Regulatory experiences with genetically modified insects

The case of *A. aegypti* OX513A in Brazil

Paulo P. Andrade

Departamento de Genética, Universidade Federal de Pernambuco, Recife, Brazil;

Info on the transgenic *Aedes aegypti* OX513A

It has two new genes: one expresses a fluorescent green marker and the other expresses a lethal protein (a transcription activator factor).

A request for a field release was submitted to the National Biosafety Commission back in 2011.

Field experiments were conducted by the proponents (Oxitec and the University of São Paulo), starting 2012

The mosquitoes were released in two neighborhoods in Bahia (Juazeiro): around 3000 inhabitants each. Semi-dry climate. Very deficient water supply and sewage system. Average income low

Risk communication very effective

The transgenic Aedes aegypti OX513A
Some hazards derived from different stakeholders perception and their risk classes

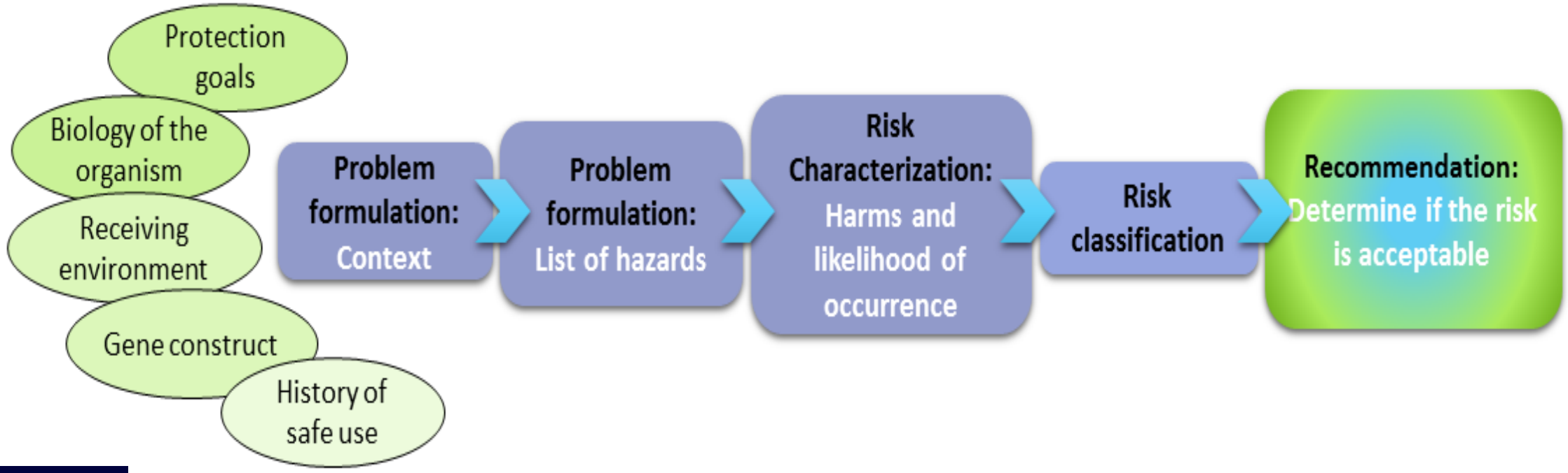
(according either to the public, to the proponents or to risk assessors)

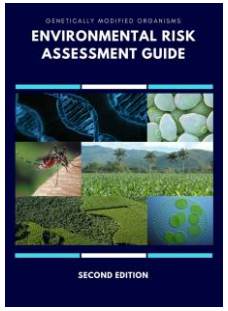
Risk perception (hazard)	Associated harm	Public outrage	Real risk level
GM mosquitoes may bite people	Disease transmission	Big	Negligible
Unexpected survival of GM mosquitoes	Ecological damage	Low	
Allergenicity and/or toxicity of two new proteins expressed	Allergy and intoxication	Low	
Horizontal flow of the transgene	Ill defined (to Zika virus?)	Moderate	
Enhanced viral transmission	Epidemics	Moderate	
Tetracycline resistant bacteria	Diseases outbreaks	Low	
Vacant niche occupation	New vectors, new diseases	Big	

Main concerns for the Commission (related to an experimental field release)

Insects can fly	But not that much...
Aedes can take rides in cars and busses	Insects will die after a few days: dead GM insects are no cause of concern
Eggs can also be spread	
Humans are involved in the trial	Male insects don't bite. The few females accidentally released are not infected. If they get infected, they die before being able to transmit the disease New proteins are not expressed in the saliva Humans don't eat mosquitos

The bulk of ***relevant*** questions were derived from the environmental risk assessment (ERA). However, **essentially all questions** from the different stakeholders were also considered in the list of hazards. No food and feed RA required





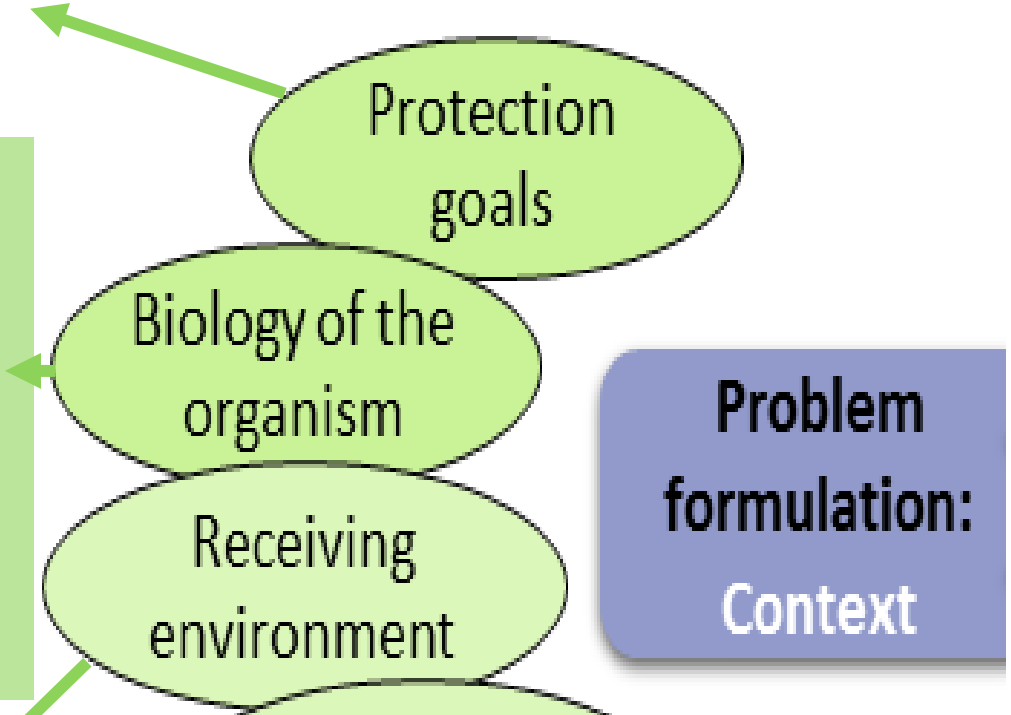
Environmental risk assessment of GMOs (Draft - June 2017)
http://www.targetdna.com.br/wp-content/uploads/2015/02/D52-ERA-Guide-with-watermark-final.pdf

Biodiversity: **none**

Problem formulation: the context

Main issue kept in mind: what are the protection goals that the commission derived for its assessment?

Non native
No sexually compatible species
Dispersion under control
No invasive potential (for OX513A)
Not important in the wild life food chain



Agri-environments/ rivers

Some kind of lethality (OX513A)

SIT? (as a comparator)

After 4 years (2010-2014) all steps from the initial assessment to the commercial release were done

No new questions were raised during the RA for commercial release. (*until the zika epidemics, 1 1/2 years after the commercial release*)

Risk communication was essential:

- To reduce opposition among many stakeholders
- To produce a positive feedback in the media

Moreover

- The technology advantages were clearly in favor of the Brazilian society (and not restricted to a small group)
- No obvious risks and a long history of successful use of biotechnology in Brazil (and elsewhere) helped a lot
- Opposition faded out rapidly. Oxitec Brasil took very positive measures to ensure

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Use of transgenic *Aedes aegypti* in Brazil: risk perception and assessment

Paulo Paes de Andrade,[a] Francisco José Lima Aragão,[b] Walter Colli,[c] Odir Antônio Dellagostin,[d] Flávio Finardi-Filho,[c] Mario Hiroyuki Hirata,[c] Amaro de Castro Lira-Neto,[e] Marcia Almeida de Melo,[f] Alexandre Lima Nepomuceno,[b] Francisco Gorgônio da Nóbrega,[c] Gutemberg Delfino de Sousa,[g] Fernando Hercos Valicente[b] & Maria Helena Bodanese Zanettini[h]

Abstract The OX513A strain of *Aedes aegypti*, which was developed by the British company Oxitec, expresses a self-limiting transgene that prevents larvae from developing to adulthood. In April 2014, the Brazilian National Technical Commission on Biosafety completed a risk assessment of OX513A and concluded that the strain did not present new biological risks to humans or the environment and could be released in Brazil. At that point, Brazil became the first country to approve the unconstrained release of a genetically modified mosquito. During the assessment, the commission produced a comprehensive list of – and systematically analysed – the perceived hazards. Such hazards included the potential survival to adulthood of immature stages carrying the transgene – should the transgene fail to be expressed or be turned off by exposure to sufficient environmental tetracycline. Other perceived hazards included the potential allergenicity and/or toxicity of the proteins expressed by the gene, the potential for gene flow or increased transmission of human pathogens and the occupation of vacant breeding sites by other vector species. The Zika epidemic both elevated the perceived importance of *Ae. aegypti* as a vector – among policy-makers and regulators as well as the general public – and increased concerns over the release of males of the OX513A strain. We have therefore reassessed the potential hazards. We found that release of the transgenic mosquitoes would still be both safe and of great potential value in the control of diseases spread by *Ae. aegypti*, such as chikungunya, dengue and Zika.

andrade@ufpe.br amarocastro@gmail.com