

Hughes Institute Poised for Growth

The imminent sale of Hughes Aircraft for billions of dollars will make the Hughes Medical Institute an awesome philanthropy

"The Howard Hughes Medical Institute must be prepared for a possible increase in disbursements in 1985," HHMI president Donald S. Fredrickson said recently in a memo to the institute's medical advisory board. In light of the fact that HHMI may soon find itself with \$150 million to spend by year's end, the admonition seems like sound advice.

Within weeks, the trustees of the Hughes Institute will decide whether to accept a bid for the Hughes Aircraft Company, the institute's sole but immensely valuable asset which was put up for sale earlier this year. Bids for the huge aerospace company are being evaluated for HHMI by Morgan Stanley, the New York securities house. Hughes Aircraft is expected to sell for \$4 billion to \$6 billion, with companies such as General Electric, General Motors, and Boeing cited by analysts as among the most likely buyers. In keeping with the Hughes penchant for secrecy, the bidders and their offerings are confidential. If everything goes according to plan, the Howard Hughes Medical Institute virtually overnight will become the wealthiest private philanthropy in the country.*

In 1953, Howard Hughes, the late billionaire recluse, created a medical institute in his own name that he hoped one day would become a stellar institution in the Rockefeller University mold (*Science*, 16 July 1976, p. 211). He named himself as sole trustee and, for business and tax purposes, made HHMI the sole owner of Hughes Aircraft. For more than three decades, the institute operated secretly on a relatively limited budget, dispersing little more than \$2 million to \$3 million a year, while the majority of Hughes Aircraft earnings were plowed back into the company. The potential for change came with Hughes' death in 1975, but it is only now, after protracted legal battles, that the HHMI is poised to become a major force in biomedical research. Its influence could be immense.

It is logical to think of HHMI as a private foundation but for years the institute has resolutely insisted that it is really a "medical research organization." The distinction, which is significant, continues to be an unresolved issue between HHMI and the Internal Revenue

Service. Under the tax code, a private foundation must distribute annually at least 5 percent of its net worth and is bound by limits on the ownership of its original asset. Thus, as a foundation, HHMI could not have owned 100 percent of Hughes Aircraft. As a medical research organization (MRO), on the other hand, the ownership provisions do not apply and only 3.5 percent of the organization's endowment must be distributed in a single year. An MRO is



Donald Fredrickson

Building a Hughes tradition.

defined as an organization "directly engaged in continuous, active conduct of medical research in conjunction with a hospital." Because Hughes himself was bound and determined to hang on to the aircraft company, designation as a private foundation was anathema. The need to try to defend its status as a MRO has, until now, determined the way HHMI operates. It accounts, for example, for the fact that academic scientists who are supported by HHMI are considered Hughes Institute employees, not grantees, and explains why their university-based laboratories are regarded as Hughes units.

In the future, the issue will assume less importance because, by deciding to sell Hughes Aircraft, the institute's newly appointed trustees have obviated the need to be exclusively an MRO. In fact, Fredrickson now envisions HHMI operating in two modes—both as an MRO,

and also as a private, grant-giving foundation.

Although responsibility for managing HHMI falls to the trustees,† decisions about the support of research have always been the purview of the institute's medical advisory board. The focus of HHMI research has been in four areas—immunology, genetics, endocrinology, and the neurosciences—and Hughes' units have been established at the nation's most prestigious research universities. The challenge facing the medical board today is to determine how and where to expand, and whether to maintain the proclivity for supporting the elite. As Fredrickson notes, "Matthew's Principle, to the effect that 'them that has gits more,' is operative in academic research."

The issues are laid out by Fredrickson in reports to the HHMI trustees, one describing a site visit to the University of Utah in Salt Lake City, another a discussion of HHMI expansion at Yale. As part of HHMI's new tradition of openness, the reports were made available to *Science*.

In November, Hughes advisors made a site visit to Utah, where the institute has a modest investment at present. Fredrickson's assessment is candid. The advisors, he wrote, "come with concerns about the capacity of the medical center to nurture an HHMI unit. In terms of its resources for supporting research, the Utah medical center is on the outer thin edge of the galaxy of research-intensive universities in which the Institute successfully operates affiliated units." At present, the center has what Fredrickson calls "trying vacancies in the chairs of biochemistry and genetics."

The Hughes people are beginning to emphasize the need for an HHMI unit to be "integrated" into the university that

†The Howard Hughes Medical Institute is incorporated in the state of Delaware where the court, in resolving a dispute about Hughes' will, reorganized the institute and ordered the appointment of nine trustees. They are: Helen K. Copley of Copley Press, Inc.; Donald S. Fredrickson; F. William Gay, former president of the Summa Corporation, a Hughes company; James Howard Gilliam, Beneficial Corporation; Hanna Gray, president, University of Chicago; William R. Lummis, a cousin of Howard Hughes; Frank A. Petito, chairman of James D. Wolfenshon, Inc.; Irving S. Shapiro, former chairman of E. I. duPont; George Thorn, professor emeritus, Harvard.

Thorn is also chairman of the medical advisory board until January 1986 when he will be succeeded by Lloyd H. Smith, professor of medicine at the University of California at San Francisco.

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houses it. The Hughes unit, described as one of the strongest scientific assets at Salt Lake, was opened in 1978 when Raymond Gesterland moved from Cold Spring Harbor. Fredrickson reported that "a pleasant laboratory was created for him by [HHMI] down the hill from the medical campus, in the department of biology where he can commune with his kind." In 1980, Raymond White moved to Utah from Stanford and has become one of Gesterland's principal HHMI colleagues. Gesterland is in genetics; White is a molecular biologist.

Recently, partly in the interest of fostering the kind of proximity that HHMI likes, Gesterland's lab was moved up the hill next to White's. Says Fredrickson, Gesterland "is sensitive to the need there for a critical mass not yet attained in the surrounding academic department. As a good citizen of the university community, he is willing to help fill the void of the missing professor of genetics."

If HHMI decides (as is quite possible) that Salt Lake is acquiring the research intensity that could support an expanded Hughes effort, one proposal it will consider is to back White in a full-scale effort to map the human genome. He recently has been urged by voluntary health groups to pinpoint on the chromosome the location of defective genes in known inherited disorders. White now has 50 or so of the approximately 150 available probes. Illustrative of HHMI operating in the MRO style, Fredrickson notes that "if we determine that the effort should be supported, HHMI will prefer to pay all costs—including those for the necessary expansion of space."

But the medical advisory board and trustees will have to evaluate several issues, he sates, in deciding whether to support the creation of such an international resource: "The question of computer capacity, relationships to other genome-mapping registries . . . , even the ethical questions arising from the possession of such sensitive data bearing on individual risk for disease."

HHMI has already decided to expand its existing units at the University of Michigan Medical School, the University of Illinois College of Medicine, the University of Texas Southwestern Medical School, and Duke University School of Medicine. As a result of the site visit to Salt Lake, expansion at Utah is down for "early attention." Another school on the early attention list is Yale, where the medical school leadership is talking with HHMI about an increased Hughes presence there.

In a report he titled "Institutions: Sparta," Fredrickson continues the pro-

cess of using the case history method of laying out issues for the HHMI trustees as they begin the process of "building a Hughes tradition." Harvard and Yale have long been home to HHMI units, but not without difficulties. "It is noteworthy," he says, "that neither of our affiliations in the two schools—best compared as rival Hellenic city states—yet exemplifies the flowering of our capacity for symbiosis."

To begin, Fredrickson describes some of the Spartan qualities that, he suggests, distinguish Yale from Harvard's Athens. At Sparta, he says, "The faculty has to be chosen carefully, but then is left alone. No one interferes with the scholars, or goes out of the way to provide for their needs." The quality of being left



The "Cloisters" at NIH

alone suits what he would like to see as an element of the new Hughes tradition; Hughes, however, would look after its scholars' needs. Citing another plus, he says "Yalies tend to be an independent lot," but he also notes that too much independence can be a hurtful thing.

The Hughes Institute has, in some quarters, a reputation for barging its way into a university (*Science*, 5 October 1979, p. 36). "HHMI has often presented a ghostly image in the past," Fredrickson says, "and the exorcism of hobgoblins of misunderstanding today is a frequent challenge to Institute management." Yale is a case in point. "Our discussions with Yale are uncovering some old wounds," he reports. "For example, when the HHMI immunology unit at Yale was created in the '70s, it was set down in the department of pathology. In all the years since, the chairman of this department and the now deceased head of the unit apparently never held a discussion, let alone reached a satisfactory agreement about their relationship." That may be apocryphal, but it illustrates Fredrickson's point about the need for "integration."

New or expanded Hughes units in the new regime will be developed with careful attention to the need for understanding and backing from the university—from the president and dean on down. Yale now wants to create a Center for

Molecular Medicine and is seeking HHMI backing. Fredrickson finds it significant that the proposal has the support of the Yale president, the medical dean, and the chairman of the department of medicine. That is just what HHMI wants to see in terms of its desire to be "integrated" within a university. Molecular medicine is the state-of-the-art field, and Hughes is interested in fostering it. Here, the potential for Hughes impact is substantial. "An infusion of new dollars into the research system can create some of the centers for molecular medicine without which each medical school fears (correctly) that it will cease to be modern." Hughes has already created a new unit in Ann Arbor and is contributing to one at Stanford. Negotiations at Yale

continue. Fredrickson says of the Yale plan, which would encompass researchers and students throughout the school, "This seems to be a venture that is both worthy of HHMI and true to our mission. . . ."

As Hughes goes about the business of creating and expanding units that fit in the medical research organization mold that has characterized HHMI from the start, it seems likely it will continue to insist upon affiliating with the elite, research-intensive universities. "We have persuaded ourselves that the majority of schools will not sustain an HHMI affiliated unit, and that a single award for laboratory science will not have an effect upon their small scientific contributions," Fredrickson says. But that pertains mainly to life in the MRO mode. The trustees already recognize that HHMI will soon be too large to operate only with the elite. In all likelihood, at Hughes there soon will also be life in the private foundation mode. For that, the call is out for innovative ideas.

To anticipate the prospect of greatly increased spending in 1985, Fredrickson began by asking present and former medical advisory board members to play "The Planning Game." The rules of the game were simply these: you have \$150 million to spend in 1 year. How would you do it, consonant with the goal of the institute to promote "human knowledge

within the field of the basic sciences. . . ."

The answers, if generally not surprising, are bound to please. Grouped by categories, the suggestions for distributing Hughes' largesse included these:

- Long-term funding for scientists of proven merit.
- Sustained support of departments or research units in outstanding scientific organizations.
- Support for selected younger career scientists.
- Support for students and young graduates.
- Funds for equipment and laboratory renovation.
- Support for centers in the emerging field of structural biology/molecular biophysics.

And, in a category Fredrickson labels "Off the (great) wall and other ideas," he got these suggestions:

- Creation of a new "China Medical Board."
- A one-time \$5 million endowment for the Institute of Medicine—the health policy branch of the National Academy of Sciences.

In the search for ideas, Fredrickson also has written to minority institutions, small universities, and to the presidents of the 70 colleges that have the highest percentage of students going on to graduate education in science.

One new HHMI venture, already under way, is the "Cloister Project." Undertaken as a joint program with the National Institutes of Health (NIH), medical students are being given a chance to study in an NIH research lab before they get their M.D.'s. The project is housed in an old convent adjacent to NIH which belonged to the cloistered Sisters of the Visitation until it recently was purchased by NIH and renamed in honor of philanthropist Mary Woodard Lasker. The "Hughes Research Scholars" generally will take their HHMI-NIH year between the second and third years of medical school. The first 25 were chosen from a pool of 70 applicants.

In its new phase, the Howard Hughes Medical Institute will not only be far richer than it has been these past three decades, it will also be far more open to public scrutiny. For an organization that has long eschewed public inquiry, it will be a welcome change. Says Fredrickson, "HHMI must leave no room for doubt that broad public interest guides its philanthropy, even if applied to narrow themes. . . . Merely being a wealthy foundation does not provide satisfaction."—**BARBARA J. CULLITON**

Dispute Reopened on Mysterious 1979 Flash

Representative John Conyers (D-Mich.) on 21 May released a report that he said presents "compelling evidence" that a mysterious double flash picked up by a U.S. satellite in 1979 was caused by a nuclear explosion off the coast of South Africa. However, the significance of part of the evidence cited by Conyers has since been disputed by the scientist who originally produced it.

A totally convincing explanation for the flash has never been developed. In 1980, for example, a group convened by the White House concluded that it was probably a small meteorite hitting the satellite, while a study by the Naval Research Laboratory (NRL) concluded that it was probably a nuclear explosion (*Science*, 29 August 1980, p. 996).

The report released by Conyers, which was prepared by the Washington Office on Africa, an anti-apartheid group, relies heavily on the NRL's analysis. It cites, for example, evidence of ionospheric disturbances and hydroacoustic data that the NRL found indicative of a nuclear explosion. Most of this information has already been widely discussed in public.

But the report also puts a great deal of significance on a previously undisclosed finding of elevated levels of radioactive iodine in the thyroids of Australian sheep shortly after the event. Ronald Walters, a Howard University professor who wrote the report, called the finding "an important missing element" in previous analyses.

The thyroid data were developed by Lester van Middlesworth of the University of Tennessee, who has been monitoring radioiodine levels in sheep thyroids for three decades. In late 1979, he found levels 4 to 6 times higher than background in thyroids of Australian sheep, a level he says is "right on the borderline of whether there is really something there or not." In the past, he has found that thyroid activity rises between 1,000 and 10,000 times background levels following an atmospheric nuclear test.

Van Middlesworth communicated his findings to the NRL group studying

the event, but did not publish them because their significance was uncertain. "It could either have been a very small contamination or a very unusual variation in background," he told *Science*. He says he was not contacted by the Washington Office on Africa when it was preparing its report, and "I would not want my data used as crucial evidence" for the conclusion that a nuclear explosive was detonated.

Walters argues that the thyroid data is part of a pattern of evidence that points to an explosion. "We can say with confidence that it occurred, but we can't be certain," he says.

In releasing the report, Conyers called for an end to all nuclear cooperation between the United States and South Africa, and called on the National Academy of Sciences to examine all the data gathered since the mysterious flash was first noted.

—**COLIN NORMAN**

Academy Proposes a Federal Trauma Center

A committee of the National Research Council and the Institute of Medicine has settled upon the Centers for Disease Control (CDC) as the most appropriate location for the study, treatment, and prevention of trauma.

Produced at the behest of the Department of Transportation (DOT), the group's report, "Injury in America," declares injury to be the "principal public health problem in America today." Accidents, the fourth leading cause of death, kill more than 140,000 people a year, one-third of them on the roads. They leave 80,000 permanently disabled from brain or spinal cord injuries. Alcohol is involved in half of all highway accidents and is heavily implicated in shootings, falls, drownings, poisonings, and burns, as well as in 80 percent of suicides.

The committee, headed by former CDC director William Foege, notes that federal research funds—about \$112 million a year—are paltry in relation to the annual treatment costs of \$75 to \$100 billion. It calls for stepped-up research, particularly on biomechanics; safer product design; new "centers of excellence," a major