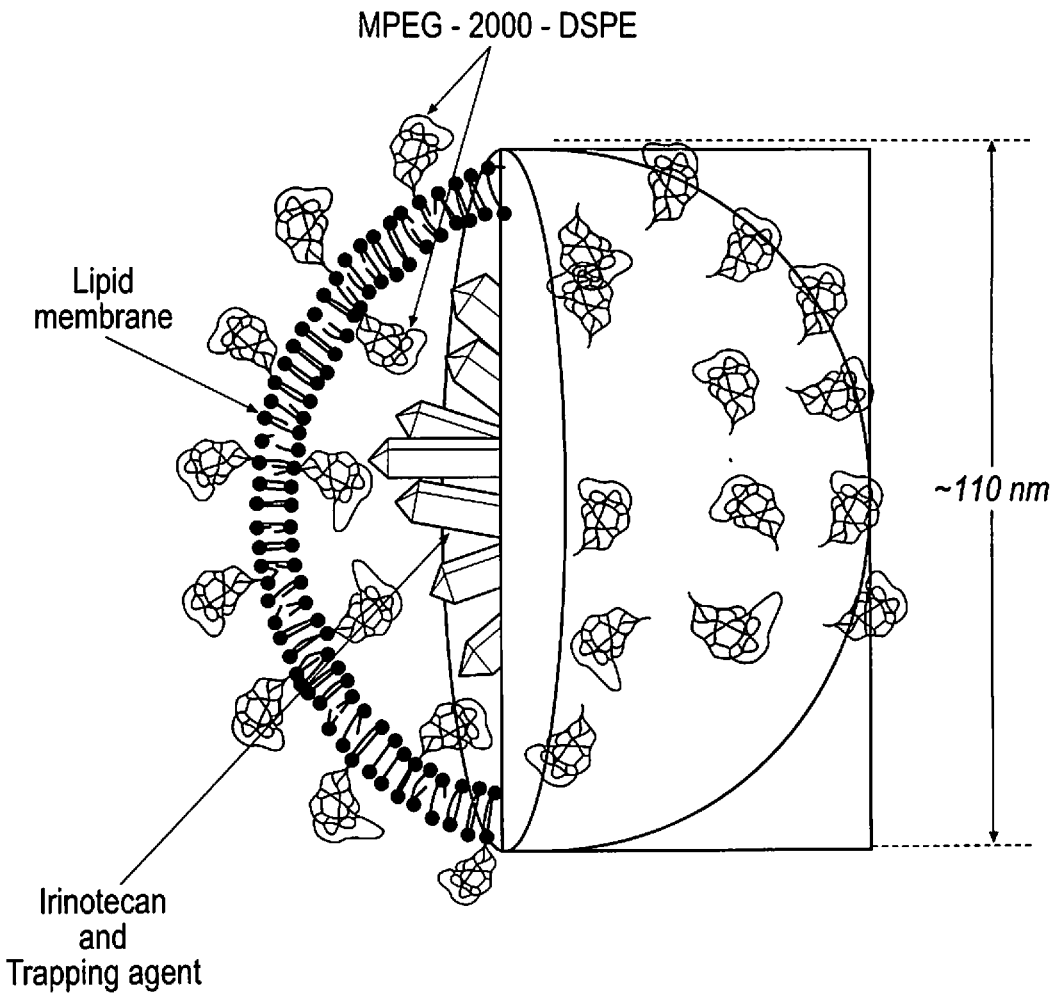

MPEG - 2000 - DSPE
Lipid membrane
~110 nm
Irinotecan and Trapping agent

FIG. 1A

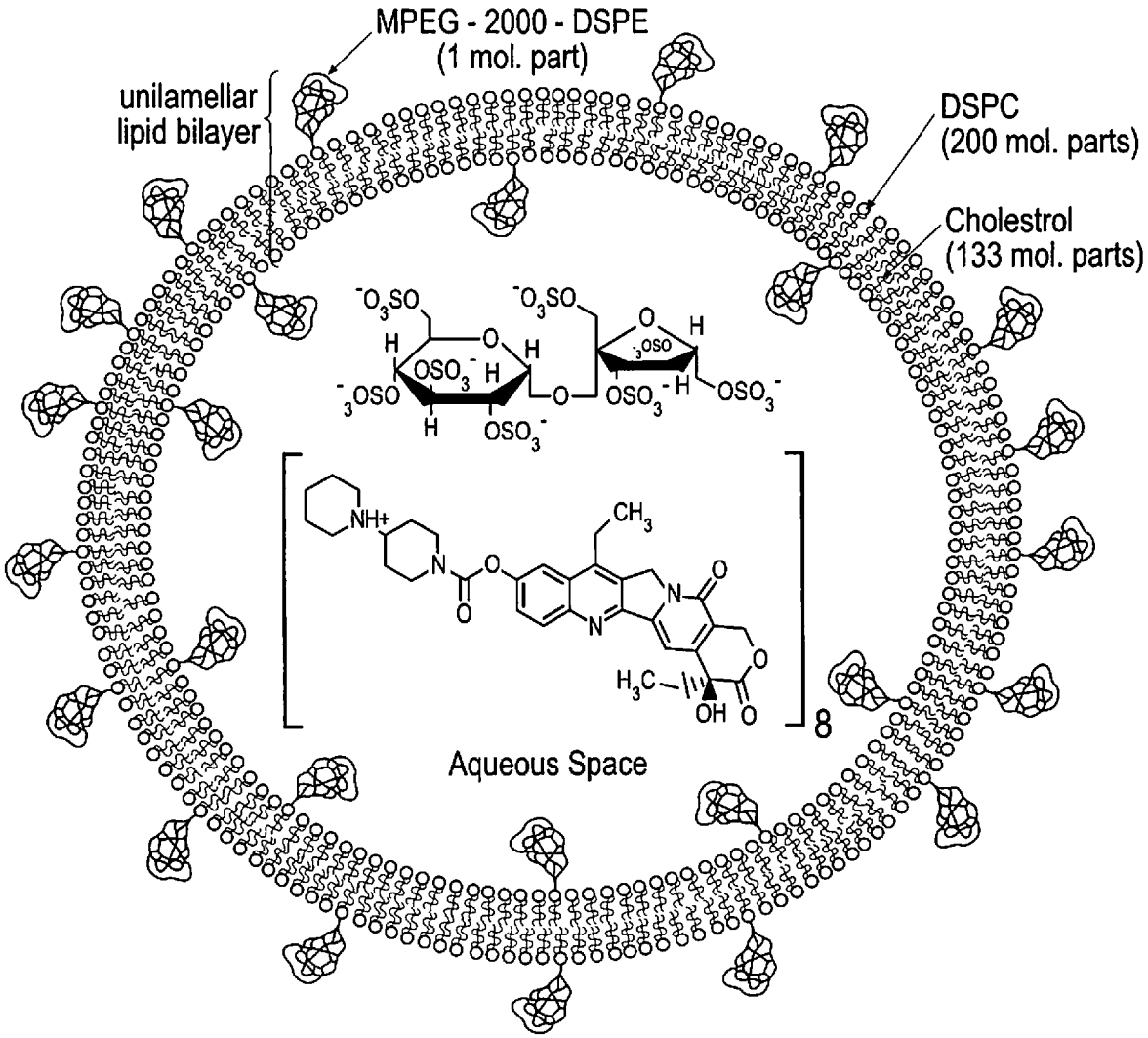

MPEG - 2000 - DSPE
(1 mol. part)
unilamellar
lipid bilayer
DSPC
(200 mol. parts)
Cholestrol
(133 mol. parts)
Aqueous Space
8

FIG. 1B

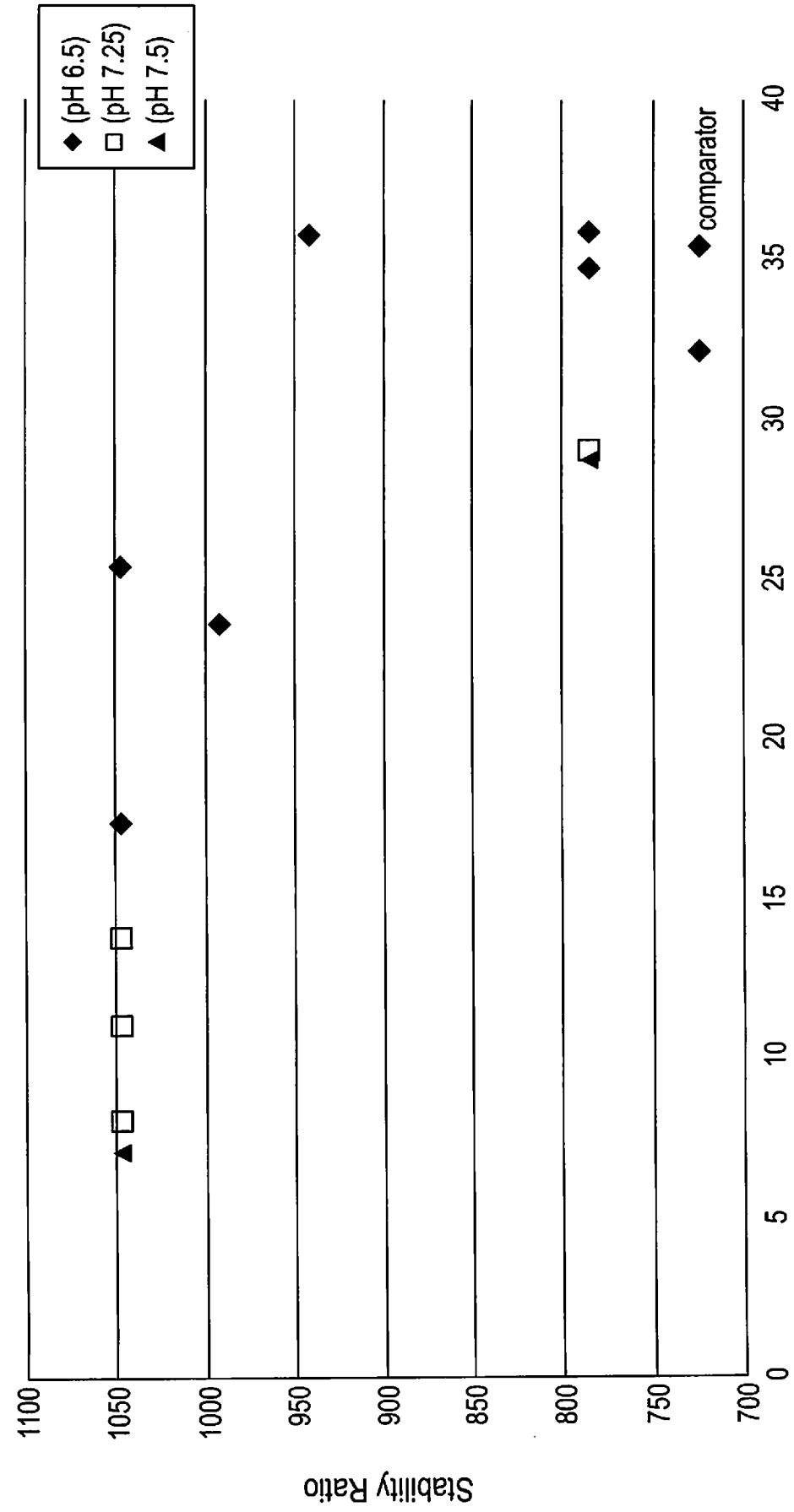

(pH 6.5)
(pH 7.25)
(pH 7.5)
comparator
Stability Ratio
1100
1050
1000
950
900
850
800
750
700
0
5
10
15
20
25
30
35
40
mol% liposomal Lyso-PC (9 mos, 4 °C)

FIG. 2A

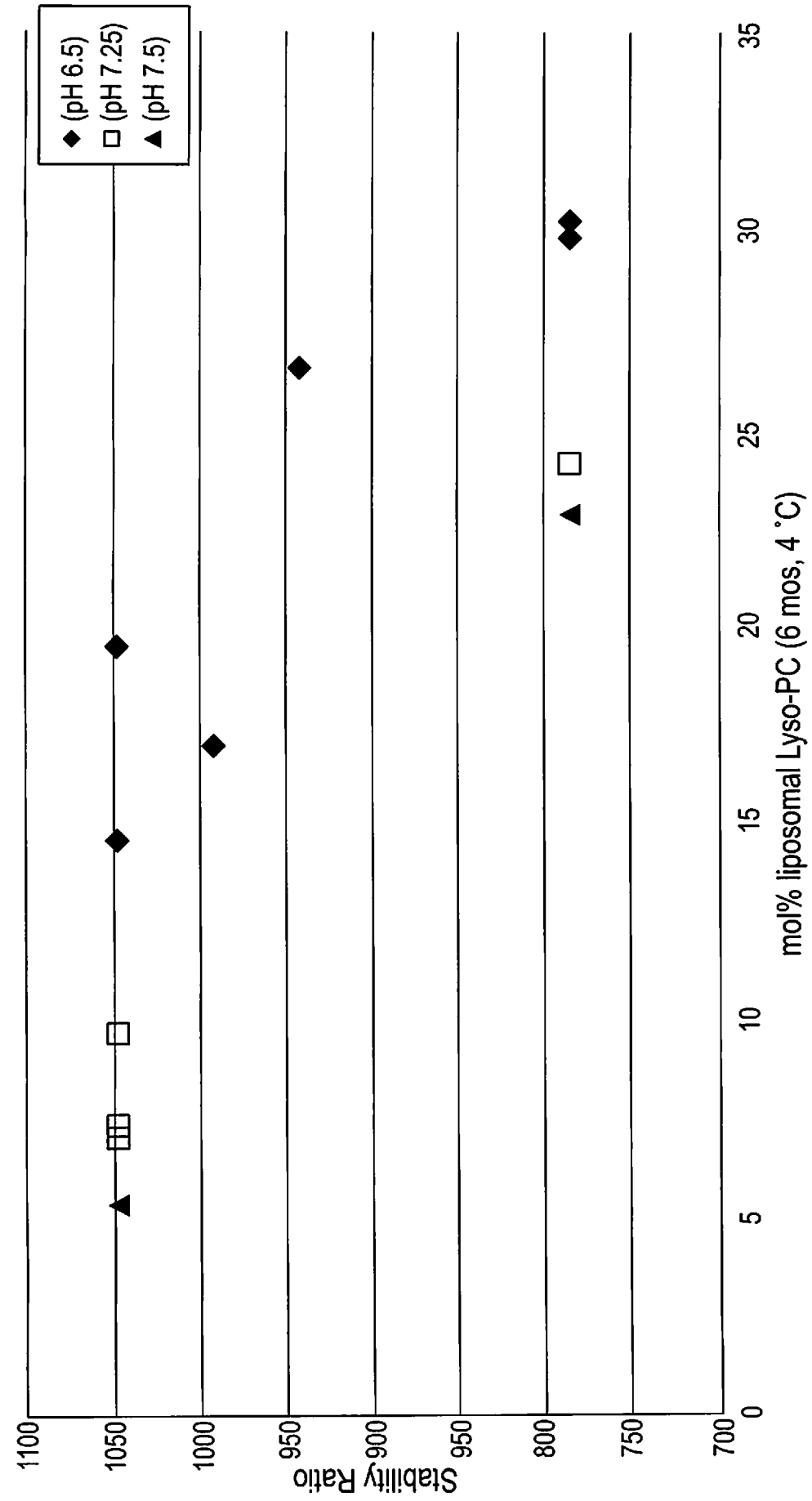

(pH 6.5)
(pH 7.25)
(pH 7.5)
Stability Ratio
1100
1050
1000
950
900
950
800
750
700
0
5
10
15
20
25
30
35
mol% liposomal Lyso-PC (6 mos, 4 °C)

FIG. 2B

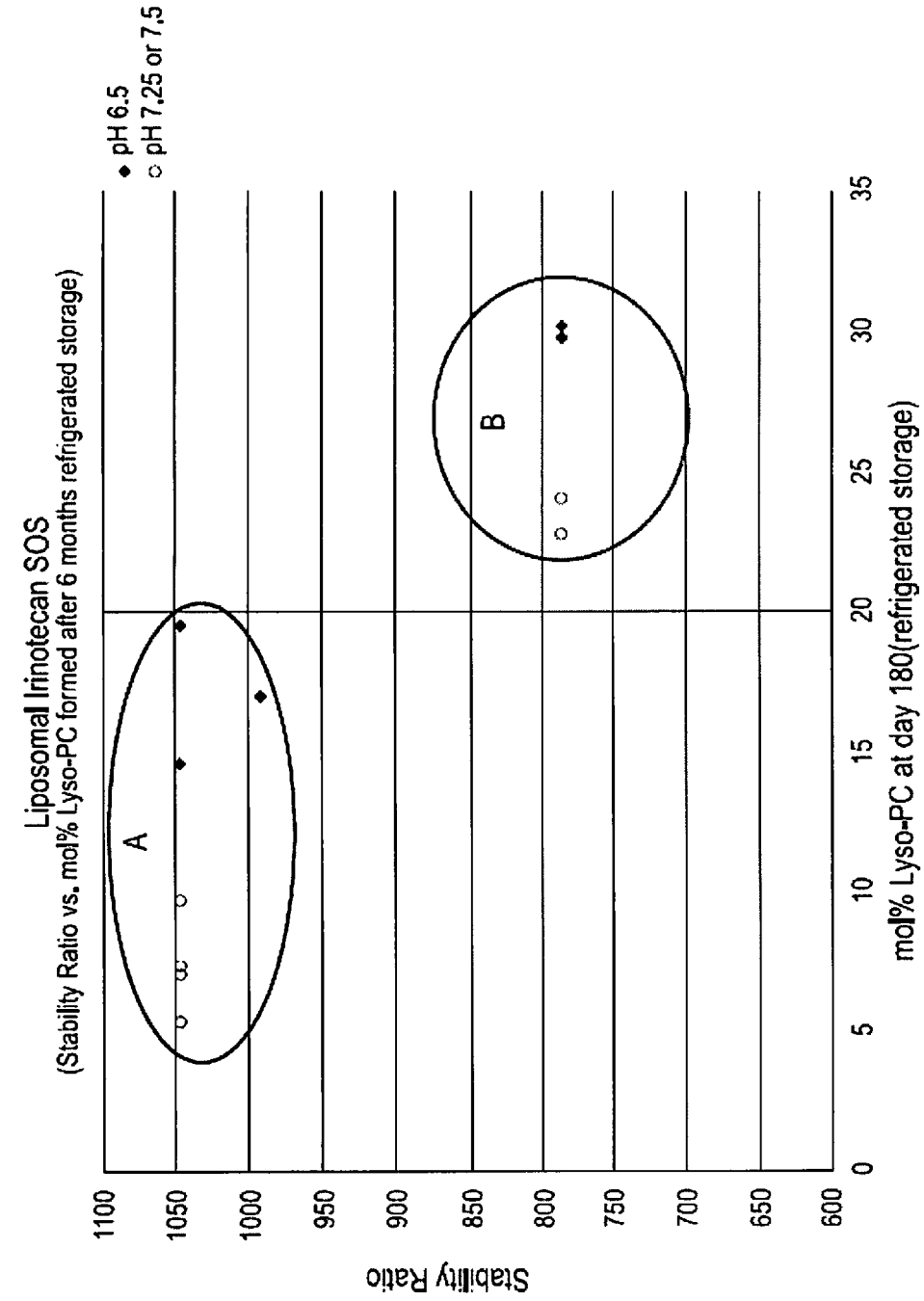

Liposomal Irinotecan SOS
(Stability Ratio vs. mol% Lyso-PC formed after 6 months refrigerated storage)
◆ pH 6.5
○ pH 7.25 or 7.5
A
B
Stability Ratio
1100
1050
1000
950
900
850
800
750
700
650
600
0
5
10
15
20
25
30
35
mol% Lyso-PC at day 180(refrigerated storage)

FIG. 2C

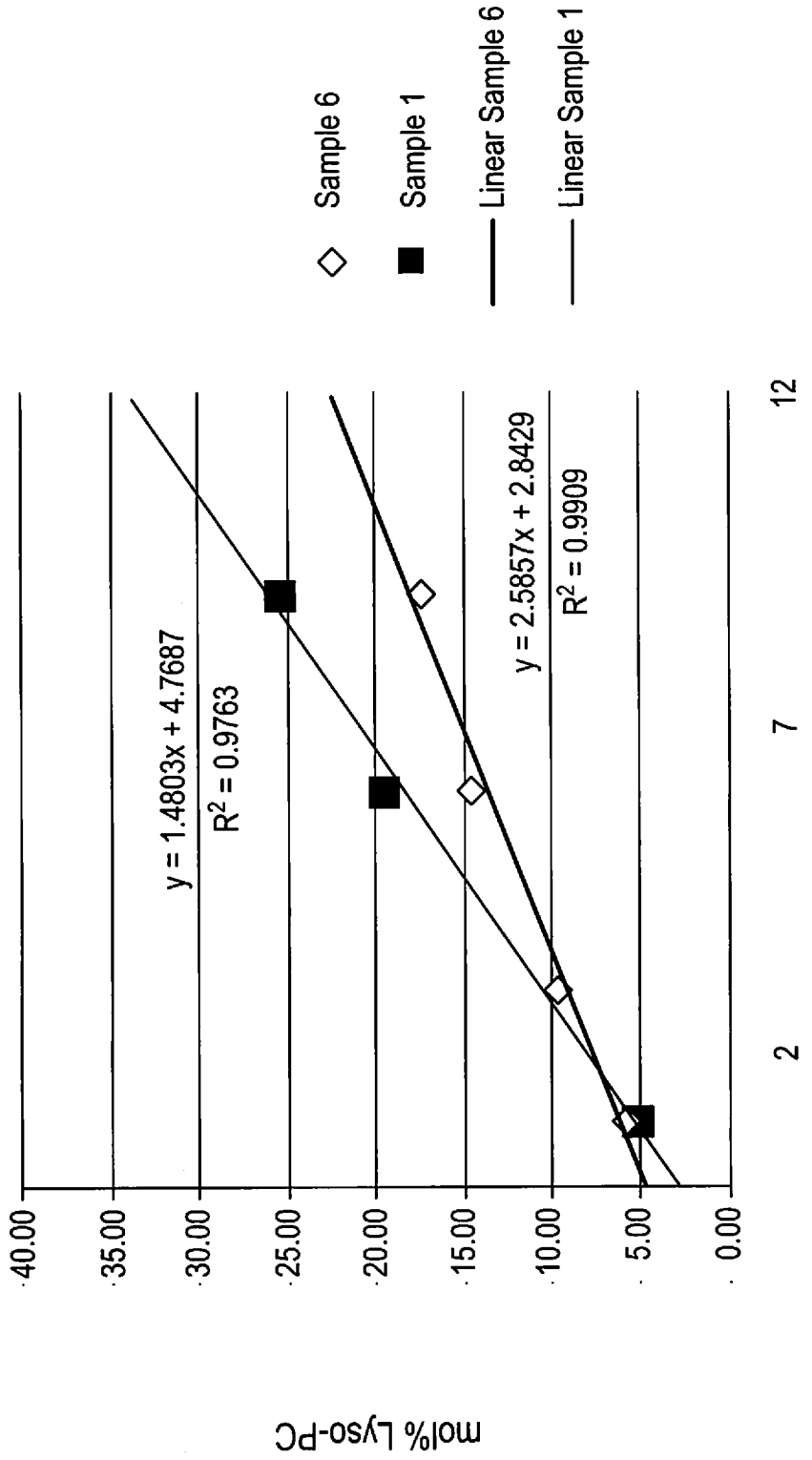

Sample 6
Sample 1
Linear Sample 6
Linear Sample 1
y = 1.4803x + 4.7687
R2 = 0.9763
y = 2.5857x + 2.8429
R2 = 0.9909
mol% Lyso-PC
40.00
35.00
30.00
25.00
20.00
15.00
10.00
5.00
0.00
2
7
12
months storage (4 °C)

FIG. 3A

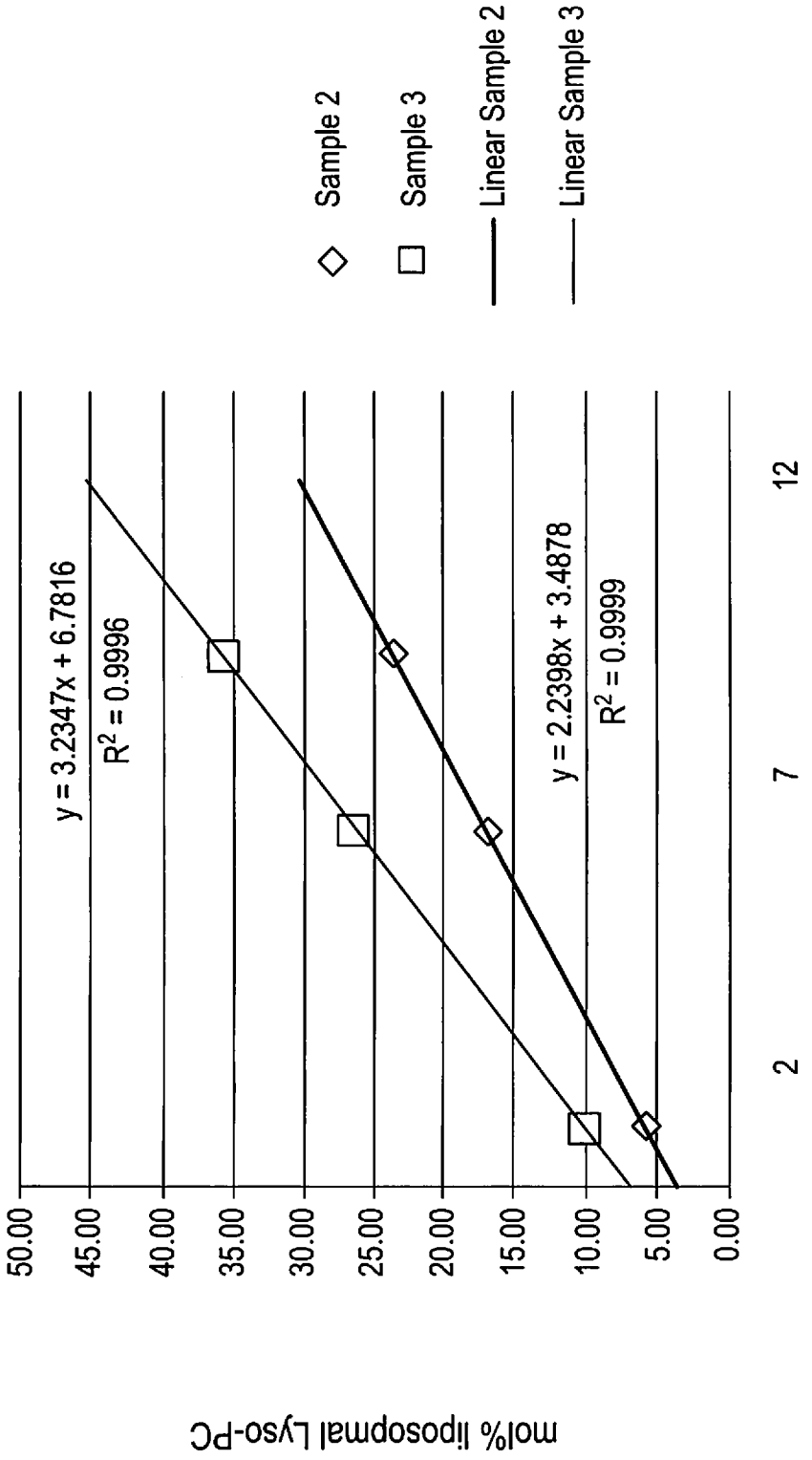

Sample 2
Sample 3
Linear Sample 2
Linear Sample 3
y = 3.2347x + 6.7816
R2 = 0.9996
y = 2.2398x + 3.4878
R2 = 0.9999
mol% liposomal Lyso-PC
50.00
45.00
40.00
35.00
30.00
25.00
20.00
15.00
10.00
5.00
0.00
2
7
12
months storage (4 °C)

FIG. 3B

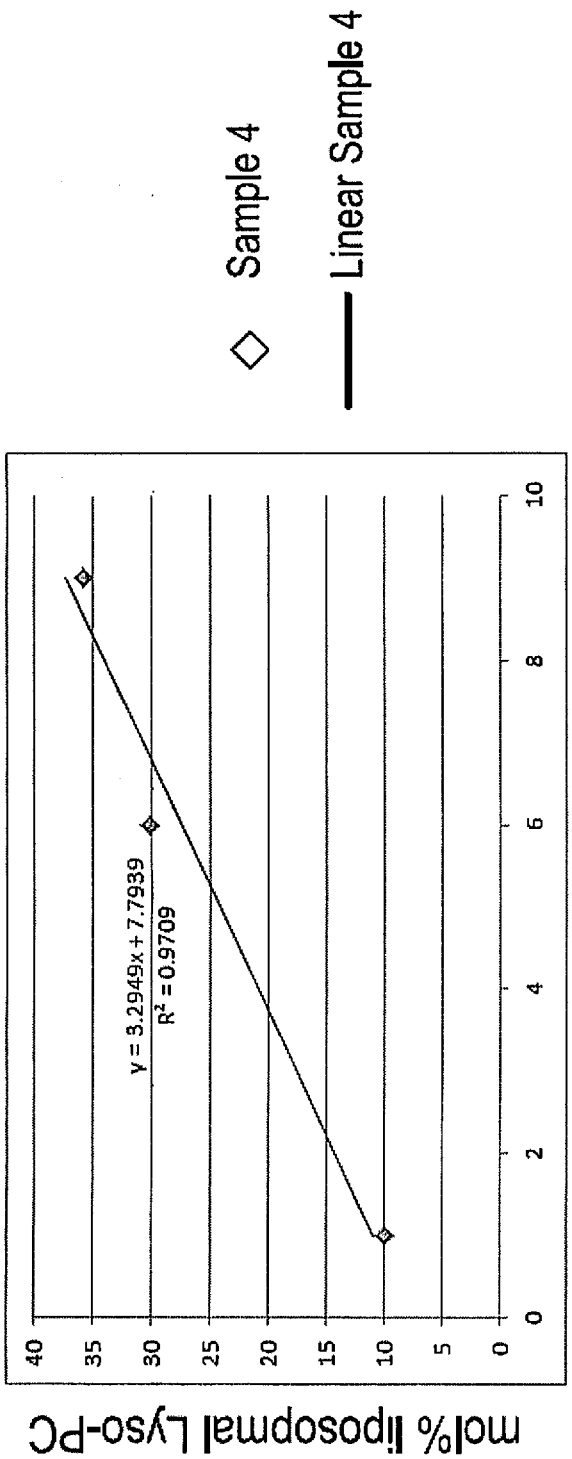

Sample 4
Linear Sample 4
mol% liposomal Lyso-PC
40
35
30
25
20
15
10
5
0
0
2
4
6
8
10
months storage (4 °C)
y = 3.2949x + 7.7939
R² = 0.9709

FIG. 3C

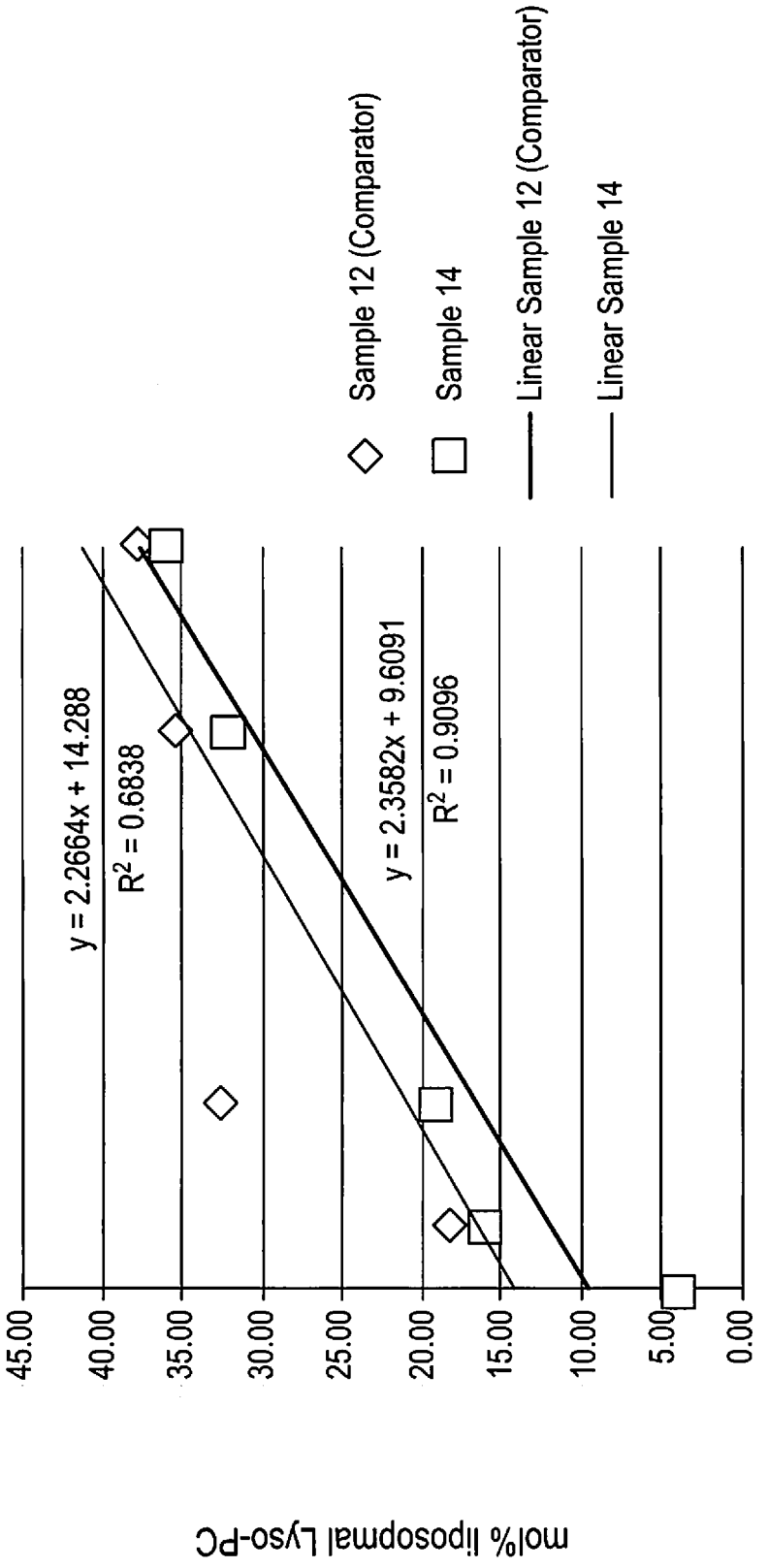

mol% liposomal Lyso-PC
45.00
40.00
35.00
30.00
25.00
20.00
15.00
10.00
5.00
0.00
2
7
12
months storage (4 °C)
y = 2.2664x + 14.288
R² = 0.6838
y = 2.3582x + 9.6091
R² = 0.9096
Sample 12 (Comparator)
Sample 14
Linear Sample 12 (Comparator)
Linear Sample 14

FIG. 3D

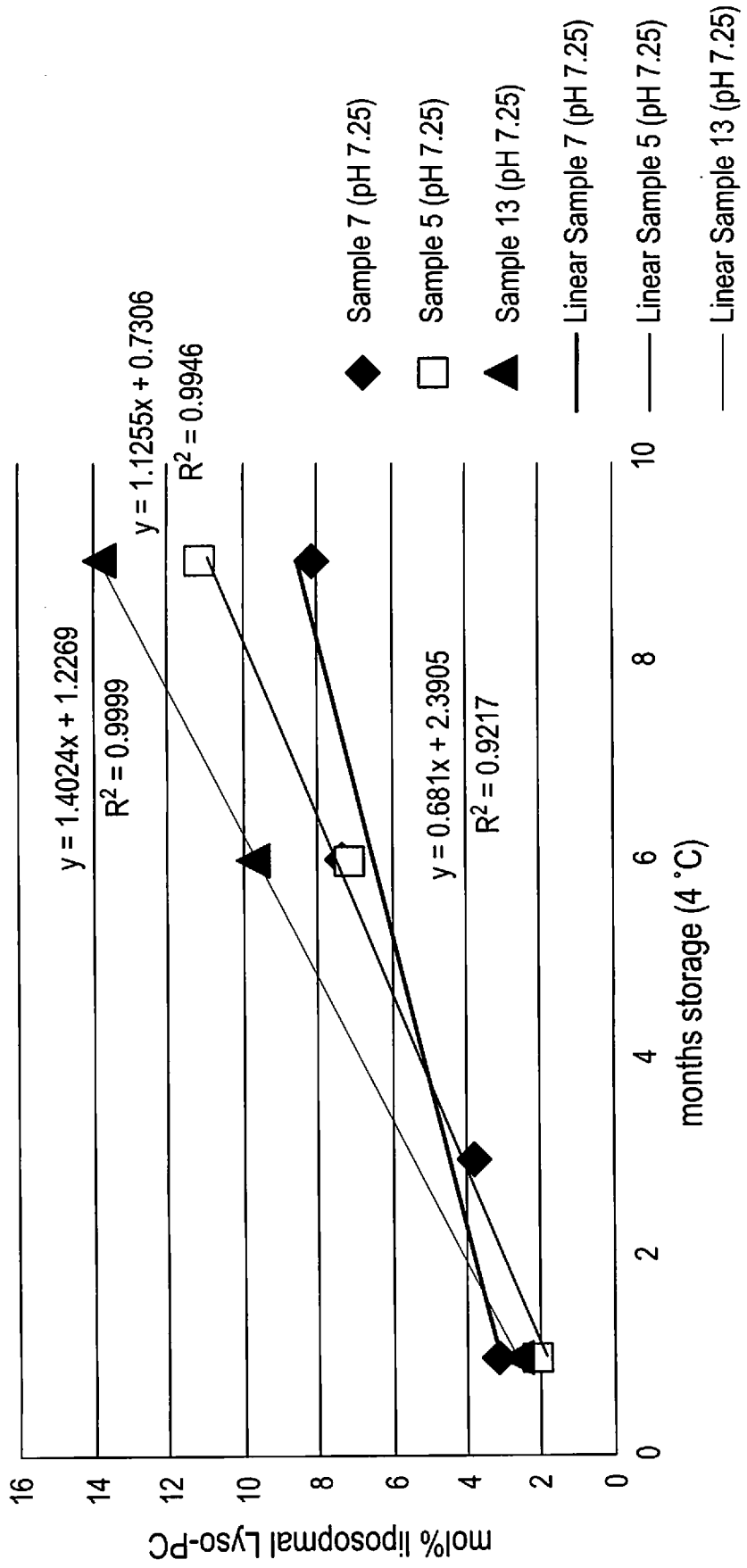

mol% liposomal Lyso-PC
months storage (4 °C)
y = 1.4024x + 1.2269
R² = 0.9999
y = 1.1255x + 0.7306
R² = 0.9946
y = 0.681x + 2.3905
R² = 0.9217
Sample 7 (pH 7.25)
Sample 5 (pH 7.25)
Sample 13 (pH 7.25)
Linear Sample 7 (pH 7.25)
Linear Sample 5 (pH 7.25)
Linear Sample 13 (pH 7.25)

FIG. 4A

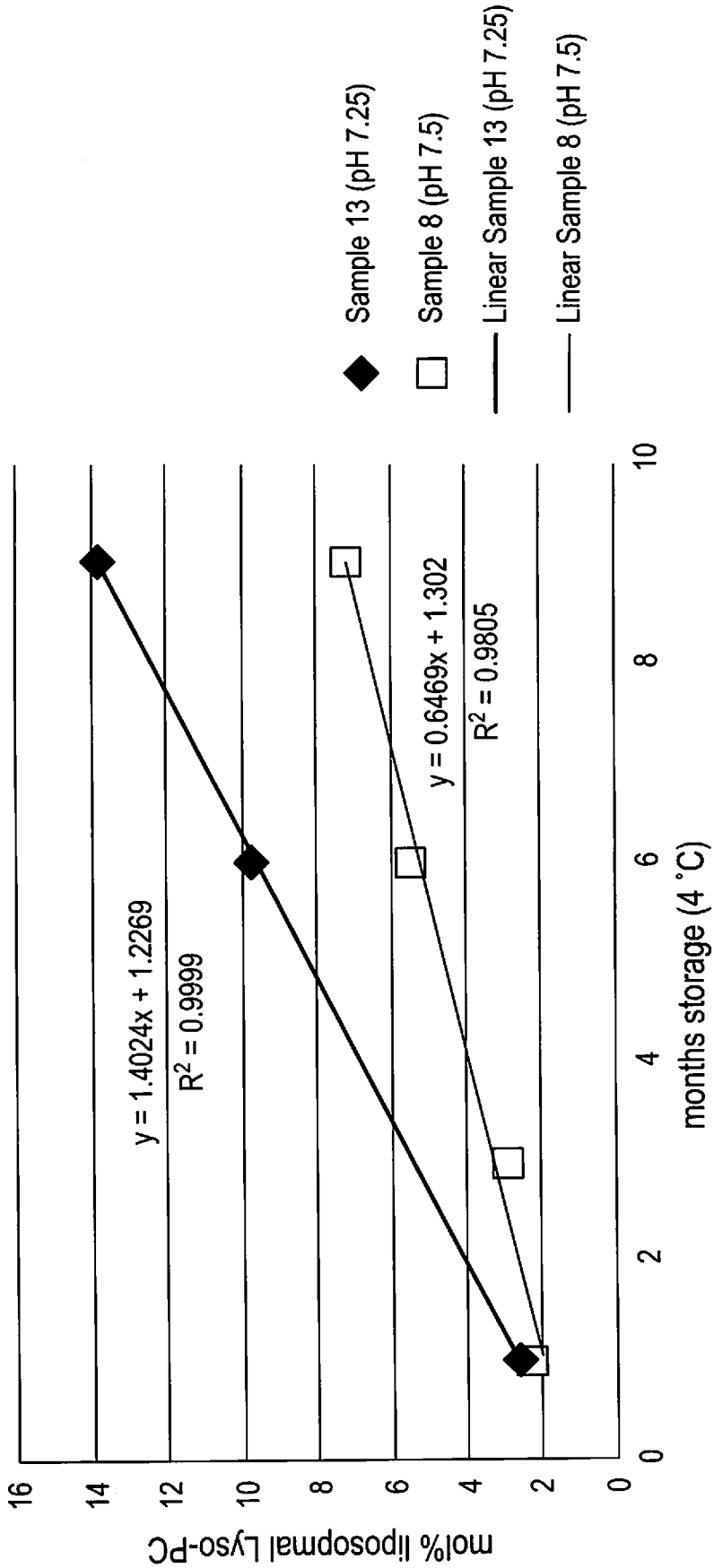

Sample 13 (pH 7.25)
Sample 8 (pH 7.5)
Linear Sample 13 (pH 7.25)
Linear Sample 8 (pH 7.5)
y = 1.4024x + 1.2269
R2 = 0.9999
y = 0.6469x + 1.302
R2 = 0.9805
mol% liposomal Lyso-PC
months storage (4 °C)
0
2
4
6
8
10
12
14
16
0
2
4
6
8
10

FIG. 4B

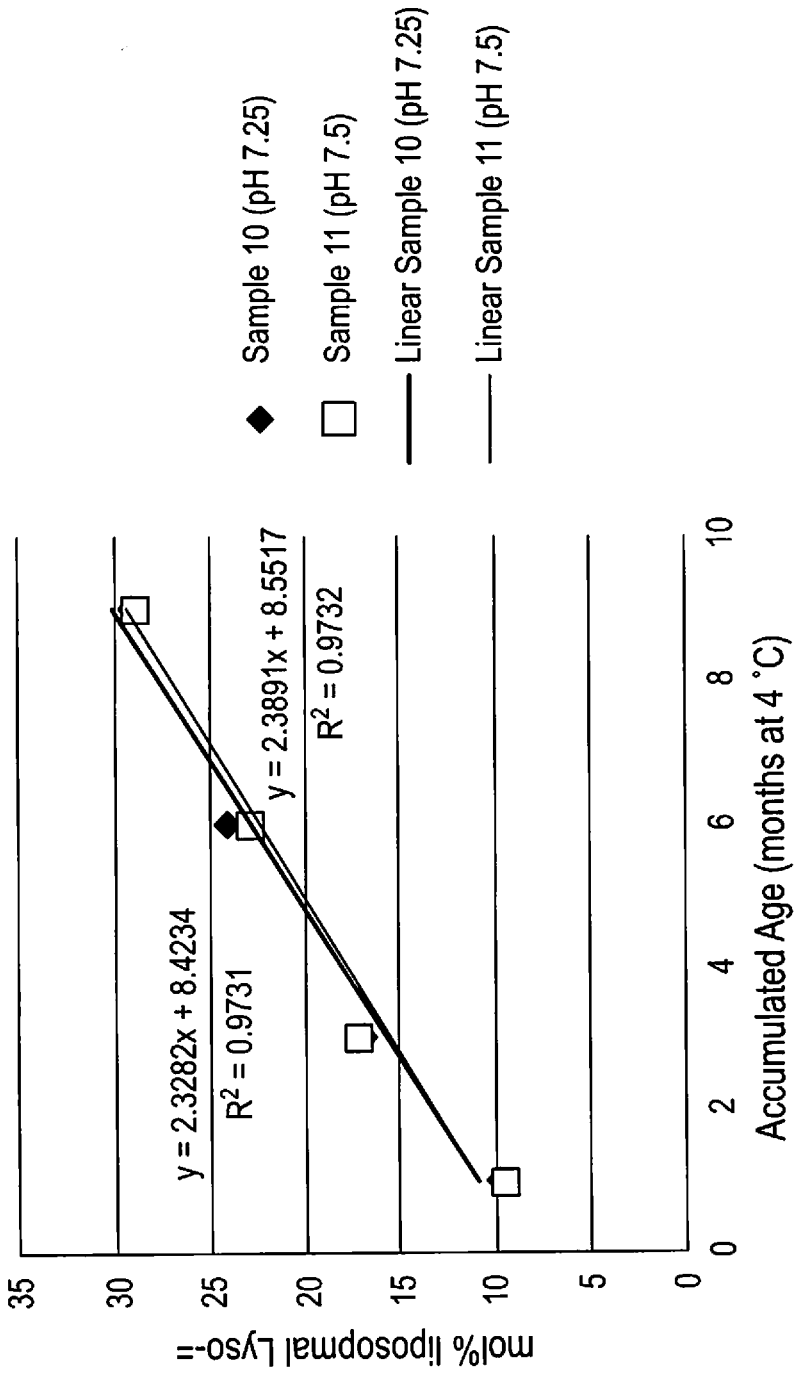

Sample 10 (pH 7.25)
Sample 11 (pH 7.5)
Linear Sample 10 (pH 7.25)
Linear Sample 11 (pH 7.5)
y = 2.3282x + 8.4234
R2 = 0.9731
y = 2.3891x + 8.5517
R2 = 0.9732
mol% liposomal Lyso-=
Accumulated Age (months at 4 °C)
0
5
10
15
20
25
30
35
0
2
4
6
8
10

FIG. 4C

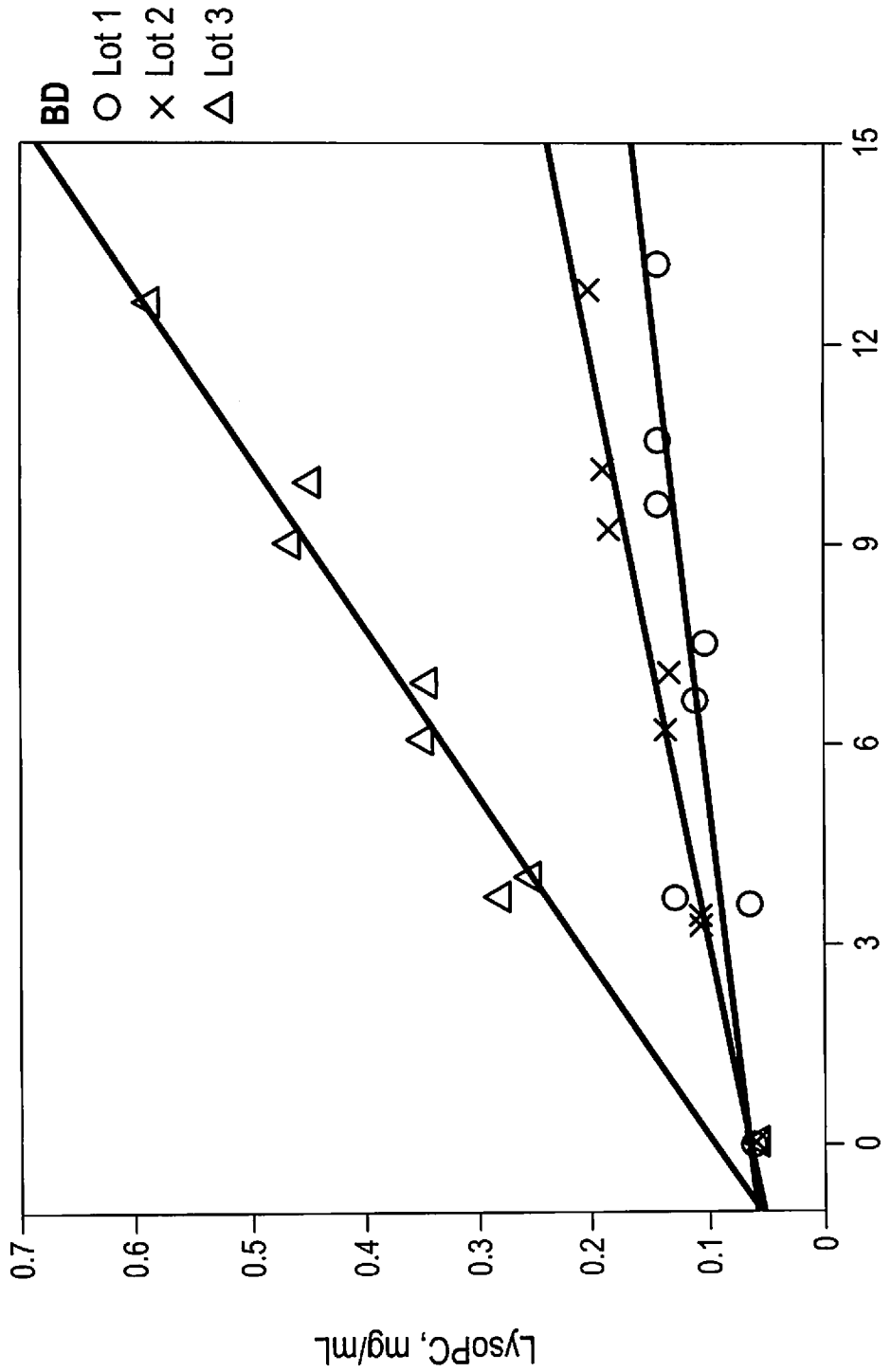

BD
O Lot 1
X Lot 2
Δ Lot 3
LysoPC, mg/mL
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
3
6
9
12
15
Accumulated Age (months at 4 °C)

FIG. 5

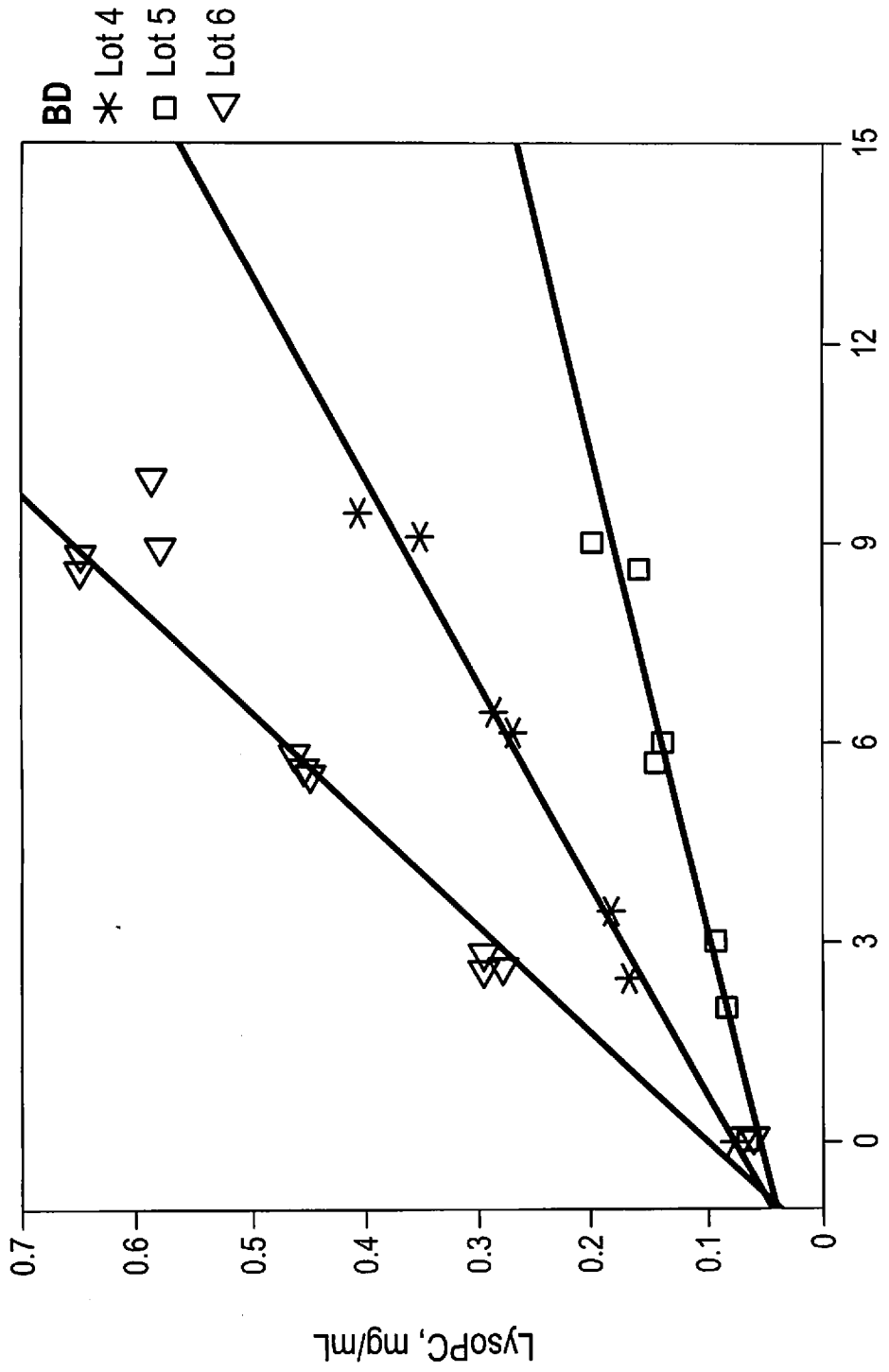

BD
Lot 4
Lot 5
Lot 6
LysoPC, mg/mL
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0
3
6
9
12
15
Accumulated Age (months at 4 °C)

FIG. 6

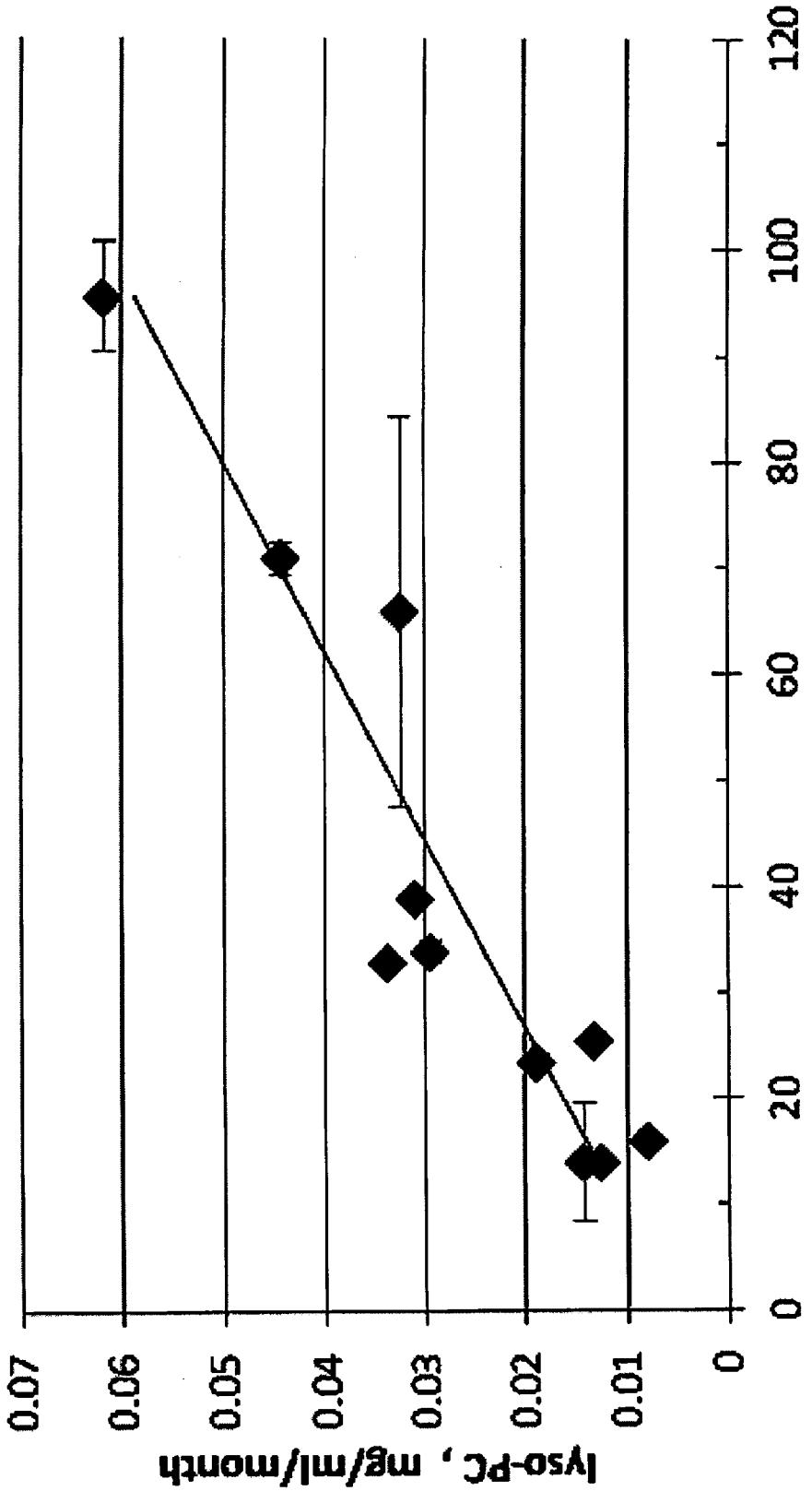

0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
lyso-PC , mg/ml/month
0
20
40
60
80
100
120
TEA, ppm

FIG. 7

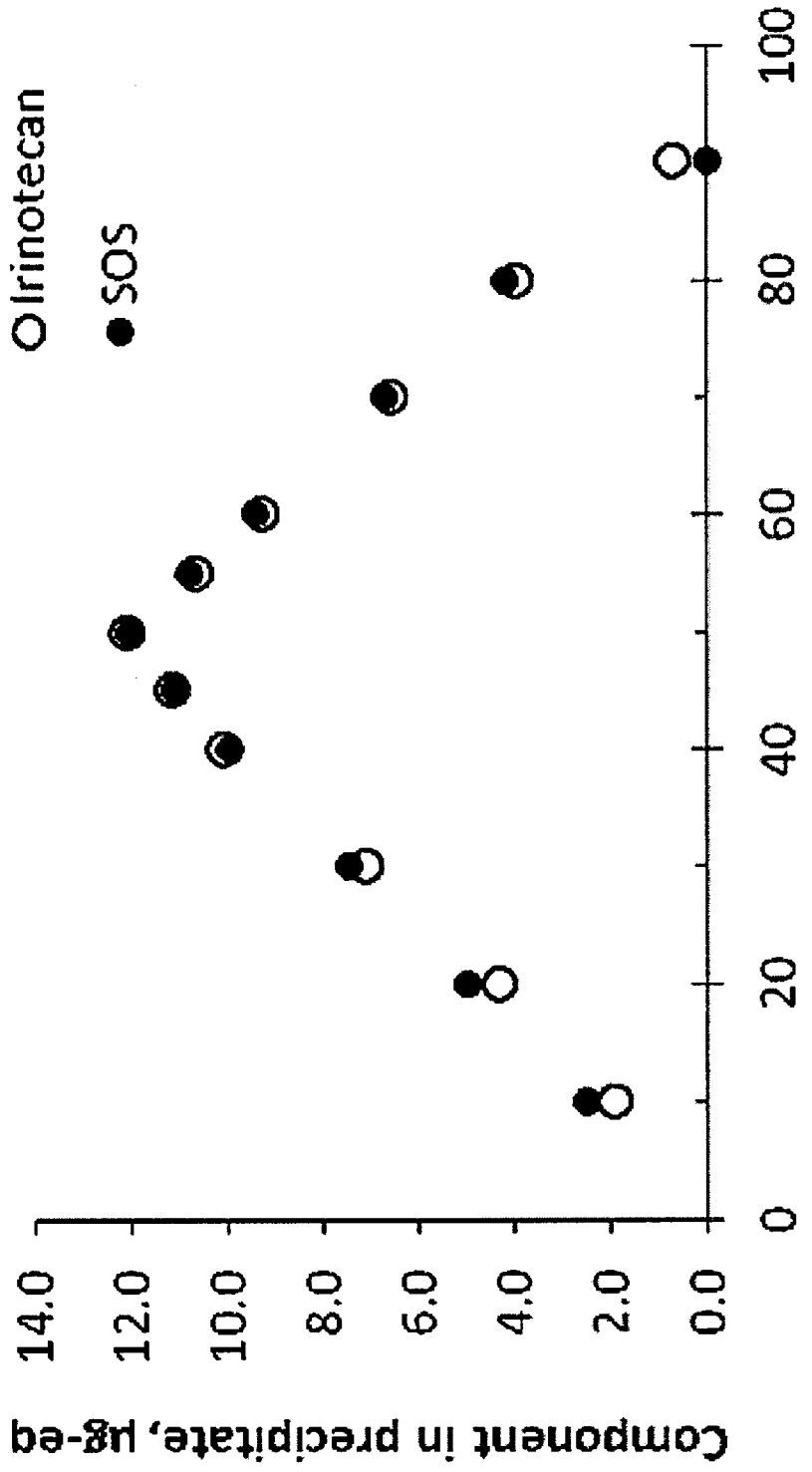

Irinotecan
SOS
Component in precipitate, µg-eq
14.0
12.0
10.0
8.0
6.0
4.0
2.0
0.0
0
20
40
60
80
100
SOS, eq. %

FIG. 8

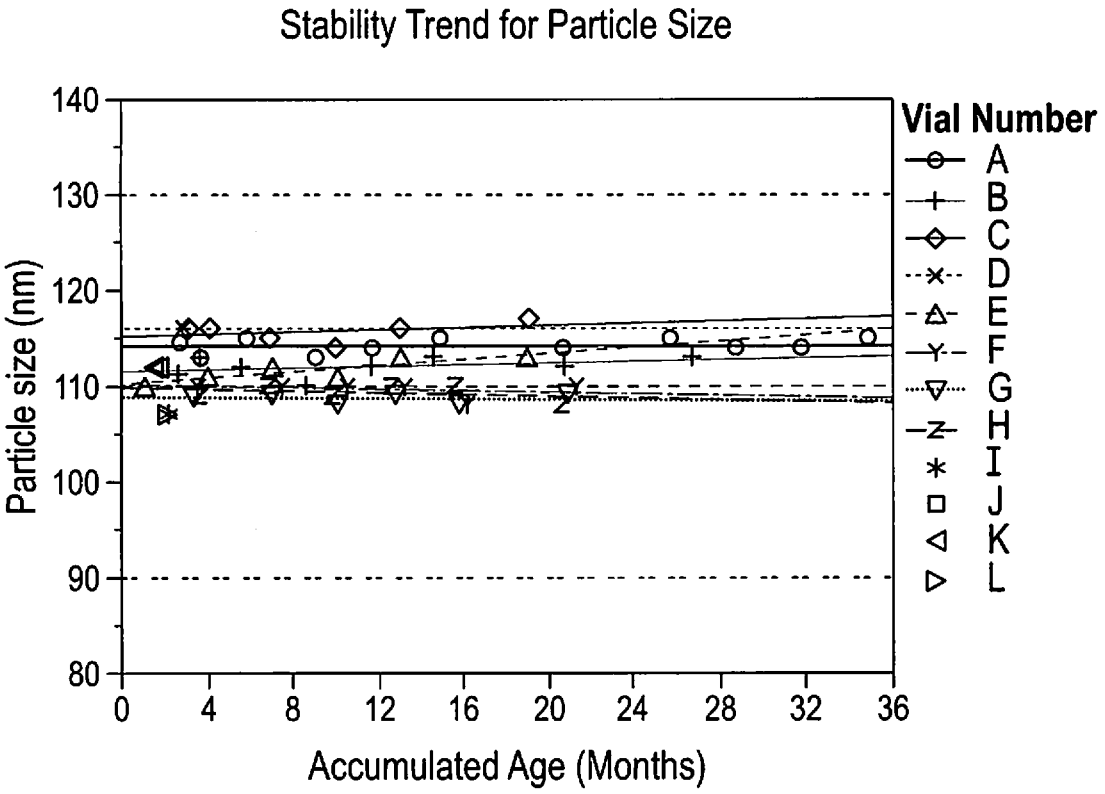

Stability Trend for Particle Size
Particle size (nm)
140
130
120
110
100
90
80
0
4
8
12
16
20
24
28
32
36
Accumulated Age (Months)
Vial Number
A
B
C
D
E
F
G
H
I
J
K
L

FIG. 9

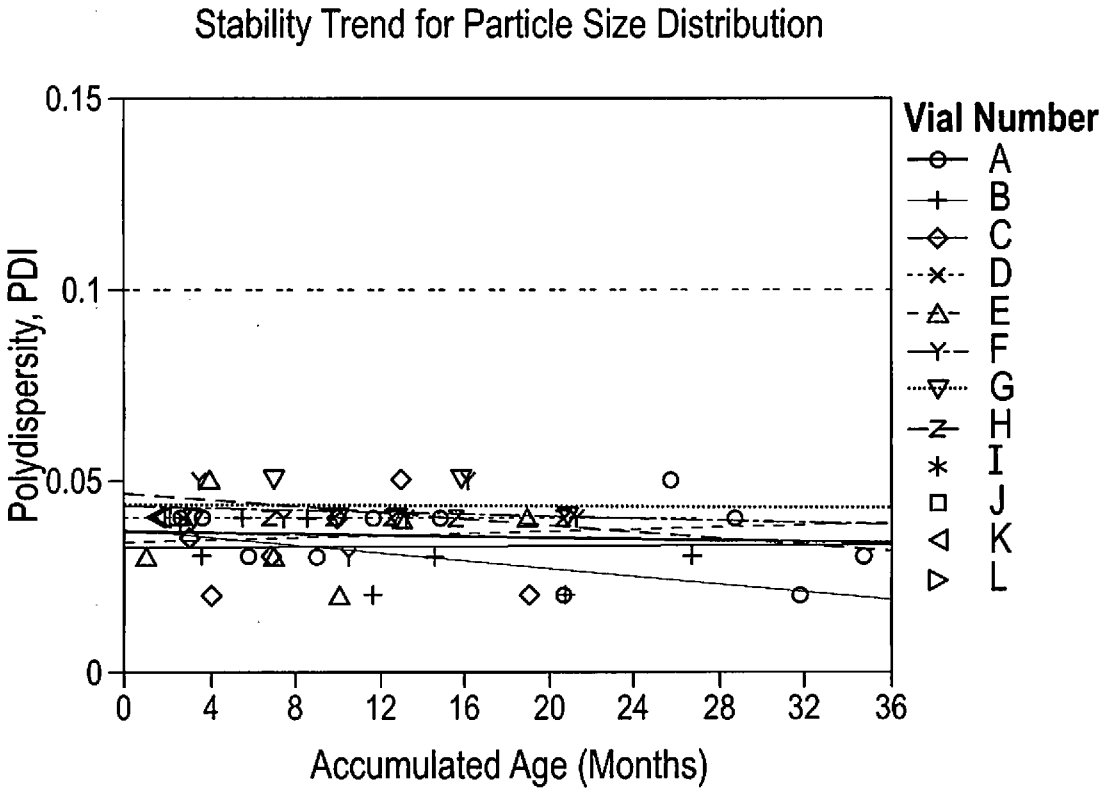

Stability Trend for Particle Size Distribution
Polydispersity, PDI
0.15
0.1
0.05
0
0
4
8
12
16
20
24
28
32
36
Accumulated Age (Months)
Vial Number
A
B
C
D
E
F
G
H
I
J
K
L

FIG. 10

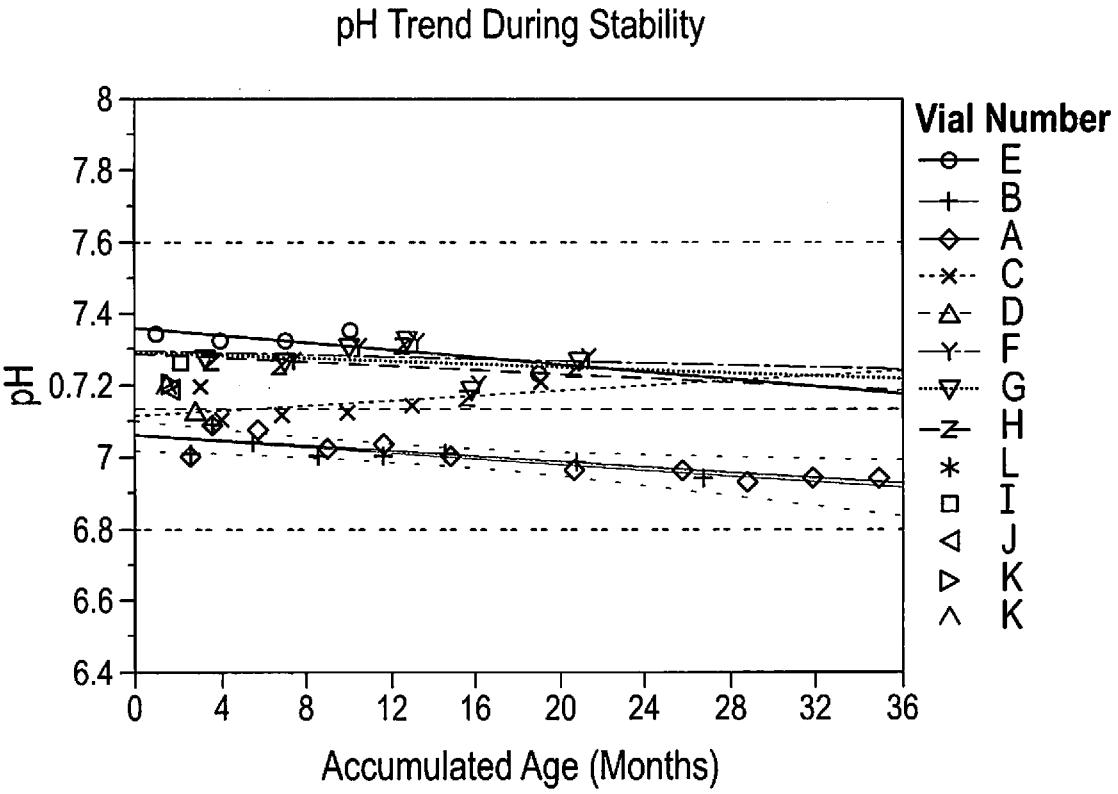

pH Trend During Stability
pH
8
7.8
7.6
7.4
7.2
7
6.8
6.6
6.4
0
4
8
12
16
20
24
28
32
36
Accumulated Age (Months)
Vial Number
E
B
A
C
D
F
G
H
L
I
J
K
K

FIG. 11A

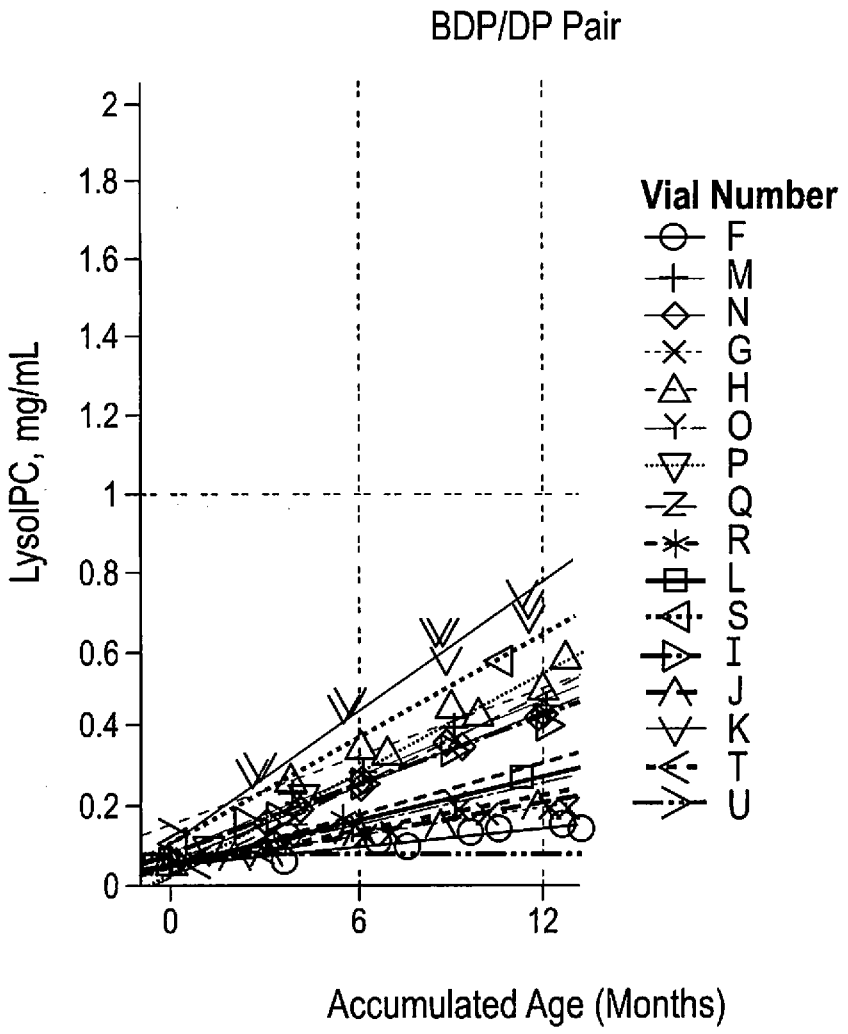

BDP/DP Pair
LysoIPC, mg/mL
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0
6
12
Accumulated Age (Months)
Vial Number
F
M
N
G
H
O
P
Q
R
L
S
I
J
K
T
U

FIG. 11B

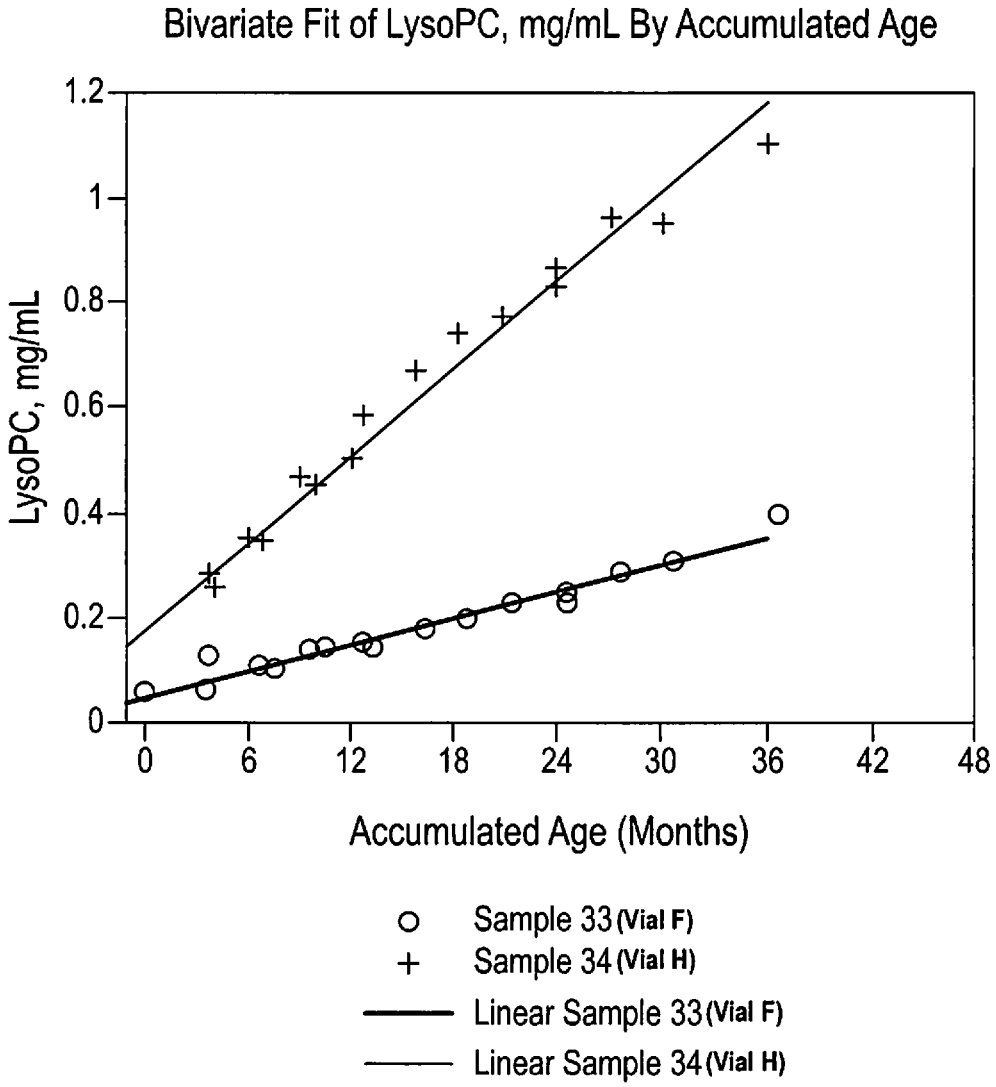

Bivariate Fit of LysoPC, mg/mL By Accumulated Age
LysoPC, mg/mL
1.2
1
0.8
0.6
0.4
0.2
0
0
6
12
18
24
30
36
42
48
Accumulated Age (Months)
Sample 33 (Vial F)
Sample 34 (Vial H)
Linear Sample 33 (Vial F)
Linear Sample 34 (Vial H)

FIG. 12

FIG. 13A

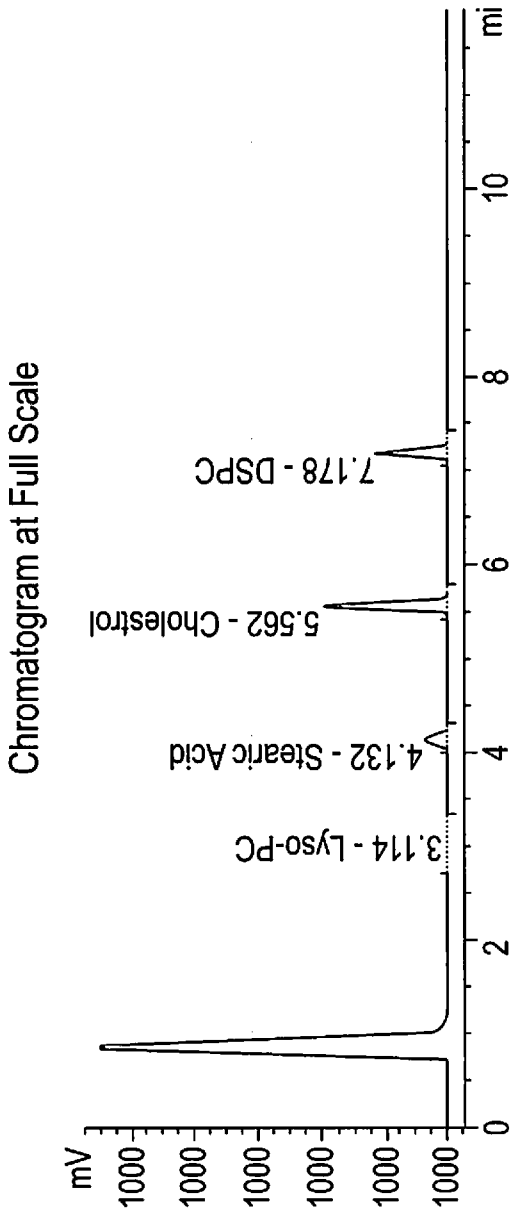


FIG. 13B

