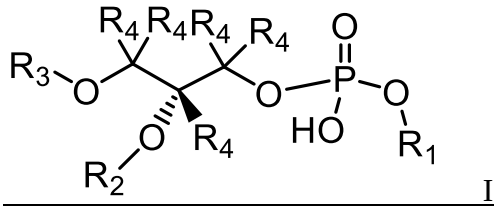
CLAIMS

1. A universal lipid quantitative standard (ULQS) comprising a plurality of isotopically labeled lipid standards, wherein the plurality of isotopically labeled lipid standards includes at least one lipid species from one or more lipid classes selected from the group consisting of: a phospholipid class, a lysophospholipid class, a cholesterol ester class, a triacylglycerol class, a diacylglycerol class, a ceramide class, and a sphingomyelin class,

wherein the phospholipid class includes one or more phospholipid species selected from the group consisting of: phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylserine (PS), phosphatidylglycerol (PG), and phosphatidylinositol (PI),

and wherein the phospholipid species are represented by the general formula I, or a pharmaceutically acceptable salt thereof:



I

wherein:

R_1 is $-(CH_2)_n-N(CH_3)_3$, $-(CH_2)_n-NH_3$, $-(CH_2)_n-C(H)(NH3)-C(O)-O^-$, $-(CH_2)_n-CH(OH)-CH(OH)$, inositol, and H;

n is 1 to 6;

R_2 is a C3 to C30 saturated or unsaturated acyl chain;

R_3 is a C3 to C30 saturated or unsaturated acyl chain; and

R_4 is independently H or an isotope of H, provided that at least one of R_4 is an isotope of H.

~~1.~~

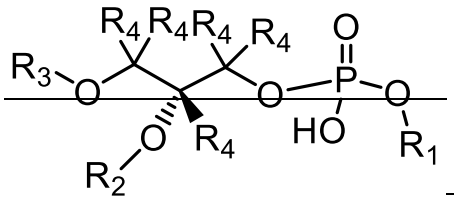
~~2. The ULQS of claim 1, wherein the plurality of isotopically labeled lipid standards includes more than 1 lipid species from one or more of the lipid classes.~~

~~3. The ULQS of claim 1, wherein the plurality of isotopically labeled lipid standards includes 2 to 25 lipid species from one or more of the lipid classes.~~

~~4. The ULQS of claim 1, wherein the plurality of isotopically labeled lipid standards includes:~~

a. 15 phospholipid species, 10 lysophospholipid species, 3 cholesterol ester species, 5 triacylglycerol species, 3 diacylglycerol species, 3 ceramide species, and 3 sphingomyelin species
b. 20 phospholipid species, 15 lysophospholipid species, 5 cholesterol ester species, 9 triacylglycerol species, 5 diacylglycerol species, 5 ceramide species, and 5 sphingomyelin species; or
c. 25 phospholipid species, 15 lysophospholipid species, 5 cholesterol ester species, 9 triacylglycerol species, 5 diacylglycerol species, 5 ceramide species, and 5 sphingomyelin species.

5. The ULQS of claim 1, wherein the lipid species for each lipid class are selected to correct for at least one of the following: ionization efficiency, extraction efficiency, and differential fragmentation efficiency of the lipid species in a sample.
6. The ULQS of claim 5, wherein the lipid species for each lipid class are further selected to cover the entire mass range or substantially all of the mass range of a lipid species present in the sample.
7. The ULQS of claim 5, wherein the concentration of the various lipid species for each lipid class are further selected to mirror the concentration of a lipid species present in the sample.
8. The ULQS of claim 1, wherein the phospholipid class includes one or more phospholipid species selected from the group consisting of: phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylserine (PS), phosphatidylglycerol (PG), and phosphatidylinositol (PI).
9. The ULQS of claim 8, wherein the acyl chains of the phospholipid species are independently selected from a saturated C3 to C30 acyl chain or an unsaturated C3 to C30 acyl chain containing from 1 to 6 double bonds.
10. The ULQS of claim 9, wherein the acyl chains of the phospholipid species are each independently a saturated or unsaturated C3 to C6 acyl chain, a saturated or unsaturated C7 to C11 acyl chain, a saturated or unsaturated C12 to C21 acyl chain, a saturated or unsaturated C22 to C30 acyl chain.
11. The ULQS of claim 8, wherein the acyl chain length of the phospholipid species are each selected such that the sum composition score for the acyl chains is an odd number.
12. The ULQS of claim 8, wherein the phospholipid species are represented by the general formula I, or a pharmaceutically acceptable salt thereof:



~~I~~

~~wherein:~~

~~R_1 is $-(CH_2)_n-N(CH_3)_3$, $-(CH_2)_n-NH_3$, $-(CH_2)_n-C(H)(NH3)-C(O)-O^-$, $-(CH_2)_n-CH(OH)-CH(OH)$, inositol, and H;~~

~~n is 1 to 6;~~

~~R_2 is a C3 to C30 saturated or unsaturated acyl chain;~~

~~R_3 is a C3 to C30 saturated or unsaturated acyl chain; and~~

~~R_4 is independently H or an isotope of H, provided that at least one of R_4 is an isotope of H.~~

~~13.~~2. The ULQS of claim 1~~2~~, wherein R_2 and R_3 are each independently a saturated or unsaturated acyl chain from 3 to 6 carbons in length, from 7 to 11 carbons in length, from 12 to 21 carbons in length, or an acyl chain from 22 to 30 carbons in length.

~~14.~~3. The ULQS of claim 2~~13~~, wherein the length of the acyl chain of R_2 is different from the length of the acyl chain of R_3.

~~15.~~4. The ULQS of claim 3~~14~~, wherein R_2 is unsaturated and R_3 is saturated.

~~16.~~5. The ULQS of claim 1~~2~~, wherein at least a subset of the phospholipid species included in the ULQS have the same R_3 group, but different R_2 groups, wherein at least one or all of the R_2 groups are unsaturated.

~~17.~~6. The ULQS of claim 1~~2~~, wherein the phospholipid species include at least one species each of PC, PE, PS, PG, and PI, the phospholipid species have the same R_3 group, but different R_2 groups, wherein the length of the R_3 group is n and the length of the R_2 group is from n-5 to n+7, and at least one or all of the R_2 groups are unsaturated.

~~18.~~7. The ULQS of claim 6~~17~~, wherein the phospholipid species include five species each of PC, PE, PS, PG, and PI and the R_3 and R_2 groups are repeated for each of the PC, PE, PS, PG, and PI species.

~~19.~~8. The ULQS of claim 1~~2~~, wherein the phospholipid species include the phospholipid species of Table 1, wherein the underlined portion corresponds to R_2, and the double underlined portion corresponds to R_3

Table 1

PC (17:0/14:1)	PE (17:0/14:1)	PS (17:0/14:1))	PG (17:0/14:1))	PI (17:0/14:1)
PC (17:0/16:1)	PE (17:0/16:1)	PS (17:0/16:1)	PG (17:0/16:1)	PI (17:0/16:1)
PC (17:0/18:1)	PE (17:0/18:1)	PS (17:0/18:1)	PG (17:0/18:1)	PI (17:0/18:1)
PC (17:0/20:3)	PE (17:0/20:3)	PS (17:0/20:3)	PG (17:0/20:3)	PI (17:0/20:3)
PC (17:0/22:4)	PE (17:0/22:4)	PS (17:0/22:4)	PG (17:0/22:4)	PI (17:0/22:4)

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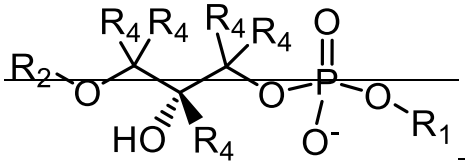
20. The ULQS of claim 1, wherein the lysophospholipid class includes one or more lysophospholipid species selected from the group consisting of: lysophosphatidylcholine (LPC), lysophosphatidylethanolamine (LPE), lysophosphatidylsphoserine (LPS), lysophosphatidylglycerol (LPG), and lysophosphatidylinositol (LPI).

21. The ULQS of claim 20, wherein the acyl chain of the lysophospholipid species is independently selected from a saturated C3 to C25 or an unsaturated C3 to C25 acyl chain containing from 1 to 6 double bonds.

22. The ULQS of claim 20, wherein the acyl chain of the lysophospholipid species is independently a saturated or unsaturated C3 to C6 acyl chain, a saturated or unsaturated C7 to C11 acyl chain, a saturated or unsaturated C12 to C18 acyl chain, a saturated or unsaturated C19 to C25 acyl chain.

23. The ULQS of claim 20, wherein the acyl chain length of the lysophospholipid species are each selected such that the sum composition score for the acyl chains is an odd number.

24. The ULQS of claim 20, wherein the lysophospholipid species are represented by the general formula II, or a pharmaceutically acceptable salt thereof:



II

wherein:

R_1 is $-(CH_2)_n-N(CH_3)_3$, $-(CH_2)_n-NH_3$, $-(CH_2)_n-C(H)(NH3)-C(O)-O^-$, $-(CH_2)_n-CH(OH)-CH(OH)$, inositol, and H;

n is 1 to 6;

R_2 is a C2 to C24 saturated or unsaturated acyl chain; and

R_4 is independently H or an isotope of H, provided that at least one of R_4 is an isotope of H.

25. The ULQS of claim 24, wherein R_2 is a saturated or unsaturated acyl chain from 3 to 6 carbons in length, 7 to 11 carbons in length, 12 to 18 carbons in length, or 19 to 25 carbons in length.

26. The ULQS of claim 24, wherein R_2 is a saturated acyl chain from 3 to 6 carbons in length, 7 to 11 carbons in length, 12 to 18 carbons in length, or 19 to 25 carbons in length.

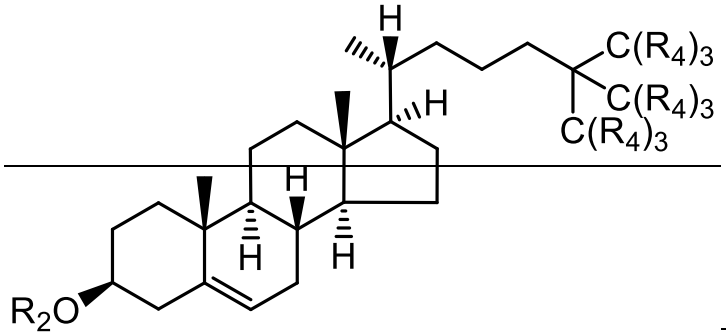
27. The ULQS of claim 20, wherein the lysophospholipid species include three species each of LPC, LPE, LPS, LPG, and LPI and the R_2 groups are repeated for each of the PC, PE, PS, PG, and PI species.

28. The ULQS of claim 24, wherein the lysophospholipid species include the lysophospholipid species of Table 2, wherein the underlined portion corresponds to R_2

Table 2				
LPC (15:0)	LPE (15:0)	LPS (15:0)	LPG (15:0)	LPI (15:0)
LPC (17:0)	LPE (17:0)	LPS (17:0)	LPG (17:0)	LPI (17:0)
LPC (19:0)	LPE (19:0)	LPS (19:0)	LPG (19:0)	LPI (19:0)

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29. The ULQS of claim 1, wherein the cholesterol ester species are represented by the general formula III, or a pharmaceutically acceptable salt thereof:



III

wherein:

R_2 is a C9 to C29 saturated or unsaturated acyl chain; and

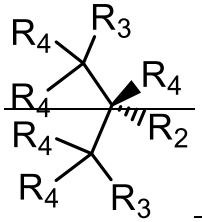
R_4 is independently H or an isotope of H, provided that at least one of R_4 is an isotope of H.

30. The ULQS of claim 29, wherein R_2 is a saturated or unsaturated acyl chain from 2 to 5 carbons in length, from 6 to 10 carbons in length, from 10 to 20 carbons in length, or from 21 to 29 carbons in length.

31. The ULQS of claim 29, wherein R_2 is an unsaturated acyl chain from 2 to 5 carbons in length, from 6 to 10 carbons in length, from 10 to 20 carbons in length, or from 21 to 29 carbons in length.
32. The ULQS of claim 29, wherein the acyl chain length of the cholesterol ester species are each selected such that the sum composition score for the acyl chains is an even number.
33. The ULQS of claim 29, wherein the cholesterol ester species include the cholesterol ester species of Table 3, wherein the underlined portion corresponds to R_2

Table 3				
CE (14:1)	CE (16:1)	CE (18:1)	CE (20:3)	CE (22:4)

34. The ULQS of claim 1, wherein the triacylglycerol class includes one or more triacylglycerol species.
35. The ULQS of claim 34, wherein the acyl chains of the triacylglycerol species are independently selected from a saturated C3 to C30 acyl chain or an unsaturated C3 to C30 acyl chain, containing from 1 to 6 double bonds.
36. The ULQS of claim 35, wherein the acyl chains of the triacylglycerol species are each independently a saturated or unsaturated C3 to C5 acyl chain, a saturated or unsaturated C6 to C10 acyl chain, a saturated or unsaturated C11 to C20 acyl chain, and a saturated or unsaturated C21 to C30 acyl chain.
37. The ULQS of claim 34, wherein the acyl chain length of the triacylglycerol species are each selected such that the sum composition score for the acyl chains is an odd number.
38. The ULQS of claim 34, wherein the triacylglycerol species contains 3 acyl chains and the length of one acyl chain is different from the length of the other two acyl chains and one acyl chain is unsaturated or each of the acyl chains are unsaturated.
39. The ULQS of claim 34, wherein the triacylglycerol species are represented by the general formula IV, or a pharmaceutically acceptable salt thereof:



IV

wherein:

R_2 is a C3 to C30 saturated or unsaturated acyl chain;

R_3 are each independently a C3 to C25 saturated or unsaturated acyl chain; and R_4 is independently H or an isotope of H, provided that at least one of R_4 is an isotope of H.

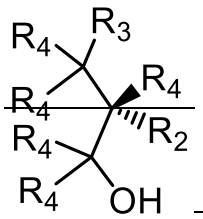
40. The ULQS of claim 39, wherein R_2 is a saturated or unsaturated acyl chain from 3 to 5 carbons in length, from 6 to 10 carbons in length, from 10 to 20 carbons in length, or from 21 to 30 carbons in length.
41. The ULQS of claim 39, wherein R_3 is a saturated or unsaturated acyl chain from 3 to 5 carbons in length, from 6 to 10 carbons in length, from 10 to 20 carbons in length, or from 21 to 25 carbons in length.
42. The ULQS of claim 39, wherein R_3 is independently an acyl chain of n atoms in length, n is 12, 14, 16, 18, 20, or 22, R_2 is independently an acyl chain from n-3 to n+5 carbon atoms, wherein R_3 is saturated when n is 12, 14, or 16 and contains 1 to 2 double bonds when n is 18, 20, or 22, R_2 contains 1 or 2 double bonds when R_2 is from n-3 to n+1 carbon atoms and R_2 contains 2 or 3 double bonds when R_2 is from n+2 to n+5 carbon atoms.
43. The ULQS of claim 39, wherein the triacylglycerol species include the triacylglycerol species of Table 4, wherein the underlined portion corresponds to R_2 and the double underlined portion correspond to R_3

Table 4		
TAG (14:0/13:0/14:0)	TAG (16:0/15:1/16:0)	TAG (18:1/17:1/18:1)
TAG (14:0/15:1/14:0)	TAG (16:0/17:1/16:0)	TAG (18:1/19:2/18:1)
TAG (14:0/17:1/14:0)	TAG (16:0/19:2/16:0)	TAG (18:1/21:2/18:1)

.

44. The ULQS of claim 1, wherein the diacylglycerol class includes one or more diacylglycerol species.
45. The ULQS of claim 44, wherein the acyl chains of the diacylglycerol species are independently selected from a saturated C3 to C30 acyl chain or an unsaturated C3 to C30 acyl chain, containing from 1 to 6 double bonds.
46. The ULQS of claim 45, wherein the acyl chains of the diacylglycerol species are each independently a saturated or unsaturated C3 to C6 acyl chain, a saturated or unsaturated C7 to C11 acyl chain, a saturated or unsaturated C12 to C21 acyl chain, a saturated or unsaturated C22 to C30 acyl chain.

47. The ULQS of claim 44, wherein the acyl chain length of the diacylglycerol species are each selected such that the sum composition score for the acyl chains is an odd number.
48. The ULQS of claim 44, wherein the diacylglycerol species contains 2 acyl chains, the length of one acyl chain is different from the length of the other acyl chain, and one acyl chain is unsaturated.
49. The ULQS of claim 44, wherein the diacylglycerol species are represented by the general formula V, or a pharmaceutically acceptable salt thereof:



V

wherein:

R_2 is a C3 to C30 saturated or unsaturated acyl chain;

R_3 is a C3 to C25 saturated or unsaturated acyl chain; and

R_4 is independently H or an isotope of H, provided that at least one of R_4 is an isotope of H.

50. The ULQS of claim 49, wherein R_2 is a saturated or unsaturated acyl chain from 3 to 6 carbons in length, from 7 to 11 carbons in length, from 12 to 21 carbons in length, or from 22 to 30 carbons in length.
51. The ULQS of claim 49, wherein R_3 is a saturated or unsaturated acyl chain from 3 to 5 carbons in length, from 6 to 10 carbons in length, from 10 to 20 carbons in length, or from 21 to 25 carbons in length.
52. The ULQS of claim 49, wherein R_3 is independently an acyl chain of n carbon atoms in length, n is 14 to 20, R_2 is independently an acyl chain from n-5 to n+7 carbon atoms, wherein R_3 optionally contains 1 or 2 double bonds, R_2 contains 1 or 2 double bonds when R_2 is from n-5 to n-1 carbon atoms, and R_2 contains 2 to 4 double bonds when R_2 is from n+2 to n+7 carbon atoms.
53. The ULQS of claim 49, wherein the diacylglycerol species include the diacylglycerol species of Table 5, wherein the underlined portion corresponds to R_2 and the double underlined portion correspond to R_3

Table 5		
DAG (17:0/14:1)	DAG (17:0/18:1)	DAG (17:0/22:4)
DAG (17:0/16:1)	DAG (17:0/20:3)	

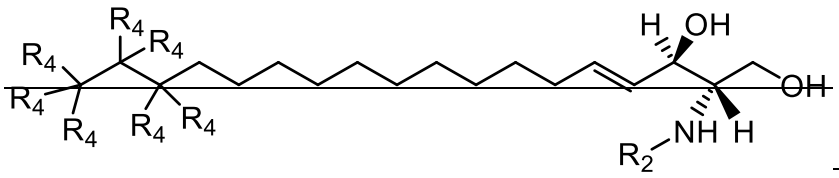
54. The ULQS of claim 1, wherein the ceramide class includes one or more ceramide species.

55. The ULQS of claim 54, wherein the acyl chain of the ceramide species is a saturated C10 to C30 acyl chain or an unsaturated C10 to C30 acyl chain containing from 1 to 4 double bonds.

56. The ULQS of claim 55, wherein the acyl chain of the ceramide species is a saturated or unsaturated C10 to C15 acyl chain, a saturated or unsaturated C16 to C20 acyl chain, a saturated or unsaturated C21 to C25 acyl chain, or a saturated or unsaturated C26 to C30 acyl chain.

57. The ULQS of claim 54, wherein the acyl chain length of the ceramide species are each selected such that the sum composition score for the acyl chains is an even number.

58. The ULQS of claim 54, wherein the ceramide species are represented by the general formula VI, or a pharmaceutically acceptable salt thereof:



VI

wherein:

R_2 is a C10 to C30 saturated or unsaturated acyl chain; and

R_4 is independently H or an isotope of H, provided that at least one of R_4 is an isotope of H.

59. The ULQS of claim 58, wherein R_2 is a saturated or unsaturated C10 to C15 acyl chain, a saturated or unsaturated C16 to C20 acyl chain, a saturated or unsaturated C21 to C25 acyl chain, a saturated or unsaturated C26 to C30 acyl chain.

60. The ULQS of claim 59, wherein R_2 is unsaturated.

61. The ULQS of claim 58, wherein R_2 is an acyl chain of 12, 14, 16, 18, 20, 22, 24, 26, or 28 carbons in length, wherein R_2 contains 1 double bond.

62. The ULQS of claim 58 , wherein the ceramide species include the ceramide species of Table 6, wherein the underlined portion corresponds to R_2

Table 6		
CER (18:1/16:1)	CER (18:1/20:1)	CER (18:1/24:1)
CER (18:1/18:1)	CER (18:1/22:1)	

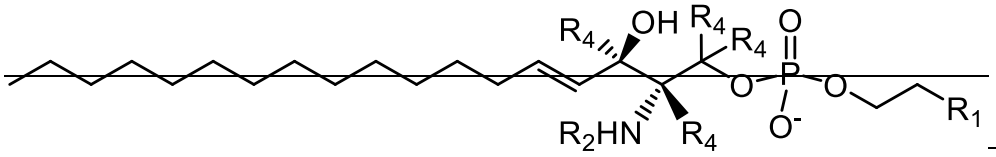
63. The ULQS of claim 1, wherein the sphingomyelin class includes one or more sphingomyelin species.

64. The ULQS of claim 63, wherein the acyl chain of the sphingomyelin species is a saturated C10 to C30 acyl chain or an unsaturated C10 to C30 acyl chain containing from 1 to 4 double bonds.

65. The ULQS of claim 64, wherein the acyl chain of the sphingomyelin species is independently a saturated or unsaturated C10 to C15 acyl chain, a saturated or unsaturated C16 to C20 acyl chain, a saturated or unsaturated C21 to C25 acyl chain, a saturated or unsaturated C26 to C30 acyl chain.

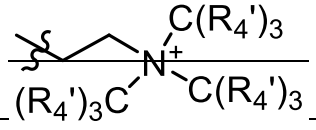
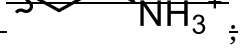
66. The ULQS of claim 63 wherein the acyl chain length of the sphingomyelin species are each selected such that the sum composition score for the acyl chains is an even number.

67. The ULQS of claim 63, wherein the sphingomyelin species are represented by the general formula VII, or a pharmaceutically acceptable salt thereof:



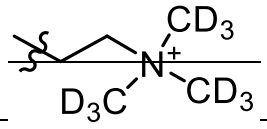
VII

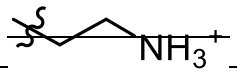
wherein:

R_1 is  or ;

R_2 is a C10 to C30 saturated or unsaturated acyl chain; and

R_4 and R_4' are each independently H or an isotope of H, provided that at least one of R_4 or R_4' is an isotope of H.

68. The ULQS of claim 67, wherein R_1 is  and R_4 is H.

69. The ULQS of claim 67, wherein R_1 is  and at least one of R_4 is an isotope of H.

70. The ULQS of claim 67, wherein R_2 is a saturated or unsaturated acyl chain from 10 to 15 carbons in length, from 16 to 20 carbons in length, from 21 to 25 carbons in length, or from 26 to 30 carbons in length.

71. The ULQS of claim 70, wherein R_2 is unsaturated.

72. The ULQS of claim 67, wherein R_2 is an acyl chain of 12, 14, 16, 18, 20, 22, 24, 26, or 28 carbons in length, wherein R_2 contains 1 double bond.

73. The ULQS of claim 67, wherein the sphingomyelin species include the sphingomyelin species of Table 7, wherein the underlined portion corresponds to R_2

Table 7		
SM (18:1/16:1)	SM (18:1/20:1)	SM (18:1/24:1)
SM (18:1/18:1)	SM (18:1/22:1)	

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74. The ULQS of claim 1 comprising at least one lipid species from the phospholipid class, the lysophospholipid class, the cholesterol ester class, the triacylglycerol class, the diacylglycerol class, the ceramide class, and the sphingomyelin class.

75. The ULQS of claim 1 comprising 5 to 40 phospholipid species, 5 to 25 lysophospholipid species, 3 to 15 cholesterol ester species, 5 to 20 triacylglycerol species, 3 to 15 diacylglycerol species, 3 to 15 ceramide species, and 3 to 15 sphingomyelin species.

76. The ULQS of claim 75, wherein the phospholipid species are selected from Table 1, the lysophospholipid species are selected from Table 2, the cholesterol ester species are selected from Table 3, the triacylglycerol species are selected from Table 4, the diacylglycerol species are selected from Table 5, the ceramide species are selected from Table 6, and the sphingomyelin species are selected from Table 7.

77. The ULQS of claim 75, wherein the phospholipid species, the lysophospholipid species, the cholesterol ester species, the triacylglycerol species, the diacylglycerol species, the ceramide species, and the sphingomyelin species are selected from Table 8.

78. The ULQS of claim 1 comprising 25 phospholipid species, 15 lysophospholipid species, 5 cholesterol ester, 9 triacylglycerol species, 5 diacylglycerol species, 5 ceramide species, and 5 sphingomyelin species.

79. The ULQS of claim 78, wherein the phospholipid species are selected from Table 1, the lysophospholipid species are selected from Table 2, the cholesterol ester species are selected from Table 3, the triacylglycerol species are selected from Table 4, the diacylglycerol species are selected from Table 5, the ceramide species are selected from Table 6, and the sphingomyelin species are selected from Table 7.

~~80. The ULQS of claim 78, wherein the phospholipid species, the lysophospholipid species, the cholesterol ester species, the triacylglycerol species, the diacylglycerol species, the ceramide species, and the sphingomyelin species are selected from Table 8.~~

~~81. The ULQS of claim 80, wherein the sum composition score for the phospholipid class is 27:1 to 43:4, the sum composition score for the lysophospholipid class is 11:0 to 23:0, the sum composition score for the cholesterol ester class is 11:1 to 25:4, the sum composition score for the triacylglycerol class is 43:1 to 55:2, the sum composition score for the diacylglycerol class is 27:1 to 43:4, the sum composition score for the ceramide class is 12:1 to 28:1, and the sum composition score for the sphingomyelin class is 12:1 to 28:1.~~

~~82. The ULQS of claim 80, wherein the sum composition score for the phospholipid class is 31:1 to 39:4, the sum composition score for the lysophospholipid class is 15:0 to 19:0, the sum composition score for the cholesterol ester class is 14:1 to 22:4, the sum composition score for the triacylglycerol class is 47:1 to 51:2, the sum composition score for the diacylglycerol class is 31:1 to 39:4, the sum composition score for the ceramide class is 16:1 to 24:1, and the sum composition score for the sphingomyelin class is 16:1 to 24:1.~~

5