CLAIMS:

1. A process for manufacturing a therapeutic enzyme substance, the process comprising:

(a) providing a liquid comprising a therapeutic enzyme that is substantially free of cells, wherein the liquid is fed into a multi-column chromatography system (MCCS);

(b) performing two unit operations of (i) capturing the therapeutic enzyme in the liquid using a hydrophobic interaction or an anion exchange resin and (ii) inactivating viruses, using the MCCS; and

(c) further purifying the therapeutic enzyme by performing hydrophobic interaction chromatography, viral inactivation, cation exchange chromatography, or affinity chromatography, to yield a therapeutic enzyme substance.

2. The process of claim 1, wherein the liquid is selected from the group consisting of: liquid culture medium removed from a perfusion bioreactor containing a culture of mammalian cells that secrete the therapeutic enzyme, liquid culture medium removed from a fed-batch bioreactor containing a culture of mammalian cells that secrete the therapeutic enzyme, and a clarified liquid culture medium from a culture of bacteria or yeast cells that secrete the therapeutic enzyme.

3. The process of claim 2, wherein the liquid is liquid culture medium removed from a perfusion bioreactor containing a culture of mammalian cells that secrete the therapeutic enzyme.

4. The process of claim 3, wherein the mammalian cells are Chinese hamster ovary (CHO) cells.

5. The process of claim 1, wherein the use of the MCCS involves column switching.

6. The process of claim 1, wherein the MCCS utilizes at least two chromatography columns.

7. The process of claim 1, wherein the MCCS utilizes at least two chromatographic membranes.

8. The process of claim 1, wherein the MCCS utilizes at least one chromatography column and at least one chromatographic membrane.

9. The process of claim 1, wherein MCCS is a periodic counter current chromatography system (PCCS).

10. The process of claim 9, wherein the PCCS comprises a four-column PCCS.

11. The process of claim 1, wherein step (c) includes the use of an additional MCCS.

12. The process of claim 11 wherein the use of the additional MCCS involves column switching.

13. The process of claim 11, wherein the additional MCCS utilizes at least two chromatography columns.

14. The process of claim 11, wherein the additional MCCS utilizes at least two chromatographic membranes.

15. The process of claim 11, wherein the additional MCCS utilizes at least one chromatography column and at least one chromatographic membrane.

16. The process of claim 1, wherein the liquid is held in a break tank, before being fed into the MCCS.

17. The process of claim 1, wherein the process is integrated and runs continuously from step (a) through step (c).

18. The process of claim 1, further comprising:

(d) filtering the therapeutic enzyme substance.

19. The process of claim 18, further comprising:

(e) formulating the therapeutic enzyme substance into a pharmaceutical composition.

20. The process of any one of claims 1-19, wherein the therapeutic enzyme is a recombinant galactosidase.

21. The process of claim 20, wherein the recombinant galactosidase is a recombinant α-galactosidase-A.

22. A process for manufacturing a therapeutic enzyme substance, the process comprising:

(a) culturing therapeutic enzyme-secreting cells in a perfusion bioreactor comprising a liquid culture medium under conditions that allow the cells to secrete the therapeutic enzyme into the liquid culture medium, and wherein substantially cell-free volumes of the liquid culture medium are continuously or periodically removed from the perfusion bioreactor and fed into a multi-column chromatography system (MCCS);

(b) performing two unit operations of (i) capturing the therapeutic enzyme in the liquid culture medium using a hydrophobic interaction or anion exchange resin and (ii) inactivating viruses, using the MCCS; and

(c) further purifying the therapeutic enzyme by performing hydrophobic interaction chromatography, viral inactivation, cation exchange chromatography, or affinity chromatography, to yield a therapeutic enzyme substance.

23. The process of claim 22, wherein the mammalian cells are Chinese hamster ovary (CHO) cells.

24. The process of claim 22, wherein the use of the MCCS involves column switching.

25. The process of claim 22, wherein the MCCS utilizes at least two chromatography columns.

26. The process of claim 22, wherein the MCCS utilizes at least two chromatographic membranes.

27. The process of claim 22, wherein the MCCS utilizes at least one chromatography column and at least one chromatographic membrane.

28. The process of claim 22, wherein the MCCS is a periodic counter current chromatography system (PCCS).

29. The process of claim 28, wherein the PCCS comprises a four-column PCCS.

30. The process of claim 22, wherein step (c) includes the use of an additional MCCS.

31. The process of claim 30, wherein the use of the additional MCCS involves column switching.

32. The process of claim 30, wherein the additional MCCS utilizes at least two chromatography columns.

33. The process of claim 30, wherein the additional MCCS utilizes at least two chromatographic membranes.

34. The process of claim 30, wherein the additional MCCS utilizes at least one chromatography column and at least one chromatographic membrane.

35. The process of claim 22, wherein the liquid culture medium is held in a break tank, before being fed into the MCCS.

36. The process of claim 22, wherein the process is integrated and runs continuously from step (a) through step (c).

37. The process of claim 22, further comprising:

(d) filtering the therapeutic enzyme substance.

38. The process of claim 37, further comprising:

(e) formulating the therapeutic enzyme substance into a pharmaceutical composition.

39. The process of any one of claims 22-38, wherein the therapeutic enzyme is a recombinant galactosidase.

40. The process of claim 39, wherein the recombinant galactosidase is a recombinant α-galactosidase-A.