

# 9<sup>th</sup> National Seminar on Travel Medicine

17 November 2011



## FLASHES

17.20-17.35

Flashes from the 12th CISTM Boston – What's new in travel medicine: WHO/CDC news

Prof F. Jacobs, Hôpital Erasme Brussels Prof F. Van Gompel, – ITG Antwerpen

# 1 - CISTM 12 BOSTON



ISTM - CISTM12 - Windows Internet Explorer

https://www.istm.org/WebForms/Members/MemberActivities/Meetings/Congresses/cistm12/Default.aspx

Google

ISTM - CISTM12



**International**  
20 years of pro

**CISTM Congresses**

- CISTM 12**
  - Robert Steffen History of ISTM  
Presentation during the  
Opening Ceremonies
  - Organization
  - CISTM12 Program at a Glance
  - Photos - coming soon!
  - CISTM12 Program Book
  - CISTM12 Invited Speaker  
Abstracts
  - CISTM12 Free Communication  
Abstracts
  - Poster Abstracts

Done



CISTM12 Program at a Glance

Photos - coming soon!

CISTM12 Program Book

CISTM12 Invited Speaker  
Abstracts

CISTM12 Free Communication  
Abstracts

Poster Abstracts



# International Society of Travel Medicine

20 years of promoting healthy travel worldwide

1991-2011

- Manage Membership
- Congress Materials

## Congress Materials

The Congress program book and abstracts have been moved to the public CISTM12 meeting pages and you can access them by [clicking here](#).

## CISTM12 Speaker Presentation Handouts

- 21st Century Tools for Migration Medicine, Arocha
- Addressing Health Disparities in Migrant Populations – Beyond Access to Health Care, Patricia Walker
- Chagas Disease: Epidemiology in the United States and Diagnosis, J.H. Maguire
- Changing Travel Patterns From Emerging Economies, Poh Lian Lim
- Cross-Cultural Travelers, Care of Families on Return From Overseas, Michael E Jones
- Cross Cultural Travelers, Management of Psychological Probelms, S. Aebischer Perone
- Cross Cultural Travelers, Resilience Briefing



# CISTM12 Speaker Presentation Handouts

- To download for members of the ISTM

PL02.03	<b>Dengue Into the Future</b> •Dengue Vaccines: To Be or Not to Be?	Steve Whitehead
PL03	<b>The Immunocompromised Traveller</b> •Vaccine Use and Immunization in Immunocompromised Travelers •Immunosuppression and Travel Risks: A Case Based Presentation, •Overview for the Travel Medicine Specialist: Immunosuppression, Immunosuppressive Agents, and Drug Interactions,	Camille Nelson Kotton Edward Ryan Robert Orenstein
PL04	<b>Plenary Emerging Economies: Changes in Travel Patterns and Differences for Pre-Travel,</b> •Changing Travel Patterns From Emerging Economies •Travellers From Emerging Economies in South America. Implications for Travel Medicine Providers, •Travel From Emerging Economies in Asia: Differences in Behaviour, Activities and Travel Destinations,	Poh Lian Lim Cecilia Perret  Susan MacDonald
SY01.02 SY01.03	<b>Risks and Costs in Travel Medicine</b> •Low Risk High Consequence Diseases •Rabies Pre-Travel Vaccination: Who Needs It? Who Can Afford It?	Shlim Philippe Gautret
SY02	<b>Through the Eyes of a Migrant</b> •Through the eyes of a Bolivian Migrant in Switzerland, •From the Jungles of Thailand to the Ghettos of Canada: The Migration of the Karen Refugees to Toronto	Yves Jackson Meb Rashid
SY04	<b>Water-Related Hazards</b> •Water-borne (non-enteric) Infections in Travelers, •Misconceptions in Schistosomiasis Management, •Marine and Aquatic Hazards,	Eli Schwartz Marc Mendelson Bernard Stockman

# 2 - TOPICS from BOSTON



Typhoid fever

Yellow fever

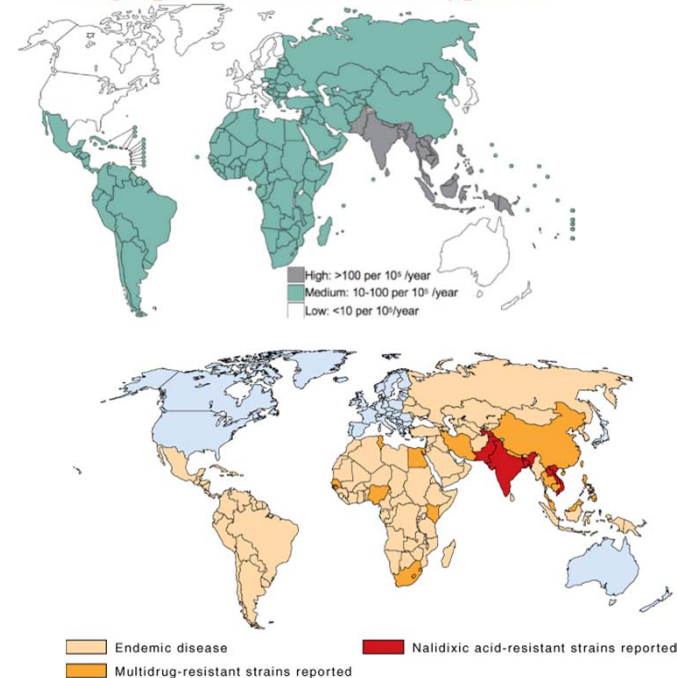
Giardiasis

Rabies

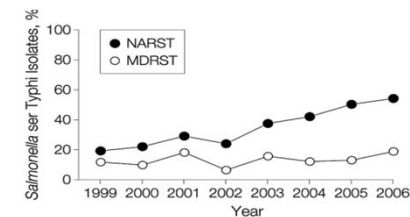
# Typhoid fever: resistance to quinolones

- 22 million new cases annually;
- 200,000 deaths annually worldwide
- Greatest burden in the Indian Subcontinent and SE Asia
- Pereira PO 03.11: clinical case
  - a 35-year-old man
  - admitted for typhoid fever due to
  - *S. typhi* resistant to nalidixic acid but susceptible for quinolones
  - Relapse after 14 days of treatment with ciprofloxacin.
  - Cure after treatment with cefotaxime and azithromycin
- The quinolone-susceptible, nalidixic acid-resistant strains may be associated with clinical failure or delayed response to quinolone

Geographic Distribution of Typhoid



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: <http://www.accessmedicine.com>  
Copyright © The McGraw-Hill Companies, Inc. All rights reserved.



Imported cases in USA

Isolates tested,	
No.	167 177 197 195 334 304 318 324
Laboratories in NARMS,	
No.	17 17 17 28 54 54 54 54

Lynch JAMA 2009



It's recommended to test for nalidixic resistance in all extra-intestinal *Salmonella* isolates

# Typhoid fever

- In returning travelers and immigrants seen at a Bronx municipal hospital 2005-2010 (Farmakiotis PO03.04)
  - 17 patients with *S. typhi*; median age 7y (2-47)
  - 16/17 required hospitalization (2 in ICU)
  - 82% history of recent travel (14/17 from Bangladesh and Pakistan)
  - None of these patients received pre-travel vaccination
  - Antimicrobial susceptibility
    - 76% (12/17) resistant to nalidixic acid
    - 23% (4/17) resistant to ampicillin and cotrimoxazole;
    - 1 was resistant to ciprofloxacin
    - All were susceptible to 3<sup>rd</sup> generation cephalosporins
- Combination therapy with ceftriaxone and azithromycin for *Salmonella paratyphi A* bacteremia among Israeli travelers to Nepal (Meltzer PO 03.08)
  - Outbreak occurred during October 2009 (< Chabad House in Pokhara)  
→ 36 patients hospitalized in Israel
  - PFGE: single bacterial strain, **all resistant to ciprofloxacin**
  - Treatment
    - 12 pts: ceftriaxone for 14 days
    - 17 pts: ceftriaxone for 14 days + azithromycin for the first 7 days
  - All the patients recovered uneventfully.
  - Time for defervescence:
    - 3.2 +/- 1.7d (combination therapy)
    - 6.3 +/- 1.7 d (monotherapy)



p=0.0006

# Delayed antibody response to yellow fever vaccination in elderly coincides with prolonged viraemia.

- YF vaccine:
  - It can cause vaccine-associated disease that resembles wild type yellow fever (yellow fever vaccine associated viscerotropic disease (YEL-AVD))
- Risk of YEL-AVD
  - 60-69 y: 1.1/100.000 doses x 4.4
  - > 70y: 3.2/100.000 x 13.4 fold higher than young adults
- Droukens FC 05.06: humoral response against YF-17D in elderly subjects to investigate the mechanism of YEL-AVD.
  - YF primovaccination: 2 groups



	Young volunteers (18-28y)	Elderly travelers (60-81y)	p
N of patients	30	28	
Day 10 Seroconversion GMT	77% 0.18 IU/ml	50% 0.017 IU/ml	0.004
Day 14 Seroconversion GMT	100% 4.8	100% 2.7	0.035
Viremia	60%	68%	P= 0.03
Viral levels	+	++	

Elderly subject (age>60y) had  
 → a delayed antibody response  
 → higher viraemia

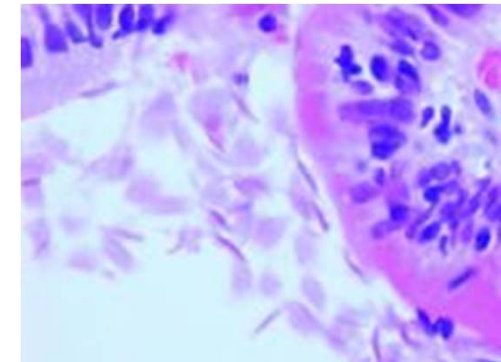
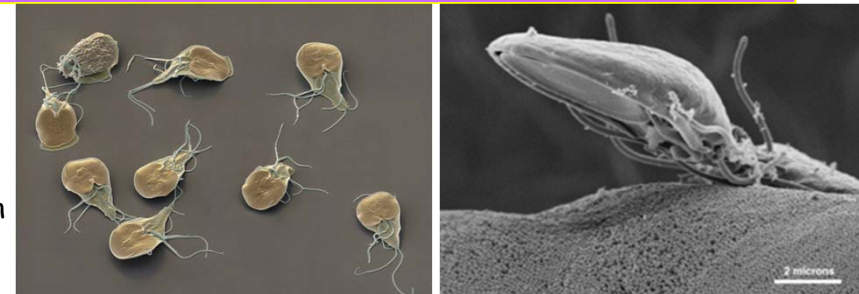
We hypothesize that this allows attenuated virus to cause higher viraemia levels that may result in severe disease





# Nitroimidazole resistant *Giardia intestinalis* in travellers

- **Giardiasis**
  - Prevalence in stools: 1-20%
  - Waterborne, foodborne, person to person transmission
  - Incubation 1-2 weeks
  - Parasite and host factors determine the course of infection
  - Stool examination:
    - 60-80% single stool
    - 90% 3 stools
  - Examination of duodenum
- **Cure rate:**
  - Tinidazole 2g once 92%
  - Metronidazole 250 mg tid 5-7 d 88%
  - Nitazoxamide 500mg tid during 3 days 90%
  - Alternative: quinacrine and paromomycine
- **Treatment failure common with all agents**
- **Different from**
  - True drug resistance
  - Cure followed by reinfection
  - Acquired lactose intolerance
- **Munoz FC 01.02 Barcelona**
  - 95 patients with *G. intestinalis*
  - 34% India, 3% SE Asia, 33% Sub-Saharan Africa, 24% Latin America, 4% Mediterranean basin
  - In 21/95 (22%), persistent *Giardia* after treatment.
    - 14 patients with quinacrine -> 100% efficacy



# Rabies



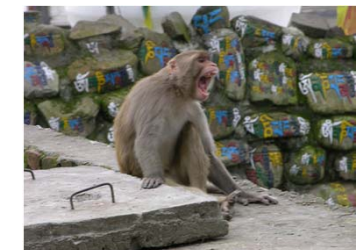
- Rabies cases in travelers:  
17 cases the last 10 years  
(! Philippines!)



- Rabies exposure
  - In expatriates 6-44/1000/year 1.6/1000/month
  - In tourists 0.3-23/1000/year 1.9/1000/month
  - Overall 0.2% (0.1-2.3%) at risk of bite per month of stay in endemic countries



- Risk factors (Geosentinel) 320 injuries in travelers
  - 67% in Asia study in Marseille (North Africa)
  - Travel duration:
    - 85% < 3 months 53% < 4 weeks → short-term = long term
    - Bangkok >50% exposed during the first 10 days (in Nepal monkey bites)
  - Dogs > monkey (in Nepal monkey bites)
  - Younger age
  - Tourists
- Vaccination coverage:
  - expatriates (30%) > tourists (13%)
- Price of the vaccine: 22 € (Europe) 200\$ in US, Canada



# Risk of possible exposure to rabies among travelers from developed countries in SE Asia

(FC 07.01; Piyaphanee Bangkok)

- In May 2010-Jan 2011, **3213** travelers from developed countries were invited to fill a questionnaire in the departure hall of Bangkok
  - They had completed their trip and were departing to destinations outside SE Asia
  - 70% European, 18% Australian-New Zealander, 11% American and Canadian
- Up to 75% had sought health information before this trip but **only 37% had received information about rabies**
- Rabies pre-exposure vaccination:
  - **15%** 3 doses
  - **11%** only 1-2 shots
  - **73%** no vaccine
- The risk of being bitten was **0.56%**, and icked **3%** (on the average stay of 28 days)
- Among those bitten, only **20%** went to the hospital to get rabies post-exposure





# Rabies postexposure prophylaxis (PEP)

- **Uwanyiligira, Lausanne FC 07.02**
  - 72 patients had consulted for rabies prophylaxis after potential exposure abroad
  - Animals responsible for exposure:
    - dogs (40), cats (6), monkey (18), bats (3), others (5)
  - 11/ (8/72) had received PEP with 3 doses of vaccine
  - Care abroad:
    - 42 patients who sought care abroad
    - Median Delay for PEP: 0 days (0-14 d)
    - Only 5/38 patients (13%) without pre-departure rabies vaccination had received Ig
  - Care in Switzerland:
    - 30 patients
    - Median delay for PEP: 10 days (0-327)
    - Of the 66 patients in whom antibody titers were available on day 21 after start of PEP, 4 (6%) did not have a protective antibody titer (> 0.5 IU/ml)
- **Gautret Clin Microbiol Infect 2010; 17, 445-447**
  - 45 injured travelers in Bali:
  - Most travelled
    - for a short time (<3 weeks),
    - for tourism purposes,
    - frequently with organized travel itineraries
  - Only 4 received pre-travel rabies vaccination
  - Majority of animal-related injuries < monkey
  - 38 had indication for IG, only 2 had received Ig



Countries of exposure



# Immunogenicity of a modified intradermal pre-exposure rabies vaccination schedule

- Intradermal vaccination:
  - cheaper but
  - recommended only if there is sufficient time to perform serology 2 to 3 weeks post vaccination and confirm immunity prior to travel
- Modified intradermal schedule TRID 2:
  - can be completed in a shorter time compared to standard intradermal schedule:
  - 2 ID of 0.1 ml of human diploid cell rabies vaccine administered on day 0 and 7
- 420 travelers
  - seroconversion rate 94.3% at 21 days post-vaccination
  - Antibody levels were significantly lower in the older age groups ( $p=0.003$ )
- This schedule is highly effective, with similar immunogenicity to the standard intradermal schedule





Date: **Wed 24 Aug 2011**  
RABIES - USA: (NEW YORK), SOLDIER,

INTERNATIONAL SOCIETY FOR INFECTIOUS DISEASES **ProMED**mail

Published Date: 2011-08-24 16:30:16  
Subject: PRO/EDR> Rabies - USA: (NY) soldier, RFI  
Archive Number: 20110824.2577

RABIES - USA: (NEW YORK), SOLDIER, REQUEST FOR INFORMATION  
\*\*\*\*\*

A ProMED-mail post  
<http://www.promedmail.org>  
ProMED-mail is a program of the  
International Society for Infectious Diseases  
<http://www.isid.org>

Date: Wed 24 Aug 2011  
Source: Syracuse.com, ex The Post-Standard [edited]  
[http://www.syracuse.com/news/index.ssf/2011/08/fort\\_drum\\_soldier\\_diagnosed\\_wi.html](http://www.syracuse.com/news/index.ssf/2011/08/fort_drum_soldier_diagnosed_wi.html)

Army officials are trying to determine where and how a Fort Drum soldier contracted rabies but believe he got the virus while stationed out of the country, officials said this morning [24 Aug 2011].

"The soldier did not contract rabies in New York State, rather, he likely contracted the disease during a recent overseas deployment," Fort Drum officials said in a prepared statement.

The soldier was diagnosed on Friday [19 Aug 2011] and is undergoing treatment. People in close contact with the soldier are being notified to assess whether they need post-exposure rabies vaccination, officials said.

They declined to identify the soldier or disclose where he had been stationed or was being treated, citing his rights under federal health privacy laws.

The Army Medical Command is working with the Centers for Disease Control and Prevention, the U.S. Forces and Central commands, the state Health Department and other agencies to determine where

Done Internet | Protected Mode: Off 115% 17:46 14/11/2011

# 3 - update consensus 2011



*Update november 2011*  
**BELGIAN**  
**CONSENSUS MEETING**  
on TRAVEL MEDICINE  
June 20, 2011

Belgian  
Scientific Study  
Group on Travel  
Medicine

Pr. A. Van Gompel (ITG)  
Pr. F. Jacobs (Hôp. Erasme, ULB)  
Pr. P. Lacor (UZ-Brussel)  
Dr. Ph. Leonard (CHU-ULg)  
Pr. W. Peetermans (U.Z. - K.U.Leuven)  
Dr. S. Callens(UZ.- U.Gent)  
Dr. S.Quoilin (iph.fgov.be)  
Dr.P. Soentjens (Belgian Army)  
Pr. B. Vandercam (CHU. St. Luc, UCL)  
Pr. Y. Van Laethem (CHU. St. Pierre, ULB)

# Vaccinations



# RABIES-1

- Prophylactic rabies vaccine is no longer available via WIV.
- Rabies vaccine is commercially available in Belgium – can easily be delivered by the pharmacists in town or in the hospitals.
- According to a guideline from 1984 the **“*Vaccin Rabique Inactive Merieux HDCV*”** from Sanofi is **yet reimbursed** (final price about 6 euro per dose) if delivered by the pharmacist (also those in the hospitals)
- The two vaccines are interchangeable and can be used for subsequent vaccination.





WETENSCHAPPELIJK INSTITUUT  
VOLKSGEZONDHEID  
INSTITUT SCIENTIFIQUE  
DE SANTÉ PUBLIQUE

Directie Overdraagbare en Besmettelijke Ziekten  
Dienst Rabiës – Humane behandeling

Aan de Directies van ziekenhuizen  
Aan de Apotheken van ziekenhuizen  
Aan de farmaceutische Verenigingen

Het Wetenschappelijk Instituut Volksgezondheid (WIV) zal vanaf 01/06/2011 niet meer instaan voor de verspreiding van het vaccin tegen rabiës dat preventief wordt toegediend.

Het WIV zal blijven instaan voor de curatieve verspreiding van het vaccin en de immunoglobulinen tegen rabiës (PEP, Post-Exposure Prophylaxis). U kan ook nog bij ons terecht voor medisch en veterinair advies ad hoc.

Het vaccin tegen rabiës is beschikbaar bij twee firma's:

Sanofi-Pasteur-MSD  
HDCV Vaccin Rabiës  
Contactpersoon: Marianne HEYMANS  
13 Jules Bordetstraat - 1140 Brussel  
T. 02 702 33 54

N.V. Novartis Pharma S.A.  
Vaccin Rabipure  
Medialaan 40 bus 1 - B-1800 Vilvoorde  
T: +32 2 246 16 11  
F: +32 2 242 37 59

PhD Michaël Kalař  
Operationeel directeur  
Overdraagbare en Besmettelijke Ziekten

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1050 Brussel | België  
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.be

# RIZIV - INAMI

## Detail van de specialiteit

De specialiteit is vergoedbaar sinds **01-04-1984** als **originele specialiteit** met RIZIV code **00126302**.

**VACCIN RABIQUE INACTIVE MERIEUX HDCV**

SANOFI PASTEUR MSD / AVENTIS  
PASTEUR MSD

1 dosis Rabiesvirus, geïnactiveerd

J07BG01

1 ml oplossing voor injectie in 1 injectieflacon poeder voor oplossing voor injectie  
en 1 voorgevulde spuit oplosmiddel voor oplossing voor injectie

injectie-subcutaan

Vergoedingsmodaliteiten											
CNK Code	Aflevering	Tarifieringseenheid		Hoofdst.- Paragr.	Model Macht.	Groep	prijs (€)	basis Vergoed. (€)	Tussenkost v/d Patient		
									WIGW(€)	Actief (€)	
2231-967	Publiek	1 verpakkingsverpakking		I	-	B-201	30,38	30,38	6,09	10,24	
0721-829	Ambulant	1 injectieflacon voorgevulde spuit) (+		I	-	B-201	30,3800	30,3800			1*
0721-829	Hospitaal	1 injectieflacon voorgevulde spuit) (+		I	-	B-201	30,3800	30,3800			2*
Niveau buiten bedrijf :							28,6600	28,6600			

Voor deze specialiteit is het forfaitaire vergoedingssysteem van toepassing voor gehospitaliseerde patiënten.

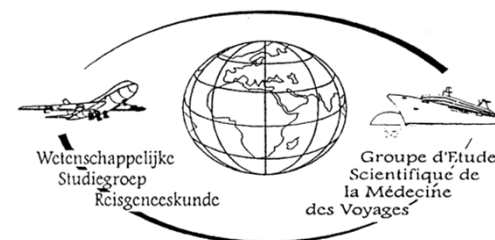
# RABIES-2

- The vaccination scheme is 3 shots within one month.
- So the only once needed booster dose can be given after one year or later.
- This is the basis whereafter the patient remains for **at least 20-30 years (probably lifelong)** boostable
- Every shot counts, so even if a second or third dose is delayed.
- It is safe to measure the rabies antibody titer after the third shot if delayed doses where given (e.g. more than 12 months).

# RABIES-3

- The postexposure rabies management remains the responsibility of the WIV/IPH/ISP
- After the postexposure rabies vaccination series, the same longterm (**probably** lifelong) boostability is present.

# YELLOW FEVER



## Yellow Fever Vaccination Recommendations in Africa, 2010

- low risk area, but yellow fever vaccination is recommended by the Belgian scientific study group on travel medicine, unless there is a contra-indication for vaccination
- vaccination recommended
- vaccination not recommended





# YELLOW FEVER

2011



## Yellow Fever Vaccination Recommendations in the Americas, 2010




-  low risk area, but yellow fever vaccination is recommended by the Belgian scientific study group on travel medicine, unless there is a contra-indication for vaccination
-  vaccination recommended
-  vaccination not recommended



TABLE 2. Contraindications and precautions to yellow fever vaccine administration

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**Contraindications**

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- Allergy to vaccine component
  - Age less than 6 months
  - Symptomatic HIV infection or CD4<sup>+</sup> T-lymphocytes <200/mm<sup>3</sup> (or <15% of total in children aged <6 years)\*
  - Thymus disorder associated with abnormal immune function<sup>†</sup>
  - Primary immunodeficiencies
  - Malignant neoplasms
  - Transplantation
  - Immunosuppressive and immunomodulatory therapies<sup>†</sup>
- 

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**Precautions**

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- Age 6–8 months
- Age ≥60 years<sup>†</sup>
- Asymptomatic HIV infection and CD4<sup>+</sup> T-lymphocytes 200–499/mm<sup>3</sup> (or 15%–24% of total in children aged <6 years)\*
- Pregnancy
- Breastfeeding

# YELLOW FEVER

- MAIL

From: Fons Van Gompel

Sent: wo 28/09/2011 17:19

To: 'meda@brusselsairport.be'; 'anneliesaerssens@hotmail.com'; 'Nathalie.ausset@uclouvain.be'; 'benedicte.belge@europarl.europa.eu'; 'Nadine.broquet@ec.europa.eu'; 'Ghislaine.Braibant@telenet.be'; 'Ghislaine.Braibant@stpierre-bru.be'; 'fbuttafu@ulb.ac.be'; 'steven.callens@ugent.be'; 'sabrina.capaert@hap.be'; 'Sabrina.capaert@erasme.ulb.ac.be'; 'reinoud.cartuyvels@jessazh.be'; 'petraclaes@skynet.be'; 'petra.claes@europarl.europa.eu'; 'Monique.coppens@health.fgov.be'; 'coutisse.af@scarlet.be'; 'christine.crem@skynet.be'; 'benedicte.delaere@uclouvain.be'; 'Andre.delandtsheer@nbb.be'; 'Isabelle.delbeke@ec.europa.eu'; 'rdemeest@ulb.ac.be'; 'Paul.demunter@uzleuven.be'; 'marc-deridder@skynet.be'; 'Jerome.deroubaix@cfwb.be'; 'surveillance.sante@cfwb.be';

Cc:

Subject: Souh Africa requires yellow fever vaccination from all travellers from and to Zambia (in addition to the list of yellow fever risk countries) from 1 October 2011



In the mail of 6 august 2011 it was said “NB. !!!! on July 21 the South African Department of Health has issued a press release which states that the yellow fever vaccination certificate is NO LONGER a requirement for entry into South Africa from Zambia or vice versa !!!!! <http://www.doh.gov.za/docs/pr/pr0721-f.html> “

BUT now it is officially [www.doh.gov.za](http://www.doh.gov.za) <http://www.doh.gov.za/diseases.php?type=19>

26 Aug 2011	Zambia added to list of countries requiring Yellow Fever vaccination
26 Aug 2011	Yellow Fever policy amendment [pdf] attachement
20 Jul 2011	Yellow Fever Guidelines [pdf] attachement

The RSA has reviewed its yellow fever vaccination requirements policy, which will be effective from 1 October 2011.

1. As of 1 October 2011, all travellers from and to Zambia, in addition to the list of yellow fever risk countries below, will be required to show proof of yellow fever vaccination (unless in possession of a valid waiver certificate).
2. Travellers transiting airports in countries with risk of yellow fever transmission will be required to show proof of yellow fever vaccination, regardless of the amount of time spent at the airport



From: Fons Van Gompel

Sent: wo 28/09/2011 17:19

To: 'meda@brusselsairport.be'; 'anneliesaerssens@hotmail.com'; 'Nathalie.aussetlet@uclouvain.be'; 'benedicte.belge@europarl.europa.eu'; 'Nadine.broquet@ec.europa.eu'; 'Ghislaine.Braibant@telenet.be'; 'Ghislaine.Braibant@stpierre-bru.be'; 'fbuttafu@ulb.ac.be'; 'steven.callens@ugent.be'; 'sabrina.capaert@hap.be'; 'Sabrina.capaert@erasme.ulb.ac.be'; 'reinoud.cartuyvels@jessazh.be'; 'petraclaes@skynet.be'; 'petra.claes@europarl.europa.eu'; 'Monique.coppens@health.fgov.be'; 'coutisse.af@scarlet.be'; 'christine.crem@skynet.be'; 'benedicte.delaere@uclouvain.be'; 'Andre.delandtsheer@nbb.be'; 'Isabelle.delbeke@ec.europa.eu'; 'rdemeest@ulb.ac.be'; 'Paul.demunter@uzleuven.be'; 'marc-deridder@skynet.be'; 'Jerome.deroubaix@cfwb.be'; 'surveillance.sante@cfwb.be';

Cc:

Subject: South Africa requires yellow fever vaccination from all travellers from and to Zambia (in addition to the list of yellow fever risk countries) from 1 October 2011



South Africa will exercise the following measures to all travellers from yellow fever risk countries who are unable to produce a valid yellow fever vaccination certificate at the port of entry:

- . refuse entry; or
- . quarantine until their certificate becomes valid, or for a period of not more than six days; or
- . those with an exemption certificate due to medical reasons will be allowed entry and required to report any fever or other symptoms to the health authorities and be placed under surveillance.

In the discussions in the ISTM-travelmed discussiongroup (in attachment) it became very clear that South Africa will require yellow fever vaccination also from the very low risk regions

(<http://www.itg.be/itg/GeneralSite/MedServ/Images/Gele%20koorts%20Afrika%2002.jpg> &

<http://www.itg.be/itg/GeneralSite/MedServ/Images/Gele%20koorts%20Zuid%20Amerika%2002.jpg>), even in case of a stop-over, no matter how short or how long.

They will NOT give the vaccine themselves at arrival nor implement quarantine, they will put the passenger on a direct retour flight

# Vaccine 1998



Vaccine 17 (1999) 1042–1046

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Vaccine

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## Recent immunization against measles does not interfere with the sero-response to yellow fever vaccine

Isabel Stefano<sup>a</sup>, Helena K. Sato<sup>a</sup>, Claudio S. Pannuti<sup>b</sup>, Tereza M. Omoto<sup>a</sup>,  
George Mann<sup>c</sup>, Marcos S. Freire<sup>c</sup>, Anna M.Y. Yamamura<sup>c</sup>, Pedro F.C. Vasconcelos<sup>d</sup>,  
Gabriel W. Oselka<sup>a</sup>, Lilly W. Weckx<sup>a</sup>, Maria F. Salgado<sup>a</sup>, Lucelene F.O. Noale<sup>a</sup>,  
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## Mutual interference on the immune response to yellow fever vaccine and a combined vaccine against measles, mumps and rubella

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# Combination of YF-vaccine and MMR-vaccine

- Administration of two live-attenuated vaccines can be done simultaneously without relevant influence on immunogenicity.
- For measles and varicella the doses, when not given simultaneously, must be separated by 30 days because of the interferon production induced by the first vaccine shot.
- This is not so for the combination of measles and yellow fever vaccination.  
CDC says that any interval can be used if yellow fever vaccination is indicated, irrespective when measles vaccine was given previously. ....
- *Studies are actually ongoing that might change this advice :*

## combination of measles and yellow fever vaccination

- Subjects injected YFV and MMR **simultaneously** had **lower** seroconversion rates – **90% for rubella, 70% for yellow fever** and **61% for mumps** – compared with those vaccinated **30 days apart** – **97% for rubella, 87% for yellow fever** and **71% for mumps**.
- Seroconversion rates for **measles** were higher than 98% in **both** comparison groups.
- Geometric mean titers **for rubella** and **for yellow fever** were **approximately three times higher** among those who got the vaccines **30 days apart**.
- For **measles** and **mumps** antibodies GMTs were similar across groups.

combination of measles and yellow fever vaccination

- MMR's interference in immune response of YFV and YFV's interference in immune response of rubella and mumps components of MMR had never been reported before but are consistent with previous observations from other live vaccines.
- These results may affect the recommendations regarding primary vaccination with yellow fever vaccine and MMR.

# Japanese encephalitis (Ixiaro®)

- Ixiaro® is commercially available in the officinal pharmacy.
- The full dose has to be used for children and adults between 3 and 18 years of age. Between the age of 1 and 3 half dose is indicated.
- The standard scheme requires 2 injections, separated by one month. Afterwards, the traveler remains boostable which means that a booster dose can be given after 12-24 months – (later boosters ? 3-5 years ?)
- When the patient was vaccinated with Jevax® previously the consensus meeting gives the advice to use two doses of Ixiaro® when Jevax® dates from five years back or more.

<http://wwwnc.cdc.gov/travel/news-announcements.htm?source=govdelivery>

- Administer JE-VC (IXIARO) off-label: JE-VC is FDA-licensed for use in adults  $\geq 17$  years of age.
- However, a health-care provider may choose to administer the vaccine off-label in children  $< 17$  years of age.
- Data from the one completed pediatric study have been published (Kaltenbock et al. Vaccine 2010;28:834-9).
- The manufacturer is currently studying a 6  $\mu\text{g}$  per 0.5mL dose (regular adult dose) for children  $\geq 3$  years of age. Additional information about the use of JE-VC in children is available from Novartis



**BOSTON 12th CISTM 2011****Abstracts – Free Communications**

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**FC07.05****Safety, Immunogenicity and Dose Confirmation for the Inactivated Japanese Encephalitis Vaccine IXIARO®<sup>1</sup>, IC51, in Filipino Children aged 3 to 12 years**

Dubischar-Kastner K.<sup>1</sup>, Kadlec V.<sup>1</sup>, Sablan B.<sup>2</sup>, Borja-Tabora C.F.<sup>3</sup>, Gatchalian S.<sup>4</sup>, Eder S.<sup>1</sup>, Schuller E.<sup>1</sup>, Taucher C.<sup>1</sup>, Westritschnig K.<sup>1</sup>, Klade C.<sup>1</sup>

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<sup>3</sup>Research Institute for Tropical Medicine, Department of Health, Manila, Philippines, <sup>4</sup>University of Philippines, Manila, Philippines

**Conclusions:**

Both tested doses of IXIARO appeared to have a comparable safety profile.

Due to higher SCR and significantly higher GMTs, the full adult dose will be pursued for further development in this age group.

# Tolérance, immunogénicité et confirmation de dose pour le vaccin inactivé contre le virus de l'Encéphalite Japonaise, Ixiaro<sup>®</sup>, IC51, chez des enfants philippins âgés de 3 à < 12 ans

Monchecourt F<sup>1</sup>, Dubischar-Kastner K<sup>2</sup>, Kadlecek V<sup>2</sup>, Sablan Jr. B<sup>3</sup>, Fay Borja-Tabora C<sup>4</sup>, Gatchalian S<sup>5</sup>, Eder S<sup>2</sup>, Schuller E<sup>2</sup>, Taucher C<sup>2</sup>, Westritschnig K<sup>2</sup>, Klade C<sup>2</sup>

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*5. University of the Philippines, Manila*

*Med Trop 2011 ; 71 : 367-370*

Based on these findings showing better SCR and significantly higher GMT **in the 6 µg/0.5 mL dose group**, use of the **full adult dose** will be continued for development of **child use**.

## Dosage and schedule

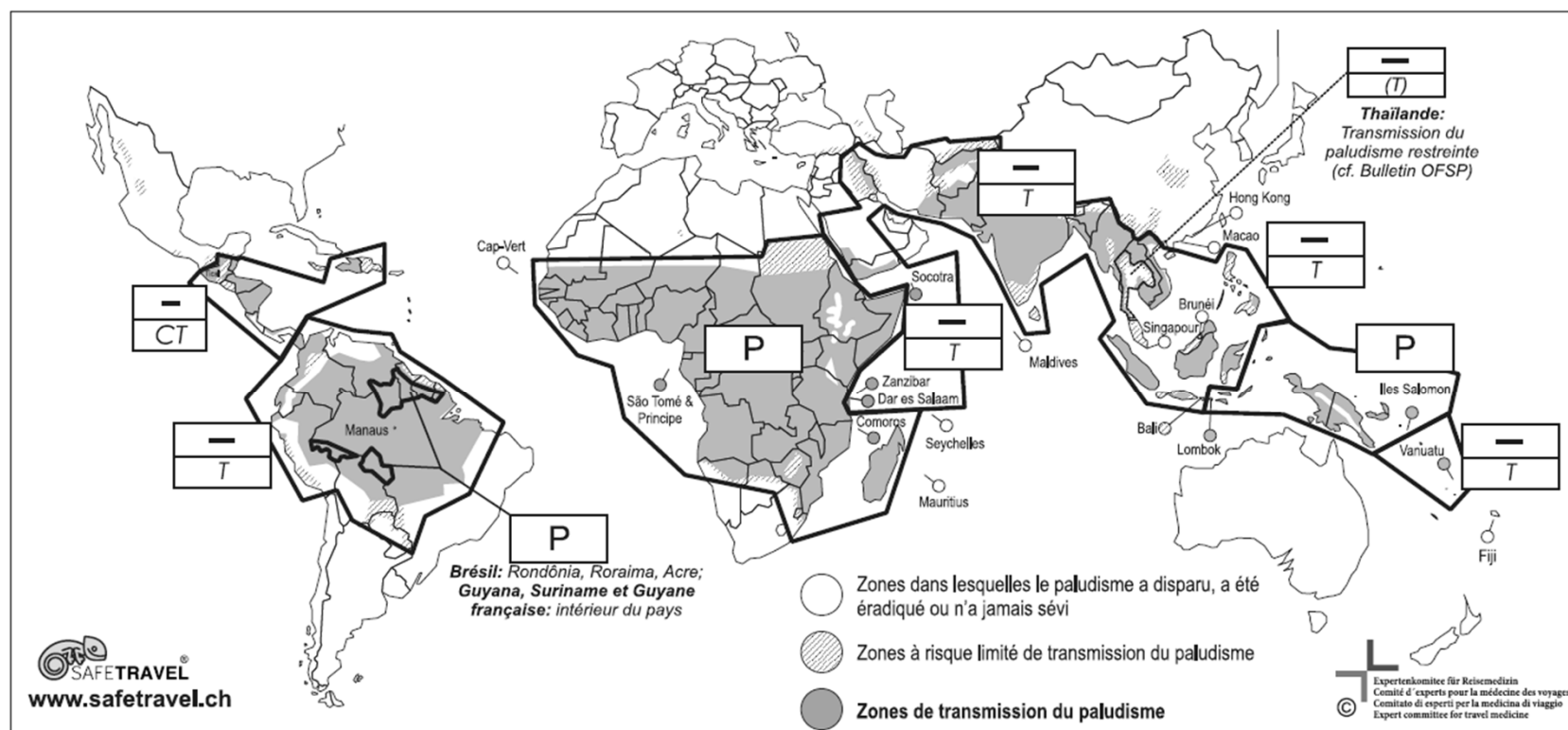
	IXIARO®	Green Cross vaccine
Infants	Not recommended	Not recommended
Children aged one year to under 36 months	Not recommended	<ul style="list-style-type: none"> <li>• First dose of 0.5ml at day 0.</li> <li>• Second dose of 0.5ml at days 7–14.</li> <li>• Third dose of 0.5ml at days 28–30.</li> </ul>
Children over 36 months and up to and including 17 years of age	*see recommendations on page 204 for use in older teenage children	<ul style="list-style-type: none"> <li>• First dose of 1ml at day 0.</li> <li>• Second dose of 1ml at days 7–14.</li> <li>• Third dose of 1ml at days 28–30.</li> </ul>
Adults aged 18 years and over	<ul style="list-style-type: none"> <li>• First dose of 0.5ml at day 0.</li> <li>• Second dose of 0.5ml 28 days after first dose.</li> </ul>	Not recommended

# Malaria



# Malaria - 1

For many countries in Asia and South America the risk is highly variable depending on area, season and way of traveling. **Strict anti-mosquito measures** (plus an **emergency self treatment** in many cases) can be discussed with the individual traveler as a valid alternative.



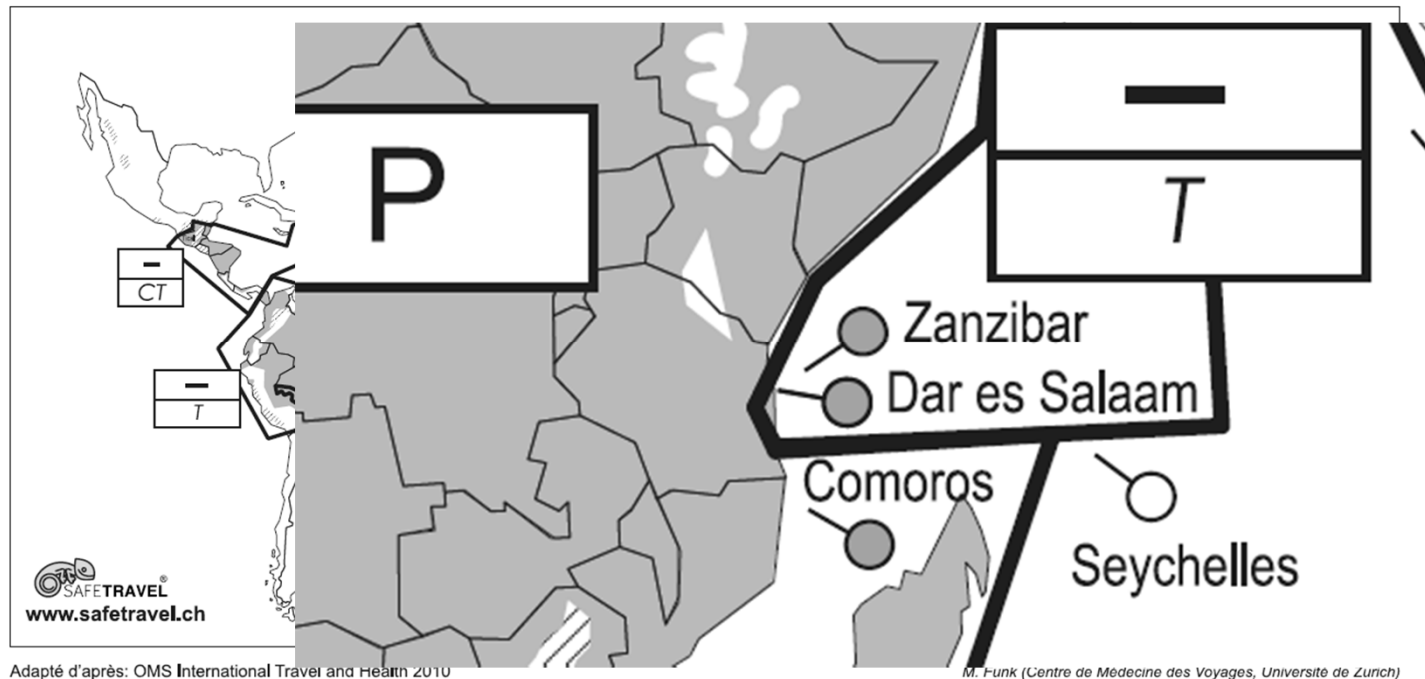
## Malaria - 2

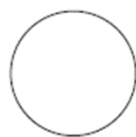
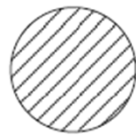

- For Zanzibar & Pemba this has become an option too.
- Several countries have a labile situation where the eradication programs seem to be successful but reintroduction can occur suddenly and unexpectedly (e.g. Dar es Salaam; Zanzibar).



2010 : Op de eilanden Zanzibar en Pemba is er malariarisico, maar in mindere mate (en de situatie kan er nog gemakkelijk verergeren)

**2011 : Volgens de Zwitsers volstaan op Zanzibar antimugmaatregelen**



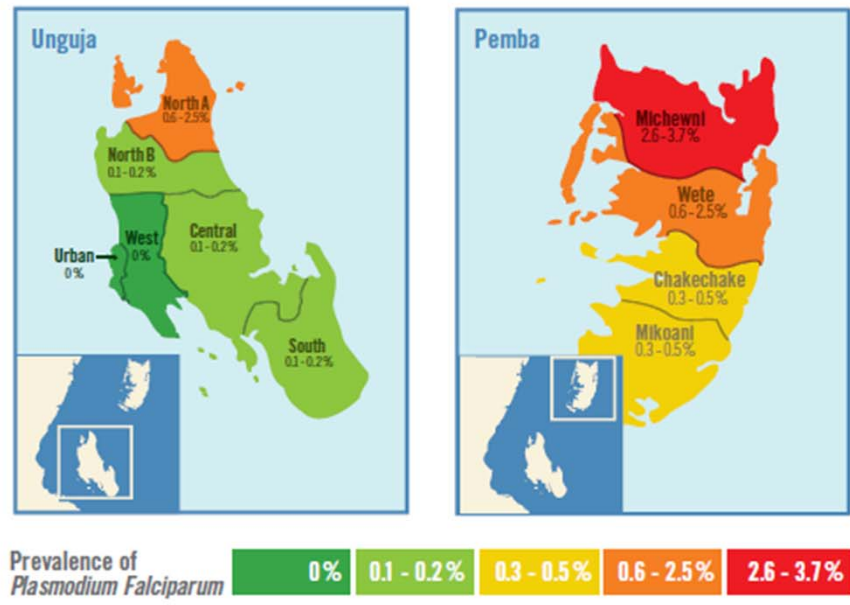
-  Zones dans lesquelles le paludisme a disparu, a été éradiqué ou n'a jamais sévi
-  Zones à risque limité de transmission du paludisme
-  **Zones de transmission du paludisme**

# MALARIA ELIMINATION IN ZANZIBAR

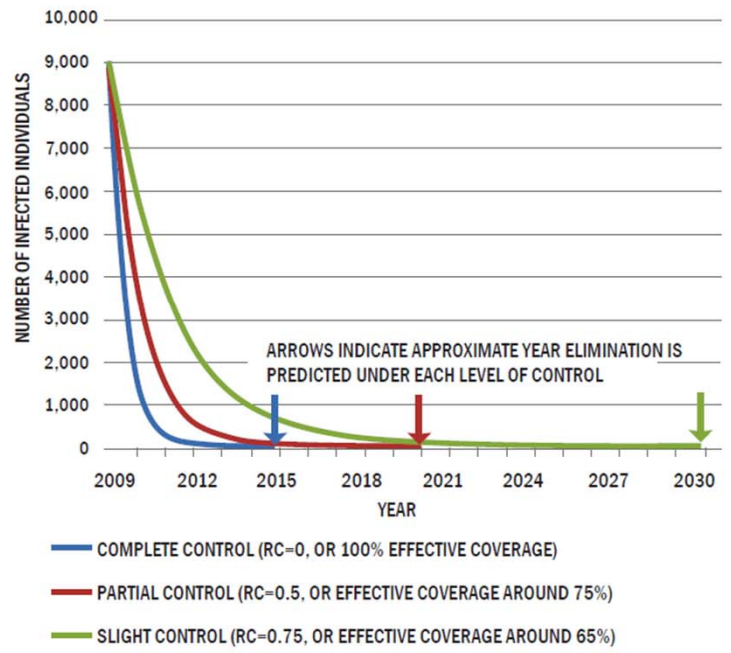
## A FEASIBILITY ASSESSMENT | OCTOBER 2009



FIGURE 3: MALARIA PREVALENCE BY DISTRICT (ZMCP, 2008) 2011



### ESTIMATED COVERAGE LEVELS AND TIME TO ACHIEVE ELIMINATION



# Malaria vaccine



- ❑ No role in travel medicine
- ❑ Explanation of adjuvant systems

# First Results of Phase 3 Trial of RTS,S/AS01 Malaria Vaccine in African Children

The RTS,S Clinical Trials Partnership\*

## ABSTRACT

### BACKGROUND

An ongoing phase 3 study of the efficacy, safety, and immunogenicity of candidate malaria vaccine RTS,S/AS01 is being conducted in seven African countries.

### METHODS

From March 2009 through January 2011, we enrolled 15,460 children in two age categories — 6 to 12 weeks of age and 5 to 17 months of age — for vaccination with either RTS,S/AS01 or a non-malaria comparator vaccine. The primary end point of the analysis was vaccine efficacy against clinical malaria during the 12 months after vaccination in the first 6000 children 5 to 17 months of age at enrollment who received all three doses of vaccine according to protocol. After 250 children had an episode of severe malaria, we evaluated vaccine efficacy against severe malaria in both age categories.

### RESULTS

In the 14 months after the first dose of vaccine, the incidence of first episodes of clinical malaria in the first 6000 children in the older age category was 0.32 episodes per person-year in the RTS,S/AS01 group and 0.55 episodes per person-year in the control group, for an efficacy of 50.4% (95% confidence interval [CI], 45.8 to 54.6) in the intention-to-treat population and 55.8% (97.5% CI, 50.6 to 60.4) in the per-protocol population. Vaccine efficacy against severe malaria was 45.1% (95% CI, 23.8 to 60.5) in the intention-to-treat population and 47.3% (95% CI, 22.4 to 64.2) in the per-protocol population. Vaccine efficacy against severe malaria in the combined age categories was 34.8% (95% CI, 16.2 to 49.2) in the per-protocol population during an average follow-up of 11 months. Serious adverse events occurred with a similar frequency in the two study groups. Among children in the older age category, the rate of generalized convulsive seizures after RTS,S/AS01 vaccination was 1.04 per 1000 doses (95% CI, 0.62 to 1.64).

### CONCLUSIONS

The RTS,S/AS01 vaccine provided protection against both clinical and severe malaria in African children. (Funded by GlaxoSmithKline Biologicals and the PATH Malaria Vaccine Initiative; RTS,S ClinicalTrials.gov number, NCT00866619.)

This article (10.1056/NEJMoal102287) was published on October 18, 2011, at NEJM.org.

## EDITORIAL



## A Vaccine for Malaria

Nicholas J. White, F.R.S.

Protective efficacy against *P. falciparum* malaria

**(55% protection against all malaria episodes)**

was at the upper end of expectations from earlier studies, whereas the **overall reduction in severe malaria (35% protection)** was slightly less than anticipated.

# Comment promedmail 21 Oct 2011

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The results published in the paper are remarkably **similar** to 2 previous studies of the vaccine.

- **Alonso** et al (**RTS,S/AS02A** vaccine - **Lancet 2005**; 366:2012-8) found in 2022 children from Mozambique after 21 month
  - a **35 per cent** protective efficacy
  - a **48 per cent** reduction in severe malaria
  
- **Bejon** et al. (**New Engl. J Med. 2008**; 259: 2521-31) included 809 children from Kenya and Tanzania who received 3 doses of **RTS,S/AS01E** and reported
  - overall protective efficacy of **56 per cent** during 7.9 months follow up.

The results reported in the new study are therefore **merely confirming the protective efficacy of the previous studies.**



# Comment promedmail 21 Oct 2011

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As the vaccine reduces the number of severe malaria cases it is expected to reduce childhood mortality due to malaria, and we look forward to see these data.

Thus the studies reported over the past 6 years demonstrate that the vaccine has a protective efficacy at the same level as insecticide treated nets (ITN) presently the basic tool for malaria control in Africa.

Pending the mortality data, it will be interesting to follow how vaccine and ITNs will be used in malaria control, how the cost of the 2 interventions will compare and how effective a combination of the 2 may be.



# Efficacy of RTS,S/AS01E Vaccine against Malaria in Children 5 to 17 Months of Age

Philip Bejon, Ph.D., John Lusingu, Ph.D., Ally Olotu, M.B., Ch.B., Amanda Leach, M.R.C.P.C.H., Marc Lievens, M.Sc., Johan Vekemans, Ph.D., Salum Mshamu, M.D., Trudie Lang, Ph.D., Jayne Gould, Ph.D., Marie-Claude Dubois, M.Sc., Marie-Ange Demoitié, M.Sc., Jean-Francois Stallaert, B.Sc., Preeti Vansadia, M.H.S., Terrell Carter, M.H.S., Patricia Njuguna, M.D., Ken O. Awuondo, H.N.D., Anangisye Malabeja, M.D., Omar Abdul, M.D., Samwel Gesase, M.D., Neema Mturi, M.R.C.Paed., Chris J. Drakeley, Ph.D., Barbara Savarese, R.N., Tonya Villafana, Ph.D., W. Ripley Ballou, M.D., Joe Cohen, Ph.D., Eleanor M. Riley, Ph.D., Martha M. Lemnge, Ph.D., Kevin Marsh, F.R.C.P., and Lorenz von Seidlein, Ph.D.

## ABSTRACT

### BACKGROUND

*Plasmodium falciparum* malaria is a pressing global health problem. A previous study of the malaria vaccine RTS,S (which targets the circumsporozoite protein), given with an adjuvant system (AS02A), showed a 30% rate of protection against clinical malaria in children 1 to 4 years of age. We evaluated the efficacy of RTS,S given with a more immunogenic adjuvant system (AS01E) in children 5 to 17 months of age, a target population for vaccine licensure.

### METHODS

We conducted a double-blind, randomized trial of RTS,S/AS01E vaccine as compared with rabies vaccine in children in Kilifi, Kenya, and Korogwe, Tanzania. The primary end point was fever with a falciparum parasitemia density of more than 2500 parasites per microliter, and the mean duration of follow-up was 7.9 months (range, 4.5 to 10.5).

### RESULTS

A total of 894 children were randomly assigned to receive the RTS,S/AS01E vaccine or the control (rabies) vaccine. Among the 809 children who completed the study procedures according to the protocol, the cumulative number in whom clinical malaria developed was 32 of 402 assigned to receive RTS,S/AS01E and 66 of 407 assigned to receive the rabies vaccine; the adjusted efficacy rate for RTS,S/AS01E was 53% (95% confidence interval [CI], 28 to 69;  $P < 0.001$ ) on the basis of Cox regression. Overall, there were 38 episodes of clinical malaria among recipients of RTS,S/AS01E, as compared with 86 episodes among recipients of the rabies vaccine, with an adjusted rate of efficacy against all malarial episodes of 56% (95% CI, 31 to 72;  $P < 0.001$ ). All 894 children were included in the intention-to-treat analysis, which showed an unadjusted efficacy rate of 49% (95% CI, 26 to 65;  $P < 0.001$ ). There were fewer serious adverse events among recipients of RTS,S/AS01E, and this reduction was not only due to a difference in the number of admissions directly attributable to malaria.

### CONCLUSIONS

RTS,S/AS01E shows promise as a candidate malaria vaccine. (ClinicalTrials.gov number, NCT00380393.)

From the Centre for Geographic Medicine Research (Coast), Kenya Medical Research Institute, Kilifi, Kenya (P.B., A.O., T.L., P.N., K.O.A., N.M., K.M.); the Centre for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom (P.B., K.M.); the National Institute for Medical Research, Tanga Centre (J.L., S.M., A.M., O.A., S.G., M.M.L.), and the Joint Malaria Programme, Korogwe (J.L., S.M., J.G., A.M., O.A., S.G., C.J.D., E.M.R., M.M.L., L.S.) — both in Tanzania; Centre for Medical Parasitology, University of Copenhagen, Denmark (J.L.); GlaxoSmithKline Biologicals, Rixensart, Belgium (A.L., M.L., J.V., M.-C.D., M.-A.D., J.-F.S., W.R.B., J.C.); the London School of Hygiene and Tropical Medicine, London (J.G., C.J.D., E.M.R., L.S.); Program for Appropriate Technology in Health (PATH) Malaria Vaccine Initiative, Bethesda, MD (P.V., T.C., B.S., T.V.); the International Vaccine Institute, Seoul, Korea (L.S.); and the Mahidol Oxford Research Unit, Bangkok, Thailand (L.S.). Address reprint requests to Dr. Bejon at KEMRI, P.O. Box 230, Mombasa, Kenya, or at pbejon@kilifi.kemri-wellcome.org.

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# Safety and Immunogenicity of RTS,S/AS02D Malaria Vaccine in Infants

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## ABSTRACT

### BACKGROUND

The RTS,S/AS malaria vaccine is being developed for delivery through the World Health Organization's Expanded Program on Immunization (EPI). We assessed the feasibility of integrating RTS,S/AS02D into a standard EPI schedule for infants.

### METHODS

In this phase 2B, single-center, double-blind, controlled trial involving 340 infants in Bagamoyo, Tanzania, we randomly assigned 340 infants to receive three doses of either the RTS,S/AS02D vaccine or the hepatitis B vaccine at 8, 12, and 16 weeks of age. All infants also received a vaccine containing diphtheria and tetanus toxoids, whole-cell pertussis vaccine, and conjugated *Haemophilus influenzae* type b vaccine (DTPw/Hib). The primary objectives were the occurrence of serious adverse events during a 9-month surveillance period and a demonstration of noninferiority of the responses to the EPI vaccines (DTPw/Hib and hepatitis B surface antigen) with co-administration of the RTS,S/AS02D vaccine, as compared with the hepatitis B vaccine. The detection of antibodies against *Plasmodium falciparum* circumsporozoite and efficacy against malaria infection were secondary objectives.

### RESULTS

At least one serious adverse event was reported in 31 of 170 infants who received the RTS,S/AS02D vaccine (18.2%; 95% confidence interval [CI], 12.7 to 24.9) and in 42 of 170 infants who received the hepatitis B vaccine (24.7%; 95% CI, 18.4 to 31.9). The results showed the noninferiority of the RTS,S/AS02D vaccine in terms of antibody responses to EPI antigens. One month after vaccination, 98.6% of infants receiving the RTS,S/AS02D vaccine had seropositive titers for anticircumsporozoite antibodies on an enzyme-linked immunosorbent assay (ELISA). During the 6-month period after the third dose of vaccine, the efficacy of the RTS,S/AS02D vaccine against first infection with *P. falciparum* malaria was 65.2% (95% CI, 20.7 to 84.7;  $P=0.01$ ).

### CONCLUSIONS

The use of the RTS,S/AS02D vaccine in infants had a promising safety profile, did not interfere with the immunologic responses to coadministered EPI antigens, and reduced the incidence of malaria infection. (ClinicalTrials.gov number, NCT00289185.)

2009

## EDITORIALS



### A Hopeful Beginning for Malaria Vaccines

William E. Collins, Ph.D., and John W. Barnwell, M.P.H., Ph.D.

From the Bagamoyo Research and Training Centre of Ifakara Health Institute, Bagamoyo, Tanzania (S.A., R.O., O.J., F.M., C.M., S.O., A.U., H.M., A.J., N.S., M.S., T.A., D.M.S., M.T.); Swiss Tropical Institute, Basel, Switzerland (R.O., T.A., M.T.); Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania (S.K.); London School of Hygiene and Tropical Medicine, London (D.M.S.); Program for Appropriate Technology in Health (PATH) Malaria Vaccine Initiative, Bethesda, MD (T.C., T.V.); GlaxoSmithKline Biologicals, Rixensart, Belgium (M.-A.D., M.-C.D., A.L., M.L., J.V., J.C.); and Bill and Melinda Gates Foundation, Seattle (W.R.B.). Address reprint requests to Dr. Abdulla at the Bagamoyo Research and Training Centre, Ifakara Health Institute, Box 74, Bagamoyo Tanzania, or at [sabdulla@ihi.or.tz](mailto:sabdulla@ihi.or.tz).

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# Randomized, Double-Blind, Phase 2a Trial of Falciparum Malaria Vaccines RTS,S/AS01B and RTS,S/AS02A in Malaria-Naive Adults: Safety, Efficacy, and Immunologic Associates of Protection

The Journal of Infectious Diseases 2009;200:337–46

Kent E. Kester,<sup>1</sup> James F. Cummings,<sup>1</sup> Opokua Ofori-Anyinam,<sup>3</sup> Christian F. Ockenhouse,<sup>1</sup> Urszula Krzych,<sup>1</sup> Philippe Moris,<sup>3</sup> Robert Schwenk,<sup>1</sup> Robin A. Nielsen,<sup>1</sup> Zufan Debebe,<sup>1</sup> Evgeny Pinelis,<sup>1</sup> Laure Juompan,<sup>1</sup> Jack Williams,<sup>1</sup> Megan Dowler,<sup>1</sup> V. Ann Stewart,<sup>1</sup> Robert A. Wirtz,<sup>2</sup> Marie-Claude Dubois,<sup>3</sup> Marc Lievens,<sup>3</sup> Joe Cohen,<sup>3</sup> W. Ripley Ballou,<sup>3</sup> D. Gray Heppner, Jr.,<sup>1</sup> and the RTS,S Vaccine Evaluation Group<sup>a</sup>

<sup>1</sup>Walter Reed Army Institute of Research, Silver Spring, Maryland; <sup>2</sup>Centers for Disease Control and Prevention, Atlanta, Georgia;

<sup>3</sup>GlaxoSmithKline Biologicals, Rixensart, Belgium

(See the editorial commentary by Bremen and Plowe, on pages 317–20, and the article by Sacarlal et al, on pages 329–36.)

**Background.** To further increase the efficacy of malaria vaccine RTS,S/AS02A, we tested the RTS,S antigen formulated using the AS01B Adjuvant System (GlaxoSmithKline Biologicals).

**Methods.** In a double-blind, randomized trial, 102 healthy volunteers were evenly allocated to receive RTS,S/AS01B or RTS,S/AS02A vaccine at months 0, 1, and 2 of the study, followed by malaria challenge. Protected vaccine recipients were rechallenged 5 months later.

**Results.** RTS,S/AS01B and RTS,S/AS02A were well tolerated and were safe. The efficacy of RTS,S/AS01B and RTS,S/AS02A was 50% (95% confidence interval [CI], 32.9%–67.1%) and 32% (95% CI, 17.6%–47.6%), respectively. At the time of initial challenge, the RTS,S/AS01B group had greater circumsporozoite protein (CSP)–specific immune responses, including higher immunoglobulin (Ig) G titers, higher numbers of CSP-specific CD4<sup>+</sup> T cells expressing  $\geq 2$  activation markers (interleukin-2, interferon [IFN]– $\gamma$ , tumor necrosis factor– $\alpha$ , or CD40L), and more ex vivo IFN– $\gamma$  enzyme-linked immunospots (ELISPOTs) than did the RTS,S/AS02A group. Protected vaccine recipients had a higher CSP-specific IgG titer (geometric mean titer, 188 vs 73  $\mu\text{g}/\text{mL}$ ;  $P < .001$ ), higher numbers of CSP-specific CD4<sup>+</sup> T cells per 10<sup>6</sup> CD4<sup>+</sup> T cells (median, 963 vs 308 CSP-specific CD4<sup>+</sup> T cells/10<sup>6</sup> CD4<sup>+</sup> T cells;  $P < .001$ ), and higher numbers of ex vivo IFN– $\gamma$  ELISPOTs (mean, 212 vs 96 spots/million cells;  $P < .001$ ). At rechallenge, 4 of 9 vaccine recipients in each group were still completely protected.

**Conclusions.** The RTS,S/AS01B malaria vaccine warrants comparative field trials with RTS,S/AS02A to determine the best formulation for the protection of children and infants. The association between complete protection and immune responses is a potential tool for further optimization of protection.

**Trial registration.** ClinicalTrials.gov identifier NCT00075049.

# Long-Term Safety and Efficacy of the RTS,S/AS02A Malaria Vaccine in Mozambican Children 2009

The Journal of Infectious Diseases 2009;200:329–36

Jahit Sacarlal,<sup>1,2,5</sup> Pedro Aide,<sup>1,3</sup> John J. Aponte,<sup>1,5</sup> Montse Renom,<sup>1,5</sup> Amanda Leach,<sup>6</sup> Inácio Mandomando,<sup>1,3</sup> Marc Lievens,<sup>6</sup> Quique Bassat,<sup>1,5</sup> Sarah Lafuente,<sup>1,5</sup> Eusébio Macete,<sup>1,4</sup> Johan Vekemans,<sup>6</sup> Caterina Guinovart,<sup>1,5</sup> Betuel Sigaúque,<sup>1,3</sup> Marla Sillman,<sup>7</sup> Jessica Milman,<sup>7</sup> Marie-Claude Dubois,<sup>6</sup> Marie-Ange Demoitié,<sup>6</sup> Joelle Thonnard,<sup>6</sup> Clara Menéndez,<sup>1,5</sup> W. Ripley Ballou,<sup>6,a</sup> Joe Cohen,<sup>6</sup> and Pedro L. Alonso<sup>1,5</sup>

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(See the editorial commentary by Bremen and Plowe, on pages 317–20, and the article by Kester et al, on pages 337–46.)

**Background.** We previously reported that the RTS,S/AS02A vaccine had an acceptable safety profile, was immunogenic, and demonstrated efficacy against *Plasmodium falciparum* malaria disease for 21 months.

**Methods.** We conducted a randomized, controlled, phase 2b trial of RTS,S/AS02A in 2022 Mozambican children aged 1–4 years. We now report safety results for all randomized subjects and vaccine efficacy (VE) findings for children in the Manhiça area over the 45-month surveillance period.

**Results.** During the surveillance period, the  $VE_{(2.5-45)}$  (VE over months 2.5–45 of surveillance) against a first or only episode of clinical malaria disease was 30.5% (95% confidence interval [CI], 18.9%–40.4%;  $P < .001$ ), and the  $VE_{(2.5-45)}$  against all episodes was 25.6% (95% CI, 11.9%–37.1%;  $P < .001$ ). When the same period was considered, the  $VE_{(2.5-45)}$  for subjects protected against severe malaria was 38.3% (95% CI, 3.4%–61.3%;  $P = .045$ ). At study month 45, the prevalence of *P. falciparum* was 34% lower in the RTS,S/AS02A group than in the control group (66 [12.2%] of 541 patients vs 101 [18.5%] of 547 patients) ( $P = .004$ ).

**Conclusion.** These results show evidence that RTS,S/AS02A maintained protection during the 45-month surveillance period, and they highlight the feasibility of developing an effective vaccine against malaria. In combination with other malaria-control measures, such a vaccine could greatly contribute to reducing the intolerable global burden of this disease.

**Trial registration.** ClinicalTrials.gov identifiers NCT00197041 and NCT00323622.

# GSK - Adjuvant System

- Adjuvant system **AS01** = MPL and QS21 and liposomes
  - **AS01**-formulated vaccines : RTS,S/AS01 malaria vaccine
- Adjuvant system **AS02** = MPL and QS21 in o/w emulsion
  - **AS02**-formulated vaccines : RTS,S/AS02 malaria vaccine
- Adjuvant system **AS03** = Squalen & Tocopherol in o/w emulsion & Tween
  - **AS03**-formulated vaccines : Pandemic & prepandemic flu vaccines
- Adjuvant system **AS04** = MPL® adsorbed on aluminum salt (aluminium hydroxide or aluminium phosphate, depending on the vaccine)
  - **AS04**-formulated vaccines : Fendrix ® & Cervarix ®

**MPL = Monophosphoryl lipid A**, derived from cell wall lipopolysaccharide LPS of *Salmonella Minnesota*

**QS 21** = Extracted from the bark of a South American tree (*Quillaja saponaria*)

# Varia

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The **13th ISTM conference** will be held in Maastricht

**19 – 23 May 2013.**

The **2nd** EU-regional Maastricht Symposium on

**the Immune Compromised Traveller**  
**Monday, January 16th 2012**

Maastricht School of Management



# 13th Conference of the

International Society of Travel Medicine

Maastricht, The Netherlands

Maastricht Exposition and Conference Center (MECC)

19-23 May 2013



Local Organizing Committee (LOC) and Regional Advisory Committee (RAC)  
CISTM 2013 Maastricht The Netherlands

Chair: Gerard JB Sonder MD PhD director National Coordination Center for Travelers Health Advice LCR Amsterdam

## For Belgium

Alfons Van Gompel MD Antwerpen (Instituut voor Tropische Geneeskunde ITG Antwerpen)

Steven Callens MD PhD Gent (Universitair Ziekenhuis-Universiteit Gent UZ.- U.Gent)

Yves Van Laethem MD Brussel (Hôpital Staint-Pierre, Université Libre de Bruxelles ULB)



Early Registration: 31 December 2012  
Abstract Submission: 17 January 2013

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# SYMPOSIUM

## 2nd Euregional Maastricht Symposium on Immune Compromised Traveller

Pre-announcement



16 Jan. 2012 | Maastricht School of Management

Crossing the borders  
in health policy



# SYMPOSIUM

2nd Euregional Maastricht Symposium on  
Immune Compromised Traveller

Pre-announcement

16 Jan. 2012 | Maastricht School of Management

**REGISTRATION AT [WWW.EUPREVENT.EU/MICT/](http://WWW.EUPREVENT.EU/MICT/)**

**Participation is free of charge**

*This includes snacks, lunch and drinks at the venue, a handout of the slide presentations and certificate.*

## **DATE**

Monday January 16th 2012

09:00 - 17:10

## **LOCATION**

**Maastricht School of Management**

Endepolsdomein 150

6229 EP Maastricht, The Netherlands

*The Maastricht School of Management is located at 5 minutes walking distance from the Maastricht-Randwijck railwaystation.*

*The Maastricht Central railwaystation is at 20 minutes walking distance from the venue.*

[www.msm.nl](http://www.msm.nl)



**2nd EU-regional Maastricht Symposium on the Immune Compromised Traveller (2nd EU-MICT)**  
**Monday, January 16<sup>th</sup> 2012**  
**Maastricht School of Management**

**Preliminary programme: version October 12th, 2011**

09:00 u: Welcome and registration

09:50 u: Opening. Dr. S.H. Lowe

**Theme: Immune response and advice**

Chair: Dr. S.H. Lowe, Infectious Diseases, Maastricht University Medical Center

10:00: (25+5) Immunosuppressive drugs: mechanism of action

Prof. dr. R.J.M. ten Berge, Clinical Immunology, Academic Medical Center, Amsterdam.

10:30 u (20+5) HIV infected traveller

Dr. L. Gelinck, Internal Medicine, MC Haaglanden, The Hague

10:55 u (20+5) Traveller with a dysfunctional spleen / Dutch guideline 2011

Dr. A. Meerveld-Eggink, Internal Medicine, St. Antonius Hospital, Nieuwegein

**11:20 – 11:50 u: Pause**

**Theme: Immune response and advice (continued)**

Chair: Dr. T. Jelinek, Berlin Center of Travel and Tropical Medicine, Germany

11:50 u: (20+5) Heart transplanted patient on the move,

Prof. Dr. R. Autschbach, Cardiosurgery, University Hospital Aken, Germany

12:15 u: (25+5) Immune compromised children

Dr. J.M. van Montfrans, Pediatric Immunology and Infectious Diseases,

Wilhelmina Childrens Hospital, University Medical Center Utrecht

12:45 u: (20+5) (Empiric) Antibiotic therapy in the immune compromised host going to or returning from travel.

Dr. E. Vlieghe, Internal Medicine & Tropical Medicine, Institute for Tropical Medicine,

Antwerpen and University Hospital Antwerpen, Belgium

**Theme: Vaccination and reactivation**

Chair: Dr. L. Visser, Infectious Diseases, Leiden University Medical Center

- 14:00 u:(25+5) Reactivation of (immune mediated) disease after vaccination  
Prof. Dr. C.G.M. Kallenberg, Clinical Immunology, University Medical Center Groningen
- 14:30 u (20+5) Biologicals and vaccination / Eular guidelines  
Dr. S v Assen, Internal Medicine, University Medical Center Groningen
- 14:55 u: (15+5) Hepatitis B vaccination in HIV infected patients  
Dr. T.E.M.S. de Vries-Sluijs, Infectious Diseases, Erasmus Medical Center, Rotterdam

**15:15 – 15:45 u: Pause**

**Theme: Vaccination and reactivation (continued)**

Chair: Drs. A. Oude Lashof, Infectious Diseases, Maastricht University Medical Center

- 15:45 u: (15+5) “By the way, I am using ....”: Yellow fever vaccination in immune compromised traveller  
Drs. R. Wieten, Infectious Diseases, Academic Medical Center, Amsterdam
- 16:05 u: (20+5) Working towards national vaccination guidelines for the immune compromised patient in general - with the immune compromised traveller as catalyst: the Belgian experience so far.  
Dr. F. van Gompel, Associate Professor Internal Medicine & Tropical Medicine, Institute for Tropical Medicine, Antwerpen, Belgium
- 16:30 u: (30) Quiz.  
Dr. P.J.J. van Genderen, Internal Medicine and Travel clinic, Havenziekenhuis, Rotterdam  
Dr. A. Verbon, Internal Medicine, Erasmus Medical Center, Rotterdam
- 17:00 u: Closure: Dr. S.H. Lowe
- 17:10 u: Reception:

**END**