OFFLU avian influenza virus characterisation meeting
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HPAI virus evolution and vaccination in Indonesia

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Current Situation

Poultry Production Type

Sector 1

Industrial integrated system; high level biosecurity

Sector 2

Semi-vertical integrated system; Moderate level biosecurity

Sector 3

Small commercial poultry production; low level biosecurity

Sector 4

Village or backyard poultry; no biosecurity, mix farming

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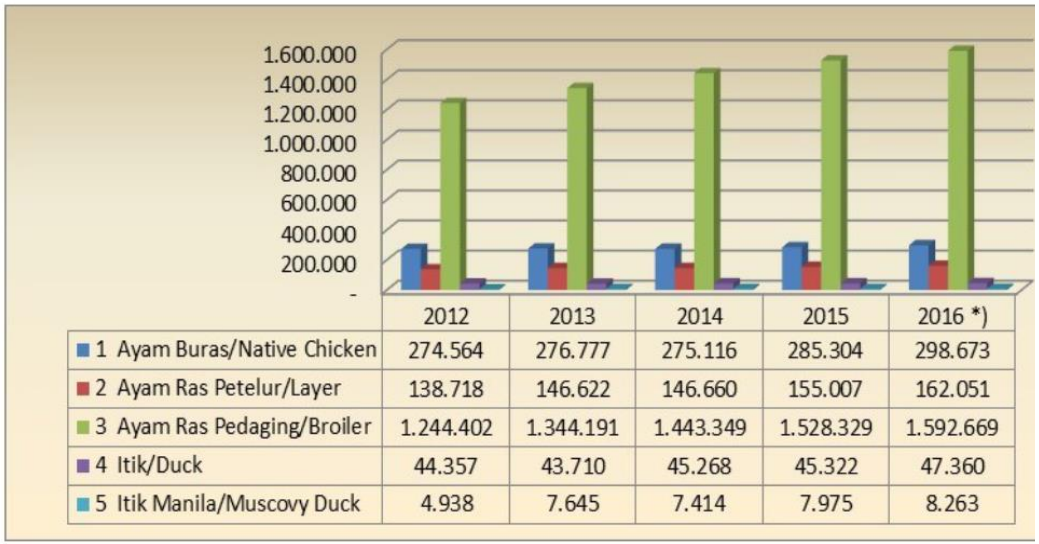
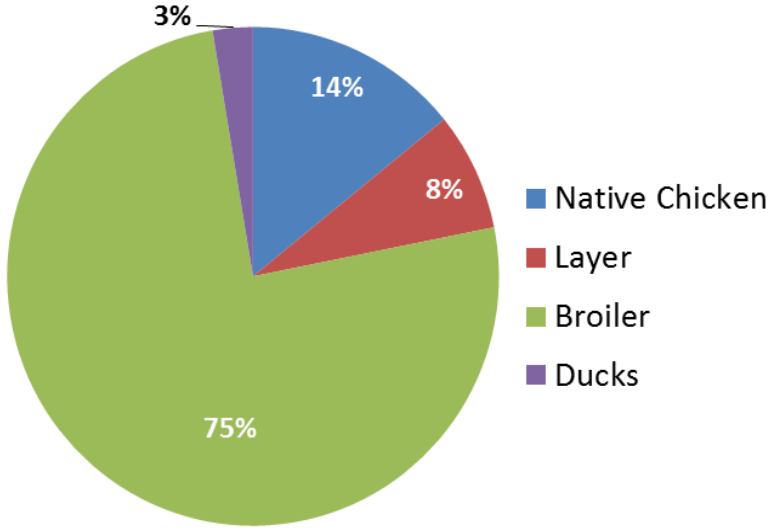
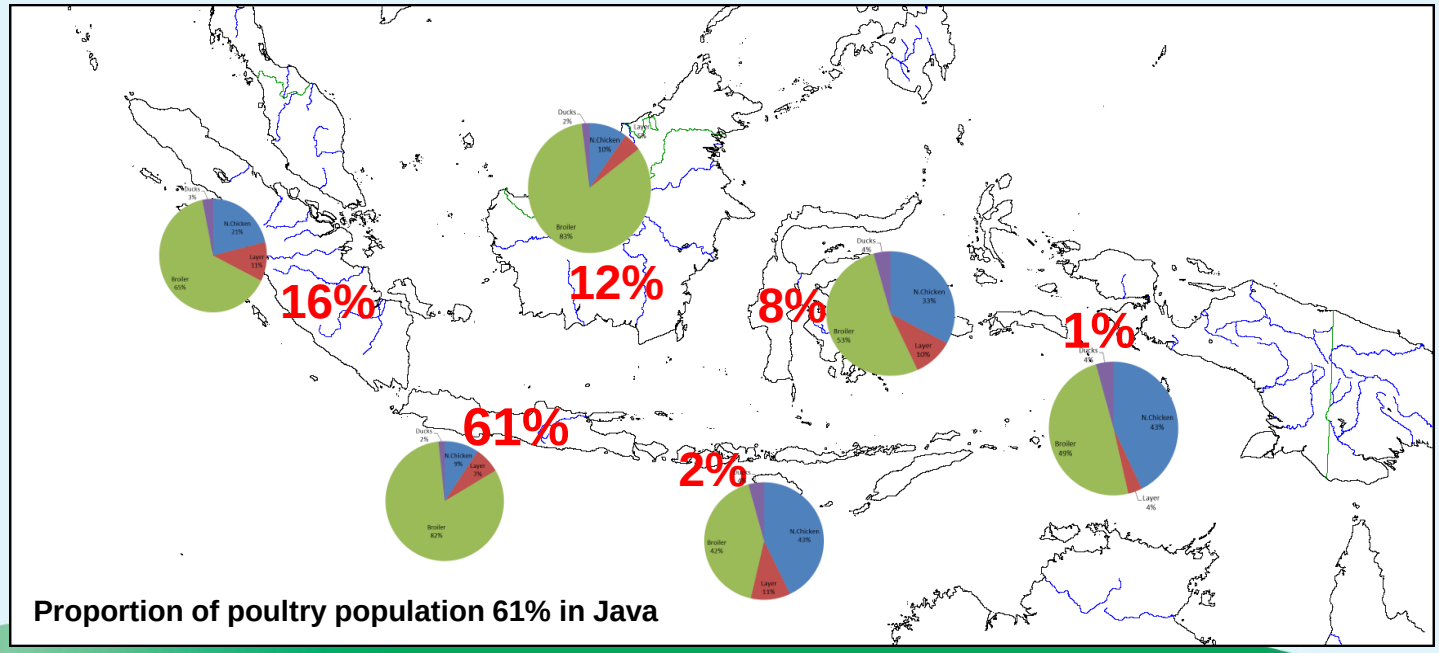
Population of poultry 2012-2016 (000 bird)



	2012	2013	2014	2015	2016 *)
1 Ayam Buras/Native Chicken	274.564	276.777	275.116	285.304	298.673
2 Ayam Ras Petelur/Layer	138.718	146.622	146.660	155.007	162.051
3 Ayam Ras Pedaging/Broiler	1.244.402	1.344.191	1.443.349	1.528.329	1.592.669
4 Itik/Duck	44.357	43.710	45.268	45.322	47.360
5 Itik Manila/Muscovy Duck	4.938	7.645	7.414	7.975	8.263

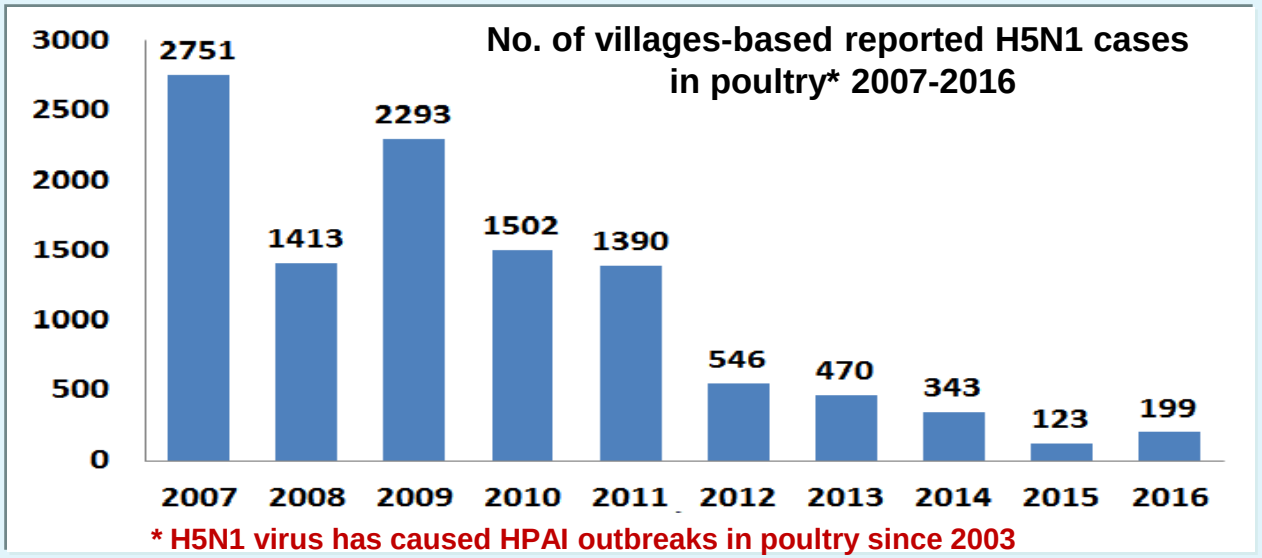


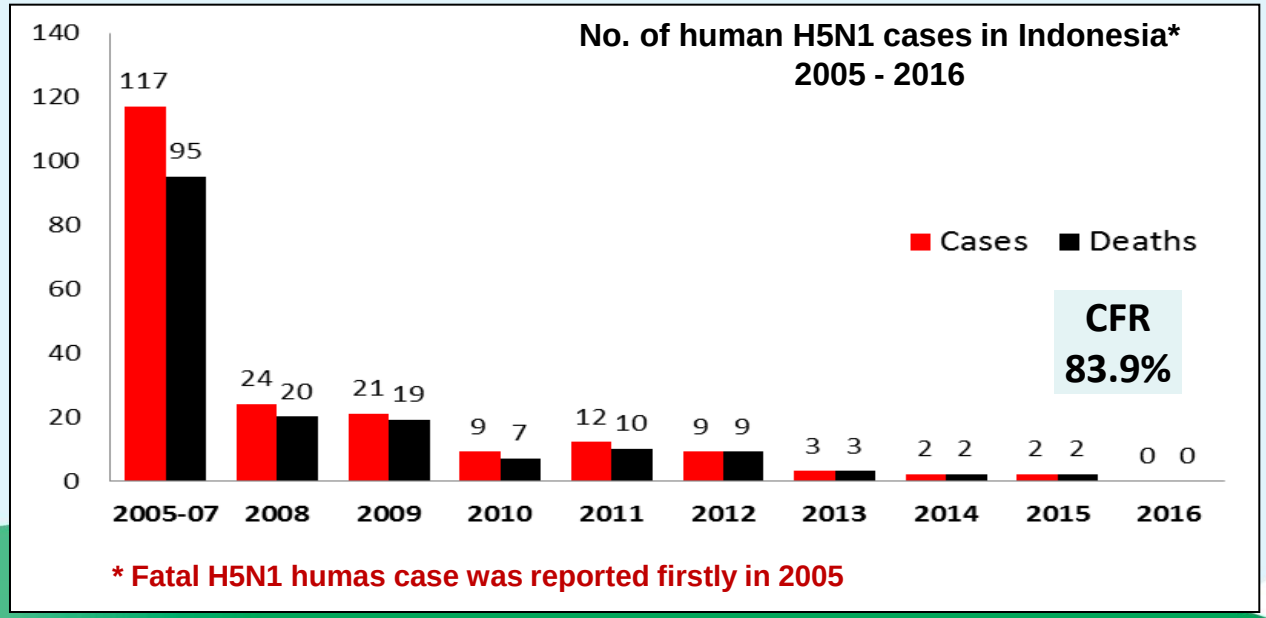


Proportion of poultry population 61% in Java

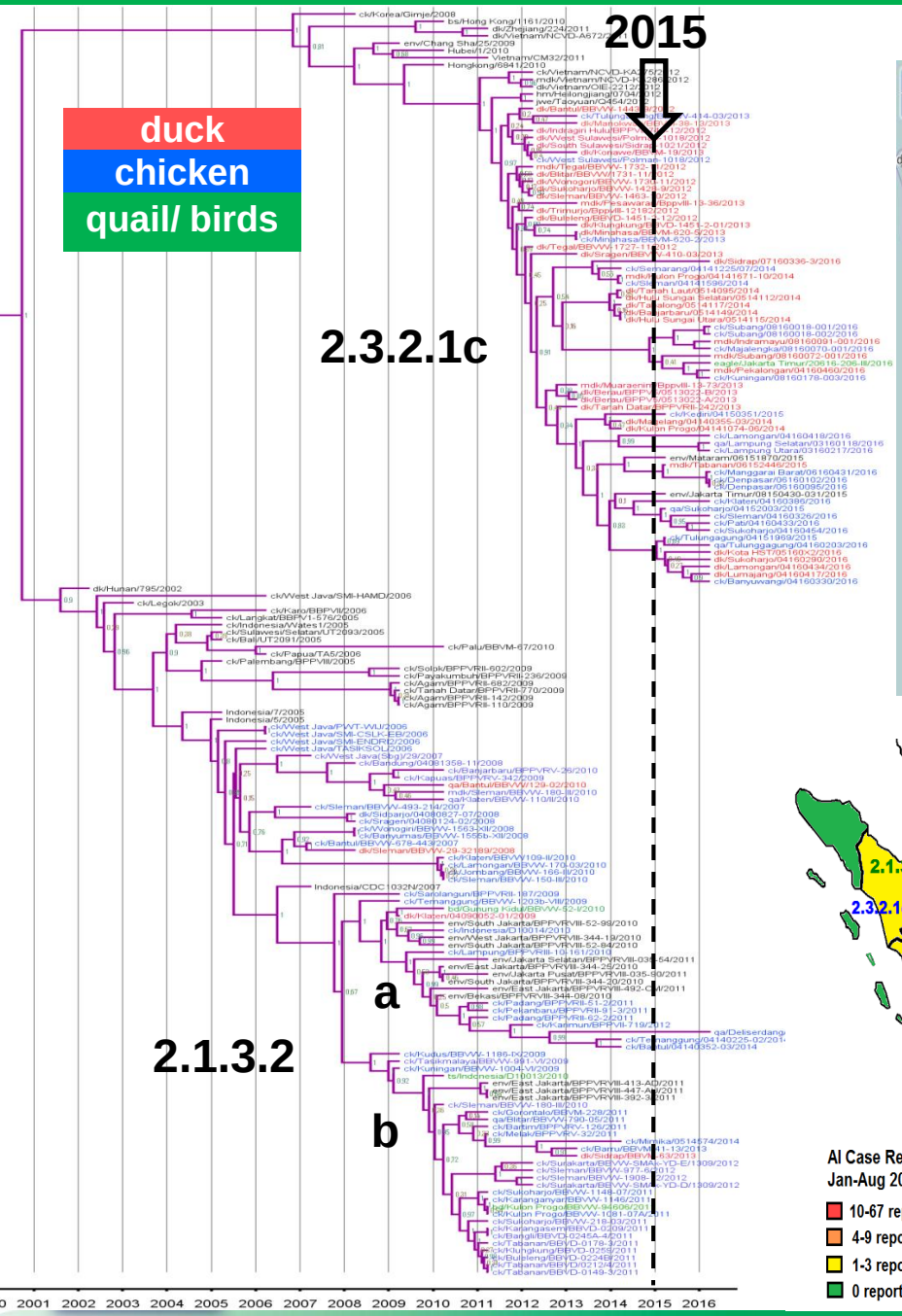
Source: Directorate General Livestock and Animal Health Services (DGLAHS), Ministry of Agriculture Indonesia

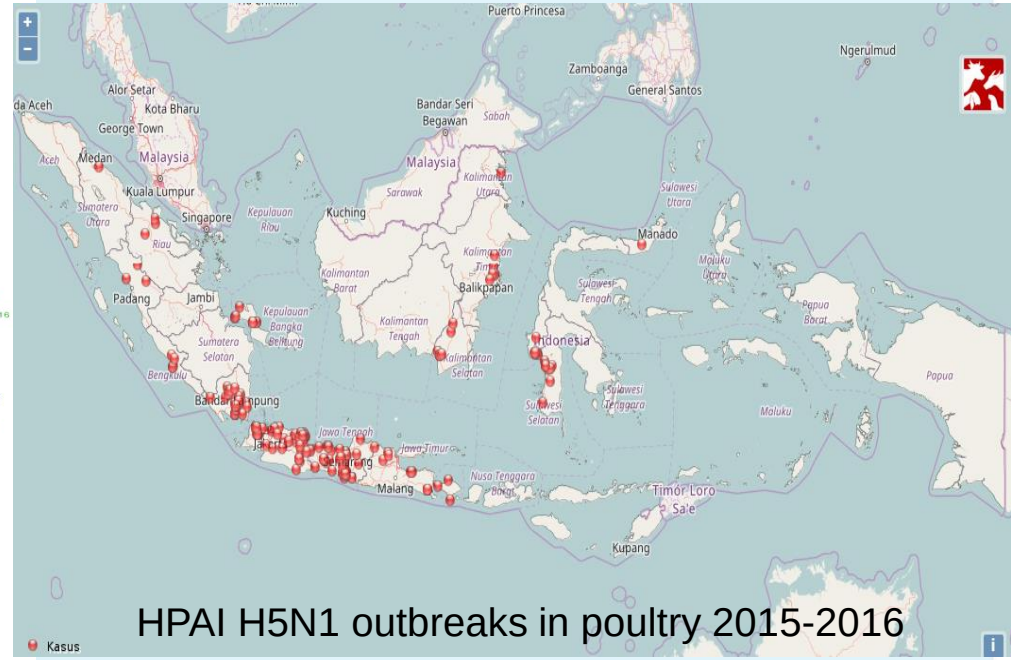
HPAI H5N1 cases in Indonesia (poultry and humans)



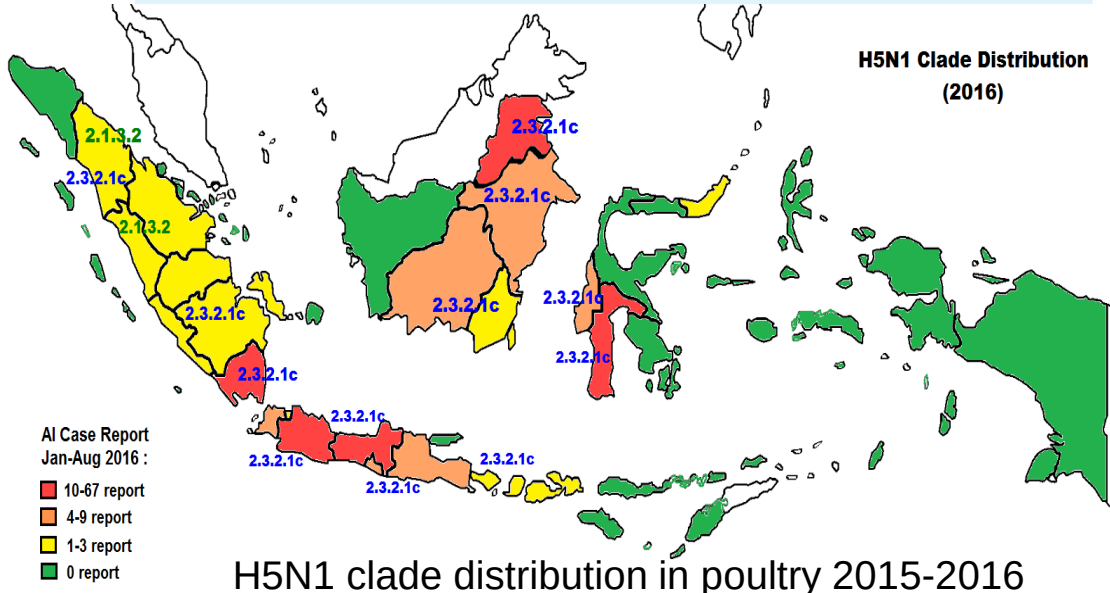


HPAI H5N1 virus evolution in Indonesia





HPAI H5N1 outbreaks in poultry 2015-2016



H5N1 clade distribution in poultry 2015-2016

Circulating HPAI viruses and vaccine in use (2012-now)

HPAI Subtype : H5N1

Clade 2.1.3.2 (group “a” and group “b”):

- Major circulating virus between 2008 and 2012
- No more detected in poultry since 2015, except in Sumatra

Clade 2.3.2.1 (group “c”):

- Detected in late 2012 causing high mortality in ducks
- Recently detected in various species including ducks, native chickens, layers, broilers, quails, pigeons, eagle
- Reassortant viruses with HA-NA-NP-PB1(2.3.2.1c) + PB2-M-NS (2.1.3.2)
- Become dominant and seems to replace Clade 2.1.3.2 viruses

HPAI H5N1 seed vaccine in use

Clade 2.1.3.2 (local strains):

- A/chicken/West Java/PWT-WIJ/2006
- A/chicken/West Java/Nagrak(30)/2007
- A/chicken/Rumtang/Tangerang-019/2009

Clade 2.3.2.1 (local strain):

- A/duck/Sukoharjo/BBVW-1428-09/2012

Vaccines are produced locally by the Indonesian companies:

1 Government:

- Pusat Veterinaria Farma

5 Private Industries:

- Vaksindo Satwa Nusantara
- Medion Farma Jaya
- Sanbio Laboratories
- Caprifarmindo Laboratories
- Shigeta-IPB

Current Vaccination Strategy

Vaccination Strategies

Phase 2004-2006:

- **Mass vaccination** in mid 2004:
  - 300 M doses available
  - Inactivated H5N1 local isolate (Legok/03-based vaccine seed)
  - **Free of charge**: backyard and small farmers (sector 4) of **any species**
- Mass vaccination continued **in 2005** and **early 2006**
- **Mid 2006** due to limited vaccines - **targeted vaccination in sector 3**:
  - Inactivated H5N1 local isolate
  - Inactivated LPAI vaccine (H5N2)
- **Vaccination in sectors 1, 2 and 3** (breeders and layers)
  - **At their own cost**
  - With coverage estimated to be 90% in commercial layer and 100% in breeding flocks

Phase 2007-2011:

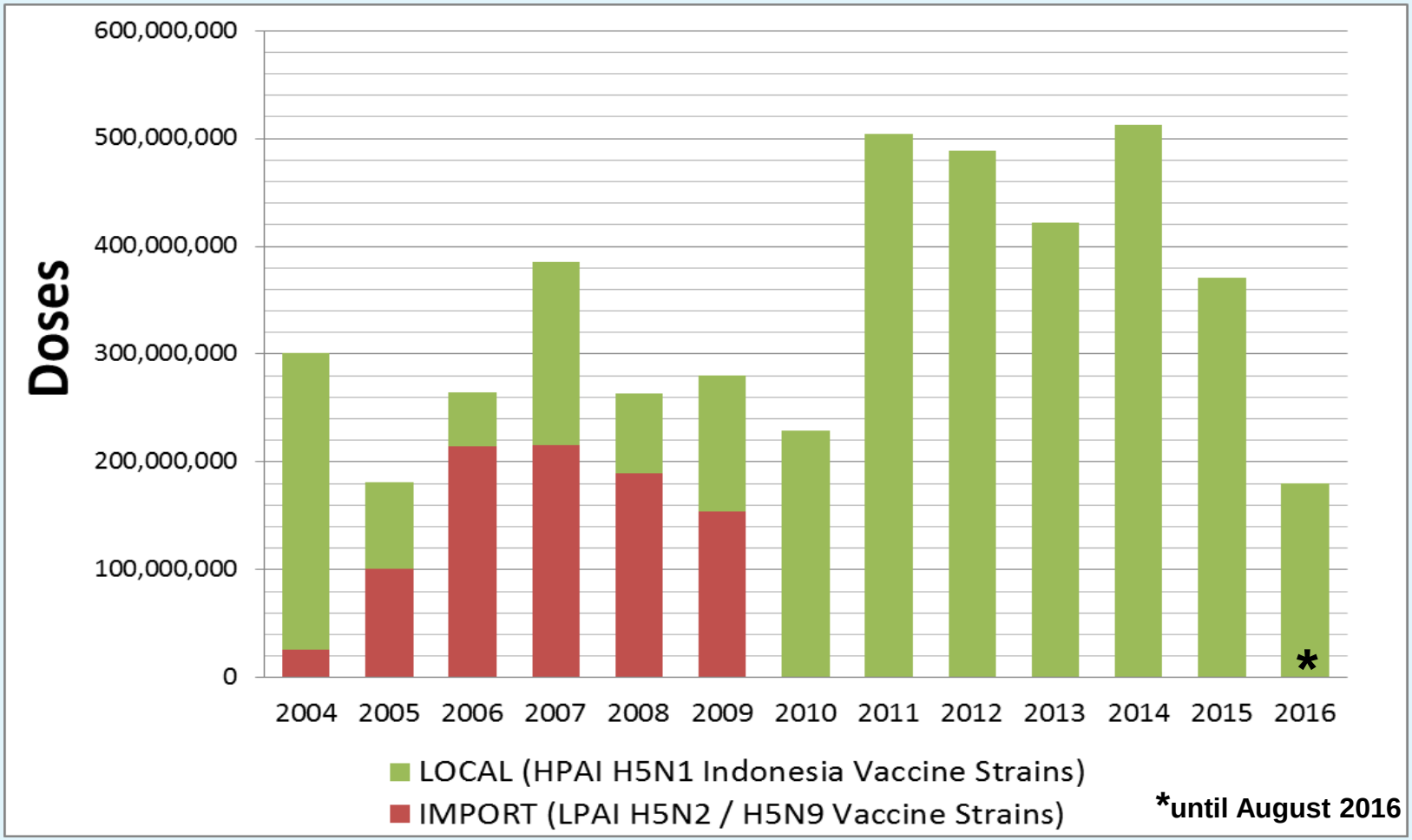
- **Vaccination in sector 4 discontinued** due to logistic problems and task of administrating vaccines to free-ranging birds
- **Continued targeted vaccination** of some populations in high risk/endemic areas for small-holder commercial farms (Sector 3) done by the district livestock services (Dinas Peternakan)
- **Vaccination in sectors 1, 2 and 3** (breeders and layers) **at their own cost**
- **OFFLU Projects started for the selection of master seed vaccines and challenge antigens** based on genetic (phylogenetics), antigenic cartography and challenge studies.

Vaccination Strategies (Phase III: 2011-Now)

- Recommendation from OFFLU Meeting Oct-2010 (at this stage clade 2.1.3.2 was dominant H5N1 virus circulating in poultry). Master seed AI Vaccine in Indonesia (local isolates) :
  1. **A/chicken/West Java/PWT-WIJ/2006**
  2. **A/chicken/Pekalongan/BBVW-208/2007**
  3. **A/chicken/Garut/BBVW-223/2007**
  4. **A/chicken/West Java (Nagrak)/30/2007**

  Challenge strains (local isolates):
  1. **A/chicken/West Java-Subang/29/2007**
  2. **A/chicken/West Java/SMI-PAT/2006**
- The vaccine that uses virus seed other which has been set by the government, particularly those of **imported vaccines**, then immediately **withdrawn from circulation and ended in December 2011**.
- Another seed vaccine (A/duck/Sukoharjo/BBVW-1428-9/2012) was introduced following the introduction and spread of Clade 2.3.2.1c viruses since 2012.
- Vaccine companies are allowed to make monovalent or bivalent vaccines from combination of reference strains of clade 2.1.3.2 and clade 2.3.2.1, or use their own seed strains **as long as originated from local isolates** and they must be **characterized antigenically** (in DIC Wates) and **pass from vaccine registration assays** (in NVDAL)

AI Vaccines use from 2004 - 2016



(source: POH-DGLAHS, 2016)

Since 2011 vaccines with only recommended seed strains or other local H5N1 strains (that passed from challenge trials) are permitted to be used in poultry (DG decree : No.3345/Kpts/LH.430/7/2011, 13 July 2011)

Mechanism:

1. Post-release vaccine monitoring
2. AI virus monitoring

Post-release AI vaccine monitoring 2013 and 2015

Monitoring AI Vaccine		
Methode	1. Collect vaccine products that used by farmers from the field 2. Potency Test by HI Test in NVDAL	
Antigen	1. A/chicken/West Java /Subang/29/2007	
	2. A/duck/Sukoharjo/BBVW 1428-9/2012	
Year	**2013**	**2015**
Number of Province	10	15
Number of District/ City	16	25
Number of Vaccine	16	30
Strain Seed vaccine	A/ck/WJ/PWT- NIJ/2006	A/ck/WJ/PWT- NIJ/2006
		A/duck/sukoharjo/BBVW-1428-9-2012

Source: Virology Lab - NVDAL

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Result of post-release vaccine monitoring 2013

Province	District/ City	Number of Vaccine	Seed Vaccine	Ag Subang	Ag Sukoharjo
				Persentase 90% titer > 4 Log 2	Persentase 90% titer > 4 Log 2
North Sumatera	Binjai	1	H5N1 Clade 2.1.3	100%	90%
	Langkat	1		100%	100%
Lampung	South Lampung	1		90%	80%
West Java	Cianjur	1		30%	0%
	Sumedang	1		80%	40%
Banten	Serang	1		100%	100%
	Tangerang	1		70%	60%
Central Java	Sragen	1		40%	20%
DIY	Kulonprogo	1		100%	100%
	Bantul	1		90%	90%
East Java	Kab.Blitar	1		100%	100%
Bali	Denpasar	1		100%	100%
	Denpasar	1		100%	60%
South Sulawesi	Pare Pare	1		100%	100%
	Sidrap	1		90%	90%
West Kalimantan	Singkawang	1		70%	70%
TOTAL		16			

INTERPRETATION

9 vaccines (orange) showed high protection against virus challenge 2.1.3 and 2.3.2
2 vaccine (purple) showed high protection against virus challenge 2.1.3 but protection < 90% against virus challenge 2.3.2
5 vaccine (yellow) showed low protection against virus challenge 2.1.3 and 2.3.2

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bbpmsoh.ditjennak.pertanian.go.id
Emilia, Ramlah, Rahajeng Setiawaty, Yati Suryati – Virology Lab -NVDAL

Result of post-release vaccine monitoring 2015

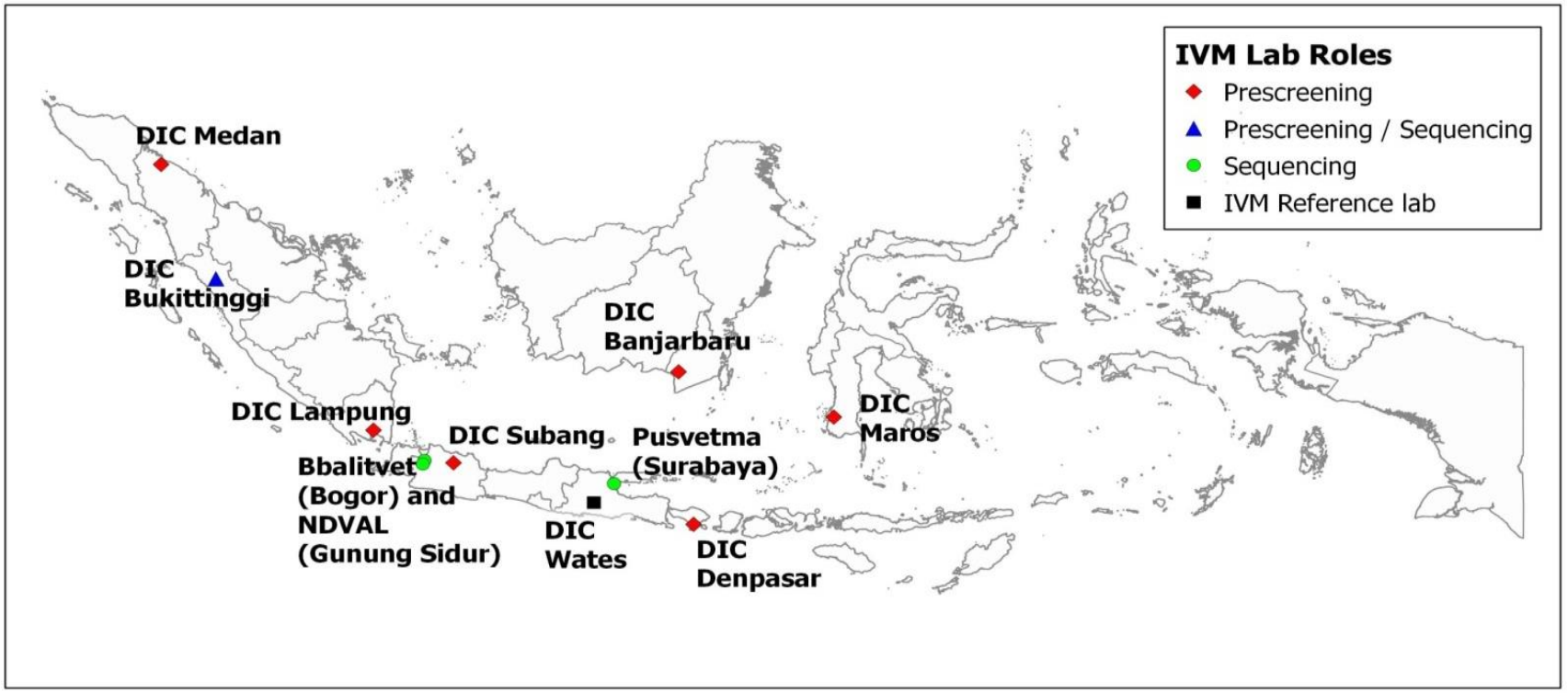
Vaccine Code	Strain Seed Vaccine	Total of Vaccine	Number of Vaccine Ag Subang 90% titer > 4 Log 2
A (Combination ND)	A/ck/WJ/PWT- NIJ/2006	2	0 (0%)
B (single)	A/ck/WJ/PWT- NIJ/2006	11	8 (72.7%)
C (single)	A/ck/WJ/PWT- NIJ/2006	9	5 (55.5%)
D (Combination ND)	A/ck/WJ/PWT- NIJ/2006	2	2 (100%)
Interpretation			
Vaccine Code A showed no protection against virus challenge 2.1.3			
Vaccine code B & C showed high protection against virus challenge 2.1.3 althought not 100%			
Vaccine code D showed 100% high protection against virus challenge 2.1.3			

Vaccine Code	Strain Seed Vaccine	Total of Vaccine	Number of Vaccine Ag Sukoharjo 90% titer > 4 Log 2
F (single)	A/duck/sukoharjo/BBVW-1428-9-2012	4	4 (100%)
G (single)	A/duck/sukoharjo/BBVW-1428-9-2012	1	1 (100%)
H (single)	A/duck/sukoharjo/BBVW-1428-9-2012	1	1 (100%)
Interpretation			
Vaccine code F, G and H showed high protection against virus challenge 2.3.2			

Source: Khusni H, Ramlah, Yati Suryati, Ketut K.N.N – Virology Lab-NVDAL

Influenza Virus Monitoring (IVM) Network

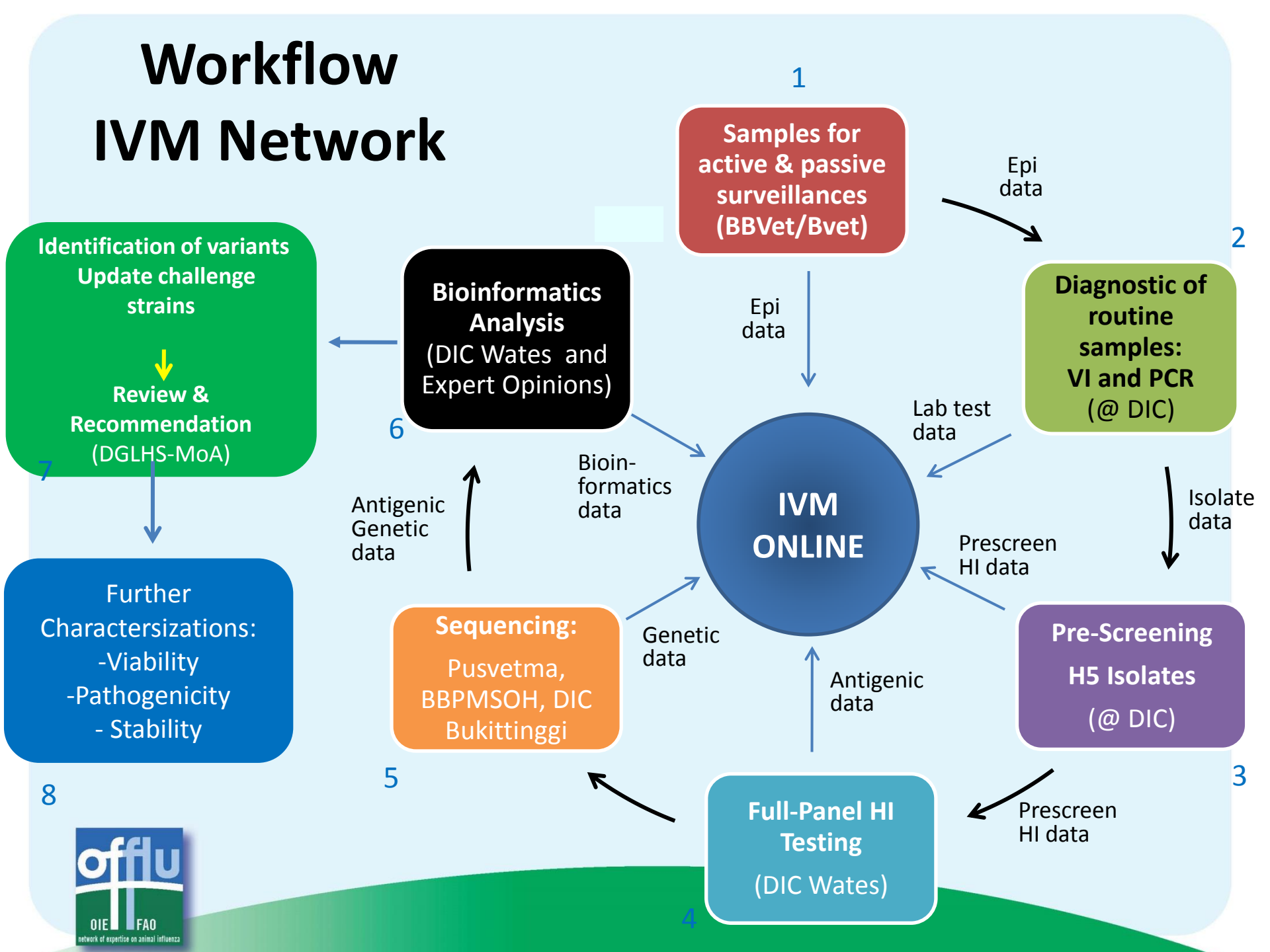
IVM: integrated and coordinated HPAI surveillance at the molecular level conducted by veterinary laboratory network in Indonesia



Aim and Objectives:

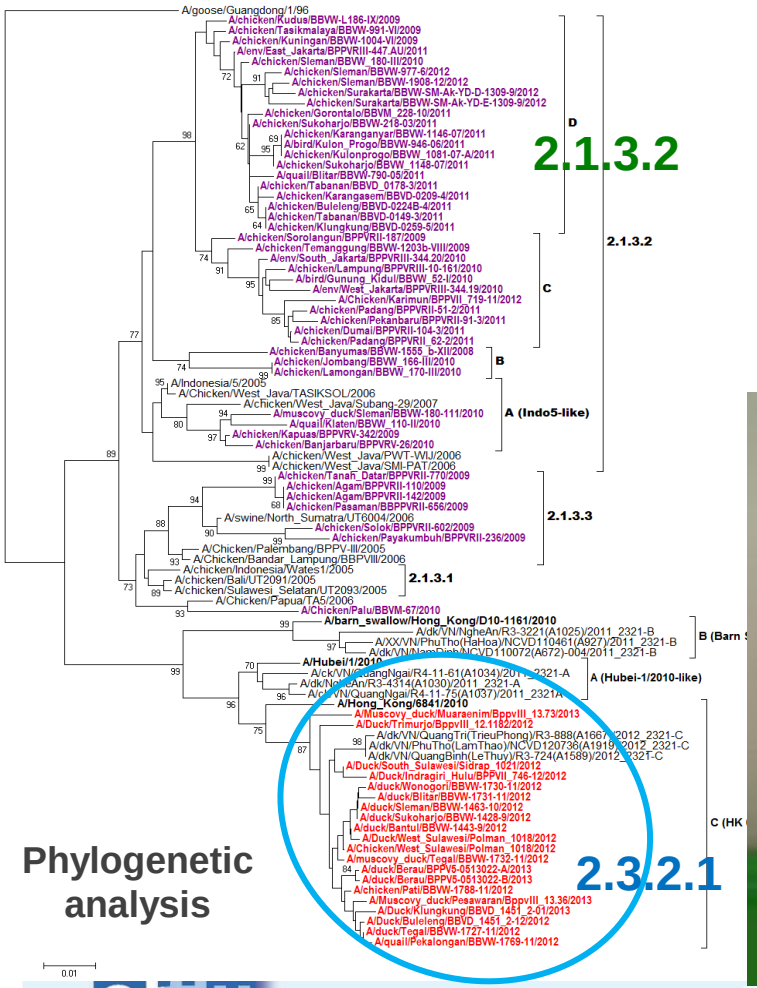
To monitor the dynamic of influenza virus circulating in animal in Indonesia and to accelerate the reporting of virus monitoring to decision makers at the national level (including recommendation of challenge strains)

Workflow IVM Network

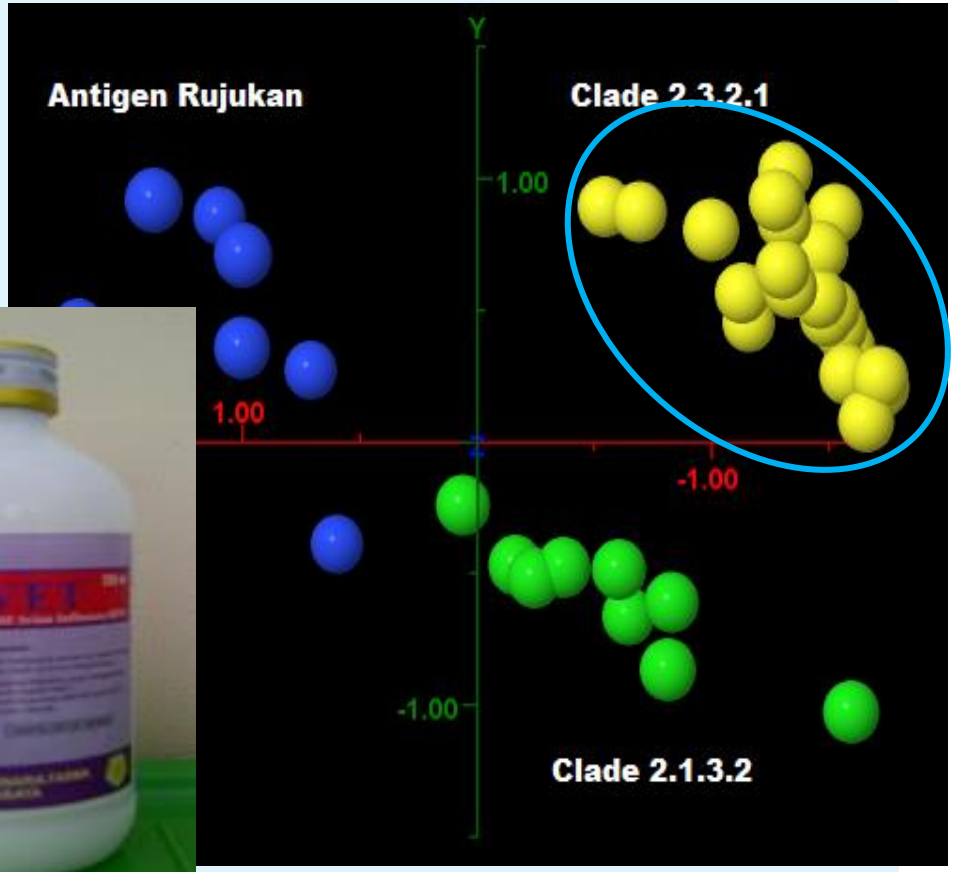


The Benefits of IVM Network approach to HPAI Surveillance :

Identification of a new clade (2.3.2.1) H5N1 virus incursion into Indonesia through genetic and antigenic analyses lead to the successful and timely development H5N1 clade 2.3.2.1 vaccine that produced locally (at PUSVETMA)



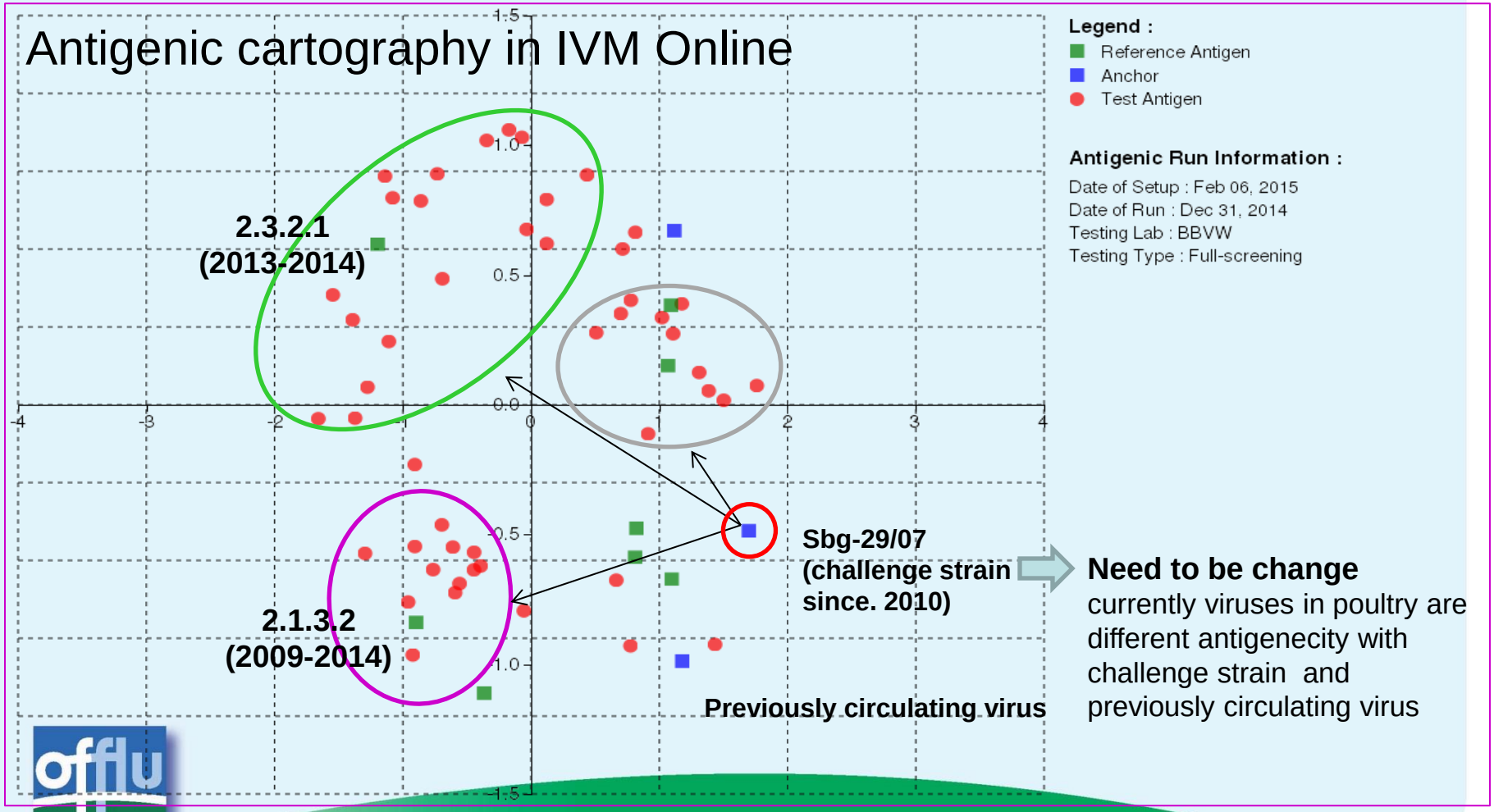
Phylogenetic analysis



2.3.2.1. vaccine

Antigenic cartography in IVM Online

The results of post vaccination monitoring show that the 2.1.3 reference antigen showed low cross protection → significant antigenic distances of newly viruses to previously circulating virus → need to change the challenge strain antigen



Summary

- HPAI H5N1 remains endemic some areas, particularly in Java, with Clade 2.3.2.1c now is predominant clade replacing clade 2.1.3.2.
- The quality of vaccines (antigenically match to circulating viruses and enough virus content/quantity per bach) is quite important to provide good protectivity.
- Improved surveillance including in the molecular level provide better understanding of epidemiology and virus evolution.
- Vaccination can be an important tool to reduce circulating H5N1 virus:
  - Needs adequate resources and commitment of management
  - Monitoring of circulating viruses and post-vaccination monitoring program are very crucial

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Acknowledgements

- Director General Livestock and Animal Health Services, Ministry of Agriculture, Indonesia
- Director of Animal Health, Directorate General Livestock and Animal Health Services (DGLAHS), Ministry of Agriculture, Indonesia
- Director of Disease Investigation Center (DIC) Wates Yogyakarta
- Directors of DICs DGLAHS, Ministry of Agriculture, Indonesia
- Director of National Veterinary Drug Assay Laboratory, Bogor
- Head of Sub-Directorate Animal Disease Surveillances (P2H), DGLAHS
- Head of Sub-Directorate Animal Drug Administration (POH), DGLAHS
- Food and Agriculture Organization of the United Nations Emergency Centre for Transboundary Animal Diseases, Jakarta, Indonesia
- Influenza Virus Monitoring Network Laboratories in Indonesia