

Advancing the Global Public Health Agenda With Commercial Clinical Research Infrastructure

Kelly T. McKee Jr, Oren Cohen

In 1967, the US surgeon general declared that “the time has come to close the book on infectious diseases” [1]. At that time, tuberculosis had become a rarity in the developed world, and the push to eradicate smallpox was just underway. Howard Martin Temin’s discovery of reverse transcriptase, which would lead to the identification of human retroviruses, would occur 3 years later. Although sporadic cases of human immunodeficiency virus (HIV) infection were likely occurring in Africa around 1970, it was not until the mid-1970s that substantial human-to-human transmission began in earnest.

In 2010, it is safe to say that infectious diseases are alive and well and will continue to be important causes of morbidity and mortality for the foreseeable future. Thanks to the wide availability of airline transportation and continued logarithmic growth of electronic connections and communications, the globe continues to shrink at breakneck speed. The pandemic of HIV infection and acquired immunodeficiency syndrome (AIDS) has ravaged sub-Saharan Africa and continues to spread on a global basis. Tuberculosis is resurgent, thanks in part to the shrinking globe and the HIV/AIDS pandemic. Malaria continues to take a million lives per year, many of them children. And 2009 saw the return of an influenza pandemic, which was caused by a molecular relative of the influenza virus that resulted in the killer pandemic of 1918.

North Carolina is at an interesting crossroads in global health. The standard of living in the state’s urban centers, which are leaders in finance, information technology, and biotechnology, is among the best in the nation. The concentration of universities and enterprises in or near Research Triangle Park, North Carolina, that are dedicated to clinical research and global health is particularly impressive, attracting investment and interest from around the world. In contrast, many of North Carolina’s rural residents have poor access to health care services, and education levels among economically disadvantaged students remain well below the national average [2]. Infant mortality rates in several counties in rural eastern North Carolina range from 15-17 deaths per 1,000 births, approximating rates in Jordan, Malaysia,

and Thailand [3]. Increasingly, parts of the developing world are looking like rural North Carolina with regard to disease prevalence [4]. The American soft drink and fast food industries are seeing unprecedented growths in sales in developing countries, and as these sought-after exports become more affordable to people in these areas, rates of obesity and diabetes have begun to soar. In India, the prevalence of diabetes is expected to increase by nearly 80%, from 2.8% to 5.0% of the population, between 2000 and 2030 [5]. In 2030, there will be approximately 79.4 million people with diabetes in India. Because diseases associated with poverty remain stubbornly prevalent in the developed world and diseases of affluence and opportunity continue to emerge in the developing world, it makes sense to investigate diseases and new treatments on a global scale via studies that accommodate as many relevant populations as possible.

Drug and vaccine development is a lengthy and expensive process, with clinical trials accounting for a substantial portion of the total costs of drug development. The complexity of trial design, the maze of regulatory requirements, the nuances and requirements of subject enrollment, and the logistics of coordinating the myriad moving parts intrinsic to large, multinational studies are some of the enormous challenges attendant to accurate and successful execution of clinical studies to determine the potential effectiveness of a drug or vaccine at the population level.

In the 1970s, the need for specialist clinical research organizations to address these complexities was recognized, and a new enterprise was born in North Carolina. Dennis Gillings, a professor of biostatistics from the University of North Carolina (UNC)–Chapel Hill, began providing statistical consulting services for firms in the pharmaceutical industry. From its earliest days in a trailer on the UNC–Chapel Hill campus, the concept that became Quintiles has grown into the largest biopharmaceutical services company in the world, with more than 20,000 employees in 60 countries. The global growth of the clinical trials industry mirrors the needs of the biopharmaceutical industry overall. In this regard, by 2007, more than 50% of clinical trial-associated activities were occurring outside of the United States

Kelly T. McKee Jr, MD, MPH, vice president and managing director, Public Health and Government Services Unit, Quintiles. He can be reached at kelly.mckee@quintiles.com.

Oren Cohen, MD, chief medical and scientific officer, Quintiles.

[6]. Primary drivers of this trend include the medical need and large number of patients in other areas of the world, the availability of skilled clinical investigators in regions of emerging importance, the harmonization of regulatory requirements, and the lower costs associated with clinical research in other regions.

Several of the largest biopharmaceutical services companies have followed Quintiles in establishing significant global footprints consisting of networks of local hospitals, investigators, laboratories, and ancillary support services to effectively coordinate and manage clinical trials. Increasingly, these footprints have expanded to the developing world (Table 1).

The resources, capabilities, and reach developed by organizations such as Quintiles for the wide range of studies conducted by the biopharmaceutical industry also have obvious appeal for drug and vaccine developers with products of potential benefit in the developing world. Biopharmaceutical companies, government agencies, and nongovernmental organizations seek to capitalize on these capabilities to avoid establishing stand-alone infrastructures, to mitigate the risk of poor or inadequate study execution, to ensure quality and ethical behavior, and, ultimately, to contain development costs. Indeed, Quintiles created a public health and government services business several years ago to meet these needs. Quintiles and similar providers of clinical services partner with numerous government, for-profit, and not-for-profit organizations in providing essential background epidemiological information, local infrastructure access, and clinical trial services to advance the development of products and better tailor the delivery of licensed products to users.

Quintiles has a particularly strong presence in sub-Saha-

ran Africa, having worked extensively in the region for more than 10 years. Quintiles has leveraged its infrastructure for local capacity building and to achieve public health objectives. Studies of experimental drugs and vaccines for prevention of HIV infection, tuberculosis, and malaria have all been successfully conducted in the region. Studies of neglected diseases, such as leishmaniasis and hookworm infection, have been conducted in other developing regions, including India and Latin America. Expanding the scope of clinical research in the developing world has been made possible by the efforts of governments, commercial organizations, nongovernmental organizations, academic medical institutions, and local communities and investigators. Partnerships are abundant, and some involve government agencies. Notable examples include the US National Institute of Allergy and Infectious Diseases and the University of Bamako in Mali, the University of Alabama-Birmingham and the University of Zambia, and Howard Hughes Medical Institute and the University of KwaZulu-Natal in South Africa. Quintiles has established partnerships with the University of Pretoria in South Africa and with the University of Ghana at the Noguchi Memorial Institute for Medical Research. In addition, the Bill and Melinda Gates Foundation funds an enormous amount of clinical research in the developing world, both directly and indirectly through partnerships and alliances. Many benefits come from these partnerships, including access to experimental treatments and vaccines by local populations with medical need, expansion of research capacity, cross-cultural scholarly activities, and employment and other economic stimuli. Ultimately, a major goal is the development and approval of safe and effective products for local populations in need. Biopharmaceutical services companies are valuable partners in achieving this objective, as they were created specifically to support efficient navigation of the drug-development process, with utmost attention to regulatory compliance.

Involvement in clinical research in the developing world raises the bar for proper ethical stewardship. Clinical staff and monitors must be well versed in International Conference on Harmonization Good Clinical Practice guidelines, the ethical principles for clinical research delineated in the Declaration of Helsinki, and local regulations. Although biopharmaceutical services companies are not directly involved in the informed-consent process, it is a critical focal point with regard to protection of vulnerable populations. Quintiles has trained hundreds of African investigators and onsite staff in the principles of good clinical practice, including issues associated with informed consent, and these efforts are now expanding around the newly established offices in Ghana and Kenya. Quintiles has also undertaken a long-term empowerment initiative in the form of a 6-month clinical research associate apprenticeship program, to address issues related to racial and gender inequality in the region. Funded by Quintiles and targeting previously disadvantaged individuals with appropriate qualifications but no

Table 1.
Quintiles Operations in Selected Countries in the Developing World

Country	Year operations began
South Africa	1990
Brazil	1997
China	1997
Estonia	1997
India	1997
Russia	1997
Thailand	2000
Peru	2003
Vietnam	2005
Indonesia	2006
Egypt	2007
Ghana	2009
Kenya	2010

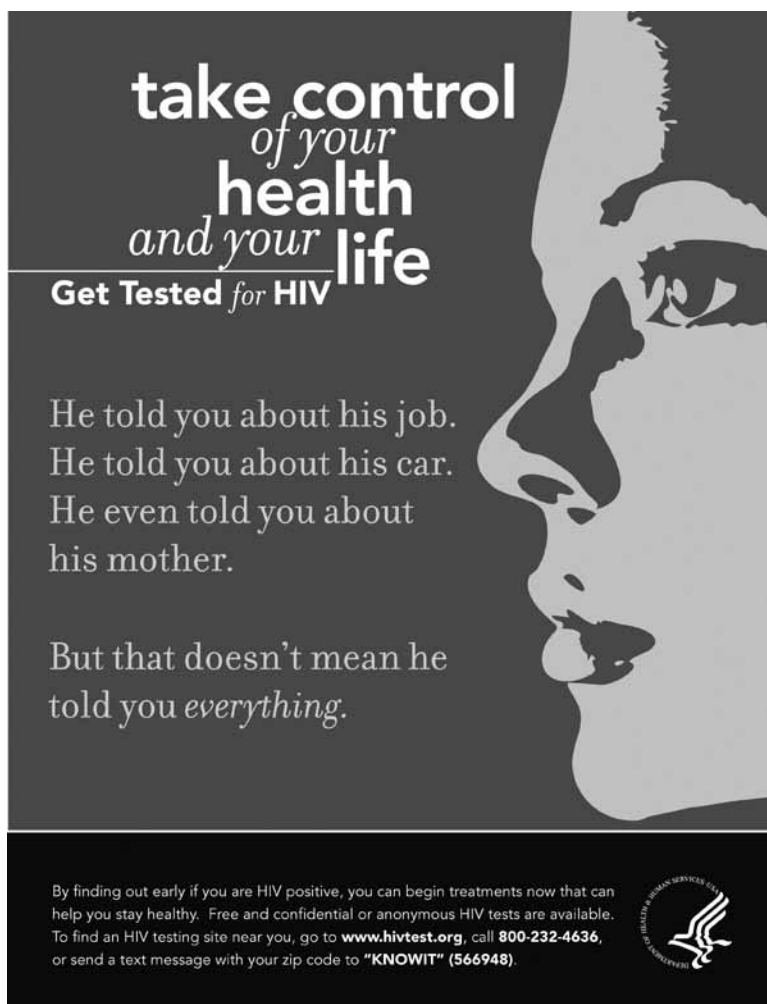
job opportunities, the program covers the soft and technical skills needed for employment in the clinical research and pharmaceutical industries. The program is intended to expand research capacity and quality in the region, and it is also contributing to economic development.

The potential exists to leverage the commercial clinical trials infrastructure in even more-creative ways. In this regard, studies of drugs and vaccines for prevention of anthrax, plague, and smallpox, as well as for other biodefense applications, have been conducted to support public health objectives. In addition, many studies of antiviral agents and vaccines to prevent influenza, including sev-

eral of the H1N1 strain involved in the influenza pandemic of 2009, have been conducted. These studies have been executed on behalf of biopharmaceutical companies and government agencies. The changing landscape of the biopharmaceutical industry and the delivery of health care pose unique challenges and opportunities. Given the moral and economic imperatives to address global public health problems, collaborative efforts between governments, nongovernmental organizations, universities, commercial organizations, and local investigators and communities will undoubtedly provide the most-compelling solutions in the developing world and North Carolina. NCMJ

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He told you about his car.
He even told you about
his mother.

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