

CLAIMS

We claim:

1. A device for in-line homogenization of a non-uniform feed stream, said device comprising a flow path comprising:
 - (a) a plug flow reactor (PFR);
 - (b) a bypass line for diverting a percentage of the non-uniform feed stream from a first location inside the PFR to a second location within the flow path;
 - (c) a pump for circulating the non-uniform feed stream through the flow path.
2. The device of claim 1, wherein the non-uniform feed stream comprises a protein or product of interest.
3. The device of claim 1, wherein the device is in-line between a first and a second process step.
4. The device of claim 3, wherein the first process is selected from the group consisting of: bind and elute chromatography and Protein A chromatography.
5. The device of claim 3, wherein the second process step is a virus inactivation step.
6. The device of claim 1, wherein the device is for virus inactivation.
7. The device of claim 1, wherein the flow path is a closed-circuit flow path.
8. The device of claim 1, wherein the device is tank-less
9. The device of claim 1, wherein the PFR comprises a tubing assembly packed in at least one chamber.
10. The device of claim 1, wherein the bypass line is an extension of the flow path that

fluidically connects to locations within the flow path.

11. The device of claim 1, wherein the second location is downstream from the first location.
12. The device of claim 1, wherein the second location is upstream from the first location.
13. The device of claim 1, wherein the second location is inside the PFR downstream or upstream from the first location.
14. The device of claim 1, wherein the pump is a pump selected from the group consisting of: a centrifugal pump and a positive displacement pump.
15. The device of claim 1, wherein the device further comprises a second pump in the flow path.
16. The device of claim 15, wherein the second pump modulates the non-uniform feed stream flow in the bypass line.
17. The device of claim 15, wherein the second pump is a pump selected from the group consisting of a centrifugal pump and a positive displacement pump.
18. The device of claim 1, wherein the non-uniform feed stream flow in the bypass line is co-current or counter-current to the non-uniform feed stream flow in the flow path.
19. The device of claim 15, wherein the non-uniform feed stream flow in the bypass line is co-current or counter-current to the non-uniform feed stream flow in the flow path.
20. A method for in-line homogenizing a non-uniform feed stream, comprising:
 - (a) Providing a non-uniform feed stream,
 - (b) Flowing the non-uniform feed stream through a flow path comprising a PFR

- bypass line and a pump;
- (c) Diverting a percentage of the non-uniform feed stream from a first location inside the PFR to a second location within the flow path;
 - (d) Circulating the non-uniform feed stream through the flow path; and
 - (e) Homogenizing the non-uniform feed stream.
21. The method of claim 20, wherein the non-uniform feed stream comprises a protein or product of interest.
22. The method of claim 20, wherein the flow path is in-line between a first and a second process step.
23. The method of claim 22, wherein the first process step is a Protein A (ProA) column chromatograph.
24. The method of claim 22, wherein the second process step is a virus inactivation step.
25. The method of claim 20, wherein the method is for virus inactivation.
26. The method of claim 20, wherein the flow path is a closed-circuit flow path.
27. The method of claim 20, wherein the PFR **(100)** comprises a tubing assembly packed in at least one chamber.
28. The method of claim 20, wherein the bypass line **(152)** is an extension of the flow path that fluidically connects to the first and second locations within the flow path.
29. The method of claim 20, wherein the second location is downstream from the first location.
30. The method of claim 20, wherein the second location is upstream from the first location.

31. The method of claim 20, wherein the second location is inside the PFR downstream or upstream from the first location.
32. The method of claim 20, wherein the pump is a pump selected from the group consisting of a centrifugal pump and a positive displacement pump.
33. The method of claim 20, wherein the method further comprises a second pump in the flow path.
34. The method of claim 33, wherein the second pump modulates the non-uniform feed stream flow in the bypass line.
35. The method of claim 33, wherein the second pump is a pump selected from the group consisting of a centrifugal pump and a positive displacement pump.
36. The method of claim 20, wherein the non-uniform feed stream flow in the bypass line is co-current or counter-current to the non-uniform feed stream flow in the flow path.
37. The method of claim 36, wherein the bypass line diverts the non-uniform feed stream with a flow rate that is about 1% to 99% of the flow rate in the flow path.
38. Method of manufacturing a product of interest by a device according to claim 1.
39. Method of manufacturing a protein by a device according to claim 1.
40. Method of claim 39, wherein the protein is a therapeutic protein.
41. Method of manufacturing a product of interest by in-line homogenizing a non-uniform feed stream according to claim 20.

42. Method of manufacturing a protein by in-line homogenizing a non-uniform feed stream according to claim 20.
43. Method of claim 42, wherein the protein is a therapeutic protein.