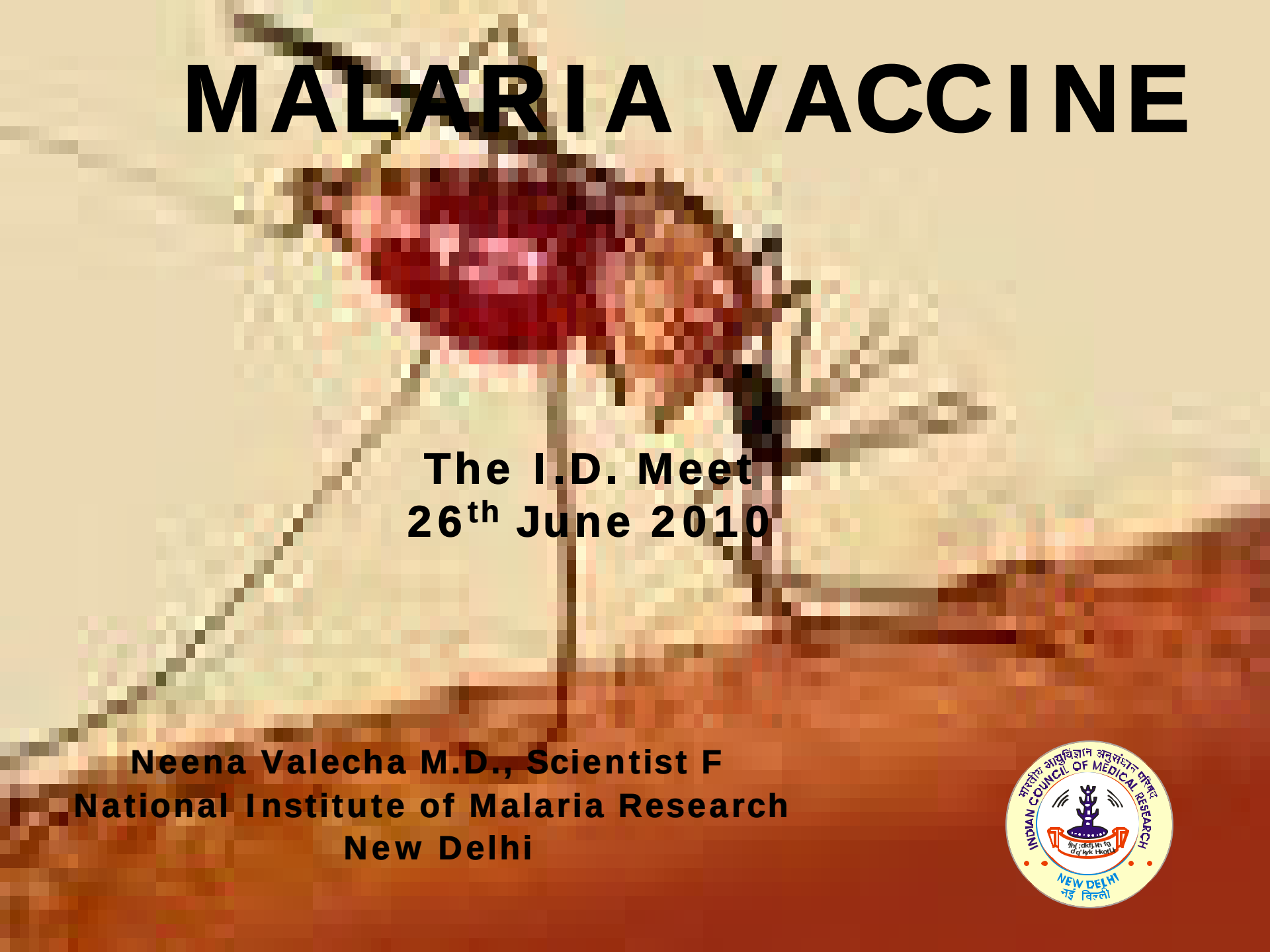
MALARIA VACCINE



The I.D. Meet
26th June 2010

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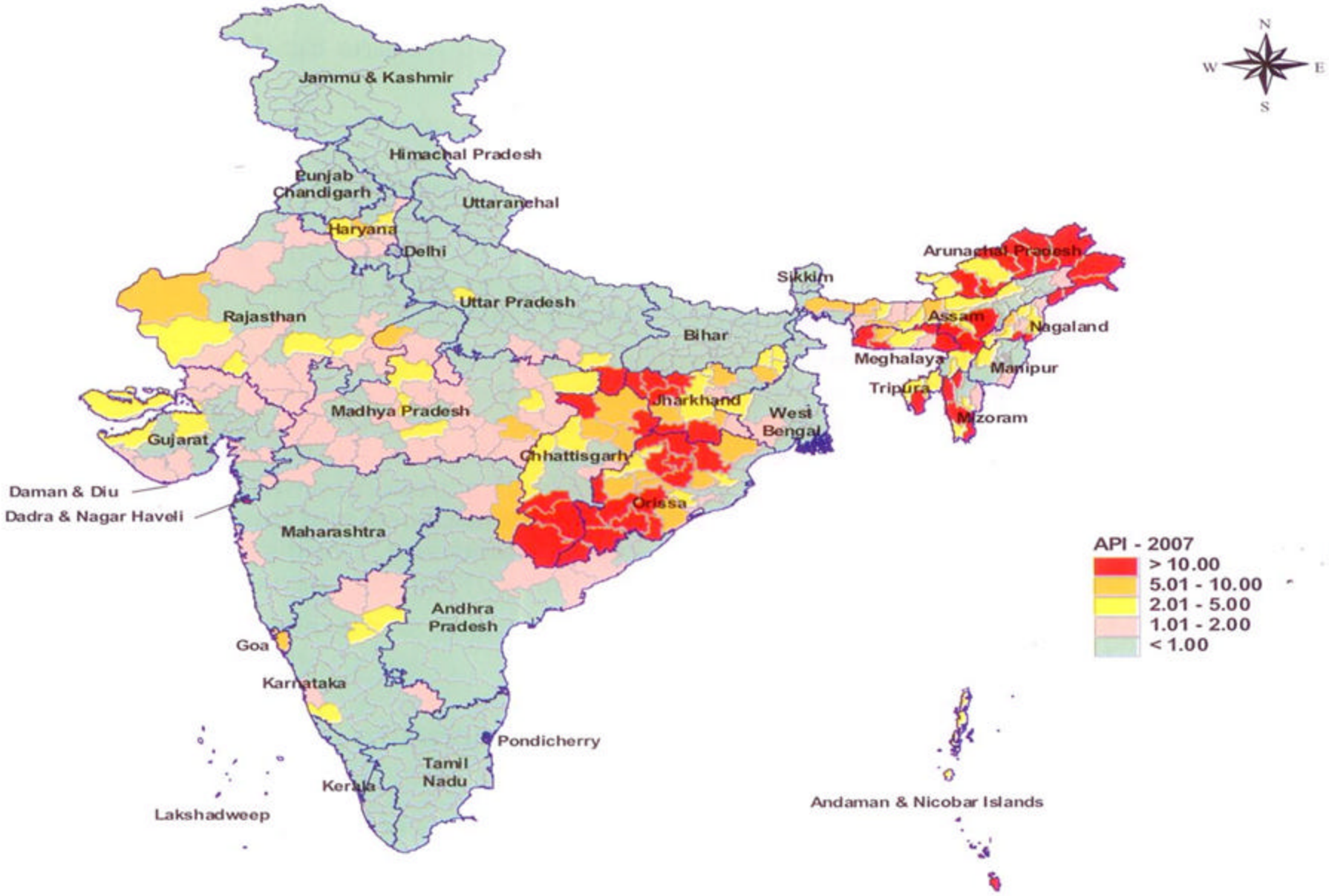
MALARIA IN INDIA (2007)

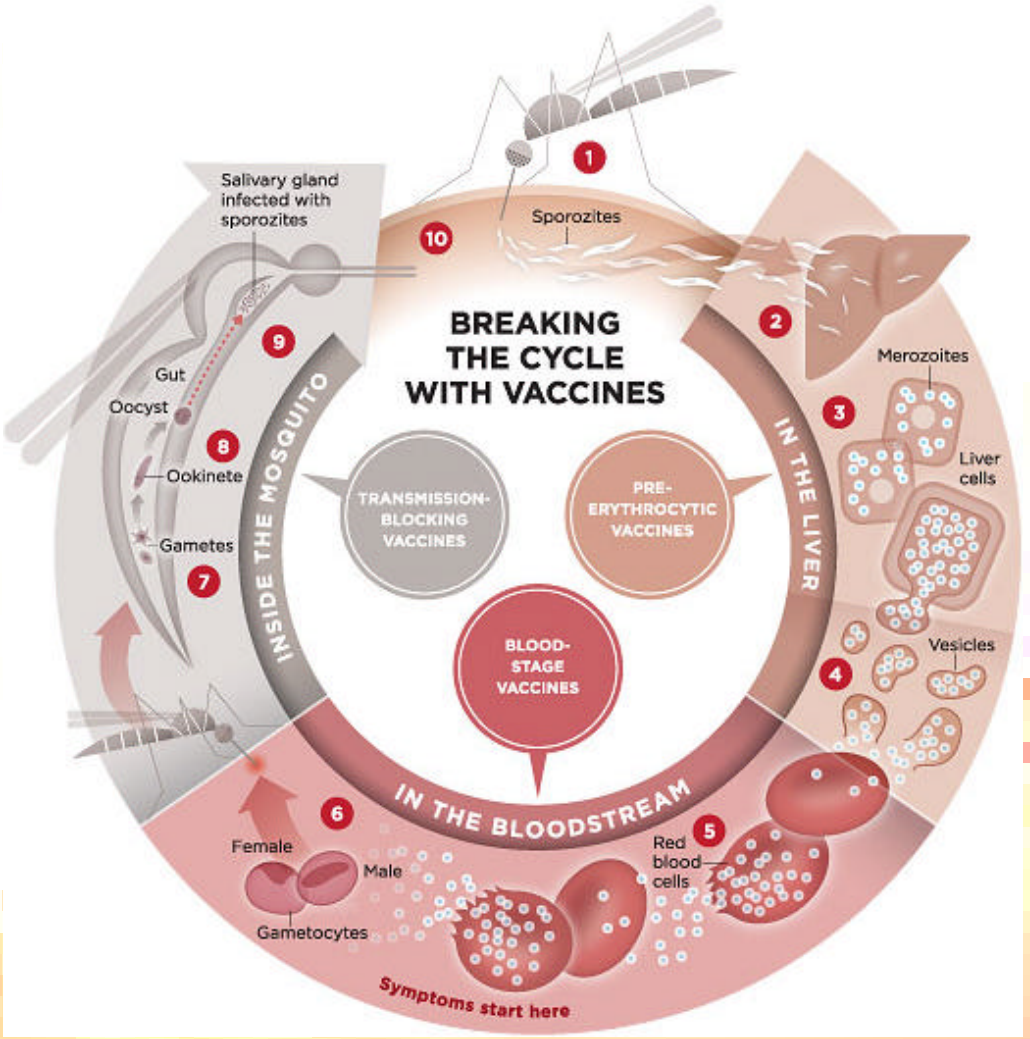


VACCINES : BASIS FOR THE DEVELOPMENT AND CHALLENGES

- Immunity develops naturally following frequent exposure to infection – antibodies to blood stage antigens
- Protective immunity by immunization with

  irradiated sporozoites – T-cells against liver stage antigens considered as effectors
- Precise nature of immunity responses (antigen specificity and magnitude, effector mechanisms) that reduce or prevent malaria infection are still not known
- Lack of animal models

MALARIA VACCINE DEVELOPMENT STRATEGIES ARE STAGE SPECIFIC



Source: www.path.org/vaccineresources/details.

MALARIA VACCINE TARGETS

- **Pre-erythrocytic stage**
  - **To stop the parasite lifecycle from progressing from the sporozoite or liver stage**
- **Erythrocytic stage**
  - **To reduce infection rather than to eliminate it, in order to protect against clinical and particularly severe disease**
- **Transmission blocking**
  - **To stop fertilization in mosquito gut and development into infective sporozoites**

MALARIA VACCINE RESEARCH

- Identification of vaccine candidates
- Parasite genome sequencing has advanced the search and several antigens have been identified
  - Pre-erythrocytic stage – CSP, SSP-2, TRAP, LSA-1, LSA-3, Exp-1 etc.
  - Erythrocytic stage – several MSP1-based antigens, MSP-2, MSP-3, MSP-5, MSP-9, AMA-1, GLURP, Pf EMP-1, EBA-175, PvDBP etc.
  - Transmission blocking – Pfs230, pfs48/45, Pfs25, Pfs28
- Selection of adjuvants
- Expression systems
- Toxicity in animals
- Preparation of antigens of international standards following GMP guidelines for clinical trials – Industrial partners
- Clinical trials

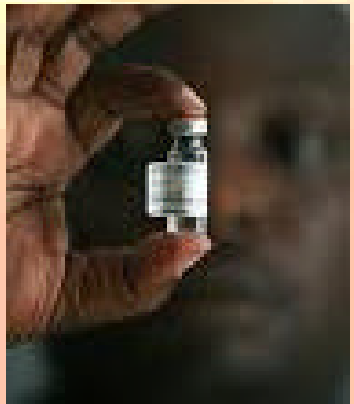
SELECTED MALARIA VACCINE TRIALS

Stage	Main target	Vaccine	Antigen	Phase	Location	Developer (Refs)
Pre-erythrocytic	Sporozoites	RTS,S– AS01/AS02	CSP	Ib/IIb	Multiple African sites	GSK[4,5]
	Hepatocytes	FP9/MVA, ME-TRAP	ME-TRAP	IIb	Kenya	University of Oxford[6,8]
	Hepatocytes	Simian adenovirus/MVA	ME-TRAP	Ia/Ib	UK	University of Oxford
	Hepatocytes	LSA-1–AS02	LSA-1	Ia/IIa	USA	WRAIR[15]
	Hepatocytes	AdHu35	CSP	Ia	USA	Crucell[11]
Blood stage	Merozoites	FMP1–AS02	$MSP\text{-}1_{42}$	Ib/IIb	Kenya/Mali	WRAIR[16]
	Merozoites	AMA1–AS02	AMA1	Ia/IIa	USA	WRAIR[17]
	Merozoites	$MSP1_{42}$–Alum, bi-allelic	MSP-1	Ia	USA	NIH[18]
	Merozoites	$AMA1\text{–}FVO_{[25\text{–}545]}$	AMA1	Ia	Netherlands	BPRC
	Merozoites	GMZ2	GLURP/MSP-3	Ia	Germany	SSI[19]
	Merozoites	PfCP2.9	$AMA1/MSP\text{-}1_{19}$	Ia	China	Wanxing[20]
Multi-stage	Sporozoites, hepatocytes, merozoites	FP9/MVA polyprotein	Six antigens	IIa	UK	University of Oxford[9]
	Sporozoites, merozoites	PEV3a	AMA1/CSP	IIa	UK	Pevion (Thompson *et al.*, unpublished data)
	Sporozoites, merozoites	Adenovirus 5	AMA1/CSP	I/IIa	USA	US Navy

VACCINES : PRESENT STATUS

RTS,S – Most advanced stage. Several trials conduced in many endemic countries in Africa

- Longest follow up was for 18 months in children. Reduced clinical malaria by 35% and severe malaria by 49% . In another study in children (5-17 months) reduced the risk of malaria episodes by 53% over 8-month followup period
- In infants in a follow up of 3 months, infection reduced by 65%. First malaria vaccine trial to establish proof-of-concept of efficacy in infants.
- Multi country and multi-centric Phase III trial launched in May 2009 in Africa in 16000 infants & children to determine efficacy and confirm safety.
- Expected to apply to submit RTS,S vaccine for approval to regulatory authorities in 2011



RESEARCH IN INDIA: VACCINES

- Identifying candidate antigens, isolation & studying their immunity profile in the population
- TWO candidate vaccines developed by ICGEB:
- JAIVAC – 1 PfMSP1-19 and PfF2 (EMVI & DBT funded) – Ready for Phase Ib
- ICGEB/BBIL PvRII (MMV)
- Bharat Biotech Ltd – clinical grade large scale production of vaccine candidates following international Good Manufacturing Practice (GMP) standards for further studies

THREE FACTORS MOST INFLUENCE FUTURE SUCCESS OF MALARIA VACCINE

Product Profile

Product profile has the strongest influence on demand

***P. falciparum* component and one year duration are important minimum requirements**

Funding

Donor funding can drive by making it available

Public markets will rely on sustainable funding to developing counties

Private markets likely to lag public markets since they do not "turn on" until higher efficacy level reached

Unlikely to be achieved in first generation vaccine

Influencer support

Support of WHO, academics, and standards – setting organizations are key to vaccine's introduction and credibility

Countries and donors both rely on key opinion leaders and WHO recommendations in deciding on which interventions to support

Thanks

National Institute of Malaria Research