

### Vaccines for NIDs EDCTP Stakeholder Forum Capitalising on cross cutting expertise

Dr Odile Leroy The Hague, 27 June 2013

# Today's Catalyst For Tomorrow's Vaccines



Priorities: Addressing the major public health gaps by:

- Broadening the initial priorities to **Diseases of Poverty**,
- *P. falciparum* to other Plasmodium species, and alternative or complementary approaches to the eradication programme of the BMGF,
- Developing priority criteria for selection of disease research based on a thorough mapping of the added value of EVI in vaccine development, ie addressing the main gaps and avoiding duplication,
- Extending the Initiative to include low income populations, not restricted to only African countries.



# SCOPE

### **Definitions:**

- Poverty Related Diseases
  - are the major cause as well as the consequence of considerable poverty in Developing Countries (DCs), particularly in Sub-Saharan Africa.
    - *HIV/AIDS, malaria and tuberculosis (TB)*
- Neglected Tropical Diseases/ NTDs, NIDs..
  - a group of tropical infections which are especially endemic in low-income populations in developing regions of Africa, Asia, and the Americas.
    - Cholera · Chagas disease · African Sleeping Sickness · Schistosomiasis · Guinea worm · River blindness · Leishmaniasis
- Diseases of poverty
  - diseases and health conditions that are more prevalent among the poor than among wealthier people

## EDCTP scope NIDs

wнo	EDCTP
Buruli Ulcer (Mycobacterium ulcerans infection)	
Chagas disease	
Dengue/Severe dengue	
Dracunculiasis (guinea-worm disease)	
Echinococcosis	
Foodborne trematodiases	
Human African trypanosomiasis (Sleeping sickness)	
Leishmaniasis	
Leprosy	
Lymphatic filariasis	
Onchocerciasis (River blindness)	
Rabies	
Schistosomiasis	
Soil transmitted helminthiases	
Taeniasis/Cysticercosis	
Trachoma	
Yaws (Endemic treponematoses)	

### **Diseases of Poverty**

		Drugs	Vaccine Preventive	Vaccine Therapeutics	
HIV/AIDS		$\checkmark$	<b>☑</b> 48	-	
Malaria	P. falciparum P. vivax	Ø	☑ 23	-	
Tuberculosis			☑ 45	$\overline{\mathbf{A}}$	
Kinetoplastids	Chagas' disease	$\checkmark$	0		
	Leishmaniasis	$\checkmark$	☑ 7	$\checkmark$	
	Trypanosomiasis Sleeping Sickness		☑ 0		
Diarrhoeal diseases	Rotavirus Enterotoxigenic E. coli (ETEC) Cholera Shigella Cryptosporidium Enteroaggregative E.coli (EAggEC)	- - V V -	<ul> <li>✓ 4</li> <li>✓ 11</li> <li>✓ 5</li> <li>✓ 7</li> <li>✓ -</li> <li>✓ -</li> <li>✓ -</li> </ul>	- - - -	

## **Diseases of Poverty**

		Drugs	Vaccine Preventive	Vaccine Therapeutics
Salmonella infections	Non-typhoidal Salmonella enterica (NTS) Typhoid and Paratyphoid fever (S. typhi, S. paratyphi A)	2 V	☑ - ☑ 6	-
Dengue		V	☑ 13	-
Helminths	Hookworm (Ancylostomiasis & Necatoriasis ) Strongyloidiasis & other intestinal	V	☑ 2	-
	roundworms		☑ -	-
	Lymphatic Filariasis (Elephantiasis)	Ø	☑ 2	-
	Onchocerciasis (River Blindness)		☑ 2	-
	Schistosomiasis (Bilharziasis)			

### **Diseases of Poverty**

		Drugs	Vaccine Preventive	Vaccine Therapeutics
Bacterial Pneumonia &	S. pneumoniae	-	☑ 13	-
Meningitis	N. Meningitides	-	<b>-</b>	-
Leprosy			<b>1</b>	-
Buruli Ulcer		V	<b>☑</b> 2	-
Trachoma		-	☑ 4	-
Rheumatic fever		-	<b>I</b> -	-
Measles		-	<b>V</b> -	-
Universal Flu			<b>V</b> -	
Rabies			<ul> <li>✓ -</li> </ul>	

# NEGLECTED TROPICAL DISEASES



# NIDs pre-requisites for Vaccine Approach

- Mapping
  - Burden of diseases
  - Public health importance
  - Analysis/modeling of vaccination impact in global context for disease control
- Feasibility
  - Antigen discovery
  - Production development
  - Clinical development

### Example: Leishmaniasis Burden of disease



- 2 million new cases (1.5 million cases of cutaneous leishmaniasis and 500 000 of visceral leishmaniasis) occur annually, with about 12 million people currently infected.
- Geographical Distribution
  - Endemic in 88 countries, 72 of which are developing countries:
  - 90% of all visceral leishmaniasis cases occur in Bangladesh, Brazil, India, Nepal and Sudan;
  - 90% of mucocutaneous leishmaniasis occurs in Bolivia, Brazil and Peru;
  - 90% of cutaneous leishmaniasis cases occur in Afghanistan, Brazil, Iran, Peru, Saudi Arabia and Syria.

# Public health importance

• Leishmaniasis is a poverty-related disease.

- associated with malnutrition, displacement,
- poor housing, illiteracy,
- gender discrimination,
- weakness of the immune system
- and lack of resources.
- Leishmaniasis is also linked to environmental changes
  - deforestation, building of dams,
  - new irrigation schemes and urbanization,
  - migration of non-immune people to endemic areas.
  - a serious impediment to socioeconomic development.
  - high morbidity but low mortality

### The Sudanese Epidemic: 1985 - 1987

#### **EUROPEAN VACCINE INITIATIVE**







>100,000 deaths (out of a population of approx. 300,000)



### EVI Workshop On The Development And Future Manufacture Of Leishmania Vaccines In India

*Capitalising on cross cutting expertise* (Univ York, IDRI, VIRBAC, MOLOGEN, NIAID, Hilleman Laboratory, THSTI-India)

York, 8 April 2013

# Leish Vaccine status

- Canine Vaccines:
  - Leishmune®
    - affinity purified glycoproteic fraction of L. donovani promastigotes, fucose-mannose-ligand (FML) + saponin
  - CaniLeish (Virbac)
    - L. infantum ES products + QA-21
  - LeishTec (Hertepe Calier Saude Animal)
    - L. donovani A2 + saponin

### Leishmania Vaccine Portfolio

	Platform	Product	PI/Affiliation	Ag ID & Formulation Assessment	Proof-of- Concept	Stage Preclinical Process Development	Clinical Development
NIAID	Recombinant Protein	N/A	Pood IDPI	x	•		
		Leish-111F	גפפט, וסאו				x
		3 New Ags	Abeijon, Detectogen Inc.	x	x		
	Nanoparticle	Nano-encapsulated LACK	Ghoroghchian, Vindico Nanobiotech Inc.		x		
		PLGA-conjugated TSA/TryP&P4	McMahon-Pratt, L2 Diagnostics		x		
	Whole Parasite	Photo-inactivated live attn. <i>L.</i> amazonensis	Chuang, Rosaline Franklin Univ.		x		
	Prime/Boost	DNA/MVA-multiple Ags	Wilson, Univ. of Iowa	x	x		
	Strategy	DNA/Protein- multiple Ags	Soong, Univ. of Texas Med. BR Galveston	x	x		
EU	Prime/Boost Strategy	AdCh63/MVA	KAYE, Univ of York				x
	DNA	DNA	LEISHDNAVAX Mologen Gemany	x	x		

# A vaccine is feasible

- Single life cycle stage responsible for disease maintenance
- No 'antigenic variation' detected to date
- Targeting of virulence determinants may not be essential for effective cell-mediated immunity
- Sub clinical infection common

➢ evidence from HIV reactivation

evidence from active disease surveillance (seropositivity, molecular diagnosis)

- Natural resistance to re-infection after clinical cure (Leishmanisation)
- Epidemiological data on cross-protection

# COMMON PRIORITIES TO ALL NTDS 'VACCINES



- Conduct research on pathogen biology and pathogen-host interactions
- Develop standardised assays and reagents...
- Identify and validate correlates of protection...
- Develop systematic criteria for prioritising and down-selecting
- Standardise clinical trial end points to enable comparison among trials
- Develop robust, accessible process development capacity

# INYVAX RULES Adjuvants





## Safety Assessment

- **INYVAX Rules** 
  - Safety Assessment in pre-licensure vaccine clinical trials (TB, Malaria)
  - Template protocol for clinical trials investigating vaccines-Focus on safety elements. Vaccine. 2013 Mar 11. pii: S0264-410X
  - Roadmap for the international collaborative epidemiologic monitoring of safety and effectiveness of new high priority vaccines. Vaccine. 2013 May 21. pii: S0264-410

# Infrastructure priorities?

- Clinical trial capacity in endemic regions
  - Liaise with other clinical platforms? (malaria, TB)
  - Liaise with EDCTP Network of Excellence
- Develop shared go/no-go decision criteria to guide decisions
  - Create a structured process to help guide and manage a portfolio
  - Create a NTDs vaccine funder group to harmonisation of decision making between donors
  - Advocacy and lobbying for innovative financing



### Advocacy for Global Coordination in NTDs vaccines

- PDPS :
  - Sabin Institute,
  - International Vaccine Institute (IVI),
  - Hillemann Laboratory (Merck MSD & Welcome Trust)
  - DNDI
  - EVI
- Research Councils
- US NIH/NLAID
- *WHO*
- *EC*
- Pharmaceutial Industry
- Biotechs

# EUROPEAN VACCINE INITIATIVE Advocacy for Global Coordination in NIDS vaccines

- Call for a NTDs vaccine funder group
  - Limited resources
  - Urgent need to define the objectives and the priorities
    - Eg Chagas diseases? Is a vaccine needed? (Perspectives of vaccination in Chagas disease revisited. Erney Plessmann Camargo. Mem. Inst. Oswaldo Cruz vol.104 supl.1 Rio de Janeiro July 2009)
      - Are we going to have a vaccine against Chagas disease in 20 years' time?
         NO
      - To whom would a Chagas vaccine be destined? Which population would be the target for a Chagas vaccine?
        - » In the 1980s, in Brazil alone, there were 25 million people at risk of infection
        - » In 2009, There is no defined population at risk of infection
        - » in Brazil, we can foresee the success of these initiatives but, just in case, it would do no harm to have a vaccine.
  - Learn from malaria/TB/HIV vaccine experience



# Many thanks for your attention