WHAT IS CLAIMED IS:

1. A method of preventing loss of copper in a solution,

wherein the solution is a cell culture medium, cell culture feed or cell culture additive comprising copper (II) and cysteine,

wherein the method comprises having substantially the same amount of soluble copper before and after filtering the solution.

2. The method of claim 1, wherein the filtering is performed with the solution comprising a dissolved oxygen (dO_2) level of at least about 6% dO_2, optionally a dissolved oxygen (dO_2) level of at least about 8% dO_2.

3. The method of claim 2, further comprising maintaining the dO_2 level of the solution at at least about 6% dO_2 (or at least about 8%dO_2) for at least about 10 minutes prior to commencing the filtering.

4. The method of claim 2 or claim 3, wherein the dO_2 levels are maintained at the required level by:

a. oxygenating the solution; and/or

b. Optimizing the filtering.

5. The method of claim 4, wherein the oxygenating comprises:
sparging the solution with a gas comprising oxygen; and/or
agitating or mixing the solution to increase contact of the solution with gas comprising oxygen.

6. The method of claim 5, wherein the gas comprising oxygen is atmosphere.

7. The method of any of claims 4 to 6, wherein optimizing the filtering comprises increasing filtration rate, filter size and/or filter capacity, such that dO_2 levels do not fall below 8% during filtering.

8. The method of any preceding claim, wherein the filtering is completed within about 24 hours of adding copper (II) to the solution.

9. The method of claim 1-5, wherein the filtering is performed within about 5 hours, about 1 hour, or about 30 minutes of adding copper (II) to the solution.

10. The method of any preceding claim, wherein the filtering is performed at a rate of at least 0.5% of the total volume per minute, optionally at least 5% of the total volume per minute.

11. The method of any proceeding claim, wherein the method comprises providing a cysteine solution and a copper (II) solution; and

the filtering comprises separately filtering the cysteine solution and the copper (II) solution, and then combining the filtered cysteine solution and the filtered copper (II) solution to form the cell culture medium, cell culture feed or cell culture additive.

12. The method of claim 11, wherein the cysteine solution comprises at least the majority of the components of the cell culture medium, cell culture feed or cell culture additive, other than copper.

13. The method of claim 11 or claim 12, wherein the cysteine solution comprises substantially all of the components of the cell culture medium, cell culture feed or cell culture additive other than copper and optionally iron.

14. The method of any of claims 11 to 13, wherein the concentration of copper in the copper (II) solution is in the range of about 0.005 μM to about 1 M.

15. The method of any preceding claim, wherein the filtering comprises sterile filtering.

16. The method of claim 15, wherein the sterile filtering comprises use of a filtration medium having a pore size of not more than about 0.5 μm, optionally not more that about 0.2 μm.

17. The method of claim 15 or claim 16, wherein the sterile filtering comprises use of a filtration medium having a pore size of at least about 0.1 μm.

18. The method of any preceding claim, wherein the cysteine is provided substantially as a cysteine derivative that does not comprise a sulfhydryl group.

19. The method of any preceding claim, wherein the cysteine is converted substantially into a cysteine derivative that does not comprise a sulfhydryl group prior to adding the copper (II) to the solution.

20. The method of claim 18 or claim 19, wherein the cysteine derivative comprises a disulfide or a thiazolidine moiety.

21. The method of any of claims 18 to 20, wherein the cysteine derivative comprises a disulfide.

22. The method of any of claims 18 to 21, wherein the cysteine derivative comprises a thiazolidine moiety.

23. The method of any of claims 18 to 22, wherein the cysteine derivative is selected from a group consisting of cystine, 4-carboxy-2-methylthiazolidine-2-carboxylate, S-sulfocysteine, S-sulfocysteinylglycine, cysteine S-linked N-acetyl glucosamine (GlcNAC-cys), homocystine, L-cysteine mixed disulfides, L-cysteine mixed peptides, S-alkylated cysteine, cysteine with a thiol-protecting group (e.g FMOC-protected cysteine), 2-methyl-1,3-thiazolidine-2, 4-dicarboxylic acid, 2-(2-carboxyethyl)21,3-thiazolidine-2, 4-dicarboxylic acid, reduced and oxidized glutathione (GSH), S-sulfoglutathione, S-acyl-GSH, S-carboxy-L-cysteine, L-2-oxothiazolidine-4-carboxylic acid, 2-alkyl-thiazolidine-4(R)-carboxylic acid, 2-aryl-thiazolidine-4(R)-carboxylic acid and carbohydrate based thiazolidines (e.g. D-ribose-L-cysteine).

24. The method of claim 23, wherein the cysteine derivative comprises cystine.

25. The method of claim 24, wherein the cysteine derivative comprises 4-carboxy-2-methylthiazolidine-2-carboxylate.

26. The method of any preceding claim, wherein the copper is in the form of a copper (II) chelate.

27. The method of claim 21, wherein the chelate comprises a chelator selected from ethylenediaminetetraacetic acid (EDTA), diethylenetriamine pentaacetic acid (DTPA), neocuprione, bathocuprione, D-penicillamine, triethylenetetramine (TETA), dimercaprol (BAL), 8-hydroxyquinoline, clioquinol, and 5,7-Dichloro-2-[(dimethylamino)methyl]-8-quinolinol (PBT2).

28. A method of preparing a cell culture medium, cell culture feed or cell culture additive comprising copper (II), cysteine, and other components, without loss of soluble copper, comprising:

providing an aqueous solution comprising cysteine and other components;

providing an aqueous solution comprising copper (II);

separately filtering the aqueous solution comprising cysteine and other components, and the aqueous solution comprising copper (II); and

combining the filtered solutions to provide the cell culture medium, cell culture feed or cell culture additive.

29. The method of claim 28, wherein preparation of the aqueous solution comprising cysteine and other components comprises dissolving and/or solubilizing cysteine and other components in water.

30. The method of claim 28 or claim 29, wherein preparation of the aqueous solution comprising copper (II) comprises dissolving a copper (II) salt in water.

31. The method of any of claims 28 to 30, wherein the concentration of copper in the copper (II) solution is in the range of about 0.005 µM to about 1 M.

32. A method of preparing a cell culture medium, cell culture feed or cell culture additive comprising copper (II), cysteine, and other components, without loss of soluble copper, comprising:

filtering a solution comprising the copper (II), cysteine, and other components to provide the cell culture medium, cell culture feed or cell culture additive.

33. The method of claim 32, wherein the filtering is completed within about 24 hours of adding the copper (II) to the solution;

optionally wherein the filtering is performed within about 30 minutes of adding copper (II) to the solution.

34. The method of claim 32 or claim 33, wherein the solution is prepared by dissolving and/or solubilizing a copper (II) salt, cysteine and other components in water.

35. The method of any of claims 28 to 34, wherein the each filtering comprises sterile filtering.

36. The method of claim 35, wherein the ~~or~~ each sterile filtering comprises use of a filtration medium having a pore size of not more than about 0.5 µm, optionally of not more that about 0.2 µm.

37. The method of claim 35 or claim 36, wherein the sterile filtering comprises use of a filtration medium having a pore size of at least 0.1 µm.

38. The method of any of claims 28 to 37, further comprising the features of any of claims 2 to 7 and 18 to 27.

39. The method of any of claims 28 to 38, wherein the other components comprise at least one carbon source, and/or at least one nitrogen source, and/or at least one vitamin, and/or at least one buffering agent, and/or at least one inorganic salt, and/or at least one trace metal other than copper, and/or at least one polyamine, and/or at least one (essential) fatty acid.

40. The method of claim 39, wherein the at least one carbon source comprises a sugar, optionally a monosaccharide or disaccharide, e.g. glucose and/or deoxyribose.

41. The method of claim 39 or 40, wherein the at least one nitrogen source comprises at least one amino acid; optionally selected from L-alanine, L-arginine, L-asparagine, L-aspartic acid, L-cystine, L-cysteine, L-glutamic acid, L-glutamine, glycine, L-histidine, L-isoleucine, L-leucine, L-lysine, L-methionine, L-phenylalanine, L-proline, L-serine, L-threonine, L-tryptophan, L-tyrosine and L-valine, or derivatives thereof.

42. The method of any of claims 39 to 41, wherein the at least one vitamin is selected from ascorbic acid, biotin, choline, D-Ca^{2+}-pantothenate, folic acid, inositol, menadione, niacinamide, nicotinic acid, paraaminobenzoic acid (PABA), pyridoxal, pyridoxine, riboflavin, thiamine, vitamin A acetate, vitamin B_{12} and vitamin D_2.

43. The method of any of claims 39 to 42, wherein the at least one buffering agent comprises carbonate, bicarbonate, phosphate, hydrogen phosphate, dihydrogen phosphate, lactate, HEPES, MOPS, BES, TES, MES, and Bis-Tris.

44. The method of any of claims 39 to 43, wherein the at least one inorganic salt comprises at least one of $CaCl_2$, KCl, $MgCl_2$, $MgSO_4$, NaCl, $NaHCO_3$, Na_2HPO_4, NaH_2PO_4 and ferric citrate chelate, or ferrous sulfate chelate.

45. The method of any of claims 39 to 44, wherein the at least one trace metal other than copper comprises ions of at least one of barium, bromium, cobalt, iodine, manganese, chromium, nickel, selenium, vanadium, titanium, germanium, molybdenum, silicon, iron, fluorine, silver, rubidium, tin, zirconium, cadmium, zinc and aluminium.

46. The method of any of claims 39 to 45, wherein the at least one polyamine comprises at least one of putrescine, cadaverine, spermine, and spermidine.

47. The method of any of claims 39 to 46, wherein the at least one essential fatty acid is selected from linoleic acid and linolenic acid.

48. A method of culturing a cell in a medium, the method comprising:

preventing loss of copper in the medium according to a method of any of claims 1 to 27, or preparing the medium according to a method of any of claims 28 to 47,

contacting the cell with the medium, and

culturing the cell in the medium.

49. The method of claim 48, wherein the cell is a eukaryotic, a prokaryotic or an archaea cell.

50. The method of claims 49, wherein the eukaryotic cell is a mammalian cell.

51. The method of claim 50, wherein the mammalian cell is selected from hybridoma cells, CHO cells, COS cells, VERO cells, HeLa cells, HEK 293 cells, PER-C6 cells, K562 cells, MOLT-4 cells, MI cells, NS-1 cells, COS-7 cells, MDBK cells, MDCK cells, MRC-5 cells, WI-38 cells, WEHI cells, SP2/0 cells, BHK cells (including BHK-21 cells) and derivatives thereof.

52. The method of any of claims 48 to 51, where the culturing the cell in the medium comprises multiplying the cell.

53. A method of making a biological product, comprising:

preventing loss of copper in the medium according to a method of any of claims 1 to 27 or preparing a medium according to a method of any of claims 28 to 47,

contacting a cell configured to express said biological product with the medium, and

culturing the cell in the medium under conditions such that the cell expresses the biological product.

54. The method of claim 53, wherein the biological product is a polypeptide, protein, peptide, hormone, virus or virus like particle, nucleic acid or a fragment thereof; optionally an antibody, or a biologically functional fragment of an antibody.

55. The method of claim 53 or 54, further comprising isolating and/or purifying the biological product.

56. A cell culture medium, cell culture feed, or cell culture additive obtainable or obtained by the method of any of claims 28 to 47.

57. Use of a cell culture medium, cell culture feed, or cell culture additive of claim 56 for culturing cells, optionally wherein the use comprises producing a biological product from said cells and / or optionally wherein the use comprises multiplying said cells.