Fighting malaria with Crispr/Cas9: Ethical implications

Perspectives from WHO

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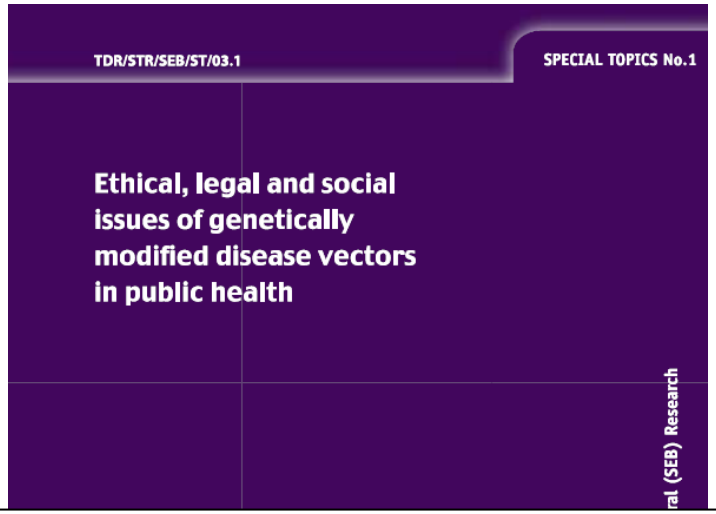
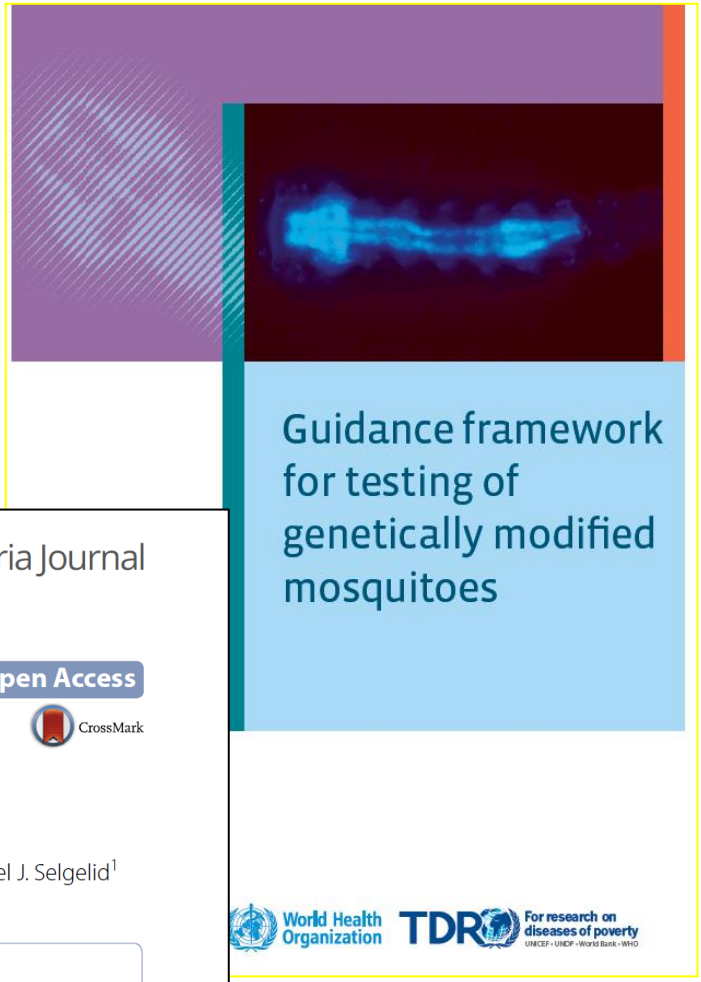
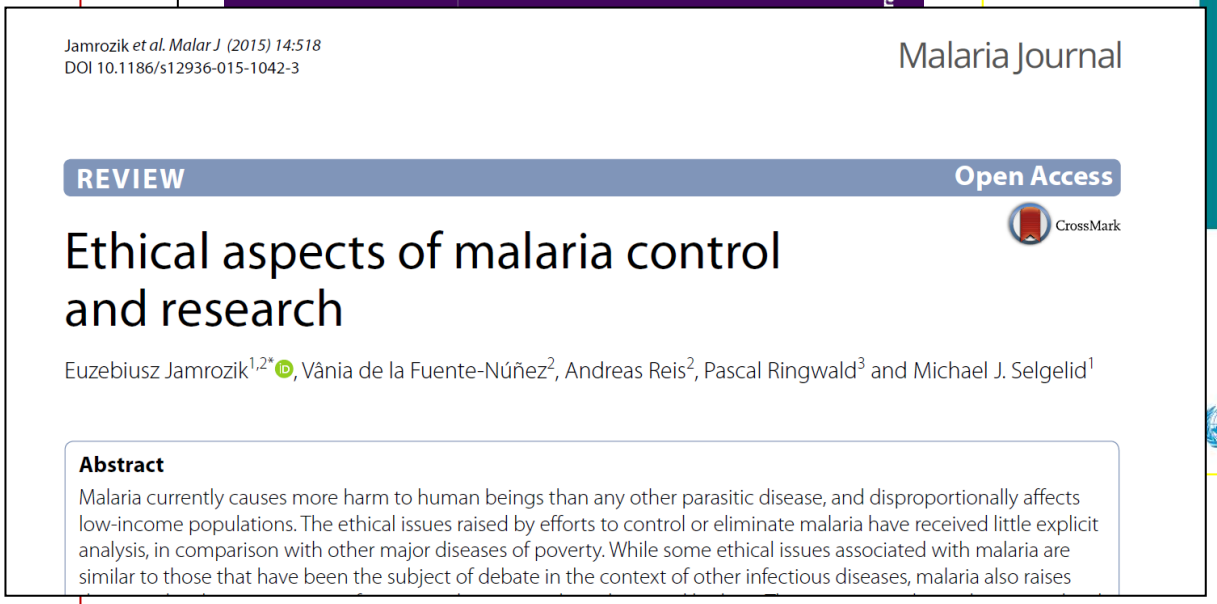
Relevant work at WHO







Relevant work at WHO

- No specific work on ethics of CRISPR/Cas9 yet
- No official position of WHO
- More reflection needed
- Welcome this initiative

Selected ethical issues

- "Eco-centrism"
- Weighing benefits and risks
- Risks to human health
- Risks/impact on eco-system
- Public engagement & acceptance prior to interventions

"Eco-centrism"

- Few intrinsic ethical concerns about killing insect pests
- Eco-centric viewpoint:
  - objections to humans modifying the eco-system
  - Opposition to killing any animals

Weighing risks and benefits

- Central ethical consideration in assessing new technologies
- **Benefits**:
  - Malaria is one of the most deadly diseases (~ 500.000 deaths/year)
  - If successful, potentially large benefits for public health

Effect of individual control measures?

Added benefit of gene drive?

Risks to human health

- Relevant interaction for human health is biting. Incidental exposure through inhalation, ingestion not likely to result in harm ?
- Likelihood of novel introduced gene flow to humans ?
- As *An. gambiae* is an important disease vector, consideration should be given to potential alterations in disease transmission; includes altered P. falciparum transmission, other human malarial transmission as well as altered transmission of other diseases
- Vector control strategies should be maintained to mitigate failure of a single control strategy – e.g. insecticide resistance

Risks/impact on ecosystem

- Likelihood of changes in population size (or elimination) to significantly harm biodiversity, whether in air on in water ?
- An. gambiae interacts with species primarily through feeding on them, being consumed as prey. These interactions require consideration for species of relevance to the assessment such as threatened or endangered species or valued species.
- Extent to which An. gambiae provides any significant ecosystem services?
- Will incidental contact with An. gambiae carrying gene drives lead to any harm?

Public engagement for testing GGM

Source: Guidance framework for testing of GMM. WHO, TDR & FNIH, 2014

A biologist releases genetically modified mosquitoes in Piracicaba, Brazil.

(Photos: Victor Moriyama/Getty Images)

Public engagement: background

- Overarching ethical principle:
  Respect for communities
- Democratic governance requires that proposals on testing of GMMs be discussed in open manner with stakeholders
- Ethical obligations broader than activities mandated by administrative laws or policies
- Regulatory compliance ≠ ethical & community engagement obligations

Public engagement: levels

- Within the project team: articulate value and social purpose of research; ethical reflection
- With the host community:
  - obligations to people living within a trial site
  - Clarify interests at stake and respond to concerns
  - Reaching agreement on whether trial should proceed
- Third parties: Individuals not immediately associated with the trial site (public health or intl. development organizations, general public) – consider and respond to concerns

Public engagement: planning

- Adequate communication & engagement plans should be put in place before the earliest stages of field testing
- Community engagement should start during collection of baseline entomological data
- Community engagement and authorization activities should be carried out in Phase 2 of the GMM testing pathway and expand in Phase 3
- In Phase 3, research ethics issues will become more prominent
- Importance of scientific team to be involved in community engagement; but need for specialized skills of social scientists & communication experts

Public engagement: How NOT to do it

Box 4.2 Disruption of the testing of male sterile mosquitoes in India

Public health scientist Robert S. Desowitz described an episode in one of his books written for a popular audience that is instructive to consider: "On a morning in 1975, a van bearing the blue-and-white logo of the World Health Organization on the door—a snake caduceus through a global map—drives into the village center. The villagers, who have a fear and loathing of snakes, regard the serpent van suspiciously. They begin to be even more suspicious when a peculiar collection of men emerges from the van—a few undoubted Indians, some strange Orientals, and some very white white men. An angry murmur of astonishment passes through the gathered group of villages when these men remove large mesh-covered cages from the vehicle, open the cages—and out flies a cloud of mosquitoes. Without a word of explanation, the snake and mosquito men then return to their vehicle and drive away. Several weeks later, the snake van appears again in the village and once more the strange foreigners release a cloud of mosquitoes from the cages. The crowd reacts—chasing the men into the van, which makes a hurried escape. A month or so later the vehicle appears again. The villagers burn it." (Desowitz, 1991:89.)

Desowitz (1991) writes that the villagers complained to parliament, and that parliamentarians accused the American scientists of conducting an experiment in biological warfare. It was later confirmed that these suspicions were entirely unfounded (Powell & Jayaraman, 2003).

Source: Guidance framework for testing of GMM. WHO, TDR & FNIH, 2014

Public engagement: Rumour management

- Rise in mosquito population due to natural causes (floods etc.) might be attributed by population to the trial
- Public opinion could quickly turn
- Key importance of managing rumours
- Specialists needed

Informed Consent

- Community agreement
- Consent of "research subjects" difficult to obtain
- Concept of GGM quite hard to explain – "control misconception"
- Opting out may be impossible
- Feasible, acceptable modality which is in line with ethical norms?

Post-trial benefits, intellectual property rights and technology transfer

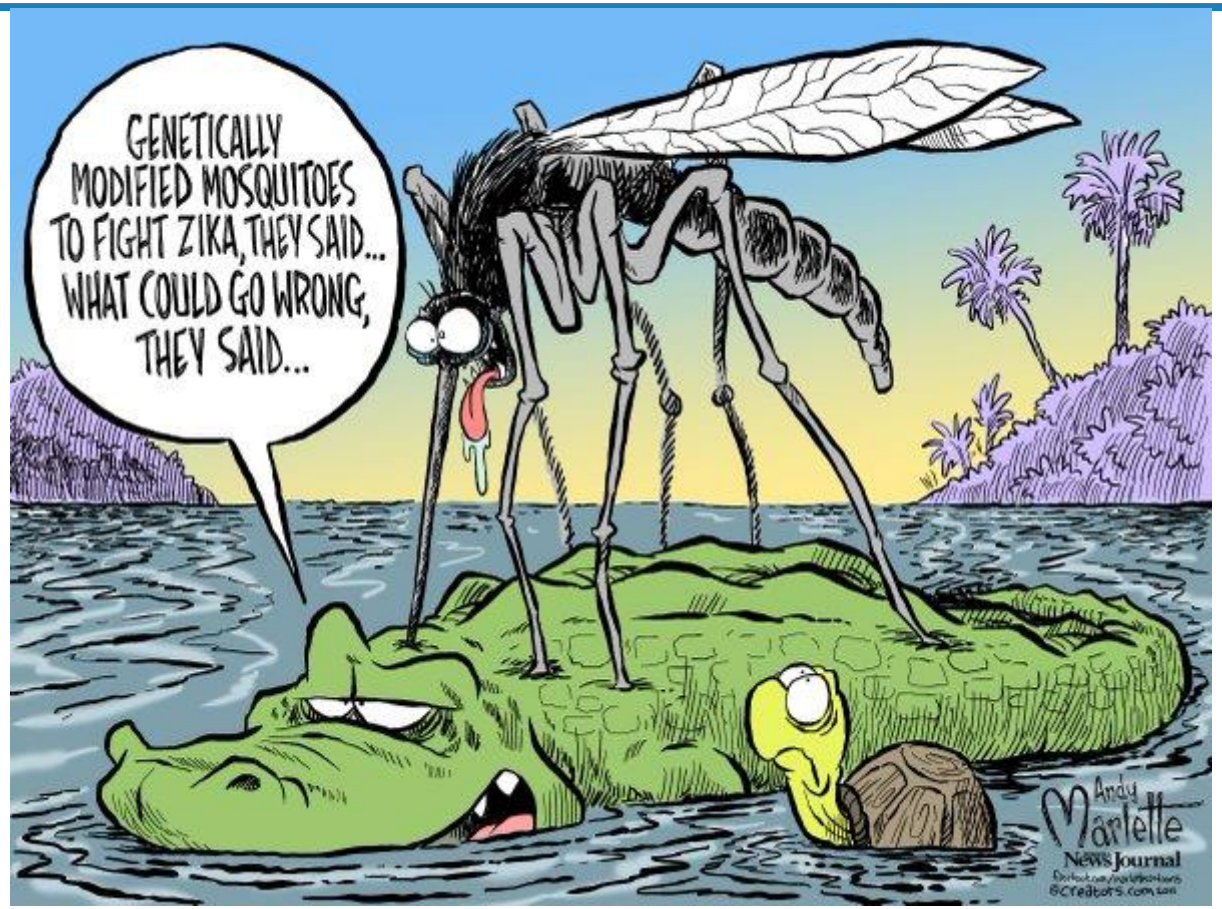
- Central concerns motivated by (global) justice
- Many commercial interests involved
- Will communities (continue to) have access to the fruits of the research? Re-introduction at different intervals needed?
- Prior negotiations with communities needed

Outlook

- More evidence on benefits and risks needed
- Community buy-in is crucial
- Rigorous monitoring & evaluation
- Annual meeting of the *Global Network of WHO Collaborating Centres for Bioethics* (Edinburgh, June 2016):

  decision to start a project to develop guidance on **ethics of vector-borne diseases**

Outlook



- Relevance for Zika, Dengue, Chikungunya etc.
- Need for further global reflection – is consensus possible?

Sources

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Thank you !

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