

CLAIMS

WHAT IS CLAIMED IS:

1. A method of making a media or a feed composition for culturing cells, comprising:
 - i) subjecting a dry powder to suspension in a moving column of a gas in a fluid bed apparatus;
 - ii) introducing at least one solvent using a sprayer into the dry powder of step (i) to form a layered base particle;
 - iii) drying the layered base particle.
2. A method of making a media or a feed composition for culturing cells, comprising:
 - i) subjecting a dry powder to suspension in a moving column of a gas in a fluid bed apparatus;
 - ii) introducing a first solvent using a first sprayer onto the dry powder of step (i) to form a base granule;
 - iii) introducing at least one second solvent using a second sprayer onto the base granule of step (ii) to form a layered base granule;
 - iv) drying the layered base granule.
3. The method of making the media or the feed composition for culturing cells of claim 1 or 2, wherein the dry powder is a basal media powder, a complete media powder, a cell culture feed, a cell culture supplement, a cell culture media or feed concentrate or an amino acid mixture.
4. The method of making the media or the feed composition for culturing cells of claim 1, wherein the first sprayer is selected from the group consisting of: a top sprayer, a bottom sprayer and a tangential sprayer.
5. The method of making the media or the feed composition for culturing cells of claim 2 or 3, wherein the first or the second sprayer is selected from the group consisting of: a top sprayer, a bottom sprayer and a tangential sprayer.
6. The method of making the media or the feed composition for culturing cells of claim 2 or 3 or 5, wherein the second sprayer is a bottom sprayer.

7. The method of making the media or the feed composition for culturing cells of any of claims 2 to 3 or 5 to 6 claims, wherein the second sprayer sprays a plurality of solvents on to the base granule to form a multilayered base granule.
8. The method of making the media or the feed composition for culturing cells of any of claims 1 or 3 to 4, wherein the second sprayer sprays a plurality of solvents on to the base particle to form a multilayered base particle.
9. The method of making the media or the feed composition for culturing cells of any of the preceding claims, wherein the second sprayer sprays the plurality of solvents sequentially, with intermittent drying steps between each spraying step.
10. The method of making the media or the feed composition for culturing cells of any of the preceding claims, wherein the second sprayer sprays the plurality of solvents sequentially, without any intermittent drying steps between each spraying step.
11. The method of making the media or the feed composition for culturing cells of any of the preceding claims, wherein each solvent in the plurality of solvents has one component in each solvent.
12. The method of making the media or the feed composition for culturing cells of claim 11, wherein each solvent in the plurality of solvents has the same components.
13. The method of making the media or the feed composition for culturing cells of claim 11, wherein each solvent in the plurality of solvents has different components.
14. The method of making the media or the feed composition for culturing cells of any of claims 1 to 11 and 13, wherein each solvent has a mixture of components.
15. The method of making the media or the feed composition for culturing cells of claim 14, wherein the components are segregated into reactive species and into sensitive species.
16. The method of making the media or the feed composition for culturing cells of claim 15, wherein the reactive species and the sensitive species are sprayed separately to give a layered granule.

17. The method of any of the preceding claims, wherein said reactive species is selected from the group consisting of one or more trace elements, one or more reactive amino acids, one or more reactive amino acids, one or more metal salts, one or more acid soluble reactive groups, one or more alcohol soluble reactive groups and one or more pH modifier groups.

18. The method of any of the preceding claims, wherein said sensitive species is selected from the group consisting of one or more polyamines, one or more vitamins, one or more growth factor and one or more labile amino acids.

19. The method of making the media or the feed composition for culturing cells of any of the preceding claims, wherein an inlet gas used in the method is at about temperature 20° C to 30° C.

20. The method of making the media or the feed composition for culturing cells of any of the preceding claims, wherein an inlet gas used in the method is at about temperature 25° C.

21. The method of making the media or the feed composition for culturing cells of any of the preceding claims, wherein the vitamins are selected from the group consisting of: vitamin B12, biotin, choline, folic acid, niacinamide, pyridoxine, riboflavin, thiamine, ascorbic acid and para-aminobenzoic acid (PABA).

22. The method of making the media or the feed composition for culturing cells of any of the preceding claims, wherein the drying step is at about temperature 50° C to 60° C.

23. The method of making the media or the feed composition for culturing cells of any of the preceding claims, wherein the base particle or the base granule is dried to a moisture content of about 0.5% to 10%.

24. The method of making the media or the feed composition for culturing cells of any of the preceding claims of any preceding claim, wherein the solvent comprises a reactive species.

25. The method of making the media or the feed composition for culturing cells of any of the preceding claims of any preceding claim, wherein the solvent additionally comprises at least one antioxidant.

26. The layered base particle or the layered base granule obtained in any of the preceding claims.

27. A method of producing a nutritive medium layered particle, a nutritive medium supplement layered particle, a nutritive medium subgroup layered particle, the method comprising making a layered media particle according to any of the preceding claims, wherein at least one layer on the base particle or base granule comprises a reactive species and/or at least one layer on the base particle or base granule comprises a sensitive species.

28. The method of any of the preceding claims, wherein said reactive species is selected from the group consisting of one or more trace elements, one or more reactive amino acids, one or more reactive amino acids, one or more metal salts, one or more acid soluble reactive groups, one or more alcohol soluble reactive groups and one or more pH modifier groups.

29. The method of claim 27, wherein said sensitive species is selected from the group consisting of one or more polyamines, one or more vitamins, one or more growth factor and one or more labile amino acids.

30. The method of any of the preceding claims, wherein the dry powder is selected from the group consisting of vitamins, bulk inorganic salts and sugars.

31. A method of culturing a cell in a liquid reconstituted from the layered media particle of any of the preceding claims, comprising:

- i) reconstituting the layered media particle in a suitable liquid or buffer; wherein said layered media particle is a cell culture medium, feed, supplement or concentrate;
- ii) culturing the cell in the reconstituted liquid under conditions favorable for the growth of the cell.

32. The method of culturing the cell of claim 31, wherein the culturing is used to produce increased amount of a polypeptide.

33. The method of culturing the cell of claims 31 to 32, wherein the polypeptide is a recombinant polypeptide.

34. The method of culturing the cell of claims 31 to 33, wherein the culturing increases product production, increasing cell growth, as compared to a culture with liquid media not made from the layered media particles.

35. A kit comprising:

- i) a first container comprising a layered particle or granule according any one of the above claims; wherein said layered particle or granule is a cell culture medium, feed, supplement or concentrate;
- ii) instructions for using the layered particle or granule for cell culture.

36. A system comprising: a liquid medium reconstituted from a layered media particles according to any preceding claim and a cell.

37. The system of claim 36, wherein the reconstituted liquid medium is used to cultivate a cell that produces a recombinant polypeptide, a virus, a secreted protein, or to cultivate a cell in suspension or a cell that is attached.

38. The making a media or a feed composition for culturing cells of any of the above claims, or, the kit of claim 35, or, the system of claims 36-37, wherein the amino acids are selected from one or more of the twenty amino acids, their salts or derivatives thereof.

39. The making a media or a feed composition for culturing cells of any of the above claims, or, the kit of claim 35, or, the system of claims 36-37, wherein the amino acids are selected one or more of glycine, alanine, arginine, aspartic acid, glutamic acid, histidine, isoleucine, methionine, phenylalanine, proline, hydroxyproline, serine, threonine, tryptophan, valine, tyrosine, cysteine and lysine.

40. Use of the layered particles or granules obtained from the methods of any of the above claims for culturing a cell.

41. The use of claim 40, wherein the cell is a mammalian cell.

42. The use of claims 40-41, wherein the cell is selected from the group consisting of CHO, BHK, HEK, 293, and VERO cells.

43. The use of claim 40-41, wherein the cell is a plant cell, an animal cell, a eukaryotic cell, a eukaryotic cell, an algal cell, a fungal cell, and a bacterial cell.