Perspective
Ethical, Social, and Cultural Considerations for Site Selection for Research with Genetically Modified Mosquitoes

James V. Lavery,* Laura C. Harrington, and Thomas W. Scott
Centre for Research on Inner City Health, Centre for Global Health Research, The Keenan Research Centre in the Li Ka Shing Knowledge Institute of St Michael's Hospital, Department of Public Health Sciences and Joint Centre for Bioethics, University of Toronto, Toronto, Ontario, Canada; Department of Entomology, Cornell University, Ithaca, New York; Department of Entomology, University of California, Davis, California

Abstract. Recent advances in technology have made strategies for disease control using genetically modified (GM) vectors more plausible. Selecting an appropriate field site for research with GM mosquitoes may be one of the most complex and significant aspects of the research process. Among the key considerations of the process is the need to address ethical, legal, and cultural (ESC) issues. No guidelines have been developed to date for this complicated and sensitive process. In this paper, we describe a site selection process and a set of preliminary considerations for addressing the ESC aspects of a research program involving genetic strategies for the control of mosquitoes as vectors for dengue viruses. These considerations reflect some of the key ESC issues for site selection decisions for research with GM vectors.

INTRODUCTION

Studies involving genetic modification of mosquitoes and other insects to make them less capable vectors (carriers) of infectious diseases1 are closer to making their move from the laboratory to the villages of developing countries, where malaria, dengue fever, Chagas’ disease, and other vector-borne diseases are most common. The establishment of caged field trials and preparation for environmental release trials of genetically modified (GM) insects mark important milestones in the evolution of vector control research and raise a host of questions about how these trials should be designed, developed, and implemented to ensure that they are ethically, socially, and culturally appropriate.

Myriad issues face researchers, research sponsors, and host communities of caged field trials and environmental release trials of GM insects, including what standards should be used for risk assessment2 and what mechanisms are most appropriate for the review and oversight of specific field trials.3 One issue that has received relatively little attention to date, but which may be one of the most complex and significant, is the process and rationale for selecting an appropriate site for the research. Site selection is a process by which an appropriate location for these trials is chosen. Some scientific criteria have been published for site selection for GM insect trials.4 There is also a growing appreciation of the kinds of ethical, social, and cultural (ESC) issues that must be successfully addressed5,6 to ensure that these trials are conducted properly. However, there is still no systematic guidance on how ESC issues relevant to site selection for research with GM insects should be approached.

Site selection is an important consideration in research with GM insects, because it is the first formal step in establishing long-term research collaborations between researchers from high-income countries and collaborators from the host endemic sites, which are primarily in low- and middle-income countries.7 The site selection process provides a brief window of opportunity for investigators to determine where their proposed research can be conducted most effectively. Because of the nature of the risks associated with either the accidental release of GM insects in caged field trials or research involving intentional environmental release of GM insects, site selection decisions must address a host of issues beyond the strictly scientific aspects. This allows the investigators to determine where the anticipated ESC issues associated with the research can be addressed most successfully.

In this paper, we describe a site selection process and a set of preliminary considerations for addressing the ESC aspects of a research program involving genetic strategies for the control of mosquitoes as vectors for dengue viruses. We believe these considerations reflect some of the key ESC issues for site selection decisions for this type of research, and we hope to stimulate further discussion and attention to them.

THE RESEARCH PROJECT

The research project for which the site selection process was conducted is one of the projects funded under the Bill & Melinda Gates Foundation’s Grand Challenges in Global Health initiative. This project aims to develop genetic strategies to prevent transmission of dengue viruses by Aedes aegypti mosquitoes by reducing the mosquito population and/or limiting the insect’s ability to serve as a disease vector. One of the project’s specific aims is to establish a field site for genetic control trials, choosing from among a number of potential sites around the world with the appropriate dengue epidemiology and Ae. aegypti ecology. Ultimately, the project aims to test the interaction of genetically modified and local wild-type mosquitoes, first in laboratory cages and then in large cage trials at the field site, to assess the relative fitness of genetically modified mosquitoes and the spread of two major effector genes designed to block transmission of dengue viruses and reduce or eliminate mosquito populations. The project does not propose or plan to release into a natural field setting any GM mosquitoes.

OUR APPROACH

As investigators on this research project, two of us (LH and TS) engaged the Advisory Service of the Ethical, Social, and...
Cultural Program for the Grand Challenges in Global Health, led by one of us (JL), for advice and assistance with the site selection process. In a preliminary meeting, we discussed the importance of community issues and some recent thinking about community consent and briefly reviewed the requirements and logistics of the site selection decision. Some concerns about community consent, which are described in detail below, led us to make a decision not to engage in large-scale community interactions before the specific site selection decision. However, we understood clearly at the outset that concerns about community authorization and participation would remain central to the site selection decision.

Similarly, the complexity of the regulatory requirements for GM insects, particularly research requiring the importation of GM insects into the host country, and the significant differences in the regulatory requirements and capacity among the candidate countries, made it clear that significant interactions with the host country regulatory authorities would be required to identify the precise criteria for the regulatory aspects of site selection in advance of the decision.

We expected that, along with scientific criteria, community engagement considerations and regulatory requirements would be the main concerns for site selection. We also expected that it would be impossible to determine the full range of criteria and considerations for effective community engagement and regulatory compliance before the actual site selection decision. Similarly, although we were aware that a broad range of community interests and stakeholders would be necessary for authentic community engagement, such as media, schools, municipal government committees, universities, and local non-government organizations (NGOs), we were equally aware that the mix of community stakeholders at any given research site would be unique. We were, therefore, careful not to assume that we could anticipate all the relevant stakeholders, as well as their roles and interests, based solely on conventional categorizations. As a result, we adopted an active, collaborative, and iterative approach to site selection— involving site visits, capacity assessment, regulatory analyses, and a range of expert consultations. Our aim was to identify key criteria, including the capacity for effective community engagement and authorization, shown by the existence of various forms of community organization and representation, and an established regulatory environment with set procedures and contacts. We used these criteria to establish a decision-making framework for site selection. This framework also enabled collaborators at the selected site as well as those at sites that were not selected to understand the rationale for the decision. We were mindful that our process might contribute to the development of a preliminary set of considerations that would be useful for others facing similar site selection decisions and that this might provide an effective starting point for further study and improvement of site selection.

THE DECISION-MAKING FRAMEWORK

We expected three broad categories of criteria to be relevant to the site selection decision: 1) scientific criteria; 2) regulatory issues and administrative authority for conducting the trials; and 3) community engagement and authorization. In this paper, we focus exclusively on categories 2) and 3) and attempt to lay out a range of considerations and their guiding rationales, which we hope will prove useful to scientists facing similar site selection decisions.

REGULATORY ISSUES AND ADMINISTRATIVE AUTHORITY

Because the research plan proposed the importation of GM mosquitoes into the host country from the United States, the authority to conduct the trials in the host country lay well beyond the agreement of the host country collaborating scientists. The prevailing international framework governing the import of GM organisms is the Cartagena Protocol on Biodiversity, an agreement under the international Convention on Biodiversity. Signatories of the Cartagena Protocol (and countries that voluntarily acceded to the terms of the agreement without being formal signatories) are required to establish mechanisms to deal with the import and regulation of GM organisms. Although there is some question about the beneficial impact of the Cartagena Protocol on international trade and collaboration involving GM insects, it has been one of the key instruments by which countries—perhaps most importantly developing countries—focus their resources around capacity building for policy and regulatory infrastructure related to the import and use of GM organisms.

The status of specific mechanisms developed by the candidate countries under their Cartagena Protocol obligations proved to be a critical factor in the site selection decision. In particular, the existence of enacted legislation governing the import and various uses of GM insects—including research uses—within a candidate country was seen to provide the most secure and reliable regulatory environment for initiating these long-term research collaborations. Enacted legislation also represented evidence of public deliberation about the use of GM organisms within the country and complemented other evidence we had sought of this type of activity.

Discussions of ethical conduct in research rarely begin with attempts to gauge the political climate and will to support the research in a host country. However, in the case of proposed research on GM insects, there are two main reasons why broad political support, in particular a demonstrated political will to embrace relevant biotechnologies to improve health, may be relevant for the site selection decision. First, it is disrespectful of communities to import a novel and potentially threatening set of technologies into a country in the absence of any legitimate state interest in these activities. Without a clear expression of such interest, it is conceivable that insufficient resources could be devoted to appropriate review and oversight, including the necessary capacity for risk assessment. As well, there might be insufficient attention paid to how shared interests between the investigators and host communities should be negotiated and realized.

A key aim in scientific research involving genetically modified organisms (GMOs) should be to generate knowledge to improve health. Thus, it is important that sufficient attention and interest be paid to these issues at the highest levels of government, to ensure that beneficial findings are translated into useful technologies for the host country. Although political will is no guarantee of success, it may be equally true that its absence may be sufficient to guarantee failure. Finally, the potential release of GM mosquitoes is controversial and
raises issues not only for communities in the host country but potentially for neighboring states. Therefore, we expected that enacted legislation governing the import and use of GMOs was the best evidence that the full range of international implications had been considered.

Identification of the most important regulatory authorities turned out to be a key issue in navigating the regulatory complexity, particularly in the larger candidate countries, in which the research use of imported GM mosquitoes crosses the jurisdiction of several public agencies and government departments. The process of determining the key authorities proved to be extremely important, because it provided a clear point of contact (in at least one candidate country) to address detailed questions related to the proposed research. The Cartagena Protocol requires each participating country to establish a national committee to oversee the implementation of its requirements. This body usually plays a leadership role in the development of legislation and regulations within the country, either through the development of draft legislation or through detailed reports that inform the legislative process. The mandates of the national committees created under Cartagena are very similar. However, depending on the size and complexity of the host country’s government and bureaucracy, the mandate may be more or less comprehensive. Thus, determining the relative influence of a candidate country’s national committee can help investigators to determine the main point of contact for their discussions, deliberations and negotiations of regulatory matters.

Cartagena provided the context for the development of new legislation to deal specifically with the import of GMOs. However, producing new legislation is complex and time-consuming, so it can take several years for a country to develop and enact the necessary legislation governing the import and various uses of GMOs. Because all research activities must conform with local laws, it is important to have a clear understanding of what laws deal with the issues in the host country, especially if specific legislation is not yet in force. It is common, under these conditions, for activities related to the import and research with GMOs to be conducted under the auspices of a battery of existing laws, each of which might address specific elements of the proposed import and research uses. The relationships among these various laws and the way authority is distributed among public agencies can be complex. Under such circumstances, it is advisable to retain an independent and competent legal advisor within the country to help ensure a fair and accurate reading of the prevailing legal requirements.

Draft guidelines and laws do not always provide clear procedures or identify all the authorities with jurisdiction, so determining whether the candidate country has had any previous experience with the importing or research uses of GM insects and following up with the participants in these processes is an important way of discovering the regulatory requirements. One of the key regulatory requirements that is often not clearly articulated or obvious to investigators is the process for application and approval for the proposed research. These processes can prove to be extremely complex, and the absence of an agreed-on process for application and approval can suggest that the system lacks the requisite maturity to actually handle applications. Although the Cartagena Protocol provides general guidance on how these processes can be structured, each national authority may differ in the specific application process, depending on the range of “competent authorities” given specific powers under Cartagena in the country and the extent to which existing legislation has articulated a clear process.

Another regulatory issue with important implications for the ethics of research involving GM insects is the requirement for risk assessment before the research, which varies from country to country. There is no widely accepted risk assessment method for caged field trials or environmental release trials of GM insects. Specific requirements for risk assessment must be explored in detail and might require negotiation and collaboration to agree on an appropriate process. This issue may be particularly contentious with respect to environmental impact assessments of the research, which may be a regulatory requirement in the country sponsoring the research and thus may be a formal requirement for the investigators, depending on their source of funding. However, the assessment may not be required by the host country. In these circumstances, the overarching concern should be to ensure that a fair and appropriate assessment of human risks and environmental impacts is conducted so that the proposed research offers a favorable balance of risks and benefits for the participating communities. The application of research laws and regulations from countries sponsoring research in low- and middle-income countries hosting the research is an ongoing point of contention in international research policy, but the debate should not impede the achievement of the substantive requirements of ethical research.

Both caged field trials and environmental release trials raise difficult questions regarding the ethics of research with human subjects. Although it is now widely accepted that collaborative partnerships with communities involved in research are an ethical requirement and that some form of community authorization is required to conduct research within communities ethically, it is less clear when these trials actually become human subjects research. Although the specific requirements will vary depending on the specific context and aims of the research, investigators should start considering the immediate human risks in both the caged field trials and the environmental release trials, but these are areas in which greater elaboration is required to achieve clear and useful guidance.

The existence of national research ethics guidelines and a national mechanism for revising and developing these guidelines in light of new and emerging challenges are important considerations in site selection for two main reasons. First, it is likely that this capacity will provide better protection for communities involved in the research, by ensuring appropriate levels of scrutiny. Second, having this capacity also makes it more likely that insights gained through the research process may be incorporated into national guidance for the benefit of the host communities and for science. Depending on the nature of the specific modifications involved in the proposed research, it may also be important to understand specific requirements related to the review, approval, and oversight of research involving recombinant DNA technologies.

COMMUNITY ENGAGEMENT
AND AUTHORIZATION

The ethics of human subjects research is dominated by concerns about informed consent, although there is growing
skepticism about the effectiveness of current informed consent practices.10 Not surprisingly, some of the initial discussions of the ethics of research involving genetically modified insect vectors have focused on the informed consent of the participating communities as a key requirement. One specific issue in site selection is whether a systematic process for obtaining community authorization or “community consent” must precede the site selection decision.5,6 This a process in which the community decides, after appropriate information and due consideration, whether to participate in the research. Although appropriate authorization from the community is an essential ethical requirement for beginning any research, it is not clear that this is best addressed during the site selection process, for several reasons. First, current approaches to community consent often involve large-scale activities that aim to canvas community knowledge, attitudes, and opinions about research with GM insects. This is time-consuming and costly, and although efficiency is not a compelling ethical goal in site selection, when the choice is among several sites in different parts of the world, and funding is provided by accountable agencies within defined time horizons, time and cost need to be considered. Second, there is a great deal of research suggesting that individual informed consent—which we have vastly more experience with than community consent—is relatively ineffective at ensuring comprehension among research participants.11 Given the very limited empirical evidence we have about the effectiveness of community consent and the added complexity of interacting with communities as opposed to individuals in the consent process, it may not be realistic to rely completely on surveys of communities’ knowledge, attitudes, and opinions collected before the site selection decision as a reliable basis for inferring authentic community authorization.

Third, undertaking large-scale surveys of knowledge, attitudes, and opinions in communities that ultimately will not be selected as research sites is not an ethically neutral matter. Health research, by its very nature, suggests a commitment to improving the lives of individuals and communities affected by various health problems. When researchers withdraw useful interventions from individuals or communities at the conclusion of clinical trials, it has given rise to concerns about abandonment and a sense of loss on the part of the individuals and communities that have helped to make the research possible.12 It seems a reasonable concern that extensive mobilization and involvement of communities before informing them that their site has not been selected for research could give rise to some similar ethical problems. Greater attention should be paid to these issues as this type of work becomes more common.

Finally, there is still considerable debate about what constitutes a “community” for the purposes of research13 and what is meant by a community decision to participate in research.14 A recent proposal suggests that a research community is best understood as the collection of individuals that shares the relevant research risks and that the precise composition of this community may not be obvious until the research is underway.15 If shared research risk is used as a defining criterion for community during site selection, it becomes clear that even the precise field sites within the candidate countries or regions must be identified for community authorization to have any effective force. However, getting some form of prior consent before a final field site selection has been made may impose burdens unnecessarily on certain groups of people who may ultimately not be involved in the research while ignoring others who may become involved as the details of field site selection unfold. Any specific field site selection involves such issues as land acquisition, political authorization, and myriad local partnerships. There is always the possibility that preliminary site decisions will be reconsidered based on subsequent scientific or other findings.

Although it has become a more common practice in the context of global health research, community engagement remains a poorly defined notion, and there is no single model of community engagement that has been shown to be effective in producing both the best ethical and scientific results.16 Some guidance has begun to emerge about ethical requirements in the context of collaborative partnerships for research,17 but it lacks the depth and elaboration required for sustained engagement and ongoing negotiation with communities. This is particularly true in situations of considerable uncertainty regarding risks and potential benefits, as is the case in research with GM insects.

There may be cases in which countries have had negative experiences with GMOs. In these countries, it is important for investigators to gauge whether the affected communities have been able to work through and resolve these issues to their satisfaction or whether these experiences have left the communities jaded and wary of GMOs in general. In the latter circumstances, it may be more respectful of these communities not to add to their concerns by initiating further activities, unless the research offers unique opportunities to engage and address these issues. However, in some cases, such as Mexico’s experience with problems related to GM maize,18 these experiences have also provided impetus for developing civil society mechanisms and improved capacity in laws, guidelines, regulations, and public institutions to ensure that the appropriate lessons are learned and applied in the future.

As with the importation of GM insects at the national level, gaining access to communities and establishing the necessary infrastructure close to the field sites requires appropriate administrative authority, either at the municipal or state level or both. Investigators must determine the extent to which the relevant administrative authorities have the necessary capacity and are able to act as good faith stewards of the best interests of the populations they serve. In some cases, a committee or representative body may exist with a mandate—such as responsibility for dengue control within a municipal or regional health authority—that might make it an ideal body for liaison with the community. In such a case, which we encountered in one of the candidate countries, the existence of such a body may also play a critical role in clarifying what constitutes the relevant “community,” by helping to describe the collection of individuals who will be exposed to any research-related risks.15 As well, a body with pre-existing authority might help to ensure a strong voice for the community in deliberations and ongoing negotiations about how the community should benefit from its participation in the proposed research. These deliberations cannot be fully realized and might require a level of community involvement that is difficult to justify before a site selection decision.

Once a specific geographic region has been identified that satisfies the necessary epidemiologic and entomologic requirements, specific plots of land must be identified and evaluated for their appropriateness as potential sites for
caged field trials and/or environmental release trials. One obvious criterion for specific site selection is the distance from homes, farms, villages, schools, factories, and other community structures. It is during this detailed field site assessment process that investigators are most likely to encounter challenges, such as concerns about potential risks. Investigators must show their fundamental commitment to optimize the safety of the community and a willingness to engage the community in meaningful dialogue. They must respect community opposition, even if this means losing preferred field sites.

Many suitable sites for caged field trials are on agricultural land. In our site selection visits, we encountered situations in which small housing structures were present either on or in the vicinity of preferred field sites. A major concern was whether placement of the field sites in these locations would result in the displacement of individuals or communities. Further study may be needed to determine the location of people’s residences and to gain a better understanding of their work patterns in the chosen locations. The potential displacement of individuals should be viewed as an important concern, requiring further work to better understand the scope of the problem and to devise appropriate solutions.

Although differences in language or in levels of fluency between investigators and host country communities and some research staff is not, in itself, a sufficient justification for not selecting a particular country or field site, language is a critical vehicle for successful collaboration. Miscommunication or incomplete communication should be spotted and addressed constructively, both out of respect for the host collaborators and to ensure that the proposed science is properly conducted.

In approaching the community engagement aspects of site selection, it is important that the relationship with the relevant community or communities is understood not as a single encounter but rather as an ongoing collaboration and negotiation of important interests. For this reason, an important site selection criterion is the capacity and readiness of the community to fulfill its responsibilities in the research collaboration. The primary requirement is that of ensuring an accurate representation of the views and interests of the community during deliberations and negotiations related to the research. In our experience, there are often local social scientists or public health officials who have personal or academic interest in community development or community capacity and who may have already had extensive interactions with and made assessments of the community. Their insights can help investigators determine who the most appropriate community representatives may be and whether research may be viewed by the community as a threat or burden or as a legitimate extension of existing, familiar activities, such as local vector control programs. The extent of the community’s experience with vector-borne diseases and the local effectiveness of existing vector control programs might be extremely relevant to the way the community views the risks associated with proposed caged field trials or the prospect of future environmental release trials of GM mosquitoes and to its representation in research negotiations and deliberations.

The extent to which the capacity of the community needs to be developed will likely vary from country to country and even from site to site within a country. Investigators must use their best judgment about how much and what types of information they require to be confident about a community’s readiness and capacity. Local social scientists or public health researchers may also be willing to engage in some ongoing data collection about various aspects of the community engagement. This could involve tracking attitudes and experiences of participating community members, or changes—positive or negative—in risk perception or community concerns related to participation in the research. There may also be universities, government agencies, or research facilities with specific interests in vector control or medical entomology that might serve as partners in the proposed research. Individuals and departments within these organizations often have extensive knowledge of the local communities affected by local vector-borne diseases and may prove to be helpful in designing and assisting in local aspects of the proposed research.

Although the idea of “community consent” raises conceptual, practical, and ethical challenges, in most cases, once the specific preferred field sites have been identified, it should be possible to identify households that lie within the immediate vicinity of the sites. They can be approached—perhaps through community groups or partners—to explain the proposed research, including the potential harms and benefits, and to explore receptivity to the research at the individual household level. As long as the number of individual candidate field sites is relatively small, it should be possible to begin this process as soon as a site is assessed and considered, and if the process culminates in some legitimate form of community authorization (e.g., by a decision by a local council), the people in the immediate vicinity can be asked more formally for their individual consent to participate in the proposed research. The presumption should always be that informed consent will be sought from identifiable individuals who are likely to be exposed to research-related risks.

Because research with GM insect vectors is ultimately oriented toward preparations for environmental release of these organisms, some consideration should be given, during the earliest phases of the site selection process, to public engagement. This is generally a broader set of activities, aimed at communicating information about new technologies or other issues of public concern, and documenting public attitudes toward these issues. Even if the proposed research does not have specific provisions for environmental release trials, investigators should anticipate the potential for such trials down the road and explore the feasibility of conducting appropriate public engagement activities. For example, in one candidate country we met with an academic with a well-developed approach to national polling around emerging social issues, including the use of GMOs. Although not specifically required for our proposed research—which currently does not include any provisions for environmental release trials—these mechanisms may prove to be important for learning about the participating communities in ways that can improve the ethics and responsiveness of the proposed research. Table 1 provides a summary of the site selection considerations described above.

**DISCUSSION**

We described the process we used to select the site for a research project involving caged field trials of GM mosquitoes for the control of dengue viruses. The ESC analysis was
an integral aspect of this site selection process, and we have presented a brief overview of the main considerations we identified and used to guide the site selection decision. This process produced important lessons.

The first lesson is that explicit attention to ESC issues in site selection allowed us to identify a wide range of considerations that may not otherwise have been taken into account in our decision. This broader view improved the quality of the site selection decision.

The second lesson is that, aside from the scientific criteria for site selection, all the other important considerations we were able to identify could be classified as either regulatory issues or criteria related to community engagement. This observation, although not definitive about criteria for site selection for research involving GM insect vectors, helps to focus on the main areas of concern that we expect will continue to be prominent themes in future site selection decisions.

The third lesson is that the criteria and considerations we described provided guidance for our decision, rather than hard, definitive requirements. This reflects the extraordinary complexity of site selection decisions and the great difficulty of anticipating every relevant consideration. The other implication is that the criteria alone cannot guarantee that site selection will be conducted in a spirit and manner that is honest, fair, and respectful of the interests of potential collaborators, particularly those whose sites are not ultimately selected. Investigators must bring to the process of site selection a well-cultivated desire to act ethically and constructively, and they must give the best interests of the host communities at least as much consideration as they do to the quality of their science.

The fourth lesson relates to the way the site selection decision was made and how the ultimate decision was explained, justified, and communicated to potential research collaborators. We sought to be as transparent and explicit about our decision and our rationale for it as the information at our disposal would allow. At the beginning of the site selection process, we were not clear about what criteria we would use to guide our decision or what weight would be given to each criterion we identified as being relevant. We explained to collaborators that we were using an iterative process to identify, review, and use the most relevant criteria to develop a decision framework as the rationale for our decision, and this information was shared with all the prospective collaborators at the conclusion of the site selection process. Because we were not able to assign precise weights to each of the relevant criteria, we adopted an “on balance” approach to the decision making. Each of us reviewed the framework and our observations about the candidate sites independently and shared our decisions with each other, providing justifications for the decision based on our framework. Through this process, it became clear that key factors, such as the existence of legislation on the import and use of GMOs, would turn out to be critical in our decision making. After the decision had been made and communicated, we received favorable feedback from the prospective sites that had not been selected, who reported that they found the site selection process fair and transparent.

Because site selection for research with GM insects is likely to become a more common activity as research increasingly moves from the laboratory to the field, further attention to ESC aspects will be needed to ensure appropriate and effective guidance for researchers and host communities. We are strongly encouraged by the continued evolution of guidance and oversight mechanisms for caged field trials and environmental release trials and by the continued development of biosafety protocols and attention to the regional capacity in biosafety and related competencies in regions likely to host this type of research. For now, we hope our framework of key considerations and lessons learned from our own site selection process will add an important dimension to the ex-
isting guidance and serve as a catalyst for additional work in this area.

Received October 30, 2007. Accepted for publication May 30, 2008.

Acknowledgments: The authors thank Michael Keating for editorial assistance and Emma Cohen and Dizayn Panjwani for help in finalizing this paper.

Financial support: This work was funded by the Bill & Melinda Gates Foundation’s Grand Challenges in Global Health initiative. JL was funded through the Ethical, Social and Cultural Program for the Grand Challenges in Global Health, and LH and TS were funded through the project “Genetic Strategies for Control of Dengue Virus Transmission,” Principal Investigator, Anthony James.

Authors’ addresses: James V. Lavery, Centre for Research on Inner City Health, Centre for Global Health Research, Keenan Research Centre, Li Ka Shing Knowledge Institute of St. Michael’s Hospital, Toronto, Ontario MSB 1W8, Canada, E-mail: jim.lavery@utoronto.ca. Laura C. Harrington, Department of Entomology, Cornell University, 3138 Comstock Hall, Ithaca, NY, Tel: 607-255-4475, E-mail: lch27@cornell.edu. Thomas W. Scott, Department of Entomology, University of California, Davis, CA, Tel: 530-754-4196, Fax: 530-752-1537, E-mail: lscott@ucdavis.edu.

REFERENCES