CLAIMS

1. A method for capturing virus like particles of interest from a mixture comprising ~~the use of an expanded bed of adsorbent; suitably~~disrupted cells of a plant; wherein said method comprises the steps of:

(i) providing an expanded bed of adsorbent comprising a resin material;

(ii) equilibrating the resin material at a pH in the range of about pH 6.0 to 8.0; and

(iii) loading the mixture onto the expanded bed of adsorbent to bind the virus like particles, wherein the degree of expansion of the expanded bed is in the range of from about 1 to 5; ~~(a) providing an expanded bed of adsorbent; (b) contacting the mixture with the adsorbent such that the virus like particles in the mixture bind the adsorbent; (c)~~

(iv) optionally washing the adsorbent; and

(~~d~~v) optionally eluting the virus like particles from the adsorbent.

2. The method according to claim 1, wherein the adsorbent is contained in a column.

~~2~~3. The method according to claim 1 or claim 2, wherein the virus like particles comprises a protein of an influenza virus.

~~3~~4. The method according to ~~claim 1 or claim 2~~any one of claims 1 to 3, wherein the virus like particles comprises a haemagglutinin; ~~suitably,~~ a haemagglutinin subtype selected from the group consisting of H1, H2, H3, H4, H5, H6, H7, H8, H9, H10, H11, H12, H13, H14, H15 or H16 or a combination of two or more thereof.

~~4~~5. The method according to any of the preceding claims, wherein the mixture comprises disrupted cells of ~~a plant; suitably wherein the plant is~~ a tobacco plant infiltrated with nucleic acid molecules that express a protein transiently in the plant, said protein being present in the virus like particles; ~~more suitably~~ wherein the mixture is or is derived from aerial parts of the plant.

~~5~~6. The method according to any of the preceding claims, wherein the beads comprise, consist or consist essentially of a material selected from the group consiting of plastics, methacrylate, an anion exchanger, diethylaminoethyl, a cation exchanger, a polysaccharide, silica, poly(styrenedivinyl)benzene, polyacrylamide, ceramic and derivatives thereof or a combination of two or more thereof; ~~suitably~~ wherein the beads comprise, consist or consist essentially of a polysaccharide selected from the group consisting of cellulose, agarose and dextran and derivatives thereof or a combination of two or more thereof.

~~6~~7. The method according to claim ~~5~~6, wherein the beads comprise an inert core that comprises, consists or consists essentially of a material selected from the group consisting of: quartz, silica, Nd-Fe-B alloy, stainless steel, zirconium oxide, zirconia, metal silicates, metal borosilicates, ceramics including titanium diboride, titanium carbide, zirconium diboride, zirconium carbide, tungsten carbide, silicon carbide, aluminium nitride, silicon

nitride, titanium nitride, yttrium oxide, silicon metal powder, and molybdenum disilide; metal oxides and sulfides, including magnesium, aluminium, titanium, vanadium, chromium, zirconium, hafnium, manganese, iron, cobalt, nickel, copper and silver oxide; non-metal oxides; metal salts, including barium sulphate; metallic elements, including tungsten, zirconium, titanium, hafnium, vanadium, chromium, manganese, iron, cobalt, nickel, indium, copper, silver, gold, palladium, platinum, ruthenium, osmium, rhodium and iridium, and alloys of metallic elements, such as alloys formed between said metallic elements and derivatives thereof or a combination of two or more thereof.

~~7~~8. The method according to any of the preceding claims ~~5 to 6~~, wherein the size of the beads that bind the particle of interest is between about 25 µm to 100 µm; ~~suitably~~particularly about 50 µm.

~~8~~9. The method according to any of the preceding claims, wherein said method comprises a pre-capture step which comprises the use of a first expanded bed of adsorbent; ~~suitably~~ wherein the size of the beads is between about 125 µm to 250 µm; ~~more suitably~~particularly about 150 µm.

~~9~~10. The method according to any of the preceding claims, wherein the adsorbent comprises, consists or consists essentially of a ligand; ~~suitably~~ wherein the ligand comprises, consists or consists essentially of a ligand selected from the group consisting of (i) benzylamine or a derivative thereof; (ii) an alkylamine or a derivative thereof; (iii) an alkenylamine or a derivative thereof; (iv) an alkynylamine or a derivative thereof, (v) an alkoxyamine or a derivative therof; and (vi) an amine of mono- or bicyclic aromatic or heteroaromatic moities or a derivative thereof, or a combination of two or more thereof; or wherein the ligand comprises, consists or consists essentially of an anion exchange resin; ~~suitably~~ wherein the anion exchange resin comprises, consists or consists essentially of a diethylaminoethyl cellulose-based ion exchange resin or comprises, consists or consists essentially of diethylaminoethyl cellulose dextran-based ion exchange resin.

~~10~~11. The method according to any of the preceding claims, wherein the conductivity of the mixture prior to contact with the adsorbent is between about 1 mS/cm to 10 mS/cm; and/or the pH of the mixture prior to contact with the adsorbent is between about pH 6.0 to pH 8.0.

~~11~~12. The method according to any of the preceding claims, wherein ~~the degree of expansion of the expanded bed is in the range of from about 1 to 5; and~~ the mixture flows through the expanded bed at a linear flow rate in the range of between about 1 cm/min to 15 cm/min.

~~12~~13. A method for capturing virus like particles of interest from a mixture comprising tobacco plant material comprising the steps of:

(i) providing an expanded bed of adsorbent comprising diethylaminoethyl cellulose dextran in a column, wherein the density of the adsorbent is between about 2.5 g/ml to 3.5 g/ml, and wherein the average adsorbent particle size is about 50 μm;

(ii) equilibrating the resin material at a pH in the range of about pH 6.0 to 8.0;

(iii) providing a mixture comprising tobacco plant material, wherein said mixture has a conductivity of between about ~~2~~ 4 mS/cm to ~~3~~ 6 mS/cm;

(iv) loading the mixture onto the column at a flow rate of about 2.5 cm/min to bind the virus like particles and wherein the degree of expansion of the expanded bed in the column is about 2;

(v) washing the loaded column using a buffer having a pH in the range of about pH 6.0 to 8.0; and

(vi) eluting the bound particle of interest from the column in one or more fractions.

~~13~~14. The method of claim ~~12~~13, wherein step (iii) comprises (a) providing whole tobacco plants that are transiently expressing a protein that is present in the virus like particles; (b) disrupting cells of the leaves and stems of the tobacco plants to produce the tobacco plant material; and (c) adjusting the pH and conductivity of the mixture by dilution with a buffer or deionized water.

~~14~~15. The method of claim ~~12~~14, further comprising prior to step (iv), a step comprising filtering the mixture of step (iii) and contacting the filtered mixture of step (iii) with a first expaned bed of adsorbents comprising polyethylenimine, wherein the size of beads is about 150 μm, to remove undesired substances from the mixture.

~~15~~16. An expanded bed of adsorbent comprising a virus like particle reversibly bound thereto resulting from the method of any one of claims 1-15.

~~16~~17. Use of an expanded bed of adsorbent for capturing a virus like particle of interest from a mixture, wherein the mixture is derived from a plant that is transiently expressing a protein, said protein being present in the virus like particle; the resin material is equilibrated to a pH in the range of about pH 6.0 to 8.0; the mixture is loaded onto the column to bind the virus like particles and the degree of expansion of the expanded bed in the column is in the range of from about 1 to 5.