CLAIMS

What is claimed is:

1. A method of reducing a hydrolytic enzyme activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising:

    a capture step;

    one or more ion exchange (IEX) chromatography steps; and

    a depth filtration step,

    thereby reducing the hydrolytic enzyme activity rate of the composition as compared to purification of the sample without the depth filtration step.

2. The method of claim 1, wherein each of the one or more IEX chromatography steps is selected from the group consisting of: an anion exchange (AEX) chromatography step, a cation exchange (CEX) chromatography step, and a multimodal ion exchange (MMIEX) chromatography step.

3. The method of claim 2, wherein the MMIEX chromatography step comprises a multimodal cation exchange/ anion exchange (MM-AEX/CEX) chromatography step.

4. The method of any one of claims 1-3, further comprising a virus filtration step.

5. The method of any one of claims 1-4, further comprising an ultrafiltration/diafiltration (UF/DF) step.

6. The method of claim 5, wherein the purification platform comprises, in order:

    the capture step;

    the CEX chromatography step;

    the AEX chromatography step;

    the depth filtration step;

    the virus filtration step; and

    the UF/DF step.

7. The method of any one of claims 1-6, wherein the depth filtration step comprises processing via a depth filter, and wherein the depth filter is a X0SP depth filter, a C0SP depth filter, a D0SP depth filter, a Polisher ST depth filter, or an EMPHAZE™ depth filter.

8. The method of any one of claims 1-6, further comprising a HIC step comprising processing via Sartobind® phenyl.

9. A method of reducing a hydrolytic enzyme activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising:

one or more ion exchange (IEX) chromatography steps;

a hydrophobic interaction chromatography (HIC) step; and

a depth filtration step,

thereby reducing the hydrolytic enzyme activity rate of the composition as compared to purification of the sample without the HIC step or the depth filtration step.

10. The method of claim 9, wherein the reduction is as compared to purification of the sample without the HIC and the depth filtration step.

11. The method of claim 9 or 10, wherein each of the one or more IEX chromatography steps is selected from the group consisting of: an anion exchange (AEX) chromatography step, a cation exchange (CEX) chromatography step, and a multimodal ion exchange (MMIEX) chromatography step.

12. The method of claim 11, wherein the MMIEX chromatography step comprises a multimodal cation exchange/ anion exchange (MM-AEX/CEX) chromatography step.

13. The method of any one of claims 9-12, further comprising an ultrafiltration/diafiltration (UF/DF) step.

14. The method of claim 13, wherein the purification platform comprises, in order:

the CEX chromatography step;

the HIC step;
the MMIEX chromatography step;
the AEX chromatography step;
the depth filter step; and
the UF/DF step.

15. A method of reducing a hydrolytic enzyme activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising:
a capture step;
one or more ion exchange (IEX) chromatography steps;
a multimodal hydrophobic interaction/ ion exchange (MM-HIC/IEX) chromatography steps; and
one or both of:
a hydrophobic interaction chromatography (HIC) step; and
a depth filtration step,
thereby reducing the hydrolytic enzyme activity rate of the composition as compared to purification of the sample without the HIC step or the depth filtration step.

16. The method of claim 15, wherein the reduction is as compared to purification of the sample without the HIC and the depth filtration step.

17. The method of claim 15 or 16, further comprising a virus filtration step.

18. The method of any one of claims 15-17, further comprising an ultrafiltration/diafiltration (UF/DF) step.

19. The method of any one of claims 15-18, wherein the depth filtration step is performed as a load filter for the MM-HIC/IEX chromatography step, as a load filter for the HIC step, or following the HIC step.

20. The method of any one of claims 15-19, wherein each of the one or more IEX chromatography steps is selected from the group consisting of: a cation exchange (CEX) chromatography step, an anion exchange (AEX) chromatography step, and a multimodal ion exchange (MMIEX) chromatography step.

21. The method of any one of claims 15-20, wherein the MM-HIC/IEX chromatography step is a multimodal hydrophobic interaction/ anion exchange (MM-HIC/AEX) chromatography step.

22. The method of claim 21, wherein the MM-HIC/AEX chromatography step comprises processing via Capto™ Adhere or Capto™ Adhere ImpRes.

23. The method of any one of claims 1-8 and 15-22, wherein the capture step comprises processing via affinity chromatography.

24. The method of any one of claims 1-8 and 15-22, wherein the capture step is performed in a bind-and-elute mode.

25. The method of claim 23 or 24, wherein the affinity chromatography is selected from the group consisting of a protein A chromatography, a protein G chromatography, a protein A/G chromatography, a FcXL chromatography, a protein XL chromatography, a kappa chromatography, and a kappaXL chromatography.

26. The method of any one of claims 1-6, and 9-25, wherein the depth filtration step comprises processing via a depth filter.

27. The method of claim 26, wherein the depth filter is used as a load filter.

28. The method of claim 26 or 27, wherein the depth filter comprises a substrate comprising one or more of a diatomaceous earth composition, a silica composition, a cellulose fiber, a polymeric fiber, a cohesive resin, and an ash composition.

29. The method of claim 28, wherein at least a portion of the substrate of the depth filter comprises a surface modification.

30. The method of claim 29, wherein the surface modification is one or more of a quaternary amine surface modification, a cationic surface modification, and an anionic surface modification.

31. The method of any one of claims 26-30, wherein the depth filter is selected from the group consisting of: a X0SP depth filter, a D0SP depth filter, a C0SP depth filter, an EMPHAZE™ depth filter, a PDD1 depth filter, a PDE1 depth filter, a PDH5 depth filter, a ZETA PLUS™ 120ZA depth filter, a ZETA PLUS™ 120ZB depth filter, a ZETA PLUS™ DELI depth filter, a ZETA PLUS™ DELP depth filter, and a Polisher ST depth filter.

32. The method of claim 31, wherein

the depth filter is the X0SP depth filter, the D0SP depth filter, or the C0SP depth filter, and wherein the processing via the depth filter is performed at a pH of about 4.5 to about 8, or

wherein the depth filter is the EMPHAZE™ depth filter, and wherein processing via the depth filter is performed at a pH of about 7 to about 9.5, or

wherein the depth filter is the Polisher ST depth filter, and wherein processing via the depth filter is performed at a pH of about 4.5 to about 9.

33. The method of any one of claims 9-32, wherein the HIC step comprises processing via a HIC membrane or a HIC column.

34. The method of claim 33, wherein processing via the HIC membrane or the HIC column is performed using low salt concentrations.

35. The method of claim 33, wherein processing via the HIC membrane or the HIC column is performed in flow-through mode.

36. The method of any one of claims 33-35, wherein the HIC membrane or HIC column comprises a substrate comprising one or more of an ether group, an ethyl group, a propyl group, an isopropyl group, a butyl group, a hexyl group, an octyl group, and a phenyl group.

37. The method of any one of claims 33-36, wherein the HIC membrane or the HIC column is selected from the group consisting of Bakerbond WP HI-Propyl™, Phenyl Sepharose® Fast Flow (Phenyl-SFF), Phenyl Sepharose® Fast Flow Hi-sub (Phenyl-SFF HS), Toyopearl® Hexyl-650C, Toyopearl® Hexyl-650M, Toyopearl® Hexyl-650S, Poros™ Benzyl Ultra, and Sartobind® phenyl.

38. The method of claim 36 or 37, wherein processing via the HIC membrane or the HIC column is performed at a pH of about 4.5 to about 7.

39. The method of any one of claims 1-38, wherein each of the one or more IEX chromatography steps comprises processing via an IEX chromatography membrane or an IEX chromatography column.

40. The method of claim 39, wherein the IEX chromatography membrane or the IEX chromatography column is selected from the group consisting of: SPSFF, QSFF, SPXL, Streamline™ SPXL, ABx™, Poros™ XS, Poros™ 50HS, DEAE, DMAE, TMAE, QAE, and MEP-Hypercel™.

41. The method of any one of claims 1-40, wherein the purification platform is for purification of a target from the sample, and wherein the sample comprises the target and one or more host cell impurities.

42. The method of claim 41, wherein the target comprises a polypeptide, preferably the target is an antibody moiety.

43. The method of claim 42, wherein the antibody moiety is a monoclonal antibody, preferably the antibody moiety is a human, humanized, or chimeric antibody.

44. The method of claim 42 or 43, wherein the antibody moiety is selected from the group consisting of: an anti-TAU antibody, an anti-TGFβ3 antibody, an anti-VEGF-A antibody, an anti-CD20 antibody, an anti-CD40 antibody, an anti-HER2 antibody, an anti-IL6 antibody, an anti-IgE antibody, an anti-IL13 antibody, an anti-TIGIT antibody, an anti-PD-L1 antibody, an anti-VEGF-A/ANG2 antibody, an anti-CD79b antibody, an anti-ST2 antibody, an anti-factor D antibody, an anti-factor IX antibody, an anti-factor X antibody, an anti-abeta antibody, an anti-CEA antibody, an anti-CEA/CD3 antibody, an anti-CD20/CD3 antibody, an anti-FcRH5/CD3 antibody, an anti-Her2/CD3 antibody, an anti-FGFR1/KLB antibody, a FAP-4-1 BBL fusion protein, a FAP-IL2v fusion protein, and a TYRP1 TCB antibody.

45. The method of any one of claims 41-44, wherein the one or more host cell impurities comprises a host cell protein, preferably, the host cell protein is a hydrolytic enzyme, and more preferably, the hydrolytic enzyme is a lipase, an esterase, a thioesterase, a phospholipase, carboxylesterase, hydrolase, cutinase, or a ceramidase.

46. The method of any one of claims 1-45, wherein the sample comprises a host cell or components originating therefrom.

47. The method of any one of claims 1-46, wherein the sample is, or is derived from, a cell culture sample.

48. The method of claim 47, wherein the cell culture sample comprises a host cell, and wherein the host cell is a Chinese hamster ovary (CHO) cell or an *E. coli* cell.

49. The method of any one of claims 1-48, further comprising a sample processing step.

50. The method of any one of claims 1-49, wherein the reduction in the hydrolytic enzyme activity rate is at least about 20%.

51. The method of any one of claims 1-50, further comprising determining the hydrolytic enzyme activity rate of the composition and/or determining the level of one or more hydrolytic enzymes in the composition.

52. The method of any one of claims 1-51, wherein the composition comprises a polysorbate, preferably the polysorbate is selected from the group consisting of polysorbate 20, polysorbate 40, polysorbate 60, and polysorbate 80.

53. A pharmaceutical composition obtained from the method of any one of claims 1-52.