The use of modified mosquitoes in Brazil for the control of *Aedes aegypti*: methodological and ethical constraints

A liberação de mosquitos "do bem" na agenda brasileira para o controle do *Aedes aegypti*: restrições metodológicas e éticas

La liberación de los mosquitos "buenos" en la agenda brasileña para el control de *Aedes aegypti*: restricciones metodológicas y éticas

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The number of dengue cases in Brazil between 1990 and 2013 [1] shows the inefficiency of control actions, which largely rely on the control of *Aedes aegypti*; also the vector for the Chikungunya virus, whose occurrence in Brazil has already been recorded [2,3], and whose control recommendations reaffirming the ones for dengue [4]. To face this challenge, there are concrete actions to consolidate the use of new technologies to control *A. aegypti*, which consist of the release of genetically modified mosquitoes or mosquitoes infected with bacteria *Wolbachia*. These harmless mosquitoes, known in Brazil as "do-gooders", are reared in laboratory to be released in the field in order to transmit their laboratory-acquired features or pathogens into the wild urban mosquitoes population, thus promoting the control of mosquito populations or the control of disease transmission in the areas they were released. With the Brazilian media publishing positive results, two of such mosquito plants were installed, in Juazeiro (Bahia) and Campinas (São Paulo) [5,6,7].

This scenario imposes some reflections and ponderations regarding the use of this new technology to control *A. aegypti* in Brazil. Initially, one must observe that in the literature (Scopus, Web of Science, BVS, SciELO, Google Scholar), to date, there are no reports on the effectiveness of this methodology for the prophylaxis of dengue. Nor there are field test reports attesting the effectiveness of *A. aegypti* population suppression with the use of this technique in Brazilian urban areas. It is important to note that these field trials must comply with the ethical practices required by research studies that include human beings, as established by the Brazilian National Health Council (NHC), Ministry of Health, as well as some recommended ethical requirements [8]. Field tests are important to check the strategic suitability in view of Brazilian social and environmental obstacles, such as difficulties to access some urban areas (for instance, *favelas*), deficiencies of sanitation services, and precarious infrastructure and organization of vector control by Brazilian public services. At this point, it must be acknowledged that the ongoing release of large amounts of laboratory-produced mosquitoes in large urban areas requires properly trained, respected and well rewarded professionals both in the field and in the laboratories to perform more complex and sophisticated procedures than those performed in the current vector-control programs. It is mandatory to have good professionals for the field work, to ensure proper effectiveness of entomological surveillance services, and to map mosquito-infestation rates that will guide de selection of sites and the intensity of mosquito releases. The relevance of these observations lies in the evidences of the poor quality of the current *A. aegyp-*

ti current surveillance services [9]. One must also consider that this strategy will demand ongoing financial support, on a level higher than the current one. Therefore, one should acknowledge the lack of an empirical base to ensure effectiveness of the continuous use of modified mosquitoes in large areas, such as districts or cities in Brazil.

On the other hand, the literature does not identify methodological conflicts that arise from such mosquito releases. There are no controversies among entomologists on the current integrated pest management paradigm as the best strategy to control vectors and pests. The integrated pest management or integrated vector management (IVM) consists of rational, integrated and synergistic use of different techniques from different control methods which, by nature, the main techniques used or avalilable to promote immediate population suppression,

such as chemical or biological insecticides, predators (for instance, fish), traps, aspirators, and the different procedures to eliminate breeding places (environmental management method) [10]. The technique of releasing modified mosquitos to mate with wild individuals is unique, because it is different from all other typically used techniques, and, at least initially, it is conflictive with immediate population suppression techniques. It does not make sense to release modified mosquitoes simultaneously with the use of insecticides, traps, predators and elimination of breeding grounds. This conflict contradicts IVM integration and synergism principles, making them impracticable.

The impossibility of ensuring effectiveness of mosquito releases, mainly for diseases prophylaxis, along with the methodological conflict within the IVM sets an ethical constraint in face of the population that lives in the targeted areas. In the endemic areas selected to release the modified mosquitoes, the population must be informed on the actual limitations and uncertainties on the prophylactic effect of such releases. The question is whether or not the residents will agree to endanger, suppress or suspend, probably for an undetermined period of time, the typical techniques used to fight the mosquitoes, such as the use of insecticides or the elimination of breeding places, and replace them for the releasing of the harmless mosquitoes, but with no assurance of success. In some cases, this replacement may represent an increase the risk of transmission in endemic areas, which hamper the compliance with the ethical requirements [8] and also the legal bio-safety rules [11]; neither would it be possible to reconcile both control strategies in the same area, sectoring or directing the different control actions according to whether or not the residents agree with the release technique.

These reflections and considerations point to constraints that are not solved by the literature. Thus, there is no reason for being optimistic in regards to the release of genetically modified or infected mosquitoes in Brazilian urban areas. One should also consider the appropriateness of further investigations before making the field releases, due to the limited knowledge on bio-ecology, and also from the effects of these releases. For instance, it is possible to identify conflicting studies on the expected effect of *Wolbachia* in the virus infections in the mosquitoes [12]. These issues should be taken into account before consenting the usage of these technologies in Brazil.

Contributors

E. D. Wermelinger was the main author involved in the design, discussion and research. A. P. Ferreira contributed to the discussion, debate and writing of the manuscript. M. A. Horta collaborated in the discussion, exchange of information and writing of the manuscript.

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