

What is claimed is:

1. A composition having a protein of interest purified from mammalian cells, surfactant and a residual amount of sialate o-acetylsterase, wherein the residual amount of sialate o-acetylsterase is less than about 5 ppm.
2. The composition of claim 1, wherein the surfactant is polysorbate 20.
3. The composition of claim 1, wherein the mammalian cells include CHO cells.
4. The composition of claim 3, wherein the CHO cells include SIAE-knockout CHO cell.
5. The composition of claim 2, wherein the sialate o-acetylsterase causes degradation of the polysorbate 20.
6. The composition of claim 1, wherein the composition is a parenteral formulation
7. The composition of claim 2, wherein a concentration of the polysorbate in the composition is about 0.01 %w/v to about 0.2% w/v.
8. The composition of claim 1, wherein the protein of interest is selected from a group consisting of a monoclonal antibody, a polyclonal antibody, a bispecific antibody, an antibody fragment and an antibody-drug complex.
9. The composition of claim 1 further comprising one or more pharmaceutically acceptable excipients.
10. The composition of claim 1 further comprising a buffer selected from a group consisting of histidine buffer, citrate buffer, alginate buffer, and arginine buffer.
11. The composition of claim 1 further comprising a tonicity modifier.
12. The composition of claim 1 further comprising sodium phosphate.
13. The composition of claim 1, wherein concentration of the protein of interest is about 20 mg/mL to about 400 mg/mL.
14. The composition of claim 1, wherein the sialate o-acetylsterase is CHO-sialate o-acetylsterase.
15. The composition of claim 1, wherein the sialate o-acetylsterase is cytosolic sialic acid esterase isoform.
16. The composition of claim 1, wherein the sialate o-acetylsterase is lysosomal sialic acid esterase isoform.
- ~~17. A composition having a protein of interest purified from mammalian cells, surfactant and a residual amount of lysosomal acid lipase, wherein the residual amount of lysosomal acid lipase is less than about 1 ppm.~~
- ~~18. The composition of claim 17, wherein the surfactant is polysorbate.~~
- ~~19. The composition of claim 18, wherein the surfactant is polysorbate, wherein the polysorbate is selected from the group consisting of polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 80, or combinations thereof.~~

20. — The composition of claim 17, wherein the mammalian cells include CHO cells.
21. — The composition of claim 18, wherein the lysosomal acid lipase causes degradation of the polysorbate.
22. — The composition of claim 17, wherein the composition is a parenteral formulation
23. — The composition of claim 18, wherein concentration of the polysorbate in the composition is about 0.01 %w/v to about 0.2% w/v.
24. — The composition of claim 17, wherein the protein of interest is selected from a group consisting of a monoclonal antibody, a polyclonal antibody, a bispecific antibody, an antibody fragment and antibody drug complex.
25. — The composition of claim 17 further comprising one or more pharmaceutically acceptable excipients
26. — The composition of claim 17 further comprising a buffer selected from a group consisting of histidine buffer, citrate buffer, alginate buffer, and arginine buffer.
27. — The composition of claim 17 further comprising a tonicity modifier.
28. — The composition of claim 17 further comprising sodium phosphate.
29. — The composition of claim 17, wherein concentration of the protein of interest is about 20 mg/mL to about 400 mg/mL.
30. — The composition of claim 17, wherein the lysosomal acid lipase is CHO lysosomal acid lipase.
31. — A method of preparing a composition having a protein of interest, comprising
culturing mammalian cells to produce the protein of interest to form a sample matrix;
contacting the sample matrix to a first chromatography resin;
washing the bound protein of interest to form an eluate;
contacting the eluate to a second chromatography resin;
collecting a flow through from washing the second chromatography resin;
contacting the flow through to a third chromatography resin;
collecting a second flow through from washing the third chromatography resin; and
filtering the second flow through by viral filtration.
32. — The method of claim 31, wherein the composition comprises less than about 5 ppm of sialate o-acetyltransferase.
33. — The method of claim 31, wherein the composition comprises less than about 1 ppm of lysosomal acid lipase.
34. — The method of claim 31, wherein the mammalian cells are CHO cells.
35. — The method of claim 31, wherein the first chromatographic resin is selected from protein A chromatographic resin, anion exchange chromatographic resin, cation exchange chromatographic resin and hydrophobic interaction chromatographic resin.

36. — The method of claim 31, wherein the second chromatographic resin is selected from protein A chromatographic resin, anion-exchange chromatographic resin, cation-exchange chromatographic resin and hydrophobic interaction chromatographic resin.
37. — The method of claim 31, wherein the third chromatographic resin is selected from protein A chromatographic resin, anion-exchange chromatographic resin, cation-exchange chromatographic resin and hydrophobic interaction chromatographic resin.
38. — The method of claim 31, wherein the first chromatographic resin is protein A chromatographic resin.
39. — The method of claim 31, wherein the second chromatographic resin is anion-exchange chromatographic resin.
40. — The method of claim 31, wherein the third chromatographic resin is hydrophobic interaction chromatographic resin.
41. — The method of claim 31 further comprising a purification step using beads having anti-sialate o-acetylcetate antibody.
42. — The method of claim 31 further comprising contacting the sample matrix to beads having anti-sialate o-acetylcetate antibody.
43. — The method of claim 31 further comprising contacting the eluate to beads having anti-sialate o-acetylcetate antibody.
44. — The method of claim 31 further comprising contacting the flow through to beads having anti-sialate o-acetylcetate antibody.
45. — The method of claim 31 further contacting the second flow through to beads having anti-sialate o-acetylcetate antibody.
46. — The method of any one of claims 41, wherein the anti-sialate o-acetylcetate antibody is of human origin.
47. — The method of any one of claims 41, wherein the anti-sialate o-acetylcetate antibody is of hamster origin.
48. — The method of claim 31 further comprising a purification step using beads having anti-lysosomal acid lipase antibody.
49. — The method of claim 31 further comprising contacting the sample matrix to beads having anti-lysosomal acid lipase antibody.
50. — The method of claim 31 further comprising contacting the eluate to beads having anti-lysosomal acid lipase antibody.
51. — The method of claim 31 further comprising contacting the flow through to beads having anti-lysosomal acid lipase antibody.
52. — The method of claim 31 further comprising contacting the second flow through to beads having anti-lysosomal acid lipase antibody.

53. — The method of claim 48, wherein the anti-lysosomal acid lipase antibody is of human origin.
54. — The method of claim 48, wherein the anti-lysosomal acid lipase antibody is of hamster origin.
55. — A method of depleting sialate o-acetyl esterase levels in a sample matrix, comprising
- contacting the sample matrix having sialate o-acetyl esterase to a resin having anti-sialate o-acetyl esterase antibody;
 - washing the resin with a wash buffer; and
 - collecting wash fractions from the washing, wherein the wash fractions have a reduced concentration of sialate o-acetyl esterase than sialate o-acetyl esterase in the sample matrix.
56. — The method of claim 55, wherein the sample matrix comprises polysorbate.
57. — The method of claim 55, wherein the resin is a magnetic bead.
58. — The method of claim 55, wherein the amount of anti-sialate o-acetyl esterase antibody to the resin is about 1 µg/g to about 50 µg/g.
59. — The method of claim 55, wherein the anti-sialate o-acetyl esterase antibody is of human origin.
60. — The method of claim 55, wherein the anti-sialate o-acetyl esterase antibody is of hamster origin.
61. — The method of claim 55, wherein the wash fractions have a two-fold reduced amount of sialate o-acetyl esterase compared to amount of sialate o-acetyl esterase in the sample matrix.
62. — A method of depleting lysosomal acid lipase levels in a sample matrix, comprising
- contacting the sample matrix having lysosomal acid lipase to a resin having anti-lysosomal acid lipase antibody;
 - washing the resin with a wash buffer; and
 - collecting wash fractions from the washing, wherein the wash fractions have a reduced concentration of lysosomal acid lipase than lysosomal acid lipase in sample matrix.
63. — The method of claim 62, wherein the sample matrix comprises polysorbate.
64. — The method of claim 62, wherein the resin is a magnetic bead.
65. — The method of claim 62, wherein the amount of anti-lysosomal acid lipase antibody to the resin is about 1 µg/g to about 50 µg/g.
66. — The method of claim 62, wherein the anti-lysosomal acid lipase antibody is of human origin.

67. — ~~The method of claim 62, wherein the anti-lysosomal acid lipase antibody is of hamster origin.~~
68. — ~~The method of claim 62, wherein the wash fractions have a have a two-fold reduced amount of lysosomal acid lipase compared to amount of lysosomal acid lipase in the sample matrix.~~
69. — ~~A method of detecting sialate o-acetyltransferase in a sample matrix, comprising:~~
~~contacting the sample matrix with a biotinylated anti-sialate o-acetyltransferase antibody;~~
~~incubating the sample matrix with a resin;~~
~~performing elution on the resin of to form an eluate;~~
~~adding hydrolyzing agent to the eluate to obtain digests; and~~
~~analyzing the digests to detect the sialate o-acetyltransferase.~~
70. — ~~The method of claim 69, wherein the resin is a magnetic bead.~~
71. — ~~The method of claim 69, wherein the elution is performed using a one or more solvents selected from acetonitrile, water and acetic acid.~~
72. — ~~The method of claim 69, wherein the hydrolyzing agent is trypsin.~~
73. — ~~The method of claim 69 further comprising adding protein denaturing agent to the eluate.~~
74. — ~~The method of claim 73, wherein the protein denaturing agent is urea.~~
75. — ~~The method of claim 69 further comprising adding protein reducing agent to the eluate.~~
76. — ~~The method of claim 75, wherein the protein reducing agent is DTT.~~
77. — ~~The method of claim 69 further comprising adding protein alkylating agent to the eluate.~~
78. — ~~The method of claim 77, wherein the protein alkylating agent is iodoacetamide.~~
79. — ~~The method of claim 69, wherein the digests are analyzed using a mass spectrometer.~~
80. — ~~The method of claim 79, wherein the mass spectrometer is a tandem mass spectrometer.~~
81. — ~~The method of claim 79, wherein the mass spectrometer is coupled to a liquid chromatography system.~~
82. — ~~The method of claim 79, wherein the mass spectrometer is coupled to a liquid chromatography multiple reaction monitoring system.~~
83. — ~~A method of detecting lysosomal acid lipase in a sample matrix, comprising:~~
~~contacting the sample matrix with a biotinylated anti-lysosomal acid lipase antibody;~~
~~incubating the sample matrix with a resin;~~

- ~~performing elution on the resin of to form an eluate;~~
~~adding hydrolyzing agent to the eluate to obtain digests; and~~
~~analyzing the digests to detect the lysosomal acid lipase.~~
84. — ~~The method of claim 83, wherein the resin is a magnetic bead.~~
85. — ~~The method of claim 83, wherein the elution is performed using a one or more solvents selected from acetonitrile, water and acetic acid.~~
86. — ~~The method of claim 83, wherein the hydrolyzing agent is trypsin.~~
87. — ~~The method of claim 83 further comprising adding protein denaturing agent to the eluate.~~
88. — ~~The method of claim 87, wherein the protein denaturing agent is urea.~~
89. — ~~The method of claim 83 further comprising adding protein reducing agent to the eluate.~~
90. — ~~The method of claim 89, wherein the protein reducing agent is DTT.~~
91. — ~~The method of claim 83 further comprising adding protein alkylating agent to the eluate.~~
92. — ~~The method of claim 91, wherein the protein alkylating agent is iodoacetamide.~~
93. — ~~The method of claim 83, wherein the digests are analyzed using a mass spectrometer.~~
94. — ~~The method of claim 93, wherein the mass spectrometer is a tandem mass spectrometer.~~
95. — ~~The method of claim 93, wherein the mass spectrometer is coupled to a liquid chromatography system.~~
96. — ~~The method of claim 93, wherein the mass spectrometer is coupled to a liquid chromatography—multiple reaction monitoring system.~~