SAFETY AND EFFICACY OF USING ORAL RABIES VACCINES IN DOGS FROM FIELD STUDIES IN THAILAND

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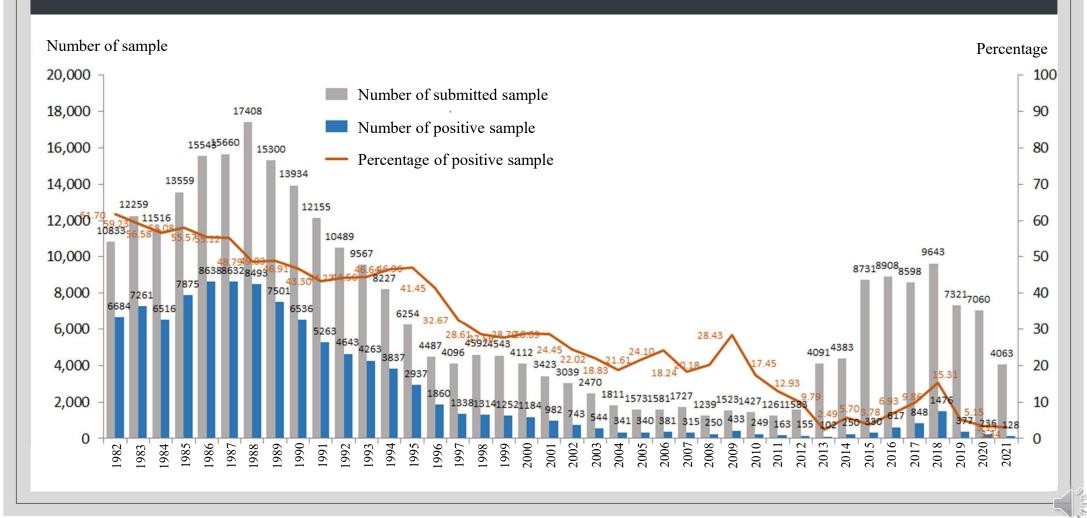




Outline

- Animal rabies situation and free-roaming dogs in Thailand
- Overall framework of oral rabies vaccine study in Thailand and the field trial studies in free-roaming dogs
- Safety of oral rabies vaccines





Data source: Thai Rabies Net, Department of Livestock Development, Thailand



Framework for oral rabies vaccine (ORVs) study in Thailand

Bait acceptance study

Feasibility and Effectiveness study

Phase 1

Phase 2

Phase 3

Phase 4

Antibody response study

Nationwide feasibility and antibody response study



OIE terrestrial 2018, Chapter 2.1.17:

"Apart from mass parenteral vaccination (carried out concurrently or sequentially), the use of oral vaccination, especially in free-roaming and inaccessible dogs, taking into account structure and accessibility of the dog population, should represent a complementary measure for the improvement of the overall vaccination coverage in dog rabies control programmes."



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Egg-flavored and fishmeal baits









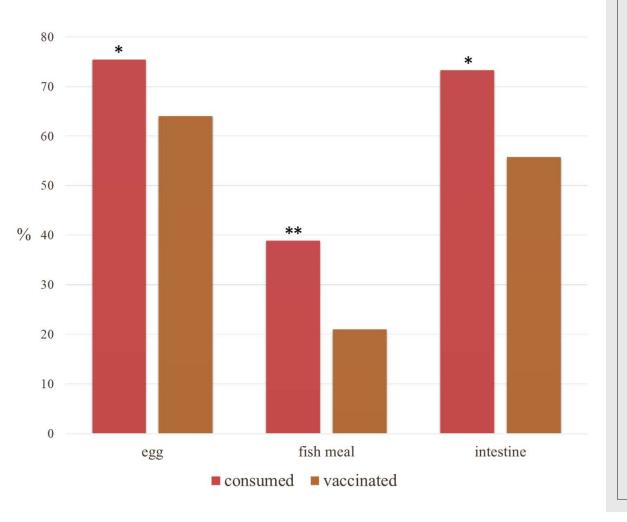
Intestine baits (in collagen cases)

Phase 1 Bait acceptance study

- Free-roaming dogs in Kamphaeng Saen campus of the Kasetsart University, and the surrounding temples in Nakhon Pathom province
- Three different bait types
 - 206 fishmeal baits (brown)
 - 196 egg-flavored baits (yellow)
 - 206 boiled pig intestine in collagen cases



The percentage of dogs consuming the offered bait type and were subsequently considered vaccinated



Phase 1 Bait acceptance study





- Assessment
 - Bait acceptance: direct oral contact
 - Consumption and handling
 - Vaccinated: dyed-water was released in the oral cavity of the dog

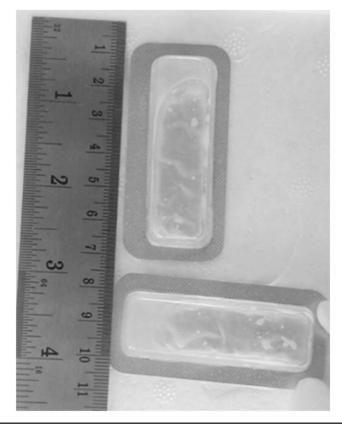
Dog shelter in Taptan, Uthai-Thani province, Thailand

Phase 2 Antibody response study

- ORV: Live Attenuated rabies virus strain SPBN GASGAS (Ceva Santé Animale, Germany)
- 46 young dogs (26 males and 20 females) at the Bangkok Metropolitan Administration's dog shelter in Taptan, Uthai-Thani province



D1	D3	D5	D7	D9	D11	D14	D15	D18	D20	D21	D23	D25	D27	D29	D31	D34	D36	D37	D39	D41	D43	D45	D45
A.	•••	A	\$	A	4	A.	4	1	N. Comments	В	•••	В	В	В	В	В	В	•••	•••	•••	C	C	C
D2	D4	D6 ,	D8	D10	D12	D13	D16	D17	D19	D22	D24	D26	D28	D30	D32	D33	D35	D38	D40	D42	D44		
B	•••	A.	E		P	B	a	B	B	₽ ₽	•••	B	B	₽ ₽	B	₽	B	•••	•••	•••	C		





B Placebo (PBS) withBait 7 dogs

RABITEC D/DOA 10 dogs

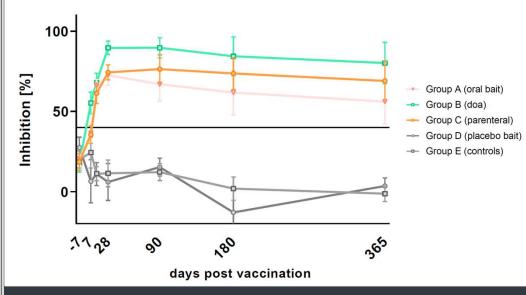
RABITEC D/Bait/Blister 15 dogs

Bayovac/SC 10 dogs

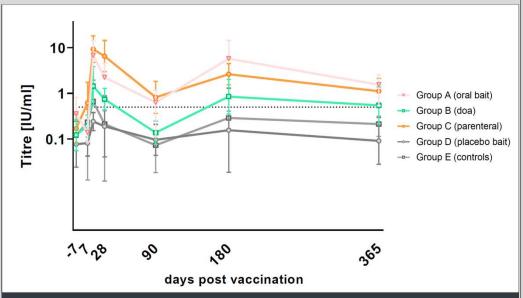
C Control 4 dogs

Cage allocation of experimental dogs

Boiled pig intestine bait and vaccine sachets



 $Rabies\ binding\ antibody\ (rVBA)$ ELISA Mean percent inhibition with standard deviation



Rabies virus neutralizing antibodies (rVNA)
Rapid Fluorescent Focus Inhibition Test (RFFIT)
Geometric mean titer with standard deviation









Egg baits and intestine baits

Phase 3 Feasibility and Effectiveness study

- SPBN GASGAS vaccine (Ceva Innovation Center GmbH, Dessau in Germany)
- Egg bait (commercial), pig intestine bait (local made), and Egg+ bait (cat liquid snack pasted on egg bait)
- 5 study areas
 - Choeng Noen municipality, Rayong
 - Phe municipality, Rayong
 - Cha Um municipality, Phetchaburi
 - Thung Song municipality, Nakhonsrithammarat
 - Tapraya, Sa Kaeo



ORV campaign



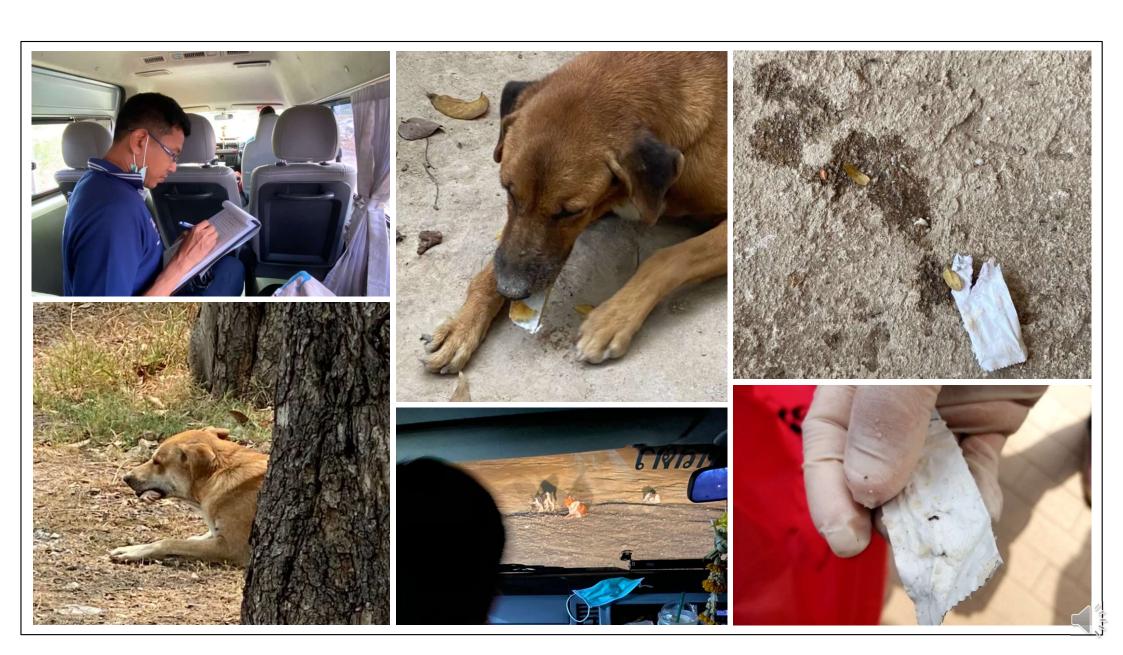












Percentage of dogs interested in bait offered, dogs that chewed very shorty ($<10~\rm s$), swallowed the sachet and considered vaccinated per bait type offered

Bait Type	No. of Dogs Offered a Vaccine Bait	No. of Dogs Interested in Bait (% [n/N]) *	Sachet Swallowed (% [n/N])	Chewing Time (<10 s) (% [<i>n</i> /N])	Vaccinated ** (% [n/N])
Intestine	1314	92.9 (1209/1302)	80.0 (929/1161)	42.5 (480/1130)	82.0 (995/1214)
Egg	338	87.3 (288/330)	32.2 (88/273)	24.0 (58/242)	83.6 (255/305)
Egg+	278	92.8 (256/276)	26.5 (65/245)	24.6 (60/244)	87.0 (235/270)
total	1930	91.9 (1753/1908)	64.4 (1082/1679)	37.0 (598/1616)	83.0 (1485/1789)

Oral rabies vaccination coverage in the free-roaming dog population in 5 study areas

Study Area	Nr. of Sites	Nr of Inaccessible Dogs	Dogs Approached (% [n/N])	Dogs Accepting the Bait & Successfully Vaccinated (% [m/M])	Vaccination Coverage Achieved (%) *
Choen Noen	59	488	77.5 (378/488)	88.1 (310/352)	68.2
Cha Um	59	789	71.7 (566/789)	79.5 (387/487)	57.0
Phe	112	564	86.5 (488/564)	81.9 (381/465)	70.9
Thong Song	77	456	87.7 (400/456)	81.2 (315/388)	71.2
Tapraya	31	147	66.7 (98/147)	94.9 (92/97)	63.2
Total	338	2444	79.0 (1930/2444)	83.0 (1485/1789)	65.6

^{*} vaccination coverage achieved (%) was calculated as follows: 100 (n/N * m/M).

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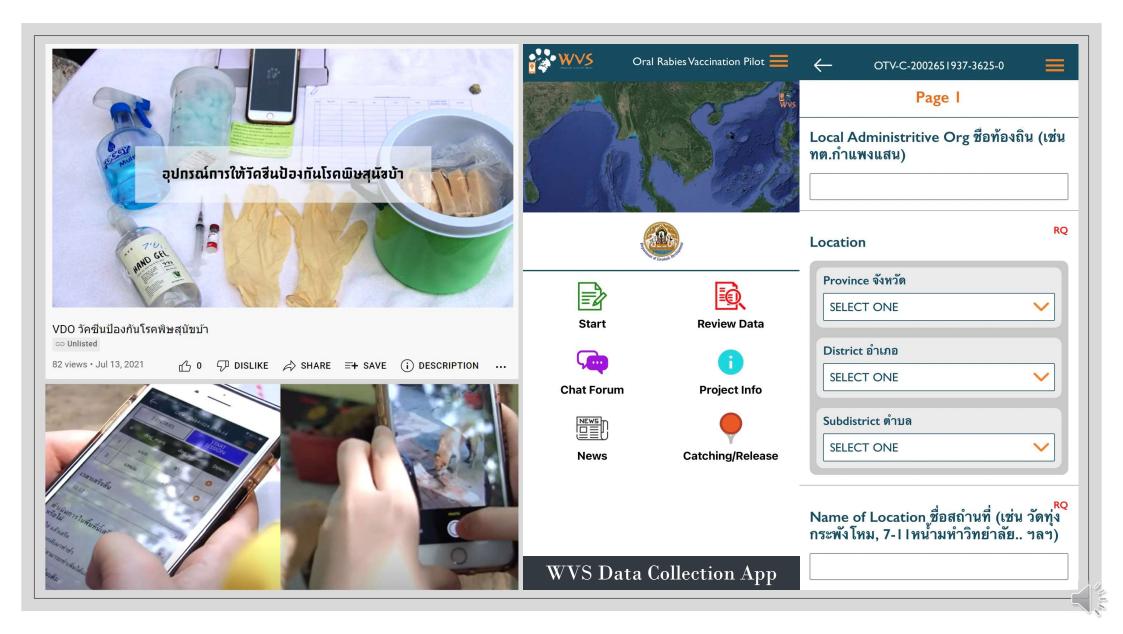




Phase 4 Nationwide feasibility and antibody response study

- SPBN GASGAS vaccine (Ceva Innovation Center GmbH, Dessau in Germany)
- Egg bait and Egg+ bait (cat liquid snack pasted on egg bait)
- 12 study areas in all region of Thailand
- Serological monitoring following ORV in 5 study areas

12 study areas



Percentage of bait consumption and subsequently considered vaccinated

Bait type	Number of dogs offered a vaccine bait	% of bait consumption (dog chewed vaccine bait)	% of vaccinated (sachet perforation)	
Egg	1540 (84.6%)	79.9% (1231 / 1540)	93.4% (1115 / 1194)	
Egg+	280 (15.4%)	72.5% (203 / 280)	96.9% (185 / 191)	
Total	1820	78.8% (1434 / 1820)	93.9% (1300 / 1385)	

Egg baits (79.9%) were more often chewed than Egg+ baits (72.5%) (p = 0.006). There was no significant difference between bait types for the sachet perforation (p = 0.089).

Percentage of bait consumption and subsequently considered vaccinated

Ownership status	Number of dogs offered a vaccine bait	% of bait consumption (dog chewed vaccine bait)	% of vaccinated (sachet perforation)
Ownerless dogs	1379 (75.8%)	81.9% (1130 / 1379)	93.0% (1020 / 1097)
Owned dogs	338 (18.6%)	70.1% (237 / 338)	98.2% (222 / 226)
Unidentified dogs	103 (5.7%)	65.1% (67 / 103)	93.6% (58 / 62)
Total	1820	78.8% (1434 / 1820)	93.9% (1300 / 1434)

Ownerless dogs (81.9%) significantly consumed bait more than the other two dogs (p < 0.0001).

Owned dogs (98.2%) were significantly vaccinated more than the other two dogs (p = 0.011).

Serology study

Day 0

Day 28

Day 90

Serum collection

Serum collection

Serum collection

Oral rabies vaccination







Serology study

Day 0

Day 28

Day 90

Oral rabies vaccination

Serum collection

Serum collection

Serum collection

ELISA test (Bio-Rad Platelia® Rabies II ELISA)

at National Institute of Animal Health (NIAH), Department of Livestock Development, Thailand

A serum titer of ≥ 0.5 EU/ml was considered as protective level (positive)

Serology study

Day 0

Day 28

Day 90

NEGATIVE

>>> POSITIVE

>>>

POSITIVE

Successful vaccination

25 dogs (75.76%) from 33 naïve dogs

Dogaha	vo atavisti as	Successful	n voluo	
Dog cha.	racteristics	Yes (%)	No (%)	p-value
A 000	Adult	17 (77.3%)	5 (22.7%)	1.000
Age	Juvenile	7 (77.8%)	2 (22.2%)	1.000
Gender	Female	16 (72.7%)	6 (27.3%)	0.697
Gender	Male	9 (81.8%)	2 (18.2)	0.687
Oran analain atatus	Ownerless	18 (69.2%)	8 (30.8%)	0.154
Ownership status	Owned	7 (100%)	0	0.134
Social status of dog	With other dogs	22 (78.6%)	6 (21.4%)	0.572
during vaccination	Single	3 (60%)	2 (40%)	0.573

VII.

	Fastans	Successful	n volus	
	Factors	Yes (%)	No (%)	p-value
Doit type	Egg	22 (73.3%)	8 (26.7%)	0.560
Bait type	Egg+	3 (100%)	0	0.300
Charring times	More than or equal 10 times	24 (77.4%)	7 (22.6%)	0.431
Chewing times	Less than 10 times	1 (50%)	1 (50%)	0.431
Number of bait	One bait	25 (80.6%)	6 (19.4%)	0.053
consumed	Two baits	0	2 (100%)	0.033
Vassimatan	Study team	21 (72.4%)	8 (27.6%)	0.550
Vaccinator	Dog feeder & Local staff	4 (100%)	0	0.550

VIII.









Safety of ORV

- No vaccine-induced adverse effect in captive dogs for 1-year observation period
- No adverse effects in dogs or humans after ORV campaign









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Conclusion

- Oral rabies vaccine improved vaccine coverage in free-roaming dog population in Thailand.
- Well cooperation from the community is needed to increase accessibility of the free-roaming dogs.
- The application of ORV SPBN GASGAS vaccine strain for free-roaming dogs in Thailand offers a safe and efficacious.

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Federal Research Institute for Animal Health

 ${\bf Acknowledgement}$