



OXITEC

Advanced Informed Agreement Notification

Information Required Under Regulation (EC) No 1946/2003 of the European Parliament and of the Council of 15 July 2003 on Transboundary Movements of Genetically Modified Organisms

ANNEX I INFORMATION REQUIRED IN NOTIFICATIONS UNDER ARTICLE 4

(a) Name, address and contact details of the exporter.

Oxitec Ltd
71, Innovation Drive
Milton Park
Abingdon, Oxfordshire
OX14 4RQ
United Kingdom
Tel: 01235 832393
Email: info@oxitec.com

(b) Name, address and contact details of the importer.

Instituto Conmemorativo Gorgas de Estudios de la Salud
Avenida Justo Arosemena y Calle 35
APDO. 0816-02593
Panamá,
República de Panamá
Tel: +(507)527-4800
E-mail: informatica@gorgas.gob.pa

(c) Name and identity of the living modified organism, as well as the domestic classification, if any, of the biosafety level of the living modified organism in the State of export.

OX513A *Aedes aegypti*
Containment level: 1

(d) Intended date or dates of the transboundary movement, if known.

Not known at present

(e) Taxonomic status, common name, point of collection or acquisition, and characteristics of recipient organism or parental organisms related to biosafety.

Aedes aegypti (Diptera: Culicidae)

The parent strain is the Rockefeller wild type laboratory strain which was originally obtained from a colony based in the UK.

(f) Centres of origin and centres of genetic diversity, if known, of the recipient organism and/or the parental organisms and a description of the habitats where the organisms may persist or proliferate.

Aedes aegypti originated in Africa however is currently distributed throughout all subtropical and tropical regions across the globe, as an invasive species. As this mosquito species is highly anthropophilic it predominantly survives in and around domestic and peridomestic urban environments.

(g) Taxonomic status, common name, point of collection or acquisition, and characteristics of the donor organism or organisms related to biosafety.

(i) The Cabbage looper moth (*Trichoplusia ni*)

The Cabbage looper moth has an extensive global range throughout Central and North America as well as being detected in Northern Europe, most of Russia, the Middle East, Asia, parts of Africa, and most of the Indo-Australian region however it is a pest of particular notoriety in the United States and Canada where it can impact on agricultural brassica species. The moth is seasonal with an erratic yearly occurrence predicted to be due to recurring cycles of a nuclear polyhedrosis virus. Adult moths are present year round in the warmer climates of the southern United States although in colder climates such as Canada the adults will only be present in the summer months after migrating long distances from warmer climates (Capinera 1999).

Thibault et al. (1999) describes the transposable element, piggyBac which was isolated from a lepidopteran cell culture (*Trichoplusia ni*) this transposon has been well studied and used in a number of insect transformations. (Handler 2002) This genetic element enables stable integration of the inserted genetic elements into the genome of *Aedes aegypti*. (Sethuraman, Fraser et al. 2007)

(ii) *Drosophila melanogaster* (Vinegar fly)

Drosophila melanogaster has a widespread global distribution which has radiated from its original range in Africa and parts of Asia. *Drosophila* are known to be present throughout North, Central and South America and most of Europe, Asia and the outer regions of Australia. The distribution of the fly is limited to areas with a permissible temperature range, (development is impossible below 12°C and above 32.5°C) (Economos and Lints 1986) and access to water. *Drosophila* are associated with rotting fruits, females lay eggs in fruit that will rot in a sufficient timescale for their larvae to feed on the yeast found in the rotting fruit. The short generation time of the *Drosophila* (7 days from egg to adult) has enabled them to radiate rapidly as a species and there are a number of *Drosophila* species found worldwide. Due to their short generation time they also make excellent model organisms and have been well studied for over a century (Doktor 2008).

These studies have enabled a thorough understanding of genetic function and isolation of a number of genetic sequences, some of which can be used as promoters in different orders of organisms.

(iii) *Discosoma spp*

Discosoma genes have been used in many transgenic field releases where DsRed or a close variant have been used as a marker gene. *Discosoma* species are also known by their common name as mushroom corals and are found throughout many marine environments. *Discosoma spp* have particular fluorescence proteins which are similar to the green fluorescent protein (GFP) family of proteins. A variant of DsRed, DsRed2 has improved expression and solubility assisting its use as a marker gene and is used in the construct.

(iv) *Escherichia coli*

Escherichia coli is an intensively studied species which serves as a model organism across a range of disciplines. Its geographical range is worldwide as *E. coli* forms part of the microbiota of the lower gastrointestinal tract of mammals, including humans. There are many strains of *E. coli* most of which exist as harmless commensals however a number of pathogenic strains of *E. coli* have been recorded. The genomes of several *E. coli* strains have been completely sequenced and information from the sequencing has been used in designing constructs for genetic engineering. Sequencing of Salmonella strains, which last shared a common ancestor with *E. coli* more than a hundred million years ago have increased scientists understanding of the evolution of bacterial species (Elena, Whittam et al. 2005). The *E. coli* strains used in the generation of the tet-system are all laboratory strains listed in (Altschmied, Baumeister et al. 1988) these strains are typically benign and non-pathogenic.

(v) Herpes simplex virus type 1

Herpes simplex virus type 1 is a human virus usually associated with infections of the lips, mouth, and face. It is the most common herpes simplex virus and many people develop it in childhood. HSV-1 often causes sores (lesions) inside the mouth, such as cold sores (fever blisters), or infection of the eye (especially the conjunctiva and cornea). It can also lead to infection of the lining of the brain (meningoencephalitis). It is transmitted by contact with infected saliva. By adulthood, 30 - 90% of people will have antibodies to HSV-1. There are more than 80 herpes viruses circulating in human populations however only 8 of these are known human pathogens. Different human populations have increased susceptibility to infection with a Herpes virus but there is a worldwide distribution of Herpes within the human population, (Fatahzadeh and Schwartz 2007). Domains have been coupled to control elements from *E. coli* in order to develop the widely used tet- repressible control system which has been produced synthetically (Gossen and Bujard 1992); the domain is therefore a short fragment of DNA that has no intrinsic ability to replicate or spread in cells and can neither behave like a functioning virus nor can it provide a new route for viral transmission.

(h) Description of the nucleic acid or the modification introduced, the technique used, and the resulting characteristics of the living modified organism.

Microinjection of *Ae. aegypti* eggs with a plasmid containing a repressible lethal system based on tetracycline transcriptional activator (tTAV) and a fluorescent marker gene (DsRed2) and a non-autonomous transposon, *piggyBac* for the facilitation of integration in the *Aedes* genome. (Phuc,

Andreasen et al. 2007). The resulting characteristics of the LMO are repressible lethal phenotype in the absence of sufficient quantities of tetracycline and a constitutively expressed red fluorescent marker

(i) Intended use of the living modified organism or products thereof, namely, processed materials that are of living modified organism origin, containing detectable novel combinations of replicable genetic material obtained through the use of modern biotechnology.

The intended use is twofold: to evaluate its potential for the reduction of local populations of *Aedes aegypti* in urban areas and /or to prevent its recurrence once control in an area has been achieved.

(j) Quantity or volume of the living modified organism to be transferred.

Up to 100g OX513A *Ae. aegypti*/month for the duration of the project.

(k) A previous and existing risk assessment report consistent with Annex III.

Data and information has been submitted by Instituto Conmemorativo Gorgas de Estudio de la Salud (Gorgas Institute) Panama, to the National Biosafety Commission of the Government of Panama, in accordance with local regulations (Ley 72 de 26 de Diciembre de 2001 and Ley 48 de 8 Agosto de 2002 and Resolución 046 de 25 enero de 2012). An import permit for contained use of *Aedes aegypti* OX513A was previously granted to the Gorgas Institute (Resolución 027 de 15 enero de 2013). The National Biosafety Commission of Panama and the Comité Sectorial de Biosseguridad del Sector Salud para Organismos Généticamente Modificados conducted their own risk assessment based on the data submitted. This risk assessment has not been made available to Oxitec Ltd, nor is it in the public domain as far as we are aware. A field release permit for *Aedes aegypti* OX513A was subsequently issued by the Government of Panama (Resolución CNB N° 01-2014). A copy of the field release permit is attached.

(l) Suggested methods for the safe handling, storage, transport and use, including packaging, labelling, documentation, disposal and contingency procedures, where appropriate.

The shipments will be at least double contained and sent with the relevant import permits. Methods for transport, opening and disposal of *Aedes aegypti* are included with the shipment, but are summarised here: *Double containment only to be opened under contained conditions (ACL1 equivalent or above). Store and transport above 4°C. Notify importer/exporter in case of loss or damage. Materials only to be disposed of by importer or exporter.*

(m) Regulatory status of the living modified organism within the State of export (for example, whether it is prohibited in the State of export, whether there are other restrictions, or whether it has been approved for general release) and, if the living modified organism is banned in the State of export, the reason or reasons for the ban.

The LMO is used under the Contained Use Regulations (2000) in the state of export, the UK. *Aedes aegypti* is also regarded as a carrier species for animal pathogens, imports of which are regulated under The Importation of Animal Pathogens Order 1980 by the Department of Environment Food and Rural Affairs (DEFRA).

(n) Result and purpose of any notification by the exporter to other States regarding the living modified organism to be transferred.

The LMO has been previously notified to the Cayman Islands, Malaysia and Brazil. The purpose of these notifications was for assessing the LMO in the environment for use as an *Aedes aegypti* population control agent.

(o) A declaration that the above-mentioned information is factually correct.

To the best of our knowledge the information contained within this notification is factually correct at the time of writing.

References:

Altschmied, L., R. Baumeister, K. Pfeleiderer and W. Hillen (1988). "A threonine to alanine exchange at position 40 of Tet repressor alters the recognition of the sixth base pair of *tet* operator from GC to AT. ." The EMBO Journal **7**(12): 4011-4017.

Doktor, P. (2008). "The humble fruit fly, *Drosophila melanogaster*." Retrieved 16/07/2012, 2012, from <https://scitechlab.wordpress.com/2008/11/02/the-humble-fruit-fly-drosophila-melanogaster/>.

Economos, A. C. and F. A. Lints (1986). "Developmental temperature and life span in *Drosophila melanogaster*. I. Constant developmental temperature: evidence for physiological adaptation in a wide temperature range. ." Gerontology **32**(1): 18-27.

Elena, S. F., T. S. Whittam, C. L. Winkworth, M. A. Riley and R. E. Lenski (2005). "Genomic divergence of *Escherichia coli* strains: evidence fro horizontal transfer and variation in mutation rates. ." International Microbiology **8**: 271-278.

Fatahzadeh, M. and R. A. Schwartz (2007). "Human herpes simplex virus infections: Epidemiology, pathogenesis, symptomatology, diagnosis, and management. ." J Am Acad Dermatol **57**(5): 737-763.

Gossen, M. and H. Bujard (1992). "Tight control of gene expression in mammalian cells by tetracycline-responsive promoters." PNAS **89**(12): 5547-5551.

Handler, A. (2002). "Use of the *piggyBac* transposon for germ-line transformation of insects." Insect Biochem Mol.Biol. **32**: 1211-1220.

Phuc, H. K., M. H. Andreasen, R. S. Burton, C. Vass, M. J. Epton, G. Pape, G. Fu, K. C. Condon, S. Scaife, C. A. Donnelly, P. G. Coleman, H. White-Cooper and L. S. Alphey (2007). "Late-acting dominant lethal genetic systems and mosquito control." BMC Biology, **5**:(11): 1-11.

Sethuraman, N., M. J. Fraser, P. Eggleston and D. O'Brochta (2007). "Post-integration stability of *piggyBac* in *Aedes aegypti*." Insect Biochem. Mol. Biol. **37**: 941-951.

República de Panamá



Instituto Conmemorativo Gorgas de Estudios de la Salud

20 de enero de 2014
Nota No.0030/DG/ICGES/14

Dra. Camilla Beech
Asesora de Asuntos Regulatorios
Oxitec, Ltd.
Londres, Inglaterra

Estimada Doctora Beech:

Es para nosotros de complacencia saludarla y hacerle llegar a usted la Resolución CNB-01-2014 de 14 de enero de 2014, en la cual la Comisión Nacional de Bioseguridad para los Organismos Genéticamente Modificados, aprobó la solicitud realizada por el Instituto Conmemorativo Gorgas de Estudios de la Salud, para la segunda fase de experimentación de liberación controlada de *Aedes aegypti* RIDL machos en la comunidad de Nuevo Chorrillo.

Atentamente,



Dr. Néstor Sosa
Director General del ICGES

Adj.Lo Indicado

/hs

“ LÍDERES DE LA INVESTIGACIÓN, COMPROMETIDOS CON LA SOLUCIÓN DE LOS PROBLEMAS DE LA SALUD ”

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RECIBIDO HOY:

FIRMA:

21 Enero 14
Donis Alegría
J07-0605

REPÚBLICA DE PANAMÁ
COMISIÓN NACIONAL DE BIOSEGURIDAD PARA
LOS ORGANISMOS GENÉTICAMENTE MODIFICADOS

Resolución CNB No. 01 -2014
(De _____ de _____ de 2014)

La Comisión Nacional de Bioseguridad para los Organismos Genéticamente Modificados,
en uso de sus facultades legales

CONSIDERANDO:

Que mediante la Ley 72 de 26 de diciembre de 2001, la República de Panamá se adhiere al Protocolo de Cartagena sobre Seguridad de la Biotecnología del Convenio sobre la Diversidad Biológica, hecho en Montreal, el 29 de Enero de 2000;

Que la Ley 48 de 8 de agosto de 2002 crea la Comisión Nacional de Bioseguridad para los Organismos Genéticamente Modificados y los Comités Sectoriales de Bioseguridad Agropecuario, de Salud y de Ambiente para los Organismos Genéticamente Modificados y dicta otras disposiciones;

Que de conformidad con la precitada excerta legal, ésta tiene la finalidad de establecer y coordinar las políticas del Estado panameño relativas a la bioseguridad, el ordenamiento y manejo de los organismos modificados genéticamente, productos y sus derivados y productos que los contengan, para prevenir los riesgos y minimizar los impactos sobre el ambiente, la diversidad biológica, la salud humana y la producción agropecuaria, que puedan resultar de las actividades que se realicen mediante el uso de la biotecnología moderna;

Que la Resolución 046 de 25 de enero de 2012 crea el Comité Sectorial de Bioseguridad del sector Salud para Organismos Genéticamente Modificados (CSBS) y conforma los miembros que lo integran;

Que la Comisión Nacional de Bioseguridad refrenda la evaluación de riesgo de la información y la autorización para la continuidad de la segunda fase del Proyecto "Evaluación de una nueva alternativa para el control de *Aedes aegypti* mediante el uso de mosquitos transgénicos en Panamá"

Que el Comité Sectorial de Bioseguridad del sector salud para Organismos Genéticamente Modificados revisó y evaluó toda la documentación suministrada por el Instituto Conmemorativo Gorgas de Estudios de la Salud.

Que luego de ello, en reunión celebrada el día 7 de enero del año en curso, los miembros del precitado Comité deliberaron sobre la aprobación de la solicitud presentada, concluyendo en la inexistencia de impedimentos para su aprobación.

Que de conformidad con la Ley 48 de 2002, los permisos para realizar actividades de investigación, manejo confinado, ensayos con organismos genéticamente modificados en invernadero, casa malla, lotes experimentales y desarrollo tecnológico a nivel de investigación, serán autorizados o negados por los Comités Sectoriales.

Que en atención a todo lo antes expuesto, se

RESUELVE:

ARTÍCULO PRIMERO: Aprobar la solicitud realizada por el Instituto Conmemorativo Gorgas de Estudios de la Salud para la segunda fase del Proyecto "Evaluación de una nueva alternativa para el control de *Aedes aegypti* mediante el uso de mosquitos transgénicos en Panamá", el cual consiste en la liberación controlada (fase de experimentación n°2) de *Aedes aegypti* RIDL machos en la comunidad de Nuevo Chorrillo, Arraiján, a fin de

Resolución CNB No. 01 -2014 de 14 de ENERO de 2014.

determinar la eficiencia del precitado OVGM en el control biológico del vector del dengue (*Aedes aegypti*) en campo.

ARTÍCULO SEGUNDO: Solicitar al Instituto Conmemorativo Gorgas de Estudios de la Salud la entrega de informes periódicos en cuanto al avance de la investigación.

ARTÍCULO TERCERO: El Comité Sectorial de Bioseguridad del Sector Salud dará seguimiento y monitoreará cada una de las etapas de la investigación.

ARTÍCULO CUARTO: La presente Resolución rige a partir de la fecha de su firma.

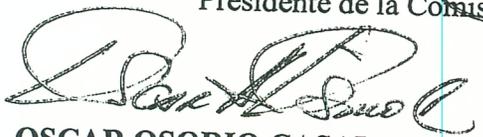
FUNDAMENTO LEGAL: Ley 72 de 26 de diciembre de 2001, Ley 48 de 8 de agosto de 2002 y Resolución 046 de 25 de enero de 2012.

COMUNÍQUESE Y CÚMPLASE.

LUIS EDUARDO CAMACHO G.

Ministro de Comercio e Industrias y

Presidente de la Comisión Nacional de Bioseguridad encargado



OSCAR OSORIO CASAL

Ministro de Desarrollo Agropecuario y

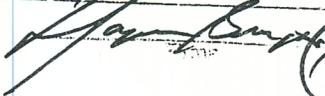
Secretario de la Comisión Nacional de Bioseguridad

MINISTERIO DE COMERCIO E INDUSTRIAS
SECRETARÍA GENERAL

Es copia Auténtica de su original

Panamá, 15 de enero

de 2014.



REPÚBLICA DE PANAMÁ

DECRETO N.º 2

De 2 de Enero de 2014

Que designa al Ministro de Comercio e Industrias y Viceministro de Comercio Interior e Industrias, encargados

EL PRESIDENTE DE LA REPÚBLICA,
en uso de sus facultades constitucionales y legales,

DECRETA:

- ARTÍCULO 1.** Designese a **LUIS EDUARDO CAMACHO**, actual Viceministro de Comercio Interior e Industrias, como Ministro de Comercio e Industrias, encargado, del 6 al 24 de enero de 2014, inclusive, mientras el titular, **RICARDO A. QUIJANO J.**, esté ausente del cargo.
- ARTÍCULO 2.** Designese a **NORIEL SALERNO**, actual Secretario General del Ministerio de Comercio e Industrias, como Viceministro de Comercio Interior e Industrias, encargado, del 6 al 24 de enero de 2014, inclusive, mientras **LUIS EDUARDO CAMACHO**, ocupe el cargo de Ministro, encargado.
- PARÁGRAFO.** Estas designaciones rigen a partir de la Toma de Posesión del cargo.

COMUNÍQUESE Y CÚMPLASE.

Dado en la ciudad de Panamá, a los 2 días del mes de Enero de dos mil catorce (2014).

RICARDO MARTINELLI BERROCAL
Presidente de la República

