation to Map and Sequence the Human Genome

Before the

Subcommittee on International Scientific Cooperation
Committee on Science, Space and Technology
United States House of Representatives

October 19, 1989

Mr. Chairman and Members of the Subcommittee:

Thank you for the opportunity to present testimony on NIH efforts to ensure effective international scientific cooperation in genome research and to explain the importance of mapping and sequencing the human genome.

At the National Institutes of Health, the Human Genome Program is being managed by the National Center for Human Genome Research, established officially on October 1, 1989. The Center evolved from the Office for Human Genome Research, a coordinating unit within the Office of the Director, NIH, in recognition of the growth of the program over the last two years and the high priority NIH places on mapping and sequencing the human genome. Overall advice and guidance to the Genome Program at the National Institutes of Health is provided by the Program Advisory Committee on the Human Genome. I am pleased to be able to testify for the first time as Director of the National Center for Human Genome Research.

The task of determining the human DNA sequence is now firmly established as a national objective. Similar to the 1961 decision made by President Kennedy to send a man to the moon, the United States has committed itself to a highly visible and important goal. We did not know if we could successfully reach the moon -- we already know it is possible to map and sequence the human genome. Though the final monies needed to completely

determine the sequence of the three billion chemical components of human DNA called base pairs are on an order of magnitude smaller than those needed to let Americans explore the moon, the impact of the Human Genome Program on human life is likely to be as great or greater. A more important set of instruction books will never be made available to human beings.

Gene mapping and analysis will be key tools of biology in the 21st century. When finally interpreted, the genetic messages encoded within our DNA molecules will provide the ultimate answers to the chemical underpinnings of human existence. They will not only explain how we function as healthy human beings, but also provide us with a new understanding of such widespread illnesses as heart disease, hypertension, certain cancers and diabetes, that touch the individual lives of so many millions of our citizens. Determining the location and structure of specific genes on the 23 pairs of human chromosomes is a major step toward discovering new methods to prevent or treat the 4,000 inherited diseases that are caused by single-gene defects, or the many more genetic defects that involve an inherited susceptibility to disease. The sooner the entire genome is mapped and sequenced, the sooner scientists can get on with the real work of human biology: understanding what the genes do.

Every gene is a unique fragment of DNA. These genes are strung along the 23 pairs of chromosomes present in every cell in the human body. Finding the location of individual genes on a chromosome and analyzing these genes down to their chemical

components is now possible on a large scale. The National Institutes of Health has supported most of the basic research that has brought us to this threshold, especially the phenomenal explosion of biologic knowledge emanating from the invention of recombinant DNA technology in the early 1970's. Because of the generous funding provided by Congress to the National Institutes of Health, the United States is clearly the leader in this field of research.

The possibility of knowing our complete set of genetic instructions seemed an unreachable scientific objective in 1953 when Francis Crick and I discovered the helical structure of DNA. Then, there existed no way to determine the sequence (i.e., the precise structural composition) of even very short DNA molecules, much less the totality of human DNA. New techniques derived from recombinant DNA technology have made it possible to isolate individual genes. Researchers can chop up DNA at identifiable points that act as landmarks, mix and match pieces of DNA in various organisms, grow unlimited quantities of these fragments in bacteria, and take DNA apart and put it back together again. They have learned to make DNA from laboratory chemicals and to note its tiniest variations. Scientists also have learned to "sequence" DNA, that is, determine the order in which the four chemical components, called A, T, C and G occur. Breakthroughs in recombinant DNA technology allowed Walter Gilbert and Fred Sanger to develop their powerful sequencing techniques -- for which they won the Nobel Prize in 1980 -- that now make the

sequencing of short stretches of DNA a routine laboratory procedure. Technology is still inadequate for the sequencing of long stretches of DNA.

Mapping and Sequencing of Model Organisms

The sequencing of the genomes of relatively simple organisms such as bacteria and yeasts are intended to go hand-in-hand with, if not ahead of, that of the human genome. Experience has shown that information derived from studies of the biology of model organisms is a critical key in understanding and interpreting human biology. Knowledge of the simpler structures of the genes of bacteria and budding yeasts can facilitate the task of distinguishing the DNA sequences that actually carry a gene's instructions (exons) from the much more prevalent noncoding (intron) components whose functions are not fully understood. The sequences of a large number of individual genes in model systems and in the human are already complete, with the total number of base pairs sequenced approaching 25 million. However, this number pales by comparison with the 3 billion base pairs in human DNA.

The best understood organism to date is the intensively studied bacterium Escherichia coli (or E. coli), with over 800,000 base pairs out of a total of 4.7 million in its genome already established. There are a number of labs in both the United States and Japan that are working to complete the E. coli sequence. We have good reasons for believing that success will

come within the next decade. The mere statement that how E. coli functions will one day be completely known is an extraordinary scientific assertion. The sequencing of the yeast genome would be an even more dramatic achievement.

Elucidation of the genomes of multicellular organisms like Caenorhabditis elegans, or C. elegans (a simple round worm of 100 million bases), and Drosophila (the fruit fly with 150 million bases) are equally important scientific landmarks. Their much more complex genomes provide the instructions for the extraordinary set of events that allow fertilized eggs to develop into functional adults. Both the C. elegans and Drosophila scientific communities are starting to make plans for deciphering the DNA messages of their respective organisms.

The main mappers of C. elegans are planning to start pilot sequencing efforts that they hope will bring the cost down quickly to less than $1 per base pair. The NIH Program Advisory Committee on the Human Genome unanimously endorsed the concept of a collaborative United States/United Kingdom pilot project, co-funded by the NIH and the Medical Research Council of the U.K., for sequencing the entire genome of C. elegans, with the goal of establishing the total C. elegans genome by the year 2000. We anticipate that applications for this project will be submitted this fall. The Drosophila community will probably propose a project with a similar timetable. Here again, it would be advantageous if the final sequencing effort could be shared between Europe and the United States, as these nation's

scientists are the primary researchers working on these model organisms.

Mapping and Sequencing the Human Genome

The human genome, which is almost 1000 times larger than that of E. coli and is distributed over 23 pairs of chromosomes, is a much more formidable objective. Here, the approach of coordinating small groups of individuals working at a large number of different sites is unlikely to be sufficient, unless there are dramatic changes in technology. The time involved in completing the human genome would more than exceed the lifetimes of those working in this area.

Therefore, we must design a strategy where economies of scale are sought and found. In order to do this, we need to establish research centers where groups of 15-20 individuals from many disciplines can pool their talents. These research centers must become the foci for collaboration with other investigators, for sharing and distribution of materials, and for data collection on an international scale.

The National Center for Human Genome Research has announced its plan to establish such research centers at academic and industrial sites, with three centers planned for fiscal year 1990. Additional centers are planned to be initiated in subsequent years. Some of these centers will focus on sequencing the genome of a model organism, some will focus on the physical map of a human chromosome, and others will focus on a particular

technology. I want to point out that the Department of Energy has established three centers in their National Laboratories that are very similar in concept to the NIH centers. I also expect that research centers will be established abroad and be funded by other nations.

All genome research centers will be expected to foster collaboration among scientists with similar research interests across the world. Obviously, we will take great care to ensure that centers do not duplicate each other's work. At the moment this is not a problem as there is so much work to do. On the contrary, we need to encourage scientists to take on some of these challenging objectives.

NIH and DOE Cooperation

The National Institutes of Health and the Department of Energy have developed a remarkably close working relationship on the Human Genome Project. This relationship was highlighted by a joint meeting of the advisors to the DOE and NIH which was held this past August at Cold Spring Harbor. The agenda was to prepare a joint NIH/DOE five year plan for the Genome Project. For the first time the question before us was not whether to start a human genome program, but how best to carry it out. The meeting was the culmination of the close cooperation between the agencies in the past two years and illustrated how the two agencies can bring complementary strengths to this project. It also was gratifying to see how much scientific progress has been

made since the project commenced in 1987. A copy of the NIH/DOE plan will be available in early December and we will be glad to share it with you at that time.

Technological Advances

Several significant improvements in technology have occurred in the last two years. There are now better cloning vectors that allow for the isolation and amplification of larger pieces of DNA. This facilitates the task of making physical maps because fewer pieces of DNA have to be assembled. Methods for localizing pieces of DNA on chromosomes using microscopes also have been improved. A third improvement is the application of a method called PCR, for polymerase chain reaction, to mapping. This is a chemical method for isolating and making large amounts of a desired piece of DNA. It allows specific segments of DNA to be located, even if they are buried in large amounts of other DNA. This method has had a revolutionary impact on the genome project and has made many experiments much simpler.

Recently, a proposal was made by several members of the original National Research Council Committee on Mapping and Sequencing the Human Genome that presents a system for collecting information from physical mapping projects in a common language. This new approach is referred to as sequence-tagged sites (STS) and will allow the data from diverse physical mapping techniques to be integrated into a common map. The STS proposal would also eliminate the need for large central repositories of DNA, as the

information about STS locations could be used to regenerate any desired piece of DNA easily.

In the area of database development, the National Center for Human Genome Research will collaborate with NIH's recently established National Center for Biotechnology Information at the National Library of Medicine as well as with the Department of Energy. The National Center for Biotechnology Information was created to pursue research in biological information handling, particularly with respect to human molecular biology. Efforts of the National Center for Biotechnology Information are closely coordinated with the Human Genome Program through frequent staff interaction and through use of the same advisory groups.

Ethical and Legal Considerations

Many ethical, legal and social questions arise from the use of the information and capabilities that flow out of the Human Genome Program. Therefore, the National Center for Human Genome Research will provide support for studies that investigate such concerns. Starting in fiscal year 1990, at least 3% of the NIH Human Genome Program budget will be available for activities that address ethical, legal and social issues related to the project. The NIH Program Advisory Committee created an ethics working group to plan and coordinate this part of our Human Genome Program. The working group held its first meeting on September 14-15, 1989. At this meeting, the group began to develop a detailed plan for addressing the ethical issues arising from the

application of knowledge gained as a result of the Human Genome Program. This plan also will be available in early December.

International Cooperation

The NIH is fully aware that the importance, complexity, and cost of the effort to map and sequence the human genome makes international cooperation desirable, if not essential. Most developed countries are already formulating strategies to undertake aspects of this international effort, and some developing countries are interested in participating in the research as well. To date, only the United States, the United Kingdom (U.K.), Italy and the Commission of the European Community (EC) have announced independent human genome initiatives, but there are good reasons for believing that France, the USSR, Japan, and possibly Canada will join the effort.

The Human Genome Program will require a number of years, substantial resources, and the development of increasingly sophisticated technology. Storage, comparison and retrieval of the information produced also will require a high level of international cooperation to ensure that basic scientific information is freely accessible to all. The project is much bigger than any one country, and there are certainly enough challenges to go around.

Cooperation already exists between the United States and the Commission of the European Community and the U.S. and the United

Kingdom. Representatives of the Commission of the European Community, the United Kingdom and Canada have participated in meetings of the NIH Program Advisory Committee on the Human Genome. Similarly, members of my staff attended two meetings of the European Community's Human Genome Initiative Working Group, and the chairperson of the NIH Program Advisory Committee's ethics working group will attend the next meeting of the European Community's Study Group on Ethics.

In the past year, I have travelled to England, Italy, France and the Soviet Union to confer with scientists working on human genome research. In addition to representatives of these countries, officials from Japan, Belgium, Denmark and the Federal Republic of Germany have visited my staff to get information about our programs. All parties unanimously endorse the concept of cooperation and are eager to work together. From the start of the Human Genome Program, we have made it a policy that genome related meetings and workshops conducted or planned by the NIH will include international representation.

How to ensure that nations work together instead of indulging in costly competitive races for the same chromosomal objectives will be a challenge. Open communication, sharing of basic scientific data and collaborative efforts are probably the most productive methods for preventing duplication of research efforts and costly international competitions. A number of prominent international molecular biologists and human geneticists have banded together to form "The Human Genome

Organization" (HUGO). This organization is in the process of being formally established. We support the role of HUGO as the principal international coordinating group for human genome research. HUGO could greatly facilitate the free and open exchanges of data that we all want to be features of the Human Genome Program. Knowing the sequences of half of the human chromosomes without having access to the other half would be unbearably frustrating. Sharing of the human DNA database is much more likely to occur if large-scale mapping and sequencing efforts are undertaken by all the major industrial nations that want to use the data.

Another challenge for us is to strike the proper balance between the necessity for international scientific collaboration and the need to promote the United States' competitive position in biotechnology. We do know that science cannot and will not advance when basic scientific data is shrouded in secrecy. By fully involving the U.S. industrial sector in the genome program from the very beginning we hope to ensure that these companies are in the best possible competitive position. The U.S. biotechnology industry is strong and leads the world in this field. There is every reason to think that they will meet the challenges facing them successfully.

Mr. chairman, I am very excited by the prospects for the Human Genome Project. I am gratified by how much has already been accomplished both scientifically and in terms of

international cooperation, and I am optimistic that we will be successful in carrying this project to completion.

I would be pleased to answer any questions that you or Members of the Subcommittee may have about the Human Genome Program.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health

Memorandum

Date October 17, 1989

From Program Analyst, Division of Legislative Analysis, OSPL

Subject Final Testimony for Hearing on the Role of International Cooperation in Mapping the Human Genome

To See Below

Attached for your information is the final testimony for the hearing on the role of international cooperation in mapping the human genome, to be held on Thursday, October 19, 1989. Dr. James D. Watson, Director of the National Center for Human Genome Research will testify before the House Science, Space, and Technology Subcommittee on International Scientific Cooperation [chaired by Ralph M. Hall (D-Tex.)]. Also attached is the Subcommitte press release on the hearing.

Thank you for your previous comments on this testimony.

Kristin Olsen Kiser

Kristin Olsen Kiser

Attachments

Addressees:
Dr. Moskowitz
OD Staff
BID Legislative Contacts
DLA Staff

COMMITTEE ON SCIENCE, SPACE AND TECHNOLOGY
U.S. HOUSE OF REPRESENTATIVES
WASHINGTON, D.C. 20515

SUBCOMMITTEE ON INTERNATIONAL SCIENTIFIC COOPERATION

Hearing on "The Role of International Cooperation in Mapping the Human Genome"

Thursday, October 19, 1989
9:00 a.m. - 10:30 a.m.
Room 2325, Rayburn House Office Building

Witness List

Dr. James D. Watson
Director, National Center for
Human Genome Research
National Institutes of Health
Bethesda, Maryland

Dr. Robert O. Hunter, Jr.
Director, Office of Energy Research
Department of Energy
Washington, D.C.

Dr. George F. Cahill, Jr.
Treasurer of the Human Genome
Organization (HUGO) and Special
Assistant to the President
Howard Hughes Medical Institute
Bethesda, Maryland

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0204

NEWS from:
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
U.S. House of Representatives

Robert A. Roe, Chairman

Robert S. Walker
Ranking Republican Member

#101-111
October 17, 1989
For Immediate Release

ISC SUBCOMMITTEE TO HOLD HEARING ON THE ROLE OF INTERNATIONAL COOPERATION IN MAPPING THE HUMAN GENOME

Congressman Ralph M. Hall (D-TX), Chairman of the Subcommittee on International Scientific Cooperation (ISC), announced today that the Subcommittee has scheduled a hearing on "The Role of International Cooperation in Mapping the Human Genome." The hearing will be held on Thursday, October 19, 1989 at 9:00 a.m. in Room 2325 of the Rayburn House Office Building. The hearing will focus on: the status of international efforts in mapping the genome; the appropriate level of international involvement and financial "burden sharing" in the mapping effort; and the implications of international cooperation on U.S. scientific and industrial competitiveness.

The Subcommittee will receive testimony from Dr. James Watson for the National Institutes of Health (NIH) and Dr. Robert Hunter, Jr. for the Department of Energy (DOE). Dr. Watson received a Nobel Prize for his work as the co-discoverer of DNA and is the Director of the National Center for Human Genome Research at NIH. Dr. Hunter is the Director of Energy Research at DOE and oversees the DOE laboratories performing genome-related research. The Subcommittee will also receive testimony from Dr. George Cahill, Jr., Treasurer of the Human Genome Organization (HUGO), a non-profit organization which was recently formed to promote international cooperation in mapping the human genome.

The ISC subcommittee has been actively involved in the "big science" projects before the Congress, such as the Superconducting Super Collider and the Space Station, which require balancing the need for international cooperation and resources with competitiveness and technology transfer concerns. The hearing on international cooperation in mapping the human genome represents a continuation of the ISC efforts to develop a technology policy which strikes a balance between these needs.

Congressman Hall commented, "It is important for the U.S. to make sure that the basic research effort required to develop a map of the human genome is shared equitably among our international scientific partners. At the same time, the nation that leads in applications resulting from a human genome map will have an international competitive advantage in pharmaceutical, biotechnology and related industries. The challenge facing the U.S. is to balance the need for international scientific cooperation in basic research, while ensuring the ability of U.S. industry to compete in applications."

The Subcommittee's Ranking Republican Member, Congressman Ron Packard (R-CA) said, "The human genome represents the complete set of instructions for making a human being. A complete map could lead to new pharmaceutical products or treatments for genetic diseases with worldwide applications, such as Alzheimer's, sickle-cell anemia, cystic fibrosis, muscular dystrophy, heart disease and cancer, among others. Mapping the human genome will be a massive scientific effort which will require the talents and resources of the international scientific community."

Congressman Robert A. Roe (D-NJ) is the Chairman of the Committee on Science, Space and Technology, and Congressman Robert S. Walker (R-PA) is the Committee's Ranking Republican Member.

Staff Contacts: Chuck McElyea or Robert Palmer (202) 226-3636
Catherine Rawlings (202) 226-3641

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COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
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Staff Contacts: Chuck McElyea or Robert Palmer [redacted]
Catherine Rawlings [redacted]

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COMMITTEE ON SCIENCE, SPACE AND TECHNOLOGY
U.S. HOUSE OF REPRESENTATIVES
WASHINGTON, D.C. 20515

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Assistant to the President
Howard Hughes Medical Institute
Bethesda, Maryland

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Department of Energy
Washington, DC 20585

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Room 8E-070, Forrestal Building

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TO: Pam LoKKeN Telephone: [redacted] 413

This transmittal consists of 6 pages, excluding this cover sheet.

FROM: Bev Gaines Telephone: 586-4697 Verification
CR20

Date: 10/16 Time: 1:05

UNCLASSIFIED ONLY

Pam,
Here is cy of DOE's 10/19 test for HSS&T. We have not commented DOE's written ans

Mr. Chairman and Members of the Subcommittee:

I am pleased to be here today to discuss the international aspects of the Department of Energy's Human Genome Program. The Human Genome Program is consistent with the Department of Energy's (DOE) traditional missions to evaluate the health effects of energy-related agents and to utilize DOE resources for beneficial applications in biology and medicine. The Program represents a new approach, based on modern biology and technology, to the mission of evaluating the potential effects of low doses of radiation and chemicals on human populations. The knowledge gained from human genome research will greatly enhance understanding of the molecular basis of genetic diseases, cancer, immune deficiencies, and individual susceptibilities and resistance to environmentally induced diseases. The Program is a direct outgrowth of four decades of DOE research, utilizing the unique capabilities of the national laboratories. The aim of this focused program is to develop the resources and technologies that will lead to a complete description of the human genome at the molecular level. My statement will summarize our national activities and focus on the relatively new or planned human genome research around the world.

<u>On The National Scene</u>

DOE and the National Institutes of Health (NIH) are the only two Federal agencies with formal human genome programs. The DOE and NIH programs are coordinated under the umbrella of a Memorandum of Understanding (MOU). DOE, with a budget of $27.6 million in fiscal year 1990 for the Human Genome Program, is emphasizing the construction of physical maps of each of the 24 different human chromosomes; development of the computational tools needed to

enter, retrieve and analyze mapping and sequencing data in large databases; and development of new, innovative concepts and technologies for mapping and sequencing, and for rapid, cost-effective analysis of DNA base sequences. Postdoctoral training in all aspects of human genome research is also supported.

The Department is aggressively pursuing the involvement of American industry in the genome program. Interactions that are developing between industry and the national laboratories, where the major part of the DOE effort is centered, are expected to facilitate the ultimate commercialization of innovative technologies. An example is the formal cooperative effort between industry and the Los Alamos National Laboratory Human Genome Center for shared funding and staffing of research related to computational sciences and instrumentation development.

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DOE and NIH, with the assistance of their respective advisory committees, are developing a national plan for the human genome program with DOE and NIH components. The plan will be submitted to appropriate Congressional committees in February 1990.

In addition, the Department is represented on the Genome Subcommittee of the Committee for Life Sciences of the Office of Science and Technology Policy Federal Coordinating Council for Science, Engineering and Technology (FCCSET). The National Science Foundation and the United States Department of Agriculture are also represented. Although they do not have human genome programs, they are developing plant genome initiatives.

On The International Scene

Foreign scientists and governments have voiced interest in establishing human genome programs, and there is research underway in a number of countries. However, few countries have funded a major effort, and, at this point, genome research activities are not formally coordinated on an international level. The Department's program office is sensitive to these situations and interacts on an informal basis with scientists and administrators concerned with human genome interests and efforts from around the world. The Department has supported meetings and workshops to which foreign scientists have been invited, and American scientists have been invited to meetings in other countries, as well. DNA sequence information is freely and regularly exchanged between our GenBank database at the Los Alamos National Laboratory, and the European and Japanese DNA sequence databases. Research results from laboratories in the free world are shared through publications in the open scientific literature. We will be closely following the development of human genome research around the world and will pursue more formal cooperation at an appropriate time.

The Japanese, Europeans and the Soviets are beginning to support human genome related research. Although Japan does not yet have a coordinated human genome project, there are efforts underway to assemble a massive DNA sequencing ability, largely through the support of industrial interests.

The European Economic Community (EEC) is launching a $17 million program over three years to increase cooperation among national genome research projects in the 12 member states. At this time, these projects are small and carried out independently. The EEC is planning to integrate European efforts into any future collaborations with U.S. scientists.

In addition to the EEC program, several European countries are discussing plans to initiate their own large-scale projects. The Italian effort, which is in the planning stage, is expected to have a budget of approximately $5 million over five years. The United Kingdom is beginning a program at a level of about $15 million over three years. In France, a new genome program is also in the planning stage.

The USSR has a 1989 genome budget in international currency equivalent to about $1 million, in addition to 25 million rubles for internal use. The Soviets plan to organize centers for DNA cloning, mapping and sequencing. We understand that the Peoples Republic of China is debating whether or not it should attempt a small entry into the human genome arena. The United Nations Educational, Scientific and Cultural Organization has allotted $0.5 million in support of genome-related activities, but these are for the most part not research oriented.

Probably the most visible organization involved with international aspects of human genome research is the Human Genome Organization (HUGO). It was conceived in 1988 to assist with coordination of national efforts; facilitate exchanges of research resources; encourage public debate; and provide information and advice on the implications of human genome research. It is incorporated in Switzerland, independent of any government, and is seeking support on an international level. Following a model based on the U.S. National Academy of Sciences, new members are elected from among participants in genome research. Its 42 founding members represented 17 countries and included 3 scientists who are funded by our genome program. In 1989, an additional 178 members, including 12 participants in DOE-funded genome projects, were elected. The Department will continue to closely follow HUGO's activities.

In summary, the Department's Human Genome Program is a well-coordinated, focused program of research and development activities with clearly defined goals and objectives. We are coordinating our work with other Federal agencies with similar and complementary interests, and are also informally interacting with foreign scientists and science administrators as their various countries begin to put their human genome efforts in place.

This concludes my prepared testimony. I would be happy to answer your questions.

Committee on Rules (H-312), 5-9486—CONTINUED
Staff Director.—Leo Coco.
Minority Counsel.—Don Wolfensberger (421 CHOB), 5-7985.
Staff.—Michael Harrison (1629 LHOB), 5-1037.

Science, Space, and Technology (full committee)

(2321 RHOB, phone 5-6371; FAX: 5-8280, meets first and third Tuesdays of each month)

chairman:

~~Robert A. Roe, of New Jersey.~~
George E. Brown, Jr., of California.
James H. Scheuer, of New York.
Marilyn Lloyd, of Tennessee.
Doug Walgren, of Pennsylvania.
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Harold L. Volkmer, of Missouri.
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Jack Buechner, of Missouri.
Constance A. Morella, of Maryland.
Christopher Shays, of Connecticut.
Dana Rohrabacher, of California.
Steven Schiff, of New Mexico.
Tom Campbell, of California.

SUBCOMMITTEES

[The chairman and the ranking minority member are ex officio members, with vote, on all subcommittees]

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Lee H. Hamilton, of Indiana.
George E. Brown, Jr., of California.
James H. Scheuer, of New York.

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SCIENCE, RESEARCH AND TECHNOLOGY

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TESTIMONY TO

SUBCOMMITTEE ON INTERNATIONAL SCIENTIFIC COOPERATION

OF THE

COMMITTEE ON SCIENCE, SPACE AND TECHNOLOGY

U.S. HOUSE OF REPRESENTATIVES

HUMAN GENOME ORGANIZATION (HUGO)

George F. Cahill, Jr., M.D. (testifying)
HUGO Treasurer

The history of HUGO is a short one: the suggestion of an international coordinating organization was raised at a Cold Spring Harbor meeting on the genome in late April, 1988 - by Sydney Brenner of Cambridge University, who also suggested the name Human Genome Organization and the acronym HUGO. At a rump session held in Cold Spring Harbor on April 30, 1988, Dr. Victor A. McKusick of Johns Hopkins and probably the most distinguished clinical geneticist in the United States, if not the world, was asked to convene an international group to consider the proposal in more detail. A founding council of 42 members was convened in Montreux, Switzerland, in early September 1988; 31 of the members were present. The meeting was largely supported by the Howard Hughes Medical Institute. The broad outline for Articles of Incorporation and Bylaws was laid out and the following officers were elected: President, Victor McKusick; Vice Presidents, Walter Bodmer, Jean Dausset, and Kenichi Matsubara; Secretary, John Tooze; Treasurer, Walter Gilbert (resigned February, 1989; replaced by George Cahill, June 1989); others on the executive council, Charles Cantor, Malcolm Ferguson-Smith, Leroy Hood, Lennart Philipson, and Frank Ruddle. Of the aforementioned, McKusick, Gilbert, Cahill, Cantor, Hood and Ruddle are Americans; Bodmer, Tooze and Ferguson-Smith are British; Dausset, French; Matsubara, Japanese; and Philipson a Swede working in Heidelberg, Germany as Director of the European Molecular Biology Laboratory. By secret ballot of the 219 members, prior to September 15, 1989, Francis Collins, an American; Sydney Brenner, Kay Davis and Ed Southern, all three British; Andrei Mirzabekov of the USSR and Jean-Louis Mandel of France were elected. This Council of 15 will elect three more members prior to the scheduled meeting of the full Council on December 2 and 3, 1989, in Bethesda.

Presently, HUGO is organized and incorporated in Geneva, Switzerland, (to emphasize is international character) and will soon also be incorporated in the State of Delaware (to satisfy grantors in the U.S.) It has an elected membership of about 150 distinguished scientists representing 23 countries. Its affairs will be run by the Council of 18 members from which the president and 3 vice presidents of HUGO are elected. HUGO has taken steps to establish offices in Bethesda, Maryland, London, and Osaka. The establishment of an office in Moscow is also under discussion.

At its meeting in Montreux, the HUGO Founding Council decided to follow an "academy model" in setting up HUGO. By this it is meant that it will have a membership elected on

merit. In the conduct of the work of HUGO, it is understood that some persons will be co-opted to the several committees who are themselves not members of HUGO. In this respect, the organization will follow the well-known practice of similar academies in setting up work parties.

The Human Genome Organization (HUGO) was conceived and established with the general purpose of promoting international collaboration in the human genome initiative. The purposes as stated in its Charter are as follows:

a. To assist with the coordination of research on the human genome and in particular to foster collaboration between scientists with a view toward avoiding unnecessary competition or duplication of effort; to coordinate this research with parallel studies in model organisms;

b. To coordinate and facilitate the exchange of data and biomaterials relevant to human genome research and through a training program, to encourage spreading of the related technologies;

c. To encourage public debate and provide information and to advise on the scientific, ethical, societal, legal and commercial implications of human genome projects.

To carry on the work of HUGO in specific areas, five committees have been established:

a) The Human Gene Mapping Committee. This Committee is an outgrowth of the Human Gene Mapping Workshops that have been occurring, on an international basis, since 1973. These provide a valuable background for the entire human genome initiative and a model of a chromosome-by-chromosome strategy in organizing the work.

b) The Mouse Mapping Committee. The study of model organisms, especially those in which a great deal of genetic information already exists, such as the mouse, is seen as highly valuable to the human genome initiative. Through its sponsorship of this mouse gene mapping committee, HUGO will play a major role in coordinating the studies in the human and the mouse.

c) The Physical Mapping Committee. This committee will concern itself with questions such as the desirability of creating various types of libraries of cloned DNA segments from specific chromosomes and the mechanisms for making these generally available.

d) The Data Base Committee. This committee potentially will have the most important role in coordinating the entire international effort. The data, i.e., the map information and the sequence itself, are not only the main product of the human genome initiative, but the sequence data, according to the strategy laid out by Olson, Cantor, Hood and Botstein, would provide the basis for the entire mapping and sequencing. [STS method (STS = sequence tagged sites.) Science, Sept. 29, 1989]

e) Committee on Ethical, Societal, Legal and Commercial Issues.

The concept of HUGO appears to be accepted worldwide with enthusiasm by scientists because they recognize the need for a coordinating body of this type. This enthusiasm is reflected by the fact that there are already realistic possibilities of financial support from the governments of at least 3 countries: Italy, Canada, and Australia.

HUGO was, from the beginning, set up consciously on the pattern of EMBO (European Molecular Biology Organization), which was first established in the mid 60s, initially with private funding from the Volkswagen Foundation and Interpharma (a pharmaceutical consortium). It then went to predominantly, although not exclusively, a multinational governmental funding; 17 nations now contribute to the support of EMBO. The funding of HUGO to this point has been exclusively from non-governmental sources, although multinational governmental support appears promising in the near future.

The support of HUGO has come so far predominantly from the Howard Hughes Medical Institute, the Lucille P. Markey Charitable Trust and the Wesley Foundation, all of these being U.S. institutions, and also from the Imperial Cancer Research Fund in the UK. The level of funding has been modest, approximating $100,000 to date.

HUGO was not conceived as a grant-giving organization to pass-through funds for conducting basic research. HUGO is seen as an organization for coordinating the basic research taking place in each country and funded predominantly by that country. For example, the work effort may be organized on a chromosome-by-chromosome basis. There may be several laboratories working on the same chromosome or chromosome arm and these laboratories may be located anywhere in the world. One laboratory, however, under the aegis of HUGO, will take the lead in collating the information as it is developed. Seeing that the job gets finished in a scientifically acceptable manner is one very important role for HUGO.

Regarding data sharing, existence of chromosome-by-chromosome consortia will tend to discourage, at the grass roots level, most data restrictions. Clearly, to be a recognized member of the consortium, free exchange of data with those working in the same area of the genome will be a condition of membership. At this time, the sequence data do not seem patentable or copyrightable. The data do not themselves represent intellectual property. The discovery of the significance of the particular sequences, e.g., discovery of their function with characterization of important endogenous molecules that may have growth factor, psychotropic or other pharmaceutical usefulness will, be a spin-off from the genome project that could be, and perhaps should be, patentable. HUGO will assist in examining these new legal issues.

The regional offices will eventually become the mechanisms for the collection and distribution of data through networking. The offices will be expected to maintain information on the characteristics and availability of biomaterials and technology, thus promoting the major coordinating functions.

Currently, HUGO coordinates its efforts with those of the Department of Energy through Charles Cantor as a member of the HUGO Council. Several members of the HUGO Council, including Lee Hood and McKusick, are members of the Advisory Committee to the Center on Human Genome Research of the NIH. The HUGO Council has among its present 15 members, the 5 leading figures in the UK effort (including Bodmer and Brenner), and the leader of the effort in Japan (Kenichi Matsubara) and the genome leaders in every other country who are represented either on the Council or in the Membership. By its By-laws, one third of the Council (six members) will be elected annually, four by the Members and two by the Council in order to keep a broad geographic representation.

The cost of the Human Genome Mapping Project has been placed at approximately 200 million dollars a year for about 15 years. Some would say there are other related costs of the Project, especially in the area of ethics. However, the techniques and technology developed for the complete mapping and sequencing of the human genome will also create immense financial benefit when applied to economic plants and animals and to pathogenic organisms, yet alone to improving human health and curing disease. It has been said that this effort will provide the foundation of all biological science for the next century.

The estimate of 10 to 15 years for complete mapping and sequencing the human genome was predicated on the existence of international cooperation although the cost (200 million

dollars a year) was estimated exclusively on the US effort. It is difficult to estimate the amount of time necessary to sequence the human genome without international cooperation. It is totally inconceivable that such an activity would be done without an open, active, and coordinated international effort. The human genome belongs to the entire human race.

Additionally, international cooperation is essential to getting the work done. It would certainly be more expensive and would take longer to map the human genome if it were to be done as an isolationist activity of the US. Duplication of effort would undoubtedly result because significant programs are already underway in the UK and Japan, for example. The human genome initiative is not purely a technologic venture, particularly during this time. For this science to proceed with anything short of complete international cooperation would do major damage to science in general. There is another major point, overlooked in most discussions. Americans are hybrids, by and large, of numerous and diverse genetic backgrounds. Knowledge of genomes in founding cultures is crucial to our own well-being, a somewhat selfish but scientifically sound fact. International cooperation is crucial for Americans as well as the rest of mankind.

A main societal issue raised by the Human Genome Initiative and its results is the fact that the gap will be widened between what we know and what we can do about it. The dilemma presented by Huntington's disease, for example, will be magnified and distributed over many disorders and predispositions. The issues relate to the potential misuse of genome information by employers in the work place, by insurers, in the military service or in schools, etc. HUGO is participating in, and plans to sponsor in the future, conferences that address these issues at the international level, with cross-cultural considerations. HUGO met jointly with UNESCO in Paris in February 1989 and in Moscow in June 1989 to discuss societal and ethical issues raised by the Human Genome Initiative, with particular reference to developing countries. HUGO also just co-sponsored with Science Magazine, a highly successful international conference, Human Genome I, held in San Diego October 2-4, 1989. At this conference, some of the ethical issues were raised, even though the thrust of the meeting was on biological and technological advances.

In summary, as stated many times, the mapping and sequencing of the human genome will serve as both the dictionary and encyclopedia for all biology on this planet for decades to come. This effort is about and, therefore, involves all humankind. To be truly successful,

the project must also be an expedient, efficient, and complete one. This may only occur through enthusiastic international cooperation, coordination, and collaboration. HUGO could provide both the leadership and inspiration to nurture worldwide activities that help us realize our greatest scientific achievements.

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United States Senate

COMMITTEE ON COMMERCE, SCIENCE,
AND TRANSPORTATION

WASHINGTON, DC 20510-6125

October 25, 1989

Dr. James D. Watson
Director
Center for Human Genome Research
National Institutes of Health
Department of Health and Human Services
9000 Rockville Pike
Bethesda, MD 20205

Dear Dr. Watson:

The Senate Subcommittee on Science, Technology, and Space would appreciate your testimony at a hearing on the human genome initiative. Senator Albert Gore, Jr. will chair the hearing on Thursday, November 9, 1989, at 10:00 a.m. in Room 253 of the Russell Senate Office Building.

The hearing will examine the human genome initiative and the benefits it may provide. In September, the Subcommittee held two hearings on national science and technology policy where the setting of research priorities was a central theme, and at this hearing the [redacted]Subcommittee hopes to discuss how high a priority the human genome initiative should be. We would like you, as director of the NIH human genome initiative, to describe the human genome initiative, outline the goals of the NIH program, and summarize its accomplishments to date. We are also interested in the technology that may result from this program and the possible applications of that technology in the future.

Enclosed, you will find a copy of the Rules of Procedure for Witnesses for the hearing. Please note that you will be asked to summarize the main points of your testimony. Your written statement in its entirety will be printed in the record.

If you have any questions regarding the hearing, please contact Mike Nelson of the Majority Staff at [redacted] or Fiona Branton of the Minority Staff at [redacted]. We very much appreciate your efforts to provide this important information to the Committee and the Senate.

Sincerely,

ALBERT GORE, JR.
[redacted]hairman
Subcommittee on Science,
Technology, and Space

ERNEST F. HOLLINGS
Chairman
Committee on Commerce,
Science, and Transportation

U.S. SENATE COMMITTEE ON COMMERCE, SCIENCE, AND TRANSPORTATION

RULES OF PROCEDURE FOR WITNESSES

In order to ensure that Committee hearings are run as efficiently as possible, and to ensure also that witnesses are given equitable treatment in delivering their testimony, the following rules for witnesses have been determined. Please review them carefully.

1. The Commerce Committee requires sixty-five (65) copies of testimony from each witness. Testimony shall be submitted as follows:

   Not less than ~~five (5)~~ three (3) working days before the hearing, fifteen (15) copies of your prepared testimony shall be delivered to the Commerce Committee, SD-508 Dirksen Senate Office Building, Washington, D.C. 20510. Ten (10) copies shall be marked to the attention of the Majority staff person responsible for the hearing and five (5) copies shall be marked to the attention of the Minority staff person responsible for the hearing.

   In addition, two (2) copies of a one or two page summary of the testimony shall be submitted for the Chairman and the Ranking Minority Member, marked to the attention of the Majority and Minority staff persons.

   Twenty-four (24) hours before the start of the hearing, an additional fifty (50) copies of your full testimony shall be delivered to the Hearing Clerk, SR-254 Russell Senate Office Building, for distribution to the Members of the Committee, the press, and the public.

2. Oral Testimony on the day of the hearing:

   Witnesses (both individual and panel members) will be permitted five (5) minutes to summarize their main points. Their written testimony shall be submitted in its entirety and printed in the record. When possible and appropriate, panels of witnesses having common interests will testify together.

Exceptions to any of the above rules may be made by the Chairman, or the presiding Committee Member, when deemed necessary and appropriate.

U.S. HOUSE OF REPRESENTATIVES

COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY

SUITE 2321 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515
(202) 225-6371

October 6, 1989

Dr. James D. Watson
Associate Director for Human Genome Research
National Institutes of Health
Room 201, Building #1
9000 Rockville Pike
Bethesda, Maryland 20892

Dear Dr. Watson:

The Subcommittee on International Scientific Cooperation of the Committee on Science, Space, and Technology has scheduled a hearing on Thursday, October 19, 1989 to review plans for international cooperation in mapping the Human Genome. I am pleased to invite you to testify at the October 19th hearing, which will begin at ~~9:30~~ 9:00 a.m. in Room 2325 of the Rayburn House Office Building.

The Subcommittee hearing will examine several areas with regard to the Human Genome mapping project. These will include: 1) the status of international efforts to map the Human Genome, 2) the appropriate level of international involvement and financial "burden-sharing" in the mapping effort, and 3) the implications of international cooperation on the U.S. scientific and industrial competitiveness.

Testimony from the hearing will be used to assess the need for new policies to promote international cooperation in mapping the Human Genome, while ensuring the ability of U.S. industry to compete effectively in the fields of biotechnology, pharmaceutical development and equipment manufacture.

In this regard, we would ask that, during your testimony, you address the following questions:

1. What are the potential benefits and costs of the Human Genome mapping project?

2. What is the status of Human Genome mapping activities outside the U.S.? What is the level of these activities in comparison to U.S. activities? What are current plans for joint international cooperation to map the Human Genome? Will the Human Genome be divided up internationally to reduce duplication of efforts?

3. How long will it take to sequence the Human Genome with international cooperation?, without international cooperation?

4. Does the U.S. have adequate resources to complete the project alone? Where do we need international cooperation? What is the status of international cooperation?

5. How do we assure that all countries involved will assume a fair share of the basic research underlying the Genome mapping effort (i.e., will the U.S. pay for the entire effort, while the rest of the world benefits?) Will NIH funds be used to support international efforts?

6. What current private sector resources are being directed toward the Genome mapping effort? Are these resources adequate? How will technology or information be transferred to the private sector as the Genome is mapped?

7. How are competitive concerns such as sequencing technology, equal access to data and intellectual property protection being addressed? Will there be any data restrictions for "foreign" researchers? Will these restrictions impact international cooperation?

8. What are the social and ethical issues which will be raised by the Genome mapping effort and how will they be addressed at an international level?

9. How is the National Institutes of Health's Genome mapping effort being coordinated with efforts at the Department of Energy?

10. Do you see any need for legislation aimed at increasing international cooperation, ensuring U.S. competitiveness, or addressing ethical issues?

Your written statement may be of any length and will be included in its entirety in the published hearing record. You also may be asked during the hearing to respond to additional written questions for inclusion in the record.

Please be advised that under Committee rules, the proceedings of the hearing will be printed strictly in verbatim form. The testimony will be published as delivered: only typographical and transcriptional errors will be edited in the transcript.

In preparation for the hearing, thirty copies of your prepared statement should be forwarded to the Subcommittee on International Scientific Cooperation, Room 822, House Annex #1, Washington, D.C. 20515, at least 48 hours before the hearing. In addition, fifty copies should be delivered to Room 2325 at least thirty minutes before the hearing for distribution to the public and the press.

If you have any questions, please do not hesitate to contact Bob Palmer or Chuck McElyea, at [redacted].

Sincerely,

Ralph M. Hall

RALPH M. HALL, Chairman
Subcommittee on International
Scientific Cooperation

Questions for NIH

1. What are the potential benefits and costs of the Human Genome mapping project?

2. What is the status of Human Genome mapping activities outside the U.S.? What is the level of these activities in comparison to U.S. activities? What are current plans for joint international cooperation to map the Human Genome? Will the Human Genome be divided up internationally to reduce duplication of efforts?

3. How long will it take to sequence the Human Genome with international cooperation?, without international cooperation?

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7. How are competitive concerns such as sequencing technology, equal access to data and intellectual property protection being addressed? Will there be any data restrictions for "foreign" researchers? Will these restrictions impact international cooperation?

8. What are the social and ethical issues which will be raised by the Genome mapping effort and how will they be addressed at an international level?

9. How is the National Institutes of Health's Genome mapping effort being coordinated with efforts at the Department of Energy?

10. Do you see any need for legislation aimed at increasing international cooperation, ensuring U.S. competitiveness, or addressing ethical issues?

Questions for DOE

1. What are the potential benefits and costs of the Human Genome mapping project? What are the potential non-human spinoffs of the techniques and technology being developed?

2. How long will it take to sequence the Human Genome with international cooperation?, without international cooperation?

3. What is the status of Human Genome mapping activities outside the U.S.? What is the level of these activities in comparison to U.S. activities?

4. Does the U.S. have adequate resources to complete the project alone? Where do we need international cooperation? Will limiting international cooperation improve U.S. competitiveness in the biotechnology and pharmaceutical industry?

5. How are competitive concerns such as sequencing technology, equal access to [foreign] data and intellectual property protection being addressed? How will the DOE laboratories involved in the mapping effort transfer technology to U.S. companies? Will there be any data restrictions for "foreign" researchers? Will these restriction impact international cooperation?

6. How do we assure that all countries involved will assume a fair share of the basic research underlying the Genome mapping effort (i.e., will the U.S. pay for the entire effort, while the rest of the world benefits?) Will DOE funds be used to support international efforts?

7. What current private sector resources are being directed toward the Genome mapping effort? Are these resources adequate?

8. What are the social and ethical issues which will be raised by the Genome mapping effort and how will they be addressed at an international level?

9. How is the Department of Energy's Genome mapping effort being coordinated with efforts at the National Institutes of Health?

10. Do you see any need for legislation aimed at increasing international cooperation, ensuring U.S. competitiveness, or addressing ethical issues?

Committee on Science, Space, and Technology

2321 Rayburn House Office Building, Washington, DC 20515 (202) **225-6371**

Jurisdiction: (1) Astronautical research and development, including resources, personnel, equipment and facilities; (2) Bureau of Standards, standardization of weights and measures and the metric system; (3) National Aeronautics and Space Administration; (4) National Aeronautics and Space Council; (5) National Science Foundation; (6) Outer space, including exploration and control thereof; (7) Science scholarships; (8) Scientific research, development, and demonstration, and projects therefor, and all federally owned or operated nonmilitary energy laboratories; (9) Civil aviation research and development; (10) Environmental research and development; (11) All energy research, development, and demonstration, and projects therefor, and all federally owned or operated nonmilitary energy laboratories; (12) National Weather Service. In addition to its legislative jurisdiction under the preceding provisions of this paragraph (and its general oversight function under clause 2(b)(1) of House Rule X), the committee shall have the special oversight function provided for in clause 3(f) with respect to all nonmilitary research and development.

Ratio: 30/19.

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SPACE SCIENCE AND APPLICATIONS
2324 Rayburn House Office Building
Washington, DC 20515
(202) 225-7858

Jurisdiction: Legislation, general and special oversight and all other matters relating to the National Aeronautics and Space Administration (except aeronautical research and technology); commercial space activities relating to the Department of Transportation and the Department of Commerce; outer space, including exploration and control thereof, space applications, space commercialization, space communications and related matters; and research and development of earth-observing systems.

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INTERNATIONAL SCIENTIFIC COOPERATION
822 House Office Building Annex I
Washington, DC 20515
(202) 226-3636

Jurisdiction: International scientific cooperation; international technology transfer; international cooperative R&D (including global change; space station; nuclear and non-nuclear energy, the superconducting super collider, and international cooperative funding therefore); international scientific and technological competitiveness; international information and communications policy (including scientific data banks, technical communications and translation, and SARSAT); resolutions of joint cooperation with other national parliamentary committees on science and technnology; international trade policy and its effect on science and technology and on R&D; international agriculture research policy (including the international implications of genetic engineering); and international intellectual property rights.

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Minority
Special Assistant Catherine O. Rawlings 225-3641
Staff Assistant Georgette Schaefer 225-8772

(continued on next page)

a b

Subcommittee Chairman

Congressional Quarterly

Ralph M. Hall (D) Texas - 4th District
Of Rockwall - Elected 1980

BIOGRAPHICAL DATA
(Prepared: July 1989)

Born: May 3, 1923, Rockwall County, Texas.
Education: Attended Texas Christian U., 1943; U. of Texas, 1946-47; Southern Methodist U., LL.B. 1951.
Military Career: Navy, 1942-45.
Occupation: Lawyer; businessman.
Family: Wife, Mary Ellen Murphy; three children.
Religion: Methodist.
Political Career: Rockwall County judge, 1950-62; Texas Senate, 1963-73; sought Democratic nomination for lieutenant governor, 1972.
Capitol Office: 236 Cannon Bldg. 20515; 225-6673.

IN WASHINGTON
(Prepared: July 1989)

Hall's conservative voting record is not the kind the Democratic leadership generally appreciates. But on Energy and Commerce, he is a favorite of Chairman John D. Dingell, even though the two do not always see eye-to-eye. Hall's folksy sense of humor and encyclopedic supply of rural Texas stories can defuse tense confrontations, and his political acumen gives him considerable influence when he decides to weigh in on an issue.

That is not to say that Hall is one of the committee's more active members. He makes no pretense of being a workaholic, but when issues important to the energy industry come up, Hall makes his presence felt.

When the committee debated nuclear-accident liability legislation in 1987, Hall offered an amendment to allow utility lawyers to get paid before victims if damage claims exceed the compensation fund. Success required the panel to reverse an earlier decision, but working with industry lobbyists, Hall chalked up a 22-20 win.

Hall also played a role in the committee's 1988 approval of a product liability bill, a longtime industry priority. One of Hall's pro-business amendments - to prohibit states from classifying as "environmental" any injuries that might otherwise fall under product liability - was backed by chemical manufacturers and condemned by consumer activists. Another, more popular, amendment aimed to limit "frivolous" lawsuits by plaintiffs and delaying tactics by defendants. Both proposals passed, though the bill died at the end of the 100th Congress.

Hall's prime interest, however, is oil and gas, and he is known as a shrewd advocate for decontrol. After years of bitter stalemate, Energy and Commerce passed a decontrol bill by voice vote in early 1989. "I wouldn't be more surprised to see my old dog Red sharing his food with the cats," he said of the

unanimity, "or the mockingbird not flying down to peck at the squirrels."

On the whole, Hall more often than not is at odds with his party. He tested the limits of his independence in 1985, when he voted "present" rather than support Thomas P. O'Neill Jr. for Speaker. He viewed with equanimity the possibility that the leadership might retaliate by removing him from Energy and Commerce. "I wouldn't blame them if they did," he said cheerfully. "I do what I have to do, and they do what they have to do."

AT HOME
(Prepared: July 1989)

An early starter in politics, Hall was elected judge in his home county while still in law school. After 12 years, he moved up to the state Senate and spent a decade there, rising to become president pro tem.

In 1972 Hall entered statewide politics, running for lieutenant governor on a conservative platform. But he finished fourth in the Democratic primary, retired from politics and concentrated on business.

When 4th District Democratic Rep. Ray Roberts announced his retirement in 1980, Hall decided to re-enter politics. His opponent in the primary was Jerdy Gary, the son of a former Oklahoma governor. Hall contrasted his Texas upbringing with Gary's Oklahoma roots, and won nomination with 57 percent.

Because of Ronald Reagan's popularity among the 4th's voters, Hall's November contest with Republican John H. Wright turned out to be closer than expected. Though Wright, a Tyler business manager, was well-known only in the eastern part of the district, Reagan's strong showing helped Wright pull 48 percent. But Republicans have not mounted a comparable challenge since. In 1988, he had his best presidential-year showing yet, winning two-thirds of the vote.

One way Hall heads off opposition is to make his feelings about national Democratic politics unmistakably clear; chosen as an uncommitted delegate to the Democratic convention in 1984, he opted not to go, commenting acerbically that he "didn't want to elbow some gay guy out of the way to get to a committee meeting."

WITNESS LIST

Tentative

Dr. James Watson
Director, National Center for Human Genome Research
National Institutes of Health

Dr. Robert Hunter
Director, Office of Energy Research
Department of Energy

Dr. George F. Cahill
Vice President, Scientific Training and Development
Howard Hughes Medical Institute
[Dr. Cahill is representing The Human Genome Organization (HUGO)]

FOR RELEASE ON DELIVERY

Testimony by

Dr. James D. Watson, Director
National Center for Human Genome Research

National Institutes of Health
Public Health Service
Department of Health and Human Services

On International Scientific Cooperation to Map and Sequence the Human Genome

Before the

Subcommittee on International Scientific Cooperation
Committee on Science, Space and Technology
United States House of Representatives

October 19, 1989

Mr. Chairman and Members of the Subcommittee:

Thank you for the opportunity to present testimony on NIH efforts to ensure effective international scientific cooperation in genome research and to explain the importance of mapping and sequencing the human genome.

At the National Institutes of Health, the Human Genome Program is being managed by the National Center for Human Genome Research, established officially on October 1, 1989. The Center evolved from the Office for Human Genome Research, a coordinating unit within the Office of the Director, NIH, in recognition of the growth of the program over the last two years and the high priority NIH places on mapping and sequencing the human genome. Overall advice and guidance to the Genome Program at the National Institutes of Health is provided by the Program Advisory Committee on the Human Genome. I am pleased to be able to testify for the first time as Director of the National Center for Human Genome Research.

The task of determining the human DNA sequence is now firmly established as a national objective. Similar to the 1961 decision made by President Kennedy to send a man to the moon, the United States has committed itself to a highly visible and important goal. We did not know if we could successfully reach the moon -- we already know it is possible to map and sequence the human genome. Though the final monies needed to completely

determine the sequence of the three billion chemical components of human DNA called base pairs are on an order of magnitude smaller than those needed to let Americans explore the moon, the impact of the Human Genome Program on human life is likely to be as great or greater. A more important set of instruction books will never be made available to human beings.

Gene mapping and analysis will be key tools of biology in the 21st century. When finally interpreted, the genetic messages encoded within our DNA molecules will provide the ultimate answers to the chemical underpinnings of human existence. They will not only explain how we function as healthy human beings, but also provide us with a new understanding of such widespread illnesses as heart disease, hypertension, certain cancers and diabetes, that touch the individual lives of so many millions of our citizens. Determining the location and structure of specific genes on the 23 pairs of human chromosomes is a major step toward discovering new methods to prevent or treat the 4,000 inherited diseases that are caused by single-gene defects, or the many more genetic defects that involve an inherited susceptibility to disease. The sooner the entire genome is mapped and sequenced, the sooner scientists can get on with the real work of human biology: understanding what the genes do.

Every gene is a unique fragment of DNA. These genes are strung along the 23 pairs of chromosomes present in every cell in the human body. Finding the location of individual genes on a chromosome and analyzing these genes down to their chemical

components is now possible on a large scale. The National Institutes of Health has supported most of the basic research that has brought us to this threshold, especially the phenomenal explosion of biologic knowledge emanating from the invention of recombinant DNA technology in the early 1970's. Because of the generous funding provided by Congress to the National Institutes of Health, the United States is clearly the leader in this field of research.

The possibility of knowing our complete set of genetic instructions seemed an unreachable scientific objective in 1953 when Francis Crick and I discovered the helical structure of DNA. Then, there existed no way to determine the sequence (i.e., the precise structural composition) of even very short DNA molecules, much less the totality of human DNA. New techniques derived from recombinant DNA technology have made it possible to isolate individual genes. Researchers can chop up DNA at identifiable points that act as landmarks, mix and match pieces of DNA in various organisms, grow unlimited quantities of these fragments in bacteria, and take DNA apart and put it back together again. They have learned to make DNA from laboratory chemicals and to note its tiniest variations. Scientists also have learned to "sequence" DNA, that is, determine the order in which the four chemical components, called A, T, C and G occur. Breakthroughs in recombinant DNA technology allowed Walter Gilbert and Fred Sanger to develop their powerful sequencing techniques -- for which they won the Nobel Prize in 1980 -- that now make the

sequencing of short stretches of DNA a routine laboratory procedure. Technology is still inadequate for the sequencing of long stretches of DNA.

Mapping and Sequencing of Model Organisms

The sequencing of the genomes of relatively simple organisms such as bacteria and yeasts are intended to go hand-in-hand with, if not ahead of, that of the human genome. Experience has shown that information derived from studies of the biology of model organisms is a critical key in understanding and interpreting human biology. Knowledge of the simpler structures of the genes of bacteria and budding yeasts can facilitate the task of distinguishing the DNA sequences that actually carry a gene's instructions (exons) from the much more prevalent noncoding (intron) components whose functions are not fully understood. The sequences of a large number of individual genes in model systems and in the human are already complete, with the total number of base pairs sequenced approaching 25 million. However, this number pales by comparison with the 3 billion base pairs in human DNA.

The best understood organism to date is the intensively studied bacterium Escherichia coli (or E. coli), with over 800,000 base pairs out of a total of 4.7 million in its genome already established. There are a number of labs in both the United States and Japan that are working to complete the E. coli sequence. We have good reasons for believing that success will

come within the next decade. The mere statement that how E. coli functions will one day be completely known is an extraordinary scientific assertion. The sequencing of the yeast genome would be an even more dramatic achievement.

Elucidation of the genomes of multicellular organisms like Caenorhabditis elegans, or C. elegans (a simple round worm of 100 million bases), and Drosophila (the fruit fly with 150 million bases) are equally important scientific landmarks. Their much more complex genomes provide the instructions for the extraordinary set of events that allow fertilized eggs to develop into functional adults. Both the C. elegans and Drosophila scientific communities are starting to make plans for deciphering the DNA messages of their respective organisms.

The main mappers of C. elegans are planning to start pilot sequencing efforts that they hope will bring the cost down quickly to less than $1 per base pair. The NIH Program Advisory Committee on the Human Genome unanimously endorsed the concept of a collaborative United States/United Kingdom pilot project, co-funded by the NIH and the Medical Research Council of the U.K., for sequencing the entire genome of C. elegans, with the goal of establishing the total C. elegans genome by the year 2000. We anticipate that applications for this project will be submitted this fall. The Drosophila community will probably propose a project with a similar timetable. Here again, it would be advantageous if the final sequencing effort could be shared between Europe and the United States, as these nation's

scientists are the primary researchers working on these model organisms.

Mapping and Sequencing the Human Genome

The human genome, which is almost 1000 times larger than that of E. coli and is distributed over 23 pairs of chromosomes, is a much more formidable objective. Here, the approach of coordinating small groups of individuals working at a large number of different sites is unlikely to be sufficient, unless there are dramatic changes in technology. The time involved in completing the human genome would more than exceed the lifetimes of those working in this area.

Therefore, we must design a strategy where economies of scale are sought and found. In order to do this, we need to establish research centers where groups of 15-20 individuals from many disciplines can pool their talents. These research centers must become the foci for collaboration with other investigators, for sharing and distribution of materials, and for data collection on an international scale.

The National Center for Human Genome Research has announced its plan to establish such research centers at academic and industrial sites, with three centers planned for fiscal year 1990. Additional centers are planned to be initiated in subsequent years. Some of these centers will focus on sequencing the genome of a model organism, some will focus on the physical map of a human chromosome, and others will focus on a particular technology. I want to point out that the Department of Energy

has established three centers in their National Laboratories that are very similar in concept to the NIH centers. I also expect that research centers will be established abroad and be funded by other nations.

All genome research centers will be expected to foster collaboration among scientists with similar research interests across the world. Obviously, we will take great care to ensure that centers do not duplicate each other's work. At the moment this is not a problem as there is so much work to do. On the contrary, we need to encourage scientists to take on some of these challenging objectives.

NIH and DOE Cooperation

The National Institutes of Health and the Department of Energy have developed a remarkably close working relationship on the Human Genome Project. This relationship was highlighted by a joint meeting of the advisors to the DOE and NIH which was held this past August at Cold Spring Harbor. The agenda was to prepare a joint NIH/DOE five year plan for the Genome Project. For the first time the question before us was not whether to start a human genome program, but how best to carry it out. The meeting was the culmination of the close cooperation between the agencies in the past two years and illustrated how the two agencies can bring complementary strengths to this project. It also was gratifying to see how much scientific progress has been made since the project commenced in 1987. A copy of the NIH/DOE

plan will be available in early December and we will be glad to share it with you at that time.

Technological Advances

Several significant improvements in technology have occurred in the last two years. There are now better cloning vectors that allow for the isolation and amplification of larger pieces of DNA. This facilitates the task of making physical maps because fewer pieces of DNA have to be assembled. Methods for localizing pieces of DNA on chromosomes using microscopes also have been improved. A third improvement is the application of a method called PCR, for polymerase chain reaction, to mapping. This is a chemical method for isolating and making large amounts of a desired piece of DNA. It allows specific segments of DNA to be located, even if they are buried in large amounts of other DNA. This method has had a revolutionary impact on the genome project and has made many experiments much simpler.

Recently, a proposal was made by several members of the original National Research Council Committee on Mapping and Sequencing the Human Genome that presents a system for collecting information from physical mapping projects in a common language. This new approach is referred to as sequence-tagged sites (STS) and will allow the data from diverse physical mapping techniques to be integrated into a common map. The STS proposal would also eliminate the need for large central repositories of DNA, as the information about STS locations could be used to regenerate any desired piece of DNA easily.

In the area of database development, the National Center for Human Genome Research will collaborate with NIH's recently established National Center for Biotechnology Information at the National Library of Medicine as well as with the Department of Energy. The National Center for Biotechnology Information was created to pursue research in biological information handling, particularly with respect to human molecular biology. Efforts of the National Center for Biotechnology Information are closely coordinated with the Human Genome Program through frequent staff interaction and through use of the same advisory groups.

Ethical and Legal Considerations

Many ethical, legal and social questions arise from the use of the information and capabilities that flow out of the Human Genome Program. Therefore, the National Center for Human Genome Research will provide support for studies that investigate such concerns. Starting in fiscal year 1990, at least 3% of the NIH Human Genome Program budget will be available for activities that address ethical, legal and social issues related to the project. The NIH Program Advisory Committee created an ethics working group to plan and coordinate this part of our Human Genome Program. The working group held its first meeting on September 14-15, 1989. At this meeting, the group began to develop a detailed plan for addressing the ethical issues arising from the application of knowledge gained as a result of the Human Genome

Program. This plan also will be available in early December.

International Cooperation

The NIH is fully aware that the importance, complexity, and cost of the effort to map and sequence the human genome makes international cooperation desirable, if not essential. Most developed countries are already formulating strategies to undertake aspects of this international effort, and some developing countries are interested in participating in the research as well. To date, only the United States, the United Kingdom (U.K.), Italy and the Commission of the European Community (EC) have announced independent human genome initiatives, but there are good reasons for believing that France, the USSR, Japan, and possibly Canada will join the effort.

The Human Genome Program will require a number of years, substantial resources, and the development of increasingly sophisticated technology. Storage, comparison and retrieval of the information produced also will require a high level of international cooperation to ensure that basic scientific information is freely accessible to all. The project is much bigger than any one country, and there are certainly enough challenges to go around.

Cooperation already exists between the United States and the Commission of the European Community and the U.S. and the United

Kingdom. Representatives of the Commission of the European Community, the United Kingdom and Canada have participated in meetings of the NIH Program Advisory Committee on the Human Genome. Similarly, members of my staff attended two meetings of the European Community's Human Genome Initiative Working Group, and the chairperson of the NIH Program Advisory Committee's ethics working group will attend the next meeting of the European Community's Study Group on Ethics.

In the past year, I have travelled to England, Italy, France and the Soviet Union to confer with scientists working on human genome research. In addition to representatives of these countries, officials from Japan, Belgium, Denmark and the Federal Republic of Germany have visited my staff to get information about our programs. All parties unanimously endorse the concept of cooperation and are eager to work together. From the start of the Human Genome Program, we have made it a policy that genome related meetings and workshops conducted or planned by the NIH will include international representation.

How to ensure that nations work together instead of indulging in costly competitive races for the same chromosomal objectives will be a challenge. Open communication, sharing of basic scientific data and collaborative efforts are probably the most productive methods for preventing duplication of research efforts and costly international competitions. A number of prominent international molecular biologists and human geneticists have banded together to form "The Human Genome

Organization" (HUGO). This organization is in the process of being formally established. We support the role of HUGO as the principal international coordinating group for human genome research. HUGO could greatly facilitate the free and open exchanges of data that we all want to be features of the Human Genome Program. Knowing the sequences of half of the human chromosomes without having access to the other half would be unbearably frustrating. Sharing of the human DNA database is much more likely to occur if large-scale mapping and sequencing efforts are undertaken by all the major industrial nations that want to use the data.

Another challenge for us is to strike the proper balance between the necessity for international scientific collaboration and the need to promote the United States' competitive position in biotechnology. We do know that science cannot and will not advance when basic scientific data is shrouded in secrecy. By fully involving the U.S. industrial sector in the genome program from the very beginning we hope to ensure that these companies are in the best possible competitive position. The U.S. biotechnology industry is strong and leads the world in this field. There is every reason to think that they will meet the challenges facing them successfully.

Mr. chairman, I am very excited by the prospects for the Human Genome Project. I am gratified by how much has already been accomplished both scientifically and in terms of

international cooperation, and I am optimistic that we will be successful in carrying this project to completion.

I would be pleased to answer any questions that you or Members of the Subcommittee may have about the Human Genome Program.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health

Memorandum

Date FEB 23 1989

From Director, NIH

Subject Proposed Organizational Change in the National Institutes of Health - ACTION

To Robert E. Windom, M.D.
Assistant Secretary for Health

ISSUE

Attached for your concurrence is a proposal to convert the Office of Human Genome Research (HNAB) in the Office of the Director (OD), NIH, to the National Center for Human Genome Research (HN3) effective October 1, 1989. This reorganization is in recognition of the high priority placed on mapping and sequencing the human genome and the substantial funding for this program proposed in the FY 1990 President's Budget.

DISCUSSION

On April 18, 1988, you approved our request to establish the Office of Human Genome Research (OHGR) within the OD/NIH with a staffing level of five positions. At that time NIH had a budget of $17 million for human genome research and was proposing a budget of $27.6 million for FY 1989. Under the current arrangement, OHGR activities have been primarily focused on planning and coordinating functions for the genome project and establishment of the NIH Program Advisory Committee on the Human Genome. Responsibility for administering grants and contracts funded with genome dollars has been with the National Institute of General Medical Sciences (NIGMS).

At the time of our initial request, we indicated our intention to establish the National Center for Human Genome Research (NCHGR) as a second-echelon line component of the NIH with its own research budget and grant-dispensing mechanisms, once the funding level for this activity increased. The prospect of a budget of $100 million for genome research in FY 1990 signals the need to move forward with the proposal to convert the OHGR to a Center effective October 1, 1989.

The Center will assume responsibility for all funds appropriated for the Human Genome program at NIH and will develop a broad research program on complex genomes that is a centrally planned, systematic, targeted effort to create detailed maps of the genomes of several organisms. Technology development, utilizing a variety of extramural grant and contract mechanisms and, possibly, intramural research, will be a major focus in the effort to develop a broad research program on complex genomes. Research goals and long-range plans will be formulated with the guidance of the NIH Program Advisory Committee on the Human Genome.

The Center will continue to perform the functions provided by the current OHGR (coordination, integration, planning, and progress review). Given the broad involvement by a number of Federal agencies and other funding organizations in research related to the characterization of complex genomes, coordination activities will be given added emphasis. The new Center will be the focal point for coordination within NIH, and will be the DHHS point of contact for Federal interagency coordination, collaboration with industry and academia, and international cooperation.

Specifically, the Center will be responsible for all planning and coordinating functions for the genome project, some of which are currently carried out by the BIDs. The establishment of the Center, however, will not have the effect of intruding upon existing interests of other BIDs. Rather, by supporting the development of general genome-related information and materials, the Center's activities will support and encourage the genetics activities of the categorical institutes. For example, there will continue to be a very close relationship between the research interests of the Center and the research interests of NIGMS, particularly the Genetics program. The close relationship in areas of interest between the Center and NIGMS represents an opportunity for synergism and mutual progress.

Center staff and the NIH Program Advisory Committee on the Human Genome will develop new initiatives, as well as recommend establishment of working groups and other activities requiring intense staff support. Initial efforts will include the establishment of genome research centers, a research training program, and new resources, and the improvement and expansion of existing resources. Relative to data base projects in molecular biology planned or underway within NIH components (Division of Research Resources, National Library of Medicine, and the National Institute of General Medical Sciences), the Center will provide leadership in the development of a trans-NIH plan for Genome Research and Biotechnology Information Systems.

While the NIH has traditionally taken the position opposing the establishment of new categorical organizations in response to emerging health problems, we have endorsed the creation of organizational entities when the conclusion was reached that they were needed. For example, the Division of Environmental Health Sciences was elevated to the National Institute of Environmental Health Sciences when it was determined that the health research programs of the Division had developed to a level requiring Institute status. Too often new organizations are promoted to focus attention on, and gain additional resources for a particular disease. This is clearly not the issue in this instance in that the Administration has already acknowledged the importance of this initiative and has committed itself to increasing resources in the FY 1990 budget.

Transition from Office to Center - The expansion of existing functions and the assumption of new duties requires that the current FY 1989 OHGR staffing level be increased from five to 23 positions and that some overhead functions, such as personnel and other administrative services, be shared. This expansion of staff is necessary if the Center is to assume full responsibility for managing a program of $100 million in FY 1990.

IMPACT

As stated above, the FY 1989 OHGR staffing will be increased from its current level of five (including one SES) positions to 23. This staffing increase will be accomplished within the current NIH FTE ceiling. Effective October 1, the OHGR staff (including the SES position) will be transferred to the new Center, and augmented with the remaining needed positions from within the FY 1990 budget. There will be no adverse personnel impact on involved employees, nor on NIH's EEO objectives.

The FY 1989 budget is approximately $27 million and the FY 1990 President's Budget request includes $100 million for funding the Human Genome Initiative. These funds have been included in the budget requests for the National Institute of General Medical Sciences ($99,088,000) and the Office of the Director ($912,000). Since the genome set-aside is a line item in the NIGMS budget, transfer of these funds will not affect other NIGMS programs. It is expected that a separate appropriation will be requested for the new Center in FY 1991.

RECOMMENDATION

I recommend that you indicate your concurrence with this organizational change by signing the attached memorandum to the Assistant Secretary for Management and Budget.

James B. Wyngaarden

James B. Wyngaarden, M.D.

Attachments
Memorandum to the Assistant Secretary for Management and Budget from the Assistant Secretary for Health
Federal Register notice
Organization charts

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Memorandum

Date

From Acting Assistant Secretary for Health

Subject Proposed Organizational Change in the National Institutes of Health - ACTION

To Anthony S. McCann
Assistant Secretary for Management and Budget

ISSUE

Attached for your concurrence is a proposal to convert the Office of Human Genome Research (HNAB) in the Office of the Director (OD), NIH, to the National Center for Human Genome Research (HN3) effective October 1, 1989. The NIH is requesting an effective date of October 1, rather than the date of signature, because of the lead time needed to recruit additional resources so as to be fully operational as a Center when funds are available on October 1. This reorganization is in recognition of the high priority placed on mapping and sequencing the human genome and the substantial funding for this program proposed in the FY 1990 President's Budget.

BACKGROUND

On April 18, 1988, the request to establish the Office of Human Genome Research (OHGR) within the OD/NIH with a staffing level of five positions was approved. At that time NIH had a budget of $17 million for human genome research and was proposing a budget of $27.6 million for FY 1989. Under the current arrangement, OHGR activities have been primarily focused on planning and coordinating functions for the genome project and establishment of the NIH Program Advisory Committee on the Human Genome. Responsibility for administering grants and contracts funded with genome dollars has been with the National Institute of General Medical Sciences (NIGMS).

At the time of the initial request, NIH indicated its intention to establish the National Center for Human Genome Research (NCHGR) as a second-echelon line component of the NIH with its own research budget and grant-dispensing mechanisms, once the funding level for this activity increased.

The prospect of a budget of $100 million for genome research in FY 1990 signaled the need to move forward with the proposal to convert the OHGR to a Center. Accordingly, in January, the Director, NIH, forwarded a concept paper to then Secretary Bowen requesting his approval of the need to effect the conversion of the OHGR to a National Center, given the anticipated FY 1990 increase in funding. Concerns raised during the OS staff review of the concept paper are addressed below.

Assistant Secretary for Management and Budget

Staffing

NIH is aware that there will be no additional staffing resources provided for this organizational change and that the administrative overhead needed to establish and manage the Center must come from within the overall resources allocated to NIH in FY 1989 and FY 1990. The proposed reorganization will be accomplished within the current NIH FTE ceiling.

Assistant Secretary for Planning and Evaluation

Formal Review

NIH appreciates the Assistant Secretary's interest in ensuring that a broad range of perspectives are heard regarding the merits of this proposal. However, should OS staff determine that a review outside the formal organizational change approval process is necessary, it is hoped that this review can be accomplished expeditiously.

Administrative Support

NIH is taking steps to ensure that the difficulties inherent in setting up a new Center do not divert scientific leadership now provided by the OHGR. Specifically, some overhead functions such as personnel and other administrative services will be shared during the transition phase from office to center.

Establishment of New Institutes

While the NIH has traditionally taken the position opposing the establishment of new categorical organizations in response to emerging health problems, it has endorsed the creation of organizational entities when the conclusion was reached that they were needed. For example, the Division of Environmental Health Sciences was elevated to the National Institute of Environmental Health Sciences when it was determined that the health research programs of the Division had developed to a level requiring Institute status. Too often new organizations are promoted to focus attention on, and gain additional resources for a particular disease. This is clearly not the issue in this

instance in that the Administration has already acknowledged the importance of this initiative and has committed itself to increasing resources in the FY 1990 budget.

Assistant Secretary for Legislation

Administrative/Research Center

The Center will continue to perform the functions provided by the current OHGR, and will assume responsibility for all funds appropriated for the human genome project at NIH. The National Center will be an administrative center in that it will not set up intramural laboratories; however, it may selectively provide extra funding to the intramural laboratories of other NIH components performing research relating to the Center's objectives in order to expedite such research.

Impact on Other NIH Genetics Research Projects

The Center will be responsible for all planning and coordinating functions for the human genome project. However, traditional human genetics research, both intramural and extramural, of other NIH components will continue to be managed by the categorical institutes and will be supported and encouraged through the Center's development and sharing of general genome-related information, materials, and technology.

Impact to the National Institute of General Medical Sciences (NIGMS)

There will continue to be a very close relationship between the research interests of the Center and the research interests of NIGMS, particularly the Genetics program. The close relationship in areas of interest between the Center and NIGMS represents an opportunity for synergism and mutual progress. FY 1990 funding for the Human Genome Initiative has been included in the NIGMS budget requests. Since the genome set-aside is a line item in the NIGMS budget, transfer of these funds will not affect other NIGMS programs.

DISCUSSION

The Center will assume responsibility for all funds appropriated for the human genome project at NIH and will develop a broad research program on complex genomes that is a centrally planned, systematic, targeted effort to create detailed maps of the genomes of several organisms. Technology development, utilizing a variety of extramural grant and contract mechanisms, will be a major focus in the effort to develop a broad research program

on complex genomes. Some incremental funding may also be made available, on a competitive basis, to existing intramural laboratories that choose to pursue research related to the objectives of the genome program. Research goals and long-range plans will be formulated with the guidance of the NIH Program Advisory Committee on the Human Genome.

The Center will continue to perform the functions provided by the current OHGR (coordination, integration, planning, and progress review). Given the broad involvement by a number of Federal agencies and other funding organizations in research related to the characterization of complex genomes, coordination activities will be given added emphasis. The new Center will be the focal point for coordination within NIH, and will be the DHHS point of contact for Federal interagency coordination, collaboration with industry and academia, and international cooperation.

Center staff and the NIH Program Advisory Committee on the Human Genome will develop new initiatives, as well as recommend establishment of working groups and other activities requiring intense staff support. Initial efforts will include the establishment of genome research centers, a research training program, and new resources, and the improvement and expansion of existing resources. Relative to data base projects in molecular biology planned or underway within NIH components (Division of Research Resources, National Library of Medicine, and the National Institute of General Medical Sciences), the Center will provide leadership in the development of a trans-NIH plan for Genome Research and Biotechnology Information Systems.

Transition from Office to Center - The expansion of existing functions and the assumption of new duties requires that the current FY 1989 OHGR staffing level be increased from five to 23 positions and that some overhead functions, such as personnel and other administrative services, be shared. This expansion of staff is necessary if the Center is to assume full responsibility for managing a program of $100 million in FY 1990.

IMPACT

As stated above, the FY 1989 OHGR staffing will be increased from its current level of five (including one SES) positions to 23. This staffing increase will be accomplished within the current NIH FTE ceiling. Effective October 1, the OHGR staff (including the SES position) will be transferred to the new Center, and augmented with the remaining needed positions from within the FY 1990 budget. There will be no adverse personnel impact on involved employees, nor on NIH's EEO objectives.

The FY 1989 budget is approximately $27 million and the FY 1990 President's Budget request includes $100 million for funding the Human Genome Initiative. These funds have been included in the budget requests for the National Institute of General Medical Sciences ($99,088,000) and the Office of the Director ($912,000). Since the genome set-aside is a line item in the NIGMS budget, transfer of these funds will not affect other NIGMS programs. It is expected that a separate appropriation will be requested for the new Center in FY 1991.

RECOMMENDATION

I recommend that the Secretary sign the attached Federal Register notice.

Ralph R. Reed, M.D.

Attachments
Federal Register notice
Organization charts

4140-01

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

NATIONAL INSTITUTES OF HEALTH

Statement of Organization, Functions and

Delegations of Authority

Part H, Chapter HN (National Institutes of Health) of the Statement of Organization, Functions and Delegations of Authority of the Department of Health and Human Services (40 FR 22859, May 27, 1975, as amended most recently at 54 FR 5682, February 6, 1989), is amended to reflect the following changes within the National Institutes of Health effective October 1, 1989: (1) Abolish the Office of Human Genome Research (HNAB) within the Office of the Director, NIH; and (2) establish the National Center for Human Genome Research (HN3). These changes will more properly reflect the high priority placed on mapping and sequencing complex genomes and the expansion of the genome research effort.

Section HN-B, Organization and Functions, is amended as follows effective October 1, 1989:

(1) Under the heading Office of the Director (HNA), delete the title and statement for the Office of Human Genome Research (HNAB) in their entirety.

(2) After the statement for the Clinical Center (HNJ), insert the following:

National Center for Human Genome Research (HN3).
(1) Advises the Director, NIH, and senior staff on all aspects of genomic analysis; (2) coordinates the integration, review, and planning of genomic analysis research; (3) formulates research goals and long-range plans with the guidance of the NIH Program Advisory Committee on Complex Genomes; (4) serves as a focal point on genomic analysis research within NIH, other components of the Public Health Service, and other Federal agencies (e.g., DOE and NSF); (5) fosters, conducts, supports, and administers research and research training programs directed at promoting the growth and quality of research related to mapping and sequencing of complex genomes through: (a) research grants, contracts, and cooperative agreements to institutions and individuals; (b) individual and institutional research training awards; (c) promotion of closer interaction with other bases of genomic analysis research; and (d) collection and dissemination of research findings in these areas; (6) develops plans for the centralized, systematic, targeted effort to create detailed maps of the genomes of organisms; (7) establishes research goals and criteria for review or progress in meeting those goals; (8) sponsors scientific meetings and symposia to promote progress

through information sharing; and (9) fosters national and international information exchange with industry and academia concerning research on complex genomes.

This reorganization is effective October 1, 1989.

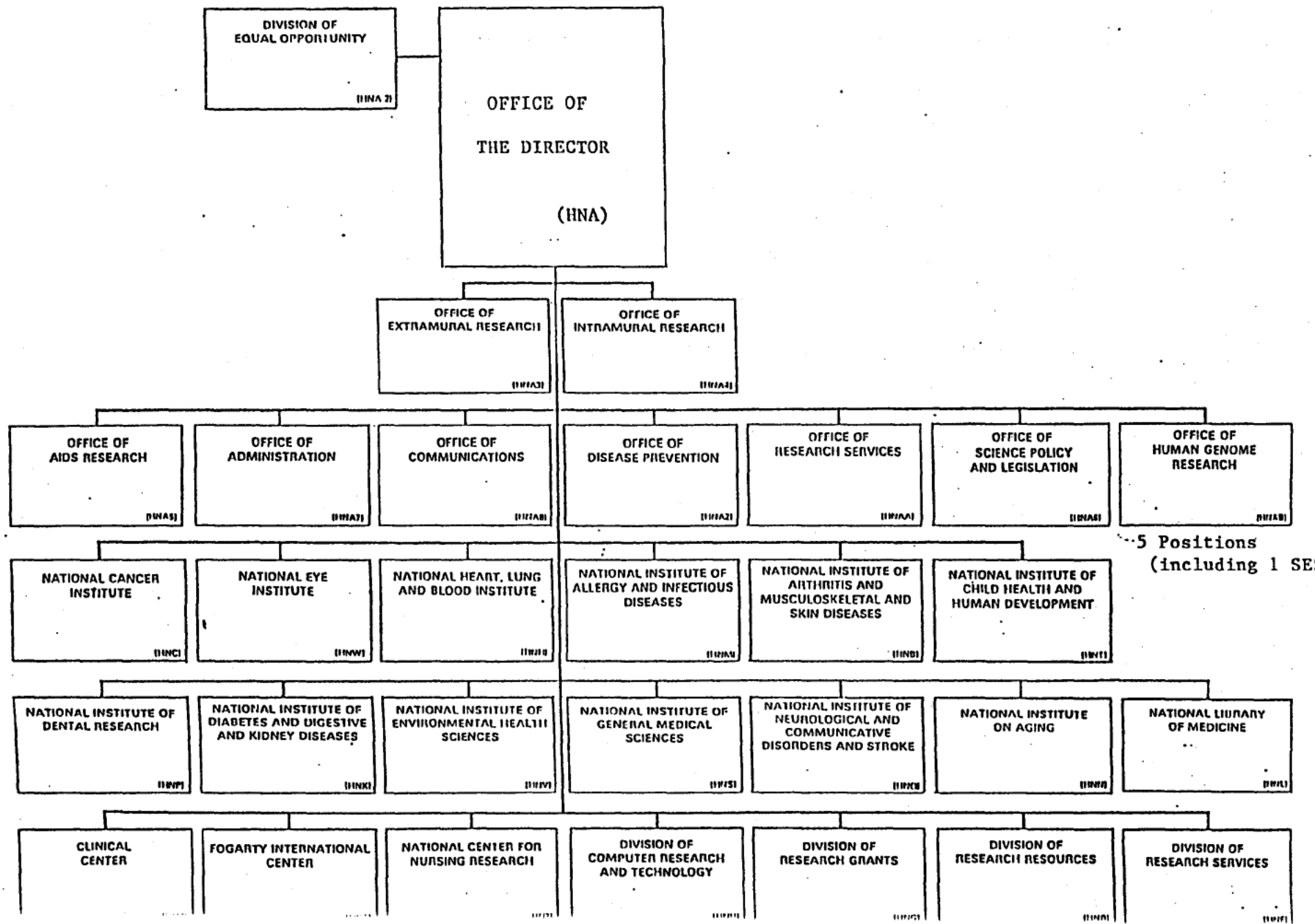
Date

Louis W. Sullivan, M.D.
Secretary

DEPARTMENT OF HEALTH AND HUMAN SERVICES

PRESENT

Public Health Service
National Institutes of Health

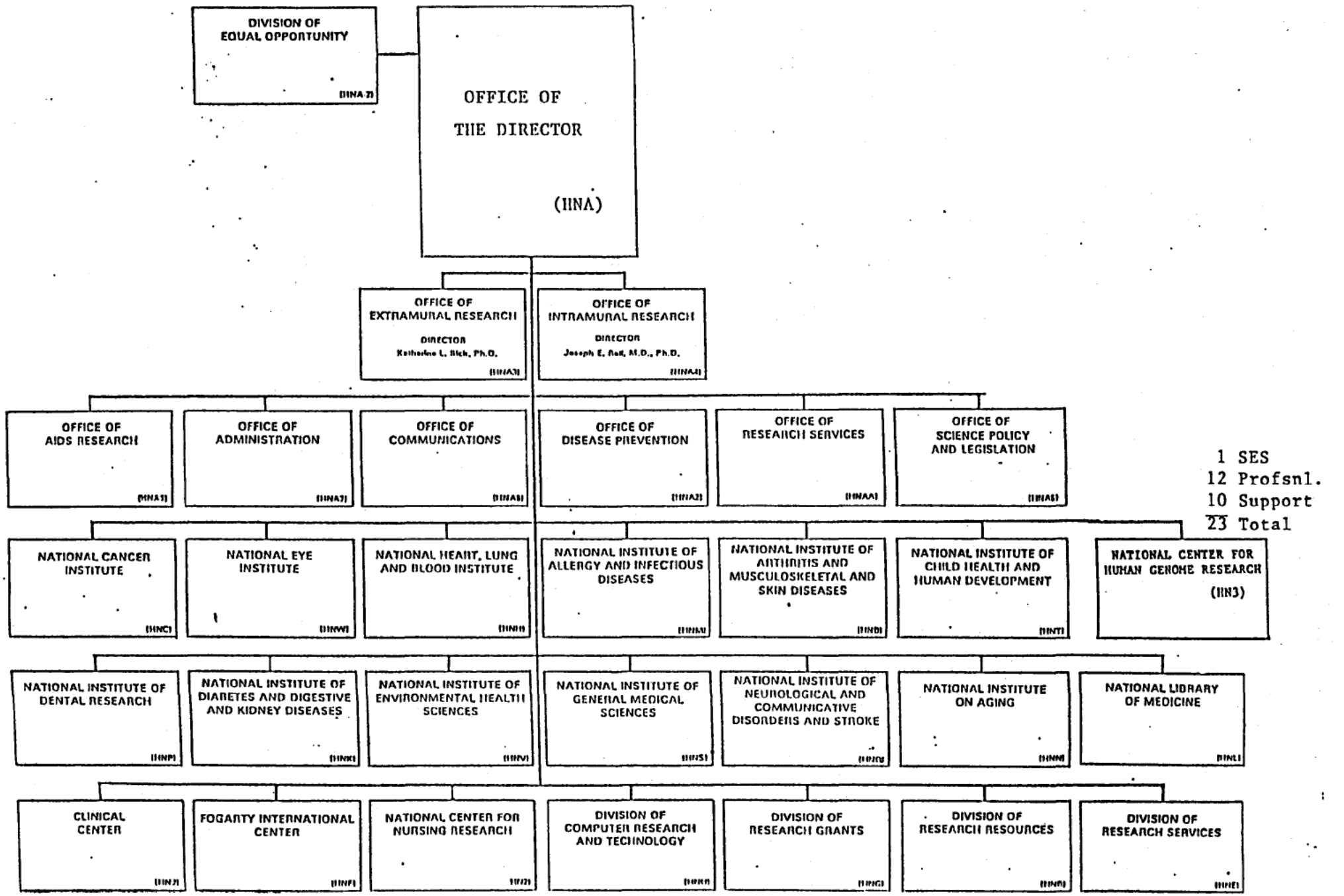


5 Positions
(including 1 SES)

DEPARTMENT OF HEALTH AND HUMAN SERVICES

PROPOSL

Public Health Service
National Institutes of Health



1 SES
12 Profsnl.
10 Support
23 Total

NATIONAL CENTER FOR HUMAN GENOME RESEARCH
(Dollars in thousands)

	FY 1988 Actual		FY 1989 Estimate		FY 1990 President's Budget		FY 1990 House Allowance		FY 1990 Senate Allowance		FY 1990 Conference Allowance	
Research Grants	No.	Amount	No.	Amount	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Proj.:												
Noncompeting			52	15,381	92	28,888	92	28,888	92	25,847	94	28,358
Competing	63	16,767	44	12,188	166	48,665	42	12,290	53	15,178	42	12,290
Subtot.,RPGs	63	16,767	96	27,569	258	77,553	134	41,178	145	41,025	136	40,648
Research Ctrs:												
Spec/comp.					3	10,000	3	8,000	3	8,000	3	8,000
Subtot.,Ctrs	0	0	0	0	3	10,000	3	8,000	3	8,000	3	8,000
Other Res.:												
Careers					25	1,685	10	674	10	674	6	404
Other	2	468			3	250	10	1,000	10	1,000	10	1,000
Subtot.,Oth	2	468	0	0	28	1,935	20	1,674	20	1,674	16	1,404
Total, Res Grant	65	17,235	96	27,569	289	89,488	157	50,852	168	50,699	155	50,052
Training	FTTP		FTTP		FTTP		FTTP		FTTP		FTTP	
Indiv.					50	1,250	50	1,250	50	1,250	50	1,250
Instit.					135	2,750	135	2,750	135	2,750	86	1,750
Total, Training	0	0	0	0	185	4,000	185	4,000	185	4,000	136	3,000
R&D Contracts					4	5,000	4	5,000	4	5,000	4	4,800
RM&S				544		1,512		2,148		2,148		2,148
Total, NCHGR		17,235		28,113		100,000		62,000		61,847		60,000

Second Meeting

Program Advisory Committee on the Human Genome

June 19-20, 1989

Ramada Inn
Bethesda, MD

ROSTER

Chairperson

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John D. Rockefeller, Jr. Professor
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Executive Secretary

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THE SECRETARY OF HEALTH AND HUMAN SERVICES
WASHINGTON, D.C. 20201

C H A R T E R

PROGRAM ADVISORY COMMITTEE ON THE HUMAN GENOME

Purpose

The Program Advisory Committee on the Human Genome will advise the NIH on all aspects of research in the area of genomic analysis. The Committee will identify opportunities to advance the ability of scientists to analyze the composition and organization of the genetic material of a number of organisms, with the goal of applying this information to the analysis of the human genome. The Committee will recommend initiatives that will promote the development of new technologies that will facilitate the acquisition, interpretation, analysis, and distribution of genetic and physical mapping information and deoxyribonucleic acid (DNA) sequence data. The Committee also will advise on research directions and identify areas of research requiring additional effort. The Committee will address the resource and training needs of the research community, as they pertain to genomic analysis.

Authority

42 U.S.C. 217a (Section 222 of Public Health Service Act as amended). This Committee is governed by provisions of P.L. 92-463, as amended (5 U.S.C. Appendix 2), which sets forth standards for the formation and use of advisory committees.

Function

The Program Advisory Committee on the Human Genome shall advise the Secretary; the Assistant Secretary for Health; the Director, National Institutes of Health; the Associate Director for Human Genome Research, National Institutes of Health; and the NIH Working Group on the Human Genome on long- and short-term planning to meet research needs for genomic analysis. Specifically, the Committee shall identify opportunities to further research on information and database technology and the methodology of genomic analysis and the characterization of the genomes of a variety of organisms, with the goal of applying this knowledge to the analysis of the human genome and ultimately to the prevention, diagnosis, and treatment of human disorders; recommend areas in which research should be stimulated; and suggest conferences, workshops, or other activities that the NIH should support to further the development of this research area.

Structure

The Program Advisory Committee on the Human Genome shall consist of 12 members selected by the Secretary, who shall be authorities knowledgeable in the fields of basic genetics, medical genetics, molecular biology, biochemistry, physical chemistry, information science, and engineering. The chair shall be selected by the Secretary from the membership and shall serve for at least one year and may be reappointed.

Members are invited to serve for overlapping four year terms, except that a member may serve after the expiration of the member's term until a successor has taken office. Terms of more than two years are contingent upon the renewal of the charter of the Committee by appropriate action prior to its expiration.

Management and support services shall be provided by the Office of the Associate Director for Human Genome Research, Office of the Director, NIH.

Meetings

Meetings shall be held at least twice a year at the call of the Chair with the advance approval of a Government official who will also approve the agenda. A Government official shall be present at all meetings. A quorum for the conduct of full committee business shall be seven.

Meetings shall be open to the public except as determined otherwise by the Secretary; notice of all meetings shall be given to the public.

Meetings shall be conducted, and records of the proceedings kept as required by applicable laws and departmental regulations.

Compensation

Members shall be paid at the rate of $200 per day for time spent at meetings, plus per diem and travel expenses as authorized by Section 5703, Title 5, United States Code, for persons in the Government service employed intermittently. Members who are officers or employees of the United States shall not receive compensation for service on the Committee.

Annual Cost Estimate

Estimated annual cost for operating the Committee, including compensation and travel expenses for members but excluding staff support, is $65,944. The estimated annual staff years of support is .45 at an estimated cost of $18,234.

Reports

An annual report shall be submitted to the Secretary; the Assistant Secretary for Health; and the Director, National Institutes of Health, which shall contain, as a minimum, the Committee's functions, a list of members and their business addresses, the dates and places of meetings, and a summary of the Committee's activities and recommendations during the year. A copy of the report shall be provided to the Department Committee Management Officer.

Termination Date

Unless renewed by appropriate action prior to its expiration, the Program Advisory Committee on the Human Genome shall terminate two years from the date of establishment.

APPROVED:

JUL 21 1988
Date

Otis R. Bowen M.D.
Otis R. Bowen, M.D.
Secretary

PROGRAM ADVISORY COMMITTEE ON THE HUMAN GENOME

FIRST MEETING

January 3 and 4, 1989

Building 31, C Wing, Conference Room 6
National Institutes of Health
Bethesda, MD

MINUTES

The first meeting of the Program Advisory Committee on the Human Genome took place on January 3 and 4, 1989, in Bethesda, MD. The following Committee members attended:

Norton D. Zinder, Ph.D., Chairman
Elke Jordan, Ph.D., Executive Secretary
Bruce M. Alberts, Ph.D.
David Botstein, Ph.D.
Jaime G. Carbonell, Ph.D.
Joseph L. Goldstein, M.D.
Leroy E. Hood, Ph.D.
Victor A. McKusick, M.D.
Maynard V. Olson, Ph.D.
Mark L. Pearson, Ph.D.
Cecil B. Pickett, Ph.D.
Phillip A. Sharp, Ph.D.
Nancy S. Wexler, Ph.D.

The following liaison members also attended:

George F. Cahill, Jr., M.D.
C. Thomas Caskey, M.D., F.A.C.P.
Mary E. Clutter, Ph.D.
Robert M. Faust, Ph.D.
Benjamin J. Barnhardt, Ph.D.

Drs. Goldstein and Clutter were unable to attend the second day of the meeting. The Committee roster and lists of speakers and others who attended are attached to these minutes.

DAY 1

Dr. James B. Wyngaarden, Director of the National Institutes of Health (NIH), began the meeting with an overview of the history of NIH's role in genetics research. He noted that NIH has invested in this type of research for several decades, by sponsoring intramural programs as well as by providing resources to the extramural scientific world. Dr. Wyngaarden reported that, in FY 1988, Congress awarded NIH the sum of $17.2 million to conduct research on the mapping and sequencing of the human genome. Following this appropriation, NIH

held a major retreat in Reston, VA, to discuss the project and determine the role NIH would play. Dr. Wyngaarden summarized the meeting's accomplishments, one of which was the creation of the Office of Human Genome Research within the Office of the Director, NIH. In addition, the meeting defined four sub-areas of the human genome project: improvement of information management, improvement of methodology, mapping of the genome, and determination of the nucleotide sequence.

Next, Dr. Wyngaarden delivered the charge to the Program Advisory Committee. He stated that the Committee is empowered to advise NIH on all aspects of the human genome project, including new technologies, new directions, training needs, etc. In addition, the Committee will be expected to assist in preparing a plan for the human genome project, which is due to be submitted to Congress in early 1990. In discussing the definition and boundaries of the project, Dr. Wyngaarden noted that virtually all Institutes of the NIH are involved in research that interacts with this program. He stated that the Office of Human Genome Research does not wish to usurp projects that have been undertaken by individual Institutes; rather, it seeks to coordinate efforts into a cohesive plan and to determine what can be done differently.

Dr. Norton D. Zinder, of The Rockefeller University, began his remarks by noting that this meeting marked the formal beginning of the NIH human genome project. He stated that obtaining the sequence of the human genome is "a priceless endeavor" and that the project will be endless: Once the sequencing has been completed, the information must be used, and the applications are almost limitless.

Dr. Zinder proceeded to set the dates for future Committee meetings. The next meeting will be held on June 19-20, 1989, and the following meeting will take place on December 4-5, 1989. The latter meeting will include discussion of the report to be submitted to Congress by March 1990.

Dr. James D. Watson, Associate Director for Human Genome Research, NIH, discussed the background and goals of the human genome project. He stated his intention to complete the project "as fast as possible within a reasonable cost." He estimated that approximately 15 to 20 years would be required to complete the entire project but that important results are likely to be produced within the next 5 years.

Dr. Watson discussed coordination of projects under the program. He felt that small laboratories consisting of 5 to 10 scientists working on special projects will probably not be sufficient to achieve program goals. Larger groups--even centers--may be necessary. Decisions about which laboratories should be encouraged to grow larger will have to be made, and this is an area in which the Office of Human Genome Research and the Program Advisory Committee must become involved.

Dr. Watson stated his belief that the human genome project must be run by the scientific community. He urged the Committee members to travel and get to know the laboratories that will be doing the work rather than simply reading their proposals. Dr. Watson also emphasized that the Advisory Committee was not convened to ratify decisions that had already been made; rather, the Committee will make decisions that will influence the direction of the program at NIH.

Dr. Elke Jordan, Director of the Office of Human Genome Research, NIH, described the function of the Office and discussed its interaction with other groups. She announced the creation of the NIH Coordinating Committee on the Human Genome, which consists of representatives from the Institutes of NIH that are involved in genome-related research (i.e., almost all the Institutes). The Coordinating Committee will facilitate communication between the Institutes and the Office of Human Genome Research. In addition, Dr. Jordan discussed the collaboration between NIH and the U.S. Department of Energy (DOE), which has been established through a Memorandum of Understanding (MOU) between the two agencies. The Health and Environmental Research Advisory Committee (HERAC) of DOE and the Program Advisory Committee of NIH will form subcommittees that will meet jointly to fulfill the requirements of the MOU.

Dr. Jordan also stated that the Office of Human Genome Research will interact with the Human Genome Organization (HUGO) to facilitate coordination of genome research internationally. She noted that representatives from other countries involved in this type of research may be invited to future Committee meetings to provide updates on their activities.

Following this presentation, Dr. Ruth Kirschstein summarized ongoing research on the human genome that is sponsored by the National Institute of General Medical Sciences (NIGMS). She described two NIH-wide program announcements, issued in May 1987, entitled "New Approaches to the Analysis of Complex Genomes" and "Computer-Based Representation and Analysis of Molecular Biology Data." Initially, solicitations sought applications involving development of methods to fragment, purify, and clone large segments of DNA; to develop ordered sets of such fragments; to explore better ways of sequencing the fragments in order to expand the genetic and physical maps of the human and other genomes; and to conduct computational analyses of data. Dr. Kirschstein also discussed the Request for Applications (RFA), published in October 1987, for research initiatives involving the human genome and those of model organisms (yeast, *Drosophila*, the mouse, and *Caenorhabditis*). She noted that two special study sections had been created to review the applications submitted by the scientific community.

Dr. Kirschstein reported that 63 grants were funded in FY 1988. The largest number of these grants involved technology development and instrumentation, and 23 were specifically related to the human genome. Dr. Kirschstein estimated that approximately $12 million will be available in FY 1989 for new research and that approximately 30 to 40 additional grants will be funded.

Dr. Irene Eckstrand of NIGMS described the Institute's plans to sponsor meetings and workshops, including the Human Gene Mapping Workshop, which is to be held June 10-17, 1989, in New Haven, CT. She also reported that NIGMS, DOE, and Howard Hughes Medical Institute will cosponsor a series of meetings on data management for physical mapping information. These meetings will deal with nomenclature, software, and data base management.

Dr. Eckstrand stated that NIGMS also plans to facilitate collaborations among investigators working on similar projects in order to improve communication and to design networks for data transfer and analysis. With these goals in mind, NIGMS will sponsor a meeting in March 1989 of approximately 25 investigators who are working on chromosome 11. In the fall of 1989, a meeting will be held to address strategies and technologies for DNA sequence determination.

During discussion of these presentations, Dr. Kirschstein stated that NIGMS had used the FY 1988 and FY 1989 funds primarily for research projects and had not allocated funds directly for training, although research grants supported training indirectly. Dr. Kirschstein also commented that NIGMS was able to provide funds for equipment needs in the scientific community but that authority for construction was not available.

Dr. Donald A.B. Lindberg provided background on the National Library of Medicine (NLM) and discussed NLM's plans to augment existing resources by developing factual data bases, particularly for microbiology and biotechnology. He described a new information model whereby data reside where they have been created, and users access the data through networks. He noted that NLM plans an active role in managing such networks. Dr. Lindberg also stated that NLM has recently funded projects on information processing and will continue to support this type of research in 1989. In addition, he mentioned that NLM has funded training grants in medical informatics for the last 20 years.

Dr. Lindberg reported that the National Center for Biotechnology Information has been established at NLM and is funded at $8 million per year. He stated that the Committee's input on optimal ways to use the Center will be sought.

Dr. Daniel R. Masys presented further detail on NLM's biotechnology information program, which focuses on problems specific to automated information systems, e.g., nonstandard vocabularies, structures, and searching methods. He stated that the National Center for Biotechnology Information has been charged with the following tasks:

- To design, develop, implement, and manage automated information systems for human molecular biology, biochemistry, and genetics;
- To perform research in advanced methods of computer-based information processing capable of representing and analyzing the vast number of biologically important molecules and compounds;
- To enable use of the systems and methods developed; and
- To coordinate international gathering of biotechnology information.

Dr. Masys summarized NLM-supported projects that have been ongoing for the last several years in the following areas:

- Development of new data bases and enhancement of existing ones, e.g., through the design of linkage schemes;
- Improvement of information retrieval and analysis; and
- Communication, including sponsorship of meetings and workshops on computational biology, e.g., the Macromolecules, Genes, and Computers Workshop to be held in the summer of 1989.

During discussion of issues surrounding the design of information systems, several participants cautioned against overstandardization in the organization of data from areas of research that are highly experimental. Dr. Masys stated

that input from the Committee would be important in making decisions about the types of data bases that should be supported (e.g., Are separate data bases for nucleic acids and proteins necessary, or would it be advantageous to combine them?). Dr. Lindberg noted that outreach is an area of major concern at NLM, and ways of educating the scientific community about available resources are being explored.

Dr. James C. Cassatt described the NIGMS-funded GenBank, a data base that contains not only sequence information but also bibliographic data and biological information pertaining to the sequences. GenBank currently contains more than 22,000 entries comprising approximately 24,000,000 base pairs, and data are available online as well as on magnetic tapes, floppy disks, and CD-ROM. GenBank also collaborates with other nucleic acid sequence data bases--the European Molecular Biology Laboratory (EMBL) in Heidelberg and the DNA Data Bank of Japan.

Dr. Cassatt stated that future challenges include insuring that GenBank data are complete and up to date. He emphasized the importance of timely data entry and reported that a user-friendly program to facilitate data entry will be available to the research community in 2 months. In addition, journals that publish sequence information will be asked to require authors to enter their data into GenBank upon acceptance of their manuscripts.

During the discussion period, several participants stressed that the Committee should work on ways to encourage investigators to enter their data into appropriate data bases quickly.

Dr. Delbert H. Dayton described the Repository of Human DNA Probes and Libraries, which is funded jointly by the National Institute of Child Health and Human Development and the Division of Research Resources (DRR). The Repository, an international facility that has served 2,667 users, provides for the reliable exchange of cloned human DNA and the distribution of chromosome-specific libraries. The American Type Culture Collection (ATCC), which operates the Repository, accepts DNA relevant to human genetic disease and focuses on genes, clones that identify restriction fragment length polymorphisms (RFLPs), and segments of importance in genetic linkage analysis. The ATCC collects well-characterized probes from investigators, expands and verifies the probes, and stores multiple samples that are distributed to interested investigators upon request. The ATCC currently receives probes at the rate of 300 per year and expects to distribute libraries at the rate of 1,000 per year by the 5th year of the contract. Probes that are likely to be heavily requested are identified through contacts with the Human Gene Mapping Library at Yale University and the Human Gene Mapping Workshops.

Following this presentation, several participants commented on the changing technology for the production of cloned DNA and noted that the ATCC will have to keep pace with these changes. Dr. Dayton stated that initial efforts to explore automation of procedures are already under way.

Dr. Caroline H. Holloway provided an overview of the Protein Identification Resource (PIR). This data base, funded by the DRR's Biomedical Research Technology Program (BRTP), collects information on protein sequences and facilitates the identification of unknown proteins. In addition, protein and nucleic acid information can be correlated, allowing the identification of

proteins based on nucleic acid sequence. Online data bases also include GenBank and EMBL. PIR is located at the National Biomedical Research Foundation at Georgetown University and has 126 universities and nonprofit organizations signed up as online users. Dr. Holloway noted that the grant that supports PIR will terminate at the same time as the GenBank contract terminates, which provides an opportunity for making decisions about collaboration between these two data bases.

Next, Dr. Holloway summarized the status of Bionet, also funded by the BRTP, which allows users access to a number of biological sequence data bases, including GenBank and PIR; software tools; and an electronic bulletin board. Bionet is operated by Intelligenetics in Mountain View, CA, and there are 867 users who subscribe.

During the discussion period, several participants noted that DRR's experience with centers should be valuable to the Committee in its efforts to determine the requirements for centers in the human genome project. There was also discussion of the differences among the grant, contract, and cooperative agreement mechanisms at NIH. Dr. Katherine L. Bick, of the Office of Extramural Research, NIH, provided clarification of these differences.

Dr. Judith Greenberg described the activities of the Human Genetic Mutant Cell Repository, an NIGMS-funded repository at the Coriell Institute for Medical Research in Camden, NJ. The Repository, also known as the Cell Bank, provides high-quality, well-characterized, contaminant-free cultures of cell lines from individuals with genetic disorders and from normal individuals. The Repository contains 4,500 cell lines, primarily fibroblasts and lymphoblasts, representing a variety of monogenic and multifactorial disorders. Chromosomal abnormalities such as duplications and deletions are also represented as well as hybridomas and myelomas. Gene mapping accounts for 12 percent of the Repository's utilization, while other utilization includes studies on the following: regulation of gene expression, cell physiology, mutagenesis, carcinogenesis, DNA synthesis and repair, and pharmacology.

Dr. Greenberg reported that, in January 1989, NIGMS awarded the Coriell Institute for Medical Research a 5-year, $5.7-million contract to continue operation of the Repository. The Repository will undertake additional activities under the new contract. For example, it will make DNA preparations from selected cell lines for distribution to investigators, which will enable distribution of DNA from somatic cell hybrids.

Following this presentation, the desirability of duplication between the Repository's pedigrees and those maintained by the Centre d'Étude du Polymorphisme Humain (CEPH) was proposed as an item for the Program Advisory Committee's consideration, given that linkage mapping is a high priority in the human genome project.

The meeting continued with an overview of genome activities in agencies other than NIH. Dr. Benjamin J. Barnhardt provided background on DOE's Human Genome Initiative, which has been undertaken to expand DOE's ability to investigate the health effects of radiation and energy-related chemicals. He stated that DOE's Human Genome Initiative encompasses three major objectives: development of resources, including overlapping sets of cloned DNA fragments prepared as

cosmids and yeast inserts; development of new mapping and sequencing technologies; and development of data base management systems, techniques for automated input of DNA sequences, and computational tools for analysis.

Dr. Barnhardt stated that DOE's intramural effort in the Human Genome Initiative is largely represented by three national laboratories: the Lawrence Berkeley Laboratory and the Los Alamos National Laboratory, which have been designated as human genome centers, and the Lawrence Livermore National Laboratory. Dr. Barnhardt highlighted other DOE-supported activities, including preparation of chromosome-specific libraries for ATCC, involvement in the National Gene Library Project, and partial support of GenBank. He stated that future goals of the Human Genome Initiative are to complete construction of linearly ordered DNA clones for chromosomes that have already been started and to initiate the construction of such clones for additional chromosomes.

During the discussion period, Dr. Barnhardt noted that DOE does not fund training directly but that the human genome centers provide training indirectly. He also described ongoing efforts at Los Alamos National Laboratory to promote technology transfer to the private sector.

Dr. George F. Cahill, Jr., summarized the genome-related activities of the Howard Hughes Medical Institute (HHMI). He stated that HHMI spends approximately $40 million per year to support investigators involved in genetics research, including those working on *Drosophila* genetics. In addition, the Institute provides support for medical students in research as well as for doctoral trainees.

Dr. Cahill stated that HHMI also funds genome resources at approximately $3.5 million per year, including the Human Genome Mapping Library (HGML), the CEPH data base, and the Online Mendelian Inheritance in Man data base, among others. HHMI plans to investigate methods of making these data bases compatible with each other. Dr. Cahill remarked that HHMI will rely heavily on recommendations from the Program Advisory Committee regarding other areas of the human genome effort that need support.

Following this presentation, several participants reiterated the importance of designing data bases that can intercommunicate. They stressed that the Committee should play a role in developing guidelines that will minimize incompatibility in future data bases.

Next, Dr. John C. Wooley described the National Science Foundation's (NSF's) support for projects focused on infrastructure in genetics, for which $50 million will be spent in FY 1989. He discussed five broad areas of special interest to NSF: instrument development, particularly during early stages; provision of instrumentation and facilities for genetic research; software development; basic genetic research (primarily on nonhuman organisms); and biological data bases. Specific NSF activities have included funding, in FY 1989, of a science and technology center dedicated to new technologies for DNA and protein chemistry. NSF is also involved in development of new software and algorithms for data base searching and development of special purpose hardware to increase the speed of biological data base searches. NSF has also collaborated with NIH to provide biomedical scientists access to resources at the NSF Advanced Computing Centers (Supercomputer

Centers). In addition, Dr. Wooley mentioned NSF's interest in the use of new technologies to advance research on corn and other agricultural plants and reported that NSF currently supports an RFLP effort in maize for $300,000 per year.

Dr. Wooley stated that NSF is committed to technology transfer and to maintaining a "pipeline" of future scientists. Funds that support the biological research centers and the science and technology centers will also support multidisciplinary and interdisciplinary training activities at these facilities.

Discussion focused on specific details related to the science and technology center that was recently funded. Dr. Zinder noted that the administrative organization of the center may serve as a paradigm for future centers that may be established by the human genome program. The question of how to evaluate the progress of such centers was raised, and Dr. Wooley stated that the peer review system would play an important role in this area.

Dr. Robert M. Faust discussed the U.S. Department of Agriculture's (USDA's) interest in the human genome effort. He stated that USDA considers mapping of plant genomes a high priority and funds mapping studies on corn and soybeans at $750,000. He also summarized recent advances in plant genetic research: Construction of RFLP marker genes has begun for corn, tomatoes, cabbage, and other crop plants; researchers have mapped three genes that control drought tolerance, five genes that have a major impact on flavor in tomatoes, and three genes involved with insect resistance in tomatoes; and a group of genes influencing yield in corn has been identified. Dr. Faust commented that USDA is interested in the human genome project primarily because of the technology that may result.

Dr. Faust also discussed the USDA Plant Genome Research Conference, which was convened in December 1988 to plan an initiative for mapping and sequencing the genomes of plants important to agriculture and forestry. Dr. Faust noted that the report developed at this conference is still in the draft stage; however, it mentioned development of a foundation of knowledge for plant science research as one of the initiative's goals. In addition, the draft report identified several criteria for selecting plants to map and sequence, including the following: Economic impact and domestic importance, maximum information transfer to other plant species, and provision of basic and fundamental insight. The draft report also mentioned features that should be incorporated in a national information network to support plant genome research: The network should be user friendly; should allow for all types of maps, quantitative information, and raw data; should be kept current through frequent updates and include a mechanism for data validation; and should be free or relatively inexpensive to users. Participants at the conference also recommended that an Office for Plant Genome Research be created at USDA to coordinate the Department's activities with other genome-related projects, such as the human genome program at NIH.

During the discussion period, several participants commented that USDA could aid the human genome effort by conducting mapping and sequencing of the genomes of agriculturally important organisms for comparative purposes.

The final segment of the first day of the meeting focused on international activities. Dr. Victor A. McKusick described the Human Genome Organization (HUGO), which was established in 1988 to facilitate international collaboration in the mapping and sequencing of the human genome. HUGO will also coordinate the efforts of investigators involved in mapping and those who work on sequencing and cloning. In addition, HUGO will coordinate research among investigators working on different species. Dr. McKusick stated that HUGO receives partial funding from HHMI but hopes to obtain multigovernmental as well as private funding.

Dr. McKusick reported that HUGO plans a wide variety of activities, ranging from international training programs to development of guidelines on ethical, social, legal, and commercial issues surrounding the human genome project. It will arrange for the exchange of data, samples, and technology relevant to genomic research and will assist in the organization and funding of the Human Gene Mapping Workshops.

There was brief discussion regarding inclusion of Third World countries in HUGO. Dr. Watson felt that, in order to keep costs down, representation in HUGO should be limited to countries that are actually doing the mapping and sequencing, rather than those interested only in the results. The Committee members stated that anyone who wishes to should be able to contribute to the human genome project.

Dr. Maynard V. Olson discussed Japan's endeavors in the area of human genome research. He reported that the Japanese have focused heavily on sequencing projects, in contrast to the approach generally taken in the United States, which is to concentrate on linkage and physical mapping, with a phase-in of sequencing as technological improvements materialize. Specifically, Japanese researchers have completed the sequence of chloroplast DNA and are currently coordinating a major effort to sequence the *E. coli* genome.

Dr. Olson noted that the interagency coordination situation in Japan is very complex, with various ministries, including the agriculture, education, and technology ministries, involved in mapping and sequencing projects. Nevertheless, Japan's hierarchal system lends itself to concentration on programmatic goals. He suggested that observation of Japan's coordination strategies may provide insights relevant to management of the human genome program in the United States.

During the discussion following this presentation, one participant noted that another aspect of Japan's management strategy has been successful coordination between academic and industrial laboratories, particularly with regard to data base management and software development.

Dr. Mark L. Pearson summarized the United Kingdom's activities in the area of technology development. He reported that British scientists have developed new techniques for the detection of sequence polymorphisms, i.e., polymorphisms between restriction sites. In addition, they have developed microsequencing methods for determining sequences at the end of restriction fragments, making it possible to generate large amounts of information that can facilitate the ordered overlapping of DNA sequences. In an effort to develop megabase-scale sequencing methods, British scientists are employing transputer technology as well as parallel processing methods that can handle

large blocks of sequences. Dr. Pearson also discussed the United Kingdom's large-scale mapping and sequencing projects, which have focused on the human genes CF, NF, and HD; viral genomes, including cytomegalovirus; plants, including *Arabidopsis*; and bacteria.

There was brief discussion following this presentation, during which the participants reiterated the need for international cooperation and sharing of data. They predicted a major role for HUGO in facilitating international communication and planning in genomic research.

Dr. Peter L. Pearson provided background on the European Economic Community's (EEC's) Predictive Medicine Program, which is planning a human genome analysis component. He reported that a working group consisting of two representatives from each of EEC's member states has been created to develop the program. This group has since been divided into the following six study groups: physical mapping, genetic mapping, advanced technologies, data base management, ethics, and training. He noted that EEC's human genome program plans to offer training fellowships that will allow less technologically advanced European countries to participate in and benefit from the program.

Dr. Pearson stated that the European approach to organization of the human genome effort involves coordination among laboratories through a network, rather than consolidation of projects in centers. It is anticipated that CEPH will form the center of the network, with which 20 European laboratories will be affiliated. Dr. Pearson also noted that a shared-costs financing arrangement will exist between EEC and laboratories that wish to participate in its human genome program.

During the discussion period, Dr. Pearson stated that coordination of effort among numerous laboratories would not preclude the possibility of two laboratories' working on the same task; in fact, he felt that a certain amount of overlap would be desirable.

There followed a general discussion of the first day's presentations. In an attempt to define the extent of interfacing activities that would be appropriate between the human genome program in the United States and similar programs in other countries, Dr. McKusick stated that the most important aspect of this interface will be exchange of data and biological resources. Such exchange would enable investigators to work more efficiently and would help to minimize duplication of effort.

Several participants sought clarification on the extent to which NIH plans to support human genome research abroad. Dr. Jordan responded by stating that NIH accepts applications for funding from foreign sources and has recently funded two foreign projects. Dr. C. Thomas Caskey commented that it is too early to contemplate major foreign funding and that resources must be kept within the United States until the U.S. program is well established. However, he stated that a small amount of money for "people movement" and collaboration between research groups would go a long way toward promoting cooperation and communication and, hence, acceleration of research.

Dr. David Botstein remarked that a spin-off of the U.S. human genome program is the long-term benefit that will be provided by the training component. A group of well-educated scientists will be poised to make use of the advances

and discoveries that result from the program. Dr. Olson concurred with the emphasis on human resources and stated that failure to address this issue adequately will lead to an "obsolete scientific personnel situation" in the future. He also cautioned against viewing acquisition of a data base containing the complete sequence of the human genome as the end point of the program. He stated that obtaining a reference sequence of the human genome will elevate the analysis of primary sequence data to a much more prominent position in biology, and predicted that state-of-the-art capability in this activity will be a prerequisite to being broadly competitive in basic research and biotechnology.

Dr. Zinder agreed with these comments and reiterated his earlier statement that sequencing of the human genome will be an "endless adventure." Following these remarks, he adjourned the first day of the meeting.

DAY 2

Dr. Zinder began the second day of the meeting by emphasizing the importance of the Advisory Committee to the human genome program. Next, he invited discussion of the biological scope of the program. The participants discussed the value of studying the genomes of model organisms at length. They agreed that the Committee should encourage such research for a number of reasons, e.g., advancement of sequencing technology and elucidation of the meaning of sequence information. They agreed in general that efforts should concentrate on five or six model organisms, preferably those for which genetic and physical mapping already have a strong start; however, several of the participants cautioned against a rigid definition of which organisms should be studied.

Dr. Watson raised the issue of the extent to which research in medical genetics should be supported by the human genome program. Dr. McKusick commented that the program is not capable of funding studies of all diseases with a substantial genetic factor. He felt that program support, at this stage, should be limited to studies on mapping of diseases that are both prevalent and caused by single-gene mutations. Several participants felt that projects in other diseases could qualify for program funding if they included the potential for technological or methodological advancement.

In terms of the technical scope of the program, the participants felt that the Committee should focus heavily on development of new technology and on making resources more available to the scientific community. Dr. Caskey emphasized the need to encourage investigation of the use of molecular biological tools in the field of cytogenetics.

The need for construction of new research space, particularly in connection with the establishment of centers, was discussed, and it was strongly urged that the Office of Human Genome Research should seek authorization to fund such construction.

Training was emphasized as an area in need of immediate attention, since the lead time required for setting up programs is likely to be lengthy. Several participants stressed the need for a forum in which students trained in technology-related disciplines, e.g., computer science, could receive training in biology, which would allow development of technological advances focused on

biological applications. Dr. Luther S. Williams of NIGMS announced that the Institute has recently launched a new training program in biotechnology that will employ an interdisciplinary, collaborative format.

Following this discussion, a working group on training was proposed, with Dr. Joseph L. Goldstein (chairman) and Dr. Leroy E. Hood as members.

Discussion moved to the topic of program management, and the advantages and disadvantages surrounding the creation of centers were debated. Dr. Olson commented that, since the Committee would not be able to micromanage numerous genome-related projects conducted by individual grantees, establishment of centers would probably be the best way to achieve programmatic goals. However, he stressed that such centers should be small and somewhat redundant in their activities, so that competition among them would insure progress. Dr. Phillip A. Sharp also supported the development of centers and noted that, in addition to providing a stimulating environment that promotes interaction among individuals, centers also provide a focus for attracting new resources.

Other issues raised in relation to centers were center-based training activities and industry participation. Dr. Zinder then proposed a working group on centers, with Dr. Phillip A. Sharp (chairman), Dr. Maynard V. Olson, and Dr. Cecil B. Pickett as members.

There was further discussion on program management, during which Dr. Watson stated that the relationship between the Office of Human Genome Research and NIGMS must be close and friendly but that the power to shape the human genome program through funding decisions should reside with the Office and its Advisory Committee. Dr. Kirschstein assured Dr. Watson and the Committee that NIGMS stood ready to assist them in achieving program goals and would carry out their decisions.

Next, Dr. Zinder moved to the topic of ethics. He estimated that, because of the high visibility of the human genome program and its potential impact on issues such as abortion and genetic screening, considerable program resources would be allocated for ethics-related work. He noted that the working group on ethics would become an important interface between the program and the public. Following these comments, he asked Dr. Nancy S. Wexler to chair the working group on ethics and also requested that Dr. Victor A. McKusick serve on this group.

Finally, a working group on data bases, which would examine extant data bases, formulate strategies for maximizing their usefulness, and examine the need for new data bases, was proposed. Dr. David Botstein was named chairman of this group. Drs. Jaime G. Carbonell and Mark L. Pearson were also appointed to this group, and Dr. George F. Cahill, Jr., was invited to serve *ex officio*.

After thanking the Committee members and the participants for their assistance in the preliminary efforts to launch the human genome project, Dr. Zinder adjourned the meeting.

I hereby certify that, to the best of my knowledge, the minutes and attachments are accurate and complete[1].

Norton D. Zinder, Ph.D.
Chairman

Elke Jordan, Ph.D.
Executive Secretary

[1] These minutes will be formally considered by the Committee at its next meeting, and any corrections or notations will be incorporated in the minutes of that meeting.

Speakers

PROGRAM ADVISORY COMMITTEE
ON THE HUMAN GENOME

January 3 and 4, 1989

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Roster

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ON THE HUMAN GENOME

January 3 and 4, 1989

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PROGRAM ADVISORY COMMITTEE
ON THE HUMAN GENOME

January 3 and 4, 1989

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Lisa White
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Pam Zurer
Chemical & Engineering News

Second Meeting

Program Advisory Committee on the Human Genome

June 19-20, 1989

Ramada Inn
Bethesda, MD

MINUTES

INTRODUCTION

The Program Advisory Committee on the Human Genome convened in Bethesda, MD, on June 19-20, 1989, to hear reports on genome-related activities at the National Institutes of Health (NIH) and other national and international agencies; to hear reports from the working groups established at the January 1989 meeting of the Committee; and to discuss the formulation of a plan for conducting the human genome project, which is due to be submitted to Congress in March 1990. The following Committee members attended:

Norton D. Zinder, Ph.D., Chairperson
Elke Jordan, Ph.D., Executive Secretary
Bruce M. Alberts, Ph.D.
David Botstein, Ph.D.
Jaime G. Carbonell, Ph.D.
Joseph L. Goldstein, M.D.
Leroy E. Hood, M.D., Ph.D.
Victor A. McKusick, M.D.
Maynard V. Olson, Ph.D.
Mark L. Pearson, Ph.D.
Cecil B. Pickett, Ph.D.
Phillip A. Sharp, Ph.D.
Nancy S. Wexler, Ph.D.

The following liaison members also attended:

Benjamin J. Barnhart, Sc.D.
George F. Cahill, Jr., M.D.
C. Thomas Caskey, M.D., F.A.C.P.
Mary E. Clutter, Ph.D.
Irene Eckstrand, Ph.D. (substituting for Ruth L. Kirschstein, M.D.)
Jerome Miksche, Ph.D. (substituting for Robert M. Faust, Ph.D.)

Dr. Miksche was unable to attend the second day of the meeting. The Committee roster and lists of speakers and others who attended are attached to these minutes.

MONDAY, JUNE 19, 1989

Welcome and Administrative Remarks

Dr. Zinder welcomed the Committee members and participants, particularly Dr. Michael Kemp from the Medical Research Council in the United Kingdom, Dr. John Rodgers from the National Research Council in Canada, and Drs. Bronwen Lodei and Peter Pearson from the Commission of the European Community. He noted that there is worldwide interest in the human genome initiative, although there is also some opposition to it. He commented on the important role of the Committee in addressing concerns of both the research community and the public over issues such as diversion of funds from other important research and social/religious implications.

Dr. Watson's introductory remarks included a brief summary of the National Academy of Sciences' 1988 report "Mapping and Sequencing the Human Genome," which stated that initial efforts should focus on mapping; on model organisms to aid interpretation of data; and on procedures to reduce costs of sequencing. He noted that, currently, sequencing costs approximately $5 per base pair; reduction of the cost to 50 cents per base pair is an objective. He also indicated that, with respect to mapping and sequencing, the unit of activity will probably be the chromosome. (This issue was discussed at length on the second day of the meeting.) He further speculated that, since many investigators in the field of genetics are "disease hunters," it may be difficult to encourage research on all the chromosomes.

Dr. Watson stated that mapping and sequencing of the human genome is "big science" in terms of the magnitude of data produced, making the participation of computer specialists knowledgeable in the field of biology essential. He noted the importance of construction to the program, so that institutions capable of conducting high-quality genome research can be given additional space and facilities in which to accomplish the work. He also stressed the importance of including a strong ethics component in the project, since the public will make decisions on how information about the human genome is used.

Dr. Jordan reported that a proposal has been submitted to the Secretary of the Department of Health and Human Services (DHHS) to elevate the Office of Human Genome Research (OHGR) to an organizational unit with funding capabilities. (This proposal was approved by the Secretary subsequent to the meeting.) She introduced new staff members who have joined the Office: Mr. James Vennetti, Acting Executive Officer; Ms. Michelle Coleman, Committee Management Officer; Dr. Bettie Graham, who will be in charge of the research grants branch; Dr. Jane Peterson (not present at the meeting), who will be responsible for the centers program; and Ms. Linda Engel, who will be in charge of the review component. Dr. Jordan also discussed the NIH's attempts to obtain authority for construction and noted that a legislative proposal to allow this has been submitted to the DHHS.

Approval of Minutes

Following these introductory remarks, Dr. Zinder called for a motion for approval of the minutes of the first Committee meeting, which was held on January 3-4, 1989. The motion was made and seconded, and the minutes were unanimously approved pending correction of the text concerning the European Community's (EC's) approach to organization of the human genome project (page 10, third paragraph). (The statements that laboratories will be coordinated "through a network" and that "CEPH [Centre d'Étude du Polymorphisme Humain] will form the center of the network" were incorrect; in fact, numerous networks will be established, and CEPH is anticipated to be a center in one such network.) Dr. Zinder then announced the dates of upcoming Committee meetings, which are as follows: December 4-5, 1989; June 18-19, 1990; and December 3-4, 1990. Dr. Watson noted that Committee

members who had been appointed originally for 1-year terms have been nominated for additional 4-year terms, and Dr. Jordan added that approval of these extended terms is pending and expected.

Reports of Significant Events

The meeting continued with reports of significant events related to the human genome program. Dr. Mark Guyer described the main features of the following meetings:

- An NIH meeting entitled "Human Genetic Maps," organized by the OHGR, was held on February 16-17, 1989. The purpose was to explore ways to reconcile and further develop linkage maps and ways to relate these to developing physical maps. Dr. Guyer noted that significant improvement in mapping techniques, including development of new types of polymorphisms to be used for linkage analysis, was evident from discussions at this meeting. Dr. Peter Pearson added that an important recommendation resulting from the meeting was for large research projects as opposed to "cottage industry." He stated that the participants also discussed the speed with which data should enter the public domain and added that compiling data from numerous laboratories can be a slow, difficult task.

- The Chromosome 11 Workshop, which took place on March 22-23, 1989, was sponsored by the National Institute of General Medical Sciences (NIGMS) and organized with the help of the chairpersons of the Chromosome 11 Committee of the Human Gene Mapping Workshops. One goal of the Workshop was to encourage the development of a physical mapping community for investigators involved in work on this chromosome in order to facilitate the exchange of information and materials. Approximately 80 percent of the laboratories involved in work on chromosome 11 sent representatives to the Workshop.

  A similar workshop on chromosome 16 was held early in June 1989. As with the Chromosome 11 Workshop, the participants appeared enthusiastic about opportunities to collaborate. Approximately six more workshops of this type are planned, as well as another chromosome 11 workshop, which is scheduled for the spring of 1990.

Dr. Guyer noted that these meetings on mapping helped to "move the field along" and provided opportunities for resolution of common problems. He then discussed several additional meetings:

- The *E. coli* Database Workshop, held in March 1989, was the first in a series being sponsored by the National Library of Medicine (NLM) and the National Science Foundation. This workshop brought molecular geneticists and computer scientists together with the goal of defining problems and needs in the field of *E. coli* biology that might be addressed by the development of databases. There will be a followup meeting in late June 1989, where these needs will be prioritized and the computer scientists will determine which can be met by existing technology and which will require new developments.

  Dr. Guyer also noted that genome-related databases for *Drosophila* and *C. elegans* have been discussed at recent national meetings, and workshops similar to the one on the *E. coli* database are planned.

- A workshop entitled "Nomenclature for Physical Mapping," which met on April 13-14, 1989, was cosponsored by the U.S. Department of Energy (DOE), the Howard Hughes Medical Institute, and the NIH. This meeting was the first in a series intended to discuss specific areas related to the management of physical mapping data. One of the conclusions of the workshop was that the name assigned to an element, such as a probe or a contig, should be unique and immutable and

should not contain biological information; rather, the name should simply identify the element. The final draft of the workshop's recommendations will be widely circulated in the scientific community in order to obtain feedback prior to a followup workshop to be held in midautumn 1989, when the final recommendations will be prepared. The recommendations will then be published in scientific journals, and journal editors will be encouraged to assist in their implementation.

Dr. Clutter briefed the Committee on the results of the May 30, 1989, *Arabidopsis* Workshop, sponsored by the National Science Foundation to discuss the feasibility of mapping and sequencing the *Arabidopsis* genome. The participants reached the consensus that the project should be undertaken. Dr. Clutter added that a meeting is scheduled for July 20, 1989, at Cold Spring Harbor, NY, to discuss a plan for the project, and that there will be an international meeting (the International *Arabidopsis* Meeting) in October 1989. She estimated that 5 to 10 years and a total of approximately $70 million will be required to complete the project. Dr. Watson noted that the United Kingdom plans to spend approximately $12.5 million over a 3-year period for research on *Arabidopsis*. He also commented on the fact that plant research in the United States has been poorly funded compared to animal research and urged greater support of plant research in the United States. He also pointed out the need to plan U.S. research on *Arabidopsis* in context with the EC's efforts.

Dr. Jerome Miksche commented that the U.S. Department of Agriculture (USDA) is also interested in participating in the *Arabidopsis* genome project. He then highlighted a variety of agricultural challenges that must be addressed, including water quality, climatic changes, sustainable agriculture, the need for new crops, new uses for crops and forest products, food quality and safety, germ plasm enhancement, and the need for alternatives to chemical pesticides, and he stressed the necessity of finding genes associated with these activities. He commented on the meager funding of plant genome research and then discussed the implementation of two recommendations of the USDA Conference on Plant Genome Research, held on December 12-14, 1988: (1) The establishment of the USDA Office of Genome Mapping and (2) the formation of a coordinating committee for science and technology. Dr. Miksche gave a detailed description of the composition and function of this committee, which comprises the following six subgroups: computer and data management; genetics and breeding; restriction fragment length polymorphism (RFLP) mapping and gene tagging; molecular genetics; physiology and biochemistry; and biotechnology endpoints. He stated that this coordinating committee is scheduled to meet on August 30-31, 1989, to refine the goals and scope of the USDA's plant genome projects and to address questions such as the following: Is more information needed on physiology, biochemistry, and underlying agricultural problems, e.g., water quality, drought, and other environmental stressors? Should research focus on specific genetic traits? Should the project define specific plants as model systems? What funding mechanisms are appropriate? Should facilities and technology development be funded? He added that the USDA's plant genome efforts will span a 10-year timeframe and will cost over $500 million. He emphasized that awards for projects will be made through a peer-reviewed grant program available to all scientists, extramural and intramural.

During discussion of this presentation, Dr. Joan Lunney of the Agriculture Research Service, USDA, mentioned that the USDA also has an active animal science component interested in genome research, and Dr. Miksche agreed that this will be a growing area in the USDA.

Dr. Olson described an international meeting held in March 1989 in Japan that discussed molecular approaches to the human genome. He reported that there was extensive discussion of model organisms, mapping and sequencing technology, human diseases, and general molecular genetics. He offered his perceptions on the status of genome analysis in Japan, stating that the existence of an advanced, monolithic plan is a misperception in the United States. He noted that basic research in biomedical science has been severely underfunded in Japan, so diversion of scarce resources is a major concern there. He also discussed Japan's *E. coli* sequencing project, an organized pilot effort that funnels support for research into academic laboratories interested in this work. He then described a

Japanese demonstration project geared toward streamlining the sequencing process by using the polymerase chain reaction (PCR) for the preparation of sequencing templates. He stated that this project is relatively small but that contracts with industry will be the next step if scaleup is warranted. He added that review of the success of this project will be rigorous.

Dr. Olson proceeded to summarize results of the second Cold Spring Harbor meeting organized to discuss mapping and sequencing of the human genome, noting that a "powerful coalescence of excitement" toward the project and "solid evolutionary improvement in techniques" were evident. He stated that, although there was no sign among any of the existing projects on chromosomes of the development of convergent physical maps, it was clear that better methods of ordering the various entry points for physical mapping of the genome, e.g., short probes, contigs, etc., along the chromosomes have been developed. Dr. Charles Cantor of Columbia University and the Lawrence Berkeley National Laboratory added that the Human Genome Organization (HUGO) Executive Committee, which was polled following the workshop, unanimously endorsed an annual meeting of this type, to be held at Cold Spring Harbor.

Dr. McKusick discussed the Human Gene Mapping Workshops, the first of which was held in 1973 and attended by 70 persons. He stated that these workshops are currently held every 2 years for the purpose of collating the accumulated information on the locations of specific genes on chromosomes. They focus on data but have plenary sessions on methodology and applications. There are individual chromosome committees as well as committees on generic topics, e.g., nomenclature. He stated that the committee model has been useful and may indicate a need for permanent committees to collect this information on an ongoing basis.

Dr. McKusick noted that 700 persons registered to attend the 10th Human Gene Mapping Workshop (HGM 10), which was held in mid-June 1989. He estimated that, based on data from this meeting, approximately 1,700 genes have been assigned to chromosomes or chromosome regions. He added that this workshop ran smoothly due to the preliminary data collection and planning accomplished at HGM 9.5, which took place in September 1988. He also attributed the success of HGM 10 partially to efficient use of computers and dissemination of abstracts to the committee chairpersons prior to the meeting. He stated that HUGO will provide the administrative basis for future HGM Workshops as well as for mouse gene-mapping workshops.

Dr. McKusick also updated the Committee on recent HUGO activities, stating that the Organization is incorporated in Geneva and has established three continental offices: one in London, one in Bethesda, and one in Osaka. He reported that HUGO has 220 elected members, including Dr. George Cahill, who was recently elected treasurer.

Dr. Barnhart reported on activities of the DOE regarding the human genome initiative. These activities included development of a quarterly newsletter and an electronic bulletin board to facilitate communication between the DOE and its contractors and grantees. He reported that there have been three Steering Committee meetings, the third having been held in April 1989. He noted that one of the topics of discussion at that meeting was the establishment of the joint DOE/NIH planning subcommittee. In addition, the Steering Committee decided to conduct a workshop where contractors and grantees can provide the DOE with an overview of their projects. This workshop is scheduled for November 3-4, 1989.

Dr. Barnhart also stated that the Steering Committee has established a working group to consider issues related to sharing of biological materials, particularly the distribution of arrayed cosmid libraries (which are in demand). Major questions need to be answered: Who should distribute these libraries, and how can the costs of distribution be recovered? Dr. Anthony Carrano, of Lawrence Livermore National Laboratory and the chairperson of this working group, explained that these libraries have not yet been characterized, and good quality control data have not yet been established. He added that the

libraries have been distributed to test laboratories but that it has been difficult, in some cases, to obtain feedback from them.

Dr. Watson added that he has endorsed a proposed brief moratorium on the distribution of arrayed cosmid libraries until a policy addressing these problems can be developed. Several Committee members objected to the proposal, however, stating that providers of research materials have an obligation to provide other investigators with the materials on which their research conclusions are based. They urged that any proposed limitations on distribution should be approached in a sensitive manner. Dr. Watson assured the Committee that its opinions on this issue would be taken into account. (This topic was discussed further on the second day of the meeting.)

Dr. Peter Pearson described recent activities of the EC's genome program. He stated that the program's final report was approved by the EC's Committee for Medical Health Research and that funding is expected in December 1989. He specifically mentioned the report's recommendation that physical mapping data become part of the public domain 1 year after being generated—a requirement that will be established by contract. He also noted that the genome program will eventually have the same organizational status as the EC's medical health research program and therefore will come under "new management." Dr. Pearson added that the EC's genome program contains an ethics study group, which will be a standing committee that will evolve with the program. He mentioned that Dr. Wexler, chairperson of the NIH Program Advisory Committee's ethics working group, will attend the next meeting of the European counterpart. In response to a question from the Committee concerning whether the EC's genome program would consider helping to fund programs involving foreign (e.g., Japanese or U.S.) investigators in conjunction with European teams, Dr. Pearson stated his belief that multigovernmental funding would strengthen genome-related projects.

National Center for Biotechnology Information

Dr. David Lipman updated the Committee on the efforts of the National Center for Biotechnology Information of the National Library of Medicine (NLM) to integrate several databases containing information on *E. coli*. These databases include a working relational database for various strains stored at the *E. coli* Stock Center, a 2-D gel electrophoresis database, and a dataset that integrates genetic and physical maps of *E. coli*. He also described the Center's efforts to develop flexible, general purpose software tools that will allow investigators to design software packages for their own needs. In response to a question from the Committee on the strategy for making software tools available to users, he emphasized that outreach is a major concern at the NLM. He stated that software developed at the NLM has been demonstrated at Federation of American Societies for Experimental Biology (FASEB) and Gordon Conference meetings and that a similar approach may be taken with the molecular biology software tools. However, he emphasized that key individuals at institutions are often helpful in communicating the availability of useful tools.

Dr. Lipman also discussed a proposed project to develop a database of unpublished yeast genome sequences to be used for conducting database searches. If this project is found to be feasible, it may become a general resource at the NLM for other organisms as well.

NIGMS Report

Dr. Irene Eckstrand reported that the NIGMS plans to spend over $10 million to fund new grants by July 1, 1989. Awards to be funded are distributed as follows: 17 for mapping (both genetic and physical), including 10 for human chromosomes and 7 for model systems; and over 20 for technology development, including 5 for sequencing technology, 3 for computer technology, and 16 for other technological innovations. She stated that the NIGMS also plans to award supplements to stimulate the

development of physical mapping databases for specific chromosomes. She added that remaining monies would be used to support OHGR activities and special projects.

Following this presentation, there was discussion regarding the priority scores of the applications that had been received. Dr. Eckstrand stated that awards were made on the basis of the importance of the projects to the human genome program as a whole (not rigidly on the basis of priority scores). She estimated that approximately one-third of the proposals received were funded. Dr. Caskey commented that Dr. Watson's proposal of limiting the term of genome-related grants to 3 years had been presented to the National Advisory General Medical Sciences Council but was not accepted; the consensus of the Council was to adopt the recommendations of the study sections concerning individual grants.

Reports From Working Groups: Center Grants, Training Grants, Databases, and Ethics

The meeting continued with reports from the working groups established at the January 1989 Committee meeting. Dr. Sharp presented the recommendations of the working group on center grants, which consisted of Drs. Richard Axel, Ronald Davis, Daniel Nathans, Maynard Olson, Cecil Pickett, and Dr. Sharp himself as chairperson. The group proposed that the NIH use the core center grant mechanism (P30) to support the infrastructure for genome research at qualifying institutions. He stated that the center grant envisioned by the working group would be similar to that of the National Cancer Institute and would have the following eligibility requirements: The institution must have significant ongoing research on genome-related projects and a specific long-term objective, e.g., physical mapping of particular chromosomes; it must be domestic and can be academic, nonprofit or for profit; it should preferably be a single institution, although consortia will be eligible; and it should be willing to collaborate with industry, since the private sector has resources that may help achieve the goals of the human genome program. He added that the working group recommended a 5-year term for this type of grant, with review 3 years after initiation to allow for a 2-year phaseout of unsuccessful centers. The Committee accepted these recommendations.

Dr. Sharp stated that core centers funded by this mechanism would provide the following: a stable environment for large-scale undertakings, which would include projects funded by other NIH mechanisms as well as other sources; opportunities for interdisciplinary collaboration, rapid dissemination of information, and sharing of resources; an administrative structure to facilitate collaboration with the private sector and recruitment of new investigators; and core facilities, e.g., for DNA and protein sequencing.

Dr. Sharp estimated that between $5 and $10 million will be required to operate each center but emphasized that the centers will attract funds from sources other than the human genome program.

Dr. Goldstein discussed the recommendations of the working group on training grants, which included the following members: Drs. Donald Brown, William Gelbart, Joseph Goldstein (chairperson), Leroy Hood, Gene Myers, and Luther Williams (*ex officio*). The group suggested three types of training grants in genome research: predoctoral institutional grants, individual postdoctoral grants, and senior fellowships for established investigators. The group recommended that two-thirds of the 185 training slots proposed in the FY 1990 budget for the human genome program should be for predoctoral institutional training, although Dr. Goldstein noted that the distribution would depend somewhat on the numbers of applications submitted for each type of grant. Dr. Goldstein stated that the theme of all these grants should be the transfer of information from one field to another, e.g., from computer science to molecular biology and vice versa. The Committee accepted these recommendations. There followed a discussion of the importance of talented technicians to the human genome initiative, during which several Committee members noted that there is a need to support good programs that train such individuals. Dr. Zinder asked the working group to reconvene to consider whether the human genome program should support training for career-level technicians.

In response to a question concerning the relationship between the human genome program's proposed training grants and those of the NIGMS, Dr. Jordan replied that there may be some overlap between the two agencies but that the genome program's training grants would focus on interdisciplinary components. She added that the OHGR would coordinate training activity closely with the NIGMS.

Dr. Botstein, chairperson of the database working group (Drs. George Cahill* (*ex officio*), Jaime Carbonell, and Mark Pearson) presented the group's recommendations. The database working group agreed that, in the short term, the scientific community needs a minimal database containing all published nucleotide and amino acid sequences, with information no more than 1 month behind the published literature. Dr. Botstein stressed that this database would provide minimal annotation but would use a format that would allow the data to be incorporated into future databases. Dr. Lipman commented that the NLM is currently developing an experimental "backbone" database similar to what the working group proposed, using information from MEDLINE and working with experts from GenBank and the Protein Information Resource. He added that multiple approaches for information retrieval are planned for this database and that linkage with other databases is also a goal. Dr. Botstein stated that the working group would prepare recommendations on long-term needs in time for the December 1989 Committee meeting. The Committee accepted these recommendations but asked the working group to consider issues related to administration of the sequence databases, specifically the roles of the NLM and the OHGR. In this regard, it was requested that the NLM prepare a position paper describing how it envisions its role in the genome project for review by the working group and the full Committee. There was also agreement that the database working group of the NIH Program Advisory Committee on the Human Genome would work with the DOE's informatics group and possibly an international group when funds from Europe become available.

Dr. Wexler discussed the activities of the ethics working group, whose members included Drs. Jonathan Beckwith, Robert Cook-Deegan, Patricia King, Victor McKusick, Robert Murray, Thomas Murray, and Dr. Wexler as chairperson. Dr. Wexler stated that the working group plans a series of interdisciplinary workshops to focus on specific issues related to the ethical, genetic, social, and legal implications of the human genome initiative for society. The first such workshop, planned for November 1989, will recommend the overall research agenda and attempt to identify issues that need to be addressed. The working group also recommended that public testimony and town hall meetings be held to "take the temperature" of the public with regard to the human genome program. She stated that the Alliance of Genetics Support Services will provide assistance in setting up these meetings.

Dr. Wexler reported that, in March 1989, she had sent a letter to various professionals involved in law, ethics, and genetics soliciting their opinions on genetics issues. She indicated that, overall, the letters she received in response were positive and highlighted the following points:

- The letters urged the Committee to consider history and precedent in order to avoid repeating the mistakes of the past. They alluded to the experience of Nazi Germany and the history of social Darwinism in the United States.

- They mentioned the unique nature of the human genome project, which will result in the capacity to predict a disease process in an individual.

- The letters advised making use of the media in order to let both the professional community and the general public know about the program and its activities.

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*Dr. Peter Pearson substituted for Dr. Cahill at the meeting of this working group.

- They raised questions concerning whose genome will be sequenced: Will there be differences between ethnic and racial groups? Will there be generalizability across groups?

- They pointed to the common understanding of "good" and "bad" genes that could cause individuals or disorders to be seen as stereotypes, whereas genetic problems should be seen as part of the general variety of human features.

- They cautioned against genetic reductionism (trivialization of the complexity of genetics—which might lead to a deemphasis of the impact of free will and a tendency toward genetic determinism).

- They raised issues of privacy and confidentiality, particularly for database families, such as the CEPH families, who are being used for genetic mapping studies. For example, if an individual is found to be at high risk for a particular disorder, should there be a provision for notifying the individual?

- The letters noted that there will be a lapse between the ability to screen for genetic disorders and the ability to treat these disorders. They advised the human genome program not to promise too much: while molecular biology offers a hopeful avenue toward treatment, cures for genetic disorders will not be available immediately.

- They pointed out insurance issues; e.g., will an insurance company have to pay benefits for an affected infant whose mother knew about the genetic disorder through prenatal genetic screening but chose to carry her pregnancy to term?

- They discussed the problem of how to integrate new genetic knowledge into mainstream medicine and the concomitant implications for malpractice issues.

- They raised the possibilities of stigmatism at the workplace and job discrimination against those prone to disorders.

- They expressed the concerns of handicapped rights groups, who are already sensitive to society's perceptions of handicapped persons, including the concern that a program to predict and prevent genetic handicaps in a sense makes the statement that people with these types of handicaps are not welcome in our culture.

Dr. Wexler stressed that, because the human genome initiative will lead to increased genetic screening capabilities and the ability to predict diseases in individuals, the program must emphasize the hopeful perspective that knowledge of the molecular basis of a disease can lead to treatment possibilities. She also emphasized that the budgets of the categorical Institutes of the NIH must be kept commensurate with that allocated for sequencing of the human genome, since these Institutes will play a major role in making use of the knowledge gained through the genome effort.

Dr. Jordan provided an overview of the types of enquiries that have been received in response to a program announcement, published on March 3, 1989, requesting proposals for research on ethical and legal issues relevant to the human genome program. She stated that the interests of the applicants varied widely, ranging from standard ethical investigations to studies of historical precedents, genetics and the law, and genetics and religion. She added that there were also applications dealing with educational approaches and conferences. She indicated that the OHGR looks forward to input from the ethics working group on specific areas on which the Office should focus.

Establishment of New Working Groups

Dr. Zinder then named the NIH representatives to the NIH/DOE joint subcommittee and planning group as follows: Drs. David Botstein, Jaime Carbonell, Maynard Olson, Mark Pearson, Nancy Wexler, and Norton Zinder. This joint subcommittee will participate in a planning retreat to work on a proposal for the overall strategy of the human genome initiative to be held this summer. He also listed the names of those anticipated to represent the DOE on this subcommittee: Drs. Sheldon Wolff, Mary Lou Pardue, Leonard Lerman, Charles Cantor, Anthony Carrano, and George Bell. Dr. Zinder noted that Drs. Lipman and Caskey, among others, would be invited to participate as consultants.

Other New Initiatives: Equipment, Intramural Research, and Physical Mapping Databases

Dr. Jordan announced that the OHGR proposes to solicit applications for supplementary funds for the purchase of equipment. Any NIH grantee working on the genome project may apply, but there must be at least 2 years of funding remaining in the grant at the time of submission of the application. (A Committee member commented on the large number of 3-year grants that have been awarded and suggested that only 1 year of remaining funds should be required.) Since this solicitation is designed to address the gap in funding for medium-priced instrumentation, the limit per item or per grant will be $100,000. Dr. Guyer briefly described a proposed Request for Applications (RFA) to support initial development of databases designed for physical mapping data. The Committee supported both these initiatives.

Dr. Jordan described a proposed NIH intramural research program whereby intramural investigators may receive funding to expand their activities in order to participate in the human genome program. She stated that, in contrast to a similar mechanism in the NIH AIDS Program, which has funded many small projects, collaboration on large projects will be encouraged. When asked whether applications from intramural investigators would be reviewed by the same study sections that review extramural proposals, Dr. Jordan replied that that would be technically difficult but that a comparably rigorous review for the intramural proposals would be conducted. Several Committee members insisted that the quality of intramural projects must be comparable to that of extramural projects. Drs. Watson and Jordan assured the Committee that every effort would be made to ensure that.

TUESDAY, JUNE 20, 1989

Program Budget

The second day of the meeting began with a brief presentation by Dr. Watson on the human genome program's budget. He indicated that the FY 1990 budget proposed by the President is for $100 million. He stated that the allotment in this budget for research center grants is $10 million, that he hoped this would increase in FY 1991, and that 10 centers would be funded by FY 1991. He added that funds for training will also probably increase in FY 1991. He reported that congressional approval of the budget is expected by the end of the fiscal year.

General Discussion

There was brief discussion on whether the Committee should establish a technology development working group. Dr. Jordan inquired as to whether the Committee perceived impediments in the funding mechanisms for technology development. Dr. Hood replied that attitudes of study section members regarding what constitutes "good science" can cause obstacles in this area and emphasized the need for

reviewers with broad technical backgrounds. The Committee decided to table the topic of a technology development working group for future consideration.

The Committee explored further the proposed establishment of research centers. A Committee member inquired as to whether one or two investigators who wished to manage a large group of investigators (30 or more), all working on a specific project, would be eligible for a center grant. Dr. Watson replied that other mechanisms, e.g., research contracts, would be more appropriate for this type of endeavor. In response to a question from the Committee concerning whether the centers would come under multiple reviews due to the various mechanisms that will contribute funds, Dr. Sharp stated that there would indeed be a bureaucracy and multiple reviews; however, because of the stability of the overall center, the failure of one component would not destroy the whole group. He noted that skilled personnel could be retained over long time periods through support from various sources, including partial support from the center grant, through the core facilities, through R01's (individual investigator grants) or P01's (program project grants), or through direct contracts.

The members discussed the possibility of centers' contracting with industry for services, which raised conflict-of-interest issues. While it was pointed out that most academic institutions have conflict-of-interest policies, the Committee members noted that institutions' guidelines vary greatly. Dr. Jordan stated that the centers would not be allowed to subcontract without approval by the NIH, and Dr. Botstein suggested that perhaps a clear statement of policy from the Committee would be sufficient to address conflict-of-interest concerns. Dr. Zinder requested that several Committee members (Drs. Alberts, Goldstein, Pearson, and Pickett) research the conflict-of-interest and disclosure guidelines at representative institutions and present information for discussion at the next Committee meeting.

New Issues: Model Systems, Rothman Proposal, Gene-Mapping Services, Hybrids, and Others

The Committee discussed at length the proposed revision of a program announcement that is intended to consolidate two broad program announcements and several RFA's that were previously published; to indicate the NIH's interest in technology development applicable to the human genome initiative; and to specify model organisms of special interest to the program, i.e., *E. coli*, *S. cerevisiae*, *D. melanogaster*, *C. elegans*, and *M. musculus*. There was significant debate on whether the wording concerning the model organisms was too restrictive, discouraging valuable research on other organisms. Several Committee members favored broadening the focus and suggested wording such as "*E. coli* and other selected prokaryotic organisms." Others believed that, if projects on many organisms are begun, few will be completed. Still others favored a narrow focus with respect to technology development applications, stating that investigators on these projects should be encouraged to work on one of the model organisms designated in the program announcement. Drs. Jordan and Guyer emphasized that the intent of the announcement was not to exclude research on other organisms but to put the burden of demonstrating the value of such research to the human genome program on the investigator. The consensus of the Committee was to broaden the focus somewhat for now.

Dr. Watson proposed that approximately 25 percent of the program's budget be devoted to physical mapping of model organisms in the initial years of the project.

Dr. Zinder opened discussion of the proposal submitted by Dr. James Rothman, which suggests Government funding of biotechnology companies on a competitive basis to sequence the proteins in novel and complex cellular organelles. Under this proposal, the companies would also provide a number of other services, e.g., complementary DNA cloning of genes encoding the structures' proteins. This work would be performed under the aegis of a principal investigator, who would be able to use the resulting data for experiments. The Committee noted that the proposal would provide for the identification of new functional genes and might attract cell biologists to the human genome program; however, several members cautioned against uncoupling the biotechnology from the "real" biology, and

others were doubtful as to whether the proposed services were vital to the objectives of the program. Dr. Zinder suggested tabling this item to give the members an opportunity to discuss the proposal with colleagues.

The Committee reviewed additional suggestions for support of gene-mapping facilities (submitted by Drs. Robert Sparkes, Thomas Shows, and Timothy Donlon) and resources for the systematic development of somatic cell hybrids (submitted by Dr. David Ledbetter). Pointing out the rapidly changing technology in these areas and the fact that similar work is being carried out on regular NIH grants, the Committee decided against support on a larger scale.

Dr. Zinder reopened the topic of distribution of arrayed cosmid libraries currently produced primarily by the national laboratories of the DOE. Dr. Cantor stated that it would be counterproductive to bar the distribution of ordered arrays at this time. He added that ordered arrays will be distributed after they have been well characterized, although there are still unresolved issues concerning who will bear the costs of distribution and how data developed from use of the arrays will be collected. The Committee supported this view.

Dr. Watson informed the Committee of an opportunity to join British investigators working on sequencing the *C. elegans* genome. He indicated that the project would involve sequencing 15,000,000 base pairs per year and would take approximately 6 years to complete. He suggested that perhaps half this work could be done in the United States, and half could be conducted in the United Kingdom. He estimated that a 3-year grant of approximately $600,000 per year would be needed to explore the feasibility of the project, provided an equal sum was contributed by the United Kingdom. He noted that the Medical Research Council would receive a grant proposal to help fund the United Kingdom's activities on the project, and Dr. Kemp stated that the Council was interested in this collaboration. Several Committee members commented that the project would offer a unique resource and pointed out that the community of investigators working on *C. elegans* already has an outstanding record of sharing information and materials. The Committee unanimously endorsed the concept of joint funding of such an effort.

Units of Scientific Management

The Committee discussed Dr. Watson's proposal that the chromosome be the scientific unit of management for the human genome project. Several members strongly urged that, if this strategy is adopted, information that will be useful as better technology is developed must be collected and made available as a by-product of chromosome-oriented activities. They specified that the type of information that would be of long-term use would be sequences that uniquely identify pieces of DNA, and this information must be entered into the public domain so that any laboratory can use it. Dr. Zinder called on Drs. Hood and Olson to develop a specific proposal for how to address this issue prior to the next meeting and also for the establishment of journal publication standards that would include this requirement. Dr. Peter Pearson stated that the chromosome is "the only workable unit of management" at the infrastructure level, since work on a particular chromosome is specialized in terms of the standard tools (cell lines with break points, somatic cell hybrids, chromosome fragments, YAC's and cosmids, etc.) and expertise required for mapping and sequencing. He suggested that organization take the form of a consortium of laboratories that pool their efforts and data on an individual chromosome. Several members proposed the chromosome as the unit of database management but favored a *laissez-faire* policy for genome projects in the initial phase of the program; they supported a gradual coalescence toward organization by chromosome as the human genome project proceeds. Dr. Caskey suggested that the cooperative agreement would be a useful mechanism by which to facilitate such coalescence. Under this mechanism, the NIH would define the mission (in the case of the human genome program, the mission would be closure on a particular chromosome), and institutions and centers would compete for the opportunity to participate.

Dr. Zinder stated his belief that the program has an obligation to create a "value-free" system whereby all the chromosomes are studied, regardless of whether or not they contain genes associated with diseases. He asked for suggestions on alternative units of management if the chromosome is not to be used. Several Committee members reiterated that the issue was not whether the chromosome should be the unit of management (there was general agreement on this) but rather when this level of organization and management should be implemented. Most of the members believed that competition and technology development should be the key components of the program's initial phase, while chromosome-by-chromosome management will be necessary to bring the project to completion. Others commented on various ways to encourage coalescence. Dr. Wexler mentioned the "convening power" of the NIH to bring scientists working on particular chromosomes together with those interested in technology development, and Dr. McKusick observed that the chromosome committee model has been useful in the physical mapping community. Dr. Watson also noted the trend toward the formation of chromosome groups but agreed that it would be premature to try to organize the project on a chromosome basis at this time. He stated that the program will sponsor chromosome workshops and that HUGO will play a role in facilitating international involvement. He added that leaders interested in managing work on entire chromosomes will probably emerge as a result of these workshops. He also stated that foreign countries will be encouraged to play a management role for some of the chromosomes when the program reaches the stage where this is necessary.

Adjournment

Dr. Zinder closed the meeting by thanking the Committee members and other participants for their contributions and inviting the individuals who are not scheduled to attend the planning retreat to communicate any ideas they may have to the representatives who will attend.

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I hereby certify that, to the best of my knowledge, the minutes and attachments are accurate and complete[1].

Norton D. Zinder, Ph.D.
Chairman

Elke Jordan, Ph.D.
Executive Secretary

[1] These minutes will be formally considered by the Committee at its next meeting, and any corrections or notations will be incorporated in the minutes of that meeting.

Second Meeting

Program Advisory Committee on the Human Genome

June 19-20, 1989

Ramada Inn
Bethesda, MD

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Second Meeting

Program Advisory Committee on the Human Genome

June 19-20, 1989

Ramada Inn
Bethesda, MD

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Second Meeting

PROGRAM ADVISORY COMMITTEE ON THE HUMAN GENOME

June 19-20, 1989

Ramada Inn
Bethesda, MD

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