

Chapter 1

Introduction and Background

Introduction and Background

The Gorgas Memorial Laboratory (GML) is a research institution concerned with tropical medicine and public health. It undertakes both applied and basic research, and performs laboratory, clinical, and field research activities. GML was established in 1928 in commemoration of the work of Gen. William Gorgas in controlling yellow fever. The Laboratory is located in Panama City, Republic of Panama. It is the research arm of the Gorgas Memorial Institute of Tropical and Preventive Medicine, Inc. (GMI), a (U. S.) domestic, nonprofit corporation headquartered in Washington, D.C.

INTRODUCTION

GML is a specific subject of evaluation because of questions concerning its fiscal year 1984 appropriation. GMI is authorized by act of Congress (Public Law 70-350, as amended) to receive a yearly appropriation, not to exceed \$2 million, from the U.S. Government. The original fiscal year 1984 budget request from the Fogarty International Center (FIC)—the unit of the National Institutes of Health (NIH) given responsibility for administering the Gorgas budget request—included a budget request for Gorgas. A subsequent revision by NIH, of the NIH budget, led NIH/FIC to request no funds at all for core support of GML. Because this core support of close to \$2 million is an extremely large percentage of the total GML budget (see ch. 2), this action effectively meant that GML would have to close down.

In order to evaluate whether this action was justified on the basis of the quality of Gorgas' research and on its success in identifying needs and conducting research relevant to health concerns of Panama and tropical America* (especially Central America and the Caribbean), the requesting subcommittee and committee asked both

This technical memorandum presents the results of a review of the quality and relevance of research and related activities of GML. The evaluation was conducted at the request of the Senate Committee on Appropriations and, especially, its Subcommittee on Labor, Health and Human Services, and Education. It is part of a broader OTA assessment of the status of biomedical research and related technology for tropical medicine, also requested by the committee and subcommittee.

the General Accounting Office (GAO) and the Office of Technology Assessment (OTA) to provide relevant information.

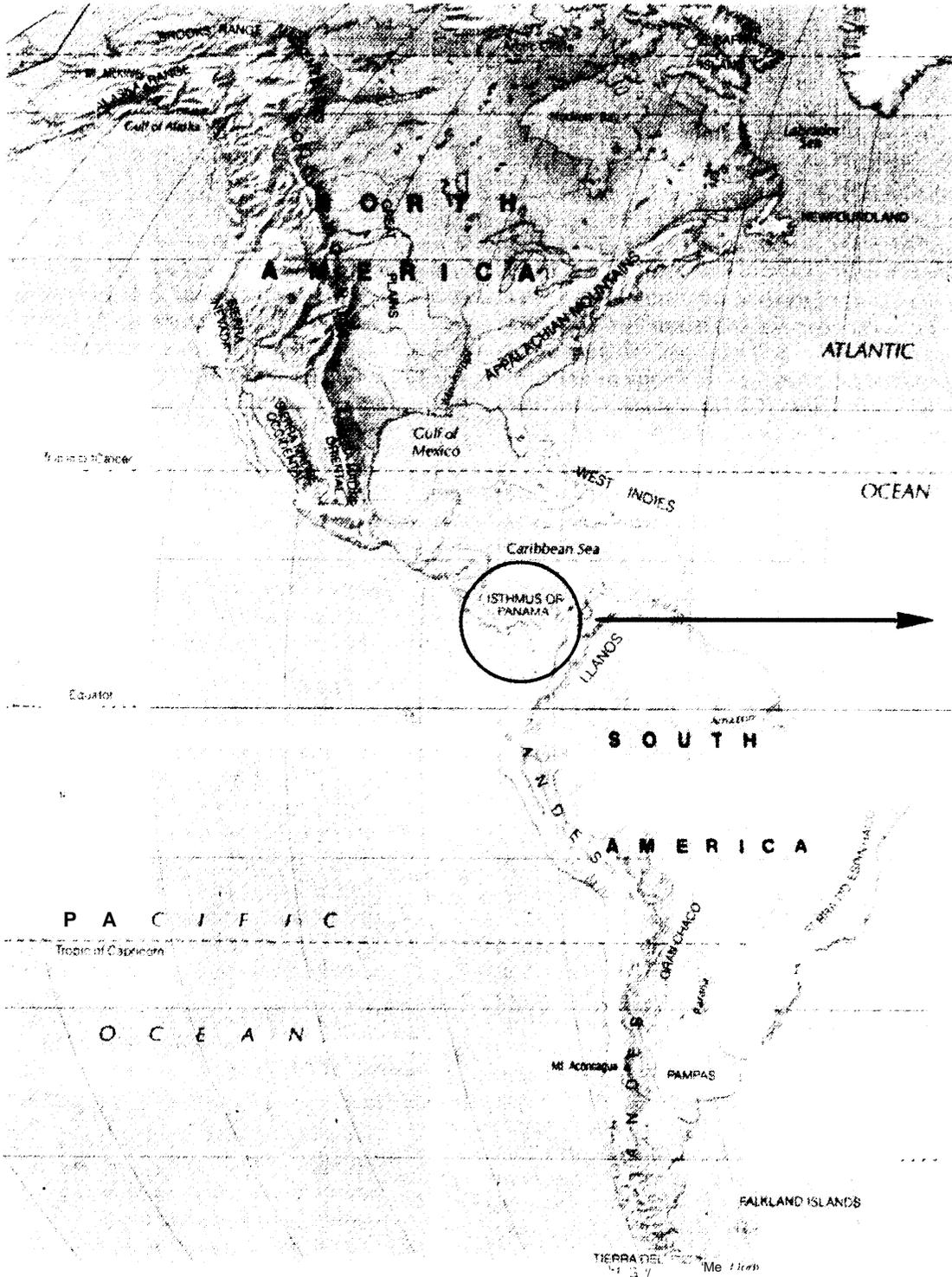
The related effort by GAO examines four topics:

1. the process of peer review used by GML before initiating research projects and after their completion,
2. efforts to broaden the financial base of GML,
3. other federally funded tropical medicine research activities, and
4. the possible impact of GML's closing on U.S.-Panamanian relations. That report is scheduled for completion in August 1983.

The OTA effort devotes some attention to the first of those four topics, but is primarily addressed to issues of:

1. the quality of GML's applied biomedical research projects, epidemiological activities, maintenance of research animal populations, and other research-related activities such as training; and
2. the relevance of GML's research and other activities to the health needs and problems of Panama, other tropical American countries, the U.S. interests, and to tropical medicine in general.

*The term tropical America here refers to the southern part of North America, all of Central America and the Caribbean, and tropical South America.



The Americas

Organization of the Technical Memorandum

The remainder of this chapter contains a summary of the findings and conclusions of the technical memorandum and background information on the Tropics, tropical diseases, and the role of research laboratories located in the Tropics. Chapter 2 presents descriptive material on Gorgas, its structure, and past and current research activities. Chapter 3 examines evidence on the quality of GML's research, public health, and training activities.

The fourth chapter presents descriptions and brief data on the status of the diseases and health problems of critical importance to tropical America and of research related to them. Gorgas's ac-

tivities are then discussed in the context of these diseases and conditions. The final chapter presents the findings and conclusions.

Appendix A presents the acknowledgments, lists the members of the Liaison Group formed by the Pan American Health Organization to provide advice to OTA on this project, and lists the OTA Health Program Advisory Committee. Appendix B is a brief presentation of other current research activities in tropical health. Appendix C is a bibliography of publications since 1975 by GML staff. Appendix D is a summary of the OTA survey of experts' opinions concerning Gorgas and its research quality and relevance. Appendix E contains a list of acronyms and a glossary of terms.

SUMMARY OF FINDINGS AND CONCLUSIONS

OTA examined the quality and relevance of tropical medicine research and related activities at GML. The evaluation of the quality of an institution such as Gorgas cannot take place without explicit recognition of certain premises:

- There is an inherent value in supporting tropical research laboratories in tropical countries. Field conditions present opportunities that cannot be duplicated by organizations such as NIH.
- Evaluations of the quality of research are inevitably, and properly, made partly on the basis of fairly objective criteria such as publications record and partly on the basis of subjective judgments by qualified individuals.
- The criteria used to judge quality, although similar in type, need to be modified and weighted differently for research performed in well-equipped, state-of-the-art laboratories than for field research laboratories.
- Relevance is directly dependent on the type and location of institution, and it should be examined from each of the appropriate viewpoints (e.g., host country, region, United States, general advancement of knowledge).

With these premises in mind, OTA examined the quality of Gorgas' research against a range of

objective and subjective criteria. There was very impressive agreement among the results of: 1) the past scientific evaluations of GML, 2) the critical evaluation of the research design and presentation of articles and manuscripts, 3) the survey of expert scientific opinion on Gorgas' quality, 4) interviews with Panamanian health officials and professionals, 5) the examination of GML staff's publications record, and 6) an examination of GML's record of competing for grants and contracts. All evidence gathered by OTA led to the finding that the overall scientific quality of GML is high, especially when considered in the context of GML's status as a research laboratory located in the Tropics. Quality was, naturally, not uniformly even.

OTA also found that the large majority of GML's research is highly or adequately relevant to health concerns and problems of Panama, the tropical American region, U.S. interests, and the advancement of scientific knowledge and the field of tropical medicine in general. (Table 1 lists significant accomplishments of GML in the past decade; table 2 shows significant activities during the previous period of GML's history.) The evidence for this finding lies, for the first two, in the match between tropical health problems and GML research directed at them, and from strongly

Table 1.—The Gorgas Memorial Laboratory's Major Accomplishments From 1970 to the Present

- Continued yellow fever surveillance and monitoring of vectors
- St. Louis encephalitis and Venezuelan equine encephalitis vectors and reservoirs
- Insect genetic studies using isozyme markers
- Transovarial transmission of yellow fever virus in mosquitoes
- Use of *Aotus* monkey model for testing of therapeutics
- Several new viral isolates in area
- Screening of antimalarial drugs and identification of promising therapeutic antimalarial compounds
- WHO regional center for bloodmeal analysis
- Improved identification of insect vectors: sandflies, triatomines, blackflies, etc.
- Development of cancer registry in the Republic of Panama
- Discovery of high incidence of cervical and penile cancer in Herrera Province (Republic of Panama)
- Studies of sexually transmitted diseases in the Republic of Panama (the first such studies in Latin America)
- Rapid identification of viral agent in recent epidemics of conjunctivitis and encephalitis in the Republic of Panama
- Discovery of high HTLV antibodies in the Republic of Panama
- Environmental impact assessment of Tabasara Hydroelectric project

SOURCE: Gorgas Memorial Laboratory, Office of the Director August 1983

expressed opinions and examples by various Panamanian officials and professionals.

The importance of GML to Panama cannot be judged solely on the basis of Panama's monetary contribution. Panama is going through a difficult economic period. Even so, the Ministry of Health has arranged a loan to keep GML in operation for the remainder of fiscal year 1983. The value of the land, buildings, and tax-favored status have never been adequately assessed. And to put the often criticized direct financial contribution of \$10,000 from Panama in perspective, the research budget of the Panamanian medical school is reportedly only \$20,000. As one official of the U.S. Department of State expresses it: Each year, the United States sends a message to Panama and the region by funding GML and supporting activities related to the health of U.S. and Panamanian citizens alike (51).

Activities related to the recent Panama Canal Treaty process provide a specific example of the importance of GML to Panama. As part of the

treaty, a Joint Committee on the Environment was established. Panama turned to GML, as the only institution in Panama with the necessary skills and experience, for assistance in relation to environmental protection and human and animal health, and additionally named Dr. Pedro Galindo, formerly of GML, as the senior Panamanian on the Committee.

Relevance to U.S. health interests can be found in the surveillance activities, the training activities, and the various research activities undertaken under contract to the U.S. military. There are about 20,000 U.S. Government employees and dependents in Panama; and many thousands more in nearby countries. The work of GML is directly relevant to the health of these people.

Gorgas's contributions in the areas of malaria, yellow fever, and leishmaniasis illustrate its relevance to the general advancement of knowledge (see also, tables 1 and 2).

Based on the above evidence, OTA finds that with some exceptions that occur almost entirely within the core-funded activities, the research conducted at Gorgas is relevant to the various parties at interest.

Conclusions: OTA concludes that the benefits of supporting GML justify, on scientific and other grounds, the relatively small amount of funds required. Quality and relevance are high. Withdrawing core support from Gorgas would probably not even save the amount of the appropriation, since other Federal agencies may need to either conduct or support research now carried out at GML.

Gorgas is not ideal; improvements could certainly be made. Some of the shortcomings stem from its uncertain funding. The prospect of unstable funding and perhaps closure may have kept individual scientists [from] joining GML or becoming visiting scientists there and may reduce the desire of U.S. universities to collaborate with GML on research projects.

Another example of the effect of uncertain funding has been the decision by the U.S. Navy to hold off on the next scheduled training class, because the course would extend a few weeks into fiscal year 1984. It is extraordinarily difficult to

Table 2.—Major Accomplishments of the Gorgas Memorial Laboratory, 1929-69

i. Protozoa/ Diseases of Man and Lower Animals:**Malaria:**

- 1933 and subsequently: First long-range, large-scale field tests of the antimalarial drugs, Atebrine, chloroquine, and paludrine under controlled conditions in the New World Tropics,
- 1954: First long-range field tests of DDT house-spraying to control malaria.
- 1960: Field demonstration of the effectiveness of weekly doses of pyrimethamine-primaquine drugs combined with the eradication of *Plasmodium falciparum* malaria from a tropical area.
- 1966: Demonstration that certain common human malaria parasites could be grown in certain species of Panamanian monkeys and could be transferred to man and other monkeys by blood inoculation and by bites of mosquitoes.

American Trypanosomiasis:

- 1931: First report of Chagas' disease in Panama and discovery of the vectors.
- 1959: First report of *Trypanosoma rangei* from man and wild vertebrates in Panama and demonstration of the development of the human strain in the salivary glands of *Rhodnius pallescens*.
- 1965: Demonstration that the Panamanian strain of *T. rangei* differs from the South and Central American strains in its behavior of development in the insect vector.

Leishmaniasis:

- 1965: Incrimination of seven wild vertebrates as reservoir hosts of human leishmaniasis.
- 1966: Demonstration that leishmania infection may commonly occur in the apparently normal skin of some feral animals without producing lesions.
- 1945-68: Recognition of over 70 species of *Phlebotomus* in Panama, of which 4 or 5 have been found infected with leishmania.

Animal Trypanosomiasis:

- 1932: Discovery of the vampire bat transmission of equine trypanosomiasis.
- 1932: Discovery of bovine trypanosomiasis in Panama.

Intestinal Protozoa:

- 1944: First finding of *Isopora hominis* in Panama.

II. Helminthic Diseases of Man and Lower Animals:

- 1934-35: First comprehensive survey of the worm parasites of equines in Panama.
- 1966: Finding a new human disease entity caused by *Echinococcus oligarthrus*, a little known cestode parasite of pumas and other large felines; description of the first known human case that terminated fatally; and demonstration of the life cycle of the parasite.

III. Rickettsial Diseases:

- 1946: First report of Q Fever in Panama.
- 1947: First report of murine typhus in Panama.
- 1951: First recognition of Rocky Mountain Spotted Fever in Panama.

IV. Virus Diseases:

- 1949: First demonstration of the mosquito vectors of yellow fever in Panama and Central America and the inauguration of comprehensive studies on vector ecology and transmission capabilities.
- 1957: First recovery of St. Louis encephalitis virus and recognition of human cases in Panama.
- 1958: First isolation of Ilheus virus in Central America.
- 1960: First isolation of Changuinola virus from man.
- 1961: Discovery of four new arboviruses: Madrid, Ossa, Patios, and Zegla.
- 1963: First isolation of Wyeomyia subgroup of arboviruses from man.
- 1964: Recognition of the first human case of Ilheus encephalitis.
- 1965: Finding of crab-hole mosquitoes (*Deinocerites*) as hosts for St. Louis encephalitis virus.
- 1968: First isolation of Vesicular Stomatitis virus (Indiana) from man in Panama and detection of virus transmission by the use of sentinel monkeys.

V. Medical Entomology:

- 1929: First elucidation of the human botfly, *Dermatobia hominis*, in man.
- 1935: First establishment of a laboratory colony of *Anopheles albimanus*, the main vector of malaria in Central America.
- 1944: First tests of DDT to control phlebotomine sandflies.
- 1945: First experimental trials of DDT for the control of *Simulium* spp., the vectors of *Onchocerca volvulus*, the blinding filarial parasite of man.
- 1945: First experiments with DDT for the control of *Culicoides* sandflies.
- 1945: First observations in Panama on the habits and life histories of chigger mites (*Trombiculidae*), potential vectors of disease.
- 1966: First comprehensive survey of the ticks and biting insects of Panama.

VI. Miscellaneous Projects:

- 1930-54: Comprehensive survey of the poisonous snakes of Panama and the incidence of snake bites.

SOURCE Willard H Wright, 40 *Years of Tropical Medicine Research* (Washington, D C Reese Press, 1970)

plan and carry out research related to tropical diseases without multiyear budgeting and some assurance of multiyear funding.

Gorgas itself could improve its standing and its relevance by:

- being more aggressive in its publishing,
- by making better use of its Advisory Scientific Board (see ch 5 for examples of possibilities),
- by more actively seeking out associations and collaborations with a range of universities,

- groups from other countries, and international organizations,
- by making strategic plans to move more fully into the developing areas of modern science (e.g., work with monoclonal antibodies and other immunological diagnostics, and biotechnology approaches to vaccine-related research and development), and
 - by making more of an effort to run vigorous visiting scientist and fellowship programs.

OTA concludes that the only benefit to the United States of defunding Gorgas would be savings of perhaps significantly less than \$2 million a year. The negative consequences would include loss of one of the few, high-quality, broadly relevant, tropical research institutions located in a tropical country. The standing of the United States in tropical America would inevitably suffer.

BACKGROUND

The Tropics and Tropical Diseases

The Tropics can be roughly considered to include Central America, much of South America, the South Pacific, southern Asia, and most of sub-Saharan Africa. Tropical nations are usually characterized by poverty, substandard drinking water and sanitation, hot and humid climates, poor health services, low levels of education, and in some cases swampy or jungle areas. Annual per capita income is often extremely low (as low as or even less than \$100). In tropical America, the average per capita gross domestic product was \$1,500 in 1980. However, the variation is wide, ranging from nearly \$9,000 in the Bahamas and \$2,685 in Barbados (both figures may be deceptive) to \$267 in Haiti and \$568 in Bolivia (75).

Of the world's approximately 4½ billion people, about three-quarters live in less developed countries, most of which are tropical. Of the approximately 600 million population (1980 figures) of the Western Hemisphere, about 60 percent live in Latin America, most of which is tropical.

Health status is generally poor, with high rates of infant mortality (primarily due to malnutrition, lack of prenatal care, and diarrheal and respiratory infections), widespread infection with debil-

Ironically, GML is in danger of extinction at the very time that U.S. interest in Latin America is high, and at a time when tropical medicine has never been more relevant to U.S. interests.

In summary, OTA concludes that the positive consequences of U.S. core support of Gorgas greatly outweigh the amount of funds involved. Defunding new, followed by an appreciation of the loss later and a subsequent attempt to reinstate such a research capability, may result in much larger required investments, an inability to recreate successful conditions for quality research, or both. *

*In fact, it may be impossible to recreate GML or a similar institution in the current political climate in Latin America (51)

itating disease, and high mortality and morbidity rates from all diseases except certain chronic ones associated with a higher standard of living (such as some cancers).

Any definition of "tropical disease" is arbitrary. In its strictest sense, perhaps, a tropical disease is one found—for reasons of physical environment and climate or the presence of specific disease vectors—entirely or predominantly in tropical regions.

However, a more realistic, and more useful, definition includes those diseases or conditions—such as acute respiratory infection, tuberculosis, malnutrition, or cholera—that occur or could occur in many regions, but which are considerably more prevalent in tropical areas because of the social and economic conditions that characterize many tropical countries. In countries with very low per capita gross domestic products, inadequate or unsafe water supplies and sanitation, low levels of health care services, high levels of illiteracy, and similar conditions, certain diseases are able to flourish beyond the extent that would be predicted simply on the basis of climate.

The OTA assessment, including this technical memorandum, will consider "classic" tropical dis-

eases such as malaria that fit the narrower definition, but it will more generally be guided by the broader definition. Thus, a more appropriate phrase to describe the subject of the assessment and the context in which Gorgas will be evaluated is “medicine and health in the tropics.”

The direct economic and social impacts of widespread disease are obvious, but the most substantial economic impacts may be indirect ones, affecting a country’s human resources and productivity. For example, a country whose population has an extremely high prevalence of debilitating disease loses labor resources, and productivity inevitably suffers.

In addition to the humanistic concern with the health and quality of life of people in tropical countries, and in addition to the stake that all developed countries have in the economic health and development of developing countries, there is a smaller, yet definite benefit that can accrue to the United States through support of tropical disease research and technology development. Tropical countries are no longer—if they ever really were—“exotic” far off lands seen only by adventurers. A great many people now travel to and live in tropical countries, as tourists, in the diplomatic or military service, or as employees of U.S. or multinational companies. The number of such people is most likely increasing. * “The tropics are coming closer and bringing their diseases with them” (69).

In addition, advances in tropical disease research can represent valuable knowledge in general medical science, particularly in the areas of infectious disease control, general preventive medicine, and environmental health.

The Value of Laboratories Located in the Tropics

Laboratories and field stations located in the Tropics have played a vital role in tropical disease research during this century. There is a certain point at which research taking place in tem-

perate countries, even though aimed at eventually eliminating or controlling tropical diseases, can go no further, regardless of the quality of researchers or institutions. Initially, information about the occurrence (incidence, prevalence, case-fatality rates), natural history, and transmission of diseases is necessary for the rational design of strategies to deal with diseases, and this can only be collected in the field. Finally, the fruits of research—e.g., drugs and vaccines, vector control programs—must be tested where the diseases occur: in tropical regions. These are the very minimum involvements for institutions in the Tropics.

There is absolutely no substitute for field conditions in tropical countries. This point has been made to OTA time and again by tropical health experts in academia, Government research organizations, and the U.S. military.

Apart from research, training in tropical medicine can only reasonably take place in the Tropics. Training needs and expertise have traditionally been concentrated largely in the military. Additionally, professionals with training in tropical medicine are in demand by foreign governments, academic institutions, and voluntary agencies (107).

In addition to benefits to the U.S. population from knowledge of the control of tropical diseases, the existing tropical field laboratories benefit the countries in which they are located. The country’s health science professionals who are involved in the projects or receiving training raise the level of sophistication of biomedical research in these countries. The disease problems studied are of obvious importance to the populations in these countries, and any progress in treatment or control will benefit them. An additional benefit can be a lessening of the “brain drain” that occurs in many, especially developing, countries. When a good quality research institution exists in a country, its professionals have a place and the opportunity to work and develop without emigrating and thus not depriving the country of their skills.

The U.S. Government supports a relatively small number of laboratories in tropical areas (see app. B). The Department of Defense operates eight medical research laboratories in the Tropics.

*The Increasing number of refugees in recent years serves as a dramatic example of an additional reason for regarding attention to tropical medicine as an important priority for the United States

In Latin America, the Centers for Disease Control (CDC) operates the Medical Entomology Research and Training Unit in Guatemala. CDC previously ran a field station in El Salvador, which has been closed. The United States also supports tropical health research through contributions to international development agencies and through bilateral aid.

Establishing new field laboratories is a difficult and time-consuming task. Building good relations

with the host country and becoming a productive unit may take years. The decision to eliminate an existing laboratory should consider that point.

Thus, any evaluation of GML must not only consider the quality and relevance of its research, but also its role as a research, training, and public health unit actually located in the Tropics.