What is claimed is:

1. Use of a pharmaceutical composition in the manufacture of a medicament for ~~A method of~~ reducing ~~a~~ risk of a cardiovascular event in a subject ~~on statin therapy~~ with at least one risk factor for cardiovascular disease who is at LDL-C goal, the ~~method~~ use comprising~~:~~

~~(a) identifying a subject on statin therapy and having a fasting baseline triglyceride level of about 135 mg/dL to about 500 mg/dL, optionally wherein said subject has established cardiovascular disease or has a high risk of developing cardiovascular disease; and~~

~~(b)~~ that the ~~administering to the subject a~~ pharmaceutical composition comprising ~~about 1 g to~~ about 4 g of icosapent ~~eicosapentaenoic acid~~ ethyl ~~ester~~ is to be administered to the subject per day for a period effective to reduce risk of the cardiovascular event in the subject.

2. The use of claim 1, wherein the cardiovascular event is one or more of: cardiovascular death, myocardial infarction, stroke, coronary revascularization, and unstable angina.

3. The use of claim 1, wherein the administration affects a relative risk reduction of said cardiovascular event of at least about 25%.

4. The use of claim 1, wherein the subject has a fasting baseline triglyceride level of 135 mg/dL to 500 mg/dL.

5. The use of claim 1, wherein the LDL-C goal is an LDL-C level of 40 mg/dL to 100 mg/dL.

6. The use of claim 1, wherein the subject has established cardiovascular disease.

7. The use of claim 1, wherein the subject has diabetes.

8. The use of claim 1, wherein the at least one risk factor for cardiovascular disease is selected from the following risk factors: (a) the subject is a male of at least 55 years of age or a female of at least 65 years of age, (b) the subject smokes cigarettes or has stopped smoking cigarettes within three months before administration of the pharmaceutical composition, (c) the subject has a

blood pressure of at least 140 mmHg systolic or at least 90 mmHg diastolic, (d) the subject is receiving antihypertension medication, (e) the subject is a male with HDL-cholesterol level 40 mg/dL or less or is a female with HDL-cholesterol level 50 mg/dL or less, (f) the subject has a hs-CRP level of greater than 3 mg/L, (g) the subject has a creatine clearance between 30 mL/min and 60 mL/min, (h) the subject has non-proliferative retinopathy, (i) the subject has pre-proliferative retinopathy, (j) the subject has proliferative retinopathy, (k) the subject has maculopathy, (l) the subject has advanced diabetic eye disease or a history of photocoagulation, (m) the subject has micro- or macro-albuminuria, and (n) the subject has a asymptomatic ankle-brachial index of less than 0.9

~~2.~~9. The ~~method~~ use of claim 1 wherein the pharmaceutical composition is to be administered to the subject in 1 to ~~4~~ 8 dosage units per day.

10. The use of claim 1, wherein the icosapent ethyl comprises at least about 90 wt. % of all omega-3 fatty acids in the pharmaceutical composition.

~~3.~~11. The ~~method~~ use of claim 1 wherein the icosapent~~eicosapentaenoic acid~~ ethyl ~~ester~~ comprises at least about 96 wt.% of all omega-3 fatty acids in the pharmaceutical composition.

~~4. The method of claim 1, wherein the established cardiovascular disease is determined by the presence of any one of: documented coronary artery disease, documented cerebrovascular disease, documented carotid disease, documented peripheral arterial disease, or combinations thereof.~~

~~5.~~12. The ~~method~~ use of claim 1 further comprising a step of measuring the subject's baseline lipid profile prior to administering the pharmaceutical composition to the subject.

~~6.~~13. The ~~method~~ use of claim ~~1~~ 12, wherein the subject has one or more of: a baseline non-HDL-C value of ~~about~~ 200 mg/dL to ~~about~~ 300 mg/dL; a baseline total cholesterol value of ~~about~~ 250 mg/dL to ~~about~~ 300 mg/dL; a baseline VLDL-C value of ~~about~~ 140 mg/dL to ~~about~~ 200 mg/dL; a baseline HDL-C

value of ~~about~~ 10 to ~~about~~ 30 mg/dL; and/or a baseline LDL-C value of ~~about~~ 40 to ~~about~~ 100 mg/dL.

~~7. The method of claim 1 wherein the statin therapy comprises administering to the subject a statin and optionally ezetimibe.~~

~~8.~~14. The ~~method~~ use of claim 1, wherein the subject: (a) has not been administered 200 mg or more per day of niacin and/or fibrates for at least 28 days before administration of the pharmaceutical composition~~step (a)~~; (b) has not been administered omega-3 fatty acid prescription for a period of time beginning 28 days prior to administration of the pharmaceutical composition~~step (a)~~; (c) has not ingested dietary supplements comprising omega-3 fatty acids for a period of time beginning 28 days prior to administration of the pharmaceutical composition~~step (a)~~.

~~9. The method of any of claim 8, wherein the period of time ends no earlier than about 6 months after a first administration of the pharmaceutical composition in step (b).~~

~~10.~~15. The ~~method~~ use of claim ~~8~~1, wherein ~~the~~ said period ~~of time~~ ends about 6 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or more than about 5 years after the first administration of the pharmaceutical composition ~~in step (b)~~.

16. The use of claim 1, wherein the subject is to be administered about 4 g of the pharmaceutical composition per day for at least about 3 years.

17. Use of icosapent ethyl in the manufacture of a medicament for delaying or preventing a major adverse cardiovascular event in a subject, the use comprising that about 4 g of icosapent ethyl is to be administered to the subject per day for a period effective to delay or prevent the major adverse cardiovascular event, wherein the subject is 50 years of age or older, has diabetes and at least one additional risk factor for cardiovascular disease.

18. The use of claim 17, wherein the at least one additional risk factor is selected from hypertension, smoking, retinopathy, and albuminuria.

19. The use of claim 17, wherein the subject has at least two additional risk factors for cardiovascular disease.

20. The use of claim 17, wherein subject has a baseline triglyceride level of at least 200 mg/dL.

21. The use of claim 17, wherein the major adverse cardiovascular event is selected from the group consisting of stroke, myocardial infarction, coronary revascularization, unstable angina, and cardiovascular death.

22. The use of claim 17, wherein the subject is on a statin therapy.

23. The use of claim 22, wherein the statin therapy is a stable statin therapy.

24. The use of claim 17, wherein the icosapent ethyl is present in a pharmaceutical composition and the icosapent ethyl comprises at least about 96 wt. % of all omega-3 fatty acids in the pharmaceutical composition.

25. The use of claim 24, wherein about 1 g of the pharmaceutical composition is present in each of 4 capsules.

~~11. The method of claim 1 wherein the cardiovascular event is one or more of: cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, and unstable angina.~~

~~12. The method of claim 1 wherein the cardiovascular event is one or more of: cardiac arrhythmia; cardiac arrest; peripheral cardiovascular disease requiring intervention, angioplasty, bypass surgery or aneurysm repair; and death.~~

~~13. The method of claim 1 wherein the cardiovascular event is onset of new congestive heart failure.~~

~~14. The method of claim 1 wherein the subject is administered about 1 g to about 4 g of the pharmaceutical composition per day for about 4 months, about 1 year, about 2 years, about 3 years, about 4 years, or about 5 years in step (b).~~

~~15. The method of claim 14 wherein, after administering the pharmaceutical composition in step (b), the subject exhibits one or more of (a) reduced triglyceride levels compared to baseline; (b) reduced Apo B levels compared to baseline; (c) increased HDL-C levels compared to baseline; (d) no increase in~~

~~LDL-C levels compared to baseline; (e) a reduction in LDL-C levels compared to baseline; (f) a reduction in non-HDL-C levels compared to baseline; (g) a reduction in VLDL levels compared to baseline; (h) a reduction in total cholesterol levels compared to baseline; (i) a reduction in high sensitivity C-reactive protein (hs-CRP) levels compared to baseline; and/or (j) a reduction in high sensitivity troponin (hsTnT) levels compared to baseline.~~

16. ~~The method of claim 14, wherein the subject exhibits one or more of: (a) a reduction in triglyceride level of at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, or at least about 55% as compared to baseline; (b) a less than 30% increase, less than 20% increase, less than 10% increase, less than 5% increase or no increase in non-HDL-C levels or a reduction in non-HDL-C levels of at least about 1%, at least about 3%, at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, or at least about 50% as compared to baseline; (c) an increase in HDL-C levels of at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, or at least about 50% as compared to baseline; and/or (d) a less than 30% increase, less than 20% increase, less than 10% increase, less than 5% increase or no increase in LDL-C levels or a reduction in LDL-C levels of at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, or at least about 55% as compared to baseline.~~

17. ~~The method of claim 1 further comprising assigning a plurality of control subjects to a control population,~~

~~wherein each control subject is on stable statin therapy, has a fasting baseline triglyceride level of about 135 mg/dL to about 500 mg/dL, and has established cardiovascular disease or a high risk of developing cardiovascular disease, and~~

~~wherein the control subjects are not administered the pharmaceutical composition comprising about 1 g to about 4 g of eicosapentaenoic acid ethyl ester per day.~~

~~18. The method of claim 17, wherein a first time interval beginning at an initial administration of the pharmaceutical composition to the subject in step (b) to a first cardiovascular event of the subject is greater than or substantially greater than a first control time interval beginning at initial administration of a placebo to the control subjects to a first cardiovascular event in the control subjects.~~

~~19. The method of claim 18, wherein the first cardiovascular event of the subject is a major cardiovascular event selected from the group consisting of: cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, and unstable angina caused by myocardial ischemia.~~

~~20. The method of claim 18 or 19, wherein the first cardiovascular event of the control subjects is a major cardiovascular event selected from the group consisting of: cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, and unstable angina caused by myocardial ischemia.~~

~~21. The method of claim 18, wherein the first cardiovascular event of the subject and the first cardiovascular event of the control subjects is any of: death (from any cause), nonfatal myocardial infarction, or nonfatal stroke.~~

~~22. The method of claim 18, wherein the first cardiovascular event of the subject and the first cardiovascular event of the control subjects is any of: death from a cardiovascular cause, nonfatal myocardial infarction, coronary revascularization, unstable angina, peripheral cardiovascular disease, or cardiac arrhythmia requiring hospitalization.~~

~~23. The method of claim 18, wherein the first cardiovascular event of the subject and the first cardiovascular event of the control subjects is any of: death from a cardiovascular cause, nonfatal myocardial infarction, and coronary revascularization, unstable angina.~~

~~24. The method of claim 18, wherein the first cardiovascular event of the subject and the first cardiovascular event of the control subjects is any of: death from a cardiovascular cause and nonfatal myocardial infarction.~~

~~25. The method of claim 18, wherein the first cardiovascular event of the subject and the first cardiovascular event of the control subjects is any of: death (from any cause).~~

~~26. The method of claim 18, wherein the first cardiovascular event of the subject and the first cardiovascular event of the control subjects is any of: fatal myocardial infarction and nonfatal myocardial infarction.~~

~~27. The method of claim 26, wherein nonfatal myocardial infarction includes silent myocardial infarction.~~

~~28. The method of claim 18, wherein the first cardiovascular event of the subject and the first cardiovascular event of the control subjects is coronary revascularization.~~

~~29. The method of claim 18, wherein the first cardiovascular event of the subject and the first cardiovascular event of the control subjects is hospitalization for unstable angina.~~

~~30. The method of claim 29, wherein the unstable angina is caused by myocardial ischemia.~~

~~31. The method of claim 18, wherein the first cardiovascular event of the subject and the first cardiovascular event of the control subjects is any one of: fatal stroke or nonfatal stroke.~~

~~32. The method of claim 1 or claim 18, wherein a second time interval beginning at an initial administration of the pharmaceutical composition to the subject in step (b) to a second cardiovascular event of the subject is greater than or substantially greater than a second control time interval beginning at initial administration of a placebo to the control subjects to a second cardiovascular event in the control subjects.~~

~~33. The method of claim 32, wherein the second cardiovascular event of the subject and the second cardiovascular event of the control subjects is a major cardiovascular event selected from the group consisting of: cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, and unstable angina caused by myocardial ischemia.~~

~~34. The method of claim 18, wherein the subject has diabetes mellitus and the control subjects each have diabetes mellitus.~~

~~35. The method of claim 18, wherein the subject has metabolic syndrome and the control subjects each have metabolic syndrome.~~

~~36. The method of claim 18, wherein the first cardiovascular event of the subject and the first cardiovascular event of the control subjects is any one of: new coronary heart failure, new coronary heart failure leading to hospitalization, transient ischemic attack, amputation for coronary vascular disease, and carotid revascularization.~~

~~37. The method of claim 18, wherein the first cardiovascular event of the subject and the first cardiovascular event of the control subjects is any one of: elective coronary revascularization and emergent coronary revascularization.~~

~~38. The method of claim 18, wherein the first cardiovascular event of the subject and the first cardiovascular event of the control subjects is an onset of diabetes.~~

~~39. The method of claim 18, wherein, after an initial administration of the pharmaceutical composition in step (b), the subject exhibits one or more of (a) reduced triglyceride levels compared to the control population; (b) reduced Apo B levels compared to the control population; (c) increased HDL-C levels compared to the control population; (d) no increase in LDL-C levels compared to the control population; (e) a reduction in LDL-C levels compared to the control population; (f) a reduction in non-HDL-C levels compared to the control population; (g) a reduction in VLDL levels compared to the control population; (h) a reduction in total cholesterol levels compared to the control population; (i) a reduction in high sensitivity C-reactive protein (hs-CRP)~~

~~levels compared to the control population; and/or (j) a reduction in high sensitivity troponin (hsTnT) levels compared to the control population.~~

~~40. The method of claim 18, wherein the first cardiovascular event of the subject and the first cardiovascular event of the control subjects is cardiac arrhythmia requiring hospitalization.~~

~~41. The method of claim 18, wherein the first cardiovascular event of the subject and the first cardiovascular event of the control subjects is cardiac arrest.~~

~~42. The method of claim 14, wherein a first weight of the subject determined after step (b) is less than a baseline weight of the subject determined before step (b).~~

~~43. The method of claim 14, wherein a first waist circumference of the subject determined after step (b) is less than a baseline waist circumference of the subject determined before step (b).~~

~~44. The method of any one of claims 18 to 38 or 40 to 43, wherein the first control time interval is an average, a median, or a mean of a plurality of first control time intervals associated with each control subject.~~

~~45. The method of claim 32 or claim 33, wherein the second control time interval is an average, a median, or a mean of a plurality of second control time intervals associated with each control subject.~~

~~46. The method of claim 17, wherein a plurality of subjects experience a first major cardiovascular event after an initial administration of the pharmaceutical composition in step (b) at a first incidence rate, and wherein the control subjects experience a first major cardiovascular event after an initial administration of a placebo at a second incidence rate,~~

~~wherein the first incidence rate is less than the second incidence rate.~~

~~47. The method of claim 46, wherein the first major cardiovascular event is any one of: cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, and hospitalization for unstable angina.~~

~~48. The method of claim 47, wherein the unstable angina is determined to be caused by myocardial ischemia.~~

~~49. The method of claim 46, wherein the first and second incidence rates are determined for a time period beginning on the date of the initial administration and ending about 4 months, about 1 year, about 2 years, about 3 years, about 4 years, or about 5 years after the date of initial administration.~~