CLAIMS

What is claimed is:

1. Use of about 1 g to about 4 g of ultra-pure EPA in the manufacture of a medicament for lowering triglycerides in a subject on stable statin therapy having baseline fasting triglycerides of about 200 mg/dl to about 500 mg/dl, wherein the use comprises administration to the subject the medicament comprising about 1 g to about 4 g of ultra-pure EPA per day, wherein (1) upon administration the medicament to the subject daily for a period of 12 weeks the subject exhibits at least 5% lower fasting triglycerides than a placebo controlled subject maintained on stable statin therapy without concomitant ultra-pure EPA for a period of 12 weeks, (2) the subject exhibits substantially no serum LDL-C increase, and (3) the placebo controlled subject also has baseline fasting triglycerides of about 200 mg/dl to about 500 mg/dl.

2. The use of claim 1 wherein the subject and the placebo controlled subject have baseline serum LDL-C levels of about 40 mg/dl to about 115 mg/dl.

3. The use of claim 2 wherein upon administration the medicament to the subject daily for a period of 12 weeks and maintaining the placebo controlled subject on stable statin therapy without concomitant ultra-pure EPA therapy for a period of 12 weeks, the subject exhibits a lower serum LDL-C level than the placebo controlled subject.

4. The use of claim 3 wherein upon administration the medicament to the subject daily for a period of 12 weeks and maintaining the placebo controlled subject on stable statin therapy without concomitant ultra-pure EPA therapy for a period of 12 weeks, the subject exhibits an at least 5% lower serum LDL-C level than the placebo controlled subject.

5. The use of claim 3 wherein upon administration the medicament to the subject daily for a period of 12 weeks and maintaining the placebo controlled subject on stable statin therapy without concomitant ultra-pure EPA therapy for a period of 12 weeks, the subject exhibits an at least 10% lower serum LDL-C level than the placebo controlled subject.

6. The use of claim 3 wherein upon administration the medicament to the subject daily for a period of 12 weeks and maintaining the placebo controlled subject on stable statin therapy without concomitant ultra-pure EPA therapy for a period of 12 weeks,

the subject exhibits at least 10% lower fasting triglycerides than the placebo controlled subject.

7. The use of claim 3 wherein upon administration the medicament to the subject daily for a period of 12 weeks and maintaining the placebo controlled subject on stable statin therapy without concomitant ultra-pure EPA therapy for a period of 12 weeks, the subject exhibits at least 15% lower fasting triglycerides than the placebo controlled subject.

8. The use of claim 3 wherein upon administration the medicament to the subject daily for a period of 12 weeks and maintaining the placebo controlled subject on stable statin therapy without concomitant ultra-pure EPA therapy for a period of 12 weeks, the subject exhibits at least 25% lower fasting triglycerides than the placebo controlled subject.

9. The use of any one of claims 1 - 8 wherein the ultra-pure EPA comprises at least 95% by weight ethyl eicosapentaenoate, about 0.2% to about 0.3% by weight ethyl octadecatetraenoate, about 0.05% to about 0.20% by weight ethyl nonaecapentaenoate, about 0.2% to about 0.4% by weight ethyl arachidonate, about 0.3% to about 0.5% by weight ethyl eicosatetraenoate, and about 0.05% to about 0.15% ethyl heneicosapentaenoate.

10. The use of claim 9 wherein the ultra-pure EPA comprises at least 95% by weight ethyl eicosapentaenoate, about 0.22% to about 0.28% by weight ethyl octadecatetraenoate, about 0.075% to about 0.15% by weight ethyl nonaecapentaenoate, about 0.25% to about 0.35% by weight ethyl arachidonate, about 0.3% to about 0.4% by weight ethyl eicosatetraenoate, and about 0.075% to about 0.15% ethyl heneicosapentaenoate.

11. The use of any one of claims 1 - 10 wherein the ultra-pure EPA is encapsulated in a capsule.

12. The use of claim 11 wherein the capsule comprises gelatin.

13. The use of claim 12 wherein 1 to 4 of said capsules are to be administered to the subject each day.

14. The use of any one of claims 1 - 13 wherein the statin is selected from the group consisting of atorvastatin, rosuvastatin and simvastatin.

15. The use of claim 14 wherein the subject and the placebo controlled subject have a baseline body mass index not greater than 45 kg/m^2.

16. The use of claim 15 wherein the subject is not on concomitant niacin or fibrate therapy.

17. The use of claim 1 wherein the subject and the placebo controlled subject have a baseline sitting systolic blood pressure less than or equal to about 160 mmHg and a baseline sitting diastolic blood pressure less than about 100 mmHg.

18. The use of any one of claims 1 - 17 wherein the ultra-pure EPA contains no DHA or derivative thereof.

19. Use of a triglyceride-lowering effective amount of ultra-pure E-EPA in the manufacture of a medicament for lowering triglycerides in a subject having a 10 year risk of coronary heart disease, based on ATP III risk analysis, of at least 20%.

CLAIMS

What is claimed is:

1. Use of ethyl eicosapentaenoate in the manufacture of a medicament for lowering triglycerides in a subject on stable statin therapy having baseline fasting triglycerides of about 200 mg/dl to less than 500 mg/dl, wherein the medicament is in a form suitable for administration of 2 g to about 4 g of ethyl eicosapentaenoate to the subject.

2. Use of ethyl eicosapentaenoate for the manufacture of a medicament for treating mixed dyslipidemia in a subject on statin therapy having baseline fasting triglycerides of about 200 mg/dl to less than 500 mg/dl, wherein the medicament is in a form suitable for administration of 2 g to about 4 g per day of ethyl eicosapentaenoate to the subject.

3. The use of claims 1 or 2 wherein the subject has a baseline serum LDL-C level of about 40 mg/dl to about 115 mg/dl.

4. The use of claim 3 wherein the medicament effects a reduction in serum LDL-C.

5. The use of claim 4, wherein the medicament effects at least a 5% reduction in LDL-C.

6. The use of claim 4, wherein the medicament effects at least a 5% reduction in fasting triglycerides and a reduction in LDL-C.

7. The use of claim 4, wherein the medicament effects at least a 10% reduction in triglycerides.

8. The use of claim 4, wherein the medicament effects at least a 15% reduction in triglycerides than the placebo controlled subject.

9. The use of claim 8, wherein the medicament effects a reduction in Apolipoprotein B, total cholesterol, and lipoprotein associated phospholipase A2.

10. The use of any one of claims 4 to 9, wherein the reduction(s) in the subject is compared to a second subject on statin therapy and having baseline fasting triglycerides of about 2000 mg/dl to less than 500 mg/dl who has not received the medicament.

11. The use of any one of claims 1 to 10, wherein the medicament is administered for a period of at least about 12 weeks.

12. The use of any one of claims 1 to 11, wherein the medicament comprises at least about 90%, by weight of all fatty acids administered, ethyl eicosapentaenoate.

13. The use of any one of claims 12, wherein the medicament comprises at least about 95%, by weight of all fatty acids administered, ethyl eicosapentaenoate.

14. The use of claim 13, wherein the medicament comprises at least about 96%, by weight of all fatty acids, ethyl eicosapentaenoate.

15. The use of any one of claims 1 to 14, wherein the subject is on stable statin therapy.

16. The use of any one of claims 1 to 15, wherein the statin is selected from the group consisting of atorvastatin, rosuvastatin and simvastatin.

17. The use of any one of claims 1 to 16, wherein the subject has a baseline body mass index not greater than 45 kg/m^2.

18. Use of a capsule comprising about 1 g of ethyl eicosapentaenoate in the manufacture for a medicament for lowering triglycerides and LDL-C in a subject on statin therapy and having fasting triglycerides of about 200 mg/dl to less than 500mg/dl, wherein about 2 to 4 capsules are to be orally administered to the subject per day.

19. Use of a capsule comprising about 1 g of ethyl eicosapentaenoate in the manufacture for a medicament for treating mixed dyslipidemia in a subject on statin therapy and having fasting triglycerides of about 200 mg/dl to less than 500mg/dl, wherein about 2 to 4 capsules are to be orally administered to the subject per day

20. The capsule of claim 18 or 19, wherein the capsule effects a reduction in fasting triglycerides and fasting LDL-C in the subject compared to fasting triglycerides and fasting LDL-C in a second subject on statin therapy who has not received the capsules.

21. The capsule of claim 20, wherein the capsule effects a reduction in fasting non-HDL-C compared to fasting non-HDL-C in the second subject.

22. The capsule of claim 20, wherein the capsule effects a reduction in fasting VLDL-C compared to fasting VLDL-C in the second subject.

23. The capsule of claim 20, wherein the capsule effects a reduction in fasting Apolipoprotein B compared to fasting Apolipoprotein B in the second subject.

24. The capsule of claim 20, wherein the capsule effects a reduction in fasting total cholesterol compared to fasting total cholesterol in the second subject.

25. The capsule of any one of claims 18 to 24, wherein the capsule comprises at least about 90%, by weight of all fatty acids present, ethyl eicosapentaenoate.

26. The capsule of claim 25, wherein the capsule comprises at least about 95%, by weight of all fatty acids present, ethyl eicosapentaenoate.

27. The capsule of any one of claims 18 to 26, wherein the capsule comprises no more than about 5%, by weight of all fatty acids present, docosahexaenoic acid or its esters.

28. The capsule of claim 27, wherein the capsule comprises no more than about 3%, by weight of all fatty acids present, docosahexaenoic acid or its esters.

29. The capsule of any one of claims 18 to 28, wherein the statin therapy is stable statin therapy.

30. The use of any one of claims 18 to 29, wherein the statin is selected from the group consisting of atorvastatin, rosuvastatin and simvastatin.

31. A composition comprising ethyl eicosapentaenoate for use in increasing plasma and/or serum EPA in a subject having baseline triglycerides of about 200 mg/dL to about 500 mg/dL and on stable statin therapy, wherein the composition comprises at least 96%, by weight, ethyl eicosapentaenoate, about 0.2% to about 0.5% by weight ethyl octadecatetraenoate, about 0.05% to about 0.25% by weight ethyl nonadecapentaenoate, about 0.2% to about 0.45% by weight ethyl arachidonate, about 0.3% to about 0.5% by weight ethyl eicosatetraenoate, about 0.05% to about 0.32% ethyl heneicosapentaenoate and not more than 0.05% ethyl-DHA, if any, and wherein the treatment comprises administering, daily, to the subject the composition in an amount sufficient to increase plasma and/or serum EPA levels in the subject by at least about 200% to compared to baseline.

32. The composition of claim 31, wherein upon administration of 2 g of the composition to the subject daily for a period of at least about 6 weeks, the subject exhibits an at least 200% increase in plasma and/or serum EPA compared to baseline.

33. The composition of claim 31, wherein upon administration of 4 g of the composition to the subject daily for a period of at least about 6 weeks, the subject exhibits an at least 300% increase in plasma and/or serum EPA compared to baseline.

34. The composition of claim 31, wherein the composition is administered in an amount sufficient to increase plasma and/or serum EPA levels in the subject by at least 300% compared to baseline.

35. The composition of claim 31, wherein the composition is administered in an amount sufficient to increase plasma and/or serum EPA levels in the subject by at least 400% compared to baseline.

36. The composition of claim 35, wherein the composition is administered to the subject daily for a period of at least about 6 weeks.

37. The composition of any one of claims 32, 33 or 34, wherein the subject has a baseline plasma and/or serum EPA level of not more than about 50 μg/ml.

38. The composition of claim 31, wherein upon daily administration of 4 g of the composition to the subject for a period of at least about 6 weeks, the subject exhibits an at least 400% increase in plasma and/or serum EPA compared to baseline.

39. The composition of claim 31, wherein upon daily administration of the composition to the subject, the subject exhibits an increase in serum and/or plasma DPA levels and a decrease in serum and/or plasma AA, DHA and/or DGLA levels.

40. The composition of claim 31, wherein upon daily administration of the composition to the subject for a period of at least 6 weeks, the subject exhibits an increase in serum and/or plasma DPA levels and a decrease in serum and/or plasma AA, DHA and/or DGLA levels compared to baseline.

41. The composition of claim 31, wherein upon daily administration of the composition to the subject for a period of at least 6 weeks, the subject exhibits a decrease in plasma and/or serum DHA levels by at least 16% compared to baseline, a decrease in DGLA plasma and/or serum levels by at least 31% compared to baseline, a decrease in AA plasma and/or serum levels by at least 20% compared to baseline, and/or an increase in plasma and/or serum DPA levels of at least 130% compared to baseline.

42. The composition of claim 31, wherein the composition comprises at least 96% by weight ethyl eicosapentaenoate, about 0.22% to about 0.4% by weight ethyl octadecatetraenoate, about 0.075% to about 0.20% by weight ethyl nonadecapentaenoate, about 0.25% to about 0.40% by weight ethyl arachidonate, about 0.3% to about 0.4% by weight ethyl eicosatetraenoate and about 0.075% to about 0.25% ethyl heneicosapentaenoate.

43. The composition of claim 31, wherein the composition comprises at least 98%, by weight, ethyl eicosapentaenoate, about 0.25% to about 0.38% by weight ethyl octadecatetraenoate, about 0.10% to about 0.15% by weight ethyl nonadecapentaenoate, about 0.25% to about 0.35% by weight ethyl arachidonate, about 0.31% to about 0.38% by weight ethyl eicosatetraenoate, and about 0.08% to about 0.20% ethyl heneicosapentaenoate.

44. The composition of claim 31, wherein the composition further comprises tocopherol in an amount of about 0.1% to about 0.3%, by weight.

45. The composition of claim 31, wherein the composition is present in a capsule shell.

46. The composition of claim 31, wherein an LDL-C level in the subject is reduced by at least about 5% compared to baseline.