Rijksinstituut voor Volksgezondheid
en Milieu
*Ministerie van Volksgezondheid,
Welzijn en Sport*

Potential release of genetically modified OX513A *Aedes aegypti* in Saba

environmental risk assessment

Boet Glandorf
GMO Office, RIVM

November 24, 2017

Request Saba

- ✓ Oxitec: release of GM *Aedes aegypti* to suppress local mosquito population on Saba

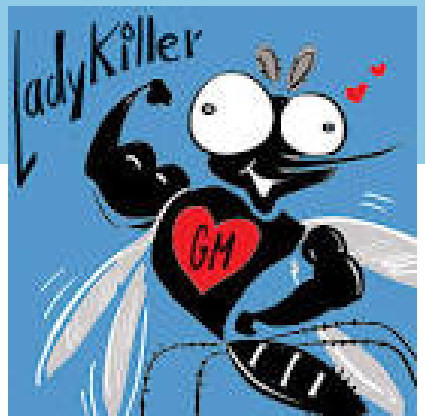
- ✓ Council of Saba requested RIVM (GMO Office) for technical evaluation of Oxitec's dossier for planned release
  (no regulatory dossier)

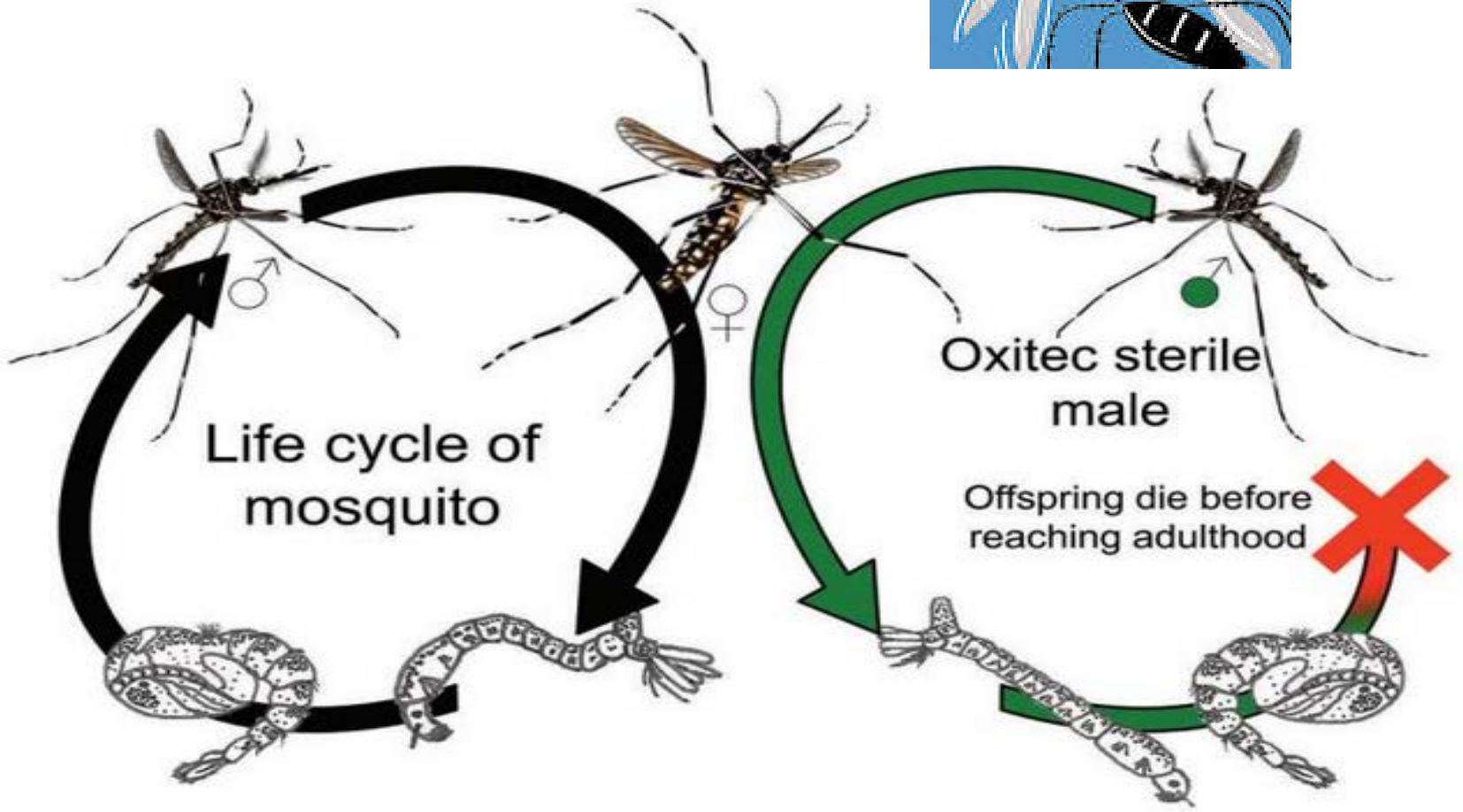


Aedes aegypti

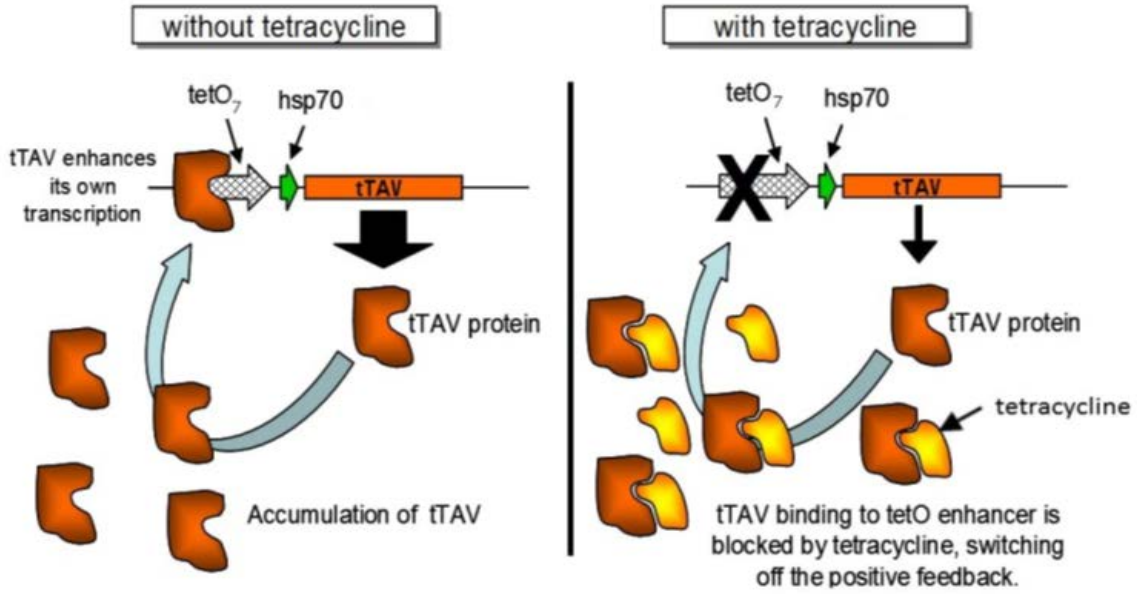
- Carrier of dengue, chikungunya and Zika
- Invasive species in many countries
- Vector control programs are in place
- More efficient control method is genetically modified *Aedes aegypti* (OX513A) (males, non-biting)
- Releases of OX513A in Malaysia, Panama, Cayman Islands and Brazil
- Also FDA concluded on environmental safety of trial in Florida

Oxitec technique





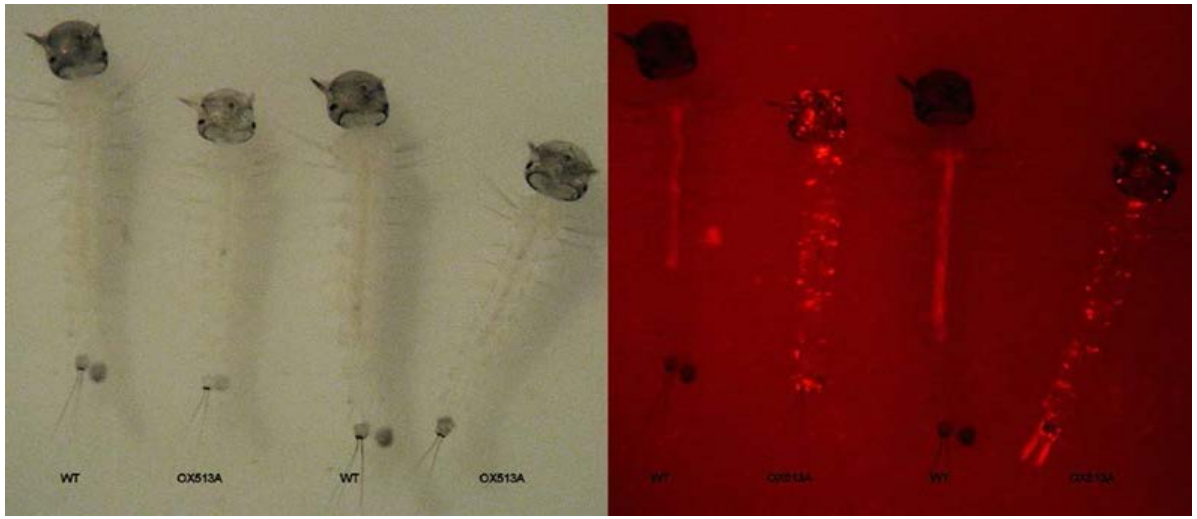
Self limiting trait tTAV



Positive feed back loop

Offspring dies before adulthood

Fluorescent marker DsRed2



Goal: eliminate local *Aedes aegypti* population on Saba

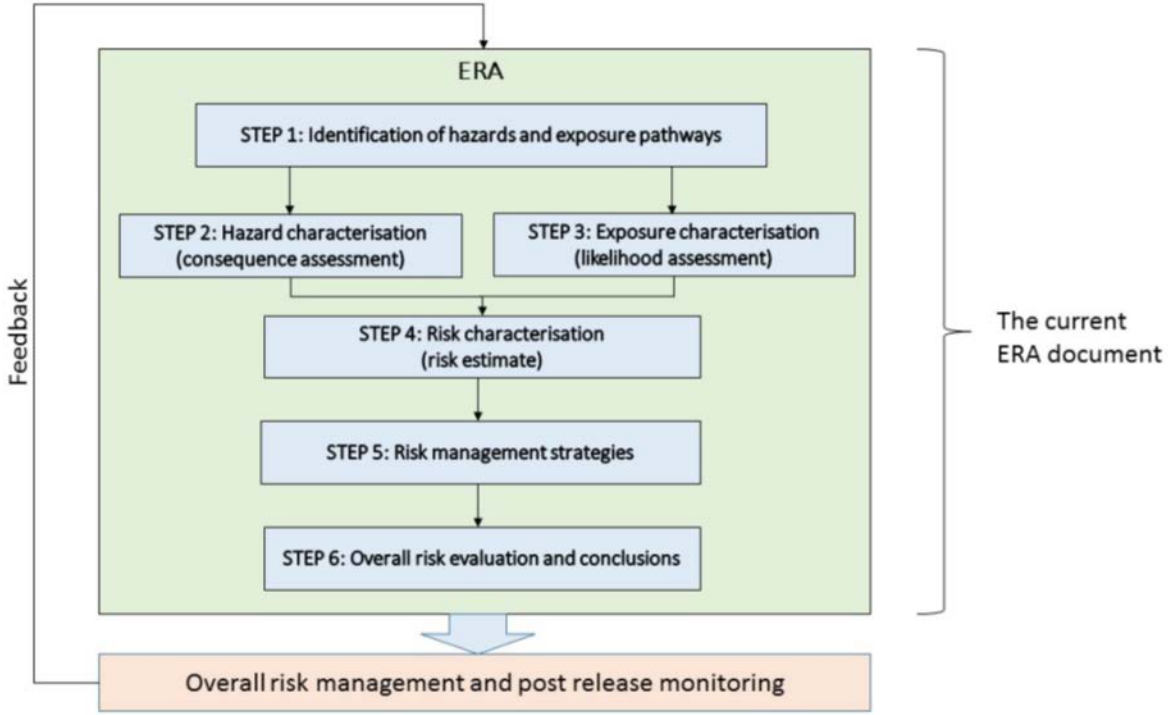
Request Saba

GMO Office agreed to perform technical evaluation, under the following conditions:

- Evaluation of potential environmental effects only, no efficacy or socio-economic/ethical aspects
- Need for complete dossier, structured according to EU Directive 2001/18/EC
- Assessment according to EFSA Guidance of GM animals (2013), also taking into account other Guidances (*e.g.* WHO, CBD)
- Protection goal of ERA is ‘human health and the environment’

Evaluation of potential adverse effects on human health and the environment as a consequence of the release of OX513A on Saba

Steps in ERA according to 2001/18/EC



Environmental risk assessment using European Guidance document

EFSA Guidance on GM insects (EFSA, 2013). Aspects to be taken into account:

- ✓ Increased persistence and invasiveness;
- ✓ Horizontal gene transfer;
- ✓ Pathogens, infections and diseases;
- ✓ Interactions with target insects;
- ✓ Interactions with non-target organisms;
- ✓ Impacts on human and animal health;
- ✓ Environmental impacts of the specific techniques used for the management of GM insects.


efsa
European Food Safety Authority

EFSA Journal 2013;11(5):3200

SCIENTIFIC OPINION

Guidance on the environmental risk assessment of genetically modified animals[1]

EFSA Panel on Genetically Modified Organisms (GMO)[2,3]

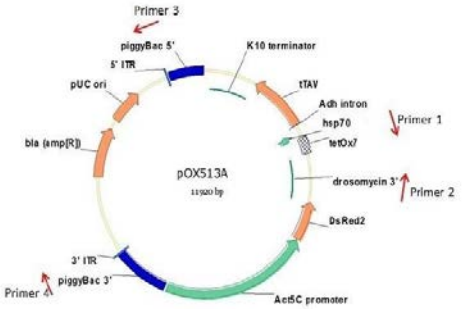
European Food Safety Authority (EFSA), Parma, Italy

Structure of dossier / ERA

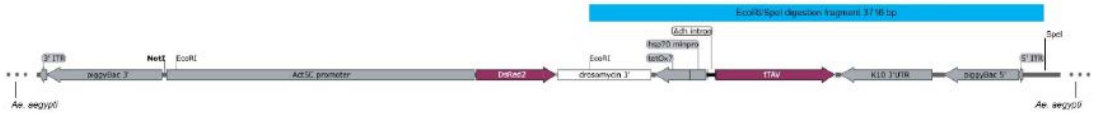
Characterisation

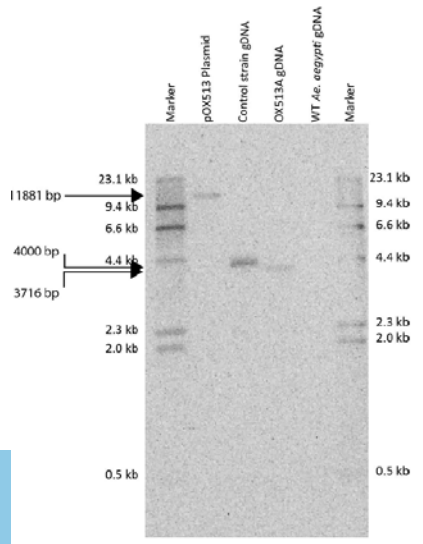
- ✓ **Parental organism**

- ✓ **DNA sequences to be inserted or deleted and method of modification**



- ✓ **GM organism and molecular characterisation**

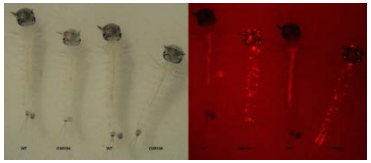




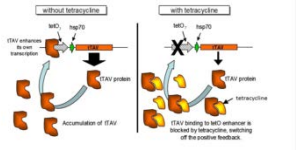
Dossier OX513A

✓ **GM organism and new traits**

+ dsRed



+ tTAV



✓ **Differences between wild type and GM**

- Life style parameters
- Response to abiotic factors (temperature, tetracycline..)
- Dispersal and longevity
- Disease transmission
- Toxicity, allergenicity
- Detection
- ...

Data of earlier releases !

Dossier OX513A

Planned activities and the receiving environment

Planned activities

- ✓ Eggs from UK
- ✓ Pupae – separation male and females, selection males
- ✓ Growth till adults
- ✓ Release in inhabited areas in (phased approach)

Receiving environment (Saba)

All abiotic and biotic aspects, including tetracycline concentrations in environment

Dossier OX513A

ERA

EFSA Guidance on GM insects (EFSA, 2013). Aspects to be taken into account:

- ✓ Increased persistence and invasiveness;
- ✓ Horizontal gene transfer;
- ✓ Pathogens, infections and diseases;
- ✓ Interactions with target insects;
- ✓ Interactions with non-target organisms;
- ✓ Impacts on human and animal health;
- ✓ Environmental impacts of the specific techniques used for the management of GM insects.

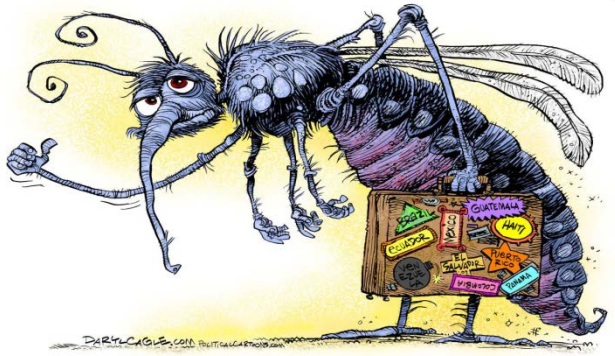
What is actually assessed in the ERA of OX513A ?

1. Potential adverse effects of introduction GM mosquitoes (new trait);

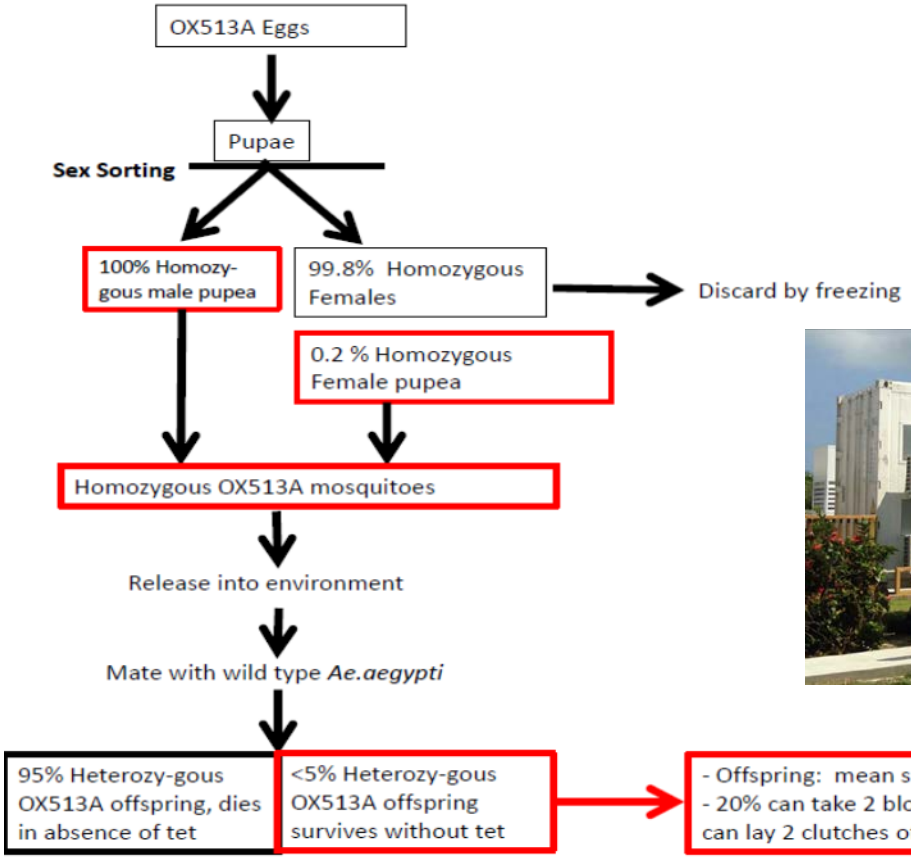
2. Potential adverse effects as a consequence of elimination of local *Aedes aegypti* population.

Other aspects: SOPS on e.g. safety of production process, separation females and males, controls, emergency measures, monitoring after introduction

Unintentional spreading from Saba by ships, airplanes



ERA-specific aspects



What is actually assessed in the ERA of GM mosquitoes ?

1. Potential adverse effects of the release of OX513A (new trait) on the environment

- ✓ more invasive in Saba?
- ✓ negatively affect predators or other non-target organisms (effect on food web)?
- ✓ toxic or allergenic for animals, humans (e.g. biting, ingestion)?
- ✓ difference in virus transmission?

Example: potential invasiveness

The hypothesis tested is that OX513A or its progeny is not more persistent or invasive in semi-natural or natural habitats than the existing wild type population.

The **key considerations** for this area of concern are (based on EFSA 2013):

- ✓ Can GM insect persist/invade?
- ✓ Can GM insect hybridise with compatible relatives?
- ✓ Does modification change fitness?
- ✓ Does modification change habitat/geographic range?

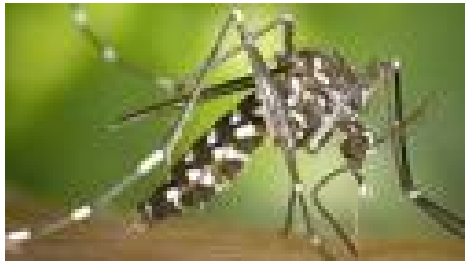
Example: potential invasiveness

Data assessment

Difference between wildtype/non-GM and OX513A with respect to:

- ✓ survival
- ✓ dispersal
- ✓ temperature response
- ✓ life table parameters
- ✓ hybridization with closely related species (*Aedes albopictus*)
- ✓ mating efficiency

…in the context of their intended release op Saba



Conclusions potential invasiveness

Conclusions on key concerns:

- ✓ OX513A can not persist/invade in Saba
- ✓ OX513A can not hybridise with *Aedes albopictus*
- ✓ Modification does not change fitness
- ✓ Modification in OX513A does not change habitat/geographic range in Saba

The GMO Office concludes that increased persistence or invasiveness of OX513A is considered to be unlikely in comparison to that of the wild type Aedes aegypti

But….. it is the intention of OX513A to suppress *Aedes aegypti* populations!

Example: interactions with NTOs

The hypothesis tested is whether OX513A, in comparison to the wild type Aedes aegypti, has no adverse effects on non-target organisms in semi-natural and natural areas taking into account current vector control.

The **key considerations**, based on EFSA (2013), are:

Effects of OX513A, in comparison to the non-GM, on:

- ✓ Abundance of natural enemies, competitors, pollinators
- ✓ Biodiversity (species of conservation value)
- ✓ Ecosystem services (pollination, decomposition)
- ✓ Abundance of host plants/host animals
- ✓ Effects of toxins or allergens on insectivorous vertebrates

Protected, charismatic and valued species on Saba

Red belied racer
Alsophis rufiventris

No habitat overlap
Does not eat mosquitoes

Saban anole
Anolis sabanus

Habitat overlap
Preference for other food sources

Conclusions NTOs

Conclusions on key concerns:

✓ **Abundance of natural enemies**

No effect due to:

- lack of habitat overlap or overlap in activity between *Aedes aegypti*/OX513A and predators
- *Aedes aegypti*/OX513A only forms a small or negligible part of the diet of predators
- predator(s) is (are) only generalist
- toxicity studies with OX513A as a sole diet demonstrate no adverse effects on predators

✓ **Biodiversity (species of conservation value)**

No effect due to lack of habitat overlap and not being a part of the diet of these species on Saba

Conclusions NTOs

✓ **Ecosystem services (pollination, decomposition)**

Aedes aegypti does not play a role in decomposition, nutrient cycling or pollination

✓ **Abundance of host plants / host animals**

Aedes aegypti has no host plants or animals

✓ **Effects of toxins or allergens on insectivorous vertebrates**

Toxicity studies with OX513A as a sole diet demonstrate no adverse effects on predators

The GMO Office concludes that OX513A, in comparison to the non-modified Aedes aegypti, is unlikely to adversely affect non-target organisms in semi-natural and natural areas, also taking into account current vector control

What is actually assessed in the ERA of OX513A?

2. Potential adverse effects as a consequence of elimination of local *Aedes aegypti* population

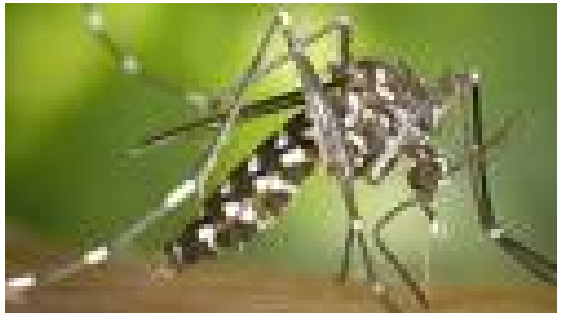
- ✓ Loss of food source for other organisms - effect on food chain?
- ✓ Herd immunity – higher infection rate after reintroduction?
- ✓ Niche replacement?

And how does this relate to current vector control strategies?

Example: pathogens, infections and diseases

e.g. niche replacement

- ✓ Closely related *Aedes albopictus* is not (yet) present op Saba.
- ✓ *Aedes albopictus* has a similar vector competence for arboviruses, such as zika, but has a different host range
- ✓ *Aedes albopictus* has a different habitat, but habitat can overlap with *Aedes aegypti*



Conclusions pathogens, infections and diseases

The GMO Office concludes that:

- ✓ It is not excluded that replacement of *Aedes aegypti* by *Aedes albopictus* on Saba would occur
- ✓ This would not lead to a change in human disease burden caused by dengue, chikungunya and zika
- ✓ The risk of zoonotic transmission of viruses from an animal reservoir to humans is increased, but the likelihood that this would occur on Saba is very low

But….replacement of *Aedes aegypti* by *Aedes albopictus* on Saba can occur with any vector control method that effectively suppresses *Aedes aegypti*

Experts involved

Experts with the following expertise:

- Mosquito-specific aspects and vector control
- Toxicity, allergenicity, herd immunity
- Molecular characterisation, and environmental aspects
- Rearing unit and SOPs
- Saba-specific aspects (ecological, tetracycline occurrence)

Contact with risk assessors from FDA and Brazil

Review by national and international experts

Conclusion RIVM report

Negligible risks for human health and the environment

concludes that potential adverse effects on human
consequence of the potential release of
under the conditions
as described
standard vector control, are
effects of non-modified *Aedes aegypti*. This is
environmental risk assessments such as from Brazil [3,4] and the
States Food and Drug Administration [5].
The GMO Office recommends post-release monitoring by an independent party, as advised by the WHO[6], on a monthly basis until populations of OX513A are below the level of detection.

Rijksinstituut voor Volksgezondheid en Milieu
Ministerie van Volksgezondheid, Welzijn en Sport

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http://www.rivm.nl/bibliotheek/rapporten/2017-0087.html

including links to all information

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News & Views (http://www.oxitec.com/news-and-views/)

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Oxitec's Friendly™ Aedes Mosquito Receives Positive Evaluation for European Standard in relation to Human Health and the Environment

July 6, 2017

RIVM concludes negligible risk of Oxitec's Friendly™ Aedes mosquitoes

GM-Mosquitoes To Fight Zika, Cleared For Takeoff, Report Says

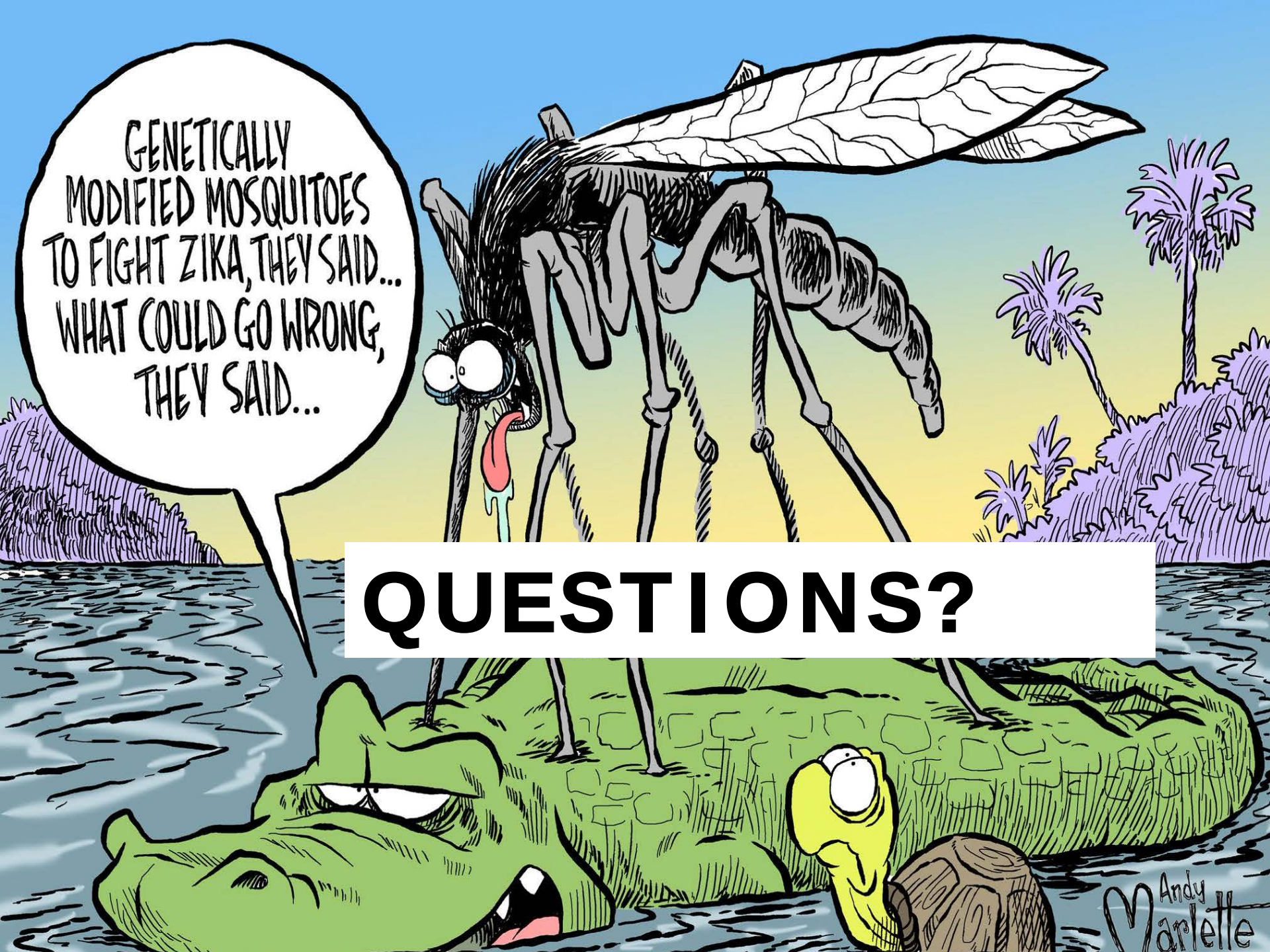
25.07.2017

15 million genetically modified mosquitoes imported to Saba in order to fight dengue and chikungunya

Breaking News from Netherlands » Saba » Health

Will there be a release on Saba?

Saba still has to decide and has to consult its population


GENETICALLY MODIFIED MOSQUITOES TO FIGHT ZIKA, THEY SAID... WHAT COULD GO WRONG, THEY SAID...
QUESTIONS?
Andy Marlette