Current surveillance knowledge from Europe – focus UK

Ian Brown

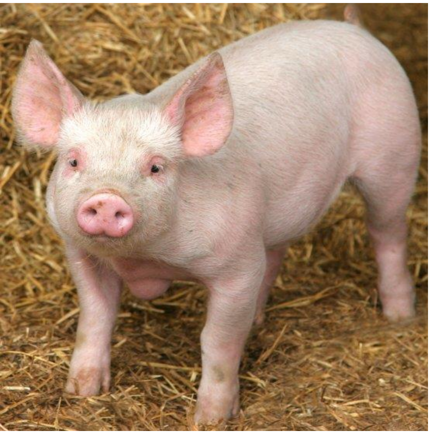
Director of OIE Reference Laboratory for Swine Influenza

Coordinator of ESNIP3

Animal and Plant Health Agency-Weybridge

OFFLU SIV group meeting, Paris, 4-5 December 2015

ESNIP1 1999-2003
Coordinator
Guus Koch, CVI Lelystad, NL



ESNIP 3 PARTNER RESULTS FROM 2014-15

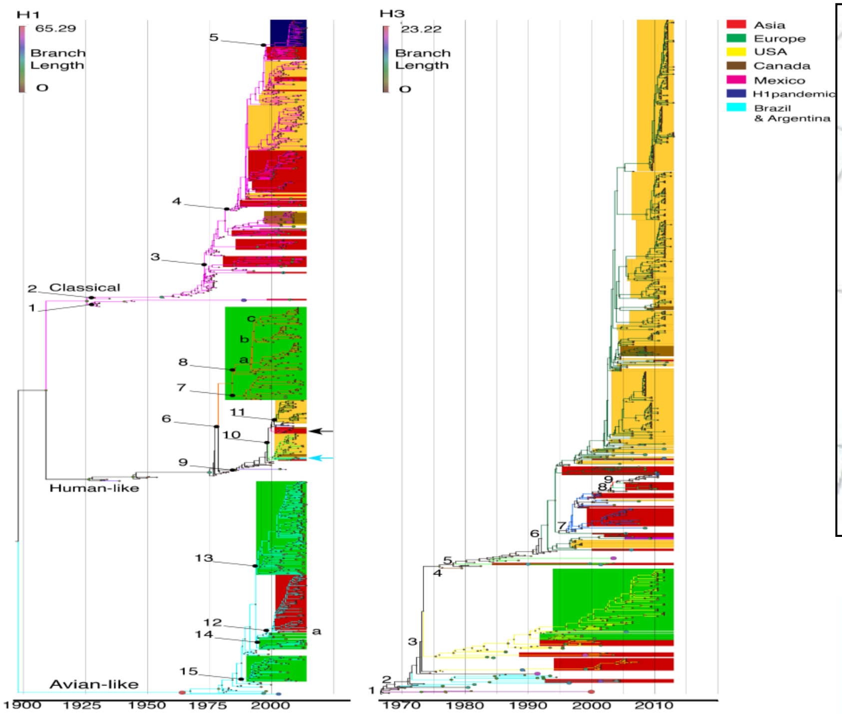
Hungary, Belgium, France, Poland, UK

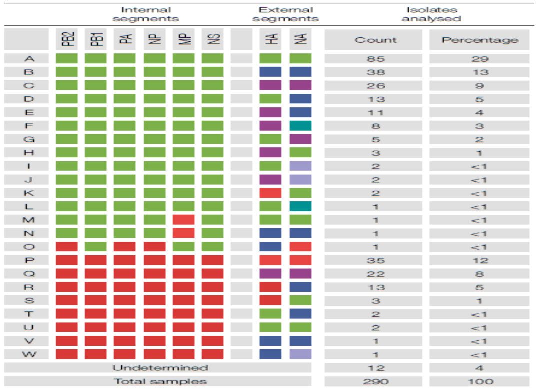
ESNIP2 2005-2008
Coordinator Kristien Van Reeth, Ugent, BE

ESNIP3
Coordinator Ian Brown, AHVLA, UK
2010-2013

ESNIP3

ESNIP3 NOVEL INSIGHTS

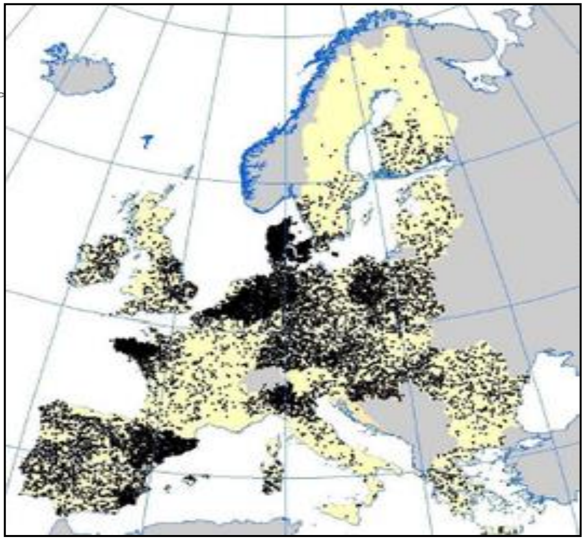


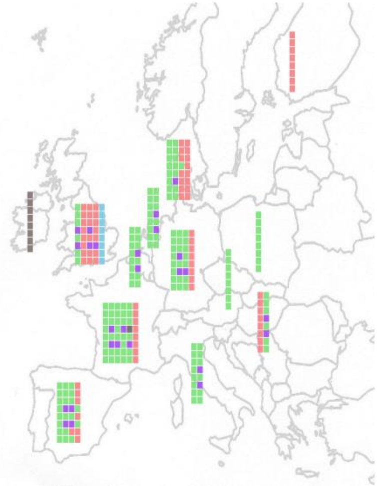


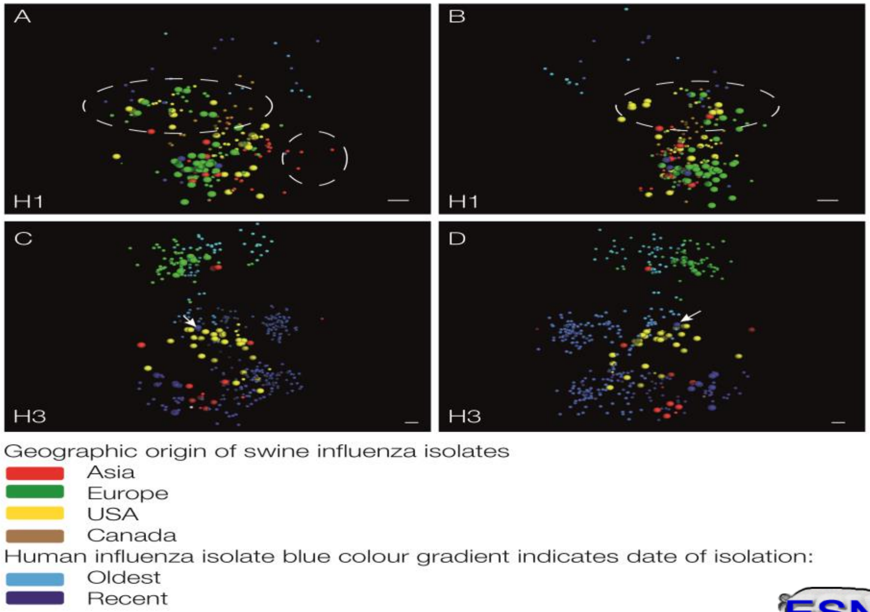
	Internal segments							External segments		Isolates analysed	
	PB2	PB1	PA	NP	MP	NS		HA	NA	Count	Percentage
A	🟩	🟩	🟩	🟩	🟩	🟩		🟩	🟩	85	29
B	🟩	🟩	🟩	🟩	🟩	🟩		🟦	🟦	38	13
C	🟩	🟩	🟩	🟩	🟩	🟩		🟪	🟪	26	9
D	🟩	🟩	🟩	🟩	🟩	🟩		🟩	🟦	13	5
E	🟩	🟩	🟩	🟩	🟩	🟩		🟪	🟦	11	4
F	🟩	🟩	🟩	🟩	🟩	🟩		🟪	▣	8	3
G	🟩	🟩	🟩	🟩	🟩	🟩		🟩	🟪	5	2
H	🟩	🟩	🟩	🟩	🟩	🟩		🟪	🟩	3	1
I	🟩	🟩	🟩	🟩	🟩	🟩		🟩	▨	2	<1
J	🟩	🟩	🟩	🟩	🟩	🟩		🟪	▨	2	<1
K	🟩	🟩	🟩	🟩	🟩	🟩		🟥	🟩	2	<1
L	🟩	🟩	🟩	🟩	🟩	🟩		🟩	▣	1	<1
M	🟩	🟩	🟩	🟩	🟥	🟩		🟩	🟩	1	<1
N	🟩	🟩	🟩	🟩	🟥	🟩		🟦	🟦	1	<1
O	🟥	🟩	🟥	🟥	🟩	🟩		🟦	🟥	1	<1
P	🟥	🟥	🟥	🟥	🟥	🟥		🟥	🟥	35	12
Q	🟥	🟥	🟥	🟥	🟥	🟥		🟪	🟪	22	8
R	🟥	🟥	🟥	🟥	🟥	🟥		🟥	🟦	13	5
S	🟥	🟥	🟥	🟥	🟥	🟥		🟥	🟩	3	1
T	🟥	🟥	🟥	🟥	🟥	🟥		🟩	🟦	2	<1
U	🟥	🟥	🟥	🟥	🟥	🟥		🟩	🟩	2	<1
V	🟥	🟥	🟥	🟥	🟥	🟥		🟦	🟦	1	<1
W	🟥	🟥	🟥	🟥	🟥	🟥		🟦	▨	1	<1
Undetermined										12	4
Total samples										290	100

🟦 A/swine/Gent/1/1984-like H3N2
🟩 Eurasian avian-like H1$_{av}$N1
▣ A/swine/Italy/4675/2003-like N2
🟪 A/swine/Scotland/410440/1994-like H1$_{hu}$N2
🟥 A(H1N1)pdm09
▨ Human seasonal-like N2

Figure 1. SIV genotypes isolated from European swine between 2009 and 2013. The 23 distinct genetic constellations are labeled A to W, with the lineage-of-origin for each segment indicated by a colored block.







Geographic origin of swine influenza isolates
🟥 Asia
🟩 Europe
🟨 USA
🟫 Canada
Human influenza isolate blue colour gradient indicates date of isolation:
🟦 Oldest
🟦 Recent

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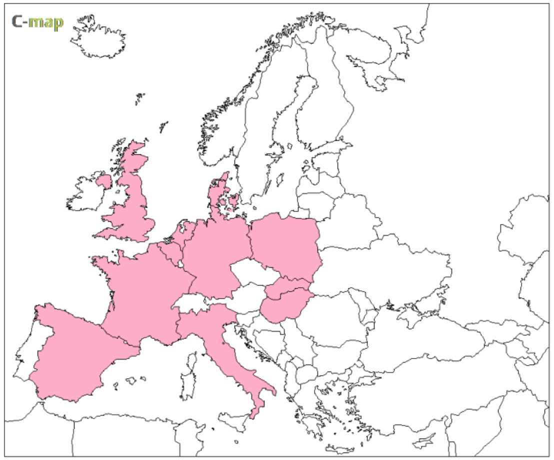
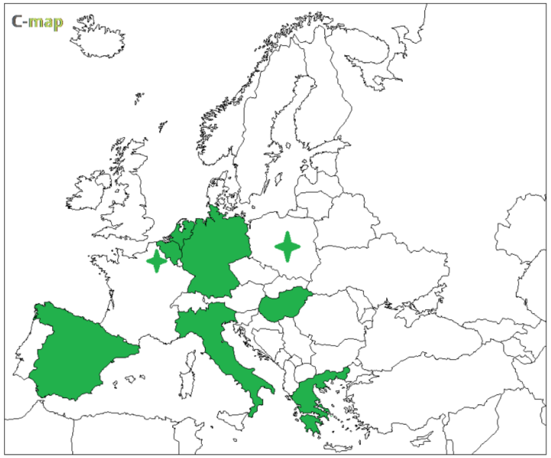
Regional variation in the epidemiology of SIV in Europe (ESNIP3) ~ 23 variants detected

H1avN1 (53%)



H3N2 (9%)

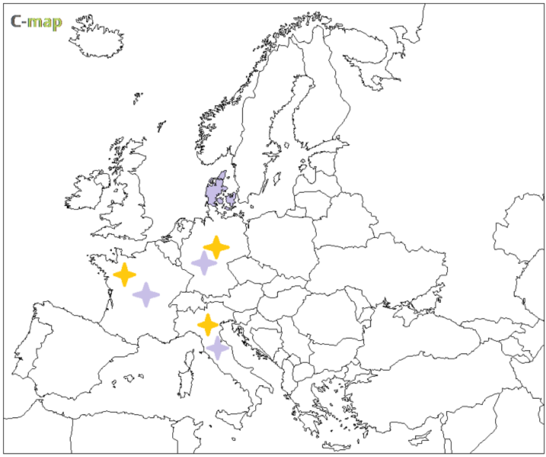


H1huN2 (16%)

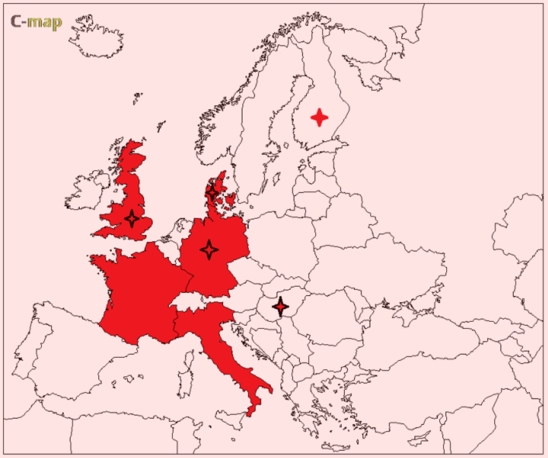
■ Enzootic lineages

✦ Epizootic lineages (occasional detections)

rH1huN1 and rH1avN2 (8%)



H1N1pdm and reass. (14%)



ESNIP3

wellcome trust
sanger
institute

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Plant Health
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Belgium: Passive Surveillance 2014-2015

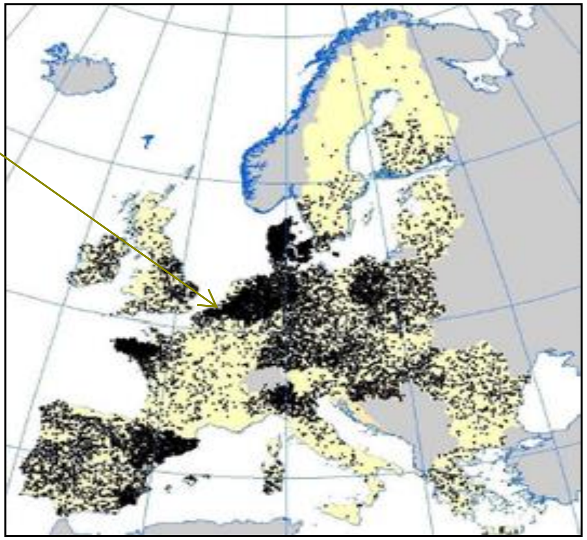
Data courtesy of Kristien Van Reeth, UGent

- 2014
  - av-like H1N1 9/22 (41%)
  - H1N2 5/22 (23%)
  - H3N2 8/22 (36%)
- 2015
  - av-like H1N1 3/3

No pdm09!?

Farm system data captured

Vaccination historically used

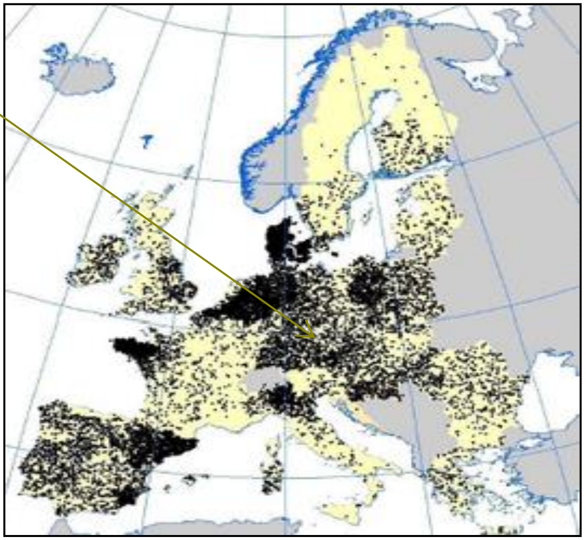


Hungary: Passive Surveillance 2014-2015

Data courtesy of Adam Dan, Veterinary Diagnostic Directorate Laboratory for Molecular Biology, Budapest

- 2014-15
  - av-like H1N1 3/4 (75%)
  - pdmH1N1 1/4 (25%)

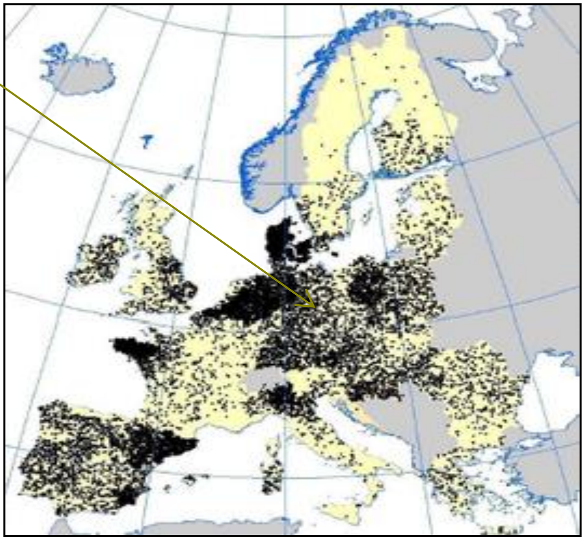
Vaccination??



Poland: Passive Surveillance 12/2014-11/2015

Data courtesy of Iwona Markowska-Daniels, NVRI, Pulawy

Country	Number of herds	Number of Influenza A positive cases -	Frequency of positive cases (%)
Poland	42	7	16,28
Slovakia	1	0	



- av-like H1N1 2/7 (29%)
- pdm09 5/7 (71%)

Farm system data captured

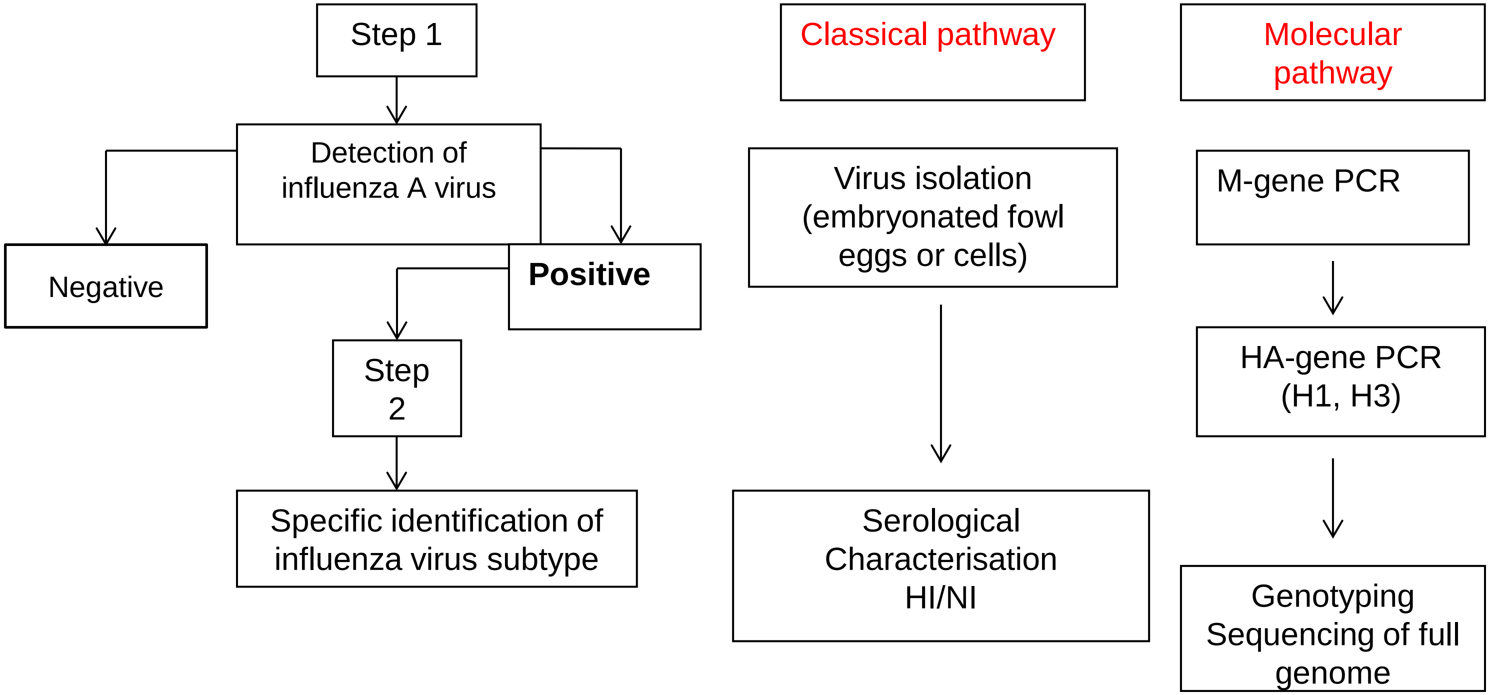
Vaccination?

Surveillance criteria – to detect virus

- Acute respiratory disease
- Necropsy
  - Viral aetiology suspected
  - Lungs with specified gross lesions
  - Lungs with any gross lesions if clinical presentation is suggestive of influenza infection
- Carcases
  - from animals which have died within 24 hours
  - presented moribund
  - up to 3 carcases/case submission

- Nasal swabs of up to 20 pigs acutely affected (pooled for PCR)

Schematic overview of diagnostic steps for confirmation of SI



Step 1

Detection of influenza A virus

Negative

Positive

Step 2

Specific identification of influenza virus subtype

Classical pathway

Virus isolation (embryonated fowl eggs or cells)

Serological Characterisation HI/NI

Molecular pathway

M-gene PCR

HA-gene PCR (H1, H3)

Genotyping Sequencing of full genome

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UK SI SURVEILLANCE RESULTS 2014

Month	No. of submissions	No. of samples submitted	No. (+ve) submissions (samples)	AVH1N1	H1N2	H3N2	PH1N1	
Jan-14	23	151	7(23)		**1**		**4**	
Feb-14	18	95	2(14)		**2**			
Mar-14	21	104	4(8)		**2**		**1**	
Apr-14	17	66	4(10)		**1**		**2**	
May-14	8	45	4(7)				**3**	
Jun-14	15	65	0					
Jul-14	12	37	4(6)		**1**			
Aug-14	20	70	0					
Sep-14	20	89	3(3)				**1**	
Oct-14	13	35	0					
Nov-14	10	19	1 (1)	**1**				
Dec-14	8	27	1 (1)					
	185			**1**	**7**		**11**	

UK SI SURVEILLANCE RESULTS 2015

Month	No. of submissions	No. of samples submitted	No. (+ve) submissions (samples)	AVH1N1	H1N2	H3N2	PH1N1	
Jan-15	15	50	2 (3)				2	
Feb-15	21	62	3 (5)		1			
Mar-15	25	99	4 (5)		1			
Apr-15	15	42	1 (2)				1	
May-15	15	47	3 (6)		1			
Jun-15	14	50	3(3)		1		1	
Jul-15	11	34	2(2)				2	
Aug-15	14	37	1(4)					
Sep-15	11	56	3 (6)				1	
	141	**477**	**22**		**4**		**7**	

SwIV pdmH1N1 surveillance across the EU

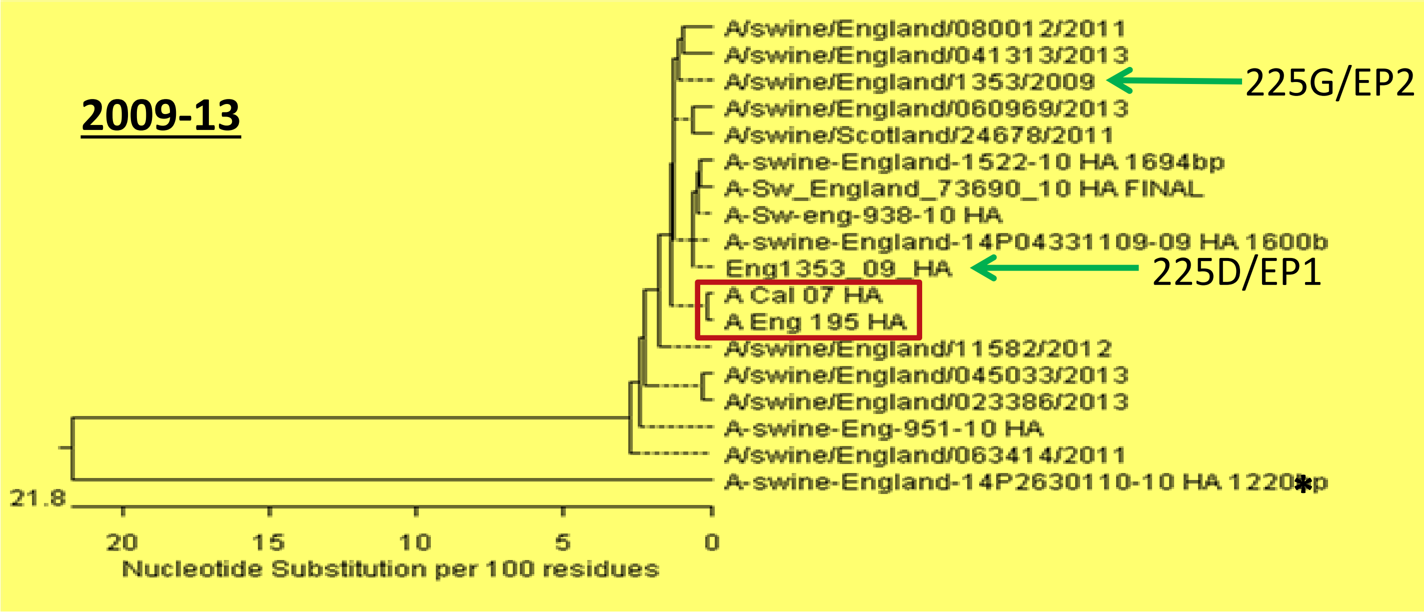
- **ESNIP 3 - 14 countries, November 2010 to October 2013**
  - pdm 194/1885 ~10% conventionally typed submissions,
  - Seq. Genotyping 12% total, European av. 8%.
  - at least 32 separate introductions from humans into swine have occurred 2009-2013 (Wats
  - ? Swine to humans.

- **UK 2009-14, pdm 60/187, 32%**
  - Nov. 2009 first detection
  - Differences in disease presentation, spread and duration,
  - mild or clinically inapparent disease in breeders
    typical respiratory disease in progeny.
  - mortality was low where disease was uncomplicated
    by environmental stresses or concurrent infections.
    Where deaths occurred in pigs infected with A(H1N1)pdm09
    influenza, they were mainly due to other infections,
    including *Strep. suis*.

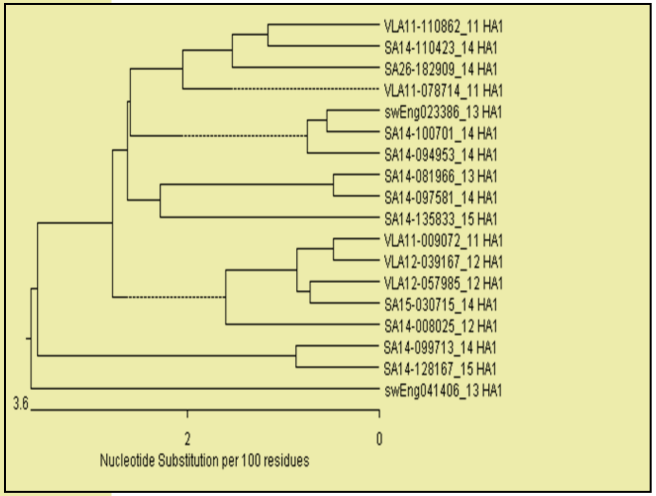
Year	pH1N1
2009	4
2010	19
2011	15
2012	8
2013	14
2014	11
2015(m6)	4
Total	64

Williamson SM et al., Vet Rec. 2012 ***[Combating Swine Influenza (COSI) UK collaboration]***

Genetic analyses for HA of UK pdm H1N1 viruses


2009-13


Clinical Samples: 2011-15



ESNIP3 A/H1N1pdm09 viruses - HA

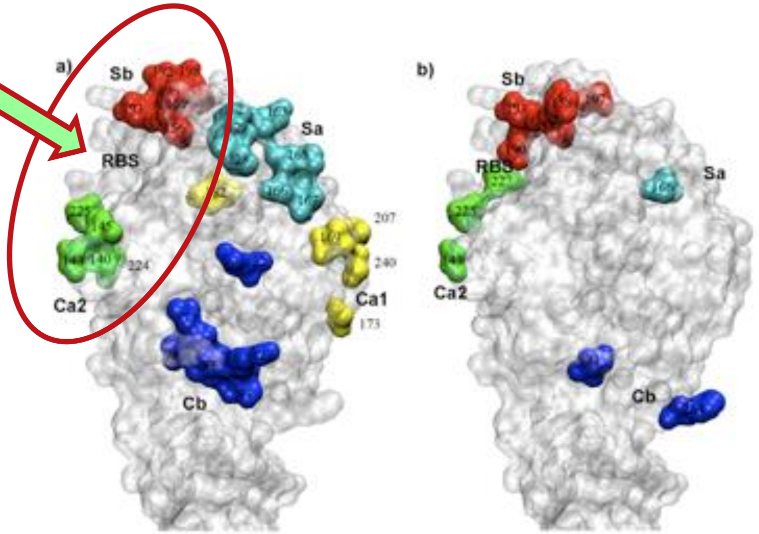
Antigenic sites : HA

A/Cal07/09 – vaccine
A/Eng195/09 – APHA typing Ag.
A/sw/Eng1353/09 – swine field isolate

All three isolates identical at all 5 Ag sites,
except 1 aa in the swine field isolate.

UK 33 swine isolates (clinical/egg grown, 18/15) most had 1-2 aa changes per Ag site, one isolate* had 1-5 aa changes / site

Ag Site	**# with AA variants**
Ca2	**17/33 (51%) – D225X**
Sb	**11/33 (33%) – D190**
Ca1	**6/33 (18%)**
Sa	**6/33 (18%)**
Cb	**3/33 (9%)**



Epizootic in humans in India with pdm09 raised concerns in swine industry

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Emergent ‘India’ human pdm virus / pigs

- K166Q T200A D225N

? Swine pdm viruses

- ➢ Worldwide the consensus in pigs is KAD

Consensus n=89
Variants n=84

K/Q	↓vacc ab sensitive
T/A	↑hu/mammalian lung
D/G/N	2,6 (URT) – 2,3 (LRT)

Variant classes – World (non clinical)

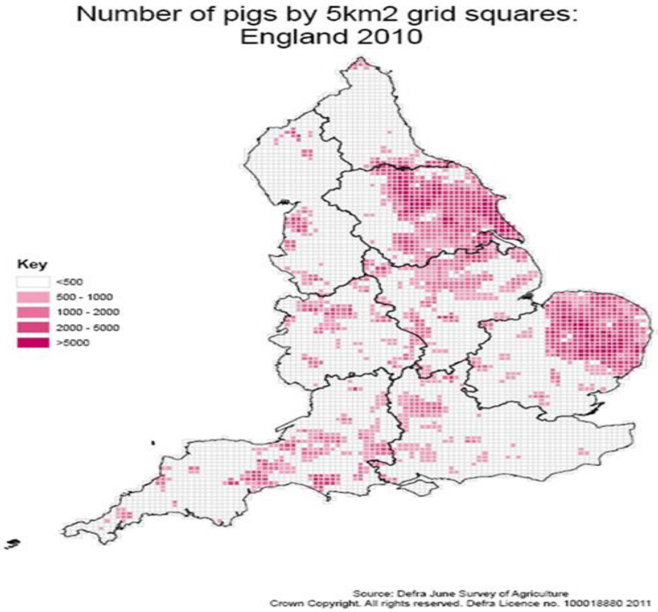
K	A	D
N (2)	T(14)	**N(10)**
T (2)	S (1)	V(1)
I(1)		**G(13)**
Q(32)		E(8)
		Y(1)

European and UK pig pdm H1N1

- Europe 15 pdm isolates sequenced (ESNIP3),
  - 14 were KAD, 1 (Poland) KAG
  - 225G variants have also been ‘isolated’ from European pigs (Belgium, France, Hungary).

- UK – 31 pdm viruses sequenced
  - 94% K (1Q, 1R),
  - 97% A (1T),
  - 75% D, 4 G (egg), 4 E (3 EP/2 clinical), 1N (clinical)

- UK clinical material n=17 2011-15,
  - 13 KAD, 1 RAD, 1 KAN, 2 KAE, 1 QAD


Number of pigs by 5km2 grid squares:
England 2010

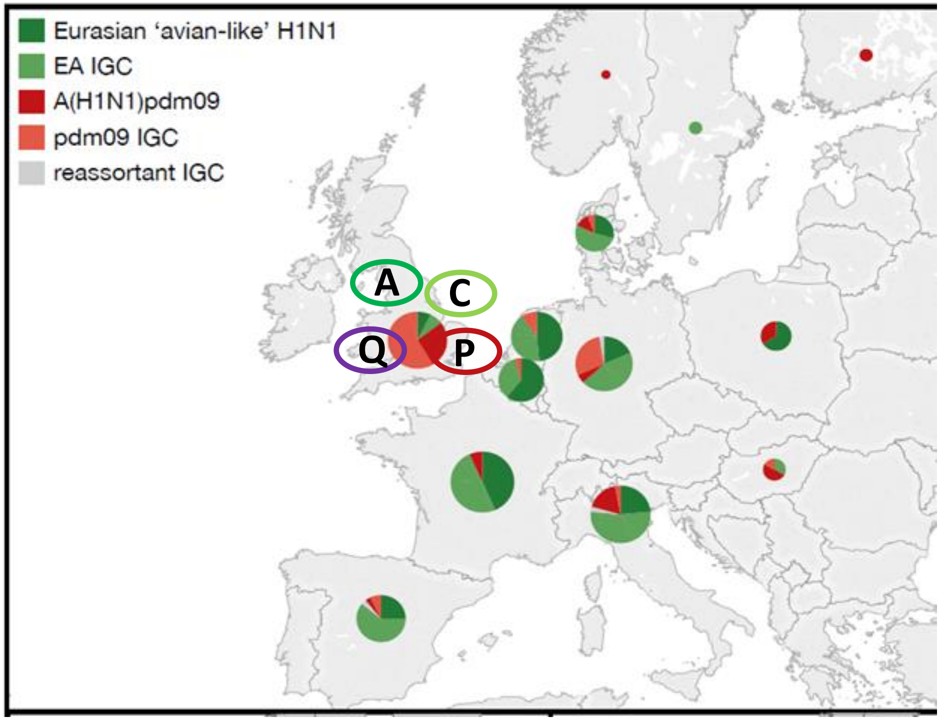
Source: Defra June Survey of Agriculture

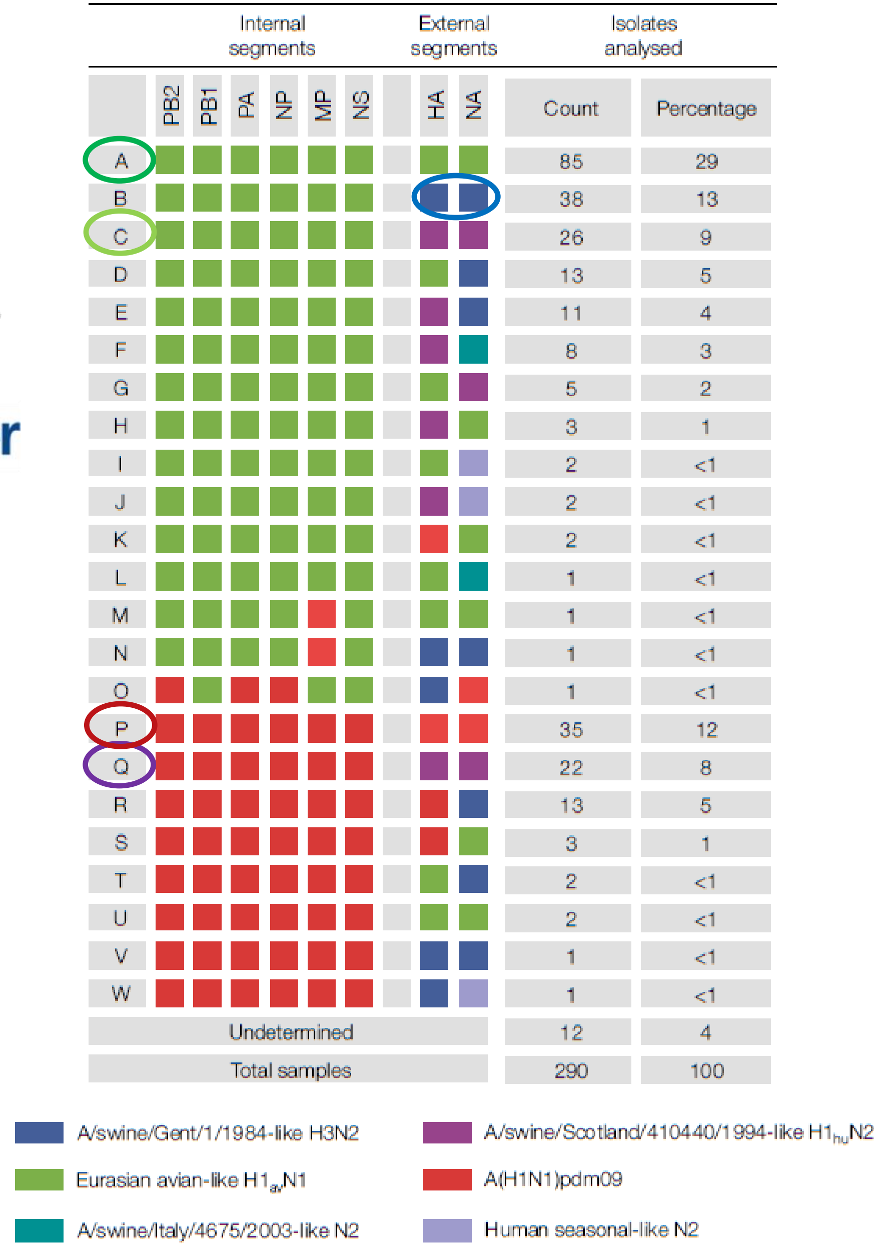
- The motif K166;T200;D225N was not selected for in European viruses analysed

- UK classical and avian-like H1N1 HA have 225G

Molecular Epidemiology and Evolution of Influenza Viruses Circulating within European Swine between 2009 and 2013.

Watson SJ[1] et al., J Virol. 2015
Oct 1;89(19):9920-31.





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J	🟩	🟩	🟩	🟩	🟩	🟩	🟪	▨	2	<1
K	🟩	🟩	🟩	🟩	🟩	🟩	🟥	🟩	2	<1
L	🟩	🟩	🟩	🟩	🟩	🟩	🟩	▦	1	<1
M	🟩	🟩	🟩	🟩	🟥	🟩	🟩	🟩	1	<1
N	🟩	🟩	🟩	🟩	🟥	🟩	🟦	🟦	1	<1
O	🟥	🟩	🟥	🟥	🟩	🟩	🟦	🟥	1	<1
P	🟥	🟥	🟥	🟥	🟥	🟥	🟥	🟥	35	12
Q	🟥	🟥	🟥	🟥	🟥	🟥	🟪	🟪	22	8
R	🟥	🟥	🟥	🟥	🟥	🟥	🟥	🟦	13	5
S	🟥	🟥	🟥	🟥	🟥	🟥	🟥	🟩	3	1
T	🟥	🟥	🟥	🟥	🟥	🟥	🟩	🟦	2	<1
U	🟥	🟥	🟥	🟥	🟥	🟥	🟩	🟩	2	<1
V	🟥	🟥	🟥	🟥	🟥	🟥	🟦	🟦	1	<1
W	🟥	🟥	🟥	🟥	🟥	🟥	🟦	▨	1	<1
Undetermined									12	4
Total samples									290	100

🟦 A/swine/Gent/1/1984-like H3N2

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▨ Human seasonal-like N2

Figure 1. SIV genotypes isolated from European swine between 2009 and 2013. The 23 distinct genetic constellations are labeled A to W, with the lineage-of-origin for each segment indicated by a colored block.

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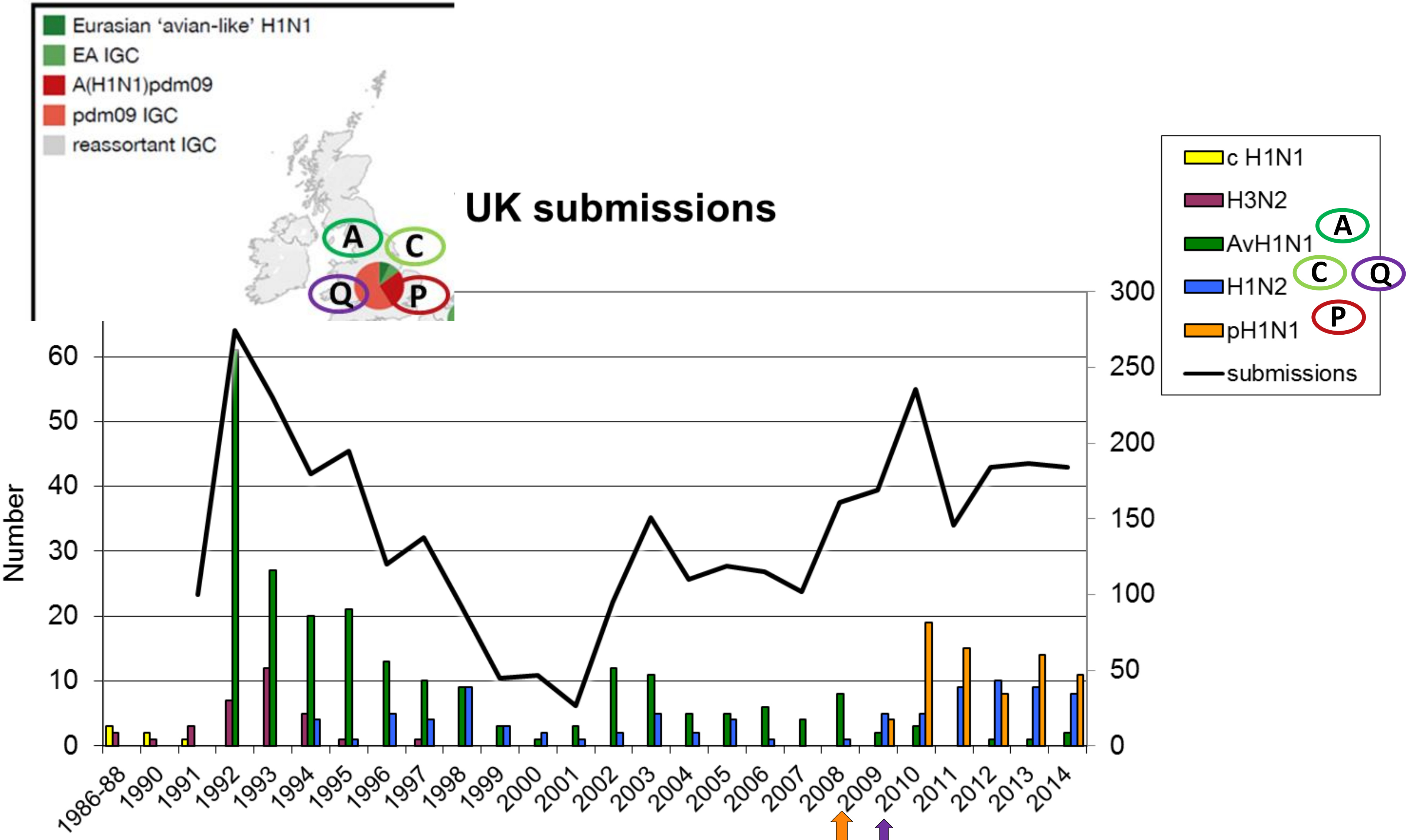
UK submissions



pdmH1N1/09 UK P

(Brookes et al., Vet Rec 2009; PlosOne 2010)

Q

swH1N2r (pdm internals)

(Howard W et al., EID. 2011)

Animal & Plant Health Agency

Perspectives from UK surveillance

- Dynamic stable since 2012
  - Pdm09
  - Hu1n2 (pdm09 cassette)
  - Avian-like virus low level; replacement after 20 years as dominant UK strain
- Viruses with pdm09 cassette of internal genes have selection advantage
- Little independent evolution to date in pdm09 HA
- Vaccination being applied increasingly

- Risks to ongoing surveillance flow!
  - Commercial vaccine manufacturers offering free testing

Acknowledgements

Department
for Environment
Food & Rural Affairs

ESNIP network

Kristien Van Reeth
Iwona Markowska-Daniel
Adam Dan
Gaelle Simon
Simon Watson
Nicola Lewis

FLUPIG

EU FP7 projects: FLUPIG #258084

Defra for funding through project SV3041

APHA flu group

Sharon Brookes


Influenza/ND team

ESNIP3

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institute

ESNIP3
European Surveillance Network for Influenza in Pigs 3 project #259949
Project website address:
http://www.esnip3.eu/index.html

Thank you for your attention

http://flu-lab-net.eu/

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