OFFLU Avian Influenza Matching (AIM) Technical Report, July 2024

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Disclaimer: This technical report uses both published nomenclature (widely used by many countries at present (i.e. "GISAID clade")[1] but not recently updated) AND unpublished nomenclature proposed by the WHO/FAO/WOAH H5 Nomenclature Working Group[2] (i.e. provisional Nextclade/LABEL clade). Throughout the report, the use of the different nomenclatures is discriminated by footnotes.

This report provides the point of view of independent OFFLU experts and does not necessarily reflect the position of the parent organisations FAO and WOAH.

Summary

OFFLU has developed a system for providing information to countries on the antigenic characteristics of circulating high pathogenicity avian influenza (HPAI) A(H5Nx) viruses of the Goose/Guangdong/1/96-lineage. This process uses reference antisera produced in chickens against either representative isolates of relevant circulating clades or isolates that are genetic representatives of vaccine seed strains (hereinafter referred to as surrogate vaccine seed strains). Contemporary viruses are tested against these sera using the HI assay and antigenic cartography is applied on the HI titers to establish the antigenic relationship between the virus antigens and available antisera. This provides a numerical value for how closely matched the circulating viruses are to the antigens used to raise the reference antisera. Greater antigenic distances between surrogate vaccine antigens and currently circulating strains indicate evolution of viral sequences through mutations that lead to increased antigenic distance over time, known as antigenic drift. As poultry vaccines are primarily designed to provide protection against a specific antigen, this antigenic drift can impact the ability of vaccine derived antibodies to bind and/or neutralise contemporary viruses. Consequently, it can become necessary to update the antigens used in vaccine formulations. Results herein provide insight on this need. Further information on the background to the approach taken and the methods applied is available in Module 1: Background report and Module 2: Guidance report. This document provides the technical results.

As of July 2024, the viruses causing the most outbreaks in poultry globally are subtype H5N1 within clade 2.3.4.4b. However, outbreaks have also been associated with other H5Nx clades, including clade 2.3.2.1a detected in South Asia, and clades 2.3.2.1c[1]/g[2]/e[2] in Southeast Asia. Due to the dominating impact of these clades on poultry, the AIM assessment focused on defining the antigenic reactivity between the sampled field viruses in these clades and representative CVVs. Following HI assessment, antigenic cartography was undertaken using eight H5N1 clade 2.3.2.1a

[1] *Smith GJ, Donis RO, World Health Organization, World Organisation for Animal Health, Food Agriculture Organization, H5 Evolution Working Group. Nomenclature updates resulting from the evolution of avian influenza A(H5) virus clades 2.1.3.2a, 2.2.1, and 2.3.4 during 2013-2014. Influenza Other Respir Viruses 2015;9(5):271-6. Available at: http://onlinelibrary.wiley.com/doi/10.1111/irv.12324/epdf. Clade 2.3.2.1c viruses have evolved into different sublineages since they were last formally classified in 2014. An updated, standardised clade nomenclature for viruses that previously fell within clade 2.3.2.1c is being developed[2] but has not yet been published.*

[2] *Provisional nomenclature was taken from the WHO/FAO/WOAH H5 Nomenclature Working Group who define "clades" using HA gene sequences, and define clades as genetically distinct, monophyletic groups of viruses. This nomenclature splits clade 2.3.4.4 into eight additional sub-clades, named 2.3.4.4a through 2.3.4.4h due to high circulating diversity within the clade and. well as sub-clades 2.3.2.1a through 2.3.2.1g for the 2.3.2.1 split.*

viruses collected between 2021 and 2023 from South Asia; one H5N1 clade 2.3.2.11 above[1]/g[1] above virus collected in 2022 from Southeast Asia; 9 H5N8 clade 2.3.4.4b viruses collected since 2020 from Europe and Asia, 74 H5N1 clade 2.3.4.4b viruses collected since 2020 from Asia, Africa and Europe and the Americas; two H5N5 clade 2.3.4.4b virus collected in Europe since 2020 and one H5N3 virus collected in Europe in 2021. Results for viruses collected in 2023 are outlined and discussed in this report. Outcomes from the analyses undertaken within this period include the following points:

- Vaccine antigens not within the clade 2.3.4.4 are antigenically distant from clade 2.3.4.4b viruses and would not be expected to be suitable candidate antigens for inactivated whole virus vaccines against these strains (figure 2).
- Subtype-specific heterogeneity over previous years was noted in antigenic distances for clade 2.3.4.4b viruses (figure 3).
- In geographically restricted regions, there is evidence of antigenic drift in viruses isolated from poultry (table 3).
- Viruses tested from wild birds in Europe did not exhibit antigenic drift (table 3).
- Clade 2.3.2.1 and clade 2.3.4.4 viruses are antigenically distinct from older virus clades including antisera raised against clade 1, clade 2.2, or clade 2.3.4 viruses (figure 2).

This report indicates that, despite extensive circulation in wild birds and global spread, HPAI A(H5Nx) viruses from wild birds don't appear to have undergone significant changes in antigenic properties. However, within poultry populations in geographically restricted areas HPAI A(H5Nx) viruses are evolving and drifting antigenically. Continued monitoring for genetic and antigenic changes, especially in countries where the virus is enzootic in poultry is crucial for early detection of antigenic change and response to update vaccines where necessary.

Vaccine seed strains

*Table 1: Seed strains of vaccines which are currently understood to be in use or have been used in the past. Where available clade information and references have been included. Clade information is described in the literature. Where sequences for the seed strain are available is noted by * and the nomenclature according to[2] included if different.*

Seed Strain / HA Gene Source	Clade[1]	Reference	Represented
A/Goose/Guangdong/96	0*	Shi et al., 2022	No
A/chicken/Vietnam/C58/04	1*	EFSA 2023	Yes
A/Vietnam/1194/2004	1*	EFSA 2023	Yes
A/Chicken/Shanxi/2/2006	7.2*	Shi et al., 2022	No
A/Chicken/Liaoning/S4092/2011	7.2	Shi et al., 2022	No
A/chicken/Legok/2003	2.1.1	EFSA 2023	Pending
A/CK/Egypt/ME1010/2016	2.2.1.1	EFSA 2023	Pending
A/Chicken/Egypt/Q1995D/2010	2.2.1.2*	EFSA 2023	Pending
A/Chicken/Egypt/RG-173 CAL/2017	2.2.1.2	EFSA 2023	Pending
A/Duck/EGYPT/M2583D/2010	2.2.1.2*	EFSA 2023	Pending
A/chicken/West Java/Pwt-Wij/2006	2.3.1.2	EFSA 2023	No
A/duck/Sukoharjo/BBVW-1428- 9/2012	2.3.2.1g[2]*	Indriani et al., 2014	Yes
A/Hubei/1/2010	2.3.2.1a[2]*	EFSA 2023	Pending
A/duck/Guangdong/S1322/2010	2.3.2.1b[2]*	Shi et al., 2022	Yes
A/chicken/Vietnam/NCVD-KA435/13	2.3.2.1c[1]/e[2]*	EFSA 2023	Pending
A/chicken/Tanggamus/031711076- 65/2017	2.3.2.1c	EFSA 2023	No
A/chicken/Liaoning/SD007/2017	2.3.2.1d	Shi et al., 2022	Pending
rgCA2/2.3.2.1d	2.3.2.1d	Kang et al., 2022	No
A/duck/Anhui/SI246/2014	2.3.2.1	Shi et al., 2022	No
A/Duck/Anhui/1/2006	2.3.4*	Shi et al., 2022	Yes
A/chicken/Guizhou/4/2013	2.3.4.4/g[2]*	Shi et al., 2022	No
A/duck/Korea/ES2/2016	2.3.4.4/e[2]*	EFSA 2023	Pending
A/Waterfowl/Korea/S57/2016	2.3.4.4	Kuruppuarachchi et al., 2022	No
A/Gyrfalcon/WA/41088-6/2014	2.3.4.4c[2]*	EFSA 2023	Yes
A/chicken/Egypt/ME-2018/2018	2.3.4.4b[2]*		Yes
A/green-winged teal/Egypt/877/2016	2.3.4.4b[2]*	EFSA 2023	Yes
A/whooper swan/Shanxi/4–1/2020	2.3.4.4b[2]*	Shi et al., 2022	Yes
A/duck/Guizhou/S4184/2017	2.3.4.4h	Shi et al., 2022	Pending
A/duck/Fujian/S1424/2020	2.3.4.4h	Shi et al., 2022	Pending
rgES3/2.3.4.4h	2.3.4.4h	Kang et al., 2022	No
A/duck/Guanzou/S4184/2017	2.3.4.4h	Shi et al., 2022	Pending
A/Duck/VietNam/QB7412	unknown	EFSA 2023	No

Panel of chicken antisera used in OFFLU AIM

Table 2: Viruses which were used in OFFLU aim to generate sera. Clade provisional nomenclature was taken from the WHO/FAO/WOAH H5 Nomenclature Working Group who define "clades" using HA gene sequences, and define clades as genetically distinct, monophyletic groups of viruses. This nomenclature splits clade 2.3.4.4 into eight additional sub-clades, named 2.3.4.4a through 2.3.4.4h due to high circulating diversity within the clade and. well as sub-clades 2.3.2.1a through 2.3.2.1g for the 2.3.2.1 split.*

Strain	Subtype	Clade[1]	Clade[2]	Similar vaccine seed strain
A/Vietnam/1194/2004/1	H5N1	1	*1*	A/chicken/Vietnam/C58/04
A/Turkey/turkey/2005	H5N1	2.2	*2.2.1*	A/swan/Hungary/4999/2006
A/Anhui/1/2005	H5N1	2.3.4	*2.3.4*	A/Duck/Anhui/1/2006
A/mynah/Indonesia/13064792-010/2013	H5N1	2.3.2.1c	*2.3.2.1g*	A/duck/Sukoharjo/BBVW-1428- 9/2012
A/chicken/Nepal/T360/2014	H5N1	2.3.2.1a	*2.3.2.1a*	A/duck/Guangdong/S1322/2010
A/Mute_Swan/Croatia/102/2016	H5N8	2.3.4.4b	*2.3.4.4b*	A/green-winged teal/Egypt/877/2016
A/mallard/Georgia/DT09382/2017	H5N8	2.3.4.4b	*2.3.4.4b*	A/chicken/ME-2018
A/chicken/Czech Republic/1175-1/2020	H5N8	2.3.4.4b	*2.3.4.4b*	
A/chicken/Bulgaria/722-1_22VIR778-1/2021	H5N1	2.3.4.4b	*2.3.4.4b*	
A/duck/Cambodia/f4k241D3/2021	H5N8	2.3.4.4b	*2.3.4.4b*	A/whooper swan/Shanxi/4–1/2020
A/great_skua/Scotland/B07779/2021	H5N1	2.3.4.4b	*2.3.4.4b*	
A/gyrfalcon/Washington/41088/6/2014	H5N8	2.3.4.4c	*2.3.4.4c*	A/Gyrfalcon/WA/41088-6/2014

Phylogenetic relationships of viruses included in the OFFLU AIM study

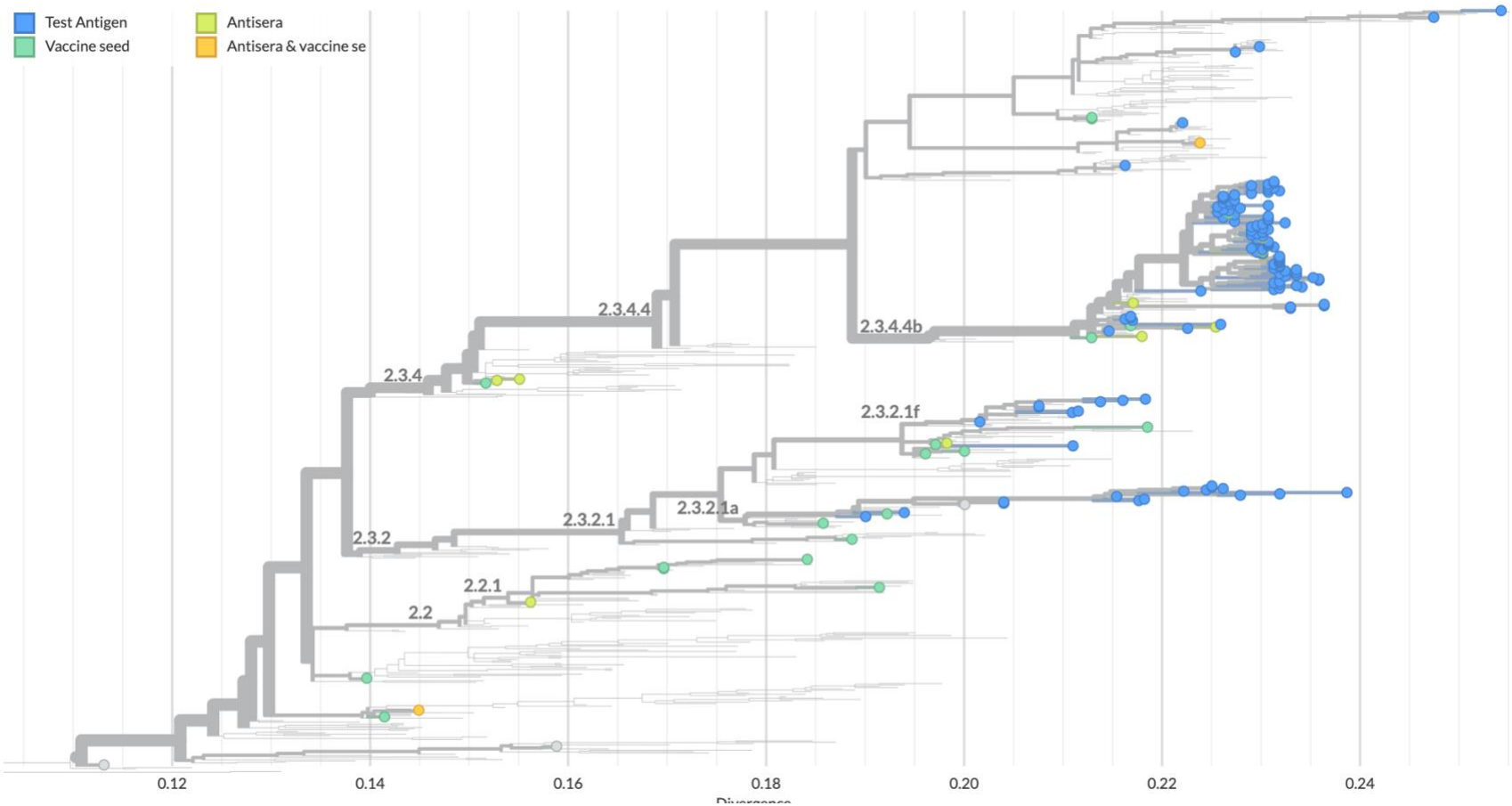

Figure 1: A maximum likelihood phylogenetic tree of the HA1 of Gs/Gd lineage H5 viruses included in this project and vaccine seed strains where sequences were available. Leaves are coloured by test antigens in this study, vaccine seed strains, antisera used in this study and antisera and vaccine seed strains used in this study. Major clades are annotated along the branches according to nomenclature, minor clade are not annotated[2]. This image was generated in Auspice using Nextclade.

Antigenic cartography

Antigenic cartography was undertaken to quantify and visualise the antigenic distances between viruses representative of vaccine seed strains and contemporary circulating viruses as described in the AIM pilot project. Maps were analysed and visualised using R Studio version 2023.03.1+446 and the Racmacs package version 1.2.9 built under R version 4.3.1 as described by Smith *et al.,* (2004) and previously used in Lewis *et al.,* (2021). For information regarding map generation and interpretation please contact an appropriate reference laboratory. Complementary genetic analysis was carried out for map testing using manually curated datasets with methods described as in the OFFLU avian data package for zoonotic influenza component of the VCM. Amino acid changes in the HA1 were visualised by reconstructing ancestry using treetime version 0.11.1 (Sagulenko *et al.*, 2018) and were compared between within-clade and within-subtype test antigens. Antigenic maps were colored according to unpublished viral clade nomenclature and subtype using the H5Nx dataset in Nextclade (Aksamentov *et al.,* 2021).

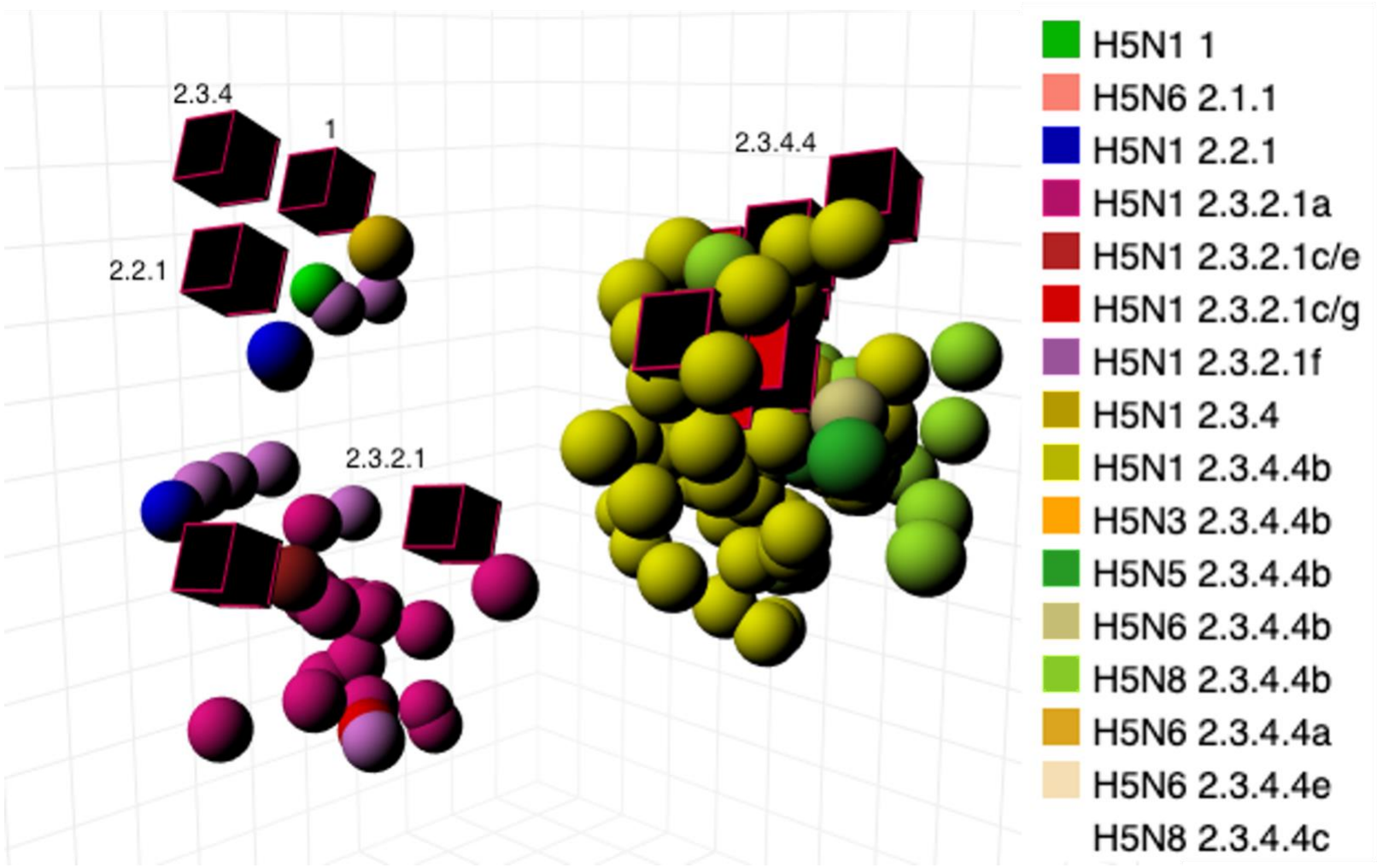

Figure 2: A 3-dimensional antigenic map showing the evolutionary relationships of H5 HPAI Gs/Gd lineage viruses. Each antiserum is represented by a red cube, for vaccine seed strains or surrogates and black cube for other. Antigens are represented as balls and are coloured by clade [1] or [2] according to the key. Each square represents one antigenic unit. One antigenic unit is representative of a 2-fold difference in HA assay titer. The corresponding table of antigenic distances can be found in table 3.

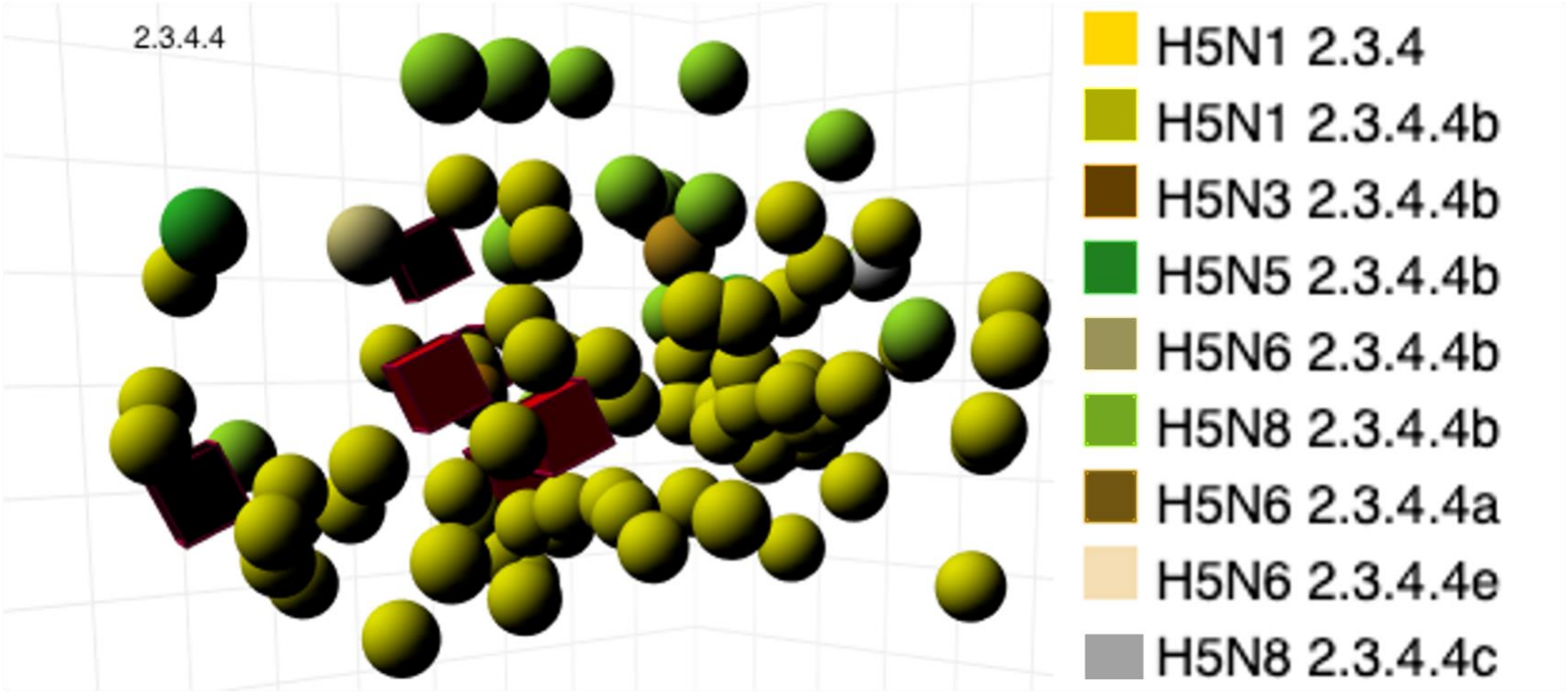

Figure 3: A 3-dimensional antigenic map showing the evolutionary relationships of H5 HPAI Gs/Gd lineage viruses of the clade 2.3.4.4. Each antiserum is represented by a red cube, for vaccine seed strains or surrogates and black cube for other. Antigens are represented as balls and are coloured by clade [1] or [2] according to the key. Each square represents one antigenic unit. One antigenic unit is representative of a 2-fold difference in HA assay titer. The corresponding table of antigenic distances can be found in table 3.

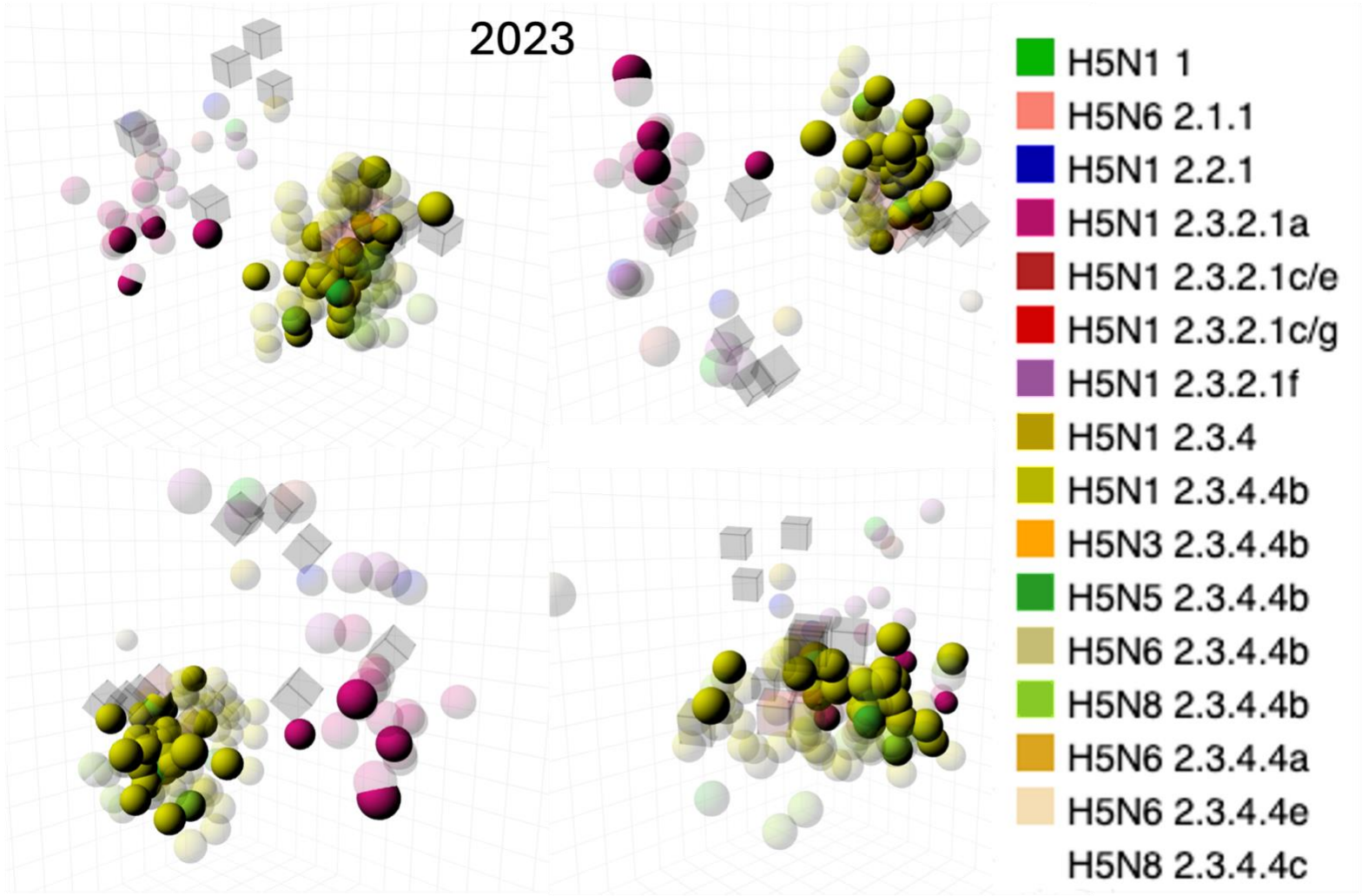

Figure 4: A 3-dimensional antigenic map showing the evolutionary relationships of H5 HPAI Gs/Gd lineage viruses. Each antiserum is represented by a red cube, for vaccine seed strains or surrogates and black cube for other. Antigens are represented as balls and are coloured by clade [1] or [2] according to the key, antigens from 2023 are highlighted. Each square represents one antigenic unit. One antigenic unit is representative of a 2-fold difference in HA assay titer. The corresponding table of antigenic distances can be found in table 3.

Table of antigenic distances

Table 3: A table of antigenic distances generated from the antigenic maps. One antigenic unit is equal to a twofold decrease in HA titer. Distances were coloured using a heat map. Vaccine antigen names are labelled in red italics next to their surrogate chicken antisera. Antigens are ordered by clade, subtype and region. ***Only antigens from viruses collected in 2023 are included in the table.***

					A/Vietnam/1194/2004/1 A/chicken/Vietnam/C58/04	A/Turkey/turkey/2005 A/swan/Hungary/4999/2006	A/Anhui/1/2005 A/Duck/Anhui/1/2006	A/chicken/Nepal/T360/2014 A/duck/Guangdong/S1322/2010	A/mynah/Indonesia/13064792-010/201 A/duck/Sukoharjo/BBWW-1428- 9/2012	A/duck/Cambodia/f4k241D3/2021 A/whooper swan/Shanxi/4-1/2020	A/mallard/Georgia/DT09382/2017 A/chicken/ME-2018	A/Mute_Swan/Croatia/102/2016 A/green-winged teal/Egypt/877/2016	A/gyrfalcon/Washington/41088/6/2014 A/Gyrfalcon/WA/41088-6/2014
				Subtype	H5N1	H5N1	H5N1	H5N1	H5N1	H5N8	H5N8	H5N8	H5N8
Year	**Clade**	**Subtype**	**Region**	**Clade**	*1*	*2.2*	*2.3.4*	*2.3.2.1a*	2.3.2.1c[1]/g[2]	*2.3.4.4b*	*2.3.4.4b*	*2.3.4.4b*	*2.3.4.4c*
2023	2.3.2.1a	H5N1	South Asia		4.8	4.8	5.6	3.9	2.7	7.5	6.6	7.2	6.2
2023	2.3.2.1a	H5N1	South Asia		6.3	6.4	7.2	5.0	3.8	8.3	7.5	8.0	7.0
2023	2.3.2.1a	H5N1	South Asia		5.3	4.8	5.8	2.9	2.3	7.3	6.5	6.4	6.2
2023	2.3.2.1a	H5N1	South Asia		4.5	3.9	4.8	2.5	1.1	4.9	4.1	3.9	4.0
2023	2.3.4.4b	H5N1	Africa		5.1	5.1	5.3	5.5	4.1	1.1	0.6	1.9	1.1
2023	2.3.4.4b	H5N1	Africa		5.9	5.9	6.5	5.4	3.3	3.7	3.1	4.0	2.8
2023	2.3.4.4b	H5N1	Africa		6.2	5.8	6.1	6.0	5.2	2.0	2.2	1.0	2.9
2023	2.3.4.4b	H5N1	Africa		6.0	6.3	6.9	6.0	3.7	4.0	3.4	4.7	2.9
2023	2.3.4.4b	H5N1	Africa		4.8	4.9	5.5	4.3	2.0	4.3	3.5	4.3	3.1
2023	2.3.4.4b	H5N1	Americas		5.1	5.7	6.1	6.0	3.6	4.0	3.3	5.1	2.6
2023	2.3.4.4b	H5N1	Americas		4.7	4.9	5.4	4.8	2.6	3.4	2.6	3.8	2.2
2023	2.3.4.4b	H5N1	Americas		5.0	5.3	5.7	5.7	3.7	2.4	1.7	3.6	1.1
2023	2.3.4.4b	H5N1	Americas		5.2	5.5	5.9	5.8	3.8	2.3	1.7	3.5	1.2
2023	2.3.4.4b	H5N1	Europe		5.0	5.3	5.7	5.5	3.5	2.4	1.7	3.4	1.2
2023	2.3.4.4b	H5N1	Europe		5.1	5.1	5.7	4.9	3.0	2.8	2.1	3.0	1.8
2023	2.3.4.4b	H5N1	Europe		4.7	4.8	5.1	5.3	3.7	1.5	0.7	2.4	0.7
2023	2.3.4.4b	H5N1	Europe		5.5	5.8	6.2	5.9	3.9	2.6	2.0	3.6	1.5
2023	2.3.4.4b	H5N1	Europe		4.9	5.0	5.4	5.2	3.4	2.0	1.3	2.6	1.1
2023	2.3.4.4b	H5N1	Europe		5.1	5.3	5.8	5.2	3.1	3.1	2.4	3.7	1.9
2023	2.3.4.4b	H5N1	Europe		5.0	5.1	5.4	5.6	4.0	1.3	0.6	2.5	0.6
2023	2.3.4.4b	H5N1	Europe		4.9	5.1	5.5	5.2	3.2	2.4	1.7	3.2	1.3
2023	2.3.4.4b	H5N1	Europe		5.0	5.4	5.8	5.6	3.5	2.7	2.0	3.8	1.4
2023	2.3.4.4b	H5N1	Europe		5.1	5.1	5.3	5.5	4.1	1.1	0.6	1.9	1.1
2023	2.3.4.4b	H5N1	Europe		5.1	5.3	5.7	5.6	3.7	2.1	1.4	3.1	1.0
2023	2.3.4.4b	H5N1	Europe		5.3	5.4	5.8	5.2	3.3	2.6	2.0	3.1	1.7
2023	2.3.4.4b	H5N1	Europe		4.5	4.6	4.9	5.2	3.6	1.5	0.7	2.3	0.8
2023	2.3.4.4b	H5N1	South Asia		4.6	4.4	4.9	4.3	2.7	2.6	1.8	2.3	1.8
2023	2.3.4.4b	H5N1	Southeast Asia		4.8	4.4	4.7	4.7	3.9	2.2	1.9	0.9	2.4
2023	2.3.4.4b	H5N1	Southeast Asia		4.9	5.5	5.6	6.2	4.2	2.1	1.5	3.8	0.8
2023	2.3.4.4b	H5N5	Europe		5.6	5.7	6.1	5.5	3.6	2.6	2.0	3.2	1.7

Main findings from contemporary viruses collected in 2023

The following text describes the distance in antigenic units of tested antigens and sera.

All viruses belonging to the 2.3.4.4b clade recorded distances ≥4.3 antigenic units (AI) to the 2.3.2.1a clade antiserum. In keeping with this result, viruses belonging to the 2.3.2.1a clade recorded distances ≥3.9 antigenic units (AI) to any of the 2.3.4.4 clade antisera. . This indicates it may be necessary to use multivalent H5 vaccines in places where multiple antigenically different viruses, or different clade viruses are co-circulating. Conclusions around antigenic diversity observed are detailed for each of the clades below:

2.3.2.1a

- For contemporary viruses (2023) isolated from South Asia we observed distances of ≥ 3.9 AU to any of the chicken antisera raised against 2.3.4.4 clade vaccine seed strains or surrogates.
- All test antigens from 2023 were 1.1-5.0 AU from chicken antisera raised against 2.3.2.1 clade surrogate vaccine antigens.
- One test antigen positioned at a distance of ≥ 3.8 AU from both chicken antisera raised against 2.3.2.1 clade surrogate vaccine antigens.
- For all test antigens we observed distances of 4.8-7.2 AU from the antiserum raised against the clade 2.3.4 clade surrogate vaccine antigen.
- For all test antigens we observed distances of 3.9-6.4 AU from the antiserum raised against the clade 2.2 surrogate vaccine antigen.
- For all test antigens we observed distances of 4.5-6.3 AU from the antiserum raised against the clade 1 vaccine antigen antiserum.

These results indicate that ***inactivated vaccines*** using antigens from clades 2.3.4.4b, 2.3.4.4c, 2.3.2, 2.2, and clade 1 viruses may not provide protection against contemporary South Asian clade 2.3.2.1a viruses. Furthermore, some inactivated vaccines using antigens from clade 2.3.2.1 viruses may no longer provide protection against all contemporary circulating clade 2.3.2.1a viruses which appear to be drifting antigenically.

2.3.4.4b

- Antisera raised against clade 1, 2.2. 2.3.4 and 2.3.2.1a vaccine seed strains or surrogates were more than 4 AU from genetic clade representative 2.3.4.4b viruses.
- Clade 2.3.2.1c[1]/g[2] antiserum was 2-5 AU from genetic clade representative 2.3.4.4b viruses.
- One clade 2.3.4.4b antigen from Africa was 2 AU from clade 2.3.2.1c/g* chicken antiserum, the rest of the contemporary antigens tested were ≥2.6 AU from clade 2.3.2.1c/g* chicken antiserum.

This indicates that ***inactivated vaccines*** using antigens against clade 1, 2.2. 2.3.4 and 2.3.2.1a, and 2.3.2.1c[1]/g[2] would not provide protection against most of the contemporary genetic clade representative 2.3.4.4b viruses.

There is some antigenic diversity among contemporary genetic clade representative 2.4.4.4b viruses which varies somewhat by region.

- All contemporary viruses tested were ≤ 5.1 AU from H5N8 clade 2.3.4.4 chicken antisera raised against vaccine seed strains or surrogates.
- All but one of the contemporary H5N1 viruses were ≤3 AU from at least one H5N8 2.3.4.4 chicken antisera raised against vaccine seed strains or surrogates.
- Contemporary H5N1 viruses tested from Africa demonstrated antigenic variability ranging between 1-4.7 AU from chicken antisera raised against H5N8 clade 2.3.4.4 vaccine seed strains or surrogates.
- Contemporary H5N1 viruses tested from the Americas demonstrated antigenic variability ranging between 1-5.1 AU from clade 2.3.4.4 chicken antisera raised against vaccine seed strains or surrogates.
- Contemporary viruses tested from Europe were 0.6-3.8 AU from chicken antisera raised against H5N8 clade 2.3.4.4 vaccine seed strains or surrogates.
- The contemporary H5N1 virus tested from South Asia was 1.8-2.6 AU from chicken antisera raised against H5N8 clade 2.3.4.4 vaccine seed strains or surrogates.
- The contemporary H5N1 virus tested from one country in Southeast Asia was 0.8-3.8 AU from H5N8 clade 2.3.4.4 chicken antisera raised against vaccine seed strains or surrogates.

Although there is some antigenic variation in clade 2.3.4.4b viruses, there did not appear to be significant changes in European wild bird viruses when comparing antigens tested since 2020, to those from 2023. Antigenic drift is observed in viruses isolated from some countries where avian influenza was introduced before 2022 and has continued to circulate in local poultry (e.g., in parts of Africa and Asia).

If vaccination is being considered within a country, it is recommended that local representative isolates be tested against several within-clade antisera to identify indicators of antigenic drift. In areas where viruses are enzootic in poultry, or where multiple clades or multiple sub-clades of viruses are circulating, vaccine challenge studies should be conducted using local representative viruses, to ascertain whether the vaccine provides protection against all contemporaneous viruses. OFFLU can provide support with any analyses or recommendations.

Future direction and information:

Reagents (antisera and inactivated viruses) generated by APHA and IZSVe under the OFFLU AIM framework can be shared, upon request, with selected partners, operating in other WOAH and FAO international reference laboratories. The objective is to enable the generation of comparative data assessing potential alteration in virus antigenicity using standardised reagents and methodologies under a defined quality framework. It should be noted, however, that careful inter-laboratory standardization and interpretation is required before data from additional laboratories can be reliably represented in the analyses.

A webinar will be held on 10th July 2024 to inform countries, CVOs and stakeholders about the OFFLU AIM project.

OFFLU value your feedback on the utility of this project. A form for comments and opinions is available at the following link.

A stakeholder meeting will be planned for 2025 to discuss the future direction of this project. If you wish to be involved, please express your interest by emailing secretariat@offlu.org

Generation of antiserum from other clade viruses including clade 2.3.4.4h, 2.3.2.1a and 2.3.2.1c[1]/e[2]/g[2] is underway. Characterisation of contemporary viruses will continue to take place; the report will be updated on an *ad-hoc* basis.

Links to other OFFLU AIM documents

OFFLU Avian influenza technical activity vaccination page

Concept note OFFLU AIM project - April 2022

OFFLU AIM presentation – February 2023

OFFLU AIM pilot report – October 2023

Module 1: OFFLU Avian Influenza Matching: Introduction and background

Module 2: OFFLU Avian Influenza Matching: guide to assessing antigenic characteristics of avian influenza viruses

Feedback form – have your say on OFFLU AIM

References

Aksamentov, I., Roemer, C., Hodcroft, E. B., & Neher, R. A., (2021). Nextclade: clade assignment, mutation calling and quality control for viral genomes. Journal of Open Source Software, 6(67), 3773, https://doi.org/10.21105/joss.03773

Indriani, R., Dharmayanti, N., 2014. Prototipe virus A/Duck/ Sukoharjo/Bbvw-1428-9/2012 subtipe H5N1 clade 2.3.2 sebagai vaksin pada itik lokal. JITV 19. https://doi.org/10.14334/jitv.v19i2.1044

Kang, Y.-M., Cho, H.-K., An, S.-J., Kim, H.-J., Lee, Y.-J., Kang, H.-M., 2022. Updating the National Antigen Bank in Korea: Protective Efficacy of Synthetic Vaccine Candidates against H5Nx Highly Pathogenic Avian Influenza Viruses Belonging to Clades 2.3.2.1 and 2.3.4.4. Vaccines (Basel) 10, 1860. https://doi.org/10.3390/vaccines10111860

Kuruppuarachchi, K.A.P.P., Jang, Y., Seo, S.H., 2022. Evaluation of Efficacy of Oil Adjuvanted H5N6 Inactivated Vaccine against Highly Pathogenic H5N6 and H5N1 Influenza Viruses Infected Chickens. Front Biosci (Landmark Ed) 27, 268. https://doi.org/10.31083/j.fbl2709268

Lewis, N.S., Banyard, A.C., Essen, S., Whittard, E., Coggon, A., Hansen, R., Reid, S., Brown, I.H., 2021. Antigenic evolution of contemporary clade 2.3.4.4 HPAI H5 influenza A viruses and impact on vaccine use for mitigation and control. Vaccine 39, 3794–3798. https://doi.org/10.1016/j.vaccine.2021.05.060

Sagulenko, P., Puller, V., Neher, R.A., 2018. TreeTime: Maximum-likelihood phylodynamic analysis. Virus Evol 4, vex042. https://doi.org/10.1093/ve/vex042

Shi, J., Zeng, X., Cui, P., Yan, C., Chen, H., 2023. Alarming situation of emerging H5 and H7 avian influenza and effective control strategies. Emerging Microbes & Infections 12, 2155072. https://doi.org/10.1080/22221751.2022.2155072

Smith, D.J., Lapedes, A.S., de Jong, J.C., Bestebroer, T.M., Rimmelzwaan, G.F., Osterhaus, A.D.M.E., Fouchier, R.A.M., 2004. Mapping the antigenic and genetic evolution of influenza virus. Science 305, 371– 376. https://doi.org/10.1126/science.1097211