First Casualty in the Biotechnology Derby

A $40-million venture has collapsed, but its backer, E. F. Hutton, is now trying to launch biotechnology tax shelters

It was going to be one of the most ambitious entrants in the overcrowded race to commercialize biotechnology: a $40-million company with branches in Israel, Ohio, and California, a link to the prestigious Weizmann Institute, a Nobel prizewinner on the staff, and, perhaps most important, the respected brokerage firm E. F. Hutton putting together the financing. The founding of the company, DNA Science, was announced with great fanfare last February, but early in August it became the conspicuous first casualty in the commercial gene-splicing derby.

A complex financial deal that would have provided capital began to unravel when some corporate investors wanted proprietary rights to DNA Science's products. It fell apart when, at the last moment, Hutton withdrew its support. On 4 August, the company's investors got their money back.

But Hutton's involvement with biotechnology is not yet over. The brokerage firm is now restructuring DNA Science, turning it into a vehicle for channeling tax shelter investments into biotechnology. Hutton, the largest dealer in tax shelters in the country, believes that the new tax bill, passed by Congress just as the original plan for DNA Science was falling apart, makes research and development an attractive area for investments designed to secure tax relief.

The collapse of the financial arrangements behind DNA Science "was a blessing in disguise, because it allows us to make use of the opportunities in the tax bill," says Nelson Schneider, the E. F. Hutton analyst who was primarily responsible for getting the brokerage firm into the biotechnology business. It was not such a windfall for Christian B. Anfinsen, winner of the 1972 Nobel Prize for Chemistry, who left the National Institutes of Health earlier this year to run DNA Science's company in Israel; he is now in Rehovot but the company no longer exists.

The DNA Science saga provides an interesting chapter in the story of how gene splicing is moving from the laboratory into the commercial world. To some, the difficulties in launching the company suggest that Wall Street's recent passion for biotechnology may have cooled, an interpretation that the venture's boosters strenuously deny.

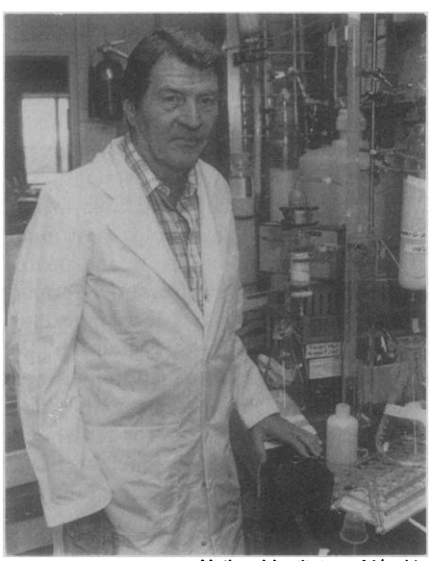
DNA Science had been taking shape over the past couple of years. The basic idea was that it would function like a holding company; its business would be conducted mostly by small subsidiary companies established near major universities to accommodate specific scientists. In essence, the subsidiary companies would commercialize products stemming from a scientist's basic research; the scientist would generally have an equity interest in the company and would be a consultant to it, but would remain on campus.

The first such venture would have linked DNA Science with the Weizmann Institute in Rehovot. A company called Taglit (Hebrew for discovery) was to be established as a joint venture to carry out a broad range of biotechnology projects with Weizmann scientists. Among them was a plan to produce genetically engineered interferon in commercial quantities and to test the substance for use against a variety of viruses. Other projects included the production of monoclonal antibodies for diagnostic testing and work aimed at improving the protein content of wheat.

The Weizmann deal was struck in February, and E. F. Hutton used the occasion to announce the establishment of DNA Science. E. Russell Eggers, a corporate high flier who had been chief executive of Loctite and before that head of Bendix International, was named president of the company. He was joined by Zsolt Harsanyi, who had headed a major study of the problems and promises of gene-splicing technology for the Office of Technology Assessment, and by Nelson Schneider. Both were made vice presidents of DNA Science.

Arrangements were subsequently negotiated for the establishment of two more subsidiary companies. One was to be a joint venture with the Battelle Memorial Institute in Ohio. And the other involved an arrangement under which DNA Science would set up a facility called Baxter Laboratories with endocrinologist John Baxter, of the University of California at San Francisco. Baxter intended to advise the new company while remaining at UCSF. The initial focus of that work would have been the production and testing of hormonal proteins, including human growth hormone.

All these deals were contingent on DNA Science raising $40 million by 28 July and that is where the problems arose. The initial goal was to raise the money from sources such as investment banks and pension plans rather than from corporations that might want to exploit the company's products themselves. "We didn't want to be a captive to anyone," Harsanyi says, noting that most of the other biotechnology companies are at least partially owned by drug companies or chemical manufacturers. In the end, however, DNA Science was forced to turn to these sources.



National Institutes of Health

Christian B. Anfinsen

"One tends not to doubt the ability of a company like E. F. Hutton to manage an enterprise like this."

Between $20 and $30 million were raised from investors outside the pharmaceutical and chemical industries. Hutton itself was prepared to invest $8 million. But the rest of the $40 million would have come from corporations, including Allied Chemical and Johnson and Johnson. In return for its cash, Allied was promised certain rights to industrial ap-

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plications of DNA Science's products or processes; Johnson and Johnson was granted similar rights to the company's pharmaceutical work. Hutton's lawyers immediately questioned the legality of such an arrangement, however, for it would have meant that the corporate investors stood to gain more from their stake in the company than other investors.

Such problems were not deemed insurmountable, but shortly before the 28 July closing date, another complication arose. Johnson and Johnson sought to negotiate more favorable proprietary rights from its investment, and the closing date was deferred for a week to see if an accommodation could be reached. About that time, however, Hutton's board of directors had second thoughts about the whole structure of DNA Science.

One concern was that the agreements with Weizmann, Battelle, and Baxter would have accounted for virtually all the initial $40-million investment. The Weizmann deal alone would have soaked up $25 million. This would have made the company very inflexible and unable to respond to any new investment opportunity that might arise. More important, Hutton's tax specialists argued that the tax bills which were then under final consideration in Congress could make R & D an attractive area for tax shelter investments, but DNA Science, as it was then structured, could not take advantage of these new opportunities.

Thus, for a variety of reasons, DNA Science's board of directors, which is dominated by Hutton executives, failed to agree on the financial arrangements by the new closing date. The deal collapsed, and the money was returned to the investors.

These developments have left Christian Anfinsen in a difficult position. He accepted an offer to become chief scientist at Taglit shortly after the agreement between Hutton and the Weizmann Institute was struck. The job was attractive, he says, because he wanted to live in Israel for a while and he thought the venture had some exciting prospects. He arrived in Rehovot on 1 July. Asked in a telephone interview why he left before the financial arrangements were signed and sealed, Anfinsen replied that "one tends not to doubt the ability of a company like E. F. Hutton to manage an enterprise like this." Now that the agreement with DNA Science has collapsed, however, Anfinsen says that alternative arrangements are being explored to keep Taglit alive, and "it is conceivable that it may be revitalized." In the meantime, he has a post as visiting professor at the Weizmann Institute.

To some observers, the difficulties encountered by DNA Science in raising noncorporate investment indicate that the financial markets have become much more cautious about biotechnology. "Companies can no longer put gene in their name and raise $5 million overnight," says Scott King of F. Eberstadt and Co. "Hundreds of millions of dollars have been invested [in biotechnology] but total sales are a few tens of millions a year if you are generous," he says. The problems with DNA Science "are a very visible sign of the greater selectivity in capital markets."

Officials of DNA Science do not agree. Harsanyi notes that the company was taking a different tack from other biotechnology ventures, by trying to tap much more conservative sources of finance, and Harsanyi argues that it was "amazing" that the company managed to raise more than $20 million from such sources.

Schneider conceded in an interview that the fund raising had not been as successful as originally anticipated, but he laid part of the blame on unforeseen difficulties in dealing with pension funds and other conservatively managed financial bodies. DNA Science had received enthusiastic commitments from the money managers of several outfits, but the deals failed to win approval from the committees that have the last word on the dispersal of funds and several large sums were withdrawn, Schneider says.

Whatever the problems encountered in raising capital for the original company, Hutton believes that the new tax law should make it easier to raise cash for a different kind of operation. Schneider says in particular that Hutton's tax specialists have found a way to structure the company to take advantage of the 25 percent tax credit for incremental investments in R & D (*Science*, 21 August, p. 843).

Although they are unwilling to discuss specific details because they believe their competitors may not yet have seen the same opportunities, officials of DNA Science say that the revamped company will essentially be financed by a collection of limited partnerships. Each partnership will contribute a separate pool of cash and have a stake in several specific projects; it will be able to take advantage of the tax credits while sharing in any subsequent profits that may come out of the work it finances. In some respects, the arrangement would work like existing schemes for channeling tax shelter

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Satellite Data Indicate Ozone Depletion

Three years ago the federal government banned the use of chlorofluorocarbons (CFC's) in most aerosol spray cans, and public anxiety about damage to the ozone layer quickly dispersed. But that action dealt with only one use of CFC's. They are still widely employed as refrigerants, foaming agents, and cleansers—uses for which there are generally no good substitutes. A fierce battle has been raging over whether such uses should be restricted.

The battle took a new turn in mid-August when reports appeared in several newspapers that satellite data have provided the first direct evidence that ozone is being removed from the upper reaches of the stratosphere. The data, obtained from two meteorological satellites, indicate a very gradual degradation of the ozone layer may be taking place about 40 km from the earth's surface.

According to Donald Heath, a scientist at the Goddard Space Flight Center who analyzed data gathered by Nimbus-4 and Nimbus-7, the rate of depletion at that altitude is about 0.5 percent a year. Heath said that he examined a 7-year series of data from Nimbus-4 and checked it against results obtained from the first 2 years of Nimbus-7. After correcting for seasonal variation, he says he found a slight year-to-year decrease in ozone concentration. "There is no way that can develop fortuitously; something real has happened in the atmosphere," he told *Science*.

The evidence linking this decrease to CFC's is far from absolute, but the ozone layer is most vulnerable to breakdown by CFC's at the 40 kilometer level, according to atmospheric models. A complete explanation of what is going on in the stratosphere must await the results of planned experiments to measure the levels of various intermediate products thought to be involved in the ozone breakdown reactions. Nevertheless, the Nimbus findings are "very significant," says Shelby Tilford, head of the atmospheric processes branch at NASA, for "they provide the first direct evidence of ozone depletion."

An interesting twist to the Nimbus

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investments into oil and gas drilling.

Some observers are skeptical that the R & D tax credits can be used in this way, however. For one thing, tax credits are only useful if a company makes taxable profits, and few biotechnology projects will be in that position for many years.

For another, the tax law specifically prohibits taxpayers from claiming credits for R & D unrelated to their own line of business, a prohibition that would seem to rule out the use of biotechnology tax shelters for wealthy individuals. Hutton, which now does about $700 million worth of business a year in tax shelters, claims to have found a way around these problems, however. "Whenever you write a 25 percent credit into the tax codes, you invite people to take advantage of it," says Schneider.

The restructured version of DNA Science would work with individual scientists in much the same way as the original company was supposed to function, and Schneider says that he hopes arrangements can still be worked out with John Baxter and with the Battelle Memorial Institute. The Weizmann Institute presents a more difficult problem, however, because the tax credits do not apply to investments outside the United States.

Hutton hopes to file the first partnership arrangements with the Securities and Exchange Commission this fall, in time for the brisk business in tax shelters that usually takes place at the end of the tax year. If the arrangements are approved, biotechnology would then take its place alongside oil and gas drilling, movie productions, real estate, and racehorses, as a focus for tax shelter investments.—COLIN NORMAN

Health Care in the Soviet Union

Rising infant mortality reflects inadequacies of a system that in many areas is primitive and ill equipped

A nation's health care system, since it touches the lives of all the inhabitants, can be presumed to supply an illuminating picture of how the society as a whole operates.

Two recent publications, one a painstaking analysis of hard-to-get Soviet statistics, and the other an American doctor's personal view of health care in the U.S.S.R., go a long way toward casting light on what goes on in this vital sector of Soviet society.

The statistical report,* issued by the Commerce Department last September, was compiled by two of the world's leading experts on Soviet health, Murray Feshbach, now at the Georgetown Center for Population Research in Washington, D.C., and Christopher Davis of the Centre for Russian and East European Studies at the University of Birmingham in England. The report documents the alarming rise of infant mortality, perhaps the most significant single indicator of a nation's health, since the mid-1960's. It is now more than double the U.S. rate, having gone from 22.9 deaths per 1000 live births in 1971 to 31.1 in 1976, the last year for which such statistics are available. And when adjusted to match U.S. criteria—the Soviets don't count deaths that occur within the first week after birth—the figure goes to 35.6 (the rate in the U.S. and Western Europe is currently under 13).

In their report, Davis and Feshbach run through a catalog of possible reasons for the rise in infant mortality. Some Soviet analysts claim the apparent changes are only the result of improved statistical reporting, but the authors reject this explanation. They say that past improvements in reporting have not resulted in a rise in the infant mortality rate; that the rise has not been confined to Central Asia where many deaths went unreported in the past; and finally that if the increase were mainly statistical, authorities would be aware of that fact and "would not be expressing so much concern about the trend." The authors go on to dismiss such factors as housing and sanitation, which they say have not worsened. Nor do regional differentials account for the phenomenon, as the rise is not confined to heavily Muslim Central Asia. Instead, they find the most likely causes to be repeated abortions (the average Soviet woman has six during her reproductive span); environmental pollution, which may cause genetic defects and miscarriages; poor management of childhood influenza (linked to malnutrition), which often turns to fatal pneumonia; and alcoholism, which has become increasingly rampant among women as well as men.

Higher mortality rates are not confined to infants; overall mortality has risen from 6.9 per 1000 in 1964 to an estimated 9.5 in 1979. This reflects a rise in death rates among men, for whom life expectancy has fallen to 63—which many observers attribute primarily to alcoholism.

That the Soviets are concerned about the trends is evidenced by the fact they have clamped down on publicizing mortality statistics in the past half-dozen years. In addition to the blackout on infant mortality data, says Feshbach, they have stopped releasing age and sex-specific data since 1974, and no data on the number of physicians by specialty have been available since 1975.

Demographer/economist Feshbach, who was one of the first to spot the "confusing" trends in infant mortality, says that one of the myths liberal America has clung to the longest is that Soviet health care is relatively immune to the difficulties that plague the rest of the system; the place where, if anywhere, socialism works. American visitors have always tended to be impressed by Soviets' claims that their system is *besplatno*, or free of charge to all.

But, according to a book by William Knaus, *Inside Russian Medicine*,† this claim loses a lot of its significance when one is exposed to the available care. Not only is much of it shockingly inadequate by American standards, both in quality of care and the availability of supplies and equipment, but, he says, a large portion of what would in America be regarded as routine services are obtainable only through *blat*, or the connections, favors, and bribes that pervade

Rising Infant Mortality in the U.S.S.R. in the 1970s (U.S. Department of Commerce, Bureau of the Census, Washington, D.C., 1980).

†Everest House, New York, 1981.

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