CLAIMS

1. A storage stabilized liposomal irinotecan composition comprising cholesterol, one or more phospholipids, and irinotecan sucrose octasulfate (SOS) encapsulated in unilamellar liposomes, said composition having:

(i) an irinotecan:total phospholipids ratio corresponding to a total of 500 grams±10% by weight irinotecan moiety per mol of total phospholipids;

(ii) a gram-equivalent ratio of from 0.85 to 1.2, as determined by the molar amounts of co-encapsulated irinotecan and sucrose octasulfate according to the formula: gram-equivalent ratio = I/(SN), where I is the molar concentration of irinotecan, S is the molar concentration of sucrose octasulfate and N = 8;

(iii) a pH before storage of from about 7.25 to about 7.5 at room temperature; and

wherein, after the first 6 months storage of said composition at a storage temperature of from 2-8° C, there is less than 20 mol % lyso-phosphatidylcholine ("lyso-PC"), relative to the total phospholipids.

2. The composition of claim 1, wherein the one or more phospholipids comprises phosphatidylcholine and PEG-phosphatidylethanolamine.

3. The composition of claim 2, wherein the phosphatidylcholine is 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC) and the PEG-phosphatidylethanolamine is N-(methoxy-poly(ethylene glycol)-oxycarbonyl)-distearoylphosphatidylethanolamine.

4. The composition of claim 3, wherein the N-(methoxy-poly(ethylene glycol)-oxycarbonyl)-distearoylphosphatidylethanolamine comprises N-methoxy-terminated polyethylene glycol (MW 2000)-distearoylphosphatidyl ethanolamine.

5. The composition of claim 4, wherein, before storage, the ratio of moles of 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC) to cholesterol is about 3:2.

6. The composition of claim 5, wherein before storage, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC) is present at a concentration of 6.1 to 7.5 mg/mL and cholesterol is present at a concentration of from 2-2.4 mg/mL.

7. The composition of claim 6, wherein after the first 6 months of said composition at a storage temperature of from 2-8° C, the composition contains less than 20 mol % lyso-PC, relative to the total phospholipids, as quantified by an HPLC method.

8. The composition of claim 7, wherein, after the first 9 months of said composition at a storage temperature of from 2-8° C, the composition contains less than 20 mol % lyso-PC as quantified by an HPLC method.

9. The composition of claim 7, wherein, after the first 6 months of said composition at a storage temperature of from 2-8° C, the composition contains less than 10 mol % lyso-PC as quantified by an HPLC method.

10. The composition of claim 7, wherein, after the first 9 months of said composition at a storage temperature of from 2-8° C, the composition contains less than 10 mol % lyso-PC as quantified by an HPLC method.

11. The composition of claim 7, wherein, after the first 12 months of said composition at a storage temperature of from 2-8° C, the composition contains less than 10 mol % lyso-PC as quantified by an HPLC method.

12. The composition of claim 7, wherein, after the first 24 months of said composition at a storage temperature of from 2-8° C, the composition contains less than 10 mol % lyso-PC as quantified by an HPLC method.

13. The composition of claim 7, wherein, after the first 6 months of said composition at a storage temperature of from 2-8° C, the composition contains less than 5 mol % lyso-PC as quantified by an HPLC method.

14. The composition of claim 7, wherein, after the first 9 months of said composition at a storage temperature of from 2-8° C, the composition contains less than 5 mol % lyso-PC as quantified by an HPLC method.

15. The composition of claim 7, wherein, after the first 12 months of said composition at a storage temperature of from 2-8° C, the composition contains less than 5 mol % lyso-PC as quantified by an HPLC method.

16. The composition of claim 7, wherein, after the first 24 months of said composition at a storage temperature of from 2-8° C, the composition contains less than 5 mol % lyso-PC as quantified by an HPLC method.

17. The composition of claim 6, wherein the composition further comprises triethylammonium or diethylammonium in a total amount of less than about 100 ppm.

18. The composition of claim 6, wherein the composition further comprises triethylammonium or diethylammonium in a total amount of less than 100 ppm.

19. The composition of claim 18, wherein the composition further comprises triethylammonium in a total amount of less than 79 ppm.

20. The composition of claim 17, wherein the composition further comprises triethylammonium or diethylammonium in a total amount of from about 10 to about 100 ppm.

21. The composition of claim 18, wherein the composition further comprises triethylammonium or diethylammonium in a total amount of from 10 to 100 ppm.

22. The composition of claim 18, wherein the composition further comprises triethylammonium or diethylammonium in a total amount of from 30 to 100 ppm.

23. The composition of claim 6, wherein the composition further comprises a total of 4.05 mg/mL 2-[4-(2-hydroxyethyl) piperazin-1-yl]ethanesulfonic acid and a total of 8.42 mg/mL sodium chloride.

24. The composition of claim 6, wherein the composition further comprises histidine buffer.

25. The composition of claim 6, wherein the gram-equivalent ratio is from 0.85 to 1.1.

26. The composition of claim 6, wherein the gram-equivalent ratio is from 0.9 to 1.1

27. The composition of claim 6, wherein the gram-equivalent ratio is from 0.9 to 1.05.

28. The composition of claim 6, wherein the gram-equivalent ratio is from 0.95 to 1.0.

29. The composition of claim 6, wherein the gram-equivalent ratio is from 0.98 to 1.0.

30. The composition of claim 6, wherein the gram-equivalent ratio is from 0.99 to 1.0.

31. The composition of claim 6, wherein the gram-equivalent ratio is from 0.85 to 1.2, as determined by the molar amounts of co-encapsulated irinotecan and sucrose octasulfate according to the formula: gram-equivalent ratio = I/(SN), where I is the molar concentration of irinotecan, S is the molar concentration of sucrose octasulfate and N = 8, with the molar amounts of co-encapsulated irinotecan and sucrose octasulfate in the composition determined by subjecting the liposomes to size-exclusion chromatography in normal saline and quantifying the amount of sulfate groups from sucrose octasulfate in the chromatographed liposomes, and quantifying the amount of irinotecan in the chromatographed liposomes.

32. The composition of claim 25, wherein the gram-equivalent ratio is from 0.85 to 1.1, as determined by the molar amounts of co-encapsulated irinotecan and sucrose octasulfate according to the formula: gram-equivalent ratio = I/(SN), where I is the molar concentration of irinotecan, S is the molar concentration of sucrose octasulfate and N = 8, with the molar amounts of co-encapsulated irinotecan and sucrose octasulfate in the composition determined by subjecting the liposomes to size-exclusion chromatography in normal saline and quantifying the amount of sulfate groups from sucrose octasulfate in the chromatographed liposomes, and quantifying the amount of irinotecan in the chromatographed liposomes.

33. The composition of claim 26, wherein the gram-equivalent ratio is from 0.9 to 1.1, as determined by the molar amounts of co-encapsulated irinotecan and sucrose octasulfate according to the formula: gram-equivalent ratio = I/(SN), where I is the molar concentration of irinotecan, S is the molar concentration of sucrose octasulfate and N = 8, with the molar amounts of co-encapsulated irinotecan and sucrose octasulfate in the composition determined by subjecting the liposomes to size-exclusion chromatography in normal saline and quantifying the amount of sulfate groups from sucrose octasulfate in the chromatographed

liposomes, and quantifying the amount of irinotecan in the chromatographed liposomes.

34. The composition of claim 27, wherein the gram-equivalent ratio is from 0.9 to 1.05, as determined by the molar amounts of co-encapsulated irinotecan and sucrose octasulfate according to the formula: gram-equivalent ratio = I/(SN), where I is the molar concentration of irinotecan, S is the molar concentration of sucrose octasulfate and N = 8, with the molar amounts of co-encapsulated irinotecan and sucrose octasulfate in the composition determined by subjecting the liposomes to size-exclusion chromatography in normal saline and quantifying the amount of sulfate groups from sucrose octasulfate in the chromatographed liposomes, and quantifying the amount of irinotecan in the chromatographed liposomes.

35. The composition of claim 28, wherein the gram-equivalent ratio is from 0.95 to 1.0, as determined by the molar amounts of co-encapsulated irinotecan and sucrose octasulfate according to the formula: gram-equivalent ratio = I/(SN), where I is the molar concentration of irinotecan, S is the molar concentration of sucrose octasulfate and N = 8, with the molar amounts of co-encapsulated irinotecan and sucrose octasulfate in the composition determined by subjecting the liposomes to size-exclusion chromatography in normal saline and quantifying the amount of sulfate groups from sucrose octasulfate in the chromatographed liposomes, and quantifying the amount of irinotecan in the chromatographed liposomes.

36. The composition of claim 29, wherein the gram-equivalent ratio is from 0.98 to 1.0, as determined by the molar amounts of co-encapsulated irinotecan and sucrose octasulfate according to the formula: gram-equivalent ratio = I/(SN), where I is the molar concentration of irinotecan, S is the molar concentration of sucrose octasulfate and N = 8, with the molar amounts of co-encapsulated irinotecan and sucrose octasulfate in the composition determined by subjecting the liposomes to size-exclusion chromatography in normal saline and quantifying the amount of sulfate groups from sucrose octasulfate in the chromatographed liposomes, and quantifying the amount of irinotecan in the chromatographed liposomes.

37. The composition of claim 30, wherein the gram-equivalent ratio is from 0.99 to 1.0, as determined by the molar amounts of co-encapsulated irinotecan and sucrose octasulfate

according to the formula: gram-equivalent ratio = I/(SN), where I is the molar concentration of irinotecan, S is the molar concentration of sucrose octasulfate and N = 8, with the molar amounts of co-encapsulated irinotecan and sucrose octasulfate in the composition determined by subjecting the liposomes to size-exclusion chromatography in normal saline and quantifying the amount of sulfate groups from sucrose octasulfate in the chromatographed liposomes, and quantifying the amount of irinotecan in the chromatographed liposomes.

38. The composition of claim 17, wherein the composition further comprises triethylammonium in a total amount of less than about 20 ppm.

39. The composition of claim 18, wherein the composition further comprises triethylammonium in a total amount of less than 20 ppm.

40. The composition of claim 33 wherein after the first 6 months of said composition at a storage temperature of from 2-8° C, the composition contains less than 10 mol % lyso-PC as quantified by an HPLC method.

41. The composition of claim 33, wherein after the first 6 months of said composition at a storage temperature of from 2-8° C, the composition contains less than 5 mol % lyso-PC as quantified by an HPLC method.

42. The composition of claim 33, wherein after the first 12 months of said composition at a storage temperature of from 2-8° C, the composition contains less than 10 mol % lyso-PC as quantified by an HPLC method.

43. The composition of claim 33, wherein after the first 12 months of said composition at a storage temperature of from 2-8° C, the composition contains less than 5 mol % lyso-PC as quantified by an HPLC method.

44. The composition of claim 33, wherein after the first 24 months of said composition at a storage temperature of from 2-8° C, the composition contains less than 10 mol % lyso-PC as quantified by an HPLC method.

45. (Allowed) The composition of claim 33, wherein after the first 24 months of said composition at a storage temperature of from 2-8° C, the composition contains less than 5 mol % lyso-PC as quantified by an HPLC method.

46. The composition of claim 33, wherein after the first 6 months of said composition at a storage temperature of 4 °C, the composition contains less than 1 mg/mL lyso-PC.

47. The composition of claim 33, wherein after the first 9 months of said composition at a storage temperature of from 2-8° C, the composition contains less than 1 mg/mL lyso-PC.

48. The composition of claim 33, wherein after the first 21 months of said composition at a storage temperature of from 2-8° C, the composition contains no more than 2 mg/mL lyso-PC when stored at 2-8 ° C.

49. The composition of claim 33, wherein after the first 12 months of said composition at a storage temperature of from 2-8° C, the composition contains no more than 2 mg/mL lyso-PC when stored at 2-8 ° C.

50. The composition of claim 6, wherein the composition further comprises less than 20 ppm of substituted ammonium ion.

51. The composition of claim 6, wherein the composition further comprises 10-20 ppm of substituted ammonium ion.