



#596: The Cartagena Protocol and genetically modified mosquitoes

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INTRODUCTION:

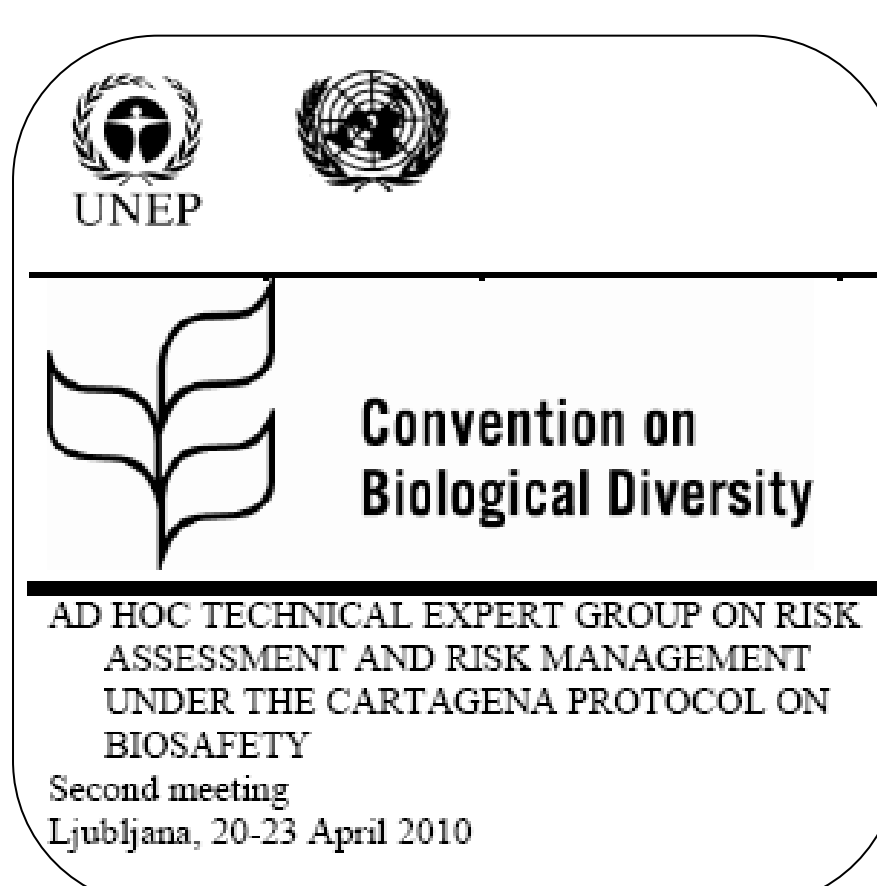
CARTAGENA PROTOCOL ON BIOSAFETY TO THE CONVENTION ON BIOLOGICAL DIVERSITY

The Cartagena Protocol:

- Fundamental document of the **United Nations** on the **responsible use** of genetically modified (**GM**) organisms.
- Applies to **GM mosquitoes** intended for **disease control**.
- But **terms** were primarily **negotiated** with concerns over the **safety** and **trade** of **GM crops** in mind.

Ad Hoc Technical Expert Group (AHTEG) on Risk Assessment and Risk Management:

- Assigned a **sub-working group** to develop **risk assessment guidelines** for **GM mosquitoes**.
- First guidance document** was **submitted** to the Parties of the Protocol **last month**.
- This is an important document outlining **potential risks** of **GM mosquitoes**; however several **overarching issues** were considered **beyond its scope**.



GM MOSQUITO STRATEGIES:

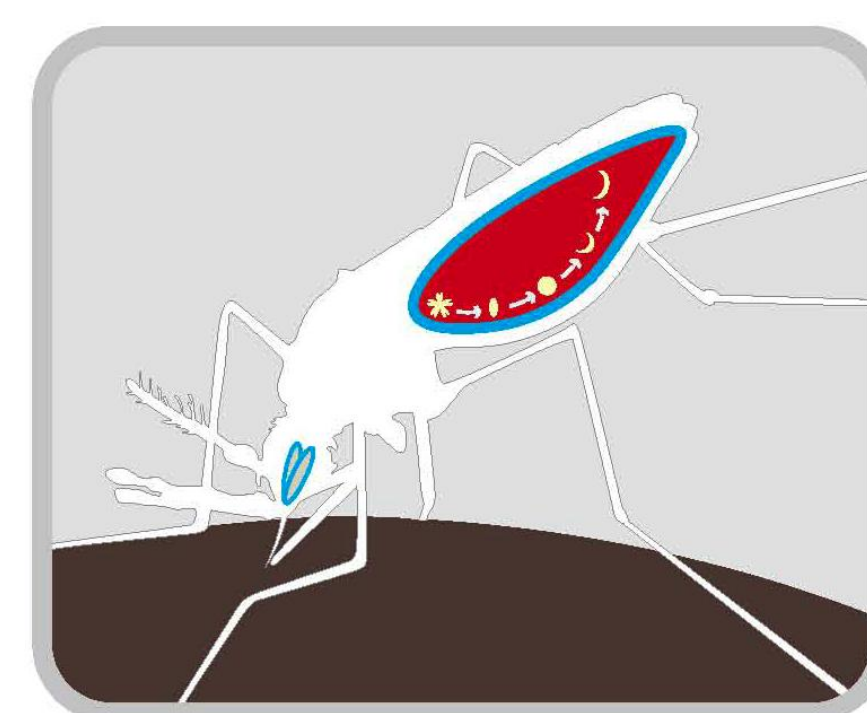
Population suppression:



- Control disease through **reducing vector population size**.
- E.g. **release of genetically sterile male *Aedes aegypti*** mosquitoes (main vector of dengue fever) that, upon mating with wild females, **produce unviable offspring**.
- Self-limiting** (transgenes are eliminated on their own).

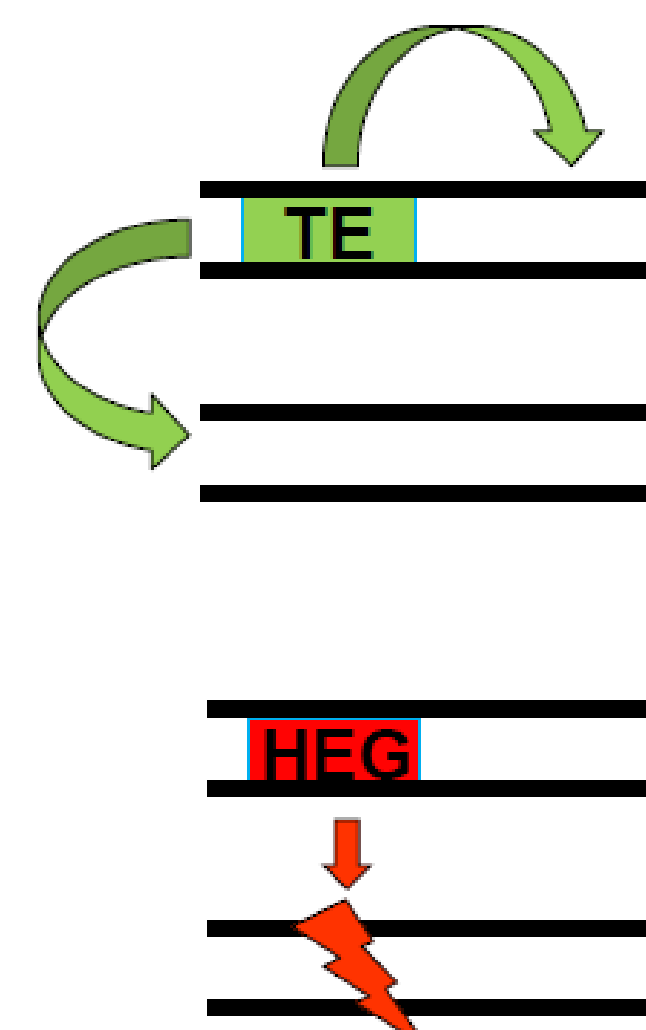
Population replacement:

- Use of a **gene drive system** to **spread disease-refractory genes** into **vector populations**, thus replacing vector populations with disease-refractory varieties.
- Self-propagating** (transgenes are capable of spreading into one, and possibly many, populations).

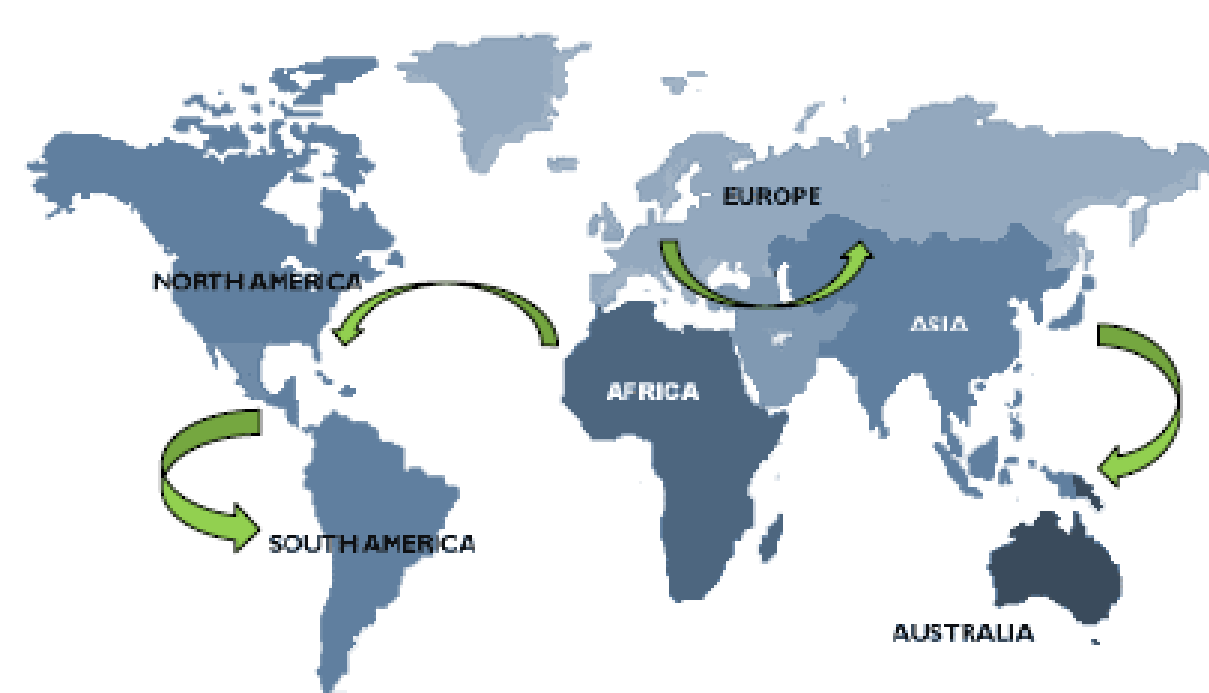


refractory gene gene drive system

INVASIVE GENE DRIVE SYSTEMS:



- Capable of **spreading** from **very low initial frequencies**. For example:
- A **transposable element (TE)** has been observed to **spread** through the **worldwide population** of ***D. melanogaster*** in a few decades.
- Other gene drive systems, such as **homing endonuclease genes (HEGs)** and ***Medea***, are being developed in ***Ae. aegypti*** and ***Anopheles gambiae***.



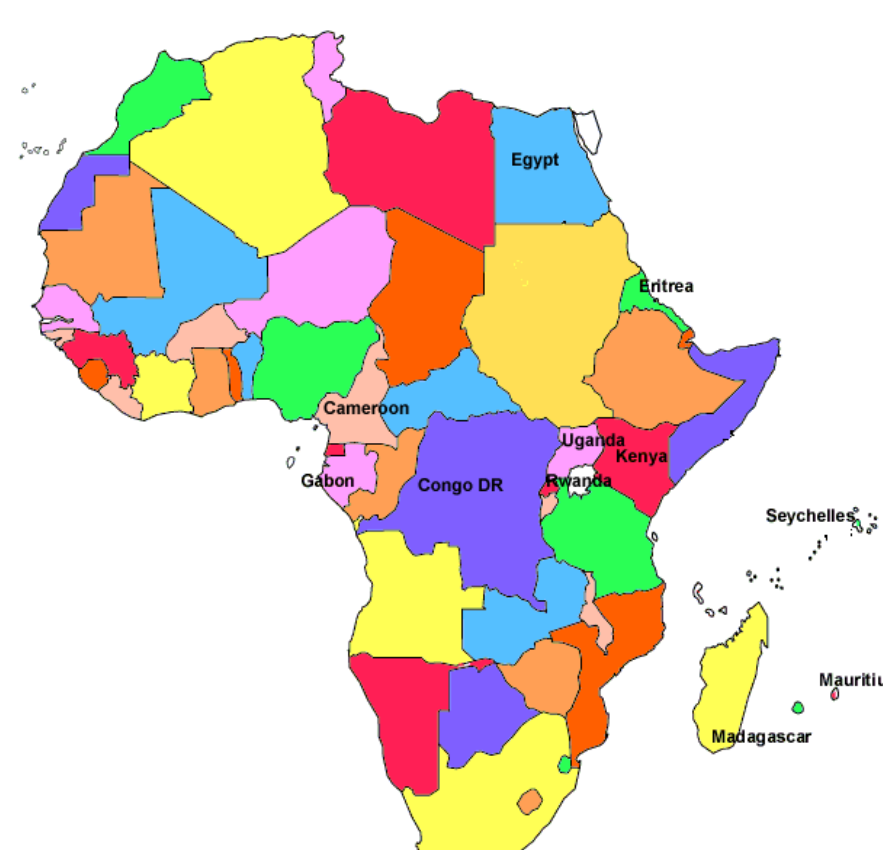
- If successful, then just a **few GM mosquitoes** carrying these constructs would be capable of **propagating genes** refractory to malaria and dengue fever through the entire **geographical range** of the species.

International regulatory issues:

- The Cartagena Protocol applies to the “**transboundary movement**” of **GM organisms**.
- Its **requirements** for a release of **GM mosquitoes** with **invasive gene drive systems** may be **almost impossible to satisfy**:
- The **Advance Informed Agreement (AIA)** procedure applies **before the first environmental release** of GM mosquitoes in **another country**.
- This grants the importing country the right to request the **exporting country** to perform a **risk assessment** at its **own expense**, part of which is to **determine the likelihood** of an “**unintentional transboundary movement**.”
- If these **movements** are **difficult to prevent**, then an **environmental release** is **not allowed**.

MULTILATERAL AGREEMENTS:

- One way around this problem is a **multilateral agreement**, **consistent** with the **Protocol**, which would acknowledge that any **release** of these mosquitoes is **intentionally international**.
- However, in the **context of Zambia's ban** on **GM food aid** in 2002 (during a famine that threatened 100,000's of lives), a **unanimous agreement** on **GM mosquitoes** spanning **Africa** and possibly beyond seems **challenging**, if not impossible.



GM MOSQUITOES IN TRANSIT AND CONTAINMENT:

Exemptions from the AIA procedure:

- The **AIA procedure** was written, in part, to **protect developing countries** against **threats to biosafety** due to a **lack of resources** to conduct their own **risk assessment**.
- During negotiations of the Protocol, however, **countries with strong biotech industries** successfully argued that **GM organisms** in transit or destined for **contained use** pose **negligible risks**, and therefore the **AIA procedure** would **restrict trade unnecessarily** if applied to them.
- This **exemption** must be **re-examined** for **GM mosquitoes** with **invasive gene drive systems** because:

- Breaches of containment** are **impossible to rule out**; and
- Just a **few escapees** could be **capable of spreading** transgenes on a **global scale**.



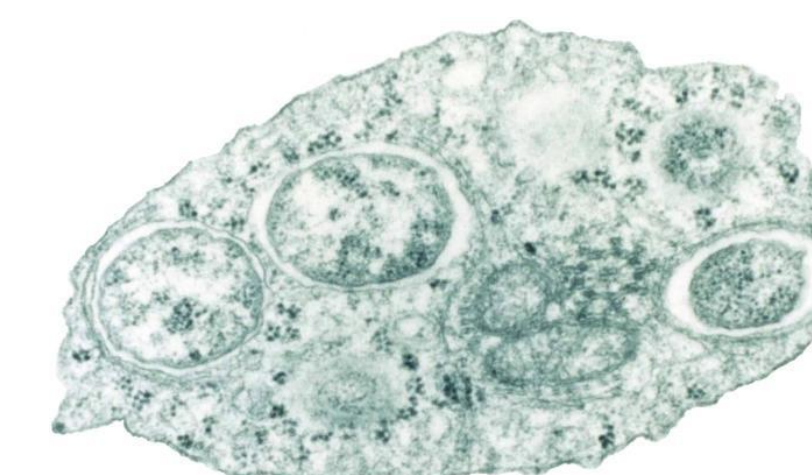
Contained field trials:

- Before an open release**, trials are being discussed that would take place in **field cages** **exposed to the ambient environment** in a **location** that the **species naturally inhabits**.
- Developing countries** are **not entitled to request** that the **importing country pay** for a preliminary **risk assessment** because the **AIA procedure** does **not apply**.



WOLBACHIA:

- Wolbachia* is an **intracellular bacterium** capable of manipulating its host's reproductive biology in a manner that **promotes its spread** through a **population**.
- An ***Ae. aegypti*** line infected with the **wMelPop strain of *Wolbachia*** has drawn attention due to a number of **physiological changes beneficial** for **disease control**:
 - Reduced mosquito lifespan**,
 - Reduced dengue viral load**,
 - Reduced ability to obtain blood meals** with age.



Inapplicability of the Protocol:

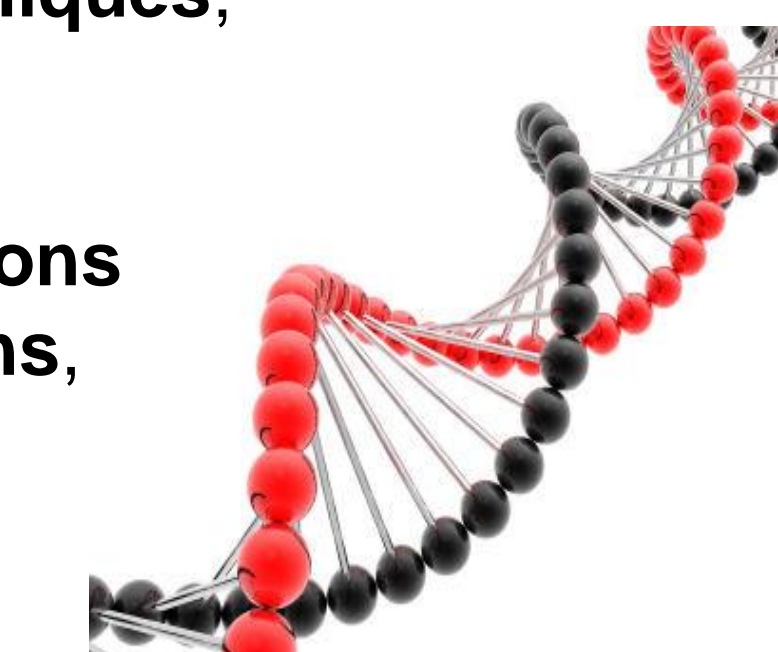
- The fact that ***Wolbachia*** is both **invasive** and **induces significant physiological changes** draws into question its wider **biosafety implications**.
- However, it is **outside the scope** of the **Cartagena Protocol** since it does not fit the definition of “**modern biotechnology**.”

CONCLUSIONS:

- Gene drive** was **not considered** when the **terms** of the **Cartagena Protocol** were first **negotiated**.
- Further discussion** is needed to **address the biosafety implications** of **GM mosquitoes** – particularly those with **invasive gene drive systems**.
- If **approval** for a release of **GM mosquitoes** with **invasive gene drive systems** is **prohibitively difficult**, the **only alternative** may be to look for **loopholes** in the legislation:

- The **Protocol applies** to **GM mosquitoes** developed using ***in vitro* nucleic acid techniques**; however, it **does not apply** to:

- Mosquitoes** with **gene deletions** produced by **traditional means**,
- Mosquitoes** infected with **non-transgenic strains** of ***Wolbachia***.



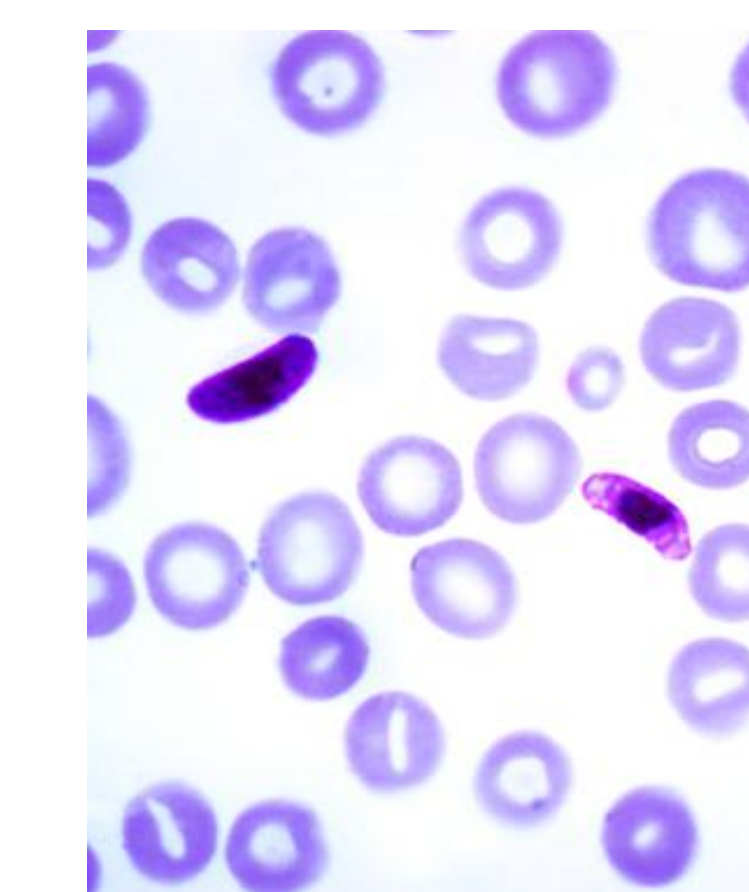
- The **Protocol applies** to movement **between Parties and non-Parties** to the Protocol; however, it **does not apply** between **non-Parties**. For example:

- United States, Canada, Australia,**
- Cote d'Ivoire, Equatorial Guinea, Sao Tome & Principe, Sierra Leone, Morocco,**
- Argentina, Chile, Uruguay, Vanuatu.**



- If **GM mosquitoes** could be considered “**pharmaceuticals for humans**”, they would be **exempt** from the Protocol, **provided** they are **addressed** by **another international agreement** or **organization**.

- The fact that **mosquitoes** are **vectors of human diseases** poses **new considerations** for a **risk-benefit analysis**.



- Ultimately, a **balance** must be sought between the **precautionary principle**, **respect for the sovereignty of states**, and the **ethical mandate** to **prevent disease** on a **global scale**.

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