Social Benefits of a Successful Biomedical Research Company: Merck

P. ROY VAGELOS
Retired Chairman and CEO, Merck and Company

THE PHARMACEUTICAL INDUSTRY has as its objective the discovery of important new medicines and vaccines to prevent and alleviate diseases and to improve health and the quality of life. Merck has been doing that successfully since 1933, when George W. Merck opened the first laboratory in Rahway, New Jersey. Through the efforts of its research scientists, the company has contributed drugs and vaccines in numerous therapeutic areas. In 1975, Bill Campbell and his research team discovered a medicine for control of animal parasites (worms) that ultimately gave Merck an opportunity few companies have ever had in history.

Campbell’s research group was searching for a medicine that would kill worms in domestic animals—horses, cattle, sheep, and pigs. To discover such a medicine, they utilized a very simple system: they put worms into the abdomen of a mouse, then fed the mouse cultures of soil microorganisms that had been collected around the world. Soil microorganisms make many interesting substances—including many antibiotics. Bill believed he might find a microorganism that would make a substance that would kill worms. The Campbell team screened soil samples sent from many parts of the world—a total of about forty thousand samples. Only one gave a very interesting response—it killed all the worms implanted in the mouse, and it did this even when the culture broth was enormously diluted, indicating that the active substance in the broth was extremely potent. The substance was isolated, identified, slightly altered chemically to improve its safety, and then tested widely for its effect on many different parasites in the Merck Research Laboratories. The unique soil microorganism came from the laboratory of Dr. Satoshi Omura of the Kitasato Institute of Japan.

This exciting new drug, called Ivermectin, was tested against all the economically important parasites that plague the business of farmers

---

1 Read 28 April 2001.
who raise livestock. These worms cause billions of dollars of damage to livestock in the United States and other countries around the world. The amazing thing about this drug was that it not only killed all the worms inside treated cattle, but also killed biting insects on the hides of the animals after a single oral or injected dose. Its amazing potency and effectiveness against a broad array of animal parasites caused the company to develop this drug for most domestic animals—including cattle, horses, sheep, pigs, and, ultimately, dogs (for heart worm). In various formulations beginning in 1978, it would become the world’s leading veterinarian product, the best-selling animal drug in history. But when Campbell’s parasitologists tested Ivermectin for possible use in humans, they discovered that it was not effective against hookworms and tape-worms, some of the most important parasites in humans; thus it would never become an important medicine for people. It was put aside for that purpose.

In 1980, Dr. Mohammed Aziz, stimulated by an observation in Campbell’s laboratory that Ivermectin was able to kill a commercially unimportant horse parasite that existed as a microfilarium during its life cycle, asked whether he could study a human microfilarial disease, river blindness. Dr. Aziz had worked earlier in his career in the World Health Organization and had been stationed in sub-Saharan Africa, where he saw many patients suffering from river blindness. This disease is caused by a parasite, Onchocerca volvulus, which infects about eighteen million people. It is transmitted by the bite of a black fly that breeds in the fast-flowing rivers of Africa and Latin America—hence the name river blindness. The disease cycle begins when a black fly bites an infected person and picks up from the skin microscopic forms of the parasite, called microfilariae. The microfilariae undergo development inside the fly, so that when the fly bites another individual, it injects into the skin a more highly developed form of the parasite. In the skin the developing parasites become mature males, about eight inches long, and females, about fifteen inches long. The males and females live together in lumps in the skin and produce millions of microfilariae, tiny worms that crawl throughout the skin causing incredible itching wherever they reach. Infected people constantly scratch their infested skin. The microfilariae also enter the eyes, where they cause inflammation and scarring with ultimate blindness. In some West African villages most of the people are infected and 60 percent of the people more than fifty-five years of age are blind. The World Health Organization (WHO) estimates that ninety million are at risk for this infection.

Dr. Aziz went to Dakar, Senegal, where he carried out a very simple clinical study. He took tiny skin snips over the hips of infected persons
and counted the number of worms (microfilariae) under a microscope. He then gave them a single oral dose of the new drug, which we renamed Mectizan®, the human formulation of Ivermectin. Testing the same way one month later, he was astonished to find the microfilariae were all gone. When he repeated the skin snips after three months, they were still completely gone—with a single dose. Dr. Aziz then undertook large-scale clinical studies with full Merck support to establish the safety and effectiveness of Mectizan® in patients infected with this parasite. These studies established that the drug could be given as a single dose once per year. The microfilariae began to reappear in the skin only at the end of a year because these people were constantly bitten by flies and re-infected. Although the medicine did not kill the adult parasites, the adult females were not able to release new microfilariae after they had been treated with Mectizan®. It became clear that annual dosing could control this disease.

As a result of the Aziz clinical studies, we knew that Mectizan® could potentially prevent river blindness. But we also recognized that this disease is prevalent among the poorest people of the world. In some of these poverty-stricken countries, only $1 a year per person can be budgeted for public health. It was clear that we would not be able to sell the medicine to these people, who would not be able to afford it even at a price of pennies per year. We then requested governments in Africa, Europe, and the United States to purchase Mectizan® from Merck (at a low price) and to supply it free to those who were infected or at risk of infection, but none agreed to do this.

In October of 1987, the French government informed Merck that it was about to approve the drug. We had gone to France for approval rather than to the U.S. Food and Drug Administration because river blindness does not exist in the United States. In France there were people who had lived in Africa; some were infected and participated in the clinical trials. Since the tests were successful, the government was willing to approve Mectizan® for human use.

Merck faced the fact that its researchers had discovered and developed Mectizan®, a medicine that could prevent river blindness. We also recognized that, if Mectizan® were widely used throughout the areas where the disease is epidemic, the disease could be eradicated. Since only humans are carriers of this parasite, if everyone in the disease area were treated with Mectizan®, all the microfilariae would be killed, and the flies would have no source for this parasite. The disease would disappear. Faced with the possibility that the medicine would not be available to most people with this disease, Merck announced in October 1987 that it would contribute the drug free to anyone in the world who needed it, for as long as it was required.
We then established an independent committee of experts to de-
cide which distribution programs were qualified to receive supplies of
Mectizan® (Mectizan® Expert Committee). We asked Dr. William H.
Foege, who had served as director of the U.S. Centers for Disease Con-
trol and was then executive director of the Carter Center in Atlanta, to
chair this committee. He has led that group since 1987. Although
Merck would supply the medicine free, we did not have the infrastruc-
ture to distribute the drug in the remote places where the infected
people often lived. A number of large organizations, including the
World Health Organization and the World Bank, as well as a number
of smaller foundations dedicated to diseases of the eye, undertook the
major challenge of distribution.

Ten years after the contribution program was started, Merck had
treated about nineteen million people, and Merck has reaffirmed its
commitment to reach about fifty million people per year. If that is
accomplished and continued for ten to fifteen years, it is projected that
river blindness, like smallpox, would be eradicated.

Merck became one of the largest and certainly most inventive phar-
maceutical companies in the world based on the accomplishments of
its research scientists. Millions of people throughout the world benef-
ited from Merck discoveries for treatment of diseases prevalent in the
developed world, such as glaucoma, high blood pressure, heart failure,
coronary heart disease, benign prostate enlargement, bacterial and
viral infections, and arthritis. People around the world share the bene-
fits of these discoveries. It is entirely appropriate that a medicine de-
veloped by this innovative company for a disease such as river blindness,
which occurs almost exclusively in the developing world, be made
available to these impoverished people. The ultimate pay-back to
Merck is that the company is able to continue recruiting some of the
best scientists in the world. They join Merck knowing that important
discoveries of the Merck laboratories will reach the patients who might
be helped, no matter what their economic status.