DEPARTMENT OF HEALTH
RESEARCH INSTITUTE FOR TROPICAL MEDICINE

Perspectives on Rabies mAb Development: Example from Academic experience

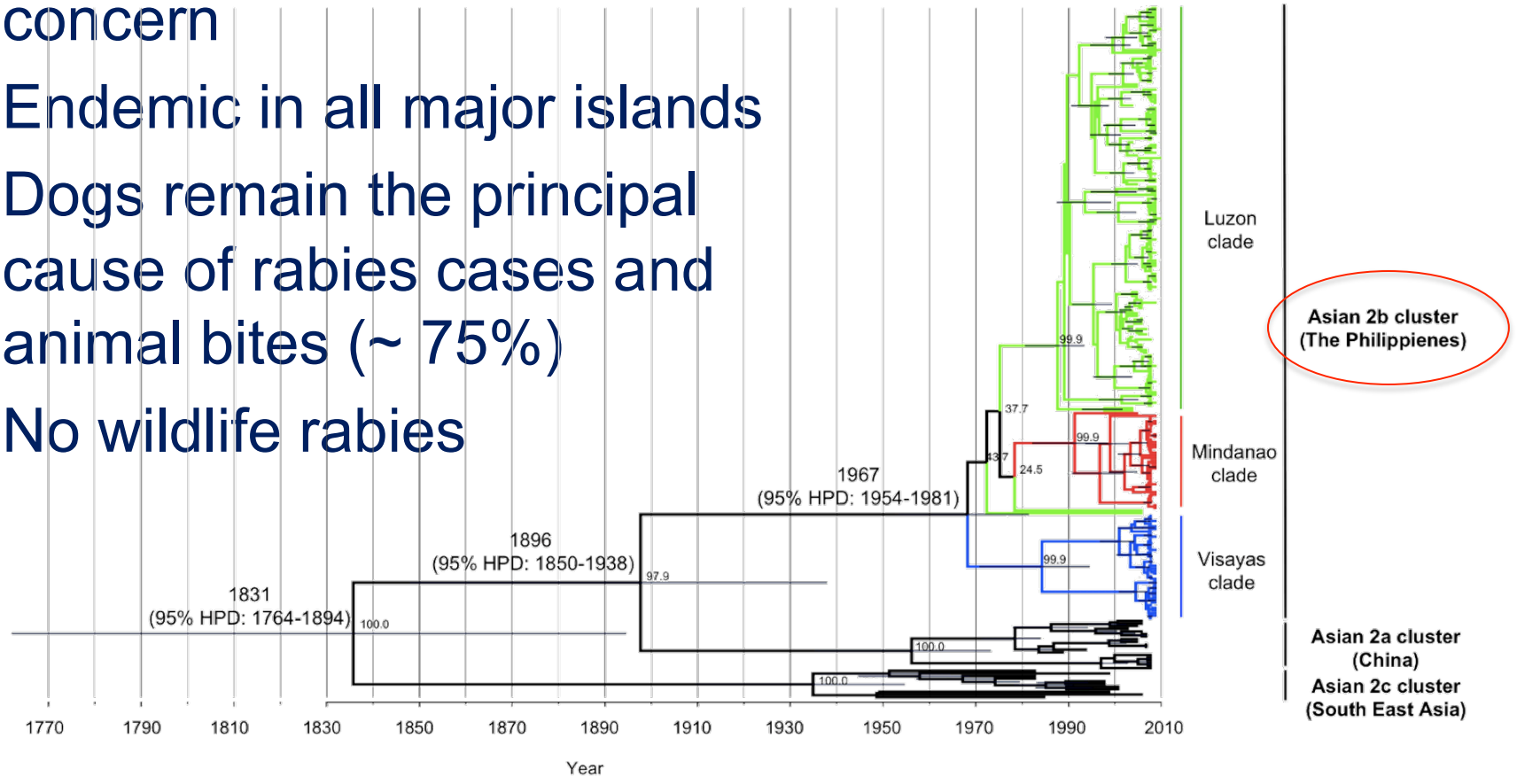
Beatriz P. Quiambao, M.D.
Research Institute for Tropical Medicine
Muntinlupa, Philippines

Disclosure

- Dr Quiambao has received research grants from Sanofi, GSK, Pfizer, Novartis, SK Chemicals and is on the speaker's bureau of Sanofi
- She has also received travel grants for attendance to meetings and presentation of research results from Sanofi, GSK and Novartis

Rabies in the Philippines

- Significant public health concern
- Endemic in all major islands
- Dogs remain the principal cause of rabies cases and animal bites (~ 75%)
- No wildlife rabies



Saito M et al, PLoS NTD 2013

Rabies in the Philippines

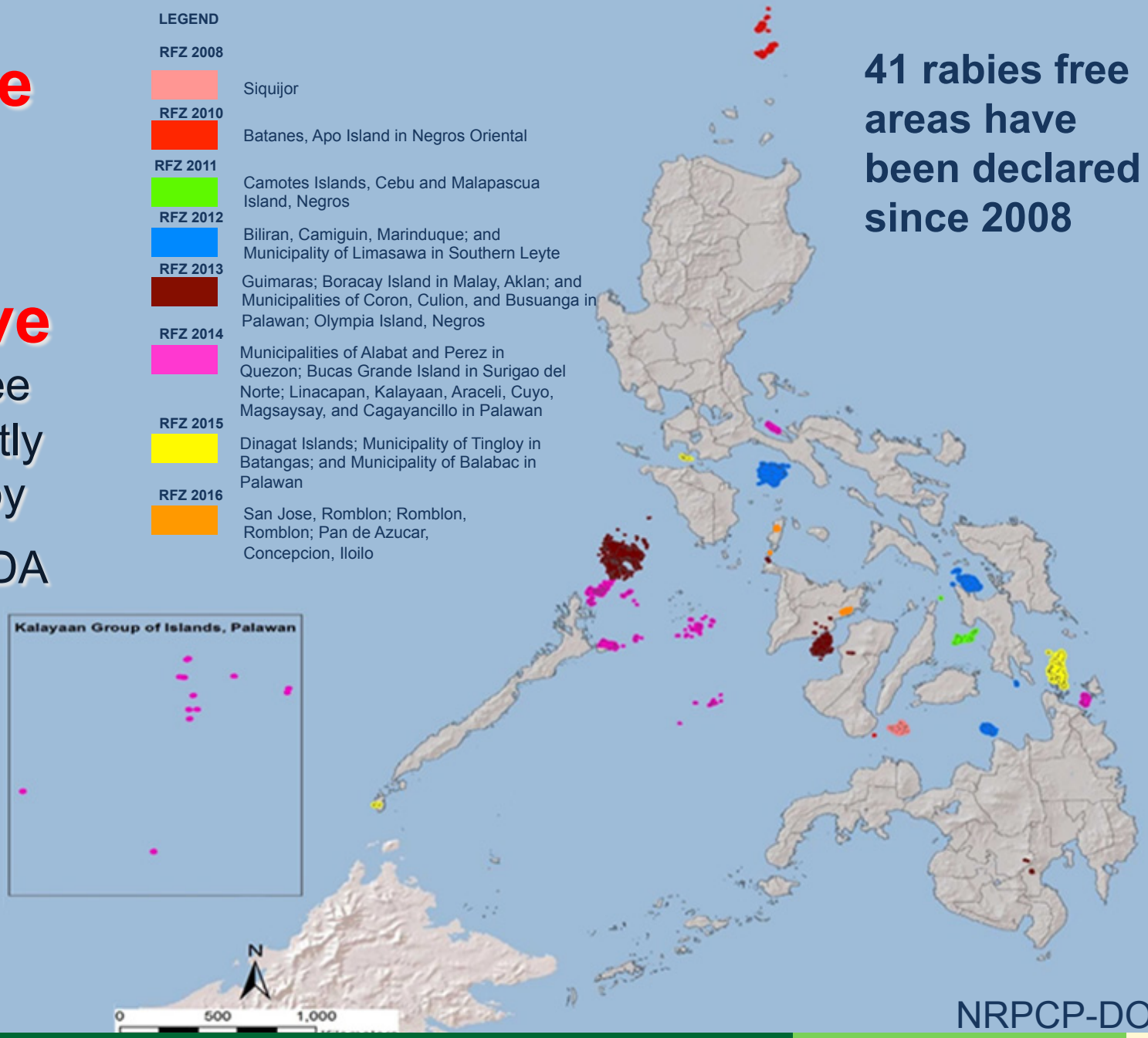
- National Rabies Prevention and Control Program is a multi-agency program headed by the Department of Agriculture in collaboration with the Departments of Health, Education and Interior and Local Government
- Rabies Act of 2007
  - Dog vaccination and registration
  - Stray dog control
  - Information/education
  - Pre-exposure andPost-exposure prophylaxis
  - Responsible pet ownership

Disease Free Zone Initiative

Rabies Free Areas Jointly Declared by

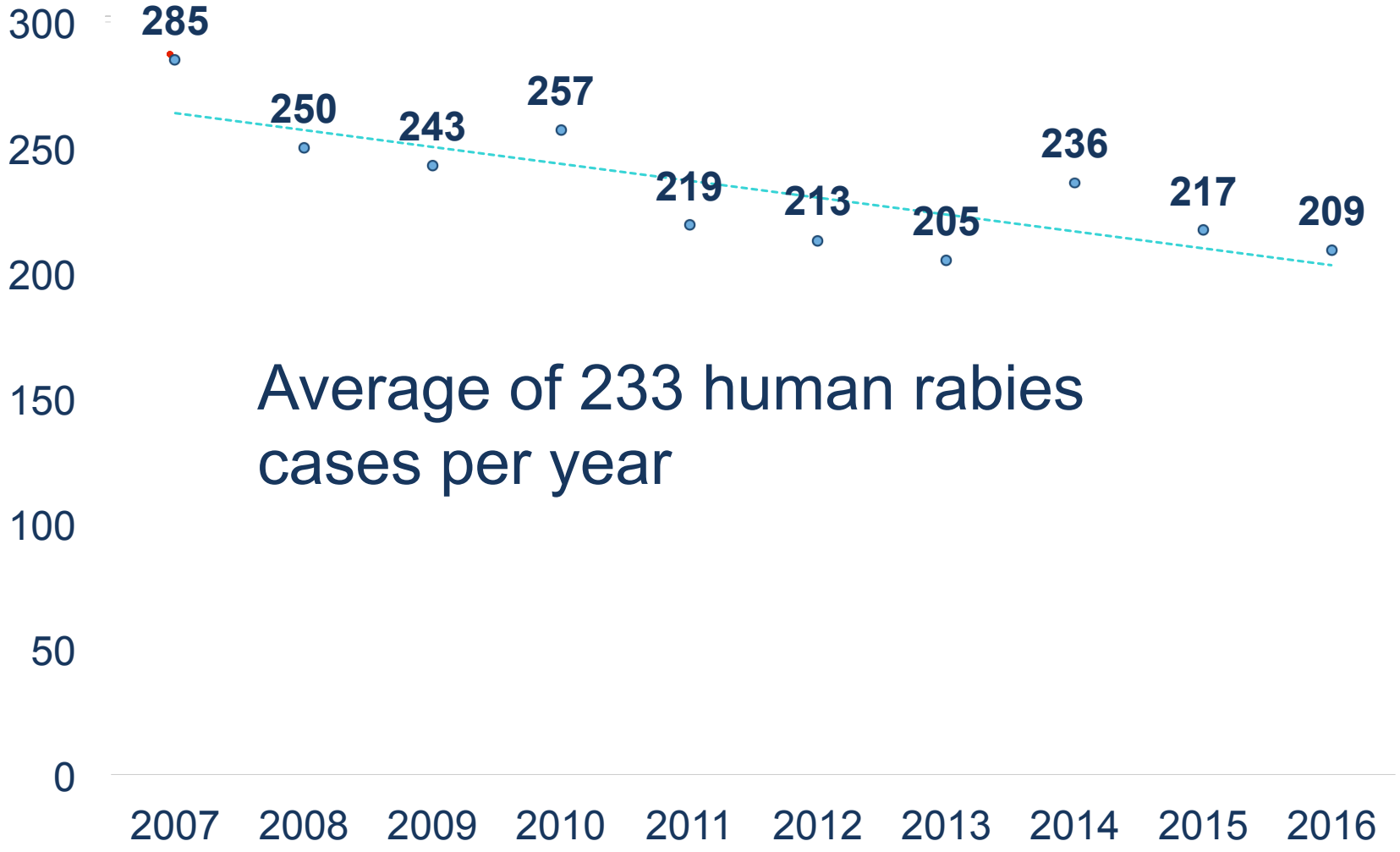
DOH and DA

41 rabies free areas have been declared since 2008

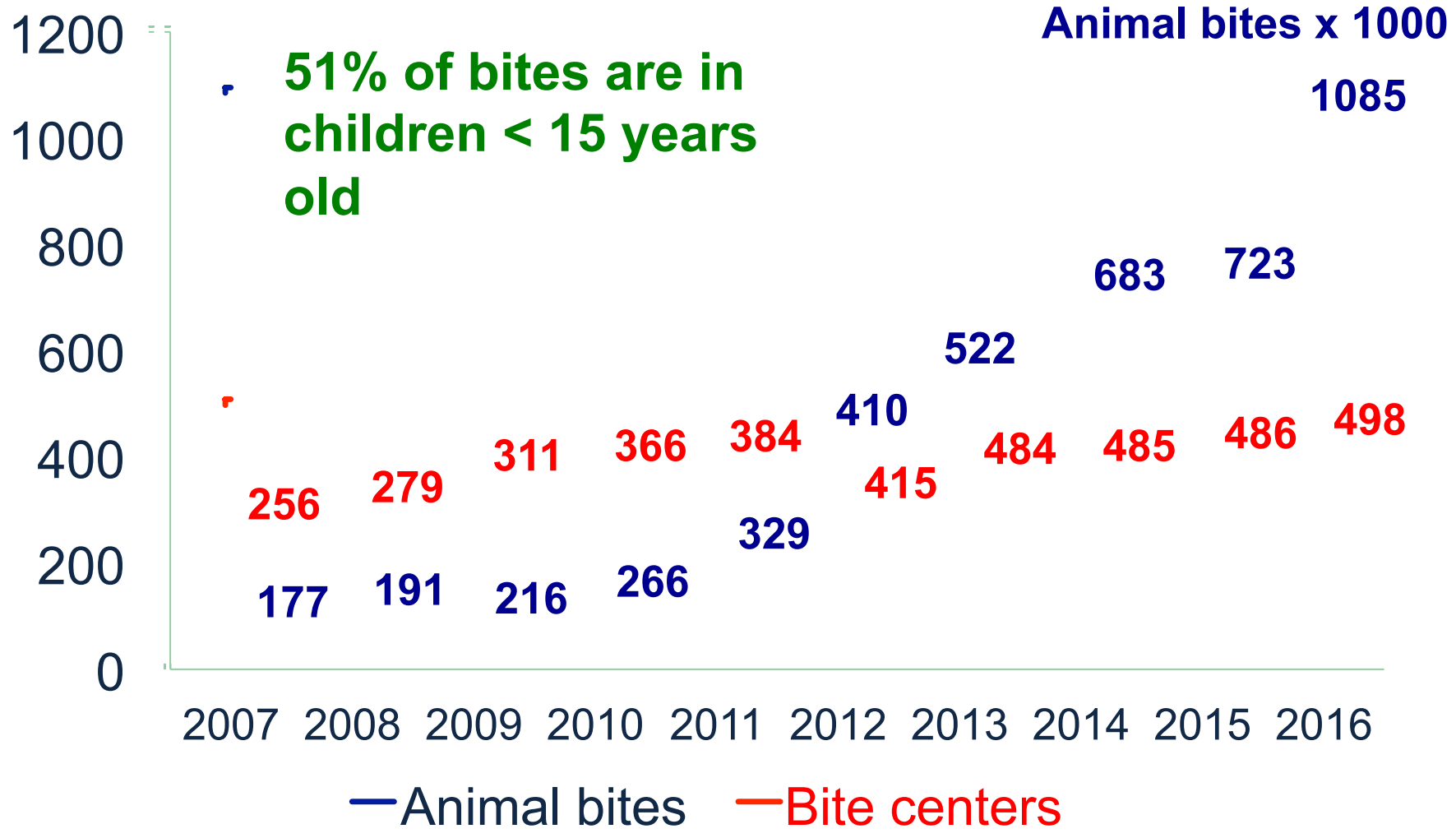


NRPCP-DOH

Human Rabies Cases (2007-2016)



Animal Bites and Bite Centers (2007-2016)



Research Institute for Tropical Medicine (RITM)

- Research arm of the Philippine Department of Health for infectious and tropical diseases
- ISO 9001 2015 accredited facility
- 50-bed hospital dedicated to patients with infectious diseases, particularly EREID
- 14 National Reference Laboratories (Dengue, Measles and other exanthems, Polio and other Enteroviruses, Influenza, Bacterial enteric diseases, Antimicrobial resistance, Mycology, TB and other mycobacteria, Malaria and other parasites, EREID, Confirmatory testing for blood donors and blood units, Rotavirus)
- Storage/distribution center for EPI vaccines; manufacturer of PCAV
- Center for Training on Infectious, Tropical and Dermatological Diseases

RITM: Rabies Capabilities

- One of 2 major government animal bite treatment centers
- Referral center for management of human rabies cases
- Rabies Laboratory for confirmation of animal and human rabies
- Research center for rabies
- Accredited training center for rabies and animal bite management and for laboratory Dx of rabies

Animal Bite Management

- Follows the WHO recommendations for PEP with some modifications
- Thai Red Cross Intradermal regimen (2-2-2-0-2) is used

Category	Management	Modification
I	Wash exposed area No rabies vaccine or RIG +/- PrEP	
II	Wash exposed area Rabies vaccine Observation of biting animal	Includes wounds which are induced to bleed
III	Wash exposed area Rabies vaccine and RIG Observation of biting animal	All bites on head and neck area are treated as Category III

Animal Bites*

* New bites

Year	Category I	Category II	Category III	Total	Category III Monthly Ave
2015	249	8857	7673	16779	639
2016	305	13287	8383	21975	698
2017 Q1	249	3767	3145	7161	1048

~ 40% of bites are in children

Animal Bites

Year	Follow-ups
2015	18,943
2016	30,662
2017 Q1-2	23,451

RITM animal bite registry

Animal Bite Management

- Use of RIG

Year	No. Category III	% given vaccine only	% given RIG + vaccine
2015	7673	33.4 %	66.6 %
2016	8383	31.5 %	56.9 %
2017 Q1	3145	17.2 %	72.9 %

- 92.5 % given as ERIG
- Since 2017, ERIG given for free

Animal Bite Management

- Completion rate of vaccination
  - 2015 – 56%; 2016 – 73%; 2017 – 59%
- Reasons for non-completion of vaccination
  - Cost
  - Biting animal is healthy
  - Time constraint (working/school)
  - Unable to come on clinic days
  - Long line at bite center
  - Fear of injection
  - Didn't understand importance of timely completion of vaccination

Human Rabies Management

- Average of 2-3 human rabies cases per month
  - 75 % males
  - 28 % children < 15 y/o
- Clinically diagnosed
- Surveillance system in place
- Supportive care given

PEP Failures

Age/ Sex	Bite	Vaccine	RIG	Incuba-tion Pd	Remarks
2.5/M	Category II; Multiple abrasions; LE	PVRV IM x 4	None	19 days	
4/F	Category III; Multiple; Severe; shoulder, neck, back	PVRV ID x 3	ERIG infiltrated and IM	19 days	Malnourished; PEP within 2 hrs; ERIG diluted 2 fold
6/M	Category III; Single laceration on lip	PVRV ID x 1→ PVRV IM x 2	ERIG infiltrated and IM	25 days	2 days delay of PEP
6/F	Category III; Multiple; back, periorbital area	PVRV IM x 4	ERIG infiltrated and IM	24 days	Vaccine on day of bite, ERIG next day
47/F	Category III; nose	PVRV ID x 3	ERIG infiltrated and IM	19 days	Vaccine and ERIG on day of bite

Laboratory Diagnosis

- Network of 20 rabies laboratories
  - Department of Agriculture
    - 18 Regional/Provincial Animal Disease Diagnostic Laboratories
    - 1 Central Animal Laboratory (PAHC)
  - Department of Health - RITM
- 19/20 labs can perform FAT; 1 performs DME
- RITM is the only laboratory performing human rabies Dx

RITM Diagnostic Capabilities

- Can do - FAT, DRIT, MIT, PCR, ELISA, RFFIT
- Currently doing: FAT, PCR, ELISA; DRIT

Year	No. Samples tested using FAT	% positive
2015	219	32.4%
2016	217	35.5 %
2017 (Jan-May)	108	43.5 %

Rabies mAb Study

- Randomized, single-blind, controlled, monocentric trial in 2008
- Objectives: safety and rabies virus neutralizing activity
- Monoclonal cocktail CL184
- Simulated rabies PEP
- 48 healthy subjects aged 5 to < 18 y/o
- 2 Groups: CL184 + PVRV vs HRIG + PVRV
- Similar immunogenicity profile
- More pain in HRIG group

THANK YOU