We claim:

1. A method of purifying Calicivirus virus-like particles (VLPs) using a multistep chromatographic process.

2. The method of claim 1, wherein the chromatographic process utilizes more than one chromatographic material.

3. The method of claim 1, wherein the chromatographic process is orthogonal.

4. The method of claim 3, wherein the orthogonal process utilizes chromatographic materials and mobile phase conditions of different physical or chemical properties.

5. The method of claim 4, wherein the chromatographic materials and mobile phase conditions are selected to retain VLPs.

6. The method of claim 4, wherein the chromatographic materials and mobile phase conditions are selected to pass through VLPs.

7. The method of claim 4, wherein the chromatographic materials and mobile phase conditions are selected to retain contaminants in VLP preparations.

8. The method of claim 4, wherein the chromatographic materials and mobile phase conditions are selected to pass through contaminants in VLP preparations.

9. The method of claim 1, wherein the sequence of the multistep chromatographic process is designed to produce VLPs meeting preset specifications.

10. The method of claim 9, wherein the VLPs are purified to greater than about 70% purity.

11. The method of claim 9, wherein the VLPs are purified to greater than about 90%.

12. The method of claim 9, wherein the VLPs are purified to greater than about 95% purity.

13. The method of claim 9, wherein the sequence of the multistep chromatographic process is designed to control the resulting composition of VLPs.

14. The method of claim 9, wherein the sequence of the multistep chromatographic process is designed to reduce contaminant levels to levels considered acceptable by regulatory agencies for pharmaceutical grade drug substance.

15. The method of claim 14, wherein the contaminant level of host cell DNA content is less than 1%.

16. The method of claim 14, wherein the contaminant level of host cell protein content is less than 5%.

17. The method of claim 9, wherein the sequence of the multistep chromatographic process is designed to make VLPs consistent with GMP regulations and suitable for pharmaceutical testing in humans.

18. The method of claim 2, wherein a solution containing VLPs is contacted with the chromatographic material.

19. The method of claim 18, wherein the solution is centrifuged without a sucrose gradient.

20. The method of claim 2, wherein a cell lysate containing VLPs is contacted with the chromatographic material.

21. The method of claim 20, wherein the cell lysate is filtered.

22. The method of claim 21, wherein the cell lysate is further purified by precipitation.

23. The method of claim 20, wherein the cell lysate is centrifuged without a sucrose gradient.

24. The method of claim 2, wherein a clarified solution containing VLPs is contacted with the chromatographic material.

25. The method of claim 2, wherein a VLP containing solution from one chromatographic step is contacted with another chromatographic material.

26. The method of claim 25, wherein the VLP containing solution is produced using recombinant methodologies.

27. The method of claim 26, wherein the VLPs and VLP proteins are produced in bacterial cells.

28. The method of claim 26, wherein the VLPs and VLP proteins are produced in insect cells.

29. The method of claim 26, wherein the VLPs and VLP proteins are produced in yeast cells.

30. The method of claim 26, wherein the VLPs and VLP proteins are produced in mammalian cells.

31. The method of claim 2 wherein the chromatographic material comprises chromatographic resin in solution, chromatographic resin in a column or chromatographic functionality incorporated into a membrane or onto a surface.

32. The method of claim 31, wherein the chromatographic material is designed for the purification of proteins or nucleic acids.

33. The method of claim 31, wherein the chromatographic material is selected from the group consisting of ion-exchange, affinity, hydrophobic interaction, mixed mode, reversed phase, size exclusion, and adsorption materials.

34. The method of claim 33, wherein the chromatographic material comprises an adsorption material.

35. The method of claim 34, wherein the adsorption material is a resin, membrane, or surface.

36. The method of claim 33, wherein the chromatographic material comprises a calcium phosphate based material.

37. The method of claim 36, wherein the chromatographic material is hydroxapatite.

38. The method of claim 33, wherein the chromatographic material comprises an ion exchanger.

39. The method of claim 38, wherein the ion exchanger is a cation exchanger.

40. The method of claim 39, wherein the cation exchanger comprises sulfate, phosphate and carboxylate derivitized chromatographic materials.

41. The method of claim 38, wherein the ion exchanger is an anion exchanger.

42. The method of claim 41, wherein the ion exchanger comprises positively charged chromatographic material.

43. The method of claim 42, wherein the positively charged chromatographic material is quaternary amine (Q) or diethylaminoethane (DEAE).

44. The method of claim 33, wherein the chromatographic material comprises a hydrophobic interaction material.

45. The method of claim 44, wherein the hydrophobic interaction material comprises one or more functional groups selected from the group consisting of methyl, ethyl, t-butyl and phenyl.

46. The method of claim 45, wherein the hydrophobic interaction chromatographic material is a methyl HIC resin.

47. The method of claim 33, wherein the reversed phase material comprises C2, C4, C8 or C18 functionality.

48. The method of claim 33, wherein the chromatographic material comprises an affinity chromatographic material.

49. The method of claim 48, wherein the affinity chromatographic material comprises antibodies, dry resins, and metals.

50. The method of claim 49, wherein the dry resin is cibachrom blue or polymixin.

51. The method of claim 33, wherein the chromatographic material comprises a size exclusion material.

52. The method of claim 51, wherein the size exclusion material is a resin or membrane.

53. The method of claim 52, wherein the resin or membrane comprises pores of the same or different sizes.

54. The method of claim 18, wherein the pH of the solution containing VLPs is adjusted to cause the retention of VLPs with contaminating materials passing through the chromatographic material.

55. The method of claim 54, wherein the pH is adjusted to less than 7.

56. The method of claim 54, wherein the pH is adjusted to greater than or equal to 7.

57. The method of claim 54, wherein the pH of the VLP containing solution is adjusted with a buffer.

58. The method of claim 57, wherein the buffer comprises phosphate, carboxylate, sulfate, acetate, citrate, tris or bis tris.

59. The method of claim 58, wherein the buffer concentration is in the range of about 10 to 1000 mM.

60. The method of claim 18, wherein the ionic strength of the solution containing VLPs is adjusted to cause the retention of VLPs with contaminating materials passing through the chromatographic material.

61. The method of claim 60, wherein the ionic strength is adjusted by anions and cations from the Hofmeister series.

62. The method of claim 61, wherein the ionic strength is adjusted by the addition of ammonium sulfate.

63. The method of claim 62, wherein the ammonium sulfate concentration is greater than about 100 mM.

64. The method of claim 62, wherein the ammonium sulfate concentration is greater than about 1 molar.

65. The method of claim 62, wherein the ammonium sulfate concentration is greater than about 2 molar.

66. The method of claim 65, wherein the ammonium sulfate concentration is about 2.4 molar.

67. The method of claim 61, wherein the ionic strength is adjusted by the addition of a phosphate salt.

68. The method of claim 67, wherein the phosphate salt is sodium phosphate.

69. The method of claim 68, wherein the sodium phosphate concentration is in the range of about 10 to 500 mM.

70. The method of claim 69, wherein the sodium phosphate concentration is about 100 mM.

71. The method of claim 2, wherein the pH of the chromatographic material is adjusted prior to VLP application by equilibration with a buffer to cause the retention of VLPs.

72. The method of claim 71, wherein the pH is adjusted to less than 7.

73. The method of claim 71, wherein the pH is adjusted to greater than or equal to 7.

74. The method of claim 71, wherein the buffer comprises phosphate, carboxylate, sulfate, acetate, citrate, tris or bis tris.

75. The method of claim 2, wherein the ionic strength of the chromatographic material is adjusted to cause retention of the VLPs.

76. The method of claim 75, wherein the ionic strength is adjusted by the addition of salt.

77. The method of claim 76, wherein the salt comprises cations and anions from the Hofmeister series.

78. The method of claim 77, wherein the ionic strength is adjusted by the addition of ammonium sulfate.

79. The method of claim 78, wherein the concentration of ammonium sulfate is greater than about 1 molar.

80. The method of claim 78, wherein the concentration of ammonium sulfate is greater than about 2 molar.

81. The method of claim 80, wherein the concentration of ammonium sulfate is about 2.4 molar.

82. The method of claim 77, wherein the ionic strength is adjusted by the addition of a phosphate salt.

83. The method of claim 82, wherein the phosphate salt is sodium phosphate.

84. The method of claim 83, wherein the sodium phosphate concentration is in the range of about 10 to 500 mM.

85. The method of claim 84, wherein the sodium phosphate concentration is about 100 mM.

86. The method of claim 18, wherein the organic solvent concentration of the VLP containing solution is adjusted to cause retention of VLPs.

87. The method of claim 18, wherein the pH of the solution containing VLPs is adjusted to cause retention of contaminating materials with the VLPs passing through the chromatographic material.

88. The method of claim 87, wherein the pH is adjusted to less than 7.

89. The method of claim 87, wherein the pH is adjusted to greater than or equal to 7.

90. The method of claim 87, wherein the pH of the VLP containing solution is adjusted with a buffer.

91. The method of claim 90, wherein the buffer comprises phosphate, carboxylate, sulfate, acetate, citrate, tris or bis tris.

92. The method of claim 91, wherein the buffer concentration is in the range of about 10 to 1000 mM.

93. The method of claim 18, wherein the ionic strength of the solution containing VLPs is adjusted to cause retention of contaminating materials with the VLPs passing through the chromatographic material.

94. The method of claim 93, wherein the ionic strength is adjusted by the addition of salt.

95. The method of claim 94, wherein the salt comprises cations and anions from the Hofmeister series.

96. The method of claim 95, wherein the salt is a phosphate salt.

97. The method of claim 96, wherein the phosphate salt is sodium phosphate.

98. The method of claim 97, wherein the sodium phosphate concentration is in the range of about 10 to 500 mM.

99. The method of claim 98, wherein the sodium phosphate concentration is about 100 mM.

100. The method of claim 18, wherein the pH of the chromatographic material is adjusted prior to contact with the solution containing VLPs by equilibration with a buffer to cause retention of contaminating materials.

101. The method of claim 100, wherein the pH is adjusted to less than 7.

102. The method of claim 100, wherein the pH is adjusted to greater than or equal to 7.

103. The method of claim 100, wherein the buffer comprises phosphate, carboxylate, or sulfate.

104. The method of claim 18, wherein the ionic strength of the chromatographic material is adjusted prior to contact with the solution containing VLPs by equilibration with a buffer to cause retention of contaminating materials.

105. The method of claim 104, the ionic strength is adjusted by the addition of salt.

106. The method of claim 105, wherein the salt comprises cations and anions from the Hofmeister series.

107. The method of claim 106, wherein the salt is a phosphate salt.

108. The method of claim 107, wherein the phosphate salt is sodium phosphate.

109. The method of claim 108, wherein the sodium phosphate concentration is greater than about 10 mM.

110. The method of claim 18, wherein the organic solvent concentration of the VLP containing solution is adjusted to cause retention of contaminating materials.

111. The method of claim 1, wherein Calicivirus virus-like particles (VLPs) comprises Norovirus and Sapovirus VLPs.

112. The method of 111, wherein the Norovirus VLPs are derived from Genogroup I, Genogroup II, or Genogroup IV Noroviruses.

113. A pharmaceutical agent prepared by the method in claim 1.

114. The pharmaceutical agent of claim 113, wherein the pharmaceutical agent is a vaccine.

115. The vaccine of claim 114, wherein the vaccine is a Norovirus vaccine.

116. An analytical reagent prepared by a method of purifying Calicivirus-like particles (VLPs) using a multistep chromatographic process, wherein the analytical reagent is purified to a desired purification level.

117. A diagnostic assay or kit comprising the analytical reagent of claim 116.

We claim:

1. A method of purifying Calicivirus virus-like particles (VLPs) comprising contacting a solution containing said VLPs with at least one chromatographic material, wherein the at least one chromatographic material is an ion exchange chromatographic material, wherein the chromatographic materials used in the method do not comprise hydroxyapatite, and wherein the VLPs are purified to greater than about 70%.

2. The method of claim 1, wherein the ion exchange chromatographic material is an anion exchange chromatographic material.

3. The method of claim 2, wherein the anion exchange chromatographic material is a DEAE-Sepharose FF resin.

4. The method of claim 2, wherein the method further comprises the use of a cation exchange chromatographic material.

5. The method of claim 1, wherein the method further comprises the use of a hydrophobic interaction chromatographic material.

6. The method of claim 1, wherein the method further comprises a precipitation step.

7. The method of claim 6, wherein the precipitation step is a PEG precipitation step.

8. The method of claim 7, wherein the PEG precipitation step is carried out prior to contacting the solution containing the VLPs with the ion exchange chromatographic material.

9. The method of claim 1, wherein the VLPs are purified to greater than about 90%.

10. The method of claim 1, wherein the method further comprises an ultrafiltration and/or diafiltration step.

11. The method of claim 1, wherein the Calicivirus VLPs are Norovirus VLPs.

12. The method of claim 11, wherein the Norovirus VLPs are Norovirus genogroup I or genogroup II VLPs.

13. The method of claim 12, wherein the Norovirus genogroup I VLPs are Norovirus genotype I.1 VLPs.