

Findings from the Technical Workshop to Create a Safe, Effective and Integrated Strategy for the Control and Elimination of *Aedes aegypti* from Puerto Rico

Hosted by the Puerto Rico Brain Trust for Tropical Disease Research and Prevention, an initiative of the Puerto Rico Trust for Science, Technology and Research.

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This Technical Workshop can be summarized by five points:

- The *Aedes aegypti* mosquito is the root cause of Dengue Fever, Chikungunya and Zika transmission.
- Experts in mosquito control and public health convened in Puerto Rico to determine the feasibility of eliminating *Ae. aegypti* infestation from the island.
- There was broad agreement that the elimination of *Ae. aegypti* and the diseases it carries is complex but feasible through Integrated Vector Management using physical, chemical and biological interventions on an area-wide basis.
- Public engagement and authorization is critical to program success including building partnerships with Puerto Rican communities and stakeholders.
- Strong leadership, dedicated program management, and autonomy of the entity charged with the execution of this campaign are essential to successful elimination.

EXECUTIVE SUMMARY: Findings from the Technical Workshop to Create a Safe, Effective and Integrated Strategy for Control and Elimination of the *Aedes aegypti* Vector from Puerto Rico.

The *Aedes aegypti* mosquito is the root cause of Dengue Fever, Chikungunya and now Zika transmission, which has brought a new level of urgency to eliminate this mosquito. On May 24, 2016 a workshop of 47 technical experts in mosquito control and public health was hosted by The Puerto Rico Trust for Science, Technology and Research. Experts focused on answering the question, “Can the *Ae. aegypti* mosquito be controlled or eliminated in Puerto Rico thereby eliminating the disease? If so, how?” Our conclusion was that it is possible to eliminate *Ae. aegypti* from Puerto Rico with a well-managed vector control program. While elimination is possible, we also concluded that the *Ae. aegypti* population could first be reduced below the threshold of disease transmission and, from that vantage point, the decision to fully eliminate this mosquito can be taken based on a cost-benefit analysis. Area-wide elimination of *Ae. aegypti* has been done before and, in our opinion, it can be done again. Our work included an assessment of the mosquito control methodologies available today, the current state of mosquito-borne disease in Puerto Rico and a review of historical elimination programs that have successfully eliminated disease-carrying mosquitoes. The full report outlines: 1) the interventions that, when properly integrated, have a high probability of controlling or eliminating *Ae. aegypti*; 2) the near-, mid- and long-term introduction of each vector control tool; and 3) the infrastructure and leadership that must be in place to ensure effective execution of the project.

Safe and effective tools to deploy the mosquito control program include physical interventions to eliminate breeding sites, chemical interventions that kill larvae and adult mosquitoes and biological interventions, notably the inundative release of male mosquitoes that cannot productively mate, thereby preventing female mosquitoes from producing the next generation; this method is broadly referred to as the Sterile Insect Technique (SIT). Integration and management across interventions along with data on mosquito populations and geographical disease burden is essential to the success of the program. The first year of a program should be the most intensive. A master plan of how interventions will be staged over time and by geography for maximum effect should be created at the outset. The plan should be widely shared as part of a community engagement strategy. Regulatory issues should be identified with an action plan for safe and expedient oversight by the appropriate agencies. In this first year, physical and chemical interventions will be prominent while biological intervention (SIT) manufacturing facilities are being constructed in Puerto Rico. Elimination of *Ae. aegypti* infestation will focus on highly burdened regions of disease in Puerto Rico, with SIT finishing the job in years two and three. From there, a “rolling front” of elimination will move on to second-tier disease-burdened regions. The decision to eliminate *Ae. aegypti* from the entire island will be taken in year four using cost-benefit analyses based on regional elimination. As elimination is achieved, on-going port-of-entry surveillance and control operations should be maintained to prevent re-infestation.

The interventions proposed were well understood with a high degree of consensus across the experts. We converged on one critical missing piece for implementing these recommendations: to effectively execute any mosquito control program requires a dedicated, autonomous mosquito control organization with the mandate to execute the program. It seems Puerto Rico is missing this basic capacity, which exists throughout the continental US in the Mosquito Control Districts (*e.g.* the Florida Mosquito Control Districts). Therefore, above all, Puerto Rico should establish a Mosquito Control Commission to carry out the *Ae. aegypti* control program and maintain it after the current crisis is solved to ensure that the island never faces this threat to human health and the economy again.

FULL REPORT: Findings from the Technical Workshop to Create a Safe, Effective and Integrated Strategy for Control and Elimination of the *Aedes aegypti* Vector from Puerto Rico.

The *Aedes aegypti* Mosquito: Root Cause of Zika, Dengue and Chikungunya Disease Transmission

The *Aedes aegypti* mosquito vector is the root cause for transmission of several serious infectious diseases including Dengue, Chikungunya, and Zika^{1,2}. Dengue has been an endemic health problem in Puerto Rico for decades and globally more than 390 million people are infected yearly³. Some estimates place Dengue infections at 3.9 billion worldwide^{4,5}. Chikungunya has caused illness, loss of the ability to work and has resulted in long lasting consequences for many Puerto Ricans⁶. The Zika epidemic, with the serious consequences of microcephaly, Guillian-Barré Syndrome and potential long-term neurological disorders, has brought a new level of urgency to eliminate *Ae. aegypti*, the source of transmission⁷. *Ae. aegypti*-transmitted diseases have also brought severe economic consequences to Puerto Rico with cumulative losses in the hundreds of millions of dollars due to associated health costs and cancelation of tourism and sporting events⁸.

A Community without *Aedes aegypti* Mosquito Infestation is Free from the Diseases It Transmits

On May 24, 2016 a workshop that brought together 47 technical experts in mosquito control and public health was convened by The Brain Trust for Tropical Disease Research and Prevention, an initiative of The Puerto Rico Trust for Science, Technology and Research. The group explored an integrated vector elimination strategy for *Ae. aegypti* in Puerto Rico. The workshop focused on answering the question, “Can the *Ae. aegypti* mosquito be eliminated thereby eliminating the disease? If so, how?”

Our workshop concluded that it is possible to eliminate *Ae. aegypti* from Puerto Rico with a well-managed vector control program. While elimination (defined as greater than 90% reduction in *Ae. aegypti* populations island-wide) is possible, we also concluded that the *Ae. aegypti* population may be first controlled and, from that vantage point, the decision to eliminate *Ae. aegypti* can be taken based on a cost-benefit analysis⁹. Health objectives are met most effectively by focusing on highly infested areas with the most disease. Area-wide elimination of *Ae. aegypti* has been done before on a scale that far exceeds that of Puerto Rico and, in our opinion, it can be done again.

Our work included an assessment of the mosquito control methodologies available today, the current state of mosquito-borne disease in Puerto Rico and a review of historical elimination programs that have successfully eliminated disease-carrying mosquitoes, for example Fred Soper’s elimination program of the African malaria vector *Anopheles arabiensis* from a 54 thousand km² area in Brazil in 1939¹⁰ or Oswaldo Cruz’s campaign against *Ae. aegypti*¹¹. These campaigns eradicated disease in the Americas through the 1950’s. However, by the 1970’s failure to maintain control measures led to the resurgence of mosquito-borne disease. Much has changed since prior “top down” elimination campaigns; we live in a dynamic, modern and democratic society. Cargo transport has facilitated the spread of *Ae. aegypti* while discarded tires and plastics have aided its breeding¹². Enforcing the clean-up of mosquito breeding sites on private property today may be more challenging but modern times have also given us powerful tools to fight this mosquito. On balance, it is our conclusion that by combining the traditional and modern tools for mosquito elimination with good leadership, the odds of successful mosquito elimination today are better than ever. This report outlines: 1) the interventions that, when properly integrated, have a high probability of eliminating *Ae. aegypti* and maintaining elimination; 2) the near-, mid- and long-term introduction of each vector control tool; and 3) the infrastructure and leadership that must be in place to ensure effective execution of the project.

Recommended Safe and Effective Physical, Chemical and Biological Strategies

Safe and effective tools for mosquito control can be grouped into three main categories: physical, chemical and biological interventions. Physical interventions include the physical elimination or removal of breeding sites. Chemical interventions are defined as the use of registered insecticides that kill mosquitoes directly. For the purposes of this study, biologically produced larvicides such as *Bti* (*Bacillus thuringiensis israelensis*), are classified as chemical interventions because they are operationally deployed identically to chemical larvicides¹³. Biological interventions refer to active living organisms that reduce mosquito populations, including mosquito-eating fish, entomopathogenic fungi, and especially the inundative release of sterile male mosquitoes preventing females from producing the next generation of mosquitoes (SIT). Finally, good intelligence on mosquito prevalence and breeding sources as well as geographical disease burden is essential to establish a baseline and monitor the success of the program.

Recommended Physical interventions emphasized the reduction of *Ae. aegypti* breeding sites (water meters and septic tanks). Physical interventions tend to be labor intensive and require a high degree of public compliance because of the need for resident participation. If well executed, community programs can empower citizens to reduce breeding areas in and around their homes, creating a community that is invested in the solution. It was recommended to engage local communities through outreach programs as well as to train and manage a large team of breeding-source reduction employees to do routine island-wide clean-up of breeding sources. Expert management of this team is recommended to bring efficiency to this labor-intensive activity. Modern, mobile phone-based communication and social media could be employed to facilitate good communication with commonly available technology. Excellent compliance will need to be enforced. However, in the Puerto Rican context, incentives may be more effective than punitive measures. Fines for failure to remove breeding sites from private property must be a strong option, but might not be the first option if incentives work.

Recommended chemical interventions. It was generally recommended to use a combination of safe (EPA approved) and effective larvicides and adulticides. *Ae. aegypti* have become resistant to many adulticides and a database of resistance should be widely disseminated to guide usage. It is important to quickly bring the regulation of insecticides in Puerto Rico in line with the continental United States and eliminate multiple layers of regulation that are peculiar to Puerto Rico¹⁴. For example, organophosphates and insect growth regulators are insecticides to which local *Ae. aegypti* are still susceptible, but regulatory issues have complicated their use specifically in Puerto Rico. Because *Ae. aegypti* is a day-biting, indoor-resting mosquito, special attention must be paid to insecticide application. Indoor Residual Spraying is most likely to control the *Ae. aegypti* vector and reduce disease if applied by trained personnel that understand where *Ae. aegypti* spends time in the house¹⁵. There is some controversy on the use of over-the-counter (OTC) products that could be used by consumers. OTC products may help people reduce *Ae. aegypti* in their homes, but there is a possibility of user abuse which puts health, safety and efficacy at risk. Outdoor residual spraying may be practical in areas where outdoor *Ae. aegypti* populations are higher than average or where access to the inside of homes/businesses is difficult. Aerial and ground spraying by truck should be guided by an understanding of how the insecticide will effectively come in contact with the target, *Ae. aegypti* or its breeding sites¹⁶. One clever way to deliver larvicides to cryptic breeding sites is to use Auto

Dissemination (AD) traps. AD traps destroy distal breeding sites as the mosquitoes visiting the AD trap pick up a larvicide and transport that agent to hidden breeding sites. Since *Ae. aegypti* breeds in places that are hard to reach, the AD trap exploits the mosquito's egg-laying behavior to find and treat hard-to-reach breeding sites¹⁷. Another emerging tool is luring adult *Ae. aegypti* to traps baited with either attractive toxic sugar baits, or moisture for resting or oviposition. Above all, a trained labor team managed by mosquito control experts is needed for the implementation and close monitoring of an island-wide chemical intervention strategy.

Recommended Biological Interventions. A major tool that has not previously been widely available at scale for mosquito control is the Sterile Insect Technique (SIT)¹⁸. This method relies on the release of male mosquitoes that effectively find and mate with females but cannot produce viable offspring. Because males do not feed on blood or transmit disease, they can be released safely in large numbers. By inundating the area with these male mosquitoes that cannot bite or productively mate with females, the population can be dramatically reduced or eliminated. Since this intervention relies on mating within the *Ae. aegypti* species only, there is no collateral damage to other insect species, mammals or birds. Because *Ae. aegypti* is a non-native invasive species that makes up only ~1% of the mosquito population, there is little if any disruption to the ecosystem upon targeted removal. The United States Department of Agriculture (USDA) presented several success stories of area-wide elimination of agriculturally important insect pests using a combination of chemical insecticides and the Sterile Insect Technique. SIT has been extensively used for over 50 years for the population control of major agricultural insect pests and disease vectors. In these cases, irradiation has been used to sterilize males, which are then released to find females and prevent future offspring¹⁹. USDA has implemented this method to eliminate insect pests with great success. Screw-worm²⁰, Pink Bollworm²¹ and Medfly²² are examples of area-wide insect elimination over geographies hundreds of times larger than Puerto Rico. Releasing insects from aircraft has proven cost-effective for covering large areas. Engineers have now developed methods to deliver sterile *Ae. aegypti* from aircraft²³.

Three types of SIT were presented that could be used to control or eliminate *Ae. aegypti*²⁴. First, a genetically engineered *Ae. aegypti* has been developed to produce males with non-viable offspring. Field results were presented from outdoor pilot programs in several countries resulting in >90% reduction of *Ae. aegypti* with this genetically engineered mosquito^{25,26}. Second, male mosquitoes may be infected with the bacterial endo-symbiont *Wolbachia* to produce males that cannot productively mate with local females if they do not carry the same bacteria²⁷. Promising semi-field results were presented and the first outdoor field trials of these infected male mosquitoes are in progress now. Finally, as demonstrated by the USDA programs, irradiation can be used to create sterile male mosquitoes. For mosquitoes, the combined irradiation and treatment with *Wolbachia* was proposed which allows the release of sterile males while at the same time ensuring that there will be no release of fertile and/or pathogen transmitting females^{28,29}. Promising semi-field results were presented and the first outdoor field trials of this combined approach are in progress now.

The experts from this workshop recommend some form of SIT as part of an Integrated Vector Management strategy to eliminate *Ae. aegypti* because of the demonstrated success in area-wide elimination of other pests by USDA. With several attractive SIT options, the right option should be chosen based on the greatest likelihood of safe and effective elimination of *Ae. aegypti* with special attention paid to logistical requirements and operational feasibility.

Monitoring of *Ae. aegypti* mosquito populations and *Ae. aegypti*-associated disease

The Centers for Disease Control and Prevention along with Puerto Rico Department of Health currently track *Ae. aegypti*-associated disease regionally across Puerto Rico, including Dengue, Chikungunya and Zika^{30,31}. We recommend supporting this disease monitoring over the course of the *Ae. aegypti* control/elimination program as the ultimate measure of program success. As an immediate indicator of *Ae. aegypti* control, we recommend the trapping and monitoring of the adult *Ae. aegypti* using Autocidal Traps of some form³². These traps are used to monitor populations, but can also be used in higher density to significantly reduce mosquito populations. Population data from trapping must be aggregated, processed and presented to track and manage program interventions. The data may also be useful to share vector elimination efforts transparently with policy makers and the public³³. With a geographical view of the *Ae. aegypti* infestation and disease distribution, the program should first focus on highly burdened areas for elimination, such as Caguas, San Juan and Ponce. Upon successful elimination in these high burden areas, the program may confidently expand to second tier burdened areas (see timeline). Continued monitoring provides feedback on intervention strategies island-wide. Monitoring of strategic areas, such as points of entry, will be indefinite and accompanied by a Quick Reaction Force (QRF) that can be deployed immediately to suppress incursions from ports of entry. Experts propose using the mosquito and disease data in conjunction with demographic data and climate and weather patterns to inform statistical modeling programs developed outside the program in academia³⁴. In the future, such models may help prevent or prepare for vector disease outbreaks globally.

Community engagement and participation

Even the most solid interventions can fail for lack of public participation, or understanding of the health objectives or consideration of the community and context of the intervention. In this case, “top-down” interventions are at risk if the community rejects the intervention at the outset or is unable to sustain the intervention over time. A modern program might be neither “top down” nor “bottom up”, but seek to hybridize the strengths of each approach^{35,36}. While the new tools for mosquito control may be more effective in eliminating *Ae. aegypti*, departures from traditional methods may bring controversy. Concerns about the environment are now featured in public consciousness and should be addressed in the pursuit of public health. In addition, active public engagement and authorization is critical to program success and we recommend building partnerships with communities and other stakeholders³⁷. We recommend the use of interviews, focus groups, and town hall meetings to understand attitudes and practices of the communities in which the programs will be executed. Household and school-based awareness programs, communication strategies and media campaigns that reach every part of the community are important. Encouraging community-based vector-control strategies that promote cleaning up breeding sites engage the community in the program while reducing the source of mosquitoes. Strategies that empower communities to contribute to the source reduction may have higher acceptance rates, visibility and impact on vector densities³⁸.

Timeline for Implementation of Interventions

Short term – first year. Experts agreed that the first year of a program should be an intensive period of activity. A master plan of how interventions will be staged over time and by geography for maximum effect should be created at the outset of the program. The plan should be widely shared and gain the support of all stakeholders as part of the engagement plan. Specific community issues should be

recognized up front with an action plan to address each issue. Regulatory issues should be identified in advance and an action plan created for safe and expedient oversight by the appropriate agencies. An over-arching mosquito control authority must be established as a first priority. In this first year, Autocidal Traps will be deployed and a monitoring system will be put into place that interfaces with the current disease monitoring at the Centers for Disease Control and Prevention and the Department of Health. This monitoring system will incorporate other relevant factors, such as climate, rainfall, mosquito dwelling and biting behaviors, characteristics of humans infected, geographical location of traps with regard to housing and other useful data. A baseline *Ae. aegypti* population map should be created paying special attention to areas of urban density and large municipalities where *Ae. aegypti*-associated diseases have been most prevalent. Physical and chemical interventions should be deployed with great vigor focusing particular attention on the training and management of the labor force that will be deployed to clean up breeding sites and deliver insecticides to the targets. Auto Dissemination (AD) traps should be deployed to get at hard-to-reach breeding sites. This first year is critical for the establishment of the SIT program, which may be fully deployed in year two. A call for proposals in the first three months will identify the appropriate SIT intervention and provider(s).

Mid-term – second and third year. In the second year, the interventions that were initiated in year one will be expanded. *Ae. aegypti* population data will become available to evaluate the effectiveness of interventions and the most effective strategies will be reinforced. In the second year, SIT will become available and, where *Ae. aegypti* populations have been knocked down, SIT may be used to regionally eliminate *Ae. aegypti*. Concentrating the SIT intervention to follow physical and chemical interventions in high-disease-burdened municipalities, such as San Juan or Ponce, should visibly drive down disease in this critical second year building momentum to reinforce the program's elimination objectives.

As regional deployment of SIT eliminates the remaining *Ae. aegypti* in high disease-burden areas, the intensity of the physical and chemical interventions may move to the second tier of disease-burdened geographies in year three. This will create a "rolling front" of *Ae. aegypti* elimination with intense physical and chemical interventions on the leading edge and SIT deployed for elimination expanding behind the leading front. Experts recommend maintaining diligent monitoring of *Ae. aegypti* and associated disease in cleared areas so that *Ae. aegypti* does not outflank the program. Continuing public engagement at this time is important as the disease burden begins to wane and the public's priorities may shift. Although not a part of vector control, by year three the possibility of vaccines to address Dengue, Chikungunya and Zika will be more apparent. While a Dengue vaccine is available in several countries, approval by the US FDA is still pending. Vaccines for Zika and Chikungunya are in development and may take more than a decade to be clinically tested and approved.

Long term – year four and five. At this point we should have a view on the "end game" and what regions remain for elimination. With the experience of the previous three years, we can examine the cost-benefit of elimination of *Ae. aegypti* versus control. As we have learned from other SIT programs for agricultural pests, elimination of *Ae. aegypti* with SIT may be less costly than allowing a low-level persistent population that can serve as a reservoir for re-infestation. Alternatively, permanent suppression of mosquito populations in towns and cities may be cheaper than constant high density monitoring and island-wide preventive sterile releases to avert re-infestation in Puerto Rico. A detailed cost-benefit analysis will be needed.

If elimination is chosen, ongoing monitoring of *Ae. aegypti* importation and spot removal is essential, as is done for the medfly SIT program maintained by the USDA in California. Using these programs as a guide the *Ae. aegypti* program in Puerto Rico may employ similar port-of-entry surveillance and island-wide monitoring to detect local mosquito outbreaks³⁹. Control measures may include continued preventative release of sterile males, lethal trapping and insecticidal control in areas that are vulnerable for introductions. Finally, if a vaccine for Dengue, Chikungunya and Zika has become available for distribution, we may consider this alternative, assuming a plan to vaccinate is in place, especially for pregnant women.

Management, Infrastructure and Capacity-Building

The interventions proposed were well understood, leading to a higher degree of consensus than expected across the 47 workshop experts. In the end, we converged on one critical missing piece for implementing these recommendations: to effectively execute any mosquito control/elimination program requires a dedicated, autonomous organization with the mandate to execute the program. It seems Puerto Rico is missing this basic capacity, which exists throughout the continental US in the Mosquito Abatement Districts (*e.g.* the California and Florida Mosquito Control Districts)^{40,41}.

Therefore, above all, Puerto Rico should establish a Mosquito Control Commission to carry out the *Ae. aegypti* control or elimination program and maintain it after the current crisis is solved. To ensure the technical capability required for program activities, we suggest that the Puerto Rico Mosquito Control Commission should be led by a mosquito control professional like those that run mosquito control districts elsewhere in the US with a long-term commitment and funding. This Director must have the authority and budget to execute an ambitious plan, just as Fred Soper had when he eliminated disease-carrying mosquitoes in his day. Because mosquito control is not an activity well suited to a medical or agricultural agency, it is imperative that the commission is independent from existing governmental structures and budgets. A Board, which may include representation from the PR Department of Health, CDC, Department of Agriculture and Natural Resources, for example, could appoint the Director. The Board should be charged solely with the oversight of the Director, with the authority for hiring the Director and holding him/her accountable for results. The Director should have complete autonomy and accountability for the elimination program. This Commission should continue over time so that once *Ae. aegypti* and the mosquito-borne diseases are under control and out of the public consciousness, a preventative program remains. The Zika, Chikungunya and Dengue epidemics occurred for lack of sustained vector control. Constant vigilance is required to prevent the resurgence of mosquito-borne diseases, those we know and those yet to emerge.

In Summary

The resurgence of serious diseases transmitted by the *Aedes aegypti* vector is one of the most urgent and important health issues for Puerto Rico today and its resolution can be found in the elimination of the vector. Vector control and preferably elimination is the only sustainable solution for Puerto Rico to thrive, turning around this crisis in public health as well as what is happening in the loss of tourism, movie production, and sporting events because of mosquito-borne diseases. Failure is not an option. Experts have made recommendations to address Dengue Fever, Chikungunya and Zika in Puerto Rico through vector control, the basis of disease transmission. The proposed first step to implement those recommendations is the formation of the Puerto Rico Mosquito Control Commission.

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