CLAIMS

1. A storage stabilized liposomal irinotecan composition comprising irinotecan sucrose octasulfate (SOS) encapsulated in liposomes comprised of cholesterol and one or more phospholipids with a ratio corresponding to a total of 500 grams ±10% by weight irinotecan moiety per mol total phospholipids, the liposomal irinotecan composition stabilized to have less than 20 mol%, with respect to total phospholipids, of lyso-phosphatidylcholine (lyso-PC) during the first 6 months of storage of the liposomal irinotecan composition at a temperature ranging from 2 to 8 °C, the liposomal irinotecan composition obtained by a process comprising the steps of:

(a) forming liposomes comprising 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), cholesterol, and methoxy-terminated polyethylene glycol-distearoylphosphatidyl ethanolamine, encapsulating a substituted ammonium salt of SOS with a sulfate concentration of from 0.4 to 0.5 M;

(b) contacting the liposomes with a solution comprising irinotecan, at a temperature above the transition temperature of the component phospholipids, thereby forming a preparation of liposomes encapsulating irinotecan sucrose octasulfate within the liposomes; and

(c) obtaining the storage stabilized liposomal irinotecan composition by at least one additional step comprising adjusting the pH of the preparation of liposomes from step (b) to a pH of from about 7.25 to about 7.50.

2. The storage stabilized liposomal irinotecan composition of claim 1, wherein the liposomes have a volume weighted mean size of 110 nm ± 20% as determined by dynamic light scattering and wherein the size is determined by the method of cumulants.

3. The storage stabilized liposomal irinotecan composition of claim 2, wherein the composition comprises unilamellar liposomes.

4. The storage stabilized liposomal irinotecan composition of claim 1, having a total irinotecan moiety content equivalent to 4.3 mg/mL irinotecan free base.

5. The storage stabilized liposomal irinotecan composition of claim 1, having less than 20 mol%, with respect to total phospholipids, of lyso-PC after a storage time ~~ranging~~ from 9 to 12 months, at a storage temperature ~~ranging~~ of from 2 to 8 °C.

6. The storage stabilized liposomal irinotecan composition of claim 1, having at least 98% of the irinotecan encapsulated within the liposomes after 6 months at a storage temperature of from 2 to 8°C.

7. The storage stabilized liposomal irinotecan composition of claim 1, comprising an isotonic HEPES aqueous buffer, wherein the HEPES aqueous buffer is present at a concentration of from 2 to 20 mM.

8. The storage stabilized liposomal irinotecan composition of claim 1, further comprising sodium chloride present at a concentration of from 130 to 160 mM.

9. The storage stabilized liposomal irinotecan composition of claim 1, wherein the irinotecan encapsulated within the liposomes is in a gelated or precipitated state as a sucrose octasulfate salt.

10. The storage stabilized liposomal irinotecan composition of claim 1, wherein the liposomes have a volume weighted mean size of from 95 to 115 nm, as measured by quasi-elastic light scattering.

11. The storage stabilized liposomal irinotecan composition of claim 10, wherein the liposomes are unilamellar.

12. The storage stabilized liposomal irinotecan composition of claim 1, comprising a total of 6.81 mg DSPC /mL, 2.22 mg cholesterol /mL, and 0.12 mg MPEG-2000-DSPE /mL, 4.05 mg/mL HEPES aqueous buffer and 8.42 mg sodium chloride/mL.

13. The storage stabilized liposomal irinotecan composition of claim 1, having a pH of about 7.25, wherein the liposomes have a volume weighted mean size of about 110 nm, as measured by quasi-elastic light scattering.

14. The storage stabilized liposomal irinotecan composition of claim 13, wherein the composition comprises unilamellar liposomes.

15. The storage stabilized liposomal irinotecan composition of claim 1, wherein the storage temperature is about 4 °C.

16. The storage stabilized liposomal irinotecan composition of claim 1, forming less than 1 mg/mL of lyso-PC after 6 months, at a storage temperature of from 2 to 8 °C.

17. The storage stabilized liposomal irinotecan composition of claim 1, wherein the substituted ammonium salt of SOS is triethylammonium SOS or diethylammonium SOS.

18. The storage stabilized liposomal irinotecan composition of claim 17, comprising triethylammonium or diethylammonium in a total amount of less than 100 ppm.

19. The storage stabilized liposomal irinotecan composition of claim 18, comprising triethylammonium or diethylammonium in a total amount of from 30 to 100 ppm.

20. The storage stabilized liposomal irinotecan composition of claim 17, having a total irinotecan moiety content equivalent to 4.3 mg/mL irinotecan free base, wherein triethylammonium or diethylammonium is present in a total amount of less than 100 ppm, and wherein the liposomes have a volume weighted mean size of about 110 nm, as measured by quasi-elastic light scattering.

21. The storage stabilized liposomal irinotecan composition of claim 1, wherein the sulfate concentration in step (a) ranges from 0.45 to 0.48 M.

22. The storage stabilized liposomal irinotecan composition of claim 3 comprising a total of 6.81 mg DSPC /mL, 2.22 mg cholesterol /mL, and 0.12 mg MPEG-2000-DSPE /mL, 4.05 mg/mL HEPES aqueous buffer and 8.42 mg sodium chloride/mL.

23. The storage stabilized liposomal irinotecan composition of claim 1, wherein the time the liposomes are contacted with the solution comprising irinotecan above the transition temperature in step (b) is from about 30 to about 60 minutes.

24. The storage stabilized liposomal irinotecan composition of claim 23, wherein the time is about 30 minutes.

25. The storage stabilized liposomal irinotecan composition of claim 1, wherein the methoxy-terminated polyethylene glycol-distearoylphosphatidyl ethanolamine is MPEG-2000-DSPE.

26. The storage stabilized liposomal irinotecan composition of claim 1, wherein the composition comprises unilamellar liposomes.

27. The storage stabilized liposomal irinotecan composition of claim 10, wherein the size is determined by the method of cumulants.

28. The storage stabilized liposomal irinotecan composition of claim 13, wherein the_size is determined by the method of cumulants.

29. The storage stabilized liposomal iinotecan composition of claim 20, wherein the_size is determined by the method of cumulants.

30. The storage stabilized liposomal irinotecan composition of claim 1, wherein the time the liposomes are contacted with the solution comprising irinotecan above the transition temperature in step (b) is about 30 minutes.

31. The storage stabilized liposomal irinotecan composition of claim 4, wherein the time the liposomes are contacted with the solution comprising irinotecan above the transition temperature in step (b) is about 30 minutes.