

The Edna McConnell Clark Foundation's Tropical Disease Research Program

PART A

MOROCCO, APRIL 1997

The hottest part of the day had passed. Michael A. Bailin, president of the Edna McConnell Clark Foundation, and his colleague Dr. Joseph A. Cook, head of the Foundation's Program for Tropical Disease Research (TDR), were traveling the highway between the towns of Zagora and Ouarzazate, where the Sahara rises to meet the Atlas Mountains.

Bailin had joined Cook in Morocco in order to observe the implementation of a program to treat trachoma, a blinding disease afflicting millions in the developing world. Previous trachoma-control field trials in Egypt, Gambia, and Tanzania had been overseen by TDR and had proven successful. The Moroccan Pilot Program was a test of how well such an effort could be run by officials of the host country.

That day, Bailin and Cook had visited the offices of the Moroccan Ministry of Health as well as those of a number of other agencies. They had entered village health clinics and observed surgeries performed to correct eye damage. They had been shown the vessels, invented by trachoma researchers in southern Africa, that used very little water (a precious resource in villages at the edge of the Sahara) but were nevertheless effective in washing out eyes. Bailin and Cook had talked with village elders about the difference the Foundation was making in the lives of the people.

The two Clark Foundation officers pulled up to the roadside hotel where they would spend the night. As they watched the shadows lengthen across the hotel *riad* (walled garden), they discussed the future of TDR. Bailin had seen for himself that the Moroccan Pilot ran smoothly, within the context of a comprehensive public health campaign administering the antibiotic azithromycin to hundreds of people vulnerable to trachoma infection. Cook explained that the pharmaceutical company Pfizer, maker of azithromycin under the brand name Zithromax, had recently indicated an interest in expanding its drug donation program beyond Morocco.

"It's a great opportunity for the Foundation to make a tremendous impact," said Cook.

"Pfizer willingness to expand its donation program is interesting," Bailin replied. "But there are lots of issues we'd have to resolve before we could commit to working with Pfizer."

Teaching Case Writing Program Director Barry Varela and writer Beth Reeves prepared this teaching case under the supervision of Professor Joel Fleishman and Senior Research Scholar Anthony So as a basis for class discussion rather than to illustrate either the effective or ineffective handling of an administrative situation.

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Forming a joint venture with a for-profit company would be an unprecedented step for the Foundation. I'm not certain we can make that kind of commitment."

The TDR program had arrived at a crossroads. Of its three major disease programs, the first, schistosomiasis, had recently concluded; the second, onchocerciasis, was in the process of wrapping up; and the third, trachoma, was already almost two years past its original target shut-down date. There might not ever come a better time for the Clark Foundation to exit tropical disease research.

On the other hand, the exit of a large funder within a specific research program could be devastating. Indeed, tropical diseases in general had suffered severe neglect by both scientists and governments before the Clark Foundation's entry into the field.

Reflecting on these matters, Bailin gazed out through an arched window in the *riad* wall and watched the sun drop behind the foothills of the Atlas Mountains. What responsibility did the Clark Foundation have for sustaining progress in a field it had long supported? Should the Foundation partner with Pfizer and recommit to fighting trachoma? After more than twenty years, should TDR be closed? Or were there other options?

AVON PRODUCTS AND THE FOUNDING OF THE EDNA MCCONNELL CLARK FOUNDATION

Edna McConnell Clark was the daughter of David Hall McConnell, the founder of Avon Products. A door-to-door book salesman, McConnell founded the California Perfume Company in 1886 when he realized that customers were buying his books mainly for the rose oil perfume included free with purchase. He recruited women to sell the perfume from their homes, an innovative business strategy that predated by some three decades American women's winning the right to vote. The strategy was successful and sales first topped \$1 million in 1920. In 1939 the company was renamed Avon Products, and in 1946 Avon was taken public through an over-the-counter offering. By 1954, Avon sales had reached \$55 million annually.

A growing but professionally unstaffed Clark Family Foundation was transformed in 1969 when Edna McConnell Clark decided, along with her husband, Van Alan Clark, and their three sons, to double the size of the foundation's endowment. They hired professional staff, renamed the organization the Edna McConnell Clark Foundation, and set out to clarify the purpose of its grantmaking. As of September 30, 1995, the Clark Foundation had assets totaling \$420 million and had made grants totaling \$500 million since its inception. In 1996, a total of \$25 million was paid out for all programs.

In 1969, when Edna McConnell Clark established the modern Clark Foundation, the Foundation defined its mission as the pursuit of activities "for the benefit of mankind." Soon that rather broad goal became "to improve conditions and opportunities for people who live in poor and disadvantaged communities." Inspired by the era of the Great Society, the Clark Foundation dedicated itself to "systems change" (also called "systems reform")—the attempt to improve the plight of individuals by seeking to influence the large institutions, organizations, and bureaucracies that affect them.

In the early 1970s, Clark Foundation trustees created programs in four areas: the poor, children, the elderly, and the developing world. In order to decide on the specific focus of the Developing World Program, in 1973 the Clark Foundation asked itself, "Given the myriad problems and enormous population at risk, which problem presented the best opportunity to make a meaningful, rather than marginal, impact?"¹

¹ Asbury, Carolyn, Barnett L. Cline, and Victoria M. Gammino, *The Edna McConnell Clark Foundation's Tropical Disease Research Program: A 25-Year Retrospective Review, 1974-1999*. New York: Edna McConnell Clark Foundation, 2000, p. 20. Retrieved from http://www.emcf.org/pdf/eval_tdrreport.pdf.

GLOBAL HEALTH ISSUES IN THE EARLY 1970S

The Global Drug Gap

Since the advent of scientific medicine and the modern pharmaceutical industry at the turn of the twentieth century, drug companies have tended to direct their research and development efforts toward diseases that are prevalent in wealthy nations and whose treatments are chronic—diseases such as diabetes mellitus, hypertension, and arthritis. By contrast, there is little money to be made in creating drugs for diseases suffered mainly by poor populations.

Over the last several decades, an additional factor has intensified the disparity of health investment. The 1962 revelation that the drug thalidomide, prescribed to pregnant women mainly in Europe as a sedative and antiemetic, had caused thousands of severe malformities in children led to legislation in the United States and other countries that required pharmaceutical manufacturers to demonstrate the safety and efficacy of drugs and vaccines before they could be sold. Higher standards for R&D—and the concomitant expectation that companies should be held liable for the products they make—can be considered to be a generally positive development for consumers in wealthy nations. However, higher R&D costs exacerbated the preexisting tendency of drug manufacturers to target their research at the common, chronic conditions of the wealthy. That the governments of wealthy nations feel little political push to help solve the health problems of their poorer neighbors is unsurprising. In recent decades less than 10 percent of global spending on health research has been devoted to the diseases or conditions that account for more than 90 percent of the global disease burden.²

Less than a decade after the legislative reforms of the 1960s helped drive up the cost of pharmaceutical R&D, experts in international health were alert to the growing global drug gap. A 1977 U.S. Centers for Disease Control report noted, “Parasitic diseases are the ‘cancers’ of developing nations, yet total international research expenditures on tropical infectious disease was only \$30 million in 1975, whereas one ‘developed’ country alone spends nine times that much on cancer research.”³

In the early 1970s, as officers at the Clark Foundation debated the goals of its Developing World Program, the global drug gap appeared to offer an opportunity, if not an obligation, for philanthropy to step in.

Control Versus Eradication

Global health advocates have long debated the effectiveness of primarily medically based disease eradication efforts versus broader-based public health solutions. (For an explanation of the differences between disease control, elimination, and eradication, see Exhibit B.) Eradication campaigns have had a history of moving in and out of favor since the turn of the twentieth century, when the Rockefeller Foundation optimistically set goals of eradicating hookworm worldwide (1913) and eliminating yellow fever in the United States (1915) through disease treatment. Both efforts failed, in the case of hookworm because the treatment reduced the severity of symptoms but rarely eliminated the parasite, and in the case of yellow fever because the virus could “hide” indefinitely in monkeys only to reemerge after treatment of humans had concluded. (In a later initiative Rockefeller scientists were successful in developing a yellow fever vaccine.⁴)

² Global Forum for Health Research, “The 10/90 Gap” Retrieved from http://www.globalforumhealth.org/Site/003__The%2010%2090%20gap/001__Now.php

³ Schultz, M., “Current Concepts in Parasitology,” *New England Journal of Medicine* (1977), 297:1259. Quoted in Asbury, Cline, and Gammino, op. cit., p. 9.

⁴ National Network for Immunization Information, “Vaccine Information: Yellow Fever.” Retrieved from http://www.immunizationinfo.org/vaccineInfo/vaccine_detail.cfv?id=28.

In the 1950s and 1960s, new developments energized the hope for disease eradication. Scientists developed vaccines for diphtheria, tetanus, poliomyelitis, smallpox, measles, mumps, rubella, and Type B meningitis.⁵ Pest control had all but eliminated malaria and plague in the United States, and animal vaccination programs had eliminated dog-to-dog rabies transmission.⁶ Improved housing had greatly reduced tuberculosis infection rates in the United States.⁷ Based on the success of these “magic bullet” campaigns to eliminate specific diseases, the World Health Organization (WHO) spent the decades of the 1950s and 1960s concentrating mainly on eradication efforts directed at tuberculosis, malaria, and smallpox, rather than on more broad-based public health improvement measures.⁸

At the same time, there were at least two prominent examples of beneficial collaborations between the public and private sectors in public health. One was the investment by the National Foundation for Infantile Paralysis in the Salk polio vaccine, and the other was Planned Parenthood’s support for birth control pill research.

However, after fifteen years (1955-1969) the WHO’s attempt to eradicate malaria had not only failed but had inadvertently promoted the spread of pesticide-resistant strains of mosquitoes and drug-resistant strains of malaria parasites.⁹ The failure of the malaria eradication program reinforced concern about the complex and unpredictable nature of global health issues and returned the WHO’s focus to promoting the development of “sewage systems, potable water, adequate food, health clinics, and rudimentary knowledge of illness and treatment”¹⁰ in areas afflicted by tropical diseases.

It was in this context—awareness of the growing global drug gap, as well as an accompanying skepticism regarding eradication efforts aimed at specific diseases—that the Clark Foundation asked itself how it could best make “meaningful, rather than marginal, impact”¹¹ in the lives of people in developing countries.

THE CLARK FOUNDATION’S PROGRAM FOR TROPICAL DISEASE RESEARCH (TDR)

Compared to very large foundations like Rockefeller and Ford, the Clark Foundation had limited resources. (Rockefeller had approximately five times, and Ford 16 times, the assets of the Clark Foundation.) Yet despite its relatively modest means, the Clark Foundation harbored lofty ambitions. Trustees and officers believed that, through the strategic leveraging of Foundation funds, small investments could yield large dividends. One of the Foundation’s early presidents, James “Jim” Henry, was a proponent of the entrepreneurial approach to systems change. As a staff member later recalled, “Jim thought the Foundation should leverage other resources, be a venture capitalist of ideas, hire broad generalist consultant types, and use planning and [auditing] to initiate and refine efforts over time.”¹²

In deciding where to focus the Developing World Program, Clark Foundation trustees identified, and explored on a preliminary basis, 13 areas of opportunity. The trustees concluded that the three areas where the Foundation’s limited funds would most likely produce

⁵ Centers for Disease Control and Prevention, “Control of Infectious Disease, 1900-1999.” *Journal of the American Medical Association*, 282(11), September 15, 1999, p. 1029.

⁶ Centers for Disease Control and Prevention, “Control of Infectious Disease, 1900-1999,” op. cit.

⁷ Centers for Disease Control and Prevention, “Control of Infectious Disease, 1900-1999,” op. cit.

⁸ Stern, Alexandra Minna, and Howard Markel, “International Efforts to Control Infectious Diseases, 1851 to the Present.” *Journal of the American Medical Association*, 292(12), September 22/29, 2004, p. 1477.

⁹ Johns Hopkins Bloomberg School of Public Health, “Background Information on Malaria.” Retrieved from http://www.jhsph.edu/Malaria/Malaria_Background.html.

¹⁰ Stern and Markel, op. cit., p. 1477.

¹¹ Asbury, Cline, and Gammino, op. cit., p. 20.

¹² Quoted in Asbury, Cline, and Gammino, op. cit., p. 1.

“meaningful, rather than marginal” results were emergency relief, craft development, and tropical disease research.¹³ (The other areas that were considered and subsequently eliminated were literacy, population and family planning, agriculture, job creation, housing and human settlements, management and management systems, health care delivery, nutrition, and the environment.¹⁴)

Tropical disease research was perfectly illustrative of the global drug gap: of all drugs approved for human use worldwide between the years 1975 and 1999, only 13 (about one percent) were developed specifically for tropical diseases,¹⁵ despite the fact that such diseases kill millions. In the early 1970s, the contributions of the ten major funders in the field had failed to achieve a critical mass of activity or funding in any one disease. After surveying the field, trustees of the Clark Foundation came to believe that a relatively small investment (relative, that is, to total international health expenditures) of targeted funding could potentially help a large number of people. In 1974, recognizing the field of tropical disease research as the “most dominant area of opportunity,”¹⁶ the Foundation renamed the Developing World Program the Program for Tropical Disease Research (TDR).

The Clark TDR program staff was small, at most times consisting of just three persons—a director, an associate, and an administrative assistant.¹⁷ Over 25 years of funding from 1974 to 1998, the Clark Foundation TDR program awarded grants totaling \$90 million for three tropical diseases: schistosomiasis, onchocerciasis, and trachoma.¹⁸ (See Exhibit A, “Timeline of the Program for Tropical Disease Research, 1969-1997.”)

Schistosomiasis Program

The first focus of the Clark Foundation’s new Tropical Disease Research program was schistosomiasis (known as “schisto” for short).

Schistosomiasis is a chronic, potentially fatal parasitic disease that affects the urinary and intestinal systems and causes serious kidney and liver damage. Symptoms of schisto are caused by the body's reaction to the eggs produced by one of five species of worms (not by the worms themselves) and range from rash, fever, severe itchiness, and flulike symptoms to seizures and paralysis. An estimated 200 million people worldwide are infected with the *Schistosoma* parasite, with approximately 120 million people symptomatic. Schisto can be found in 74 countries, mainly in South America, southeast Asia, and Africa, with 80 percent of infected people in sub-Saharan Africa.

The life cycle of worms of the genus *Schistosoma* comprise the following stages. Having been discharged into fresh water, a schistosome egg releases a microscopic motile parasite that seeks a freshwater snail host. After locating and infecting a snail, within five weeks the parasite divides, producing thousands of new parasites. The snail excretes the parasites, which penetrate on contact the skin of a person bathing or working in the infected water. The parasite moves to the blood vessels of the victim’s bladder or intestines and, within six weeks, grows into a 12- to 26-millimeter-long flatworm (also called blood fluke). Female flatworms produce 20 to 3,500 (depending on the species) eggs per day and live in the body for an average of five years (and, for one species, up to 30 years). About half the eggs produced by the worm are excreted in urine

¹³ Asbury, Cline, and Gammino, op. cit., p. 20.

¹⁴ Asbury, Cline, and Gammino, op. cit., p. 20.

¹⁵ Trouiller, Patrice, et al., “Drug Development for Neglected Diseases: A Deficient Market and a Public-Health Policy Failure.” *The Lancet*, 359, October 5, 2002, p. 2188.

¹⁶ Asbury, Cline, and Gammino, op. cit., p. 21.

¹⁷ Interview with Joseph A. Cook, January 2007.

¹⁸ Cook, Joseph A., “The Founding of the International Trachoma Initiative and the Challenges Ahead in Drug Donations for the Elimination of Blinding Trachoma.” Paper presented to the Organisation Internationale Pour La Lutte Contre Le Trachome Annual General Assembly in Paris, France, May 11, 2003.

or stool; the remaining eggs lodge in various parts of the body, causing the symptoms of schistosomiasis. Eggs that have been urinated or defecated into fresh water release the snail-seeking parasite, beginning the schistosome life cycle anew.

Thus, in order to thrive, parasitic *Schistosoma* worms demand four prerequisites: tropical climate, fresh water, lack of sanitation, and the presence of an intermediate freshwater snail host.

According to Clark's *Tropical Disease Research Program 25-Year Retrospective Review*, schisto was selected as the first focus of TDR for several reasons:

Scientific advisors to the TDR Program recommended [focusing on schistosomiasis] because the disease was widespread, affecting approximately 200 million people worldwide, had garnered few resources from the research and funding communities, and yet had some promising research already underway that could be built upon. The Foundation's \$2 million in funding for a field that had an annual budget of \$3 million afforded the Foundation an impressive debut into a significant role.¹⁹

In the early 1970s, most schistosomiasis experts believed that a multifaceted strategy of drug treatment, snail control, and intervention to reduce water contact and contamination of waterways would be most effective in controlling the disease. Elimination of schisto, while obviously ideal, was not seen as realistic—the WHO's failed malaria effort had raised doubts about eradication schemes generally. Still, the successful development of vaccines for such infectious diseases as diphtheria, pertussis, tetanus, and polio had led some experts to believe that a safe, effective, and not prohibitively expensive schisto vaccine might someday be developed. The scientific consensus held that development of a schistosomiasis vaccine was at least a decade in the future.

At its founding in 1974, the TDR schisto program concentrated its efforts on determining the economic and social impact of the disease in order to influence funding; investigating human immunity to the disease as a first step in determining whether a vaccine might be possible; improving short-term control efforts through available medicines and countermeasures; and developing better long-term control efforts.²⁰

Over the course of its first year, the schistosomiasis program was refined to include four components: 1) creating a multidisciplinary approach that would enlist a broad array of funders, governments, and other organizations in research and control efforts, 2) leveraging the field by inviting leading experts to become involved in the planning process, 3) encouraging exchange of ideas by issuing an annual review of research progress, and most importantly, 4) taking the lead among schisto research organizations by tripling the total grant budget available in the field for the provision of basic services. Later, two more components were added to the strategic plan: 5) issuing "a plan for research (the Strategic Plan for Research on Schistosomiasis) which systematically [addressed] the four research objectives above," and 6) developing a long-range plan to promote better national and international planning and funding of control efforts.²¹

That the Clark Foundation had laid out a strategic plan to achieve explicit, predetermined goals—similar in spirit to NASA's successful eight-year effort to put a man on the moon—was considered by some to be contrary to the way science (if not technology) progressed. "The idea that you tell anyone what to research was anathema," one scientist later recalled.²² Scientific

¹⁹ Asbury, Cline, and Gammino, op. cit., p. xi.

²⁰ Asbury, Cline, and Gammino, op. cit., p. 21.

²¹ "Clark Foundation Program Plan for the Developing World," November 1975. Quoted in Asbury, Cline, and Gammino, op. cit., p. 25.

²² Asbury, Cline, and Gammino, op. cit., p. 26.

outcomes couldn't be anticipated; often, breakthroughs were serendipitous, contingent upon unforeseen developments. Nevertheless, Clark Foundation officers maintained a somewhat naïvely optimistic faith that the program's goals could be achieved by force of good planning. To their credit, they recognized from the start that the strategic plan would require a five- to 10-year commitment at the least.

During the early years of the schistosomiasis program, the discovery of hybridoma cells, monoclonal antibodies, and recombinant DNA, as well as other advances in molecular biology and immunology, boosted hope that vaccine technology might indeed prove to be the "silver bullet" to eliminate schistosomiasis. However, as the years passed, a schisto vaccine seemed always to be just over the horizon, and TDR's basic six-part strategic plan remained in force.

Dr. Joseph A. Cook

In 1978, the Clark Foundation hired Dr. Joseph A. "Joe" Cook as Program Director of Tropical Disease Research. A graduate of Vanderbilt University Medical School, Cook had trained in internal medicine at the University of North Carolina-Chapel Hill and in public health at the Harvard School of Public Health. Before joining the Clark Foundation, Cook was an overseas staff member of the Rockefeller Foundation working on a project to control schistosomiasis in St. Lucia, and served as special assistant for international research at the National Institute of Allergy and Infectious Diseases in Bethesda, Maryland. According to Cook, he was hired by the Clark Foundation for his training in schistosomiasis control rather than for his foundation background. "My orientation was field research—the discovery of knowledge that could be applied in the field," Cook recalled. Of the schistosomiasis program at Clark, Cook said, "Though we were heavily involved in vaccine research through the years, my own background and experience led us to emphasize epidemiology and control perhaps more than we otherwise would have."²³

Widely respected in the scientific community, Cook was known to possess broad and deep knowledge of the tropical disease field. Foundation staff recalled how he had earned the respect and trust of public health officials in the diverse set of countries the program served. A colleague said, "[Cook] is universally admired as a terrific international practitioner."²⁴

Of the schistosomiasis program, Cook recalled:

We had very definite goals and expectations to do certain things by a certain time. Not all were successful. . . . As the process evolved, we got more explicit in honing objectives and strategies. . . . Immunologists would tell us that a vaccine was about five years away. The problem was, they told us that every five years.²⁵

During the late 1970s, the single-dose oral drugs oxamniquine, patented by Pfizer, and praziquantel, patented jointly by E. Merck and Bayer, were found to be safe and effective in treating schistosomiasis. While oxamniquine was effective against only one of the five major schisto parasites, praziquantel was found to be effective against all of them, and by 1982 it was available for human use. In light of the promise of these drugs, praziquantel especially, TDR in 1980 began scaling back its drug-development grantmaking. At a cost of about \$1 per tablet, however, praziquantel was too expensive for any of the nations in which schistosomiasis was endemic to establish a long-term schisto control program, even with the assistance of various aid agencies. Clark Foundation officers, as well as others in the international health community, repeatedly approached Bayer and Merck about the possibility of a praziquantel donation

²³ Cook interview, January 2007, op. cit.

²⁴ Quoted in Asbury, Cline, and Gammino, op. cit., p. 76

²⁵ Quoted in Asbury, Cline, and Gammino, op. cit., p. 28.

program, but the companies consistently said no.²⁶ Not until the mid-1980s, when the South Korean pharmaceutical company Shin Poong developed an alternative pathway to the creation of praziquantel (thus sidestepping Merck and Bayer's proprietary claim), did the price of the drug decline significantly, to about \$.08 to \$.10 per tablet. Even at those prices, however, a large-scale praziquantel distribution program was considered to be beyond the Clark Foundation's resources.²⁷

In 1981, Clark Foundation trustees first began to contemplate the question of how to exit the schistosomiasis program. Several considerations delayed the Foundation's exit. Despite efforts in field development—including the establishment of schisto libraries in affected parts of the world, the publication of journals such as *Tropical Doctor* and *Schisto Update*, and the cultivation of a “critical mass of first rate investigators”²⁸—global control programs were in their infancy and required the Foundation's further support. At the same time, the goal of developing a schisto vaccine still seemed viable. To officers at Clark, the Foundation's work in schisto felt unfinished. Regarding the schisto exit strategy, Foundation President Dr. Jack Coleman later recalled, “I was fully prepared to go slow in this case. There was an identifiable goal, to develop a vaccine. As long as there was hope, that persuaded me that we were right to stay the course.”²⁹

Over the course of the next six years, the Foundation refined its exit strategy, always with the hope that a vaccine would be developed. Peter Bell, president of the Foundation during the mid 1980s, later said of this period, “Increasingly we doubted we would be successful in vaccine development. . . . We decided it would not be responsible to cleave [the schisto program] off, so we decided to attenuate instead.”³⁰ The “attenuated” withdrawal strategy was based on the Foundation's belief that the availability of praziquantel (despite the high price) had reduced the need for further drug research and that the WHO could and would assume responsibility for further vaccine research. As late as 1990, TDR staff members were debating the proper course for vaccine research to take.

The Clark Foundation's board of trustees continued to feel a responsibility toward the field through the early 1990s. Rather than pull out of schistosomiasis altogether, the Foundation redirected the “attenuated” withdrawal to include a “geographic-centered approach”³¹ to grantmaking, concentrating on East and West Africa, where schisto was most prevalent. Though this shift in strategy clashed with the program's historic emphasis on scientific research, TDR staff hoped the approach would dovetail with the WHO's strategy of attacking the disease by region. The Clark schisto program finally concluded in 1994 without having discovered a vaccine.

Over the twenty-year period of its involvement in schistosomiasis, the Clark Foundation awarded grants totaling \$32.4 million (see Exhibit C). Of that total, approximately half went to immunology and vaccine research; these funds represented an estimated one third of all monies spent globally on schisto vaccine research during the period. While Foundation funding advanced the field of immunology generally, the hard fact was that, after two decades of effort, no vaccine was produced.

Scientists have asked, in retrospect, if the money spent on vaccine research would not have been better spent on promoting traditional public health measures. The answer is not clear. Despite the Foundation's early implementation of a strategic plan that included field-

²⁶ Interview with Joesph A. Cook, January 2007.

²⁷ Cook interview, January 2007, op. cit.

²⁸ Cook, Joseph A., “Memorandum RE: New Directions in Tropical Disease Research Program,” 21 August 1981. Quoted in Asbury, Cline, and Gammino, op. cit., p. 36.

²⁹ Asbury, Cline, and Gammino, op. cit., p. 36.

³⁰ Asbury, Cline, and Gammino, op. cit., p. 37.

³¹ Asbury, Cline, and Gammino, op. cit., p. 38.

strengthening measures such as the publication of journals and the sponsorship of conferences, and a lengthy and strategic-minded exit process, the schistosomiasis field faltered once Clark's money was no longer available. In the words of one researcher, "[The Foundation] believed that 'someone else' would step in to support schisto, but it was not the case."³² Another said, "The withdrawal of a major funder is very destructive to the field and related fields."³³

Yet it must be pointed out that the Clark Foundation helped develop a field where previously there had been none—just a disease, with almost no one working to fight it. When Clark exited schistosomiasis, disease researchers were not without resources. In 1999 the Carter Center began the Schistosomiasis Control Center in Nigeria, and in the years since has distributed 800,000 doses of praziquantel.³⁴ In 2002, eight years after Clark exited the field, the Bill & Melinda Gates Foundation, in partnership with Imperial College London, the WHO, and the Harvard School of Public Health, founded the Schistosomiasis Control Initiative with \$30 million in funding. As of 2006, a schisto vaccine had yet to be developed, and schistosomiasis remains a significant global health problem.

Onchocerciasis Program

In the early 1980s, as the Clark Foundation's Tropical Disease Research program began to consider phasing out of schisto research, it sought other areas of research that were consistent with its previous work as well as likely to be meaningfully influenced by the program's limited resources.

Onchocerciasis, also known as river blindness, is a parasitic infection characterized by extremely itchy, raised nodules under the skin, typically in areas of bony prominence such as the knees and elbows. In addition to disfiguring dermatitis, "oncho" infection can cause an inflammatory reaction in the cornea (the clear, tough outer layer of eye tissue that covers the iris and the pupil) and lead to the formation of cataracts (clouding of the lens) and ocular lesions. In severe cases oncho infection causes blindness.

The life cycle of the filarial parasite *Onchocerca volvulus* requires two hosts. The parasitic microfilariae (larvae) are transmitted to a human host by the bite of an infected blackfly. After migrating to subcutaneous tissue, the larvae molt to an intermediate stage; the human host shows no symptoms at this stage. After about a year, the parasite reaches adulthood. Adult *O. volvulus* females produce millions of microfilariae, which enter the host's bloodstream, inducing itching, swelling, and inflammation of the skin and the cornea of the eye. When an infected human is bitten by a blackfly, the insect ingests microfilariae, which subsequently molt within the fly host to the stage that is infective to humans, completing the life cycle. Because the larvae of the type of blackfly that hosts *O. volvulus* require well-oxygenated fresh water, onchocerciasis infection is associated with fast-flowing rivers and streams; thus the common name river blindness.

An estimated 18 million people, mainly in sub-Saharan Africa, are currently infected by onchocerciasis. Of those infected, about 270,000 are blind and another 500,000 have severe visual impairment.

In 1974 the World Bank initiated the Onchocerciasis Control Project (OCP), an ambitious program of vector control (eradication of blackflies) through aerial larvicide application (chemical spraying from airplanes and helicopters) throughout entire endemic zones. The OCP eventually encompassed numerous river systems in 11 West African countries and achieved temporary success in reducing oncho infection rates in some areas. However, blackflies, and with

³² Asbury, Cline, and Gammino, op. cit., p. 39.

³³ Asbury, Cline, and Gammino, op. cit., p. 40.

³⁴ Carter Center, "Health Programs: Schistosomiasis Control Program." Retrieved from <http://www.cartercenter.org/health/schistosomiasis/center.html>.

them onchocerciasis, soon returned to areas not subjected to active spraying. Recognizing the limited effectiveness of vector control, in 1978 the WHO opened a drug-research station in Ghana. The station devoted only modest resources toward development of an oncho vaccine.

Throughout the 1970s, the two drugs known to be effective in the treatment of oncho, diethylcarbamazine and suramin, were seldom used because they carried potentially serious side effects, including blindness, kidney damage, and death. An apparent breakthrough in oncho chemotherapy came in the early 1980s. In 1981 Merck Pharmaceutical brought to market the highly profitable drug ivermectin (brand name Mectizan) for veterinary use in the treatment of intestinal worms, lice, and mites among dogs, pigs, cattle, sheep, and other animals. A broad-spectrum antiparasite, ivermectin was found to kill in horses a worm closely related to *O. volvulus*, the parasite that causes onchocerciasis in humans. Officials from the World Health Organization, the World Bank, and other U.N. agencies urged the screening of Mectizan as a possible treatment for oncho. Researchers at Merck and the WHO soon discovered that a single annual dose of Mectizan stopped adult *O. volvulus* worms from reproducing and paralyzed the microfilariae that caused itchiness and eye lesions, thus preventing both transmission and morbidity. Field trials indicated Mectizan was safe as well as effective.

In light of the OCP's partially successful vector-control efforts and the discovery of Mectizan, the Clark Foundation saw an opening for a third line of onchocerciasis attack—vaccine research. Because next to no work had been done in the area, in 1985 the Foundation decided to direct its oncho funding toward vaccine research exclusively. By the next year, the vaccine-research effort had been refined to consist of four components:

1. Animal Models of Protective Immunity, which supported basic studies that would define the components of the immune response;
2. Immunology and Molecular Biology, which sought to identify, characterize and reproduce protective antigens;
3. Epidemiology and Pathology in Humans, which aimed to increase basic knowledge of pathogenesis as well as variation in human and species responses through assorted geographic studies; and
4. The Vaccine Testing Program, which would test candidate antigens on chimpanzees.³⁵

In 1987 Merck, in partnership with the World Bank, the WHO, UNICEF, national ministries of health, NGOs, and local communities, launched the Mectizan Donation Program (MDP). Through the MDP, Merck promised to distribute Mectizan free of charge, indefinitely, to whoever needed it worldwide. As the MDP represented a potential model for other large-scale international public-private partnerships, its success was seen by global health advocates as extremely important.

With the establishment of the MDP, the Clark Foundation asked itself two questions: 1) should it redirect some of its resources toward supporting the MDP, and 2) was there now less need for an oncho vaccine?

TDR staff members believed that Mectizan, while effective, represented only an interim measure. *O. volvulus* might eventually develop resistance to the drug, as malaria parasites had in response to the WHO's antimalarial effort. Moreover, as the World Bank's OCP had demonstrated, vector control would never succeed entirely. TDR believed strongly that the only long-term solution to oncho lay in the creation of a vaccine. After evaluating the prospects for success, in 1989 the TDR Advisory Committee decided against substantial diversification of the oncho program. It would continue to focus its effort on basic vaccine research (see Exhibit D).

³⁵ Asbury, Cline, and Gammino, op. cit., p. 49.

For the next five years TDR's oncho program furthered the science of immunology, but as in the case of schistosomiasis, the creation of a safe and effective vaccine seemed always to lie just beyond the horizon. By 1994 Clark Foundation trustees had begun to consider how to fashion an exit strategy for oncho. At that time TDR staffers believed the program "had advanced the field [of oncho vaccine research] forward sufficiently such that its sustainability, competitive edge and continued productivity would be ensured."³⁶

Over the next several years, hope arose within the Clark Foundation that an international organization would step forward to take the place of the Foundation as it withdrew from the field. Meanwhile, the Onchocerciasis Task Force, created by TDR in 1988, coordinated the activities of research institutions; administered a competitive grants program; supported publication of an oncho research bibliography, a journal, and a newsletter; disseminated information in other ways; promoted policy analysis and workshops; and sponsored a formal evaluation of the Foundation's oncho program. Despite these field-building activities, no international organization had stepped in to replace the Clark Foundation as it contemplated exiting in the mid 1990s.

In 1994, the Foundation undertook the unusual step of commissioning a formal evaluation of the onchocerciasis program. The evaluation report found that the Foundation's oncho program had "assembled materials and reagents" for continued vaccine research, furthered "understanding of host immune response," and brought together a group of high-quality researchers.³⁷ Further, the report determined that, within the community of oncho researchers, good communications and healthy competition helped to minimize inefficiencies.³⁸ While assessing overall progress in the field and making recommendations, the report also served to provide grantees with notice that the Foundation would soon cease funding the program. The evaluation concluded that though the development of an oncho vaccine was not imminent, the field had developed sufficiently that it could "stand on its own competitively."³⁹

Trachoma Program

While phasing out of schistosomiasis and entering onchocerciasis in the mid 1980s, the Clark Foundation also began considering entering the field of trachoma research.

Trachoma is a highly contagious infection of the eye caused by the bacterium *Chlamydia trachomatis* and is characterized by chronic conjunctivitis, or "pink eye." Hands, clothing, and fluid-seeking flies that have come into contact with infected eye or nose secretions can spread the bacterium. In areas of overcrowding, poor sanitation, and poverty, disease transmission can be rapid and intense, reaching prevalence rates of 90 percent among children aged 2 to 5 years.

Infection with *C. trachomatis* is not immediately threatening to sight. Rather, repeated infection can scar the eye's conjunctiva (the clear, thin skin that covers the white of the eye and the underside of eyelids) and deform the upper eyelid, causing the eyelashes to turn inward (a condition called trichiasis) and abrade the cornea. The constant scratching damages the cornea, often leading to secondary bacterial infection that worsens the condition, and eventually resulting in blindness. Because young children suffer frequent reinfection, they serve as the main disease reservoir. Trachoma is two to three times more common among women, who are infected through close contact with children, than it is among men.

Trachoma is the world's leading cause of preventable blindness from infectious disease. An estimated 600 million people worldwide are at risk of trachoma, with 150 million cases of

³⁶ Asbury, Cline, and Gammino, op. cit., p. 51.

³⁷ Hoffman, D.B., and E. Ottesan, *Review of the Onchocerciasis Research Program*. New York: McConnell Clark Foundation, March 1, 1994. Quoted in Asbury, Cline, and Gammino, op. cit., p. 54.

³⁸ Asbury, Cline, and Gammino, op. cit., p. 55.

³⁹ Hoffman and Ottesan, op. cit.

active disease. Of those with active trachoma, about 11 million individuals suffer from trichiasis requiring surgery and about 6 million are blinded. Concentrated mainly in Africa, the Middle East, and parts of Asia, trachoma is responsible for at least 15 percent of the world's blindness.

At the time of the Clark Foundation's entrance into the field, there was virtually no funding for trachoma research. TDR's strategic trachoma control plan, adopted in 1985, called for a two-pronged approach: 1) pathogenesis and immunology and 2) epidemiology and control (see Exhibit E). From the outset, the Clark Foundation's board of trustees insisted that the trachoma program's strategic plan include specific goals, including well-defined timetables for attainment of objectives.

In epidemiology and control, TDR funded valuable work, for example in designing a 12-point grading system for signs of the disease to aid in the gathering of accurate epidemiological data. Foundation-funded doctors investigated the ease and efficacy of eyelid surgery to correct trichiasis. In collaboration with the WHO and UNICEF, the Clark Foundation established programs that incorporated existing health systems in furthering disease treatment and protection and in modifying individuals' hygienic habits and water use.

The pharmaceutical company Pfizer, meanwhile, had identified the antibiotic azithromycin (brand name Zithromax), developed in the late 1980s to treat sexually transmitted chlamydia, as possibly effective in treating trachoma. (Trachoma is caused by the same bacterium that causes genital chlamydia.) Prior to the 1990s, the most effective drug in treating trachoma was the topical antibiotic ointment tetracycline. Tetracycline treatment of trachoma required that the ointment be smeared into the eyes of the patient twice a day for six weeks. Few mothers were willing to subject their children to this long and painful process. Zithromax's crucial advantage was that it could be administered and would take effect in a single oral dose.

Progress in TDR's trachoma pathogenesis and immunology program was slow. But with the implication of sexually transmitted chlamydia in HIV transmission in the late 1980s, the U.S. National Institutes of Health dramatically increased the funding of research into chlamydia. This development enabled the Clark Foundation to contemplate exiting from trachoma vaccine research. In 1991, TDR Program Director Cook stated:

. . . [U]nless a trachoma candidate vaccine for human trials is forthcoming, research on immunology and vaccine development will merge with existing efforts on the increasing problem of chlamydial infections of the genital tract and lungs. We therefore expect trachoma work to end in 1995.⁴⁰

As the 1990s progressed, the epidemiology and control side of the Foundation's trachoma program saw continued success. Trachoma had come to be understood as requiring more than a medical solution. To address the behavioral and environmental changes, as well as medical procedures, necessary to control trachoma, the Clark Foundation funded the WHO to develop a manual that described a comprehensive community strategy known as SAFE:

Surgery to correct trichiasis (i.e., the deformed eyelid caused by long-term infection),
Antibiotics to treat active disease,
Face-washing to reduce transmission, and
Environmental changes to improve water supply and sanitation.

⁴⁰ Cook, Joseph A., "Tropical Disease Research Program Statement," September 1991. Quoted in Asbury, Cline, and Gammino, *op. cit.*, p. 65.

Cook stressed the importance of the “packaging” of the SAFE strategy as an easily understood and memorable acronym. “Anything that will help people in the field to understand and remember a treatment is useful,” Cook recalled. “Just as important, the SAFE acronym helped board members at Pfizer retain the information. Eventually the SAFE acronym was translated into Swahili, Arabic, Vietnamese—wherever the strategy was used, we created an equivalent acronym in the native language.”⁴¹

Although at that time Pfizer had no international philanthropy program, it was a large, highly profitable, and growing corporation, and Clark Foundation officials believed it might be willing to embark on a relatively small altruistic venture.⁴² In 1992, Clark asked Pfizer to donate the antibiotic Zithromax in field trials of the SAFE strategy. Pfizer agreed to the donation, and trials commenced that year in Egypt and early the next year in Gambia and Tanzania. All elements of the SAFE strategy—surgery, antibiotics, facial hygiene, and environmental change—would be rigorously tested to ensure that they could be applied successfully in endemic countries. Data from the trials indicated that each individual aspect of the SAFE strategy, including Zithromax rather than tetracycline, was effective and that, taken together, the elements of the SAFE strategy would be highly effective in controlling trachoma.⁴³

Given the economic realities of the countries involved, it was clear that no market for Zithromax as a treatment for trachoma would emerge; if Pfizer was to support trachoma control, it would have to give the drug away. Motivated by the possibility of improving profoundly the lives of millions of disadvantaged people (and, no doubt, by the good publicity attendant upon a large-scale philanthropic initiative), managers at Pfizer contemplated expanding the Zithromax donation program.

As the trachoma exit target date of 1995 approached, Clark Foundation staff realized that Pfizer’s willingness to consider expanding its Zithromax donation program presented a unique opportunity and that extension of the deadline might be desirable. In the fall of 1995, TDR Program Director Cook met with Paula Luff, assistant director of International Philanthropy Programs at Pfizer, to discuss the creation of a trial trachoma control program using the SAFE strategy. The partnership was understood to be advantageous to both parties. Pfizer would gain access to Clark’s connections within governments, the scientific research community, and international and indigenous NGOs; Pfizer’s association with Clark would also win the company a measure of credibility with those entities, who tended to be suspicious of “big pharma.”⁴⁴ The Foundation, for its part, needed Pfizer’s drug as well as its financial resources.

Announced in 1995, the Moroccan Pilot Program entailed collaboration between the Clark Foundation, Pfizer, the Ministry of Health in Morocco, and Helen Keller International, a blindness-prevention nonprofit with strong ties in-country. Meanwhile, in response to the “tremendous promise”⁴⁵ shown in Egypt, Gambia, and Tanzania by the SAFE strategy, the WHO began organizing the Alliance for the Global Elimination of Trachoma by the year 2020 (GET 2020). Thirteen organizations, among them the World Bank, the African Medical and Research Foundation, the International Agency for the Prevention of Blindness, and Sight Savers

⁴¹ Cook interview, January 2007, op. cit.

⁴² Cook interview, January 2007, op. cit.

⁴³ Cook interview, January 2007, op. cit.

⁴⁴ Barrett, Diana, James Austin, and Sheila McCarthy, “Cross-Sector Collaboration: Lessons from the International Trachoma Initiative,” p. 55. Paper presented at the Workshop on Public-Private Partnerships in Public Health, April 7, 2000. Retrieved from <http://www.hsph.harvard.edu/hcpds/partnerbook/chap3.PDF>

⁴⁵ “Planning for the Global Elimination of Trachoma (GET): Report of a WHO Commission.” Geneva, Switzerland: World Health Organization, 25 & 26 November, 1996, p. 6.

International, as well as the Clark Foundation and Helen Keller International, composed GET 2020.⁴⁶

Planning and implementing the Moroccan Pilot Program proved to be an important mutual learning experience for leaders at the Clark Foundation and at Pfizer. “We felt comfortable with Clark from the beginning,” Pfizer vice president for corporate affairs Lou Clemente recalled. “We didn’t have to sell them on things that were important to us. They knew what we were about, what would be important to us. And I think we were sympathetic with what they wanted to achieve.”⁴⁷ The success of the Moroccan Pilot helped reassure Joe Cook that Pfizer was willing to be a good partner, and that it was serious about its commitment to the fight against trachoma.

The mutual trust and good will engendered by the Moroccan Pilot Program led Luff and Cook to consider expanding the partnership between Pfizer and the Clark Foundation.

THE FUTURE OF TDR

Over the years since its establishment as a professionally staffed foundation in 1969, the Edna McConnell Clark Foundation had refined its areas of interest from the originally enumerated four to a more targeted five—urban middle-school education, child welfare services, state criminal justice systems, low-income neighborhoods in New York City, and Tropical Disease Research.

For many years, professionally staffed foundations saw themselves as incubators for social projects, funding experiments and research that, if proven successful, would later be adopted and institutionalized by government. As government shrank through the 1980s and 1990s, some foundation executives began to question the viability of this approach. While its areas of interest had changed somewhat, the Clark Foundation had not wavered in its commitment, as expressed in its four domestic programs, to the philosophy of systems change. And indeed, the Foundation had made some effective grants and met with the occasional success. Yet despite years of the Foundation’s best efforts at resource leveraging, strategic planning, and other entrepreneurial techniques, and despite the millions of dollars spent, urban middle schools, child welfare, state criminal justice, and the socioeconomics of the nation’s largest city had all proven stubbornly impervious to reform. By the mid 1990s, the Foundation’s board of trustees had become frustrated by the lack of results; they had lost faith in the ability of the Clark Foundation, given its limited resources, to effect systems change.

In 1995 the board scheduled a retreat to reexamine the Foundation’s mission strategy.

Michael A. Bailin

As a result of that retreat, Michael A. “Mike” Bailin was hired as president of the Edna McConnell Clark Foundation in February 1996. As a founder and former president and CEO of Public/Private Ventures (P/PV), a nationally recognized not-for-profit organization dedicated to improving opportunities for youth in poor communities, Bailin brought with him extensive experience in nonprofit strategy and a reputation for openness to innovative approaches to philanthropy. A graduate of Dartmouth College, Bailin had earned a master’s in urban planning and a law degree from Yale University, and had practiced law and taught at Dartmouth and Franconia colleges in New Hampshire. He arrived at the Clark Foundation after more than 25 years’ experience as consultant and advisor to numerous not-for-profit organizations, including the Ford Foundation and the South Street Seaport Museum in New York City.

⁴⁶ “Report of the First Meeting of the WHO Alliance for the Global Elimination of Trachoma,” Geneva, Switzerland: World Health Organization, 30 June–1 July, 1997, p. 3.

⁴⁷ Barrett, *op. cit.*, p. 47.

From his years at P/PV, Bailin was intimately familiar with the challenges faced by grant seekers. He admitting to having “a little bit of a chip on [his] shoulder”⁴⁸ about the way grantees were required to market themselves to foundations and other sources of money. He recalled of the interview process with Clark’s board of trustees:

I told each of them, in the individual interviews, that if I were to come, I would examine every aspect of Foundation culture—practices, policies, and procedures. I said to each trustee, ‘You can count on me to make changes where there’s no evidence for effectiveness.’ They knew who they hiring.⁴⁹

Bailin’s initial impression of the Clark Foundation was that the programs were too broad and ambitious relative to the size of Foundation resources. He later stated:

[W]e were proceeding as if we had some independent leverage over social systems that had been many decades in the making—systems that were fortified by all the ramparts of bureaucracy and regulation, and thickets of intergovernmental agreements and contracts, and moats of public dollars. We were fighting battles that had tested the power and wealth of serial U.S. Congresses and presidencies. It was a battle of Homeric proportions fought with Lilliputian resources. How could we ever imagine that we could accomplish anything so significant in our lifetimes? And how would we even know if we did?⁵⁰

Bailin believed that a more realistic way for foundations to support change in society was by identifying and supporting organizations that were already showing success in achieving their goals, whatever those goals were. Bailin came to refer to this grantmaking approach as Institution and Field Building (IFB). Explaining IFB, Bailin said:

Instead of simply developing our own strategy, say around system-wide reform, and funding organizations to assist us in implementing that strategy, we would think of ourselves as investors in good products, services and ideas. That is, investing in organizations that had developed their own strategies and were having a measurable impact on disadvantaged populations. We would then take a more entrepreneurial approach and provide funding to assist with the development of sustainable programs that would have a long-term impact.⁵¹

Much of Bailin’s attention during his first year in office was focused on the Program for Justice, whose stated mission was to “[support] state policymakers working collaboratively across disparate government agencies to use correctional resources more wisely.”⁵² When Bailin arrived at the Foundation, there was a general feeling among the trustees that the time had come to close down the Justice program. The program’s director was approaching retirement, and the

⁴⁸ Nauffts, Mitch, “Newsmakers: Michael Bailin, President, Edna McConnell Clark Foundation: A High-Engagement Approach to the Field of Youth Development.” *Philanthropy News Digest* (September 2002). Retrieved from <http://foundationcenter.org/pnd/newsmakers/nwsmkr.jhtml?id=4700076>.

⁴⁹ Interview with Michael A. Bailin, September 2006.

⁵⁰ Bailin, Michael A., “Re-Engineering Philanthropy: Field Notes from the Trenches.” Speech presented at the Waldemar A. Nielsen Issues in Philanthropy Seminar Series, Georgetown University, February 21, 2003.

⁵¹ Barrett, op. cit., p. 50.

⁵² Bailin, Michael A., “Report from the President.” In *The Edna McConnell Clark Foundation 1996 Annual Report*. New York: Edna McConnell Clark Foundation, 1996.

trustees felt the program had lost its effectiveness.⁵³ Nevertheless, Bailin tried to examine the program with an open mind. If Justice could show that it was supporting effective work, he would recommend to the Foundation's trustees that the program be allowed to continue unchanged.⁵⁴ If, on the other hand, the program's grantees could not "make at least a plausible case that their work [was] getting results,"⁵⁵ he would recommend profound changes in the program.

After several months of examining program initiatives and interviewing grantees, Bailin became convinced that changes to the Justice program were warranted; indeed, he decided to close down the program altogether. However, he felt that several Justice program grantees had successfully demonstrated their effectiveness, and he wanted to ensure that those grantees would be able to continued to pursue their work even after the Clark Foundation withdrew its monetary support.

Bailin believed that, by the employing the short-term tactic of awarding relatively large and flexible grants that emphasized organizational growth and results measurement, the Foundation could achieve the long-term objective of helping grantees survive the inevitable cessation of Foundation funding. In short, Bailin would apply that approach to select Justice program grantees.

As such, the Foundation invited the Vera Institute for Justice and five other nonprofits that were doing notable work in the field of juvenile justice to apply for multiyear general support grants. The six prospective grantees were asked to identify obstacles that prevented them from attaining their goals and to explain how Foundation grants could be used to overcome those obstacles. Having convinced Bailin and the board of trustees that the funds would be put to effective use, Vera and the other organization were awarded one-time grants to increase their productive capacity, explore possibilities for relationships with one another, and tighten relationships with other organizations in the field. The six organizations would go on to form the Consortium on Juvenile Justice Reform, which met four times over the course of the three-year grant in order to learn from one another, measure progress toward overcoming obstacles, and assess the effects of the grant. The organizations continued to collaborate after the Clark grant expired.⁵⁶

Having laid the groundwork for a responsible, multifaceted strategy for exit from the Justice program, Bailin now turned his attention to the Program for Tropical Disease Research.

THE DECISION

Dr. Joseph Cook sat drinking tea with Michael Bailin in a roadside *riad* at the edge of the Moroccan Sahara. "Mike, Paula Luff at Pfizer has expressed interest in expanding the Zithromax donation effort along the lines of Merck's Mectizan program. This could be an opportunity for us to reinvest in trachoma."

Bailin listened with interest. He knew that the success of philanthropic efforts in addressing global health problems had been mixed. He was aware of the Clark Foundation's generally frustrating experience with schistosomiasis. It had taken the Foundation nearly 15 years to exit the schisto program, ultimately leaving a field that some felt had grown dependent on Clark Foundation money to fend for itself.

⁵³ Interview with Michael A. Bailin, June 2006.

⁵⁴ Bailin interview, June 2006, op. cit.

⁵⁵ Bailin, Michael A., "Philanthropy in Practice: Great Expectations Versus Getting the Job Done," *State of Philanthropy* (November 2004).

⁵⁶ "Consortium on Juvenile Justice Reform: Overview," Vera Institute of Justice, archived February 5, 2003. Retrieved from http://www.vera.org/project/project1_1.asp?section_id=5&project_id=34.

Opinions varied as to the degree of responsibility that foundations should assume with regard to their scientific fields of investment. Scientific research often needed a considerable time commitment, and critics argued that to initiate a field of research and exit it prematurely could do more harm than good. On the other hand, foundations could not be expected to commit to initiatives indefinitely.

In the 1980s, the Clark Foundation was not involved in Merck's Mectizan Donation Program for the treatment of onchocerciasis. While the Foundation's onchocerciasis program had funded a study of the socioeconomic impact of blindness in Mali and Guinea, as well as a study to assess Mectizan's effectiveness in Nigeria and Cameroon, the bulk of the program's funding had been directed at vaccine research. Bailin knew that, in retrospect, the Foundation's commitment to vaccine research had carried substantial opportunity costs. Though millions of Mectizan doses had been administered worldwide since 1987, little was known about how successful the Mectizan Donation Program had been in halting disease transmission; nor was much known about what operational factors might have limited the program's effectiveness. By investing so heavily in vaccine research, Clark's oncho program had passed up the chance to investigate these and other questions. Resolving such questions might have benefited not only the Mectizan Donation Program but other, similar drug donation initiatives, including the one now being considered by Pfizer.

Joe Cook had led TDR for almost two decades; in many ways, Bailin believed, Cook *was* the Program for Tropical Disease Research. "Joe and what he had put together were all we had there," Bailin later recalled.⁵⁷ Cook was now approaching retirement, and the board of trustees had made it clear to Bailin that they were skeptical about starting over again with a new person to head up TDR.⁵⁸ Bailin knew that the trustees were interested in the Foundation's trying new things.⁵⁹ Doing so would require resources. The Foundation devoted on average between \$4 and \$5 million per year to TDR in grant funding, and an additional \$500,000 per year in staff salaries and benefits, consultants, travel, and incidental costs.⁶⁰ For years the Foundation had divided resources equally among the five program areas. Closing down TDR would free up money for other uses.

On the other hand, 20 years of Foundation involvement in tropical disease research had won Clark a reputation in the field as a trustworthy, committed, and serious partner—institutional capital that would be lost if TDR were to be closed down.

The Foundation had been trying to formulate an onchocerciasis exit strategy for three years. Although some uncertainty existed due to the lack of a single large donor organization ready to replace Clark, Foundation staff had assured Bailin that, thanks to the institution-building efforts of the Tropical Disease Research program's Onchocerciasis Task Force, the field of onchocerciasis vaccine research was relatively stable and self-sufficient.

As for trachoma, the Foundation had been supporting research in the disease for over a decade, and the trachoma program was already two years past its target exit date. Was there a danger that the field would come to rely unhealthily on Clark money, as some believed the schistosomiasis field had?

Bailin had spent the day personally witnessing the effectiveness of the Moroccan Pilot Program in controlling trachoma. The antibiotic Zithromax, when administered within the comprehensive SAFE strategy, could potentially liberate millions of people from a painful and debilitating condition. On the other hand, Bailin remained skeptical of Pfizer. Enormous multinational pharmaceutical corporations were not known for their altruism. Pfizer, in

⁵⁷ Bailin interview, September 2006, op. cit.

⁵⁸ Bailin interview, September 2006, op. cit.

⁵⁹ Bailin interview, September 2006, op. cit.

⁶⁰ Interview with Michael A. Bailin, January 2007.

particular, had been a leader in lobbying U.S. and European lawmakers to include intellectual property on the international trade agenda,⁶¹ leading to the 1994 adoption by the World Trade Organization (WTO) of the agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS).⁶² The TRIPS agreement had been denounced by NGOs, academics, and other critics of the WTO as having the effect of exacerbating the 10/90 global drug gap by maintaining the high price of medicines in developing countries. "I was very suspicious of Pfizer," Bailin recalled. "Joe was probably more comfortable with them than I was. Maybe there was something there we could work with, but who knew?"⁶³

In response to questioning, Cook filled in some of the details of Pfizer's proposal. "Pfizer's not interested in just being a passive drug donor," he explained. "They want to be an active partner in creating public health programs using the SAFE strategy and in developing criteria for selecting the next country. The WHO is getting behind the effort to fight trachoma. You've seen how well the Moroccan Pilot is working. What do you say, Mike? Are we in or out?"

Bailin was faced with a decision. Should he recommend to the board of trustees that the Program for Tropical Disease Research be closed down? Or should one or both of the programs remain open? If so, which one, for how long, and under what criteria? Could the Foundation's experience in crafting an exit strategy from the Justice program be brought to bear on Tropical Disease Research? Was it possible for the Foundation to exit onchocerciasis in such a way that the field was strengthened rather than weakened? What about trachoma? Was the proposed partnership with Pfizer a good idea, or was that undertaking best left to some other organization?

What should Bailin do?

⁶¹ Oxfam GB, *Preventing the Cure: Corporate Lobbying and Fair Access to Medicines*. Oxford, UK: Oxfam GB, p. 6. Retrieved from http://www.oxfam.org.uk/what_we_do/issues/health/downloads/cb_pfizer.pdf.

⁶² The text of the TRIPS agreement can be found at http://www.wto.org/english/docs_e/legal_e/27-trips_01_e.htm.

⁶³ Bailin interview, September 2006, op. cit.

Exhibit A

Timeline of the Clark Foundation Program for Tropical Disease Research, 1969-1997

1969

Founding of the Edna McConnell Clark Foundation.

1973

Founding of the Clark Foundation Developing World Program.

1974

The Developing World Program renamed the Program for Tropical Disease Research (TDR).
TDR's schistosomiasis program inaugurated.

1974

World Bank initiates Onchocerciasis Control Project, eventually encompassing 11 West African countries.

November 1975

TDR's schisto program six-part strategic plan promulgated.

1978

Dr. Joseph A. Cook hired as Director of TDR.

1980

In response to development of praziquantel, TDR schisto program scales back its drug-development grantmaking.

1981

Clark Foundation trustees begin contemplating schisto exit strategy.
Pharmaceutical company Merck initiates clinical trials in Senegal of Mectizan (ivermectin) as a treatment for onchocerciasis.

1982

Praziquantel made available for use in treating schisto.

1984

TDR inaugurates trachoma program.

1985

TDR inaugurates onchocerciasis program, with heavy emphasis on vaccine research.
Trachoma program promulgates its strategic plan, calling for research into pathogenesis and immunology and into epidemiology and control.

1986

Pfizer obtains rights to market azithromycin (later tradenamed Zithromax), effective in treating chlamydia and other bacterial infections, in Western Europe and the United States.

1987

TDR adopts “attenuated” exit strategy for schisto.

Merck creates Mectizan Donation Program (MDP) to combat oncho.

1988

TDR creates Onchocerciasis Task Force to coordinate international vaccine research activities.

1989

TDR declines involvement in Merck’s MDP.

1991

TDR adopts “geographic-centered approach” to schisto grantmaking.

TDR establishes 1995 as target exit date for trachoma program.

1992

Pfizer and TDR commence field trial in Egypt of SAFE strategy including Zithromax in treating trachoma.

1993

Pfizer/TDR SAFE strategy field trial expanded to include Gambia and Tanzania.

1994

Final TDR schisto grants awarded.

Clark Foundation trustees consider exit strategy for oncho program.

1995

Discussions commence between Pfizer and the Clark Foundation to expand Zithromax donation program.

Clark Foundation trustees hold retreat to reconsider the Foundation’s mission strategy.

1996

Michael Bailin named president of the Clark Foundation.

Moroccan Pilot Program of SAFE strategy commences; entails collaboration between TDR, Pfizer, the ministry of health in Morocco, and Helen Keller International.

WHO organizes Alliance for the Global Elimination of Trachoma by the year 2020 (GET 2020).

Pfizer expresses interest in expanding Zithromax giveaway program.

1997

Bailin joins Cook in Morocco to evaluate Moroccan Pilot Program.

Exhibit B

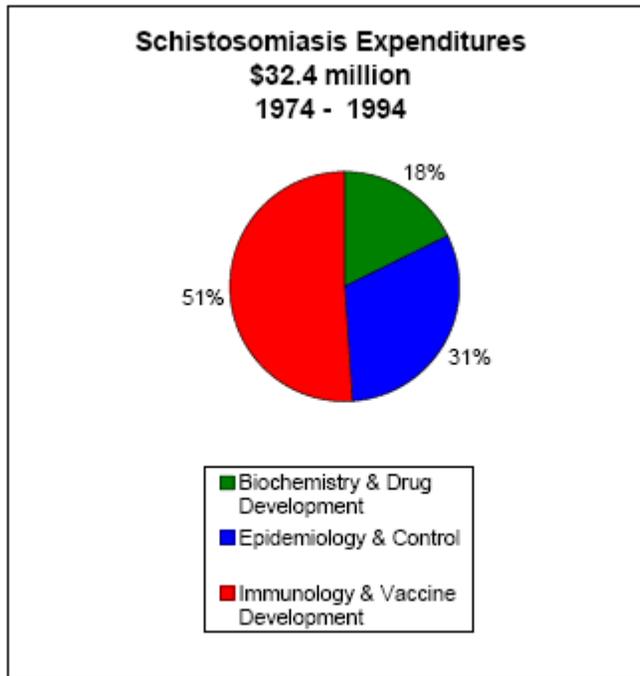
Control, Elimination, Eradication, Extinction

In an article published by the U.S. Centers for Disease Control and Prevention, Walter L. Dowdle of the nonprofit public health organization the Task Force for Child Survival and Development summarized the differences between disease control, disease elimination, elimination of infections, disease eradication, and disease extinction:

- *Control*: The reduction of disease incidence, prevalence, morbidity or mortality to a locally acceptable level as a result of deliberate efforts; continued intervention measures are required to maintain the reduction. Example: diarrhoeal diseases.
- *Elimination of disease*: Reduction to zero of the incidence of a specified disease in a defined geographical area as a result of deliberate efforts; continued intervention measures are required. Example: neonatal tetanus.
- *Elimination of infections*: Reduction to zero of the incidence of infection caused by a specific agent in a defined geographical area as a result of deliberate efforts; continued measures to prevent re-establishment of transmission are required. Example: measles, poliomyelitis.
- *Eradication*: Permanent reduction to zero of the worldwide incidence of infection caused by a specific agent as a result of deliberate efforts; intervention measures are no longer needed. Example: smallpox.
- *Extinction*: The specific infectious agent no longer exists in nature or in the laboratory. Example: none.⁶⁴

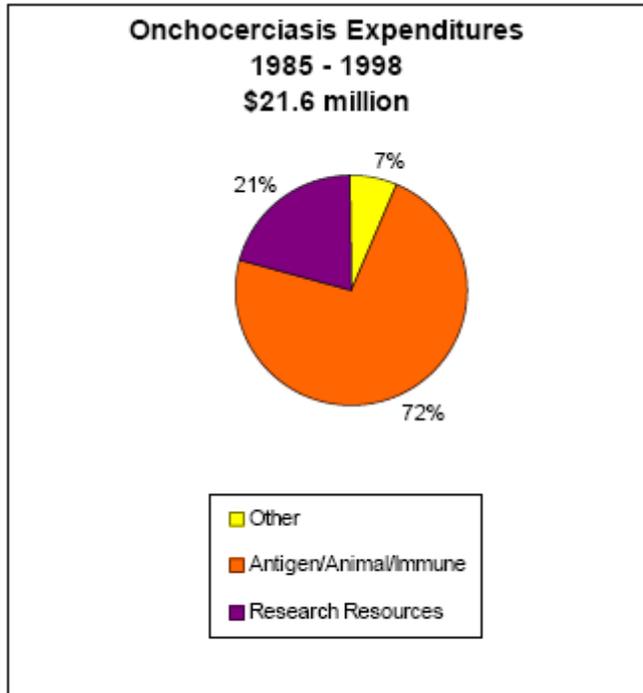
⁶⁴ Dowdle, Walter R. "The Principles of Disease Elimination and Eradication." *Morbidity and Mortality Weekly Report Supplement*, December 31, 1999, p. 24. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention. Retrieved from <http://0-www.cdc.gov.mill1.sjlibrary.org/mmwr/pdf/other/mm48SU01.pdf>.

Exhibit C



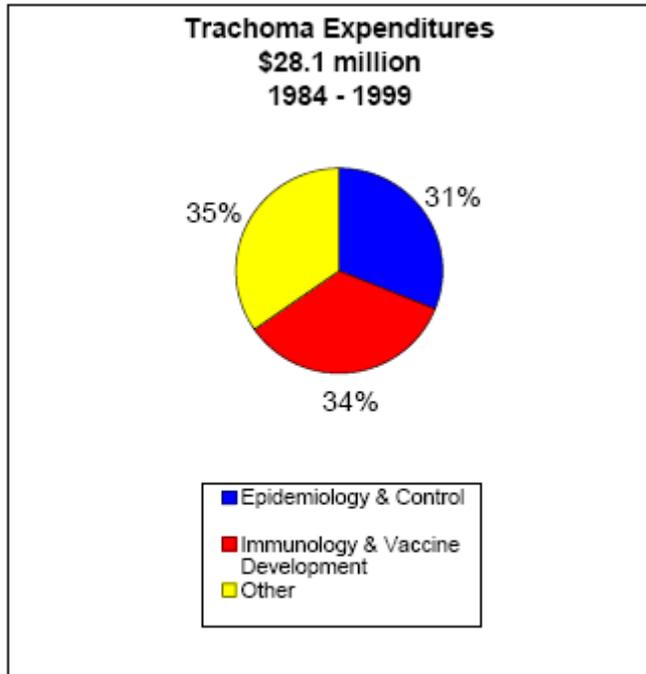
Source: Asbury, Cline, and Gammino, op. cit., p. 41.

Exhibit D



Source: Asbury, Cline, and Gammino, op. cit., p. 54.

Exhibit E



Source: Asbury, Cline, and Gammino, op. cit., p. 71.

The Edna McConnell Clark Foundation's Tropical Disease Research Program

PART B

In an interview in 2003, Bailin summarized his approach during his first few years at the Clark Foundation:

My goal, as things evolved over the first few years, was to wind down these efforts [at systems change] responsibly, and in their place assemble a program that recognizes a humbling but undeniable fact: Foundations do not, in the main, make change in this society. Grantees do.⁶⁵

Since its founding in 1974, the Tropical Disease Research program had stood out at Clark as something of an anomaly. The Foundation's other four programs addressed domestic human service problems that were enmeshed in large public bureaucracies that Clark had found impervious to change. Tropical Disease Research, by contrast, addressed international problems that could be addressed through medical/scientific research and public health measures. Bailin believed that, in essence, TDR was less in thrall to systems change than were other Clark programs.⁶⁶

In evaluating the onchocerciasis program, Bailin followed the recommendations of the 1994 formal evaluation and prepared for exit. Even though no single funder had stepped forward, Bailin believed the field was sufficiently healthy to stand on its own. In the fall of 1997 Bailin approved a grant intended to catalyze European vaccine research efforts. Over the next three years, Clark reduced its commitment to onchocerciasis as Foundation grants expired. The founding of the OnchoNet website was a product of one of Clark's last grants as it exited the field. A final Foundation-supported onchocerciasis workshop was held at Woods Hole, Massachusetts, in March 2000.⁶⁷ Participants at the Woods Hole workshop credited the Clark Foundation with helping to "catalyze and sustain the research effort."⁶⁸

Of all the Foundation's programs, trachoma was the one whose goals were most clearly established, were most measurable, and were seemingly most attainable.⁶⁹

After visiting Joe Cook in Morocco in April 1997, Bailin returned to New York. Before deciding what to do about the trachoma program, he wanted to find out more about Pfizer. He met with representatives of the company and made inquiries into the company's activities. A Clark trustee happened to know and trust Pfizer's general counsel, who vouched for the corporation's good intentions.⁷⁰

⁶⁵ Bailin, 2003, op. cit.

⁶⁶ Bailin interview, June 2006, op. cit.

⁶⁷ Asbury, Cline, and Gammino, op. cit., p. 56.

⁶⁸ Asbury, Cline, and Gammino, op. cit., p. 56.

⁶⁹ Bailin interview, June 2006, op. cit.

⁷⁰ Bailin interview, September 2006, op. cit.

In the fall of 1997, Bailin approved a grant to extend Clark's partnership with Pfizer. Bailin and the Clark board of trustees, though increasingly convinced of the efficacy of the SAFE program and of Pfizer's potential as a partner, nevertheless wanted to exit from trachoma. Bailin recalled, "We didn't want to commit the Foundation to another five years of funding trachoma while waiting for the UN or somebody else to step up. We wanted to do other things."⁷¹

Applying the principles he'd established in his Institution and Field Building approach, Bailin took the initiative in founding a new institution dedicated to implementing the SAFE strategy for trachoma control. In September 1998, the Clark Foundation awarded a \$3.2 million grant to establish the International Trachoma Initiative (ITI), a public-private partnership linking prevention with treatment and devoted to building public health infrastructure in developing countries.⁷² To ensure Pfizer that donated Zithromax would not leak into sales markets, the ITI was structured such that Pfizer itself oversaw the handling and transportation of the drug into the target countries.⁷³ Before any new project was put before the ITI board of trustees for final approval, it had to be approved by the nine-member Trachoma Expert Committee (TEC), composed of experts in tropical disease and international health, as well as representatives from Pfizer and the Clark Foundation.⁷⁴ The involvement of the TEC further reassured Pfizer that its donation program would not undermine sales of Zithromax in the developed world. Pfizer's initial commitment included providing matching funding as well as \$60 million worth of Zithromax.⁷⁵

Because ITI was an independent, stand-alone 501(c)(3) organization, the Foundation believed that "potential funders might be interested in supporting [it] whereas they might be less likely to do so if ITI were a Clark Foundation subsidiary."⁷⁶ Indeed, in its first few years of existence, besides continued support from Clark and Pfizer, the ITI received grants in excess of \$30 million from the Bill & Melinda Gates Foundation and \$8 million from the Starr Foundation,⁷⁷ as well as smaller grants from the Rockefeller Foundation, the Lavelle Fund for the Blind, and the Conrad N. Hilton Foundation.⁷⁸ Pfizer's cash and in-kind donations to the ITI totaled over \$1 billion by 2006.⁷⁹ The Clark Foundation, besides continuing to fund the ITI at the level of approximately \$1.25 million per year,⁸⁰ ensured continued accountability through the presence of one of its trustees on the board of the ITI. Clark's representative on the ITI's Trachoma Expert Committee also helped ensure accountability.

The International Trachoma Initiative would grow substantially and extend its work into dozens of developing countries in Africa and Asia. In 2005, the International Trachoma Initiative

⁷¹ Bailin interview, September 2006, op. cit.

⁷² Cook, Joseph A., "Letter from the Executive Director." In *International Trachoma Initiative 2002 Annual Report: Take a Closer Look*. New York: International Trachoma Initiative, 2002, p. 1. Retrieved from <http://www.trachoma.org/publications.php#>.

⁷³ Bailin interview, January 2007, op. cit.

⁷⁴ Bailin interview, January 2007, op. cit.

⁷⁵ Edna McConnell Clark Foundation, *Annual Report 1999*. New York: Edna McConnell Clark Foundation, 1999, p. 29. Retrieved from <http://www.emcf.org/pdf/1999ar.pdf>.

⁷⁶ Asbury, Cline, and Gammino, op. cit., p. 73.

⁷⁷ Bailin interview, January 2007, op. cit.

⁷⁸ International Trachoma Initiative, *International Trachoma Initiative 2002 Annual Report: Take a Closer Look*. New York: International Trachoma Initiative, 2002, p. 14. Retrieved from <http://www.trachoma.org/publications.php#>.

⁷⁹ Bailin interview, January 2007, op. cit.

⁸⁰ Edna McConnell Clark Foundation, *Annual Report 2005*. New York: Edna McConnell Clark Foundation, 2005, p. 30. Retrieved from <http://www.emcf.org/pdf/2005ar.pdf>.

received support and revenue totaling \$59.4 million and spent \$64.5 million⁸¹ to support health workers who distributed 16.5 million treatments of Zithromax and performed more than 77,000 surgeries.⁸² The totals, from the founding of the ITI through 2006, are just as impressive: 36.8 million antibiotic treatments applied, 221,000 surgeries performed, and hundreds of ITI projects to improve hygiene and sanitation completed benefiting millions of individuals.⁸³

⁸¹ International Trachoma Initiative, *International Trachoma Initiative 2005 Annual Report*. New York: International Trachoma Initiative, 2005, p. 16. Retrieved from <http://www.trachoma.org/publications.php#>.

⁸² International Trachoma Initiative, *International Trachoma Initiative 2005 Annual Report*, op. cit., p. 7.

⁸³ International Trachoma Initiative, *International Trachoma Initiative 2005 Annual Report*, op. cit., p. 3.