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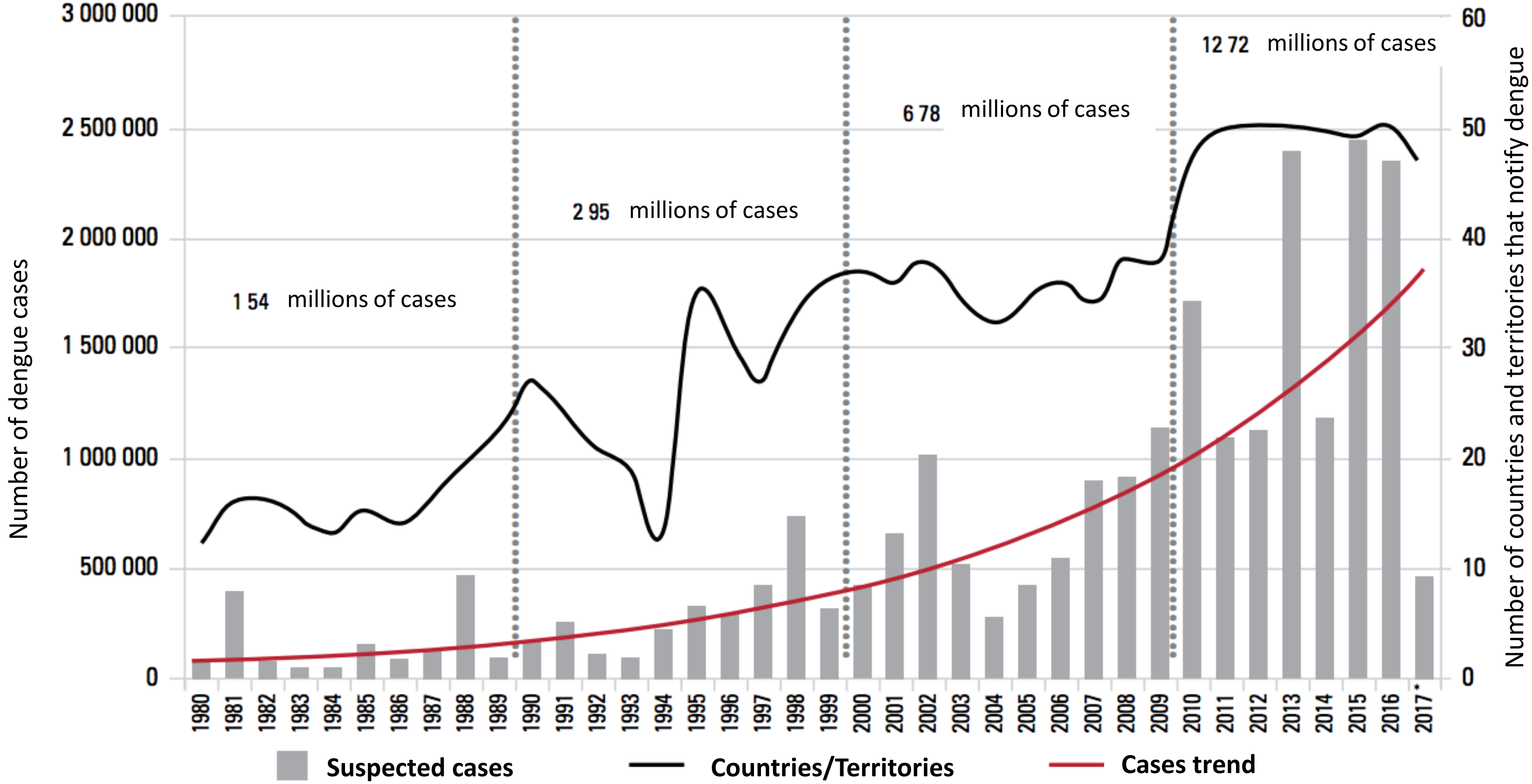
Vector-borne Diseases Global Context

Dr. Jesús Felipe González Roldán

National Centre of Preventive Programmes and Disease Control

Dengue

Number of countries and cases in America 1980-2016



*Preliminar data, epidemiological week 52

Source: Epidemiological data sent by countries to PAHO/WHO

http://iris.paho.org/xmlui/bitstream/handle/123456789/34859/OPSCHA17039_spa.pdf?sequence=8&isAllowed=y

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Dengue

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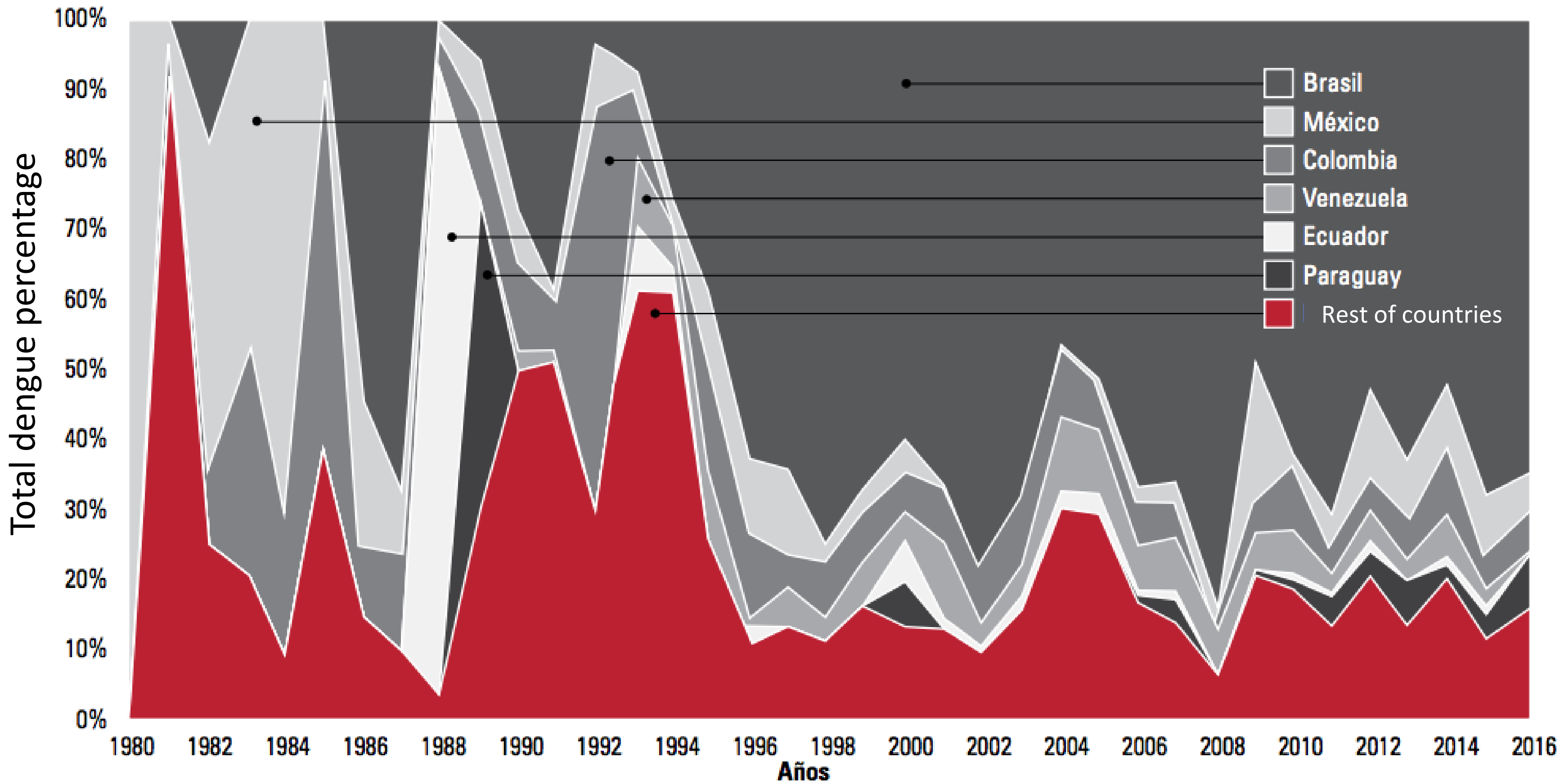

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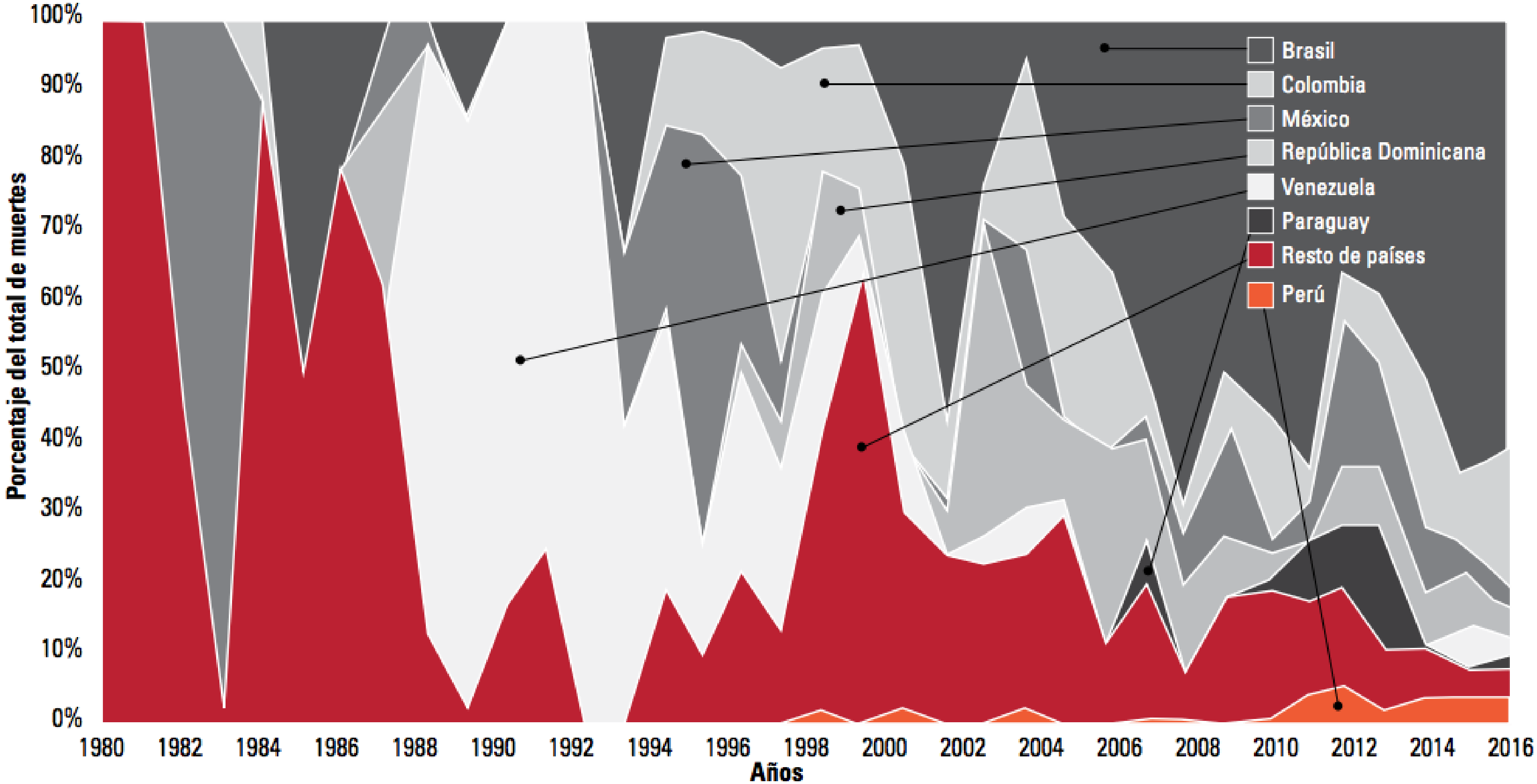
Dengue

Percent distribution of dengue deaths in the countries of America 1980-2016



Source: Epidemiological data sent by countries to PAHO/WHO

http://iris.paho.org/xmlui/bitstream/handle/123456789/34859/OPSCHA17039_spa.pdf?sequence=8&isAllowed=y

Dengue
Current situation: National

- **The control trend continues in the period 2014-2017**

Dengue cases and deaths, Mexico. 2013-2017

Data	2013	2014	2015	2016	2017	Percentage of change (2016-2017)
Dengue cases	44,162	23,760	21,552	14,112	11,344	-19.6
Dengue WS and severe	19,822	8,856	5,626	3,683	2,794	-24.1
Dengue Total	**63,984**	**32,616**	**27,178**	**17,795**	**14,138**	**-20.5**
Incidence	52.3	26.8	22.1	14.5	11.45	-21.1
Deaths	**192**	**76**	**42**	**75**	**34**	**-54.6**
Letality	**0.91%**	**0.86%**	**0.75%**	**2.02%**	**1.22%**	**-39.6**

Source: Panorama epidemiológico del dengue, Semana 52, DGE 2017
** Letality per 100 cases de Dengue with warning signs and severe

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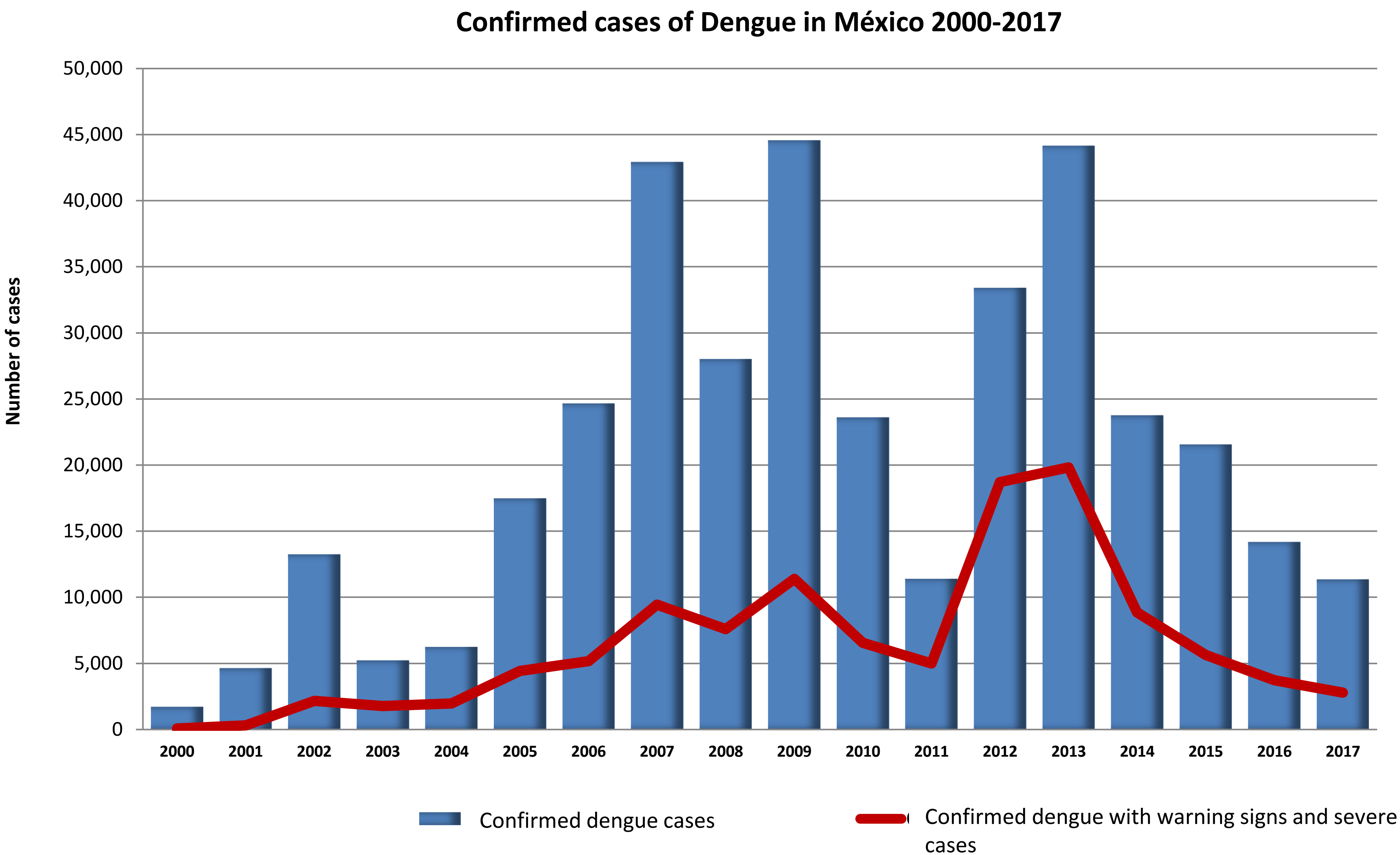
Dengue
Current situation: National



- **The control trend continues in the period 2014-2017**

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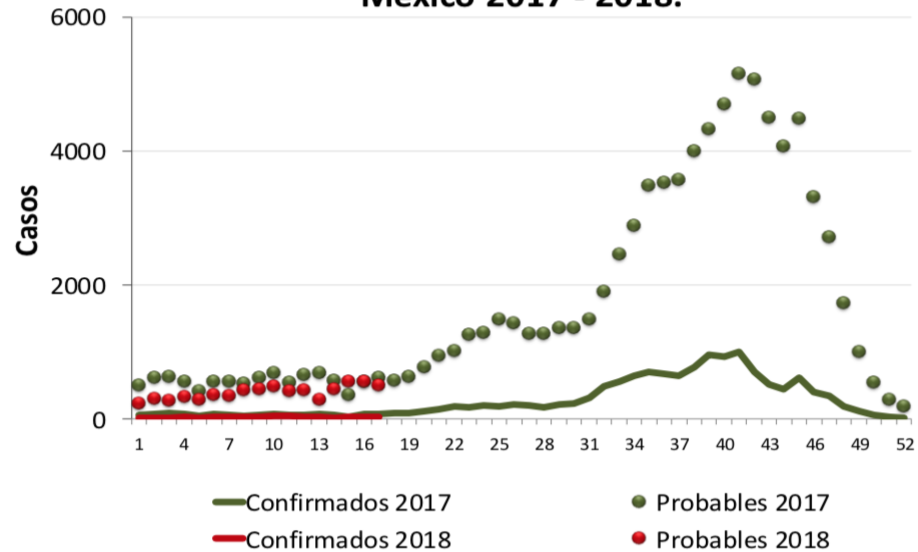
Dengue
Current situation: 2017-2018

INDICADOR	2017 SEMANA	2018 SEMANA	% de variación
DENGUE	841	140	-83.35
DENGUE WITH WS	247	332	34.41
SEVERE DENGUE	50	46	-8.00
DENGUE WITH WS + SEVERE	297	378	27.27
TOTAL CONFIRMED CASES	1,138	518	-54.48
DEATHS	3	2	-33.33
LETALITY*	1.01	0.53	-47.62

Confirmed and probable cases
México 2017 - 2018.



- **We can observe a decrease of 54.48% of confirmed cases when comparing the same of date of 2017 with 2018**
- **Around 94% of confirmed cases belong to Chiapas, Jalisco, Veracruz, Guerrero and Michoacan**

LETALITY* per 100 cases

Source: SINAVE/DGE/SALUD/Sistema Especial de Vigilancia Epidemiológica de Dengue con información al 14 de mayo de 2018 y a la semana 19 del 2017.

Zika
Current situation 2015-2018

Estado	2015-2017	2018	Total
Aguascalientes	1	0	1
Baja California	3	0	3
Baja California Sur	51	3	54
Campeche	94	0	94
Colima	297	0	297
Chiapas	821	0	821
Coahuila	336	0	335
Durango	2	0	2
Guanajuato	0	4	4
Guerrero	885	2	887
Hidalgo	277	8	283
Jalisco	432	17	448
México	27	0	27
Michoacán	67	1	68
Morelos	499	1	500
Nayarit	678	5	683
Nuevo León	949	0	950
Oaxaca	514	0	514
Puebla	225	0	225
Querétaro	17	0	17
Quintana Roo	388	0	388
San Luis Potosí	524	3	527
Sinaloa	177	5	182
Sonora	84	0	84
Tabasco	367	7	374
Tamaulipas	802	0	802
Veracruz	2,100	1	2,101
Yucatán	1,299	0	1,299
Zacatecas	1	0	1
Total	11,917	58	11,975

FUENTE: SINAVE/DGE/ Sistema de Vigilancia Epidemiológica de Infección por Zika. *Sem19-2018.

Zika virus

http://www.who.int/bulletin/es/

Zika virus infection estimates, Mexico

Juan Eugenio Hernández-Ávila,[a] Lina Sofía Palacio-Mejía,[b] Hugo López-Gatell,[a] Celia M Alpuche-Aranda,[a] Diana Molina-Vélez,[a] Leonel González-González[a] & Mauricio Hernández-Ávila[c]

Objective To assess the magnitude of the Mexican epidemic of Zika virus infection and the associated risk of microcephaly.

Methods From the reported number of laboratory-confirmed symptomatic infections among pregnant women and the relevant birth rate, we estimated the number of symptomatic cases of infection that occurred in Mexico between 25 November 2015, when the first confirmed Mexican case was reported, and 20 August 2016. We used data from the birth certificates to compare mean monthly incidences of congenital microcephaly before (1 January 2010–30 November 2015) and after (1 December 2015–30 September 2017) the introduction of Zika virus, stratifying the data according to whether the mother's place of residence was at an altitude of at least 2200 m above sea level. We used Poisson interrupted time series, statistical modelling and graphical analyses.

Findings Our estimated number of symptomatic cases of infection that may have occurred in the general population of Mexico between 25 November 2015 and 20 August 2016, 60 172, was 7.3-fold higher than the corresponding number of reported cases. The monthly numbers of microcephaly cases per 100 000 live births were significantly higher after the introduction of the virus than before (incidence rate ratio, IRR: 2.9; 95% confidence interval, CI: 2.3 to 3.6), especially among the babies of women living at altitudes below 2200 m (IRR: 3.4; 95% CI: 2.9 to 3.9).

Conclusion The Mexican epidemic appears to be much larger than indicated by estimates based solely on counts of laboratory-confirmed cases, and to be associated with significantly increased risk of microcephaly.

Zika virus
http://www.who.int/bulletin/es/

Métodos
Del número de infecciones sintomáticas reportadas en laboratorio entre mujeres embarazadas y la tasa de nacimiento relevante, estimamos el número de casos de infección sintomática que ocurrieron en México entre el 25 de noviembre de 2015, cuando se confirmó el primer caso mexicano, y el 20 de agosto de 2016. Usamos la información de los certificados de nacimiento para comparar incidencias mensuales significativas de microcefalia antes (1 de enero de 2010-30 de noviembre de 2015) y después (1 de diciembre 2015-30 de septiembre de 2017) de la introducción del virus Zika, estratificando la información de acuerdo a si el lugar de residencia de la madre estaba a una altitud de al menos 2200 m sobre el nivel del mar. Se usaron series temporales interrumpidas de Poisson, modelos estadísticos y análisis de gráficos.

Resultados
Nuestro número estimado de casos de infección sintomática que podría haber ocurrido en la población general en México entre el 25 de noviembre de 2015 y el 20 de agosto de 2016, 60.172, fue 7,3 veces más elevado que el número correspondiente de casos informados. El número mensual de casos de microcefalia por cada 100.000 nacimientos vivos fue significativamente más alto después de la introducción del virus que antes (razón de tasas de incidencia, IRR: 2,9; intervalo de confianza, IC, del 95%: 2.3 a 3.6) especialmente entre bebés de mujeres viviendo en altitudes menores a 2200 m. (IRR: 3,4; IC del 95%: 2.9 a 3.9).

Conclusión
La epidemia mexicana parece ser mucho más grande que las estimaciones indicadas basadas solamente en la contabilización de casos confirmados por laboratorio y está asociada con un incremento significativo de riesgo de microcefalia.

Boletín de la Organización Mundial de la Salud Recopilación de articulos Volumen 96: 2018 Volumen 96, Número 5, mayo 2018, 297-368

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Current Situation of Chikungunya 2014-2018

Presence of Chikungunya

Estado	2014	2015	2016	2017	2018
Aguascalientes	0	2	0	0	0
Baja California Sur	0	170	210	3	0
Campeche	0	263	22	0	0
Coahuila	0	23	3	0	0
Colima	0	991	4	1	0
Chiapas	135	691	7	4	0
Chihuahua	0	2	0	0	0
Durango	0	3	0	0	0
Guanajuato	0	14	0	1	0
Guerrero	11	1,813	37	4	1
Hidalgo	0	7	1	0	1
Jalisco	0	175	11	12	0
México	0	59	2	0	0
Michoacán	0	1,624	9	1	2
Morelos	0	713	14	5	1
Nayarit	0	46	48	1	0
Nuevo León	0	64	31	0	0
Oaxaca	7	1,203	6	1	0
Puebla	0	17	1	0	0
Querétaro	0	1	0	0	0
Quintana Roo	0	212	21	11	0
San Luis Potosi	0	8	3	3	0
Sinaloa	1	57	58	8	0
Sonora	1	365	10	0	0
Tabasco	0	58	6	0	0
Tamaulipas	0	37	80	3	0
Veracruz	0	2,301	164	6	1
Yucatán	0	1,669	11	0	0
Total	155	12,588	759	64	6

FUENTE: SINAVE/DGE/ Sistema de Vigilancia Epidemiológica de Fiebre Chikungunya. *Sem19-2018.

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Comparativo de Signos y Síntomas de Dengue, Chikungunya y Zika

SINTOMAS	DENGUE	CHIKUNGUNYA	VIRUS ZIKA
Fiebre	++++	+++	+++
Mialgias/Artralgias	+++	++++	++ ↓
Edema en Extremidades	0	0	++ ↑
Rash maculopapular	++	++	+++ ↑
Dolor retroocular	++	++	+++
Conjuntivitis	0	+	+++ ↑
Linfadenopatías	++	++	+ ↓
Hepatomegalia	0	+++	0 ↓
Leucopenia / Trombocitopenia	+++	+++	0 ↓
Hemorragias	+	0	0 ↓

Es difícil llevar a cabo el diagnóstico diferencial

Fuente: Ioos, S et. al. *Current Zika virus epidemiology and recent epidemics*. Médecine et maladies infectieuses 44 (2014): 302-3207

Integrated Management Strategy for the Prevention and Control of Dengue

Technical components:

1. **Epidemiological surveillance-> Integrated surveillance and outbreak preparation**
2. **Entomological and Entomovirological surveillance**
3. **Laboratory (including surveillance for DENV,CHIKV, ZIKAV, in humanes and in mosquitos = VEV**
4. Patient care
5. **Integrated vector management IVM**
6. Enviromental management
7. Vaccine (preparation towars the eventual introduction)

Planning, decisión making, execution and measuaring impact:

1. **Reduction of incidence**
2. **Control of entomological risk**

IVM (Integrated Vector Management)

Surveillance, diagnosis, and case management

- Entomological and entomovirological surveillance
- **Epidemiological and virological surveillance**
- Timely diagnosis and serotype detection
- **Case management in Hospitals**
- Activation of IVM from entomological risks or as inmediate response to probable cases

IVM (Integrated Vector Management)

- **Personal and enviromental risk management (integral approach with intersectorial and community participation)**
- Larvicide aplication
- **Insecticide treatment (cold and thermal)**
- Quick Indoor Residual Spraying

Integrated System of vector monitoring Prevention and Control

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CENAPRECE SALUD Instituto Nacional de Salud Pública SISTEMA INTEGRAL MONITOREO DE VECTORES

Vigilancia Entomológica y Control | Recurso Humano | Vigilancia Entomovirológica | Resistencia a Insecticidas | Especies de Importancia Médica | Promoción de la Salud

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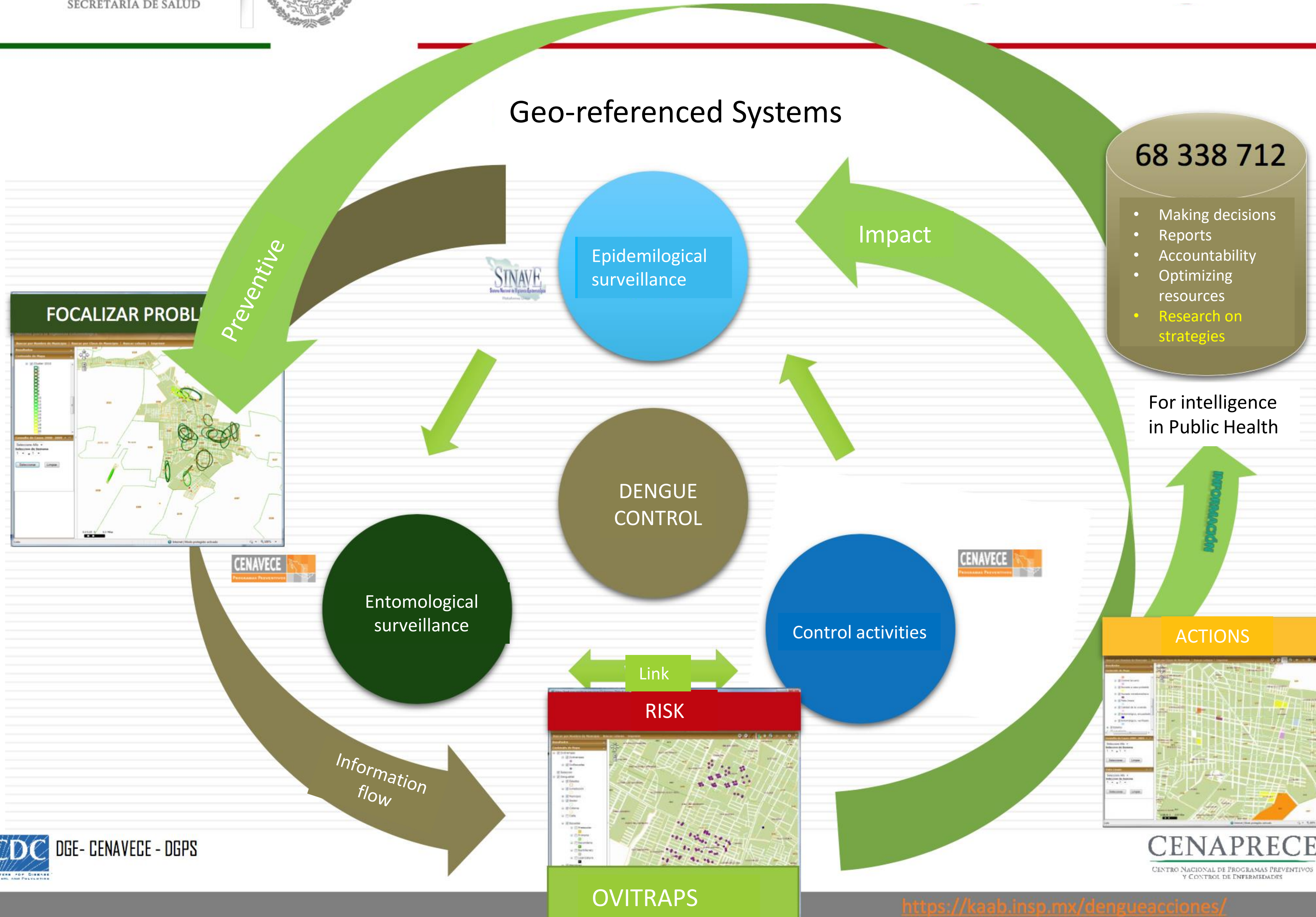
Integrated System of vector monitoring Prevention and Control

It is a set of information subsystems of vector control programmes. With capacity to receive and process data from external institutions (Epidemiological and Laboratory) and georeferenced own data (Entomological) to identify risks and make decisions based on evidence and generate knowledge.

Initial vision of the Integrated surveillance of Dengue



Charasteristics of the System

- Interoperability
  - Dinamic inteaction with the Epidemiological Sureveillance Plattform SINAVE
- Intrasectorial
  - INDRE, DGE, CENAPRECE, DGPS, COFEPRIS (Warehouses)
- National coverage
  - 32 federal entities
- Timely notification
  - Cases
  - Entomology
  - Actions

Insecticide evaluation

2013

Historical figures in the Dengue Transmission

Bottle tests during Tabasco outbreak

2014

1st Monitoring of Resistance to Insecticides-Adulticides used by the National Program

24 entities y 62 localities

2015-2017

Consolidation of the Federal Bioassay Units BU's

1st y 2nd Evaluation of the biological effectiveness of Larvicides used by the National Program

20 entities and 50 localities

2016-2018

2nd y 3rd Monitoring of Resistance to Insecticides-Adulticides used by the National Program

30 entities and 88 localities

Evaluation of the Susceptibility and Biological Efficacy of Insecticides

Entomological and Bioassay Investigation Units

- Human resources:
  113 professionals (Biól., Ing., QFB., M. in Sc., PhD. y Post PhD.)

- **14** Verified and Operating Units
- **10** Units to be Incorporated in 2018

- Identification of Species of Medical Importance and biological collections.
- Evaluation of Biological Efficacy and Resistance to Insecticides.
- Evaluation of Insecticide Application Equipment.
- Evaluation of repellents and household sprays.
- **Operative investigation**

Early Warning

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Priority localities for the prevention and control of dengue with alarm(s)

- No alarm
- One alarm
- Two alarms
- Three alarms
- Four alarms
- Five alarms
- Six alarms

Fuente: SSA/SINAVE/DGE/Sistema Especial de Vigilancia Epidemiológica de Dengue. Con información al 09/04/2018

Plataforma de Vigilancia Entomológica y Control Integral del Vector. Con información histórica del año 2011 al 11/04/2018.

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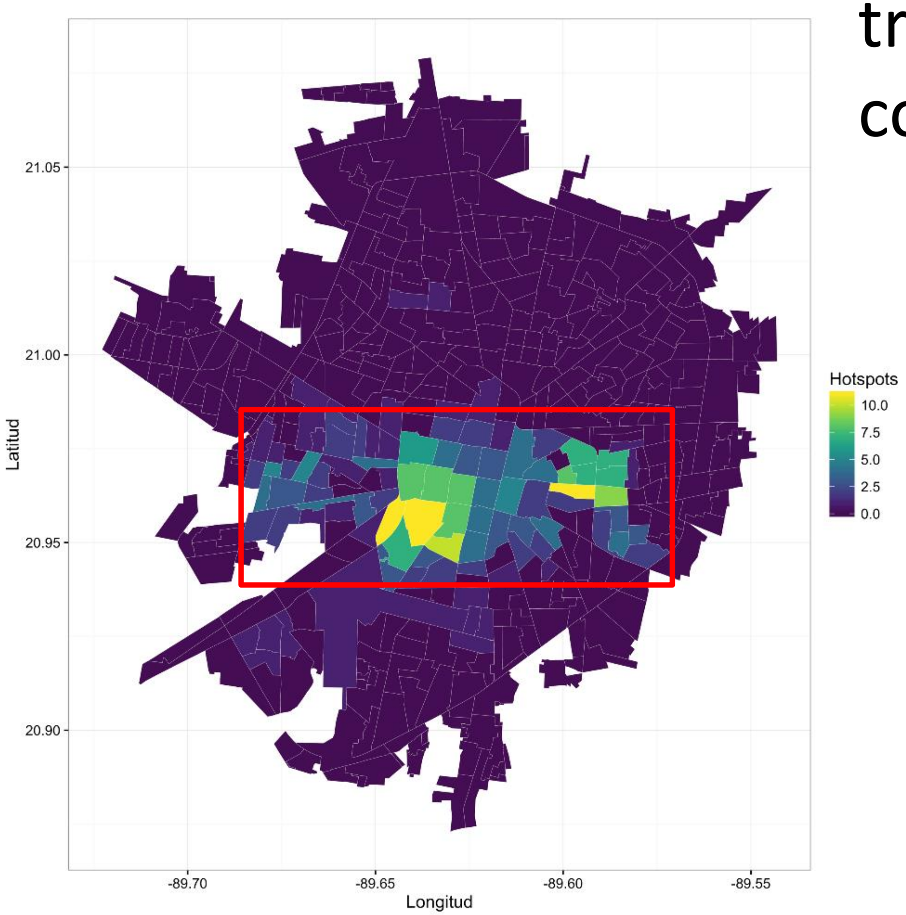
Space-Temporal Analysis

Example of the identification of hotspots in a locality



Hotspots: areas where transmission is disproportionately concentrated

- **Risk stratification model**
- **The targeting of antivector actions**
- **Efficient and effective use of the resources of the vector program**
- **Greater impact**

20-30% contribute to 60-80 of the transmission

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Sterile Insect Technique Component, to Control *Aedes Mosquitoes* as Vectors of Human Pathogens, particularly Zika Virus in Mexico

Dr. Jesús Felipe González Roldán
General Director of National Center for Preventive Programs and Disease Control

Project Team

I N S P

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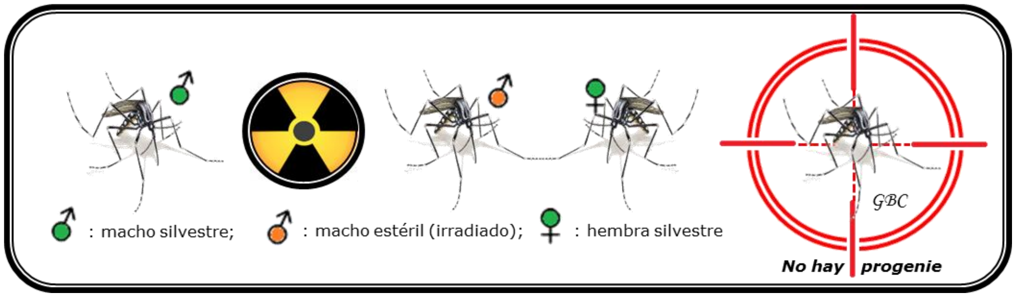

Rogelio Danis L., J. Guillermo Bond C., Carlos F. Marina F. y Pablo Liedo F.

IAEA International Atomic Energy Agency

SENASICA
SERVICIO NACIONAL DE SANIDAD, INOCUIDAD Y CALIDAD AGROALIMENTARIA

ECOSUR

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Participants

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- Pablo Liedo, (ECOSUR) Entomologist
- Ariane Dor, (ECOSUR) Antropólogo
- Javier Valle, (ECOSUR) Estadístico
- Yeudiel Gómez, (MOSCAFRUT) Irradiación
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Permits needed/obtained/requested

Liberation of sterile mosquitoes in community.

Normativity

- **The activity must belong to a research project previously authorized by the Investigation, Ethics and Biosafety Commissions of the INSP.**

- **Request authorization from the Ministry of the Environment and Natural Resources (SEMARNAT) through a Permit for the release of wildlife specimens to the natural habitat.**

✓ **Free procedure in the offices of the State Delegation located in Tuxtla Gutiérrez, Chis., With a time to issue a response of 18 working days.**

Link: **MVZ Víctor Manuel Campuzano**
SubDirector de Sanidad
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Permits needed/obtained/requested

Import of genetically diverse strain mosquitoes

Normativity

- The activity must belong to a research project previously authorized by the Investigation, Ethics and Biosafety Commissions of the INSP.

- Determine the tariff fraction of the product to be imported (it is the Universal way of identifying the product, with it determines the tariff - taxes - that the product must pay upon entering the Mexican territory and if the material requires an import permit). The Customs Law authorizes only the Customs Agent, Customs Proxy and the SHCP for the determination of the tariff item.

  ✓ If the input to be imported requires an Import Sanitary Permit, it must be processed before the SAGARPA.

Advances

May-2018

EXPERIMENTAL FIELD TAPACHULA CRISP-INSP
Surface area of 4.5 ha with electricity and water
20 minutes away from Tapachula

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Advances

Insectarium for mosquito production 10 x 30 m

Advances

2 Greenhouses for physical vigor evaluations of sterile male mosquitoes 10 x 30 m p/u

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Advances

Racks and trays for mosquito production 4 million per week

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Advances

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Advances

Hiring of personnel with federal resources for the Biofactory operation

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Advances

Genetically diverse strain o Aedes aegypti – mosquitos from 12 populations of the coast of Chiapas

Ciudad Hidalgo (14° 68" N y 92° 14" W).
Frontera hidalgo (14° 78" N y 92° 18" W).
*Tapachula (14° 90" N y 92° 26" W).
Mazatán (14° 86" N y 92° 45" W).
Huehuetán (15° 02" N y 92° 38" W).
Huixtla (15° 14" N y 92° 47" W).
*Motozintla (15° 37" N y 92° 25" W).
Escuintla (15° 32" N y 92° 66" W).
Mapastepec (15° 43" N y 92° 90" W).
*Pijijiapan (15° 69" N y 93° 21" W).
Tonala (16° 09" N y 93° 76" W).
*Arriaga (16° 23" N y 93° 89" W).

* Localidades donde se colecto *Ae. albopictus*

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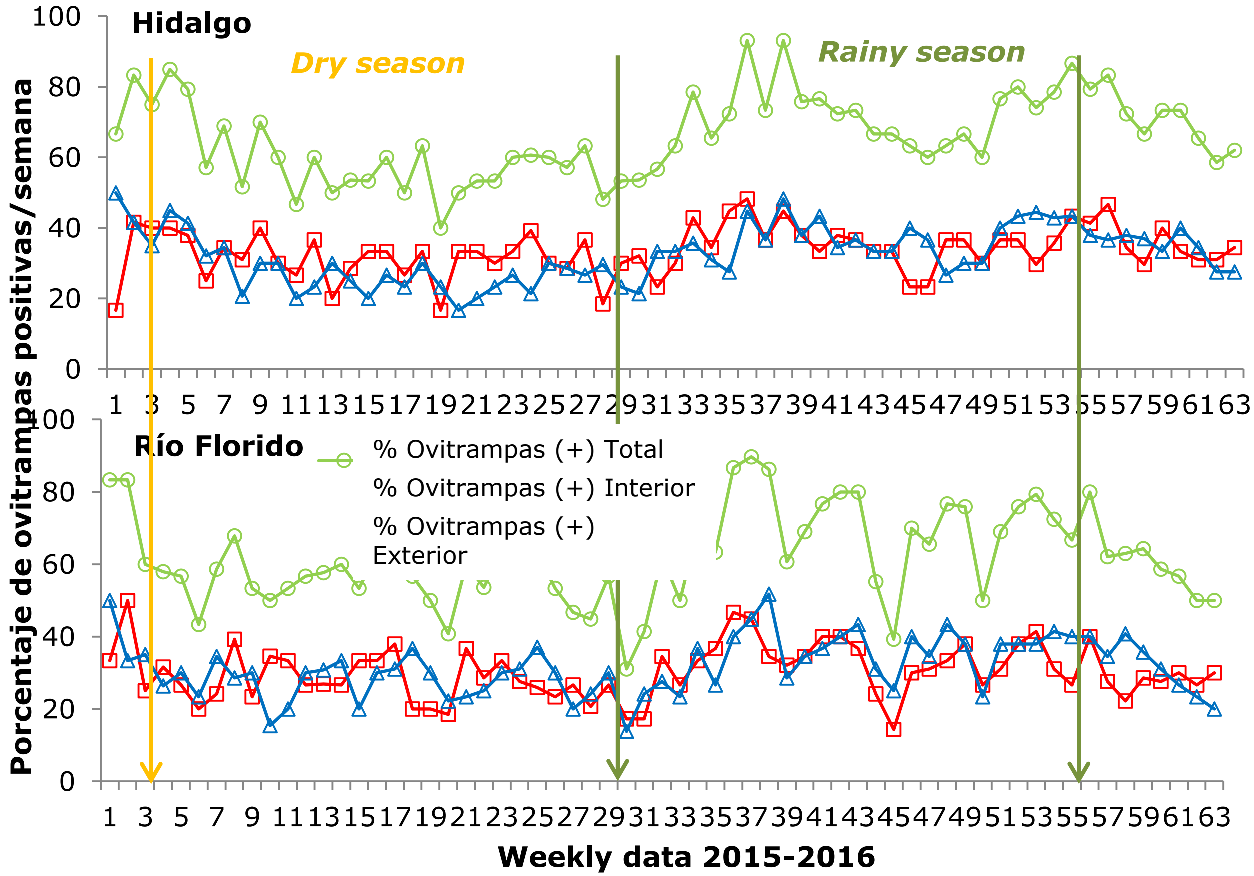
Advances

Percentage of positive ovitraps per week of sampling in two pilot communities, Hidalgo and Río Florido, Tapachula, Chiapas, Mexico.



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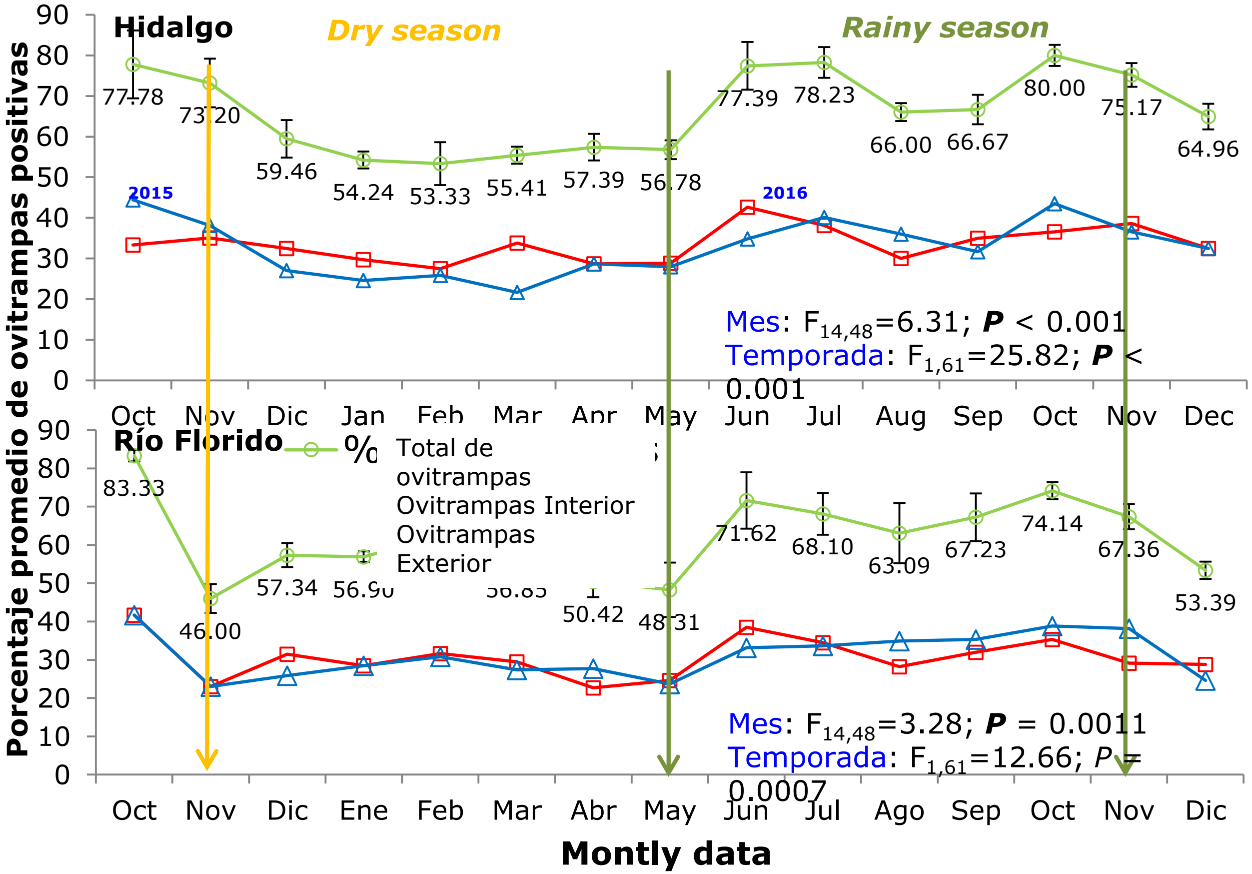
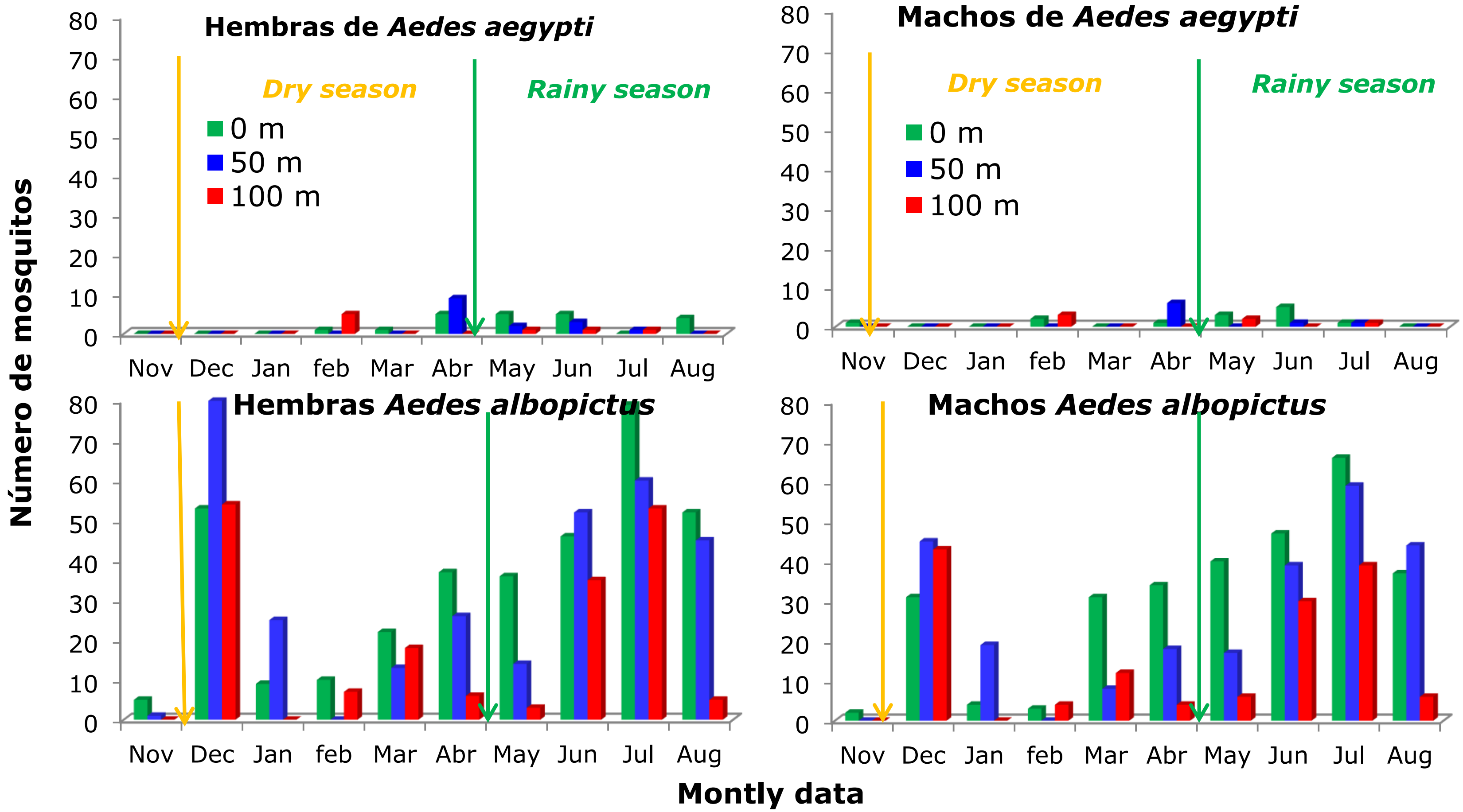
Advances

Average percentage of positive ovitraps per month of sampling in the pilot communities, Hidalgo and Río Florido, Tapachula, Chiapas, Mexico.



Advances

Number of adults of Aedes aegypti and Ae. albopictus that emerged from ovitraps located in the transects in the pilot community of Río Florido, Tapachula, Chiapas, Mexico.

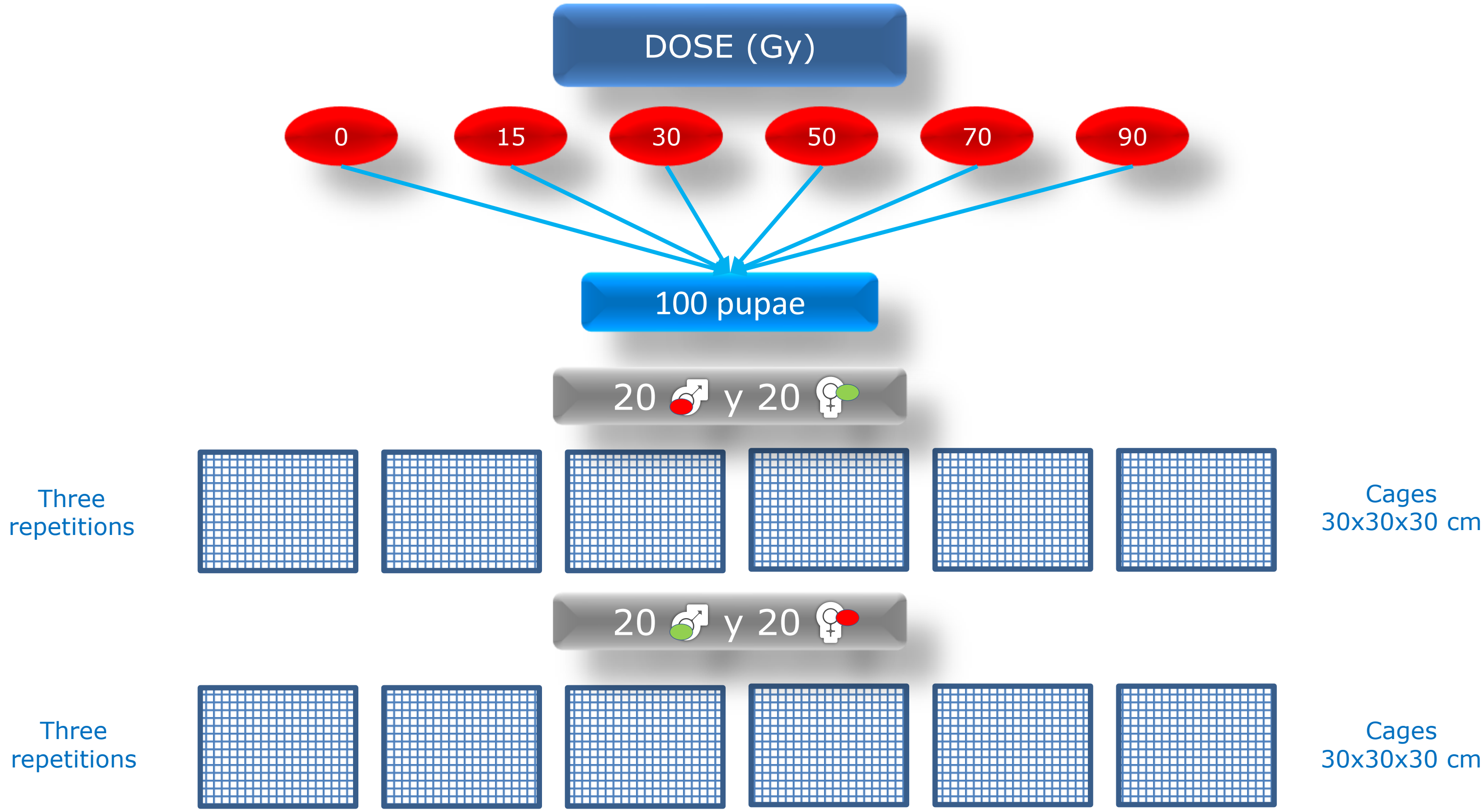


Determination of the optimal irradiation dose for the sterilization of *Aedes aegypti* and *Aedes albopictus*

Dry-storage irradiators, Model GammaBeam GB-127.

Advances

IRRADIATION (EXPERIMENTAL DESIGN) *AEDES AEGYPTI*



♂ ♀ : Males and females irradiated.

♂ ♀ : Males and females no-irradiated.

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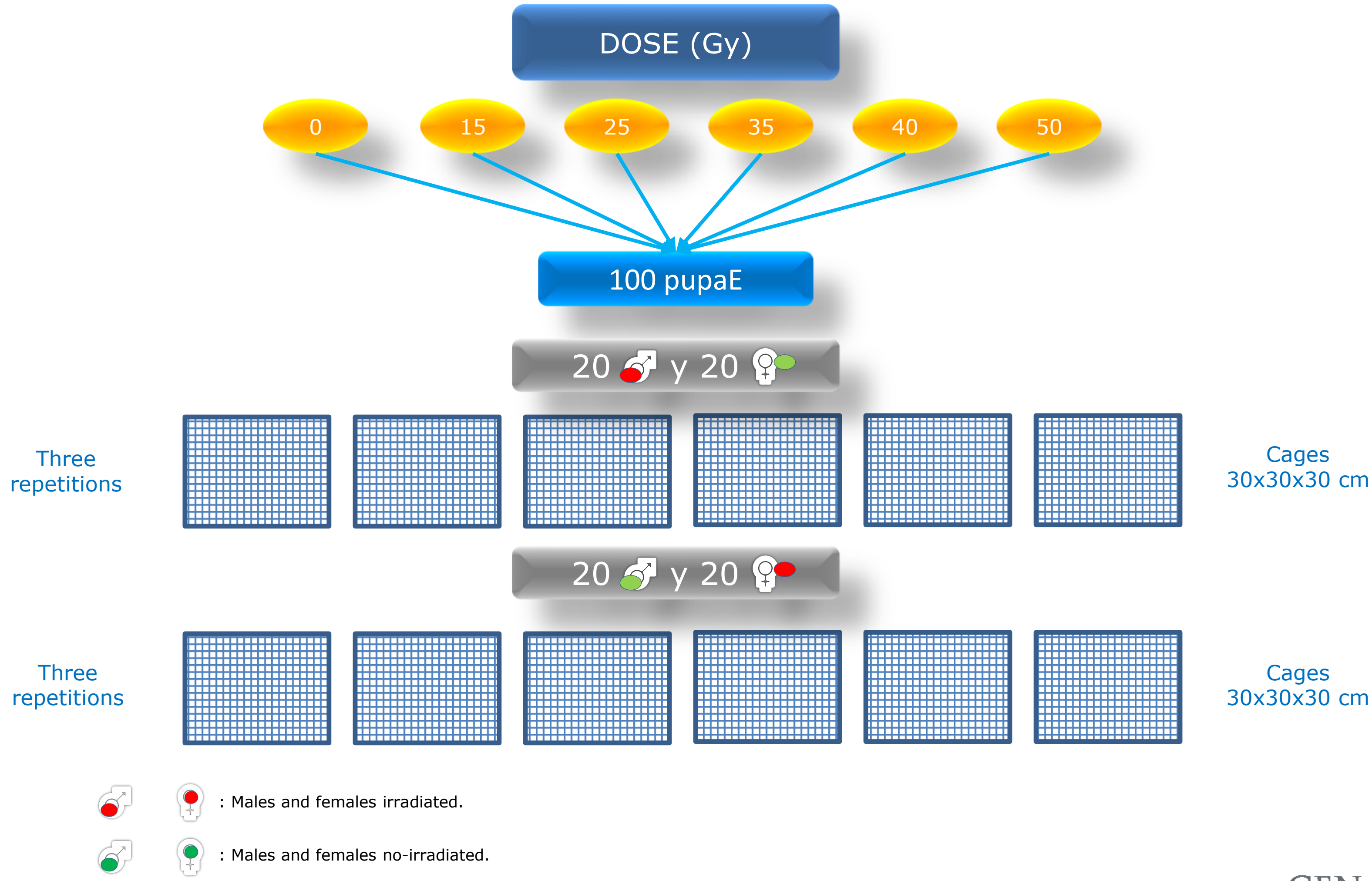
Advances

IRRADIATION (EXPERIMENTAL DESIGN) *AEDES ALBOPICTUS*



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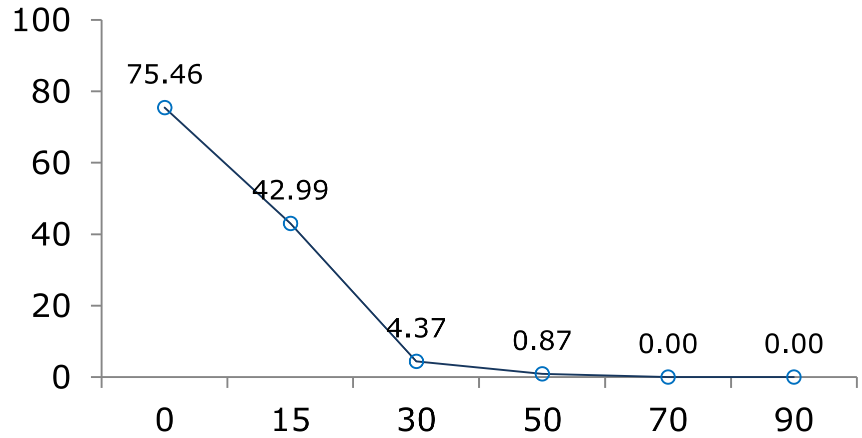
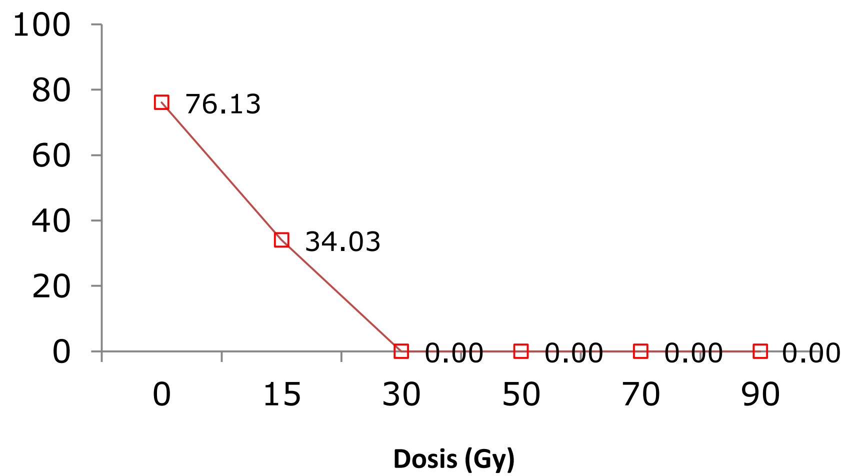
Advances

Sterility of irradiated male Ae. aegypti crossed with females as control

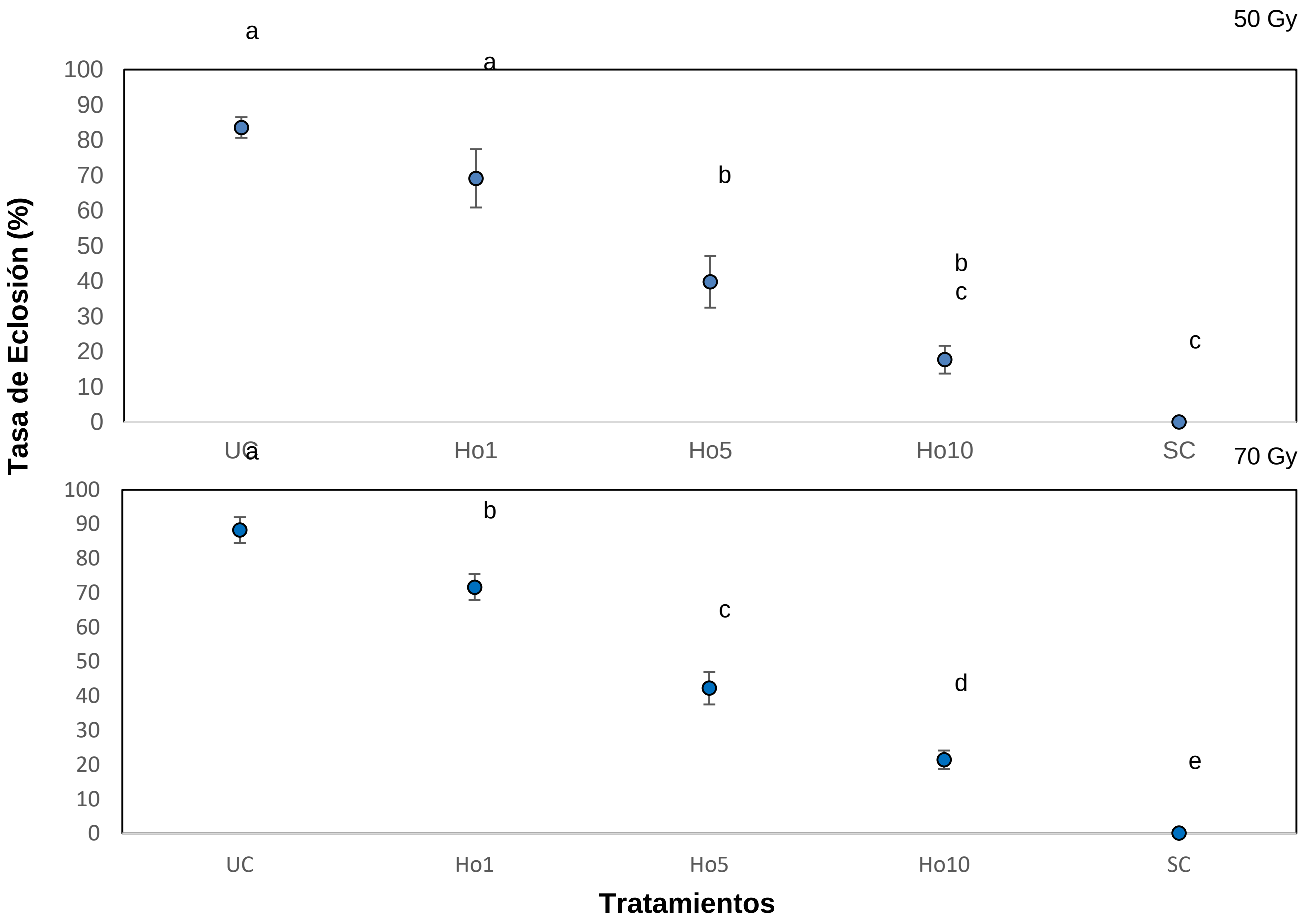


Sterility of irradiated female Ae. aegypti crossed with males as control



(Bond *et al*., 2018)

Advances



Hatching rate (%) depending on different densities (sterile males: untreated males: virgin females). UC: Control Treatment 1:1 (50 ♂ no treated: 50 ♀ vírgins); Ho1: Density 1:1:1 (50 ♂ sterile: 50 ♂ no treated: 50 ♀ vírgins); Ho5: Density 5:1:1 (250 ♂ steriles : 50 ♂ no treated: 50 ♀ vírgins); Ho10: Density 10:1:1 (500 ♂ steriles: 50 ♂ no treated: 50 ♀ vírgins); SC (Control Treatment steril): 1:1 (50 ♂ steriles : 50 ♀ vírgins). Different letters indicate significant differences.

Advances

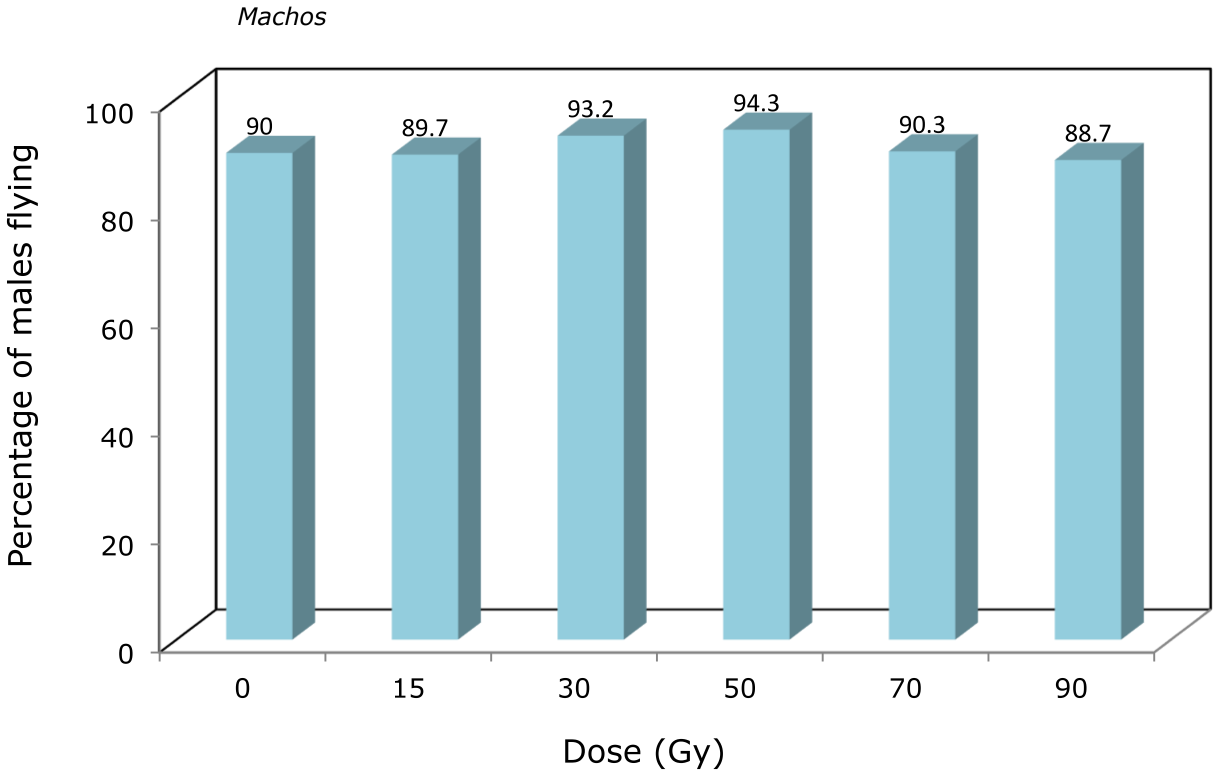
Effect of irradiation dose of pupae on the length of the ovary (Average ± SE) of *Ae. aegypti.*

Dose (Gy)	Ovarian length in mm (N)
0	1.04 ± 0.025 (30) a
15	0.97 ± 0.019 (27) a
30	0.68 ± 0.017 (30) b
50	0.70 ± 0.018 (27) b
70	0.71 ± 0.027 (30) b
90	0.66 ± 0.026 (30) b

$F_{5,168} = 52.02$; $P < 0.0001$

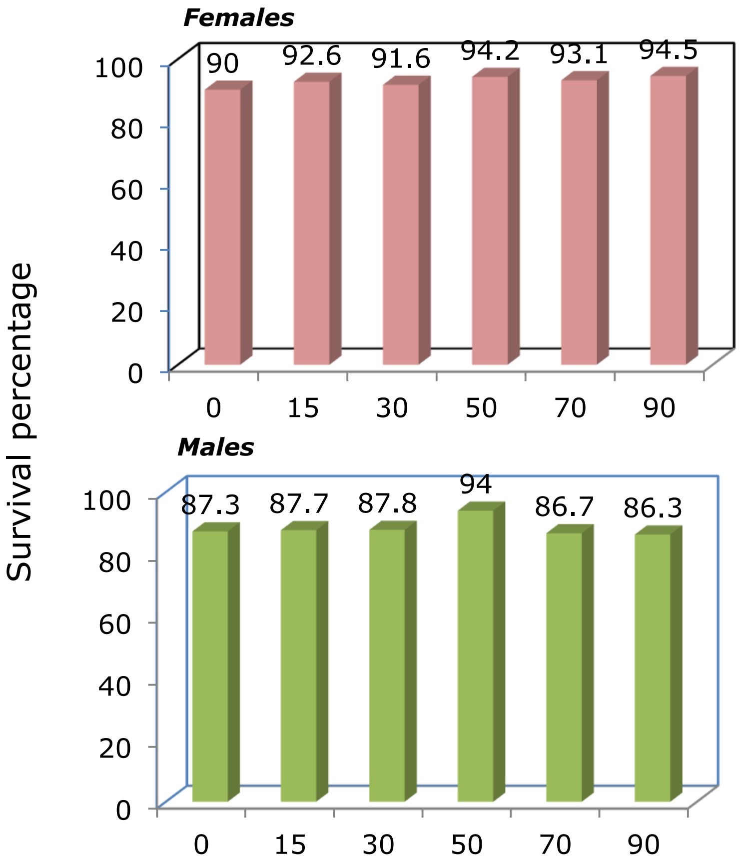
Advances

Flight capacity of irradiated males of *Aedes aegypti*



Advances

Survival of irradiated females and males of *Aedes aegypti*



Advances

Production rate of male *Aedes aegypti* pupae and sex ratio (M/H) fed with IAEA and LRD diets under light (L) and dark (O) conditions.

Treatments	Production rate of male pupae at 24h	Sex ratio at 24h M/F
IAEA-O	0.83 ± 0.015[a]	1.70 ± 0.191[ab]
IAEA-L	0.86 ± 0.033[ab]	1.76 ± 0.267[ab]
LRD-O	**0.93** ± 0.012[b]	**2.33** ± 0.163[b]
LRD-L	0.81 ± 0.012[a]	1.27 ± 0.089[ac]

(Bond *et al*., 2017)

Male pupal production rate at 24 h: $\boldsymbol{F}_{3,8}$= 7.049; $\boldsymbol{P}$=0.0123.

Proportion of sexes male / female at 24 h: $\boldsymbol{F}_{3,8}$= 5.293; $\boldsymbol{P}$=0.0265.

Advances

Life expectancy of mosquitoes *Ae. aegypti* fed with IAEA and LRD diets under conditions of light (L) and darkness (O).

Treatment	Esperanza de vida			
	Males with water	Males with sugar	Males in couple	Females in couple
IAEA-O	4.91 ± 0.0.85[a]	37.43 ± 2.37[a]	29.61 ± 1.07[a]	48.43 ± 2.27[a]
IAEA-L	4.61 ± 0.113[ab]	38.18 ± 1.14[a]	27.40 ± 3.55[a]	49.92 ± 2.27[a]
LRD-O	4.65± 0.176[b]	38.83 ± 1.72[a]	30.61 ± 0.50[a]	53.46 ± 1.38[a]
LRD-L	4.37 ± 0.077[b]	44.77 ± 1.30[a]	28.23± 1.46[a]	48.74 ± 0.49[a]

(Bond *et al*., 2017)

Males (water): $\mathbf{F}_{3,8}$=4.2; $\boldsymbol{P}$=0.045.

males (sugar): $\mathbf{F}_{3,8}$=4.0; $\boldsymbol{P}$=0.05.

Males in couple: $\mathbf{F}_{3,8}$=0.5; $\boldsymbol{P}$=0.6.

Females in couple: $\mathbf{F}_{3,8}$=1.8; $\boldsymbol{P}$=0.2.

Community Engagement Activities-Status/Progress/Planned activities

Advances

TASK	PROGRESS		
	Not yet	Ongoing	Completed
Insectary set up		X	
Surveillance sites confirmed		X	
Rearing standardized with local strain		X	
Irradiation feasibility tests (dose map + trial with mosquitoes)			X
Sterility curve			X
Competitiveness tests	X		
Mark-Release-Recapture trials		X	
Mass-rearing equipment set up		X	
Communication campaign		X	
Pilot study design strategy		X	

Mosquito release

Demonstration "Release of sterile mosquitoes with drones, as *Aedes aegypti* control method".

Practice carried out in the Tapachula Experimental Field by Group Mubarqui, part of the activities of the Annual Update Days Directed to Operative Personnel of the State Programs of Vector Control.

Scaling of the SIT for the control of Dengue vectors.

Scaling to urban communities in the Suppression of dengue vectors 2020-2022.

Study of suppression of Ae. aegypti in rural pilot communities 2018-2020.

Monitoring Eggs and adults

Release ♂ *Ae. aegypti* steriles in Ejido Hidalgo. Río Florido; Control pilot community.**2018**

Release ♂ *Ae. aegypti* steriles in Río Florido. Ejido Hidalgo; will be a witness. **2019**

Scaling of the CGS-MX brood to increase production of ♂ *Ae. aegypti*. Monitoring and estimation of the wild populations of Aedes spp. in the urban pilot communities (Metapa and Frontera Hidalgo, Chis). **2020**

Release ♂ *Ae. aegypti* steriles community with > wild population; the other will work as control.**2022**.

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