We claim:

1. A pharmaceutical composition comprising:

a binding agent that comprises an H5 hemagglutinin ("HA") polypeptide that is at least 20 amino acids in length and has an amino acid sequence that:

i) shows at least 95% identity with a corresponding portion of a reference H5 HA of SEQ ID NO: 50; and

ii) shows sequence variation from that of the reference H5 HA polypeptide in that the binding agent's sequence has a deletion at one or more positions selected from the group consisting of: 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, and combinations thereof.

2. The pharmaceutical composition of claim 1, wherein the binding agent competes in a glycan HA polypeptide interaction between umbrella topology glycan and an HA polypeptide.

3. The pharmaceutical composition of claim 1, wherein the H5 HA polypeptide amino acid sequence has a deletion of the amino acid residue at a position selected from 130, 131, 132 and 133.

4. The pharmaceutical composition of claim 2, wherein the umbrella topology glycan comprises long α2-6 sialylated glycans.

5. The pharmaceutical composition of claim 4, wherein the long α2-6 sialylated glycans are selected from the group consisting of Neu5Acα2-6Galβ1-4GlcNAcβ1-3Galβ1-4GlcNAc, Neu5Acα2-6GalNAcβ1-4GlcNAcβ1-3GalNAcβ1-4GlcNAc, Neu5Acα2-6Galβ1-4GlcNAcβ1-3Galβ1-4GalNAc, Neu5Acα2-6Galβ1-4GlcNAcβ1-3Galβ1-4GlcNAcβ1-3Galβ1-3GalNAc, Neu5Acα2-6GalNAcβ1-4GlcNAcβ1-3Galβ1-4GalNAc, Neu5Acα2-6GalNAcβ1-4GlcNAcβ1-3GalNAcβ1-4GlcNAcβ1-3Galβ1-3GalNAc, NeuAcα2-3Galβ1-3GalNAcα2-6Neu5Ac, Neu5Acα2-6Galβ1-4GlcNAcβ1-3/6GalNAc, Neu5Acα2-6Galβ1-4GlcNAcβ1-3Galβ1-4GlcNAcβ1-3/6GalNAc, Neu5Acα2-6GalNAcβ1-4GlcNAcβ1-3/6GalNAc, Neu5Acα2-6GalNAcβ1-4GlcNAcβ1-3GalNAcβ1-

4GlcNAcβ1-3/6GalNAc, NeuAcα2-6Galβ1-4GalNAcβ1-6GlcNAcβ1-3Galα2-3Neu5Ac, NeuAcα2-6Galβ1-4GalNAcβ1-3/6GlcNAcβ1-3/6Galα2-3/6Neu5Ac, Neu5Acα2-6Galβ1-3GalNAcβ1-4Galα1-3Galβ1-4Glc, Neu5Acα2-6Galβ1 -3GalNAcβ1-3Galα1-4Galβ1-4Glc, Neu5Acα2-6Galβ1-3GlcNAcβ1-3Galβ1-4Glc and Neu5Acα2-6Galβ1-4GlcNAcβ1-3Galβ1-4Glc.

6. The pharmaceutical composition of claim 2, wherein the binding agent binds to umbrella topology glycans with an affinity that is at least 50%, at least 70%, at least 80%, at least 90% or at least 100% of that observed under comparable conditions for a wild type HA that mediates infection of humans.

7. The pharmaceutical composition of claim 2, wherein the binding agent binds to umbrella topology glycans more strongly than it binds to cone topology glycans.

8. The pharmaceutical composition of claim 2, wherein the binding agent shows a relative affinity for umbrella topology glycans versus cone topology glycans of at least 2.

9. The pharmaceutical composition of claim 2, wherein the binding agent shows a relative affinity for umbrella topology glycans versus cone topology glycans of at least 5.

10. The pharmaceutical composition of claim 2, wherein the binding agent shows a relative affinity for umbrella topology glycans versus cone topology glycans of at least 10.

11. The pharmaceutical composition of claim 2, wherein the interaction occurs between the HA polypeptide and receptors found on human upper respiratory epithelial cells, the bronchus, trachea, or the deep lung.

12. An immunogenic composition comprising: a binding agent that comprises an H5 hemagglutinin ("HA") polypeptide that is at least 20 amino acids in length and has an amino acid sequences that:

i) shows at least 95% identity with a corresponding portion of a reference H5 HA of SEQ ID NO: 50; and

ii) shows a sequence variation relative to the reference H5 HA, which sequence variation includes a sequence element selected from the group consisting of:

137 Gln or Arg

155 Thr

158 Asn

160 Thr

193 Xaa, wherein Xaa is any non-basic amino acid

226 Leu, Ile or Val;

which binding agent is characterized by an activity selected from the group consisting of: it competes a glycan HA polypeptide interaction between an umbrella topology glycan and HA polypeptide; and it binds to human tissues.

13. The immunogenic composition of claim 18, wherein the sequence variation relative to the reference H5 HA additionally comprises substitutions at positions corresponding to one or more of residues 128, 159, and 224.

14. The pharmaceutical composition of claim 1, wherein the binding agent further shows sequence variation from that of the reference H5 HA polypeptide at one or more positions selected from the group consisting of: 128, 137, 155, 158, 159, 160, 193, 224, 226, and combinations thereof.

We claim:

1. A pharmaceutical composition comprising:

a binding agent that comprises an H5 hemagglutinin ("HA") polypeptide that is at least 20 amino acids in length and has an amino acid sequence using positions based on the canonical H3 numbering system that:

i) shows at least 95% identity with a corresponding portion of a reference H5 HA of SEQ ID NO: 50; and

ii) shows sequence variation from that of the reference H5 HA polypeptide in that the binding agent's sequence has a deletion at one or more positions selected from the group consisting of: 128, 129, 130, 131, 132, 133, 134, 135, 136 and combinations thereof.

2. The pharmaceutical composition of claim 1, wherein the H5 HA polypeptide further includes substitutions Q226L and G228S relative to the reference H5 HA polypeptide.

3. The pharmaceutical composition of claims 1 or 2, wherein the H5 HA polypeptide has an amino acid sequence that further differs from that of the reference H5 HA polypeptide by one or more residues selected from the group consisting of residues 192, 193, and combinations thereof.

4. The pharmaceutical composition of any one of claims 1-3, wherein the H5 HA polypeptide has an amino acid sequence that further differs from that of the reference H5 HA polypeptide by one or more residues selected from the group consisting of residues 158 or 160.

5. The pharmaceutical composition of any one of claims 1-4, wherein the H5 HA polypeptide amino acid sequence has a deletion of the amino acid residue at a position selected from 130, 131, 132 and 133.

6. The pharmaceutical composition of any one of claims 1-5, wherein the binding agent competes in a glycan HA polypeptide interaction between umbrella topology glycan and an HA polypeptide.

7. The pharmaceutical composition of claim 6, wherein the umbrella topology glycan comprises long α2-6 sialylated glycans.

8. The pharmaceutical composition of claim 7, wherein the long α2-6 sialylated glycans are selected from the group consisting of Neu5Acα2-6Galβ1-4GlcNAcβ1-3Galβ1- 4GlcNAc, Neu5Acα2-6GalNAcβ1-4GlcNAcβ1-3GalNAcβ1-4GlcNAc, Neu5Acα2-6Galβ1-4GlcNAcβ1-3Galβ1-4GalNAc, Neu5Acα2-6Galβ1-4GlcNAcβ1-3Galβ1-4GlcNAcβ1-3Galβ1-3GalNAc,

Neu5Acα2-6GalNAcβ1-4GlcNAcβ1-3Galβ1-4GalNAc, Neu5Acα2-6GalNAcβ1-4GlcNAcβ1-3GalNAcβ1-4GlcNAcβ1-3Galβ1-3GalNAc, NeuAcα2-3Galβ1-3GalNAcα2-6Neu5 Ac, Neu5Acα2-6Galβ1-4GlcNAcβ1-3/6GalNAc, Neu5Acα2-6Galβ1-4GlcNAcβ1-3Galβ1-4GlcNAcβ1-3/6GalNAc, Neu5Acα2-6GalNAcβ1-4GlcNAcβ1-3/6GalNAc, Neu5Acα2-6GalNAcβ1-4GlcNAcβ1-3GalNAcβ1-4GlcNAcβ1-3/6GalNAc, NeuAcα2-6Galβ1-4GalNAcβ1-6GlcNAcβ1-3Galα2-3Neu5Ac, NeuAcα2-6Galβ1-4GalNAcβ1-3/6GlcNAcβ1-3/6Galα2-3/6Neu5Ac, Neu5Acα2-6Galβ1-3GalNAcβ1-4Galα1-3Galβ1-4Glc, Neu5Acα2-6Galβ1 -3GalNAcβ1-3Galα1-4Galβ1-4Glc, Neu5Acα2-6Galβ1-3GlcNAcβ1-3Galβ1-4Glc and Neu5Acα2-6Galβ1-4GlcNAcβ1-3Galβ1-4Glc.

9. The pharmaceutical composition of any one of claims 1-8, wherein the binding agent binds to umbrella topology glycans with an affinity that is at least 50%, at least 70%, at least 80%, at least 90% or at least 100% of that observed under comparable conditions for a wild type HA that mediates infection of humans.

10. The pharmaceutical composition of any one of claims 1-9, wherein the binding agent binds to umbrella topology glycans more strongly than it binds to cone topology glycans.

11. The pharmaceutical composition of any one of claims 1-10, wherein the binding agent shows a relative affinity for umbrella topology glycans versus cone topology glycans of at least 2.

12. The pharmaceutical composition of any one of claims 1-10, wherein the binding agent shows a relative affinity for umbrella topology glycans versus cone topology glycans of at least 5.

13. The pharmaceutical composition of any one of claims 1-10, wherein the binding agent shows a relative affinity for umbrella topology glycans versus cone topology glycans of at least 10.

14. The pharmaceutical composition of any one of claims 1-13, wherein the interaction occurs between the HA polypeptide and receptors found on human upper respiratory epithelial cells, the bronchus, trachea, or the deep lung.

15. An immunogenic composition comprising: a binding agent that comprises an H5 hemagglutinin ("HA") polypeptide that is at least 20 amino acids in length and has an amino acid sequences using positions based on the canonical H3 numbering system that:

i) shows at least 95% identity with a corresponding portion of a reference H5 HA of SEQ ID NO: 50;

ii) shows a sequence variation relative to the reference H5 HA;

iii) includes a deletion of one or more residues within residues 128-137; and

iv) lacks glycosylation at position 158

which binding agent is characterized by an activity selected from the group consisting of:

it competes a glycan HA polypeptide interaction between an umbrella topology glycan and HA polypeptide; and

it binds to human lung tissues.

16. The pharmaceutical composition of any one of claims 1-14, wherein the binding agent further shows sequence variation from that of the reference H5 HA polypeptide at one or more positions selected from the group consisting of: 128, 137, 155, 158, 159, 160, 193, 224, 226, and combinations thereof.

17. The immunogenic composition of claim 15, wherein residue 137 in the HA polypeptide is Ala or Arg.

18. The immunogenic composition of claim 15, wherein residue 155 in the HA polypeptide is Thr.

19. The immunogenic composition of claim 15, wherein residue 131 in the HA polypeptide is Ala, Thr or Ser.

20. The immunogenic composition of claim 15, wherein residue 132 in the HA polypeptide is Ala, Thr or Ser.

21. The immunogenic composition of claim 15, wherein residue 133 in the HA polypeptide is Ala, Thr or Ser.

22. The immunogenic composition of claim 15, wherein residue 159 in the HA polypeptide is Asn.

23. The immunogenic composition of claim 15, wherein residue 159 in the HA polypeptide is Asp.

24. The immunogenic composition of claim 15, wherein residue 193 in the HA polypeptide is a neutral or an acidic amino acid.

25. The immunogenic composition of claim 15, wherein residue 226 in the HA polypeptide is Leu, Ile or Gln.

26. The immunogenic composition of claim 15, wherein residue 160 in the HA polypeptide is Ala.

27. The immunogenic composition of claim 15, wherein the corresponding portion spans at least positions 95-228 and the binding agent further shows sequence variation from that of the reference H5 HA polypeptide at one or more positions selected from the group consisting of: residues 95, 98, 128, 130, 131, 132, 133, 135, 136, 137, 138, 145, 153, 155, 156, 158, 159, 160, 183, 186, 187, 188, 189, 190, 192, 193, 194, 195, 196, 219, 221, 222, 224, 225, 226, 227, 228, and combinations thereof.

28. The pharmaceutical composition or the immunogenic composition of any one of the preceding claims for use as a vaccine in preventing and/or treating H5 influenza virus.

29. The use of the pharmaceutical composition or the immunogenic composition of any one of the preceding claims in the manufacture of a medicament for preventing and/or treating H5 influenza virus.