CLAIMS

What is claimed is:

1. A method of reconstituting Annamycin, such method comprising:
adding saline at a temperature of 37 °C ± 4 °C to one or more containers of preliposomal Annamycin lyophilizate, to form suspended liposomal Annamycin with a concentration of 0.5-1.5 mg/mL;
maintaining said one or more containers at 30-42 °C;
diluting said suspended liposomal Annamycin, with saline at a temperature of 37 °C ± 4 °C to provide diluted liposomal Annamycin at a concentration in saline of 0.3-0.7 mg/mL;
and
maintaining said one or more containers of suspended liposomal Annamycin and said diluted liposomal Annamycin at 30-42 °C during and after the dilution.

2. The method of claim 1 wherein said suspended liposomal Annamycin has a concentration of approximately 1 mg/mL.

3. The method of claim 1 or 2 wherein the total weight of the diluted liposomal Annamycin is equal to the effective dose required.

4. The method of any one of claims 1-3 wherein the suspended liposomal Annamycin is diluted by adding it into a saline-containing IV bag which is at a temperature of 37 °C ± 4 °C.

5. The method of any one of claims 1-4 wherein the temperature of the suspended liposomal Annamycin is maintained at a temperature of 37 °C ± 4 °C before, during, and after dilution.

6. The method of any one of claims 1-4 and 5 wherein the diluted liposomal Annamycin has a concentration of approximately 0.5 mg/mL.

7. The method of any one of claims 1-4 and 5-6 wherein the suspension of liposomal Annamycin is maintained at or near 37 °C and the diluted liposomal Annamycin is maintained at or near 37 °C.

8. A method of preparing an effective dose of a reconstituted liposomal formulation of Annamycin, such method comprising:

warming syringes and non-PVC IV bags, each containing saline (about) 0.9% aqueous injection USP sodium chloride at 37 °C ± 4 °C for at least about three hours, in an oven or bag warmer, wherein

the volume of saline in mL in a syringe is equal to the weight in mg of preliposomal lyophilizate Annamycin to be reconstituted, and

the volume of saline within said IV bag equivalent to the total amount of saline in all syringes, and

the volume of said IV bag is of sufficient capacity to contain the total volume of saline and liposomal Annamycin for dilution of the total dose of liposomal Annamycin;

removing a sufficient number of vials containing preliposomal Annamycin lyophilizate to provide the desired total dose of Annamycin from the freezer and allowing the vials to stand at room temperature for 30 minutes to 2 hours;

vigorously shaking each vial of preliposomal lyophilizate Annamycin to break up any dry cake;

injecting air into each vial from air filled syringes until pressure in each vial is equalized;

adding a volume of 37 °C ± 4 °C saline from a syringe kept at 37 °C ± 4 °C in an oven to a vial containing a weight equivalent vial of preliposomal lyophilizate Annamycin such that the final Annamycin concentration is approximately 1 mg/mL, maintaining negative pressure throughout the addition of saline;

immediately shaking the vial back and forth vigorously by hand for 15 seconds, then placing the vial in a resealable polyethylene storage bag;

repeating the steps of adding saline, shaking the vial, and placing the vial in the storage bag until all vials required for the total dose of Annamycin are similarly prepared;

shaking, for a second time, all vials, 2-4 at a time for 1-2 minutes;

storing all vials of reconstituted liposomal Annamycin at 37 °C ± 4 °C until ready for dilution, for 30 minutes up to 1 hour;

removing vials of reconstituted liposomal Annamycin from storage at 37 °C ± 4 °C no more than two at a time, and after gently inverting each vial once, withdrawing a foam-free suspension from the vial while maintaining negative pressure throughout the withdrawal of the suspension;

introducing the withdrawn foam-free suspension of reconstituted liposomal Annamycin slowly into a non-PVC IV bag of saline at a temperature of 37 °C ± 4 °C, prepared as described above and repeating the steps for the second vial;

repeating the steps of removing the vials, withdrawing the suspension, and introducing the

suspension into the IV bag until all vials of reconstituted liposomal Annamycin required for the total dose of Annamycin have been introduced into the non-PVC IV bag, providing an IV bag containing the final reconstituted liposomal Annamycin with a concentration of about 0.5 mg/mL; and

agitating the saline and reconstituted liposomal Annamycin in the IV bag by gently inverting the container several times, without generating foam.

9. Use of diluted liposomal Annamycin prepared by the method of any one of claims 1-4 and 6-8 for manufacturing a medicament for the treatment of cancer.

10. The use of claim 9 wherein said liposomal Annamycin is prepared as in claim 4.

11. The use of claim 9 wherein said liposomal Annamycin is prepared as in claim 5.

12. The use of claim 9 wherein said liposomal Annamycin is a prepared as in claim 7.

13. The use of any one of claims 9-12 wherein said patient is human and said cancer is selected from leukemias and lymphomas.

14. The use of claim 13, wherein said cancer is selected from the group consisting of acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphocytic leukemia (ALL), chronic lymphocytic leukemia (CLL), Hodgkin lymphoma, and non-Hodgkin lymphoma.

15. A liposomal annamycin suspension comprising

saline at 37 °C ± 4 °C, wherein the saline is a 0.9% aqueous sodium chloride solution;

0.8 mg/mL to 1.2 mg/mL of Annamycin;

32.7 mg/mL to 33.7 mg/mL of dimyristoyl phosphatidylcholine (“DMPC”);

13.6 mg/mL to 15.0 mg/mL of 1,2-dimyristoyl-sn-glycero-3-[phospho(1’-rac-glycerol)] sodium salt (“DMPG”); and

1.5 mg/mL to 1.7 mg/mL Polysorbate 20;

wherein the liposomal annamycin suspension comprises a mean particle size of about 8 μm as determined by a laser diffraction particle size analyzer.

16. The liposomal annamycin suspension of Claim 15, wherein the liposomal annamycin suspension is at a temperature of 37 °C ± 4 °C.

17. The liposomal annamycin suspension of Claim 15, wherein 50% of the particle size is distributed in the range of about 5 μm to about 10 μm as determined by a laser diffraction particle size analyzer.

18. The liposomal annamycin suspension of Claim 15, wherein 90% of the particle size is distributed in the range of about 2 μm to about 20 μm as determined by a laser diffraction particle size analyzer.

19. The liposomal annamycin suspension of Claim 15, wherein the Annamycin is at least 98% pure.

20. The liposomal annamycin suspension of Claim 19, wherein purity is determined by high performance liquid chromatography using a verified standard.

21. The liposomal annamycin suspension of Claim 15, wherein the Annamycin is at least 99% pure.

22. The liposomal annamycin suspension of Claim 21, wherein purity is determined by high performance liquid chromatography using a verified standard.

23. The liposomal annamycin suspension of Claim 16, wherein 50% of the particle size is distributed in the range of about 5 μm to about 10 μm as determined by a laser diffraction particle size analyzer.

24. The liposomal annamycin suspension of Claim 16, wherein 90% of the particle size is distributed in the range of about 2 μm to about 20 μm as determined by a laser diffraction particle size analyzer.

25. The liposomal annamycin suspension of Claim 16, wherein the Annamycin is at least 98% pure.

26. The liposomal annamycin suspension of Claim 25, wherein purity is determined by high performance liquid chromatography using a verified standard.

27. The liposomal annamycin suspension of Claim 16, wherein the Annamycin is at least 99% pure.

28. The liposomal annamycin suspension of Claim 27, wherein purity is determined by high performance liquid chromatography using a verified standard.

29. The liposomal annamycin suspension of Claim 23, wherein 90% of the particle size is distributed in the range of about 2 μm to about 20 μm as determined by a laser diffraction particle size analyzer.

30. The liposomal annamycin suspension of Claim 29, wherein the Annamycin is at least 98% pure.

31. The liposomal annamycin suspension of Claim 30, wherein purity is determined by high performance liquid chromatography using a verified standard.

32. The liposomal annamycin suspension of Claim 31, wherein the Annamycin is at least 99% pure.

33. The method of claim 1 or 8 wherein said preliposomal Annamycin lyophilizate comprises 1.8 – 2.2 wt % Annamycin; 3.0 – 3.4 wt. % Polysorbate 20; and 94.4 - 95.2 wt. % of lipids selected from DMPC and DMPG.

34. The method of claim 33 wherein the DMPC is 65.3 -67.3 wt. % and the DMPG is 27.1 – 29.9 wt. %.