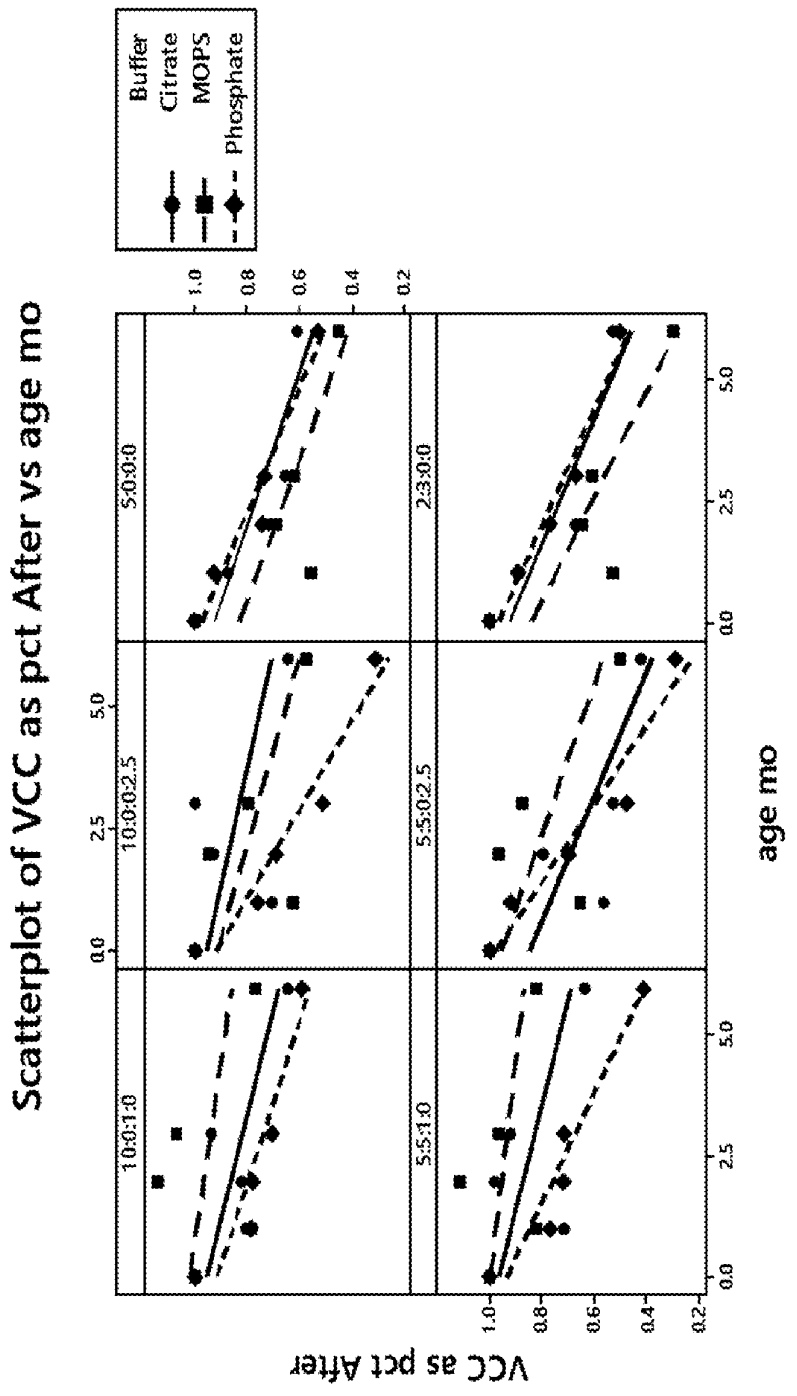

Scatterplot of VCC as pct After vs age mo
Buffer
Citrate
MOPS
Phosphate
10:0:1.0
10:0:0.2.5
5:0:0
5:5:1.0
5.5:0.2.5
2.3:0.0
VCC as pct After
age mo
Panel variable: Suc : treh : MSG : rHSA

*FIG. 1*

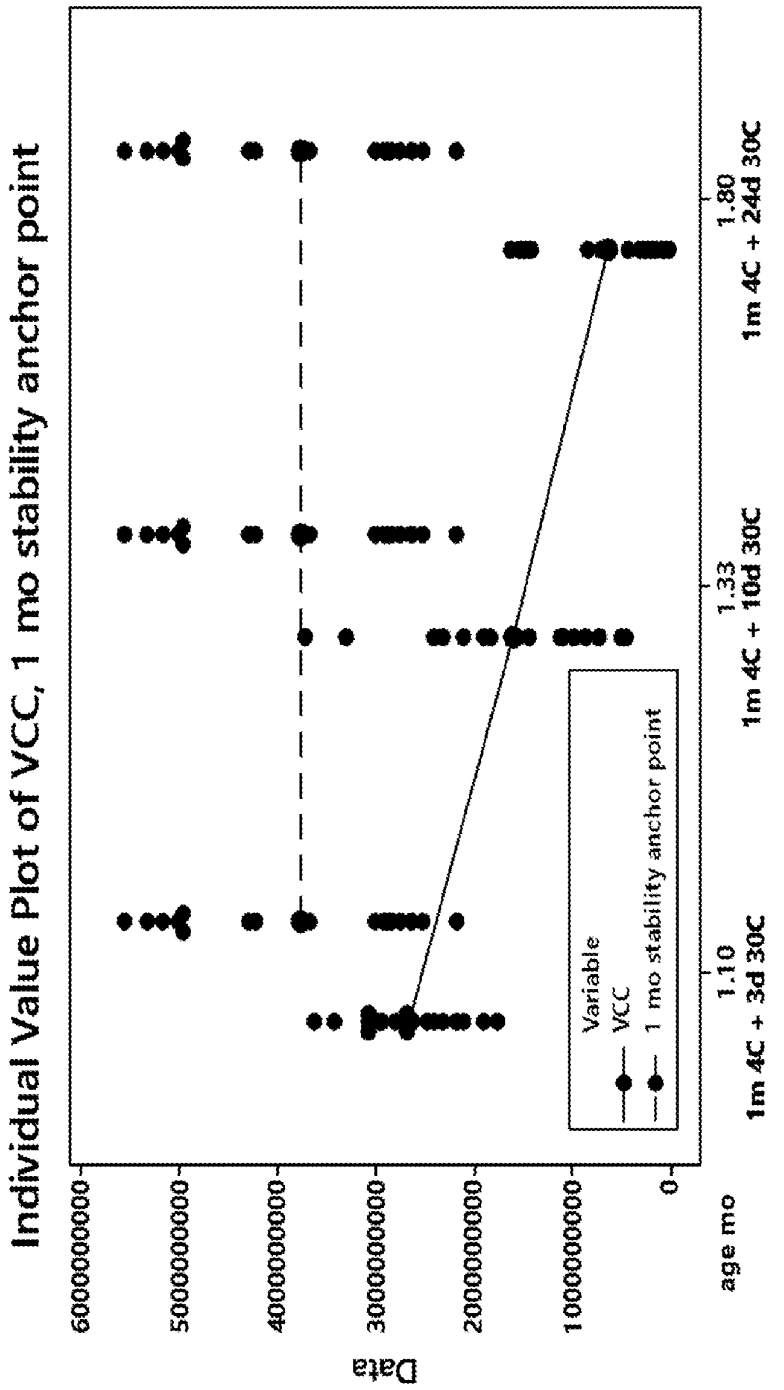

Individual Value Plot of VCC, 1 mo stability anchor point
Data
60000000000
50000000000
40000000000
30000000000
20000000000
10000000000
0
Variable
VCC
1 mo stability anchor point
age mo
1.10
1m 4C + 3d 30C
1.33
1m 4C + 10d 30C
1.80
1m 4C + 24d 30C

*FIG. 2A*

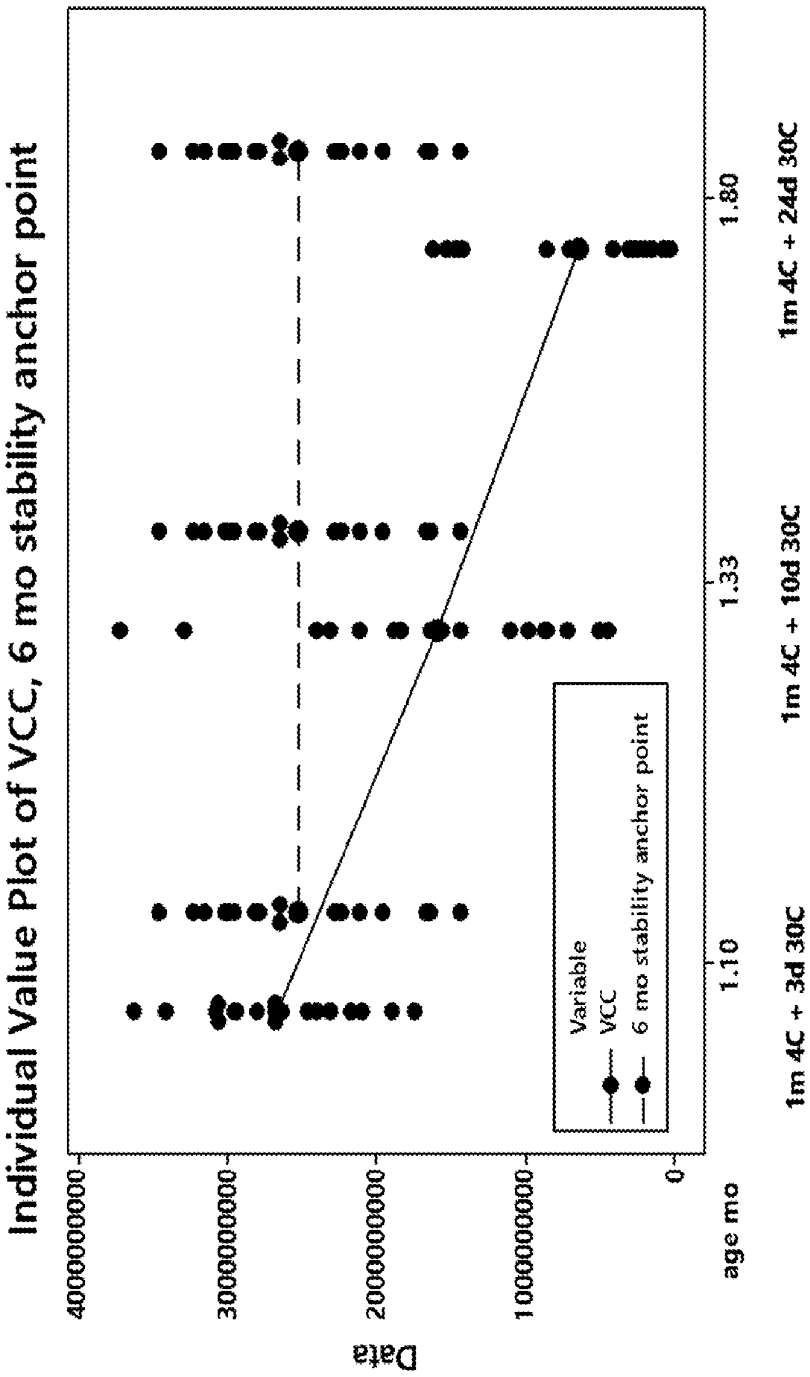
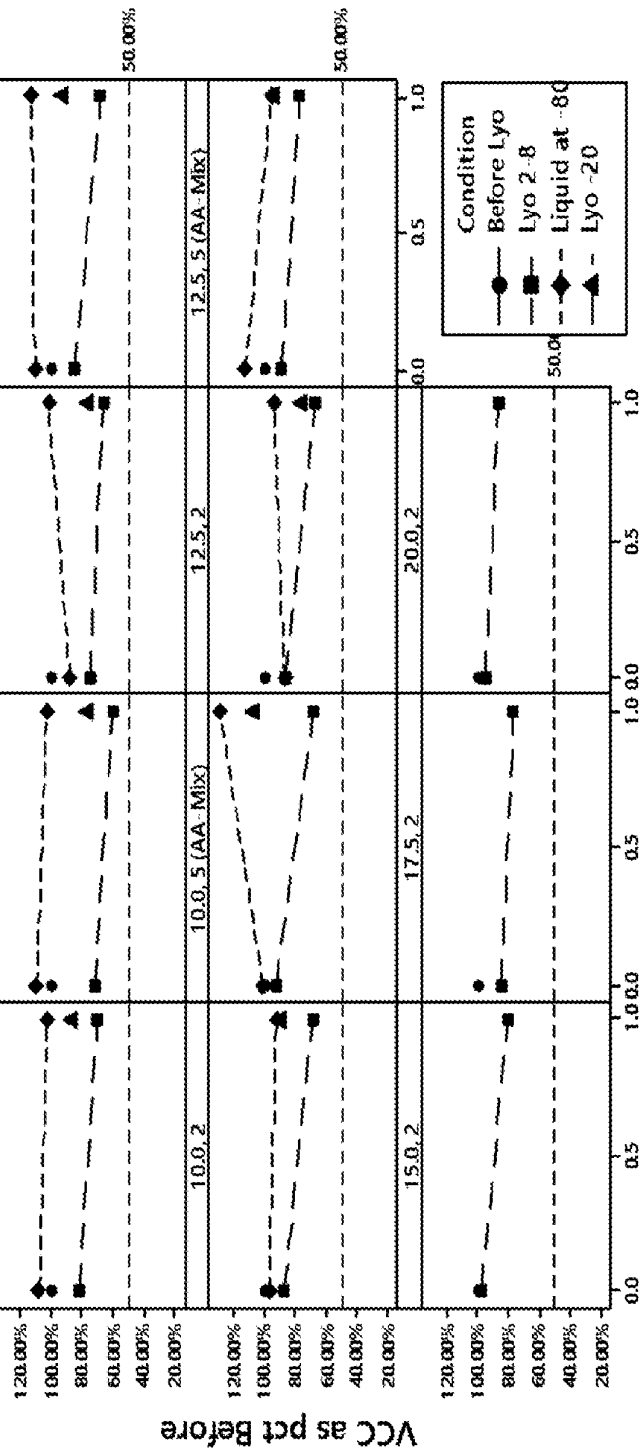

Individual Value Plot of VCC, 6 mo stability anchor point
Data
4000000000
3000000000
2000000000
1000000000
0
Variable
VCC
6 mo stability anchor point
age mo
1.10
1.33
1.80
1m 4C + 3d 30C
1m 4C + 10d 30C
1m 4C + 24d 30C

*FIG. 2B*




*Panel variables: OD in vial, Stabilizer*

***FIG. 3***

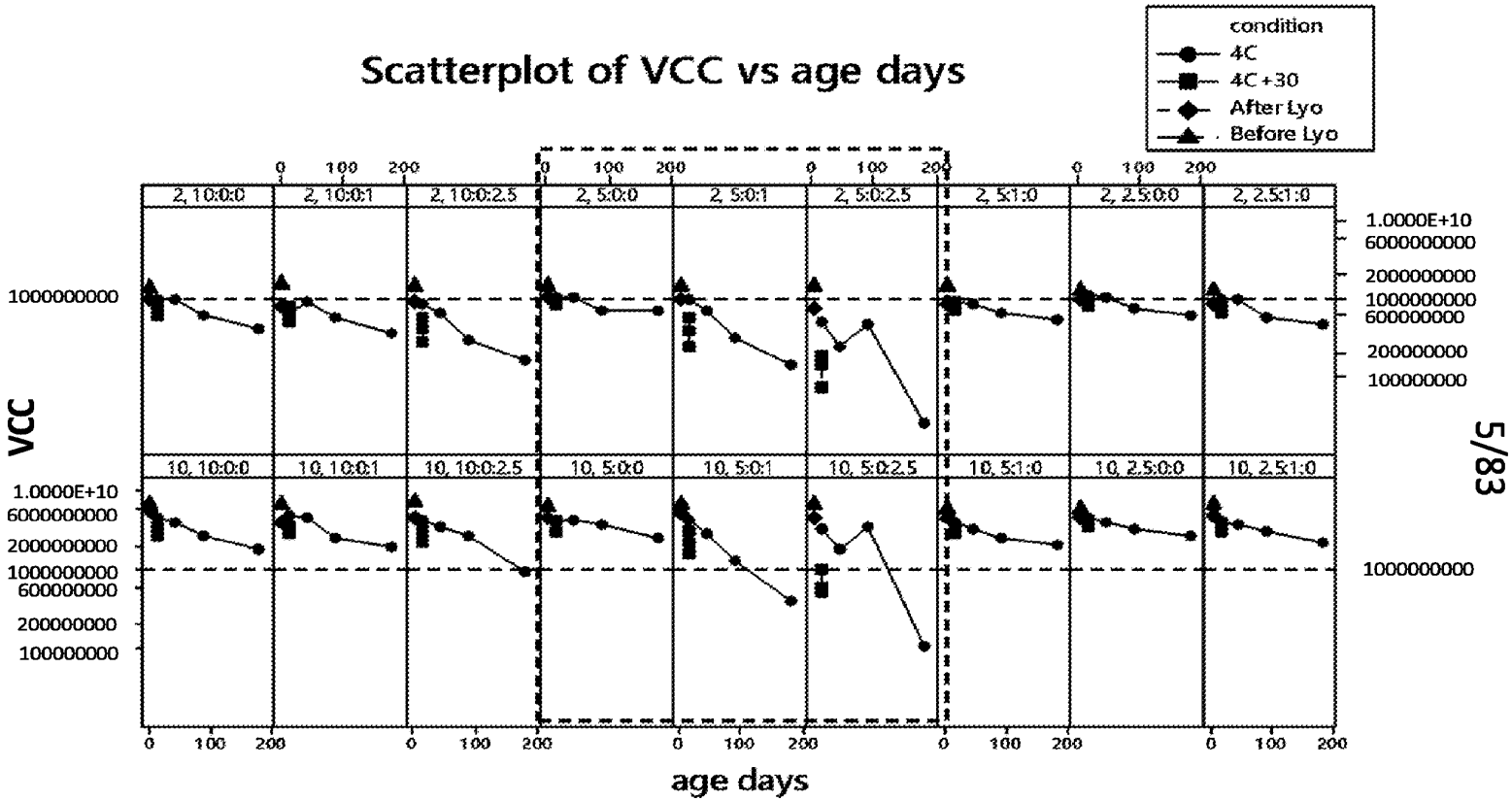

Scatterplot of VCC vs age days
condition
4C
4C+30
After Lyo
Before Lyo
2, 10:0:0
2, 10:0:1
2, 10:0:2.5
2, 5:0:0
2, 5:0:1
2, 5:0:2.5
2, 5:1:0
2, 2.5:0:0
2, 2.5:1:0
10, 10:0:0
10, 10:0:1
10, 10:0:2.5
10, 5:0:0
10, 5:0:1
10, 5:0:2.5
10, 5:1:0
10, 2.5:0:0
10, 2.5:1:0
VCC
1.0000E+10
6000000000
2000000000
1000000000
600000000
200000000
100000000
0
100
200
age days
Panel variables: OD, Suc:AAMix:rHSA

*FIG. 4*

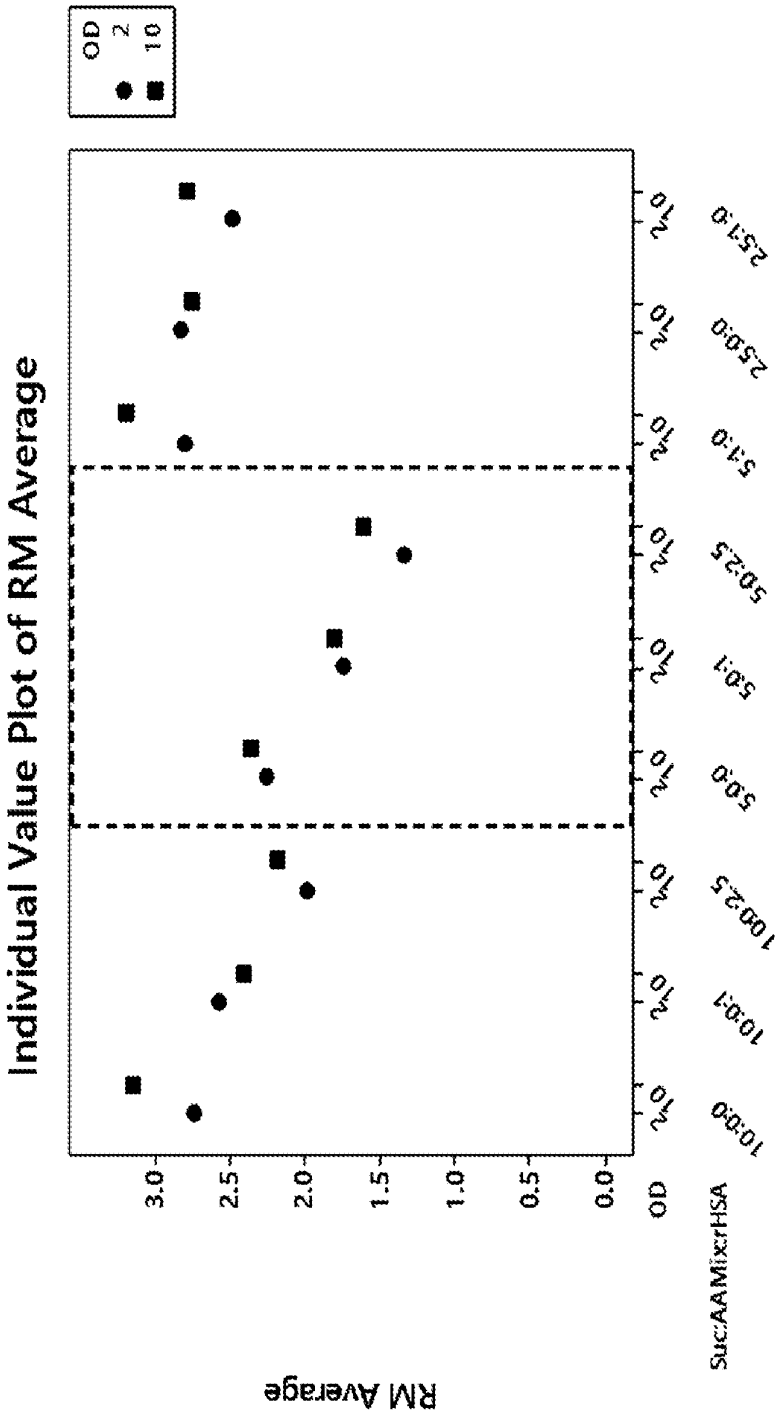

Individual Value Plot of RM Average
OD
2
10
RM Average
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Suc:AAMix:rHSA
10:0:0
10:0:1
100:2.5
50:0
50:1
50:2.5
5:1:0
2.5:0:0
2.5:1:0

*FIG. 5*

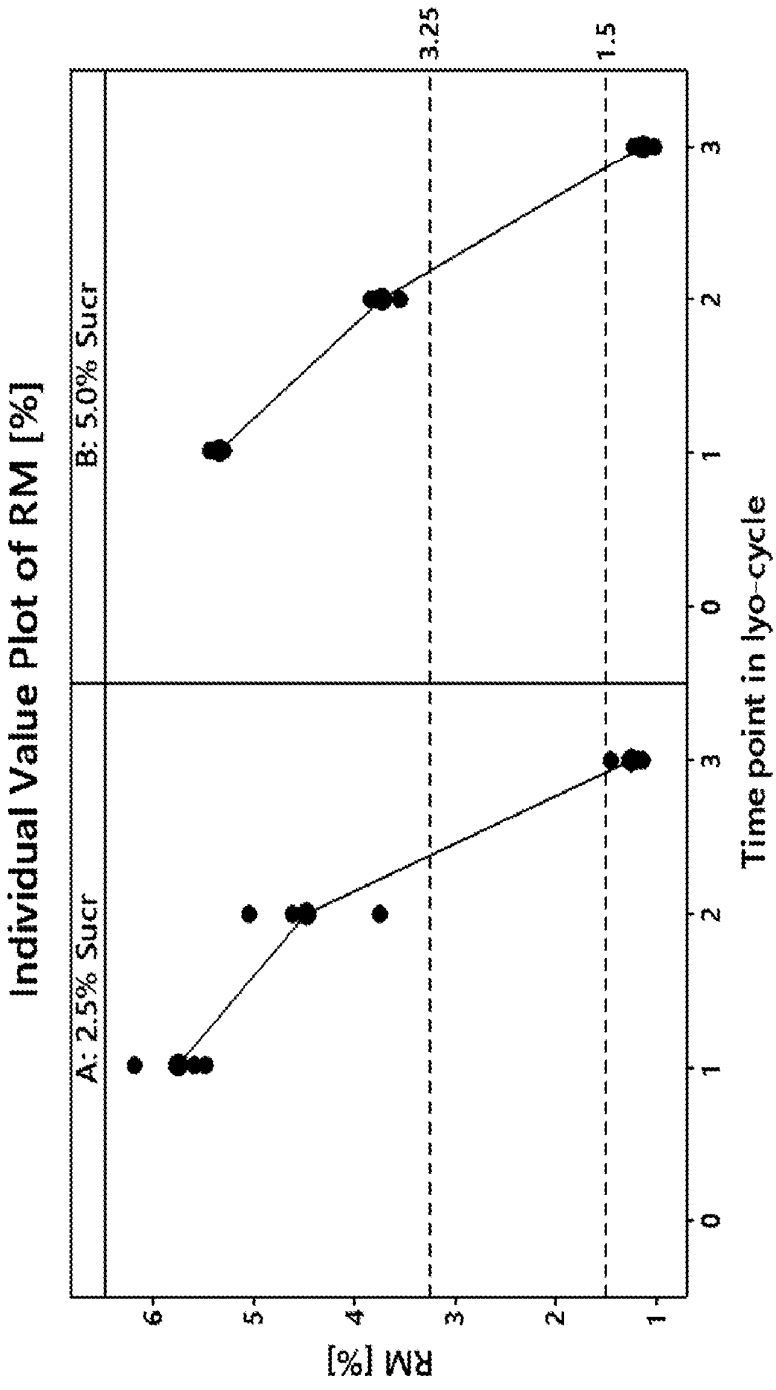

Individual Value Plot of RM [%]
A: 2.5% Sucr
B: 5.0% Sucr
3.25
1.5
RM [%]
Time point in lyo-cycle
Panel variable: Sample

*FIG. 6*

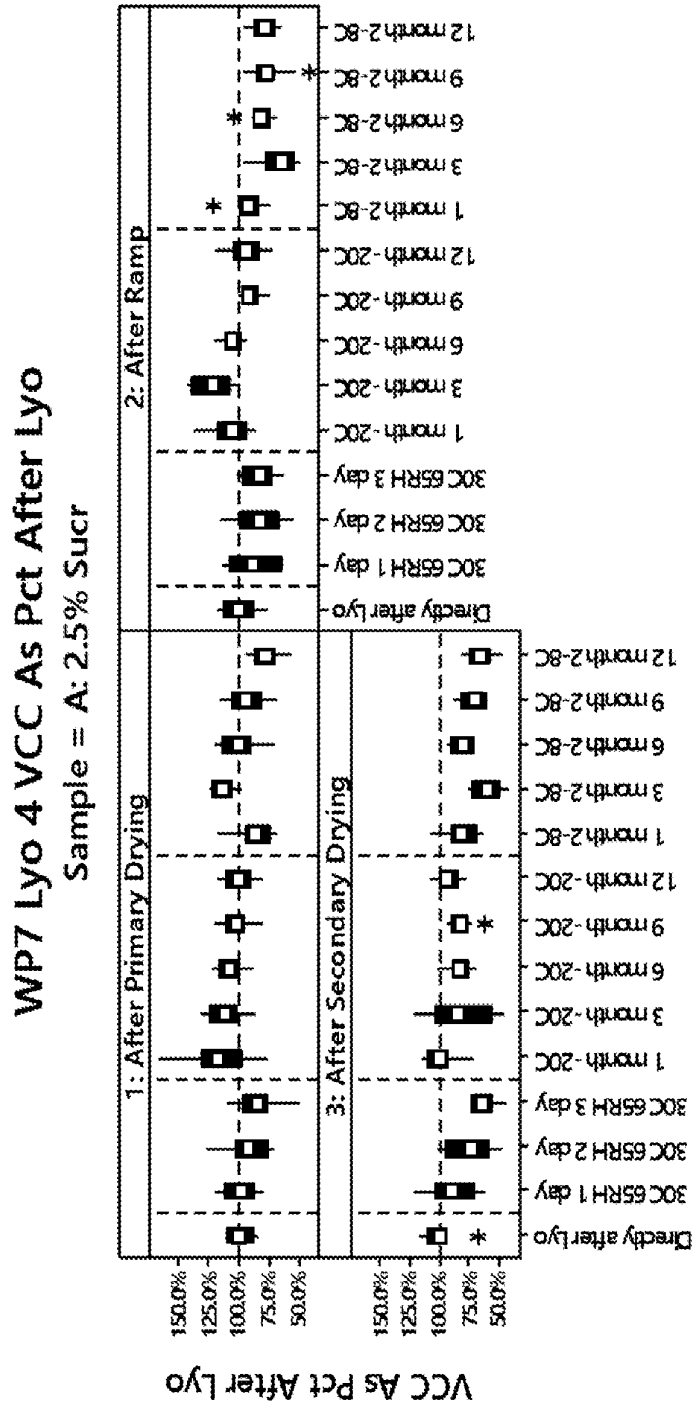

WP7 Lyo 4 VCC As Pct After Lyo
Sample = A: 2.5% Sucr
1: After Primary Drying
2: After Ramp
3: After Secondary Drying
VCC As Pct After Lyo
150.0%
125.0%
100.0%
75.0%
50.0%
Directly after Lyo
30C 65RH 1 day
30C 65RH 2 day
30C 65RH 3 day
1 month -20C
3 month -20C
6 month -20C
9 month -20C
12 month -20C
1 month 2-8C
3 month 2-8C
6 month 2-8C
9 month 2-8C
12 month 2-8C
VCC condition
Panel variable: Phase in Lyo Cycle

*FIG. 7A*

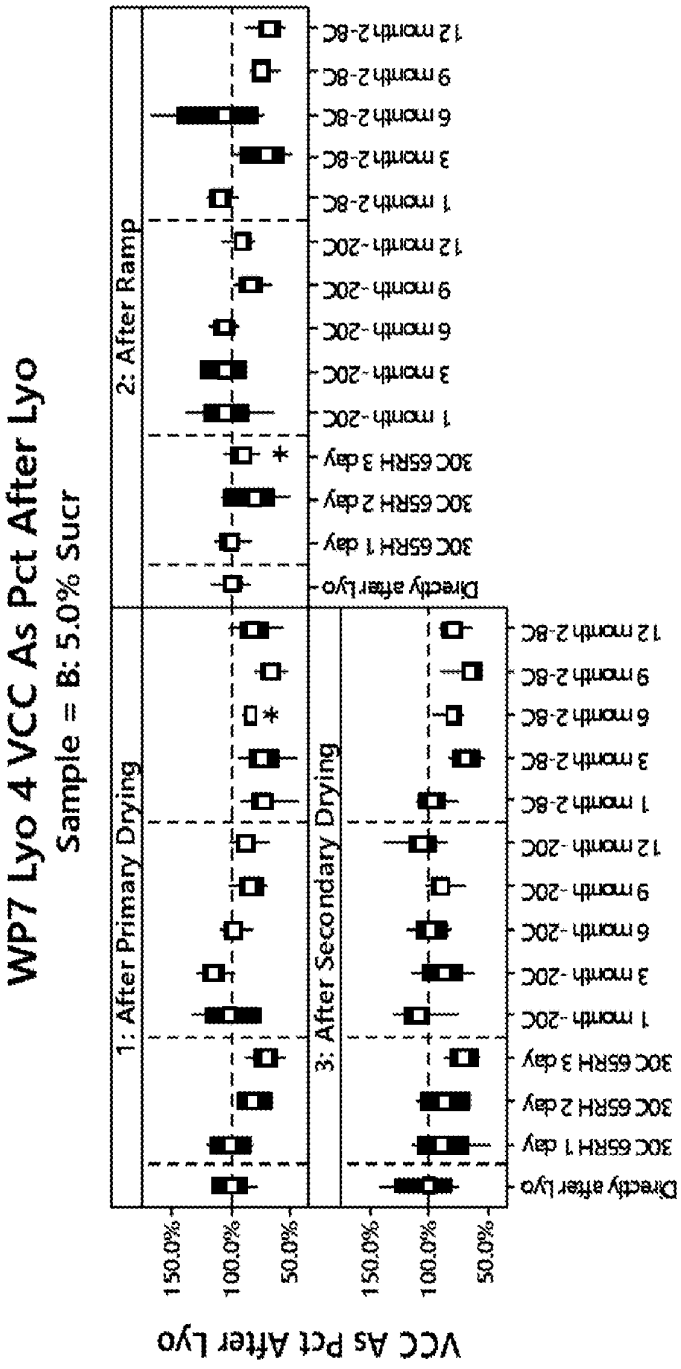

WP7 Lyo 4 VCC As Pct After Lyo
Sample = B: 5.0% Sucr
1: After Primary Drying
2: After Ramp
3: After Secondary Drying
VCC As Pct After Lyo
150.0%
100.0%
50.0%
Directly after lyo
30C 65RH 1 day
30C 65RH 2 day
30C 65RH 3 day
1 month -20C
3 month -20C
6 month -20C
9 month -20C
12 month -20C
1 month 2-8C
3 month 2-8C
6 month 2-8C
9 month 2-8C
12 month 2-8C
VCC condition
Panel variable: Phase in Lyo Cycle

*FIG. 7B*

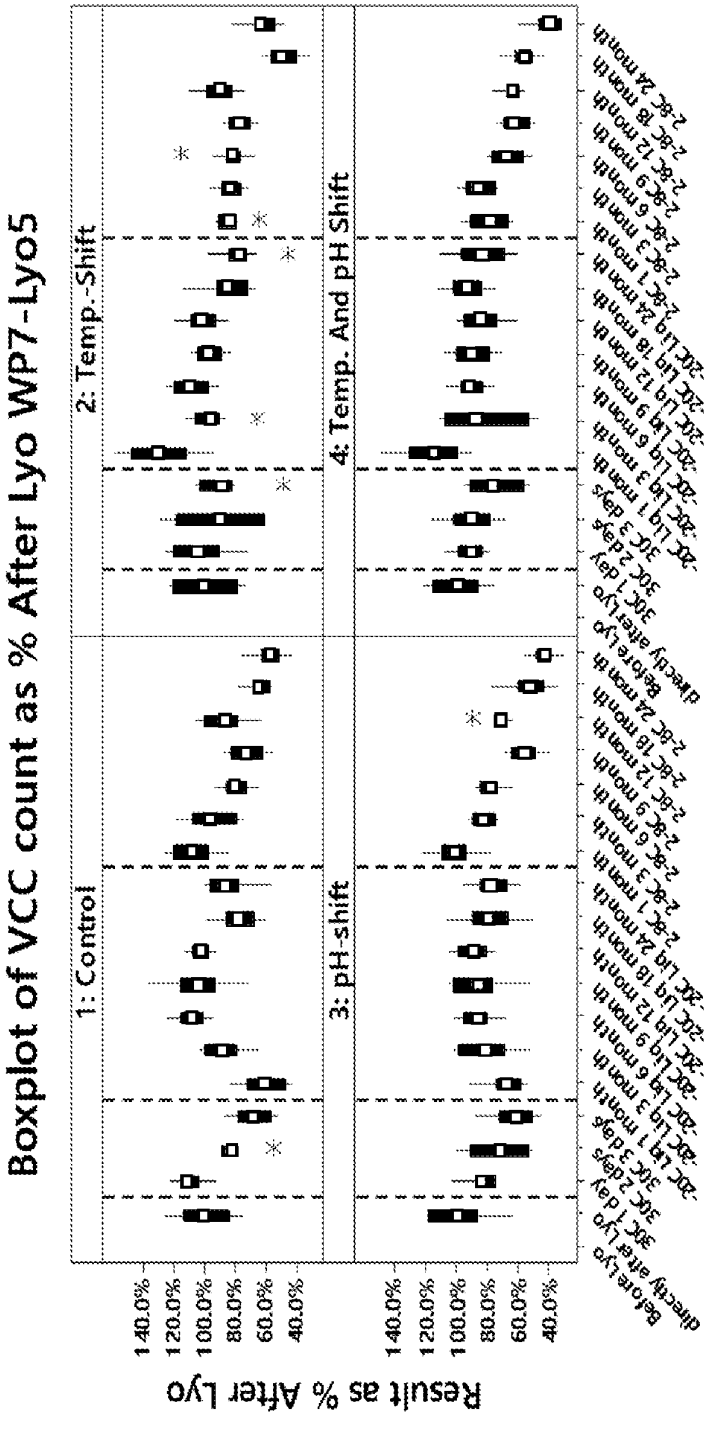

Boxplot of VCC count as % After Lyo WP7-Lyo5
1: Control
2: Temp.-Shift
3: pH-shift
4: Temp. And pH Shift
Result as % After Lyo
140.0%
120.0%
100.0%
80.0%
60.0%
40.0%
directly after Lyo
before Lyo
30C 1 day
30C 2 days
30C 3 days
30C Lyo 1 month
30C Lyo 3 month
30C Lyo 6 month
30C Lyo 9 month
30C Lyo 12 month
30C Lyo 18 month
30C Lyo 24 month
2-8C 1 month
2-8C 3 month
2-8C 6 month
2-8C 9 month
2-8C 12 month
2-8C 18 month
2-8C 24 month
Status
Panel variable: Probe

*FIG. 8*

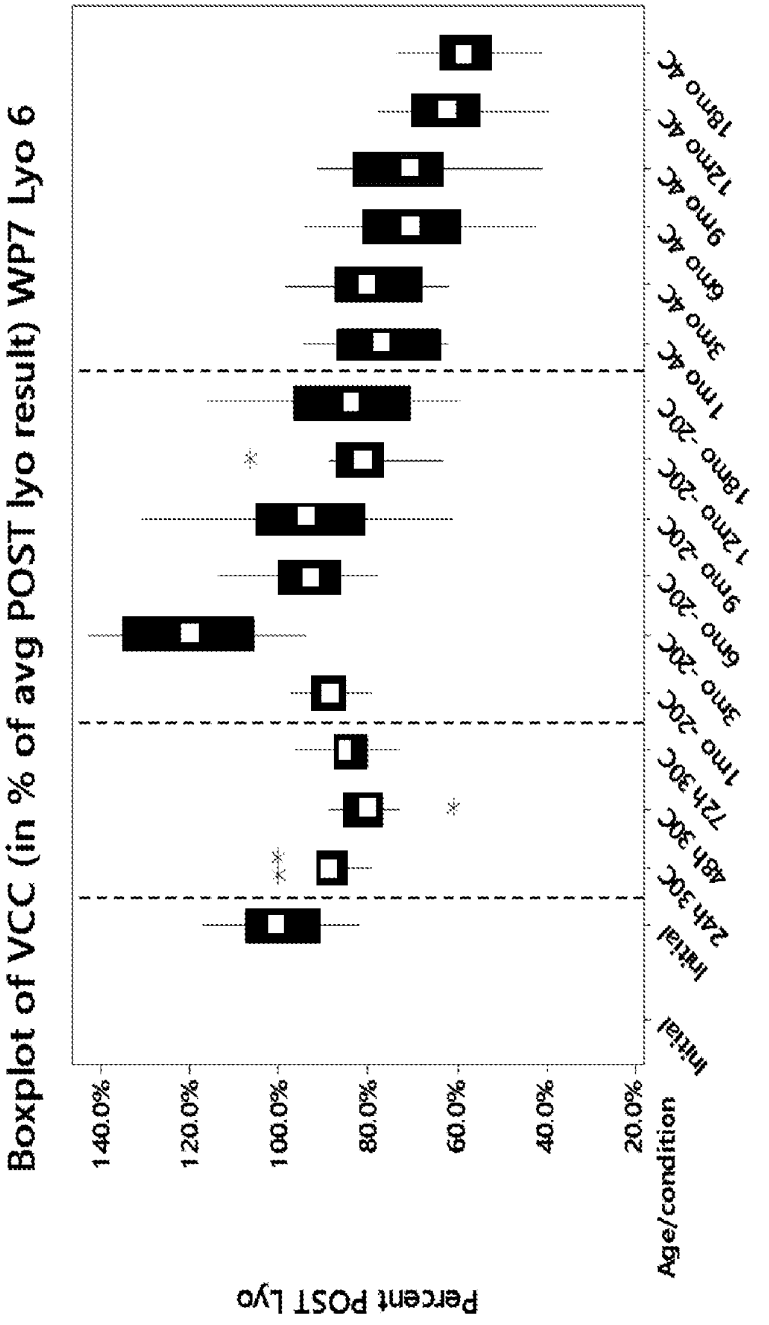

Boxplot of VCC (in % of avg POST lyo result) WP7 Lyo 6
Percent POST Lyo
140.0%
120.0%
100.0%
80.0%
60.0%
40.0%
20.0%
Age/condition
Initial
Initial
2Ah 30C
48h 30C
72h 30C
1mo -20C
3mo -20C
6mo -20C
9mo -20C
12mo -20C
18mo -20C
1mo 4C
3mo 4C
6mo 4C
9mo 4C
12mo 4C
18mo 4C

*FIG. 9*

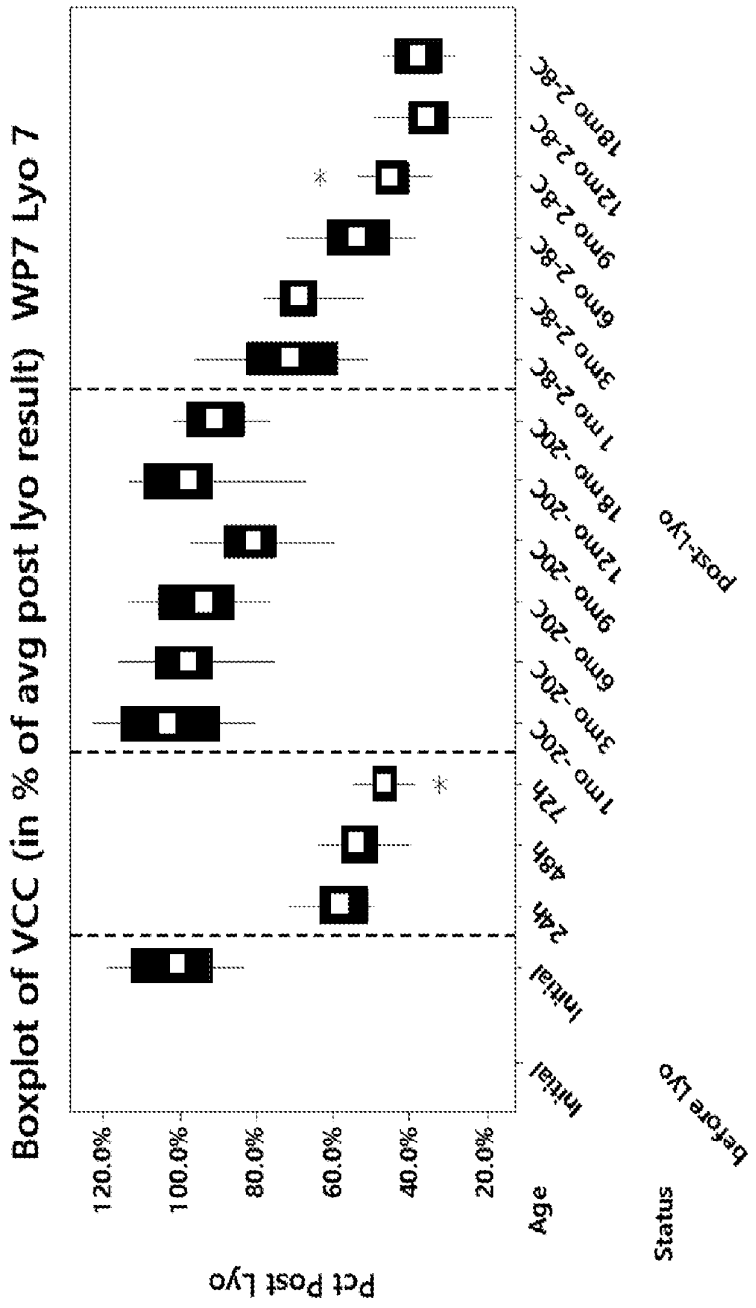

Boxplot of VCC (in % of avg post lyo result) WP7 Lyo 7
Pct Post Lyo
120.0%
100.0%
80.0%
60.0%
40.0%
20.0%
Age
Status
Initial
Initial
2dh
48h
72h
1mo -20C
3mo -20C
6mo -20C
9mo -20C
12mo -20C
18mo -20C
1 mo 2-8C
3mo 2-8C
6mo 2-8C
9mo 2-8C
12mo 2-8C
18mo 2-8C
Before Lyo
Post-Lyo

*FIG. 10*

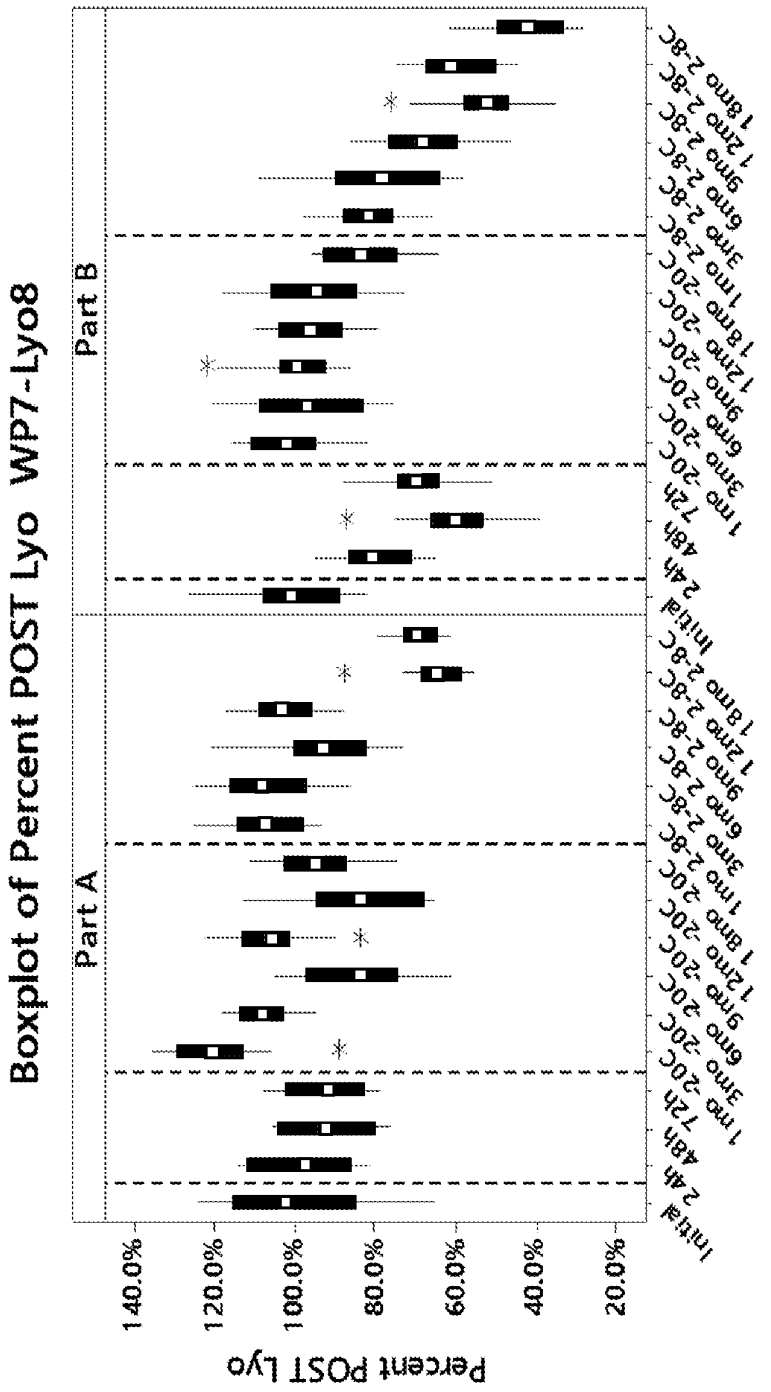

Boxplot of Percent POST Lyo WP7-Lyo8
Part A
Part B
Percent POST Lyo
140.0%
120.0%
100.0%
80.0%
60.0%
40.0%
20.0%
Initial
2 h
48h
12h
1 mo -20C
3mo -20C
6mo -20C
9mo -20C
12mo -20C
18mo -20C
1 mo 2-8C
3mo 2-8C
6mo 2-8C
9mo 2-8C
12mo 2-8C
18mo 2-8C
Age

*FIG. 11*

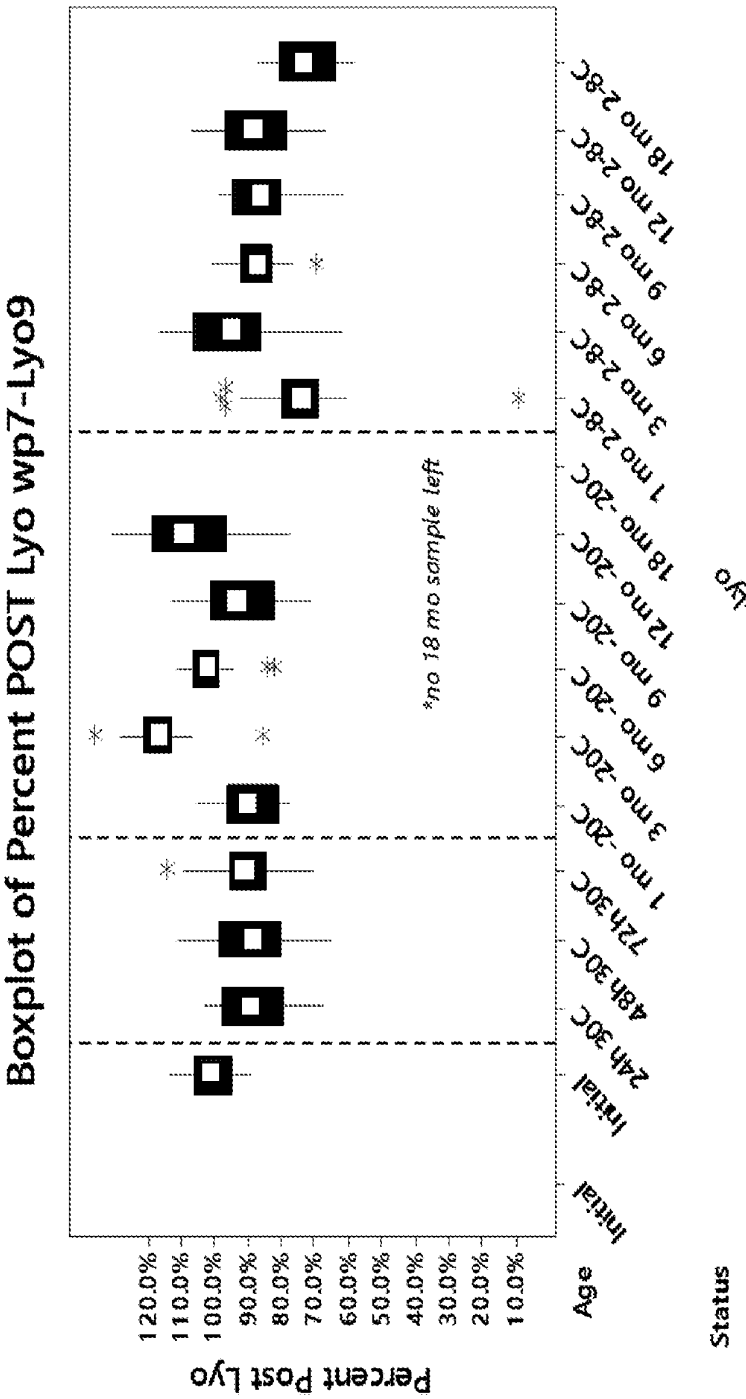

Boxplot of Percent POST Lyo wp7-Lyo9
Percent Post Lyo
120.0%
110.0%
100.0%
90.0%
80.0%
70.0%
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
*no 18 mo sample left
Age
Initial
Initial
2Ah 30C
4Bh 30C
72h 30C
1 mo -20C
3 mo -20C
6 mo -20C
9 mo -20C
12 mo -20C
18 mo -20C
1 mo 2-8C
3 mo 2-8C
6 mo 2-8C
9 mo 2-8C
12 mo 2-8C
18 mo 2-8C
Status
post-Lyo

*FIG. 12*

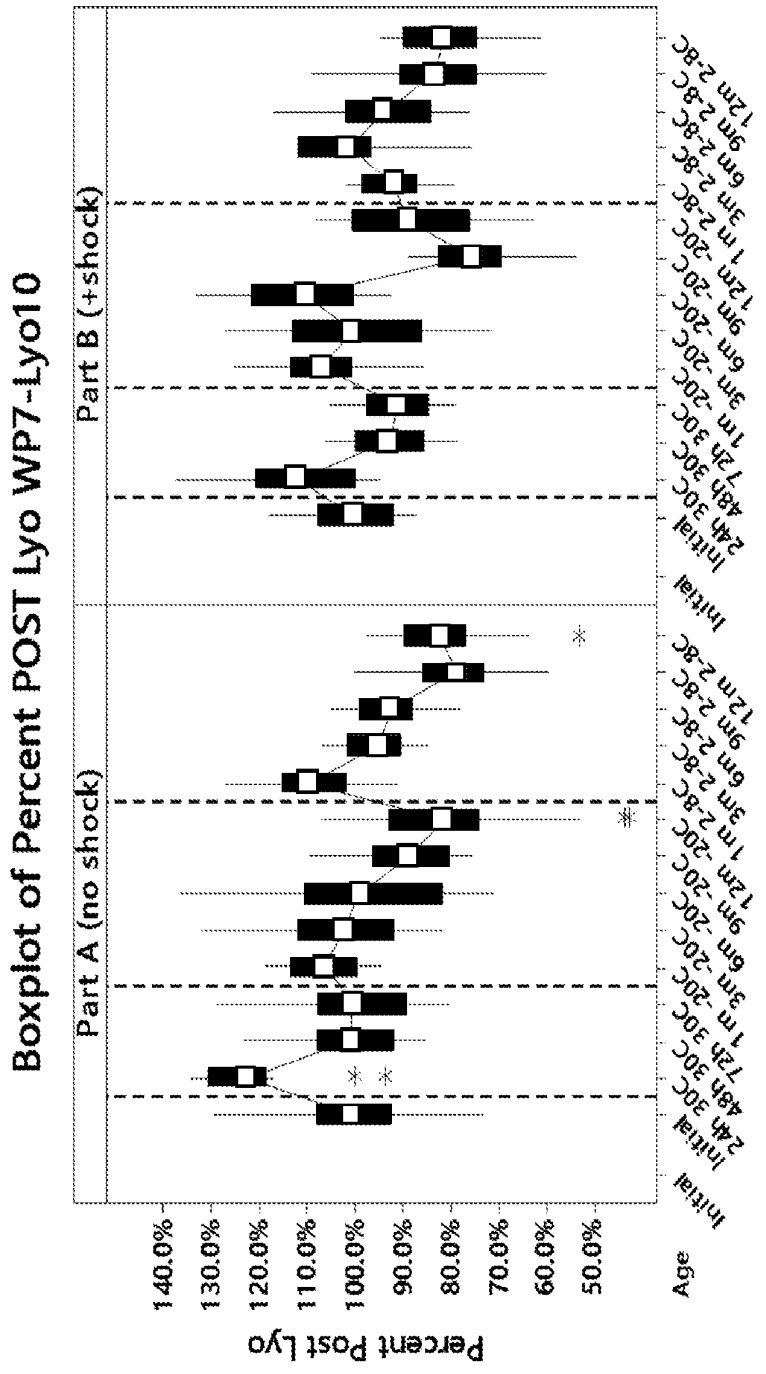

Boxplot of Percent POST Lyo WP7-Lyo10
Part A (no shock)
Part B (+shock)
Percent Post Lyo
140.0%
130.0%
120.0%
110.0%
100.0%
90.0%
80.0%
70.0%
60.0%
50.0%
Age
Initial
2Ah 30C
48h 30C
7.2h 30C
1m -20C
3m -20C
6m -20C
9m -20C
12m -20C
1m 2-8C
3m 2-8C
6m 2-8C
9m 2-8C
12m 2-8C
Panel variable Treatment

*FIG. 13*

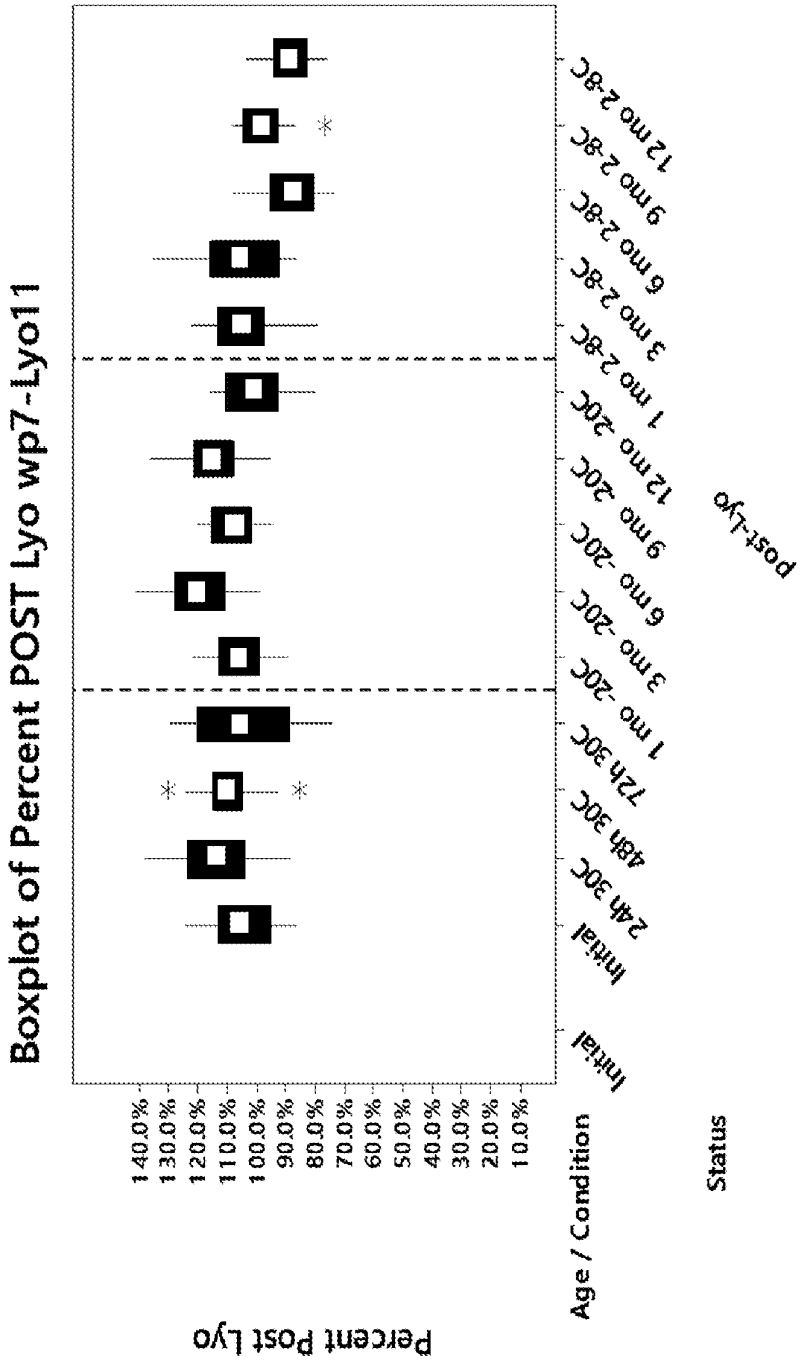

Boxplot of Percent POST Lyo wp7-Lyo11
Percent Post Lyo
140.0%
130.0%
120.0%
110.0%
100.0%
90.0%
80.0%
70.0%
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
Age / Condition
Initial
Initial
2dh 30C
4dh 30C
72h 30C
1 mo -20C
3 mo -20C
6 mo -20C
9 mo -20C
12 mo -20C
1 mo 2-8C
3 mo 2-8C
6 mo 2-8C
9 mo 2-8C
12 mo 2-8C
Status
post-Lyo

*FIG. 14*

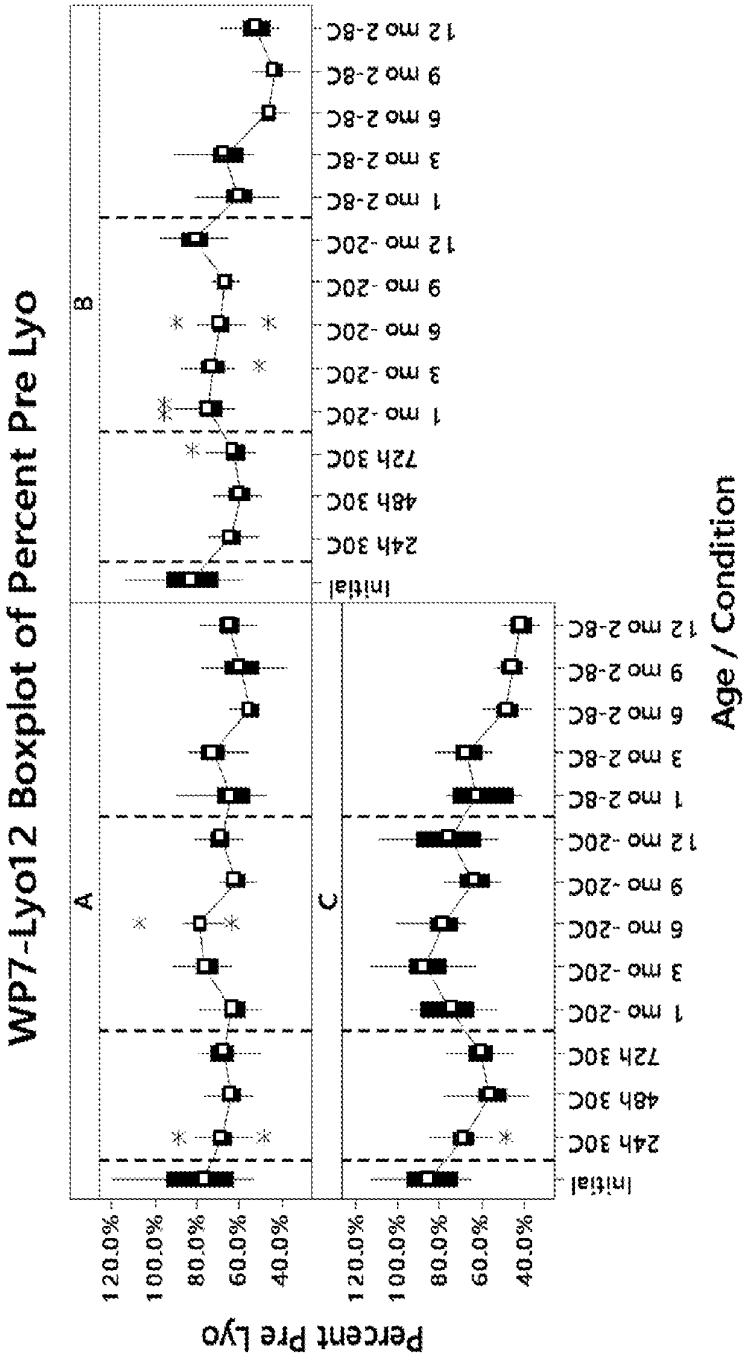

WP7-Lyo12 Boxplot of Percent Pre Lyo
Percent Pre Lyo
120.0%
100.0%
80.0%
60.0%
40.0%
A
B
C
Initial
24h 30C
48h 30C
72h 30C
1 mo -20C
3 mo -20C
6 mo -20C
9 mo -20C
12 mo -20C
1 mo 2-8C
3 mo 2-8C
6 mo 2-8C
9 mo 2-8C
12 mo 2-8C
Age / Condition
Panel variable: PART

*FIG. 15*

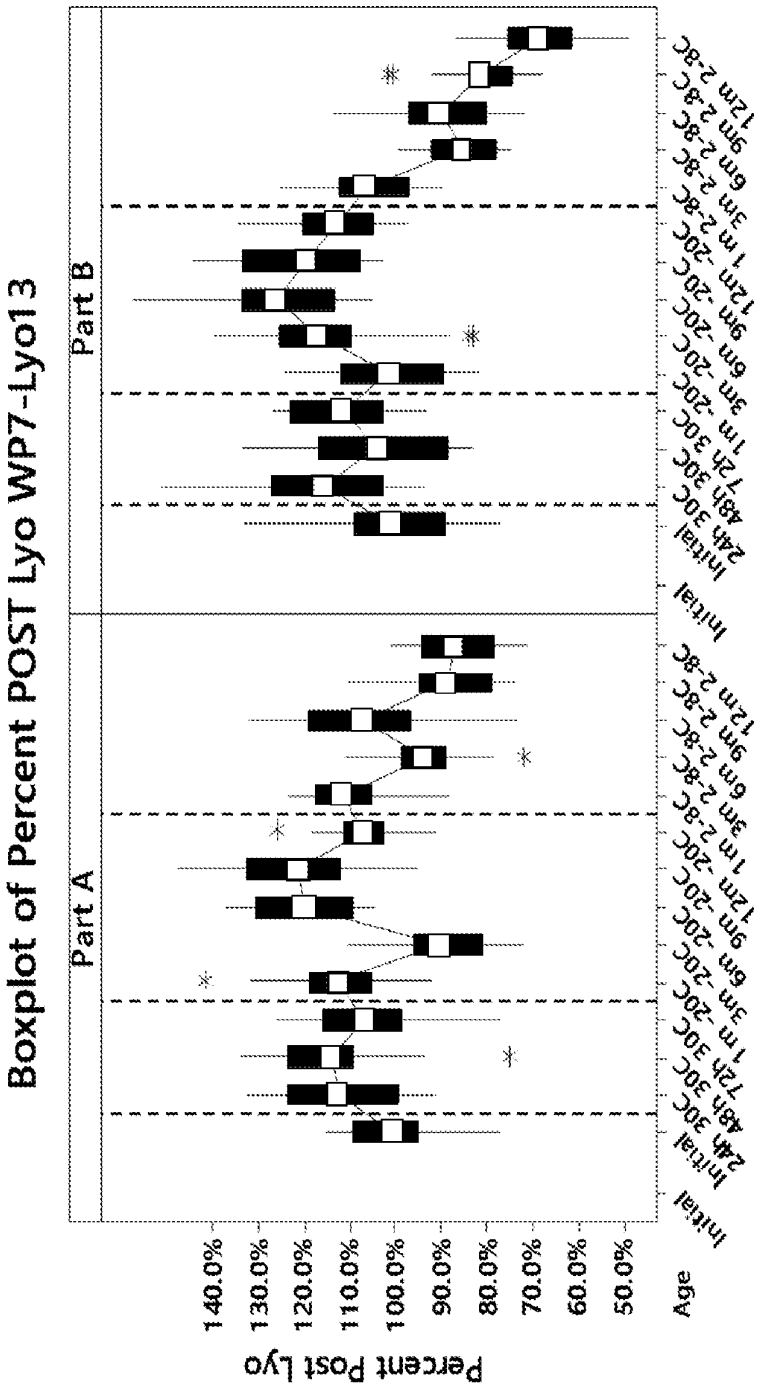

Boxplot of Percent POST Lyo WP7-Lyo13
Part A
Part B
Percent Post Lyo
140.0%
130.0%
120.0%
110.0%
100.0%
90.0%
80.0%
70.0%
60.0%
50.0%
Age
Initial
2dh 30C
48h 30C
7dh 30C
1m 30C
3m -20C
6m -20C
9m -20C
12m -20C
1m 2-8C
3m 2-8C
6m 2-8C
9m 2-8C
12m 2-8C
Panel variable: Treatment

*FIG. 16*

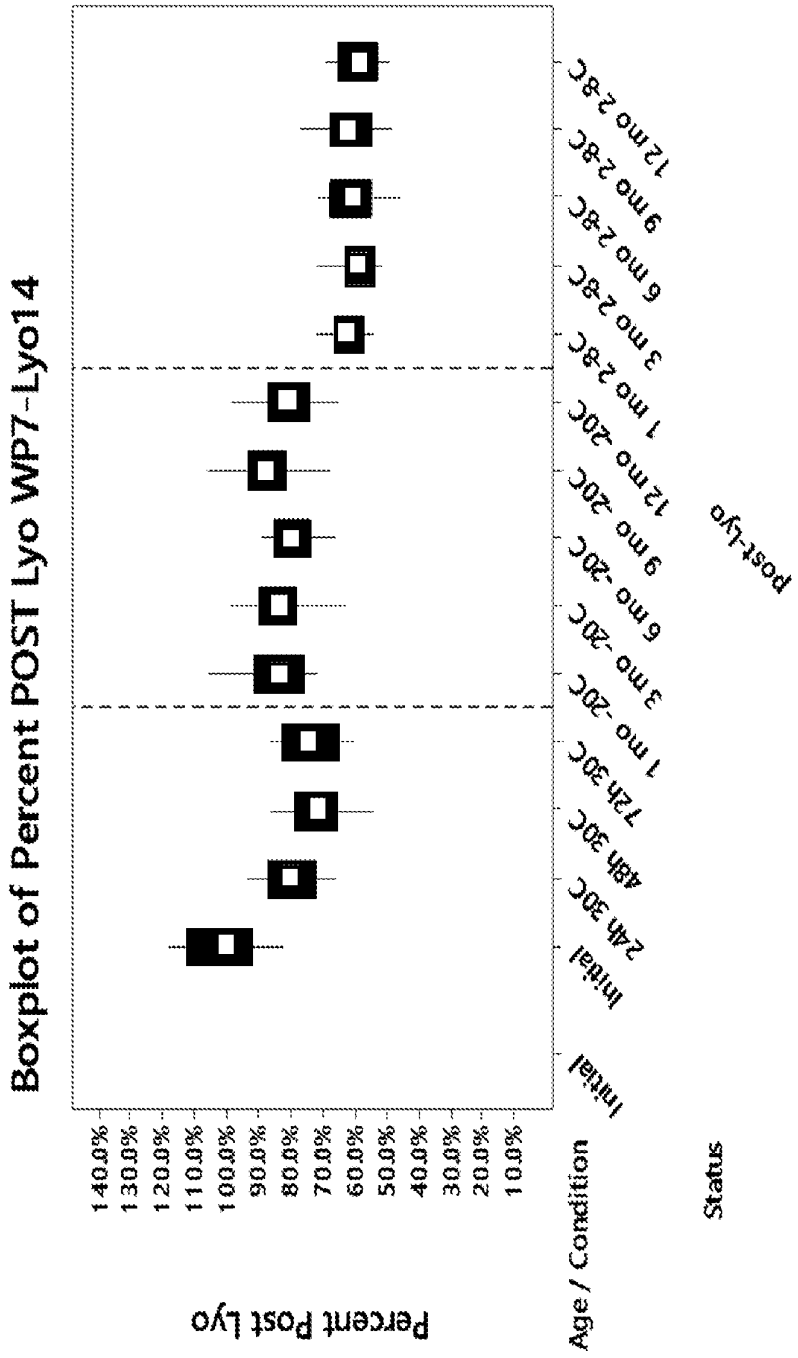

Boxplot of Percent POST Lyo WP7-Lyo14
Percent Post Lyo
140.0%
130.0%
120.0%
110.0%
100.0%
90.0%
80.0%
70.0%
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
Age / Condition
Initial
Initial
2dh 30C
4dh 30C
72h 30C
1 mo -20C
3 mo -20C
6 mo -20C
9 mo -20C
12 mo -20C
1 mo 2-8C
3 mo 2-8C
6 mo 2-8C
9 mo 2-8C
12 mo 2-8C
Status
post-Lyo

*FIG. 17*

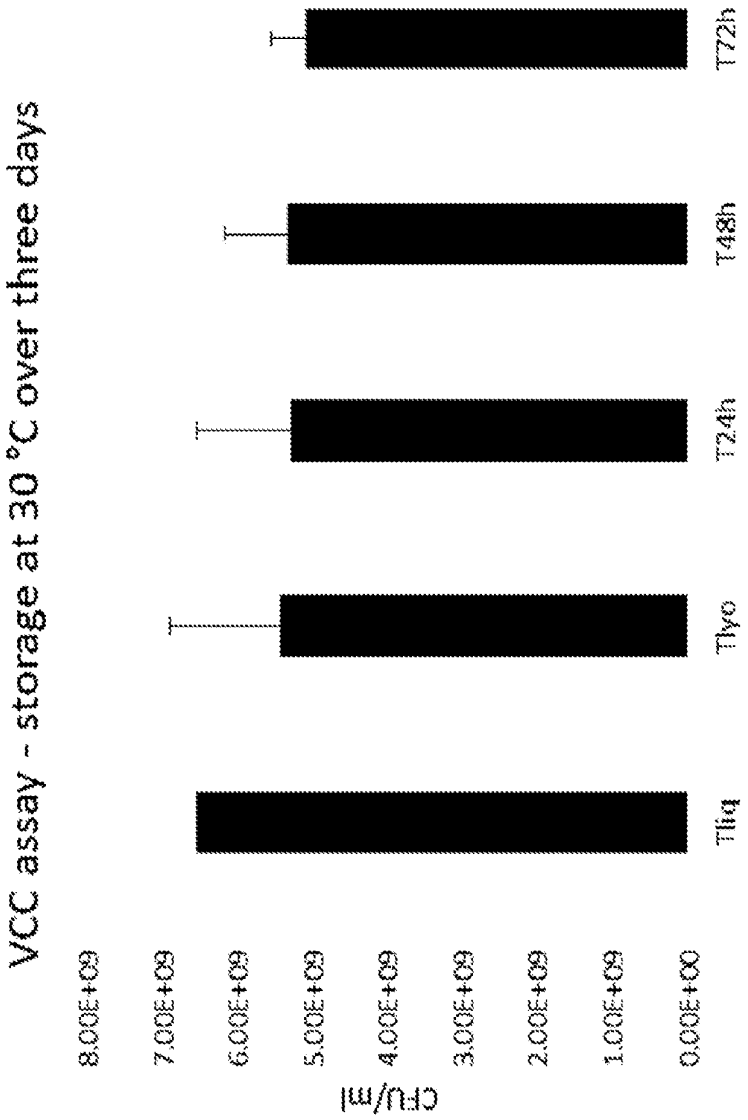

VCC assay - storage at 30 °C over three days
CFU/ml
8.00E+09
7.00E+09
6.00E+09
5.00E+09
4.00E+09
3.00E+09
2.00E+09
1.00E+09
0.00E+00
Tliq
Tlyo
T24h
T48h
T72h

*FIG. 18*

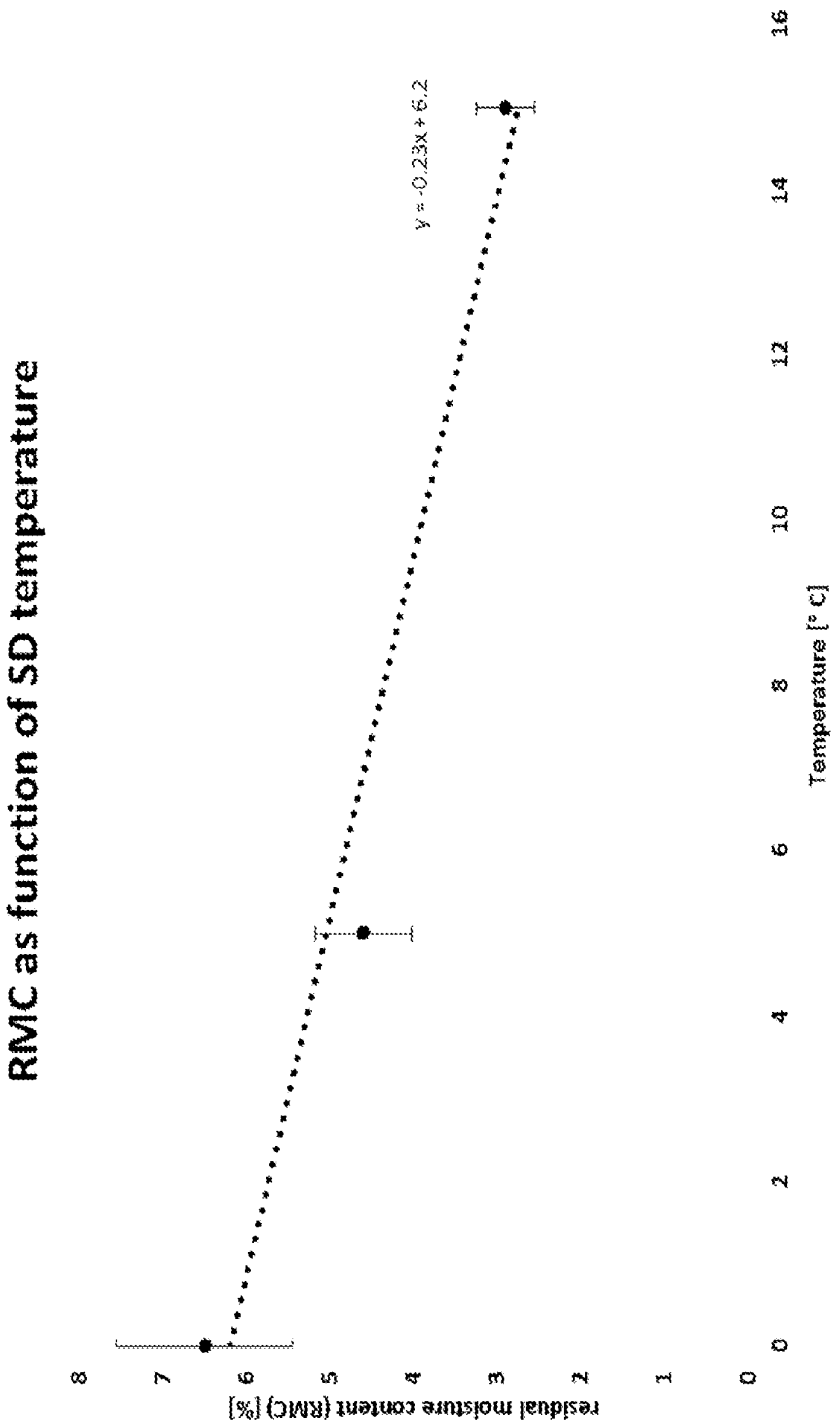

RMC as function of SD temperature
y = -0.23x + 6.2
residual moisture content (RMC) [%]
Temperature [° C]
0
1
2
3
4
5
6
7
8
0
2
4
6
8
10
12
14
16

*FIG. 19*

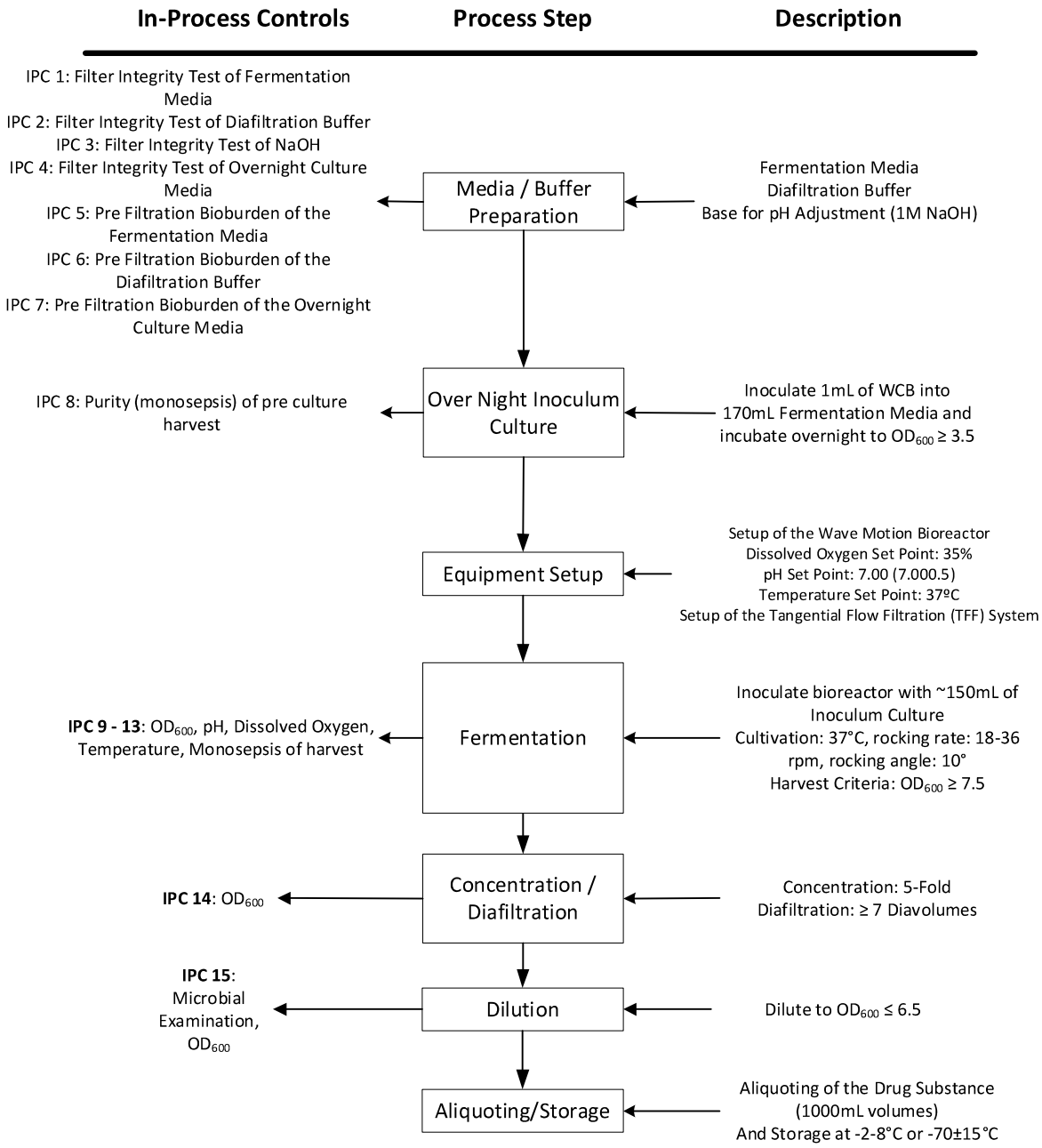

In-Process Controls
Process Step
Description
IPC 1: Filter Integrity Test of Fermentation Media
IPC 2: Filter Integrity Test of Diafiltration Buffer
IPC 3: Filter Integrity Test of NaOH
IPC 4: Filter Integrity Test of Overnight Culture Media
IPC 5: Pre Filtration Bioburden of the Fermentation Media
IPC 6: Pre Filtration Bioburden of the Diafiltration Buffer
IPC 7: Pre Filtration Bioburden of the Overnight Culture Media
Media / Buffer Preparation
Fermentation Media
Diafiltration Buffer
Base for pH Adjustment (1M NaOH)
IPC 8: Purity (monosepsis) of pre culture harvest
Over Night Inoculum Culture
Inoculate 1mL of WCB into 170mL Fermentation Media and incubate overnight to OD600 ≥ 3.5
Equipment Setup
Setup of the Wave Motion Bioreactor
Dissolved Oxygen Set Point: 35%
pH Set Point: 7.00 (7.000.5)
Temperature Set Point: 37ºC
Setup of the Tangential Flow Filtration (TFF) System
IPC 9 - 13: OD600, pH, Dissolved Oxygen, Temperature, Monosepsis of harvest
Fermentation
Inoculate bioreactor with ~150mL of Inoculum Culture
Cultivation: 37°C, rocking rate: 18-36 rpm, rocking angle: 10°
Harvest Criteria: OD600 ≥ 7.5
IPC 14: OD600
Concentration / Diafiltration
Concentration: 5-Fold
Diafiltration: ≥ 7 Diavolumes
IPC 15: Microbial Examination, OD600
Dilution
Dilute to OD600 ≤ 6.5
Aliquoting/Storage
Aliquoting of the Drug Substance (1000mL volumes)
And Storage at -2-8°C or -70±15°C

***FIG. 20***

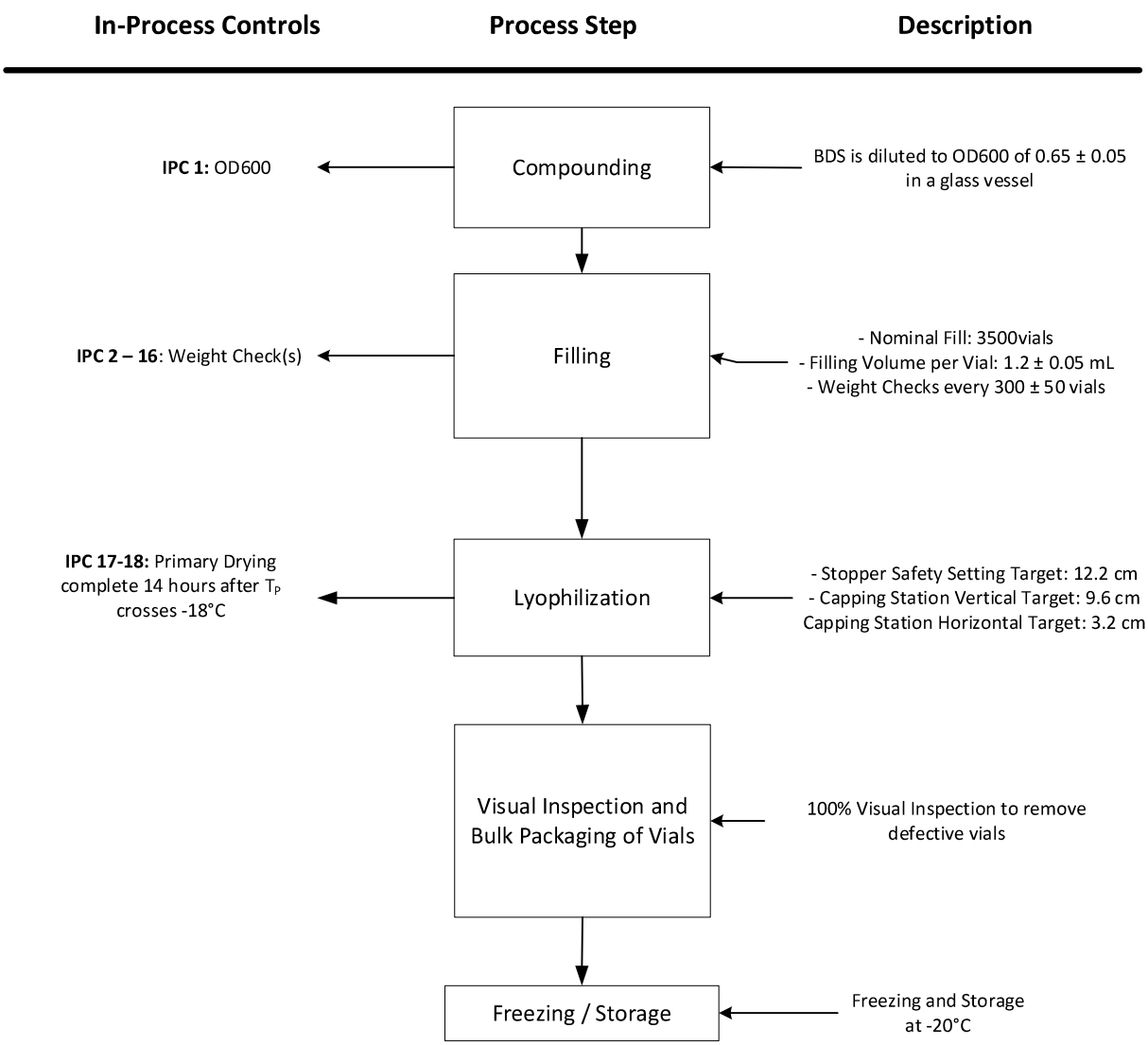

In-Process Controls
Process Step
Description
IPC 1: OD600
Compounding
BDS is diluted to OD600 of 0.65 ± 0.05 in a glass vessel
IPC 2 – 16: Weight Check(s)
Filling
- Nominal Fill: 3500vials
- Filling Volume per Vial: 1.2 ± 0.05 mL
- Weight Checks every 300 ± 50 vials
IPC 17-18: Primary Drying complete 14 hours after $T_P$ crosses -18°C
Lyophilization
- Stopper Safety Setting Target: 12.2 cm
- Capping Station Vertical Target: 9.6 cm
Capping Station Horizontal Target: 3.2 cm
Visual Inspection and Bulk Packaging of Vials
100% Visual Inspection to remove defective vials
Freezing / Storage
Freezing and Storage at -20°C

***FIG. 21***

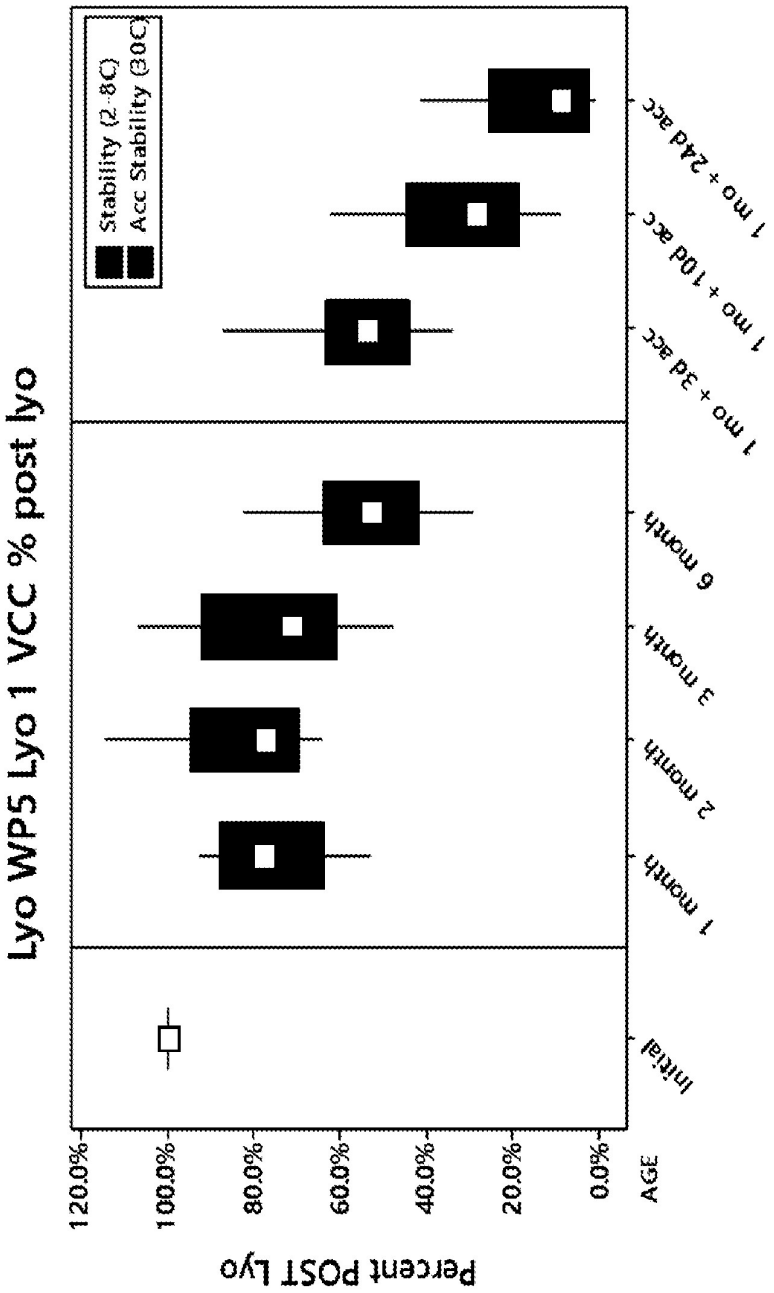

Lyo WP5 Lyo 1 VCC % post lyo
Stability (2-8C)
Acc Stability (30C)
Percent POST Lyo
120.0%
100.0%
80.0%
60.0%
40.0%
20.0%
0.0%
AGE
Initial
1 month
2 month
3 month
6 month
1 mo + 3d acc
1 mo + 10d acc
1 mo + 24d acc

*FIG. 22A*

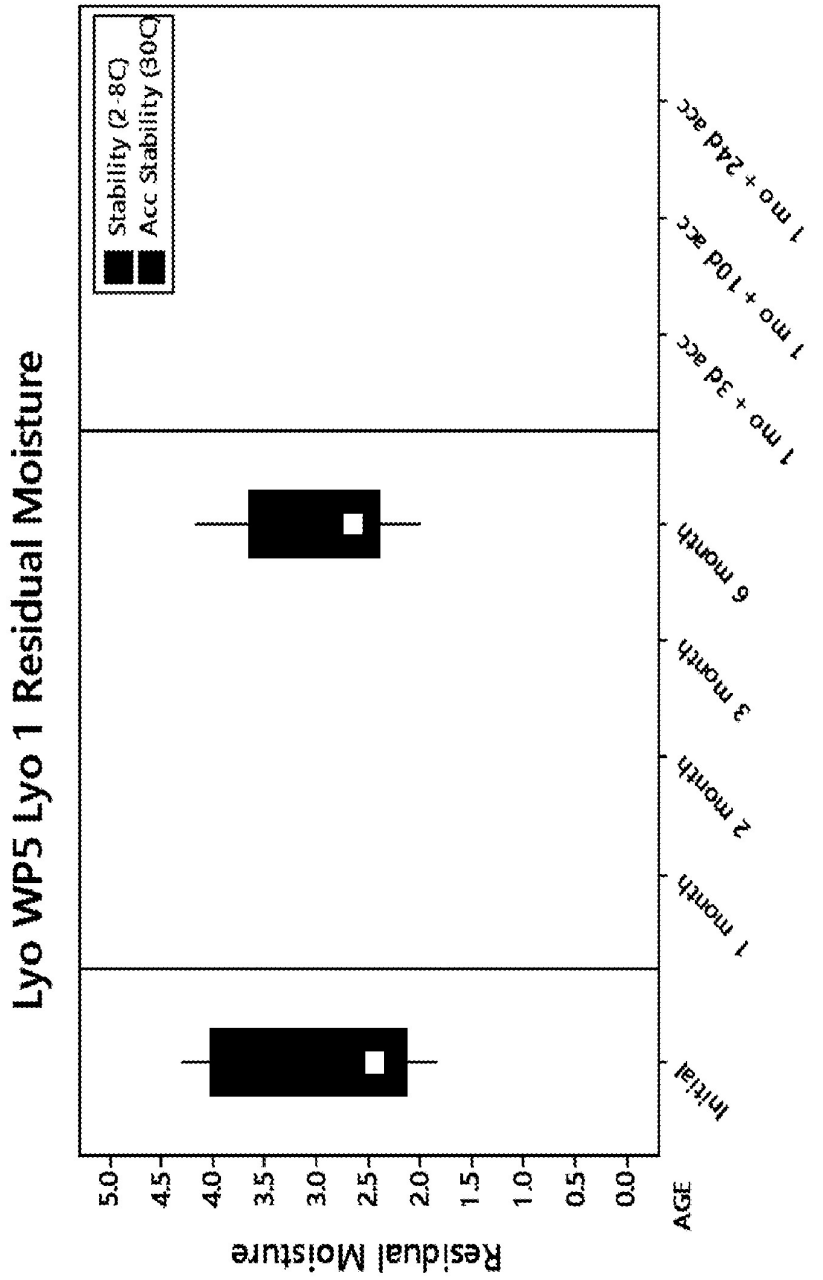

Lyo WP5 Lyo 1 Residual Moisture
Stability (2-8C)
Acc Stability (30C)
Residual Moisture
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
AGE
Initial
1 month
2 month
3 month
6 month
1 mo + 3d acc
1 mo + 10d acc
1 mo + 24d acc

*FIG. 22B*

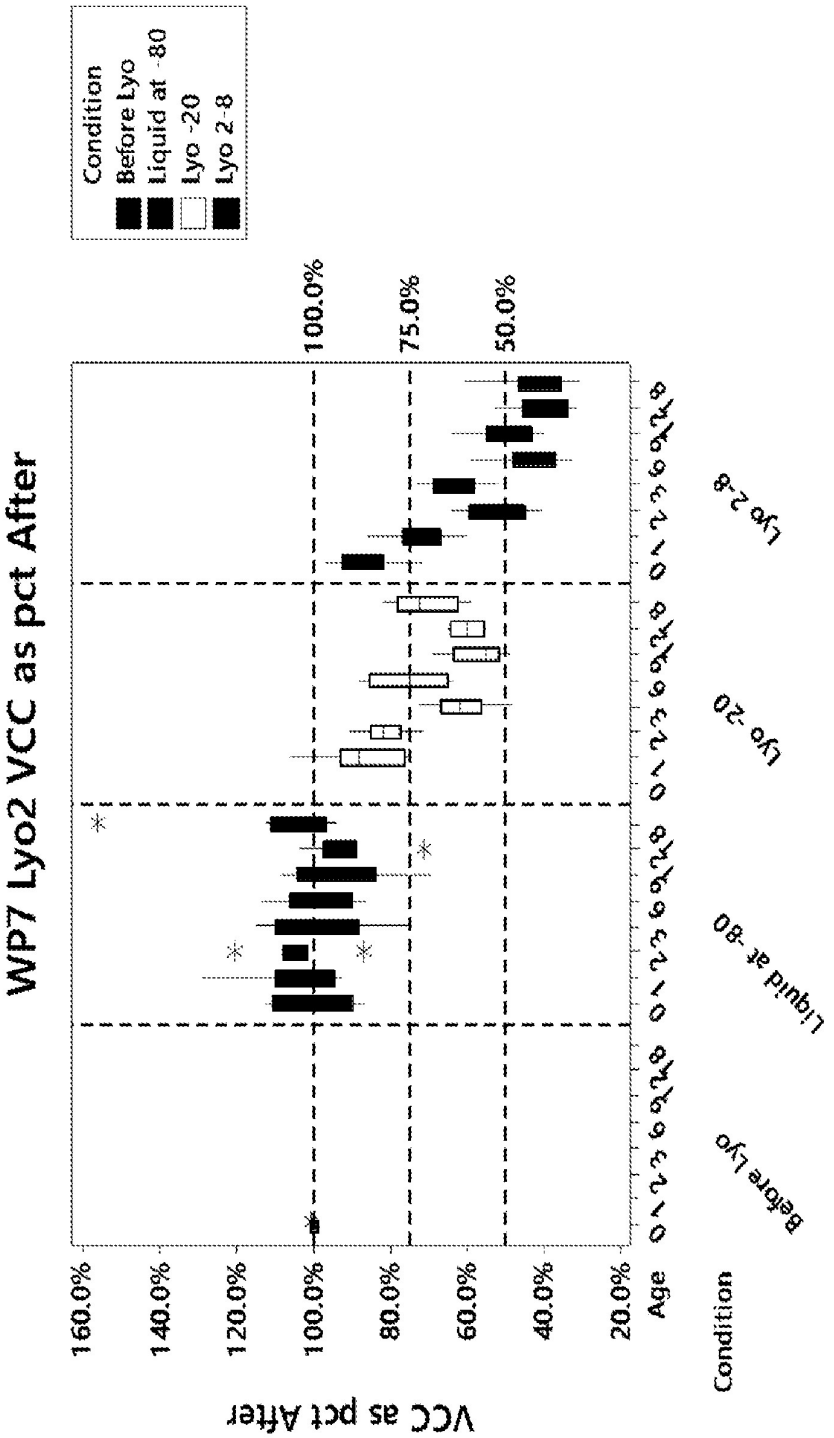

WP7 Lyo2 VCC as pct After
Condition
Before Lyo
Liquid at -80
Lyo -20
Lyo 2-8
100.0%
75.0%
50.0%
VCC as pct After
160.0%
140.0%
120.0%
100.0%
80.0%
60.0%
40.0%
20.0%
Age
0 1 2 3 6 9 12 16
Condition
Before Lyo
Liquid at -80
Lyo -20
Lyo 2-8

*FIG. 23A*

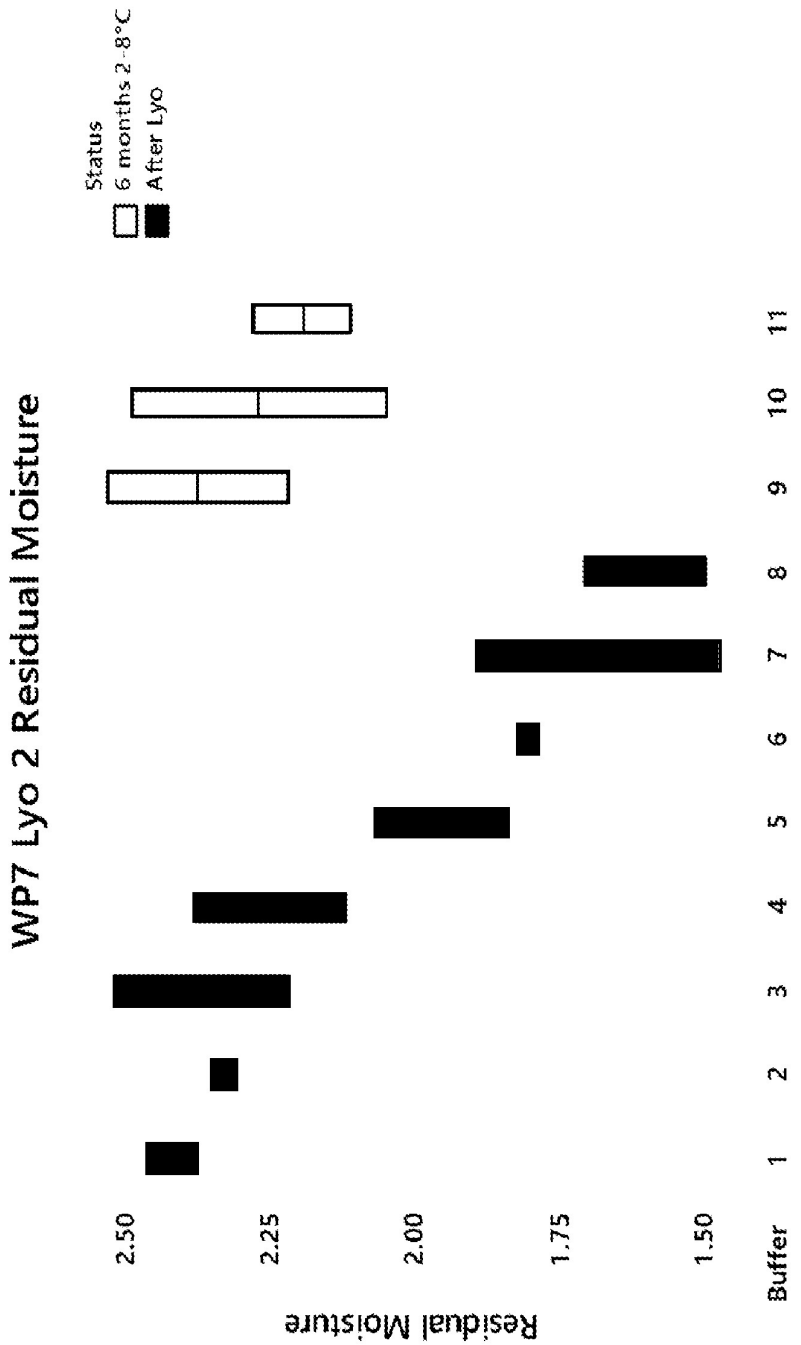

WP7 Lyo 2 Residual Moisture
Status
6 months 2-8°C
After Lyo
Residual Moisture
2.50
2.25
2.00
1.75
1.50
Buffer
1
2
3
4
5
6
7
8
9
10
11

*FIG. 23B*

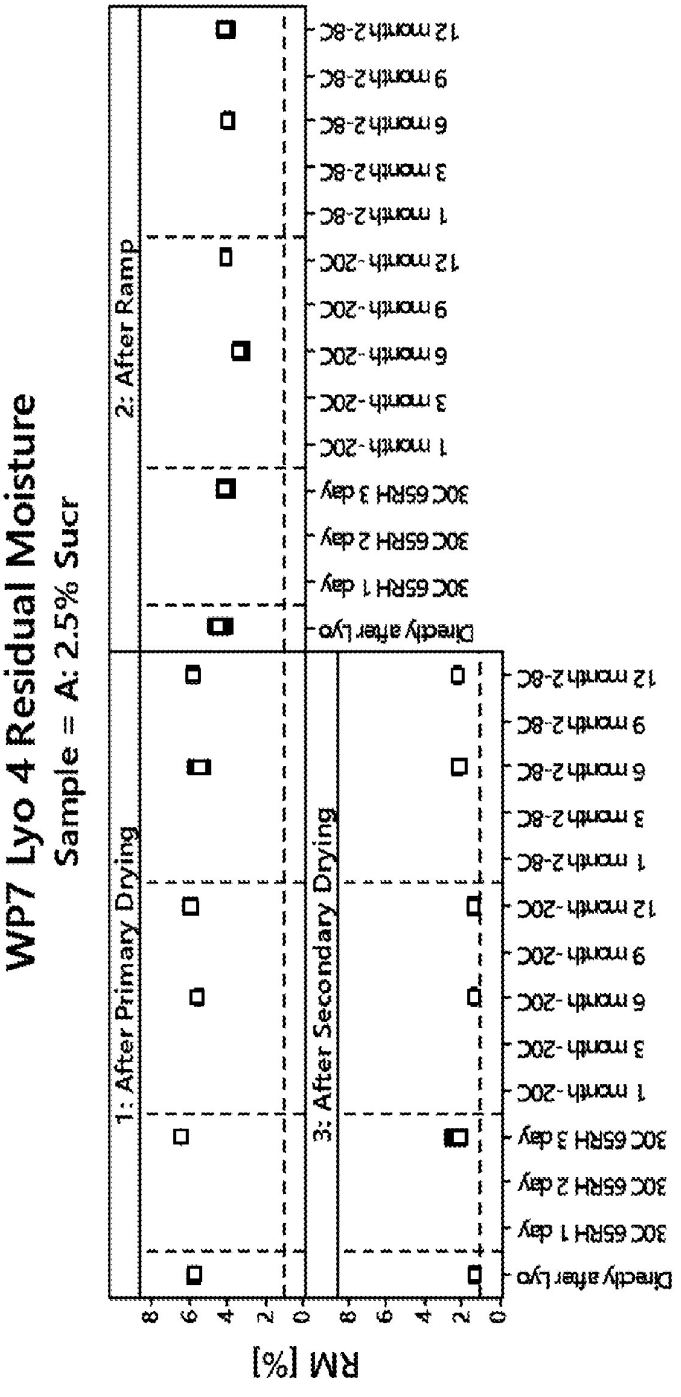

WP7 Lyo 4 Residual Moisture
Sample = A: 2.5% Sucr
1: After Primary Drying
2: After Ramp
3: After Secondary Drying
RM [%]
0
2
4
6
8
Directly after Lyo
30C 65RH 1 day
30C 65RH 2 day
30C 65RH 3 day
1 month -20C
3 month -20C
6 month -20C
9 month -20C
12 month -20C
1 month 2-8C
3 month 2-8C
6 month 2-8C
9 month 2-8C
12 month 2-8C
VCC condition
Panel variable: Phase in Lyo Cycle

*FIG. 24A*

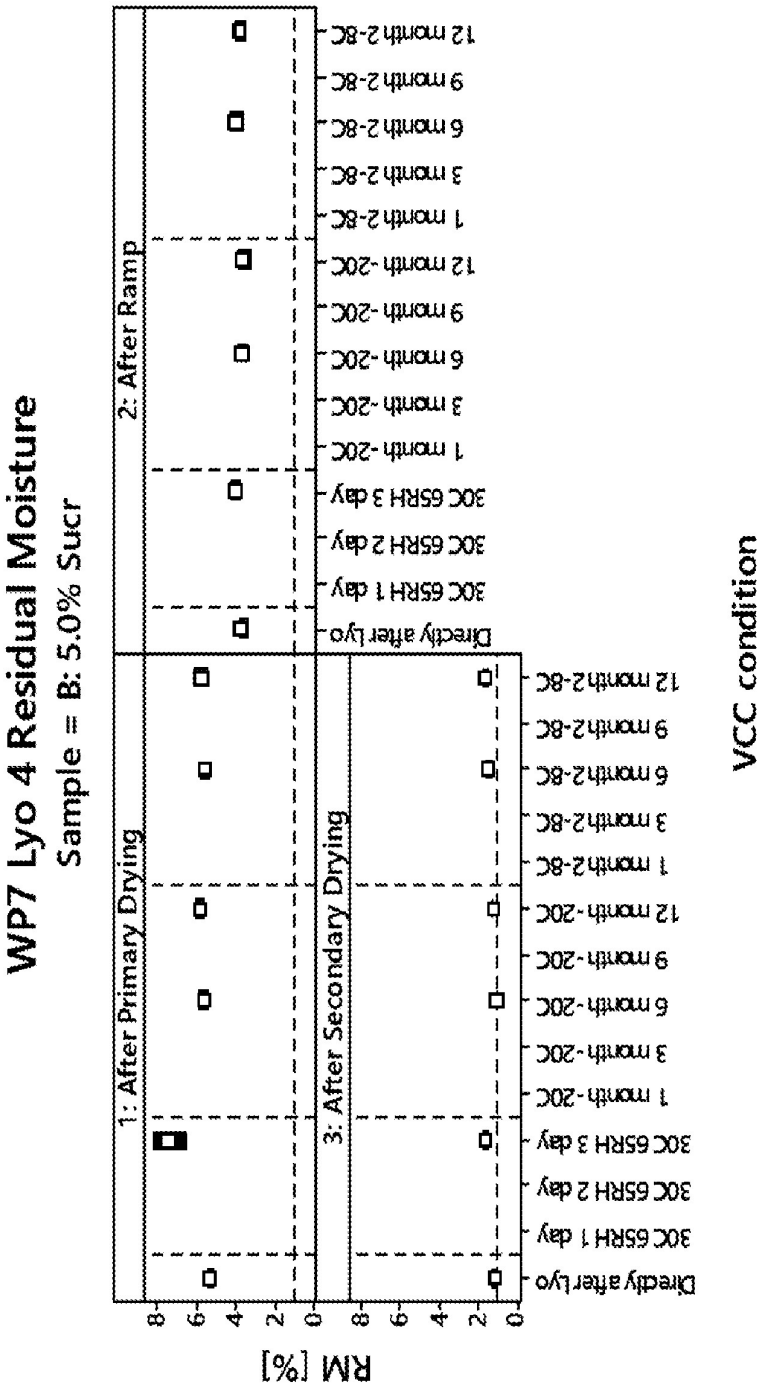

WP7 Lyo 4 Residual Moisture
Sample = B: 5.0% Sucr
1: After Primary Drying
2: After Ramp
3: After Secondary Drying
RM [%]
0
2
4
6
8
Directly after Lyo
30C 65RH 1 day
30C 65RH 2 day
30C 65RH 3 day
1 month -20C
3 month -20C
6 month -20C
9 month -20C
12 month -20C
1 month 2-8C
3 month 2-8C
6 month 2-8C
9 month 2-8C
12 month 2-8C
VCC condition
Panel variable: Phase in Lyo Cycle

***FIG. 24B***

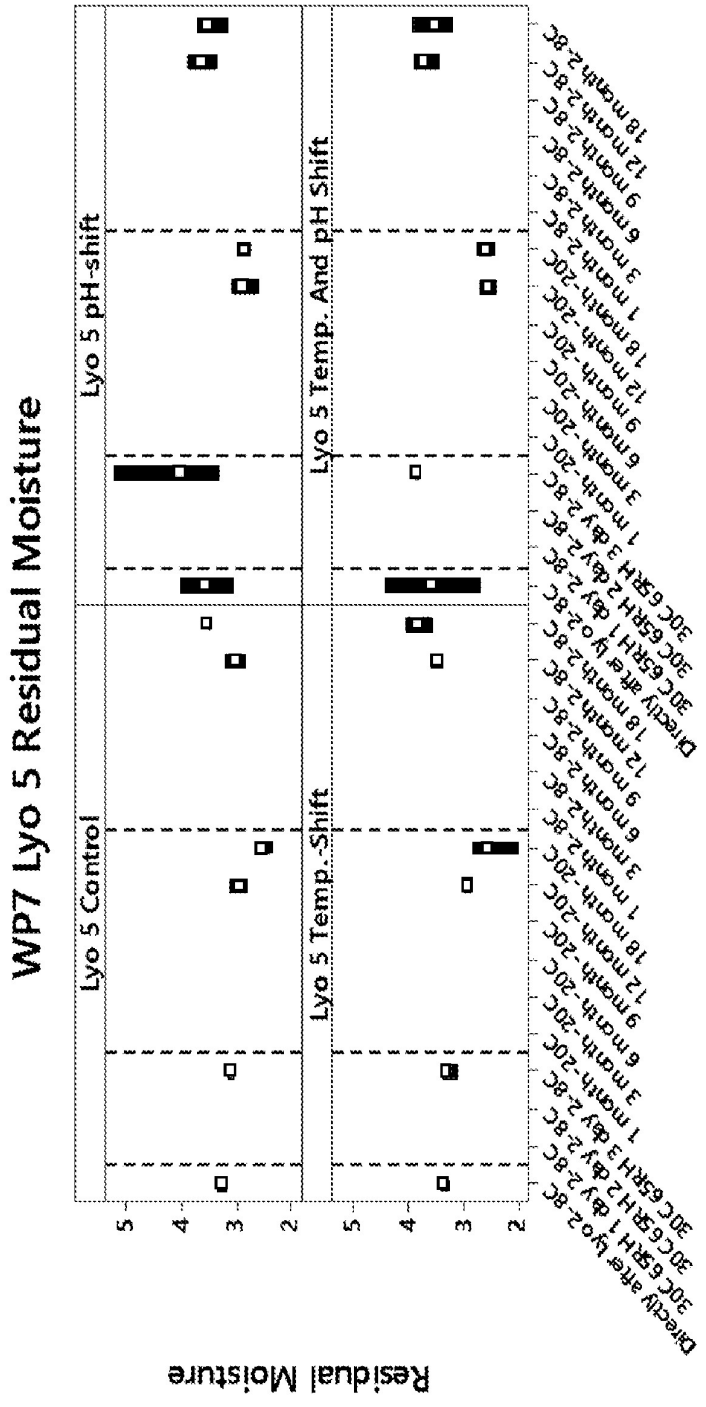

WP7 Lyo 5 Residual Moisture
Lyo 5 Control
Lyo 5 pH-shift
Lyo 5 Temp.-Shift
Lyo 5 Temp. And pH Shift
Residual Moisture
5
4
3
2
Directly after lyo 2-8C
30C 65RH 1 day 2-8C
30C 65RH 2 day 2-8C
30C 65RH 3 day 2-8C
1 month-20C
3 month-20C
6 month-20C
9 month-20C
12 month-20C
18 month-20C
1 month 2-8C
3 month 2-8C
6 month 2-8C
9 month 2-8C
12 month 2-8C
18 month 2-8C
VCC condition
Panel variable: Study Condition

*FIG. 25*

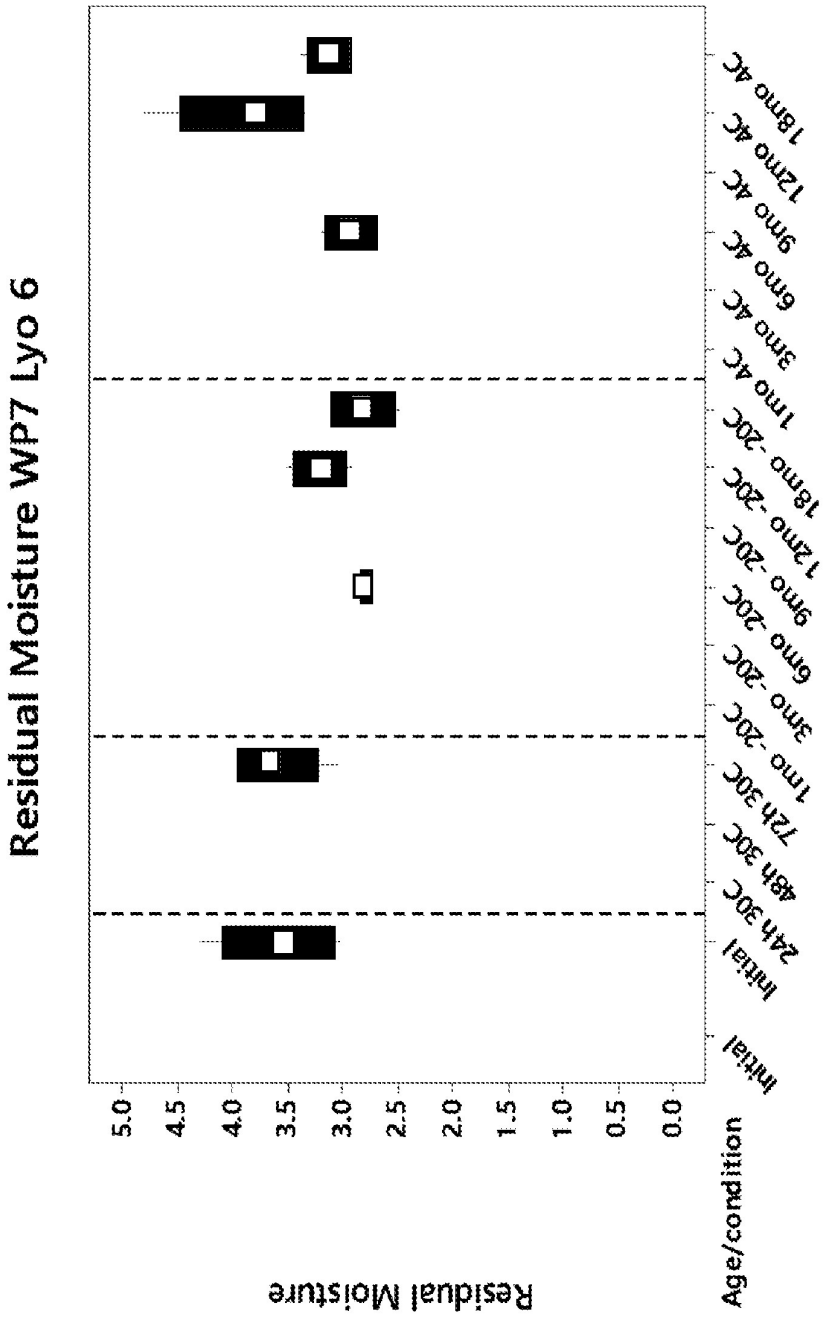

Residual Moisture WP7 Lyo 6
Residual Moisture
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Age/condition
Initial
Initial
24h 30C
48h 30C
72h 30C
1mo -20C
3mo -20C
6mo -20C
9mo -20C
12mo -20C
18mo -20C
1mo 4C
3mo 4C
6mo 4C
9mo 4C
12mo 4C
18mo 4C

*FIG. 26*

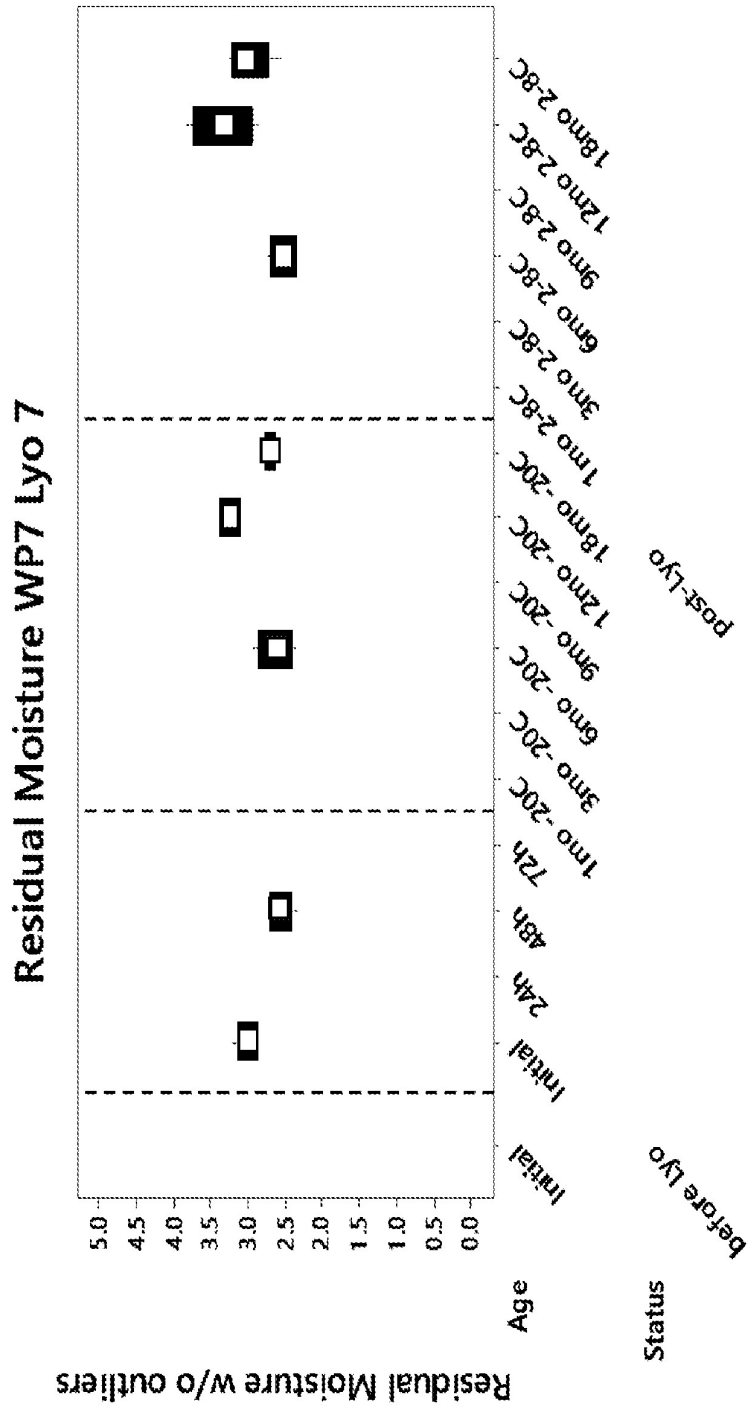

Residual Moisture WP7 Lyo 7
Residual Moisture w/o outliers
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Age
Status
Initial
Initial
2h
48h
72h
1mo -20C
3mo -20C
6mo -20C
9mo -20C
12mo -20C
18mo -20C
1mo 2-8C
3mo 2-8C
6mo 2-8C
9mo 2-8C
12mo 2-8C
18mo 2-8C
before Lyo
post-Lyo

*FIG. 27*

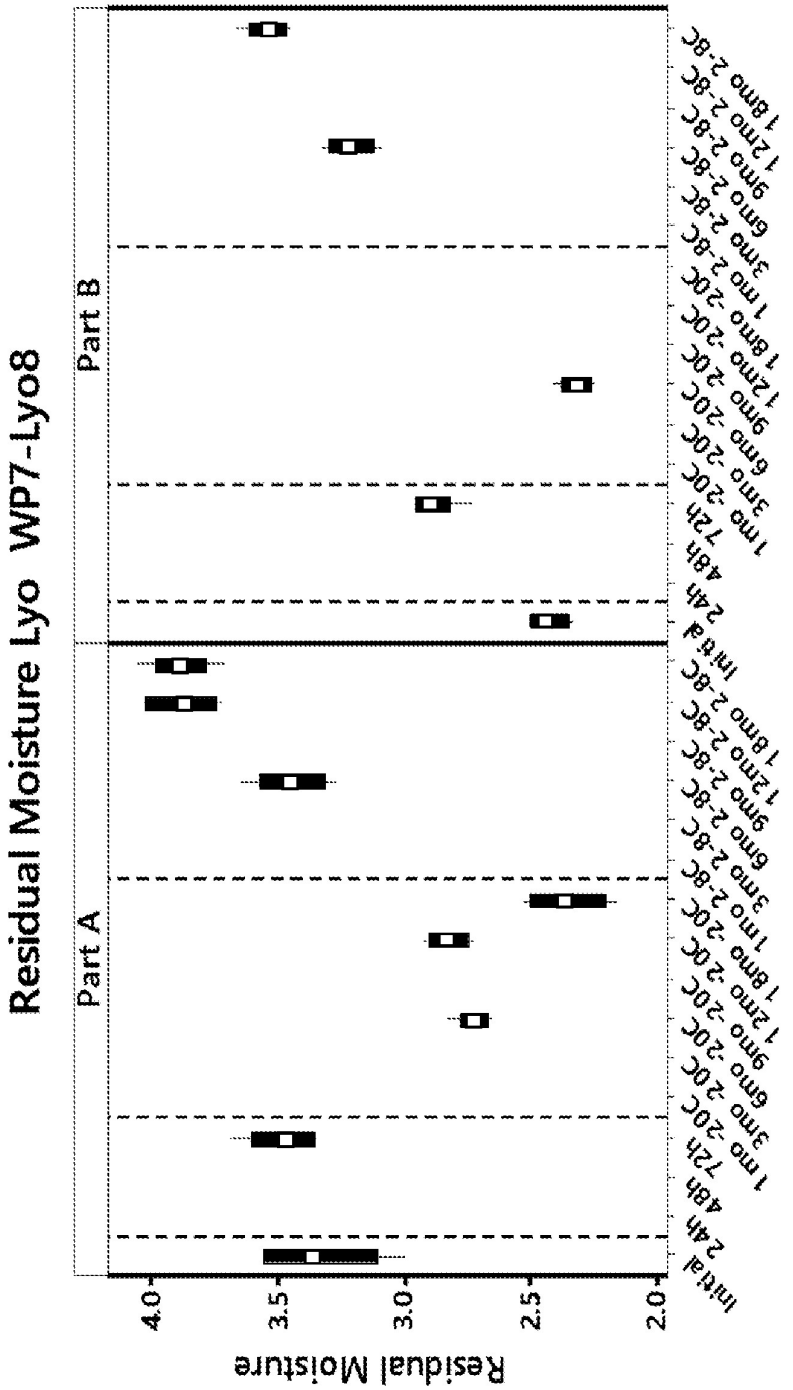

Residual Moisture Lyo WP7-Lyo8
Part A
Part B
Residual Moisture
4.0
3.5
3.0
2.5
2.0
Initial
2 h
48 h
72 h
1 mo -20C
3 mo -20C
6 mo -20C
9 mo -20C
12 mo -20C
18 mo -20C
1 mo 2-8C
3 mo 2-8C
6 mo 2-8C
9 mo 2-8C
12 mo 2-8C
18 mo 2-8C
Age

*FIG. 28*

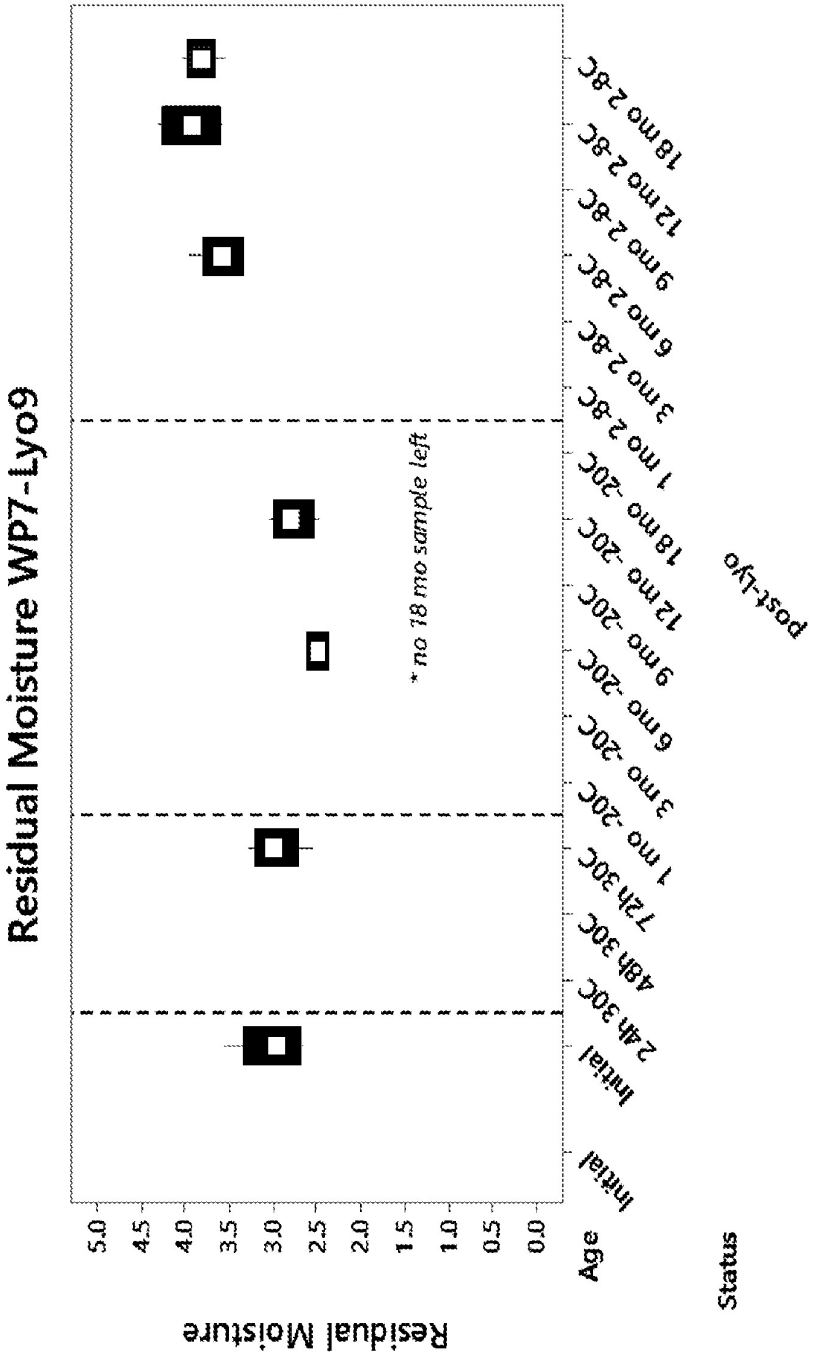

Residual Moisture WP7-Lyo9
Residual Moisture
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Age
Status
Initial
Initial
2.4h 30C
4.8h 30C
7.2h 30C
1 mo -20C
3 mo -20C
6 mo -20C
9 mo -20C
12 mo -20C
18 mo -20C
1 mo 2-8C
3 mo 2-8C
6 mo 2-8C
9 mo 2-8C
12 mo 2-8C
18 mo 2-8C
post-lyo
* no 18 mo sample left

*FIG. 29*

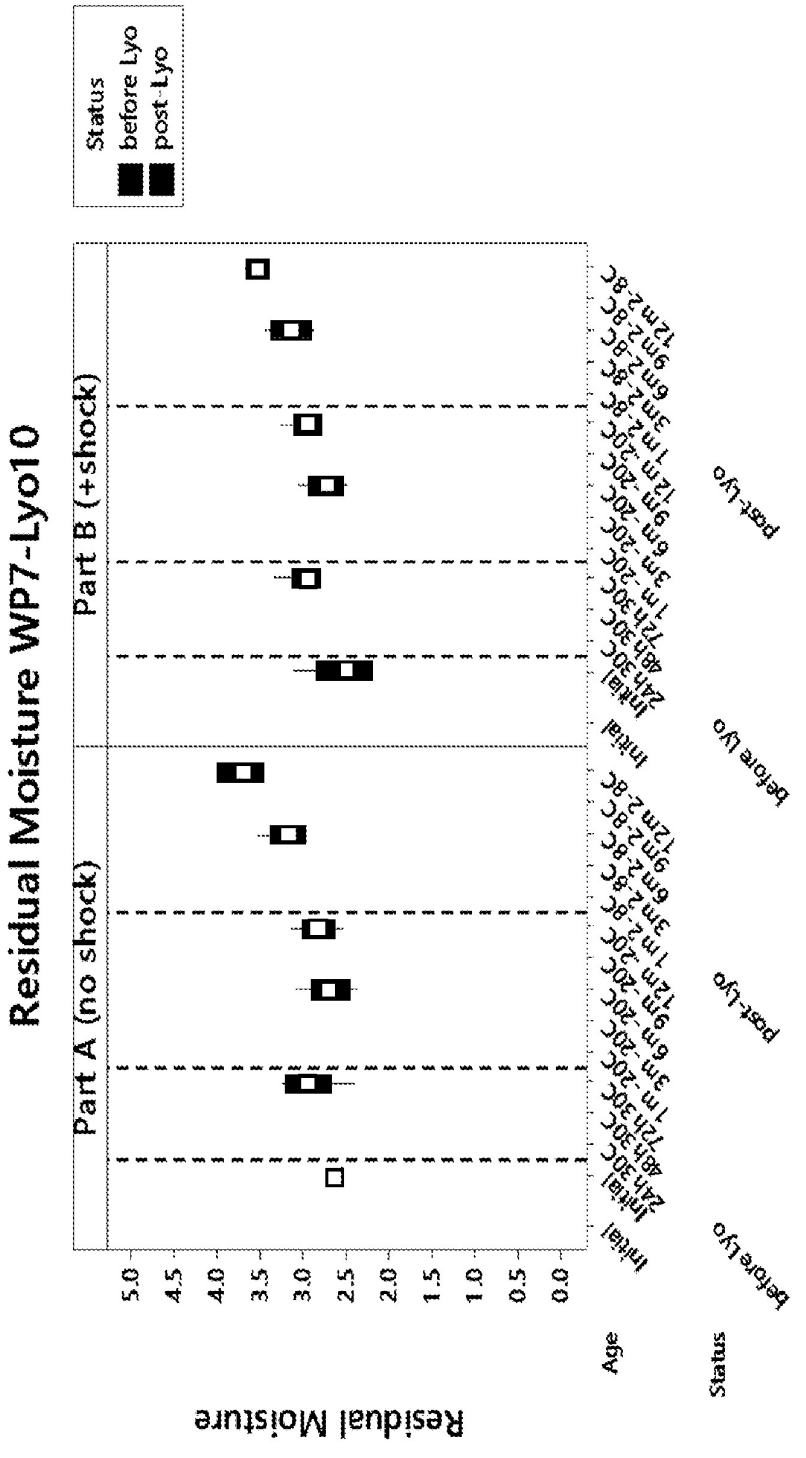

Residual Moisture WP7-Lyo10
Part A (no shock)
Part B (+shock)
Status
before Lyo
post-Lyo
Residual Moisture
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Age
Status
Panel variable: Treatment

*FIG. 30*

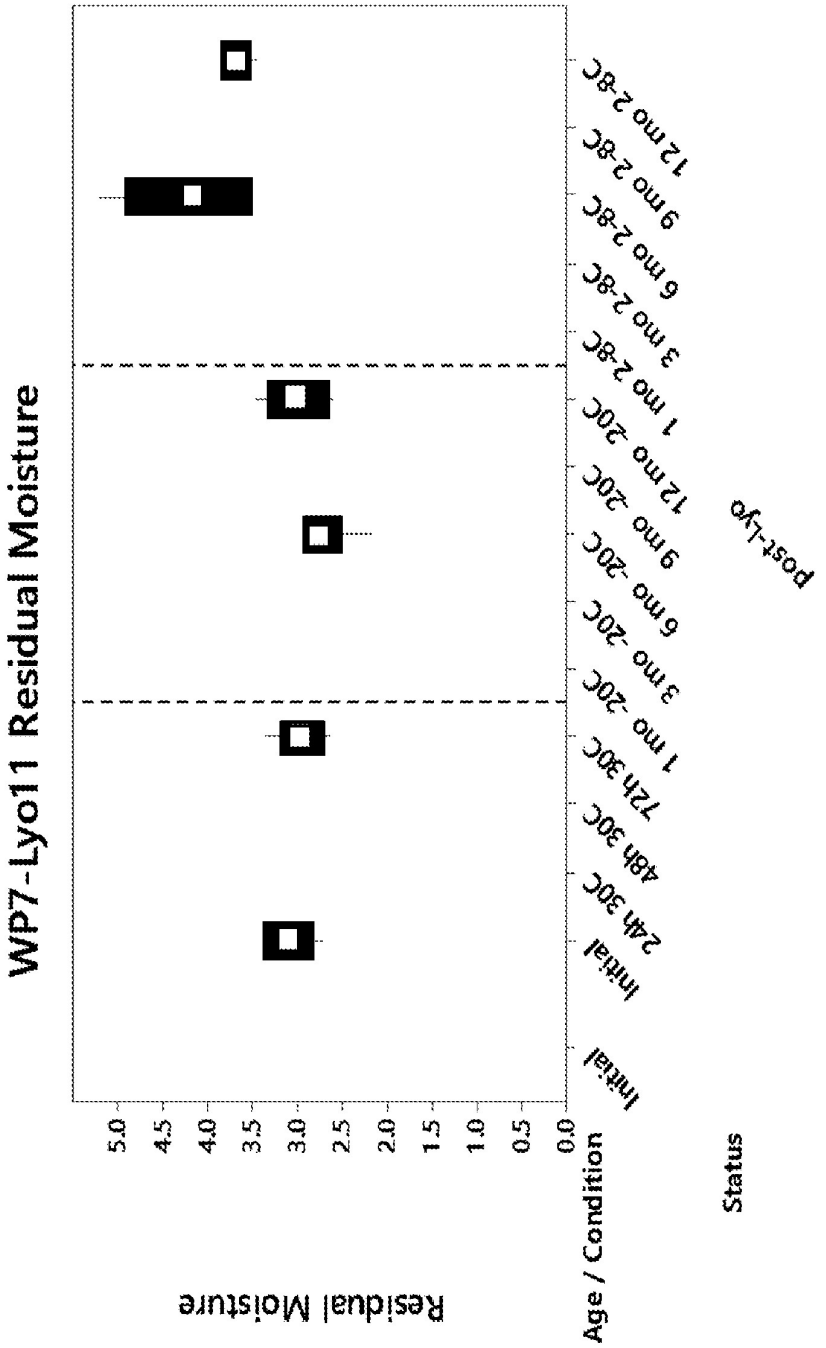

WP7-Lyo11 Residual Moisture
Residual Moisture
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Age / Condition
Initial
Initial
2Ah 30C
4Bh 30C
72h 30C
1 mo -20C
3 mo -20C
6 mo -20C
9 mo -20C
12 mo -20C
1 mo 2-8C
3 mo 2-8C
6 mo 2-8C
9 mo 2-8C
12 mo 2-8C
Status
post-Lyo

*FIG. 31*

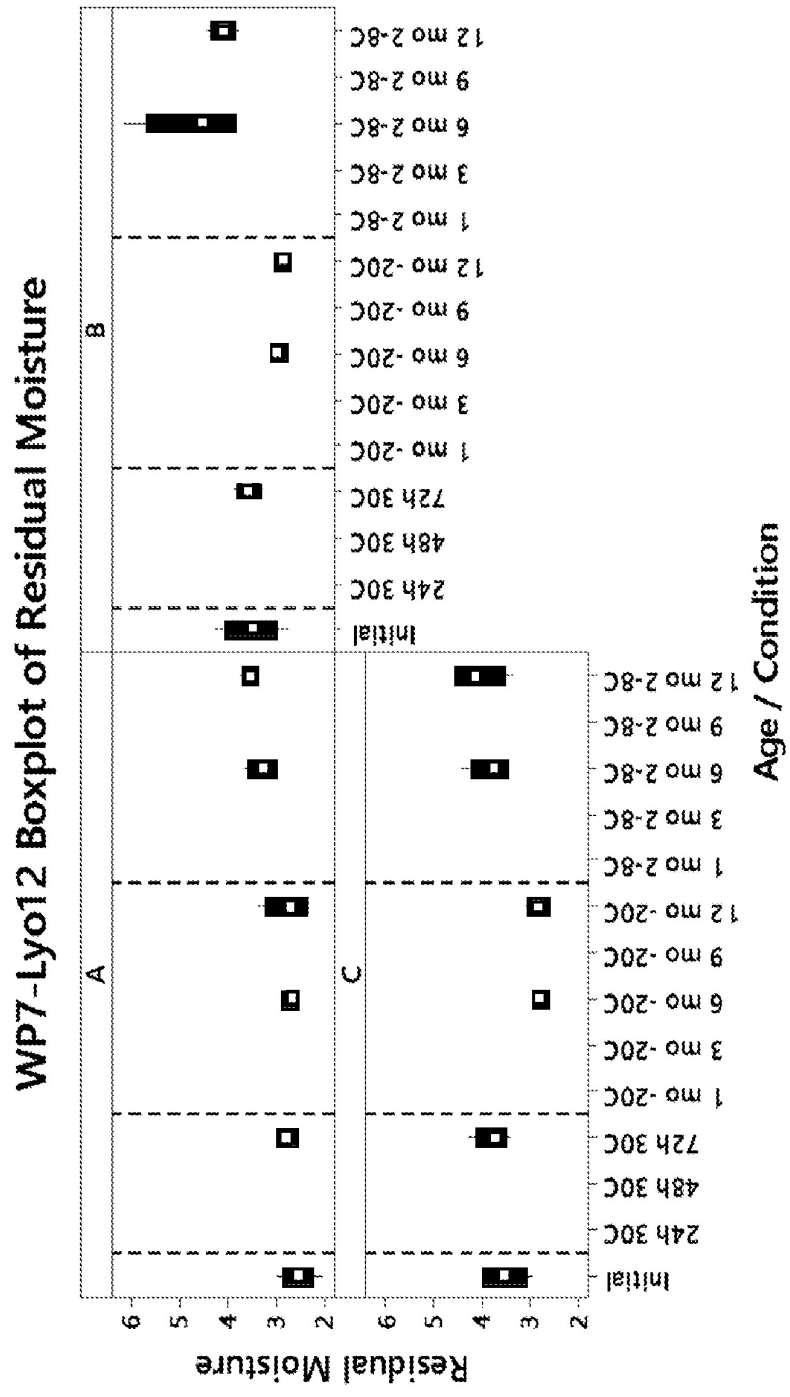

WP7-Lyo12 Boxplot of Residual Moisture
Residual Moisture
Age / Condition
Panel variable: PART
A
B
C
Initial
24h 30C
48h 30C
72h 30C
1 mo -20C
3 mo -20C
6 mo -20C
9 mo -20C
12 mo -20C
1 mo 2-8C
3 mo 2-8C
6 mo 2-8C
9 mo 2-8C
12 mo 2-8C

*FIG. 32*

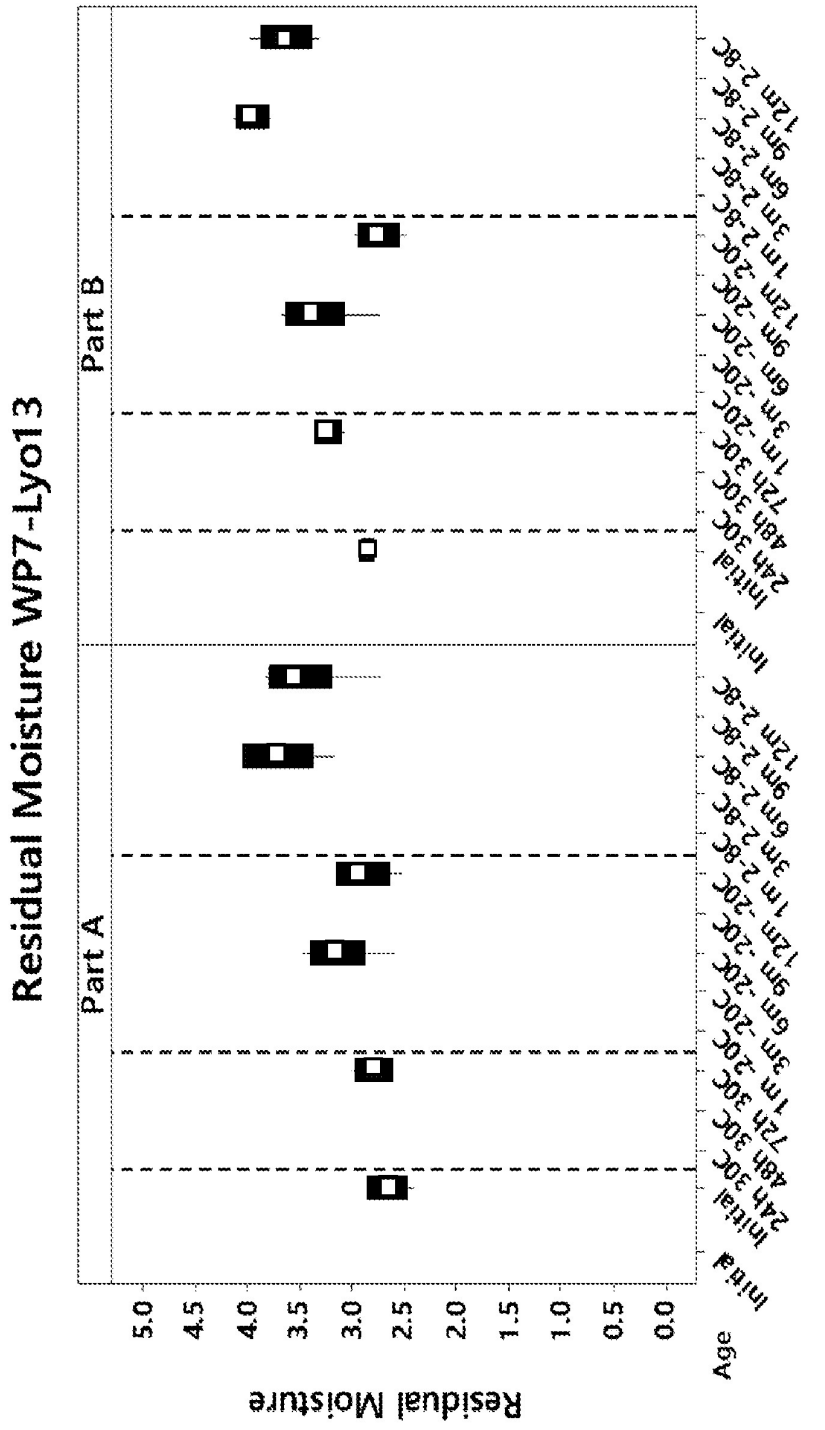

Residual Moisture WP7-Lyo13
Part A
Part B
Residual Moisture
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Age
Initial
Initial 30C 24h
Initial 30C 48h
Initial 30C 72h
Initial 30C 1m
Initial -20C 3m
Initial -20C 6m
Initial -20C 9m
Initial -20C 12m
Initial 2-8C 1m
Initial 2-8C 3m
Initial 2-8C 6m
Initial 2-8C 9m
Initial 2-8C 12m
Panel variable: Treatment

*FIG. 33*

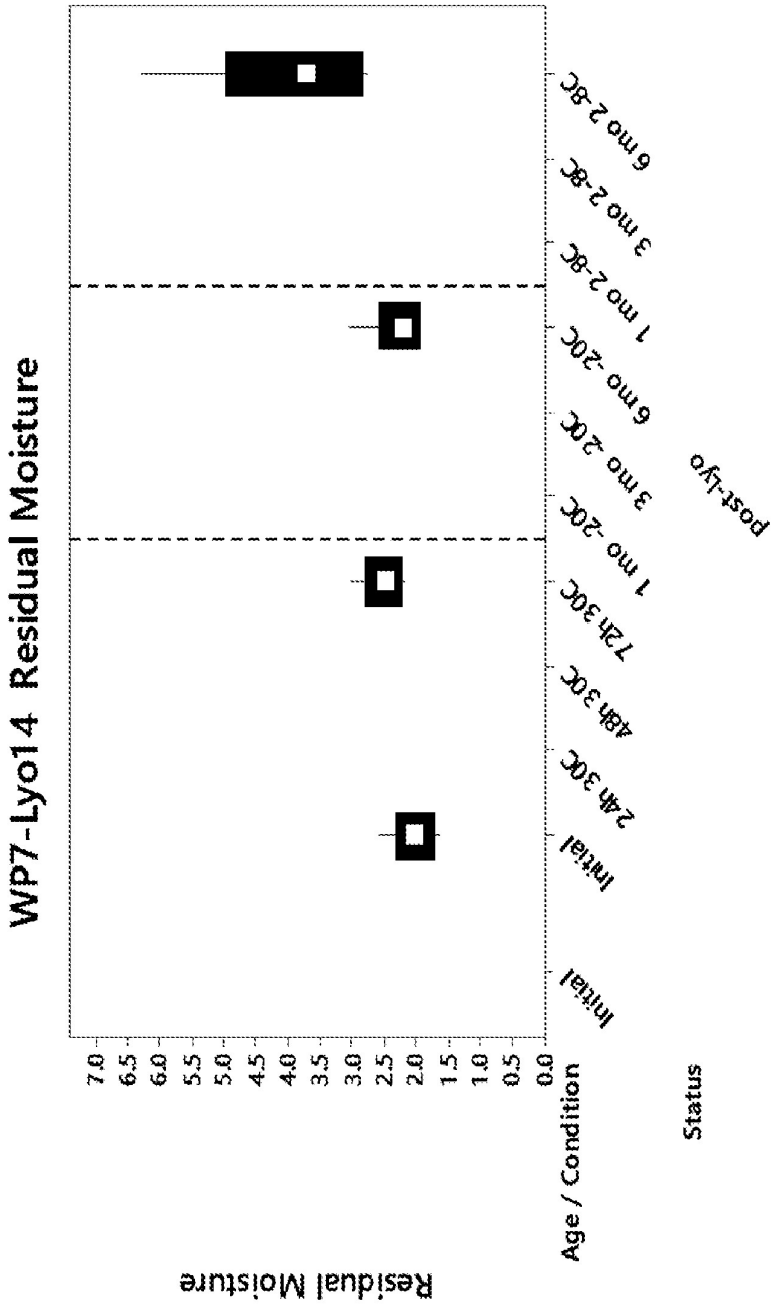

WP7-Lyo14 Residual Moisture
Residual Moisture
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Initial
Initial
2Ah 3oC
4Ah 3oC
72h 3oC
1 mo -20C
3 mo -20C
6 mo -20C
1 mo 2-8C
3 mo 2-8C
6 mo 2-8C
Age / Condition
post-lyo
Status

*FIG. 34*

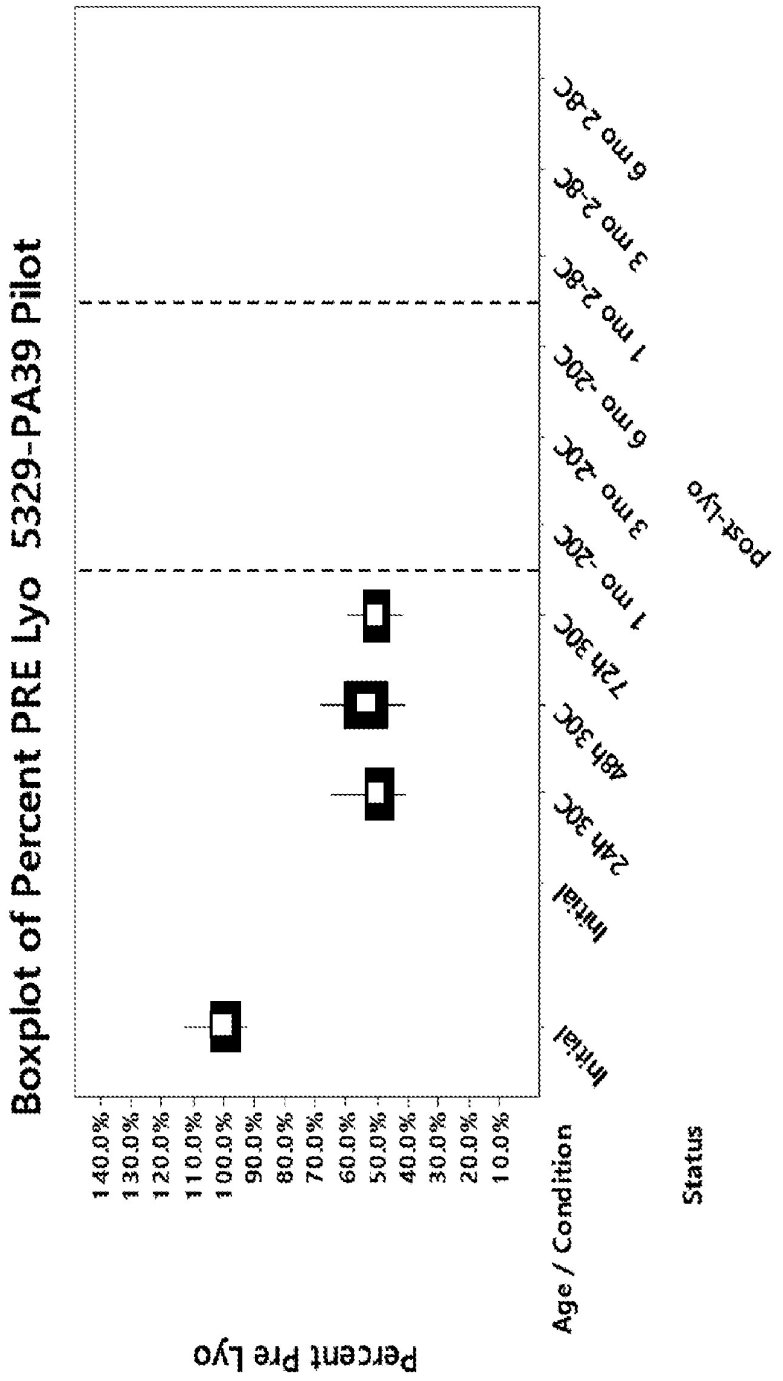

Boxplot of Percent PRE Lyo 5329-PA39 Pilot
Percent Pre Lyo
140.0%
130.0%
120.0%
110.0%
100.0%
90.0%
80.0%
70.0%
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
Age / Condition
Initial
Initial
2Ah 30C
48h 30C
72h 30C
1 mo -20C
3 mo -20C
6 mo -20C
1 mo 2-8C
3 mo 2-8C
6 mo 2-8C
Status
post-Lyo

*FIG. 35*

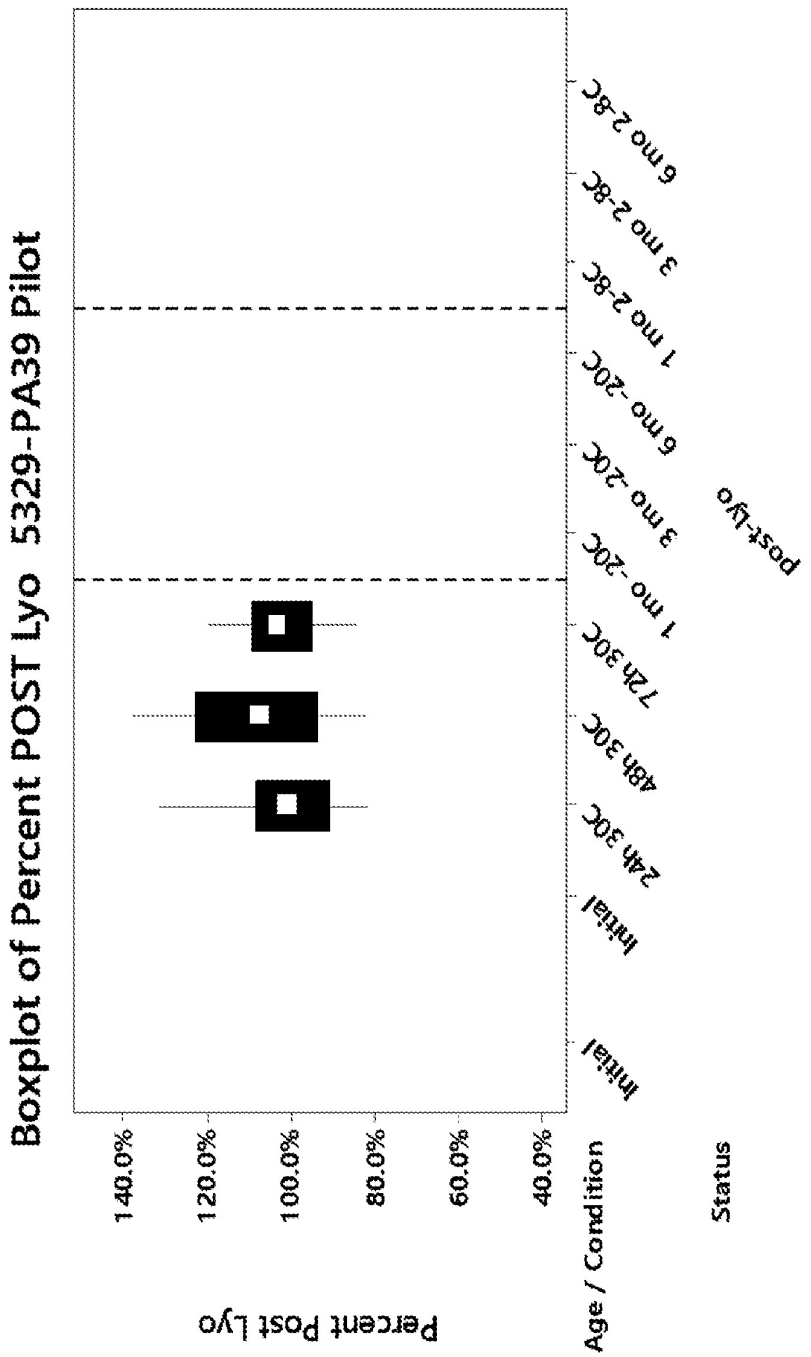

Boxplot of Percent POST Lyo 5329-PA39 Pilot
Percent Post Lyo
140.0%
120.0%
100.0%
80.0%
60.0%
40.0%
Age / Condition
Initial
Initial
2Ah 30C
48h 30C
72h 30C
1 mo -20C
3 mo -20C
6 mo -20C
1 mo 2-8C
3 mo 2-8C
6 mo 2-8C
Status
post-Lyo

*FIG. 36*

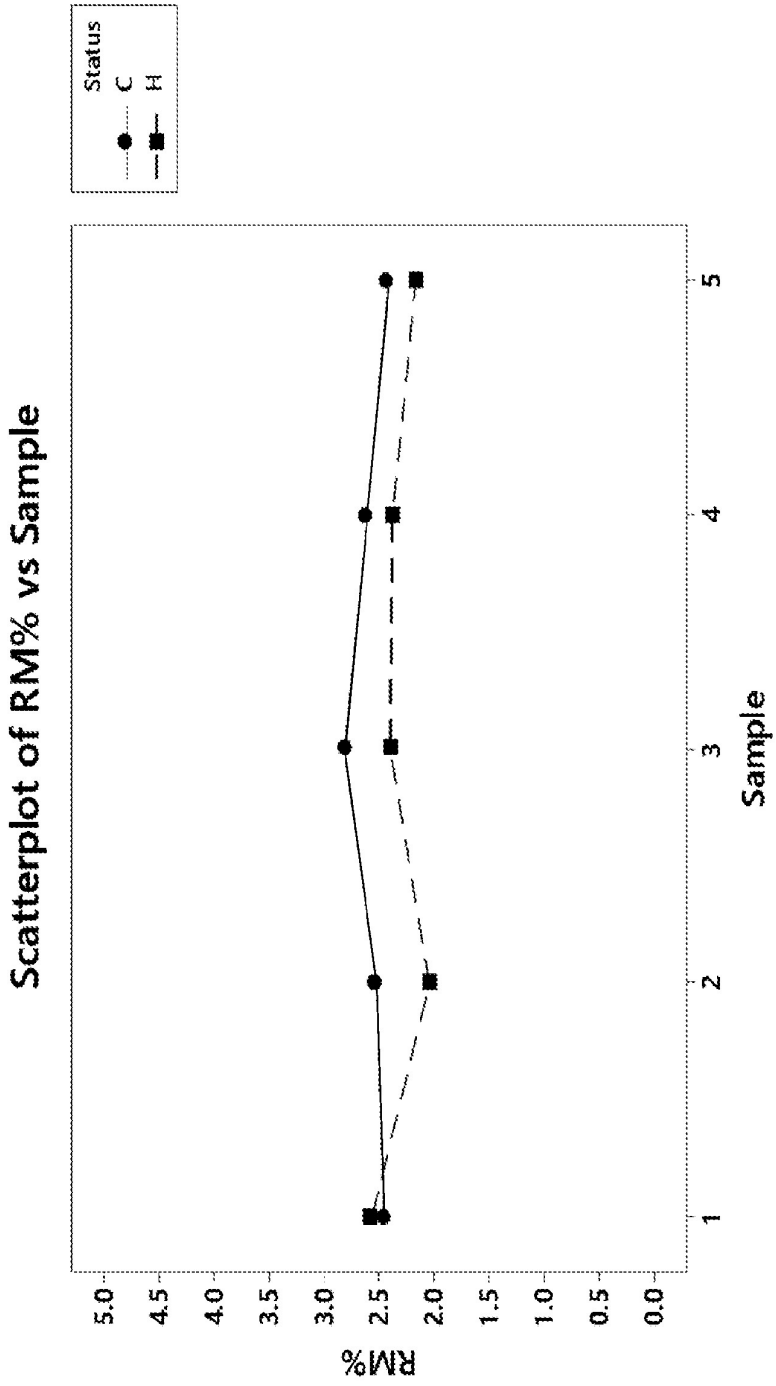

Scatterplot of RM% vs Sample
Status
C
H
RM%
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1
2
3
4
5
Sample

*FIG. 37*

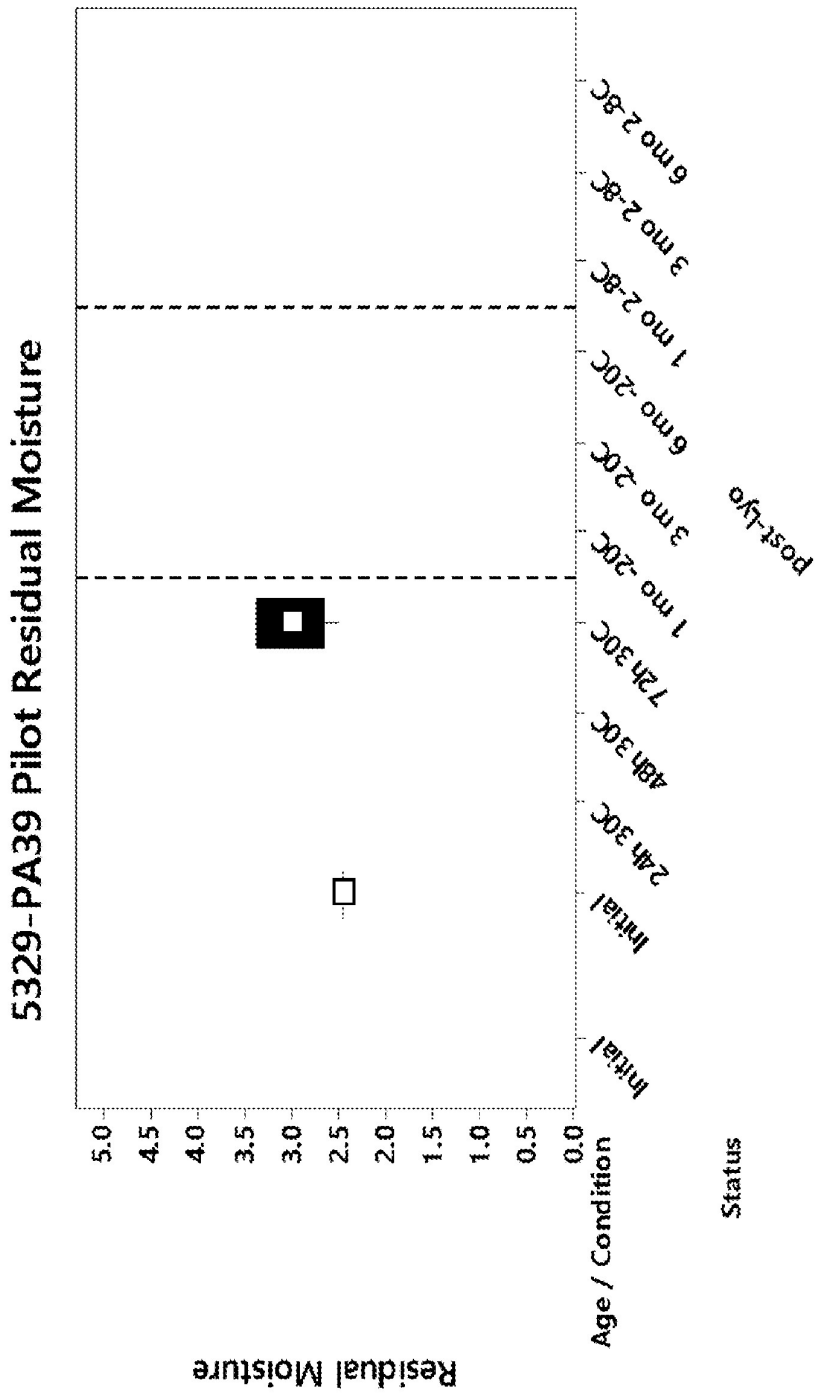

5329-PA39 Pilot Residual Moisture
Residual Moisture
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Age / Condition
Initial
Initial
2dh 30C
4dh 30C
72h 30C
1 mo -20C
3 mo -20C
6mo -20C
1 mo 2-8C
3 mo 2-8C
6 mo 2-8C
Status
post-lyo

*FIG. 38*

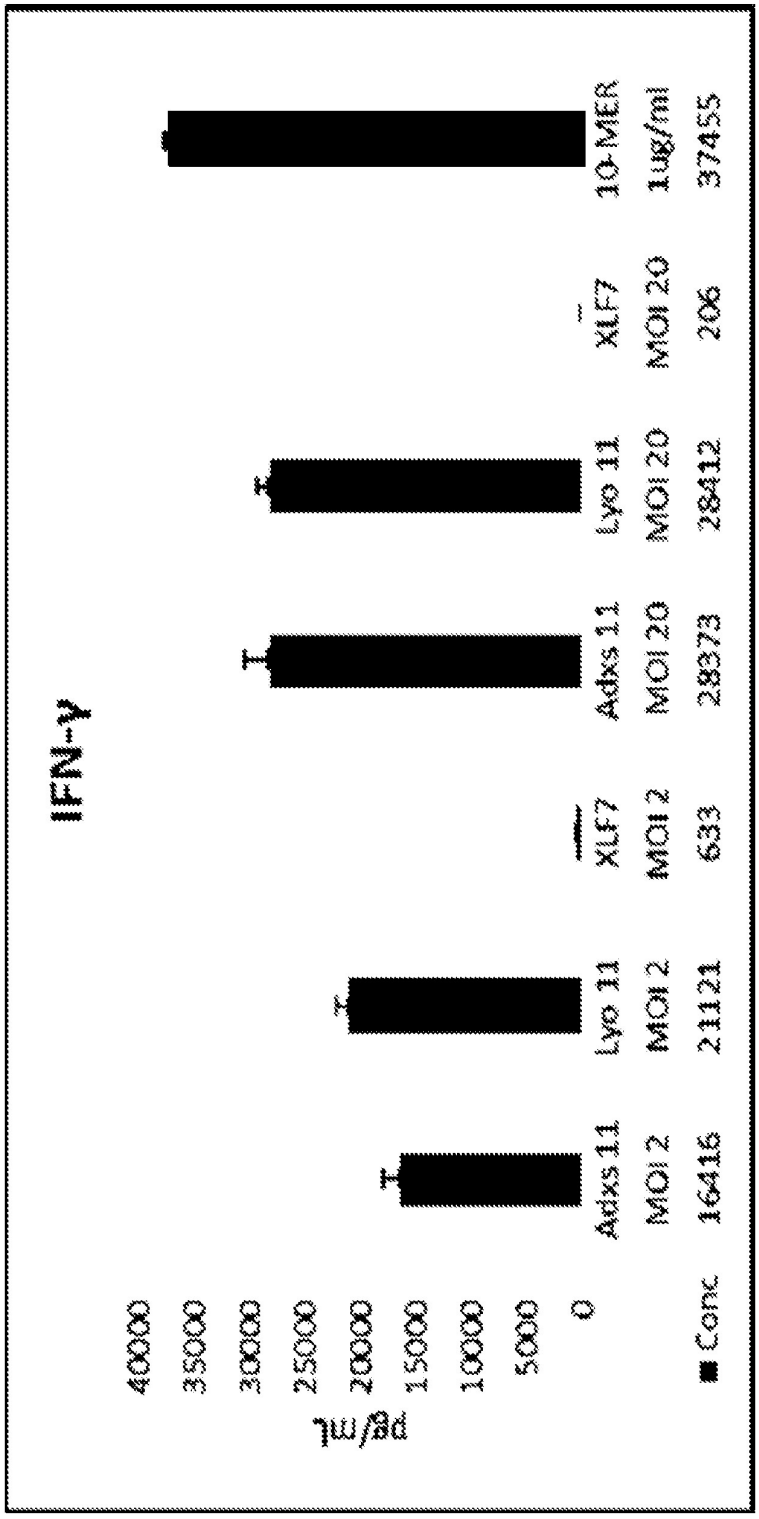

IFN-γ
pg/mL
40000
35000
30000
25000
20000
15000
10000
5000
0
Conc
Adxs 11
MOI 2
16416
Lyo 11
MOI 2
21121
XLF7
MOI 2
633
Adxs 11
MOI 20
29373
Lyo 11
MOI 20
28412
XLF7
MOI 20
206
10-MER
1ug/ml
37455

*FIG. 39*

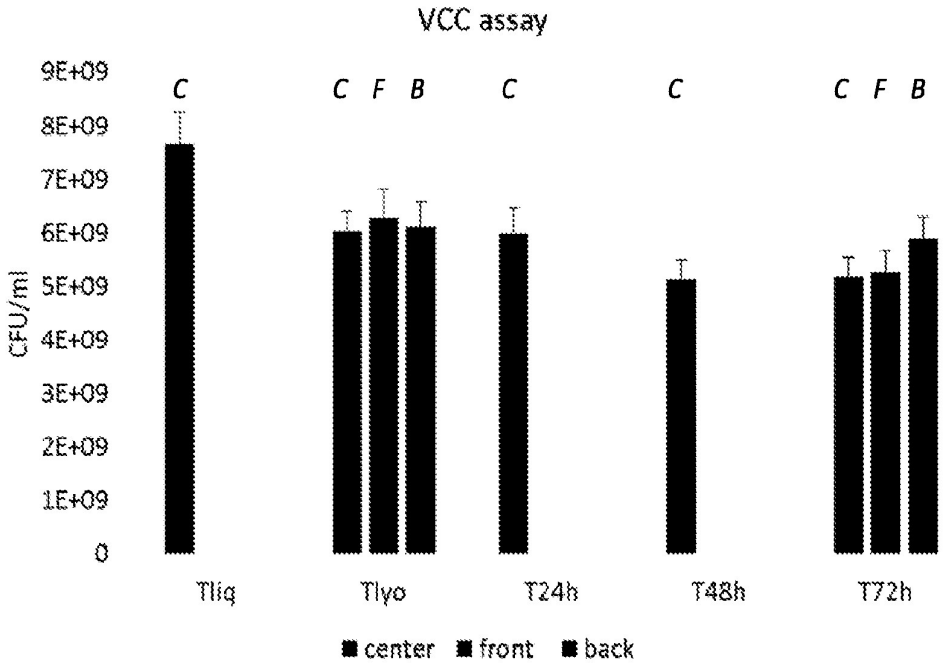



*FIG. 40A*

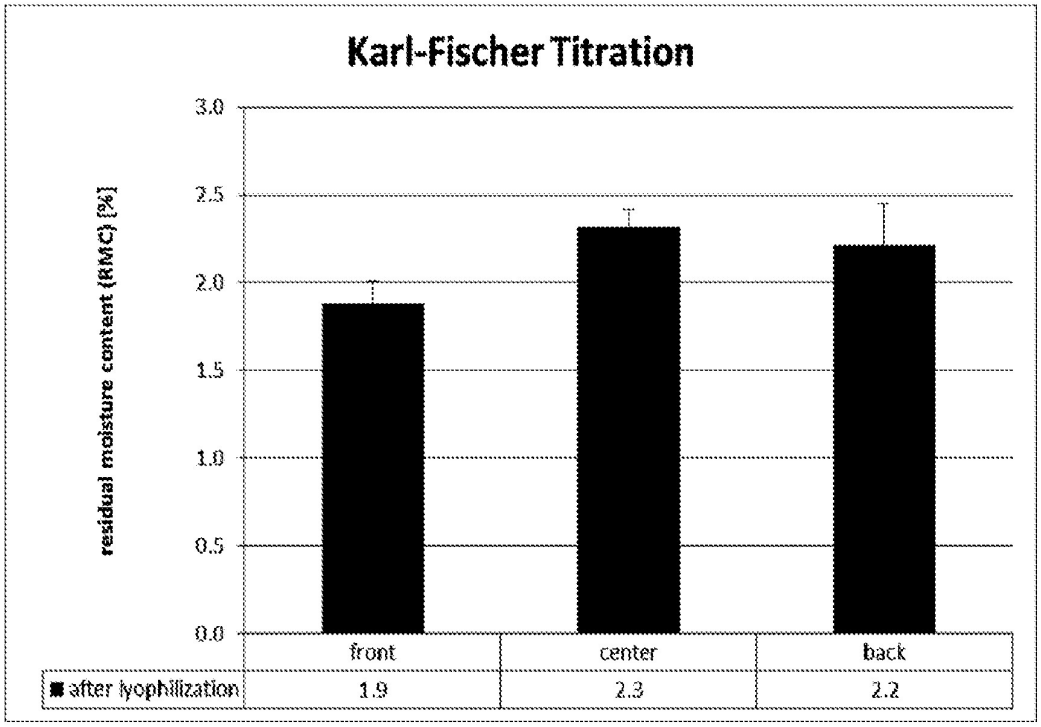



*FIG. 40B*

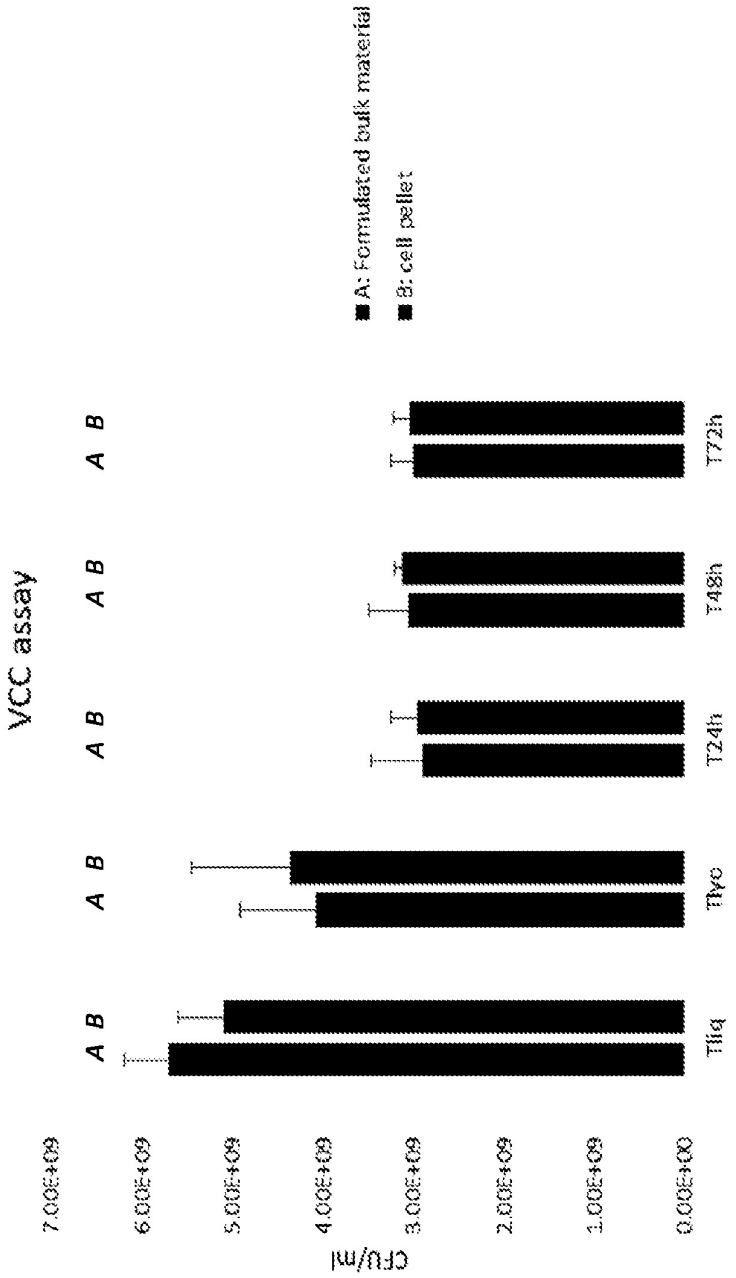

VCC assay
A: Formulated bulk material
B: cell pellet
CFU/ml
7.00E+09
6.00E+09
5.00E+09
4.00E+09
3.00E+09
2.00E+09
1.00E+09
0.00E+00
A B
Tliq
Tlyo
T24h
T48h
T72h

FIG. 41A

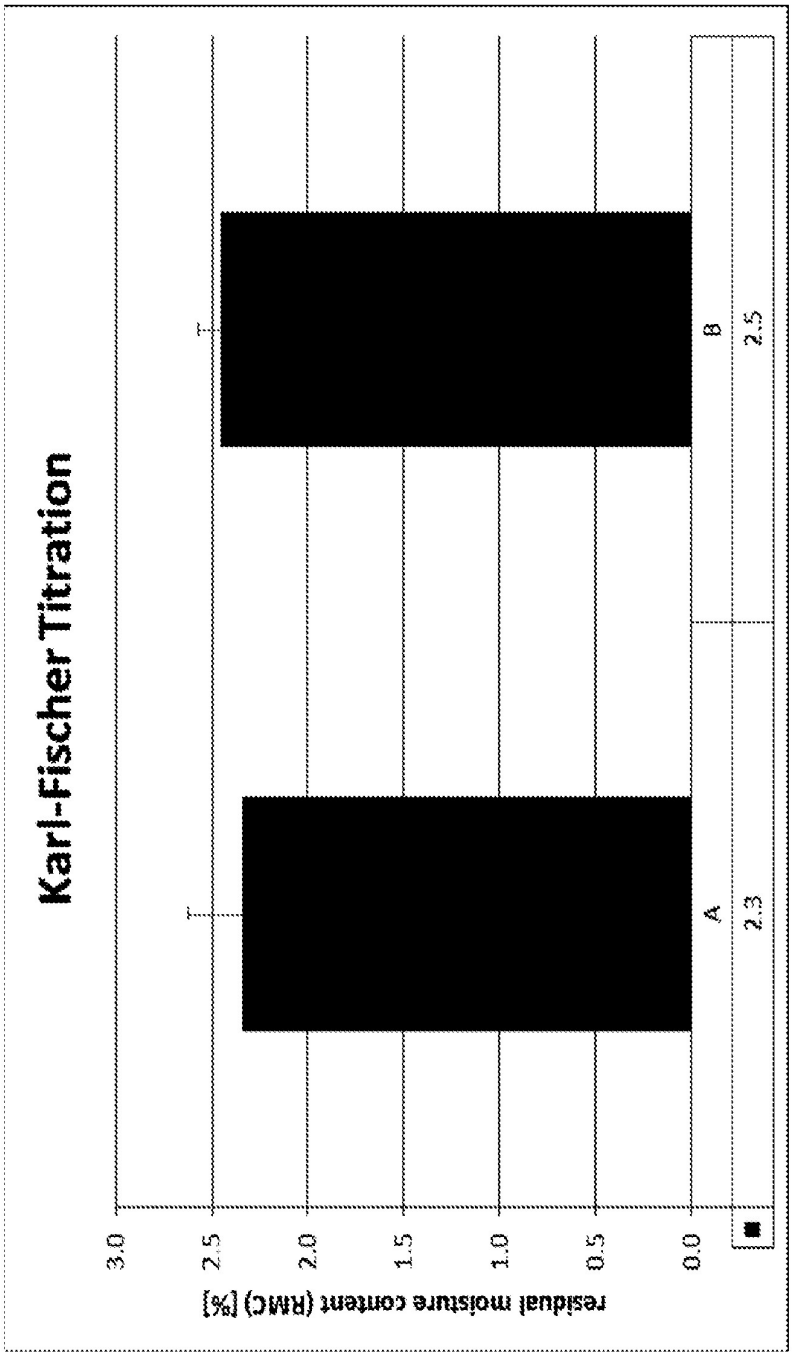

Karl-Fischer Titration
residual moisture content (RMC) [%]
3.0
2.5
2.0
1.5
1.0
0.5
0.0
A
B
2.3
2.5

*FIG. 41B*

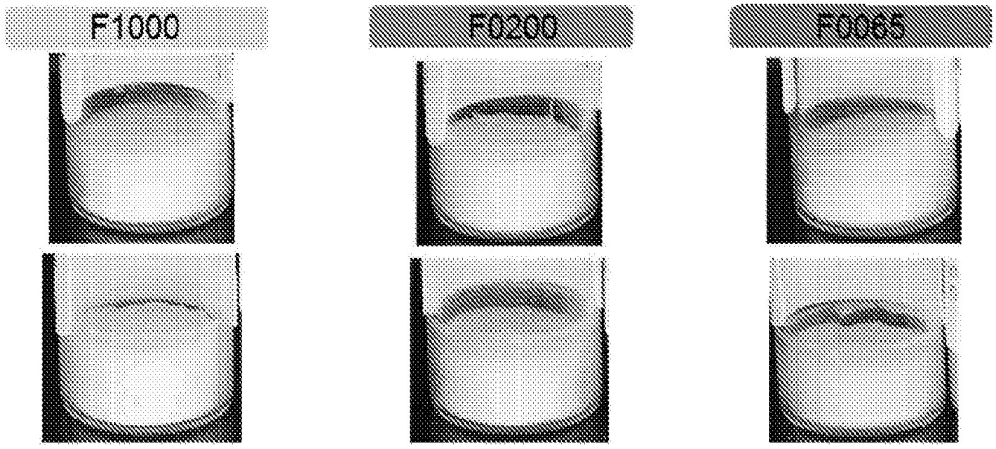



*FIG. 42A*

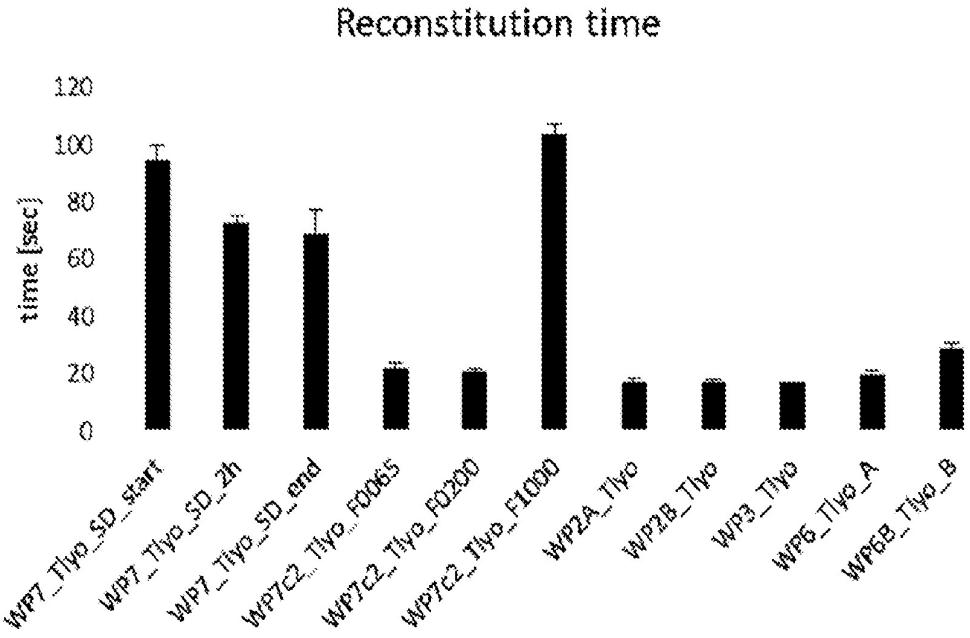



*FIG. 42B*

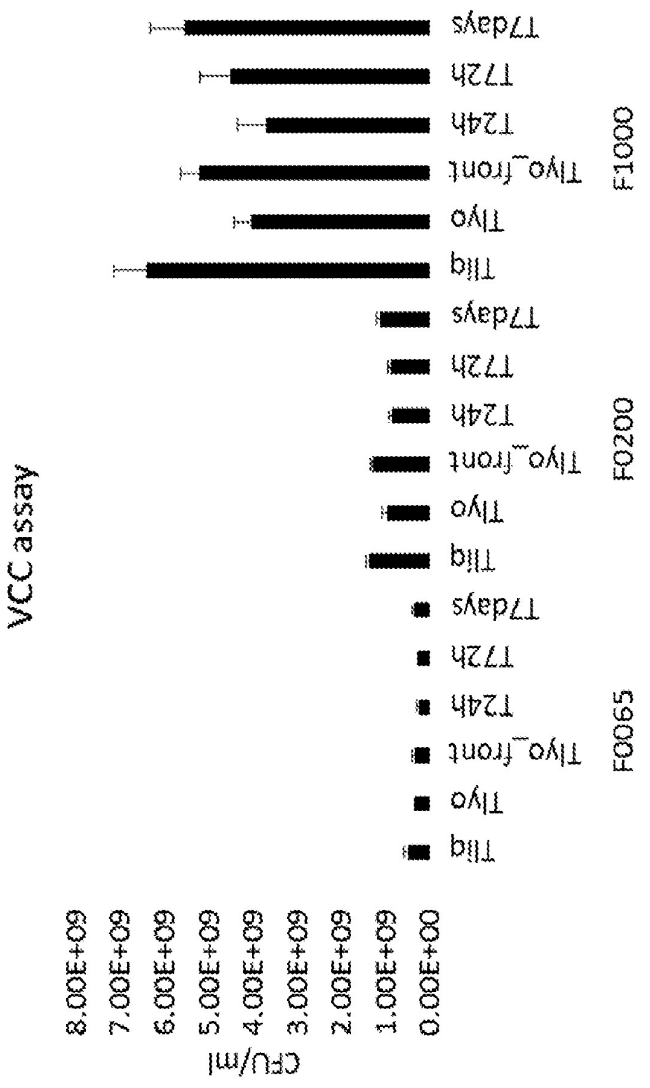

VCC assay
CFU/ml
8.00E+09
7.00E+09
6.00E+09
5.00E+09
4.00E+09
3.00E+09
2.00E+09
1.00E+09
0.00E+00
Tlla
Tlyo
Tlyo_front
T24h
T72h
T7days
Tlla
Tlyo
Tlyo_front
T24h
T72h
T7days
Tlla
Tlyo
Tlyo_front
T24h
T72h
T7days
F0065
F0200
F1000

*FIG. 43*

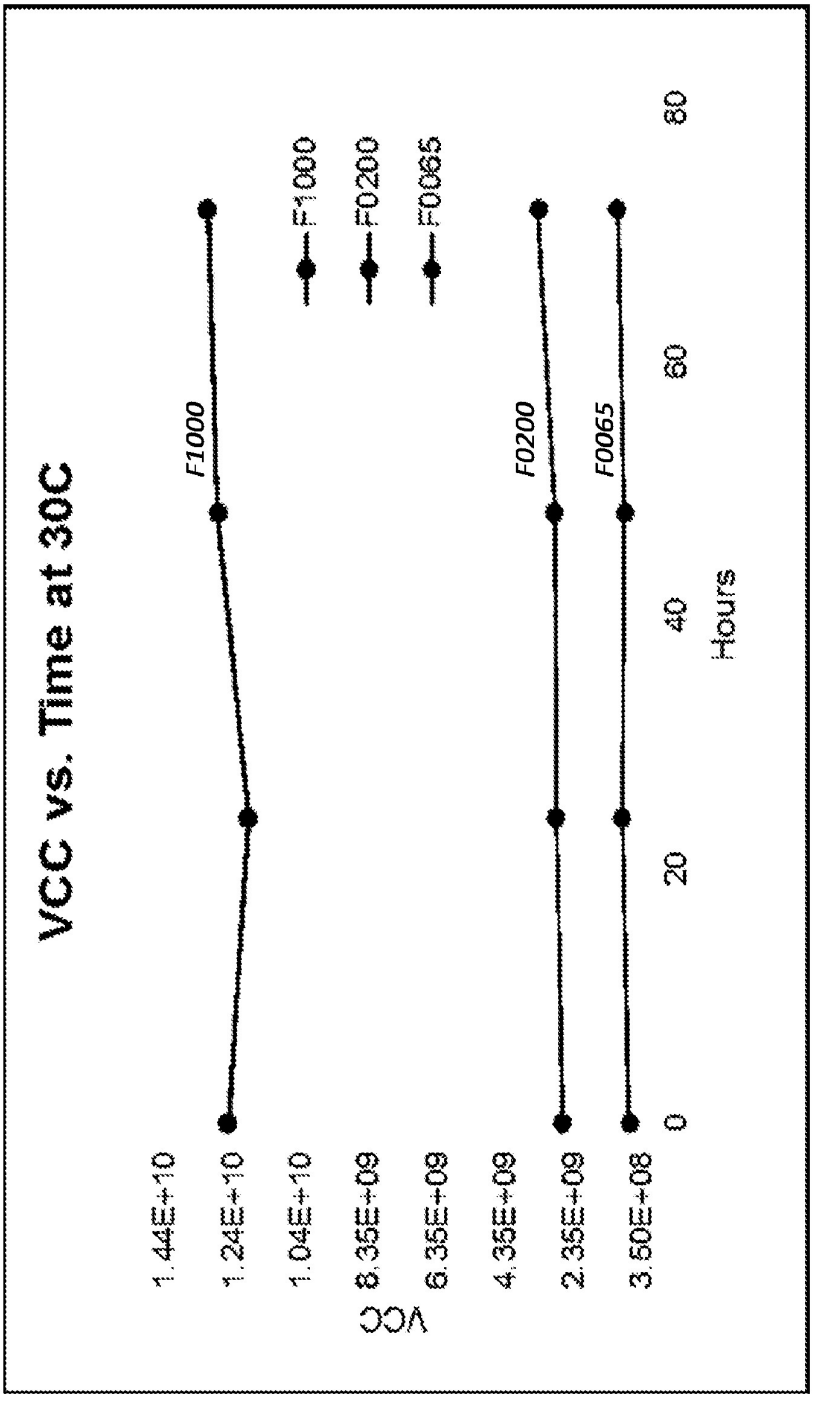

VCC vs. Time at 30C
F1000
F0200
F0065
1.44E+10
1.24E+10
1.04E+10
8.35E+09
6.35E+09
4.35E+09
2.35E+09
3.50E+08
VCC
0
20
40
60
80
Hours

FIG. 44A

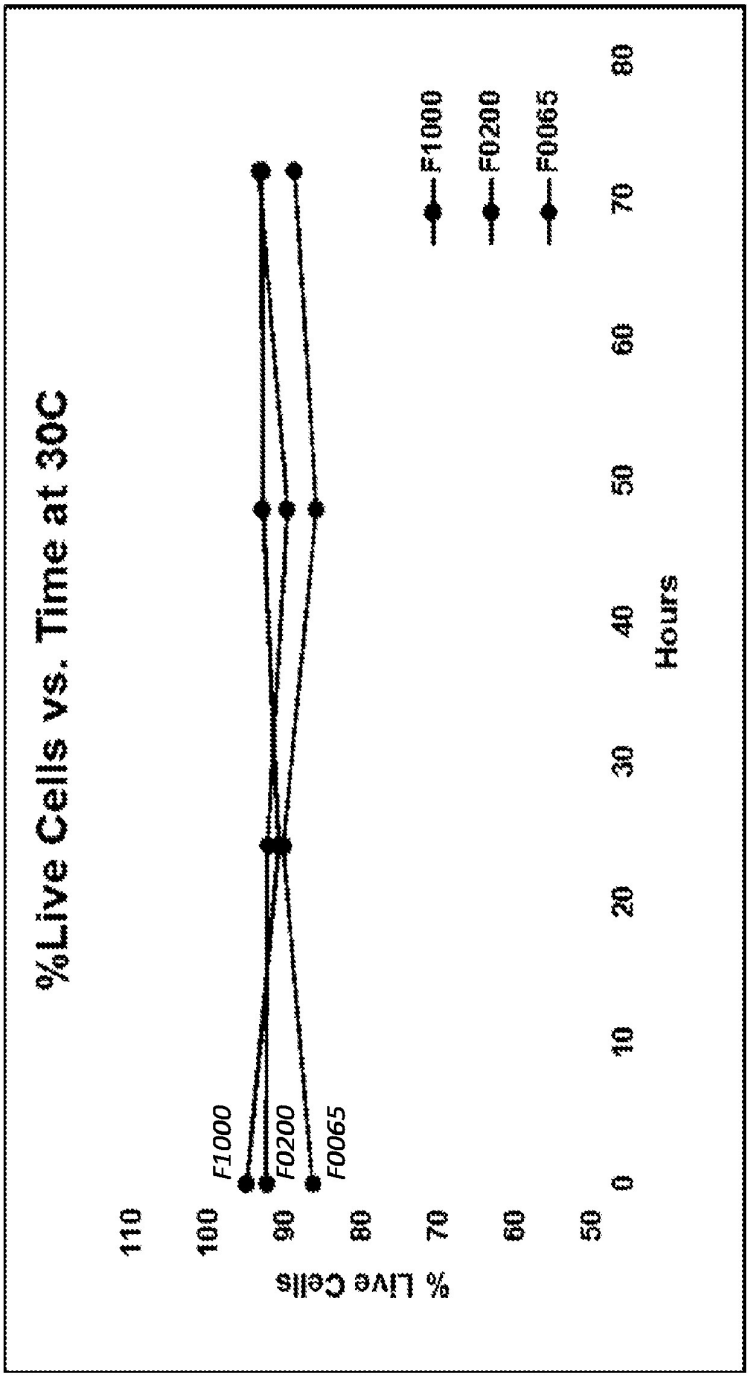

%Live Cells vs. Time at 30C
% Live Cells
Hours
F1000
F0200
F0065
110
100
90
80
70
60
50
0
10
20
30
40
50
60
70
80

*FIG. 44B*

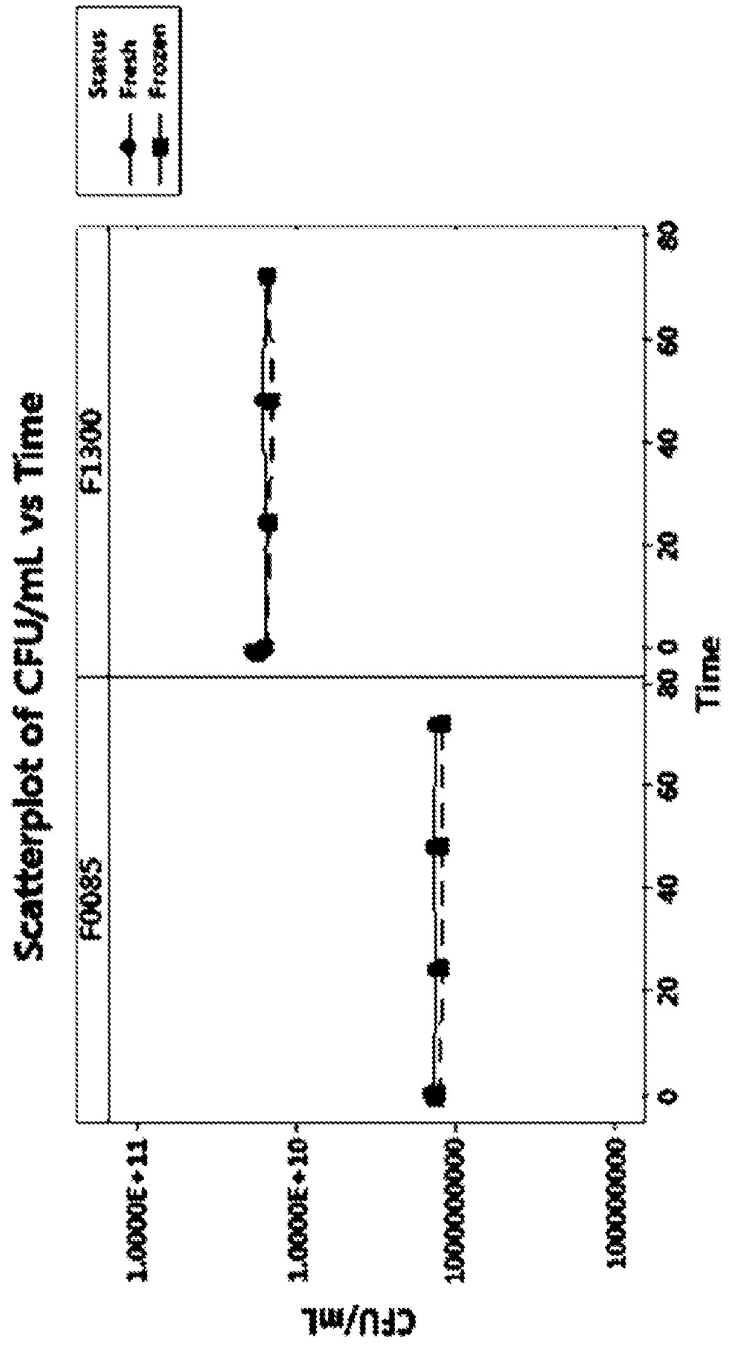

Scatterplot of CFU/mL vs Time
F0085
F1300
Status
Fresh
Frozen
CFU/mL
1.0000E+11
1.0000E+10
1000000000
100000000
Time
0
20
40
60
80
Panel variable: WPB Lot

FIG. 45A

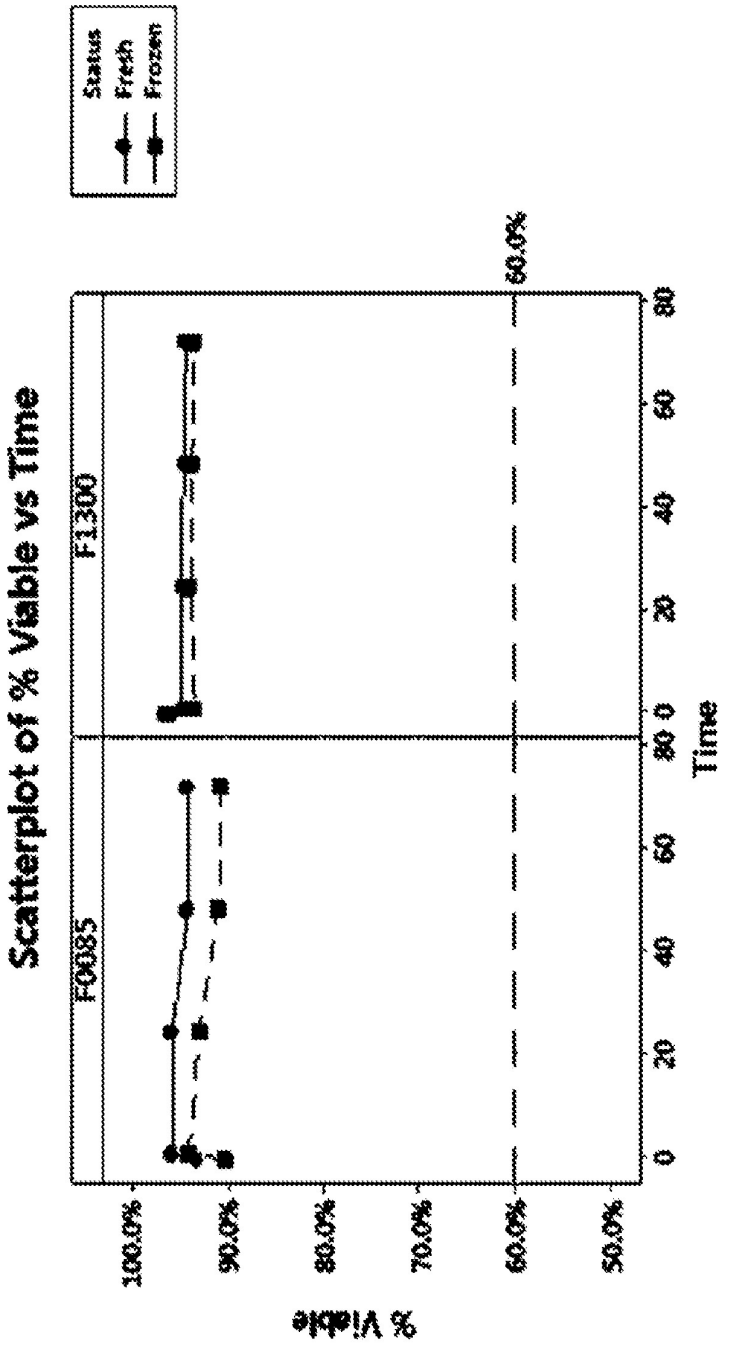

Scatterplot of % Viable vs Time
F0085
F1300
Status
Fresh
Frozen
60.0%
% Viable
100.0%
90.0%
80.0%
70.0%
60.0%
50.0%
0
20
40
60
80
Time
Panel variable: WP8 Lot

*FIG. 45B*

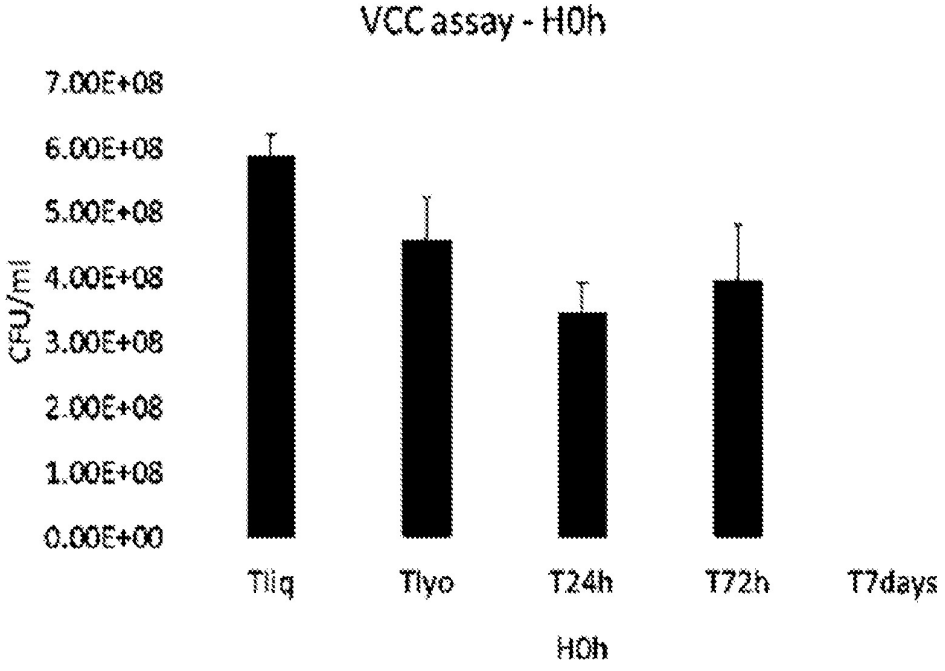



*FIG. 46A*

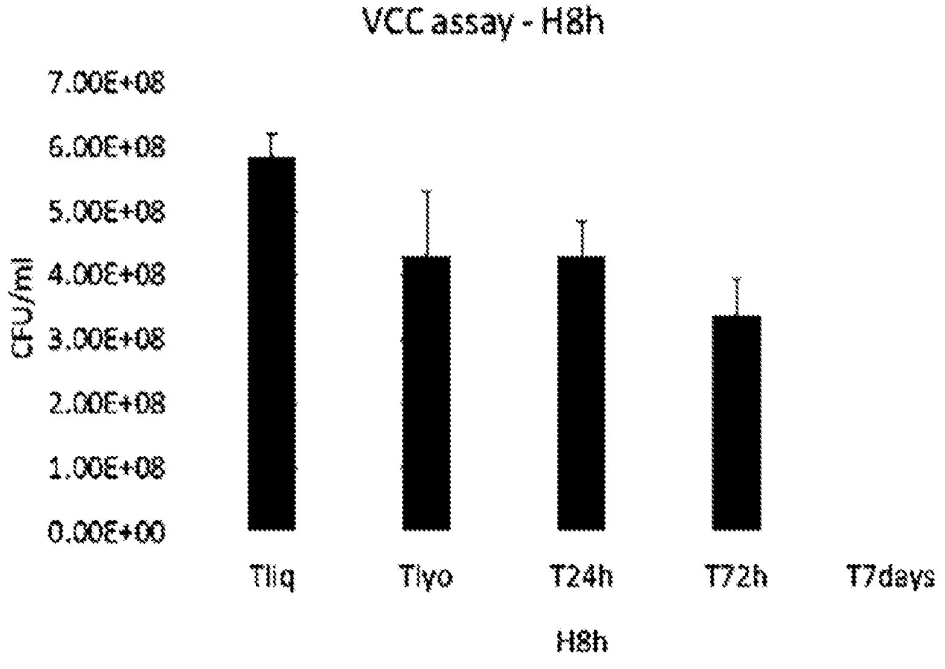



*FIG. 46B*

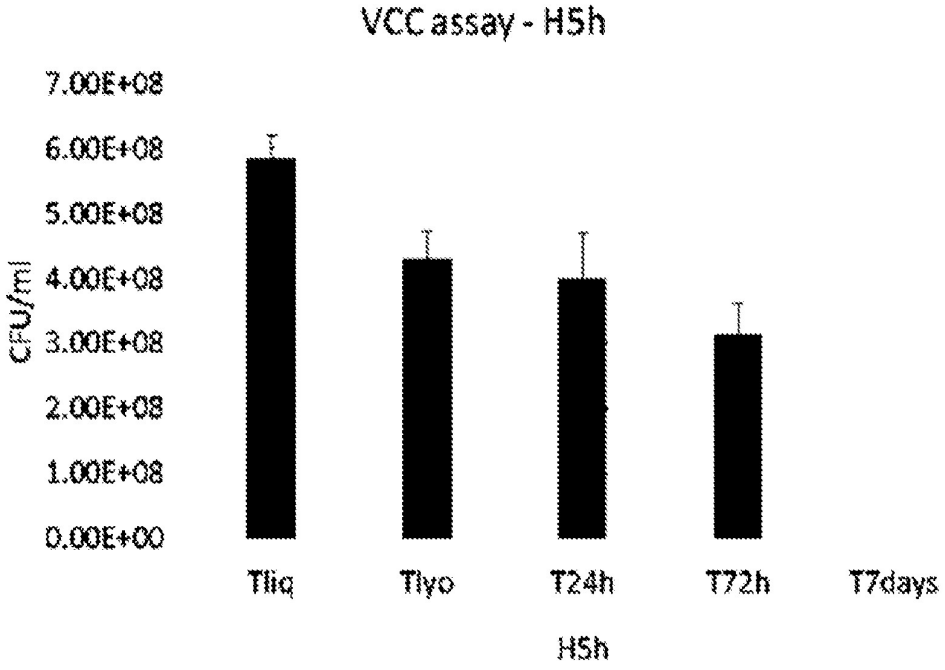



*FIG. 47A*

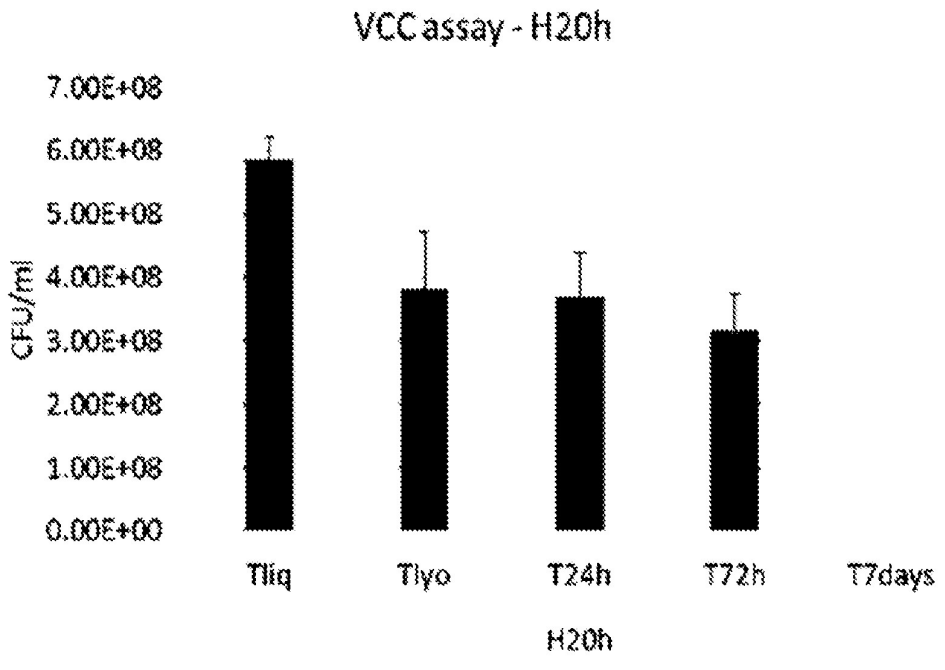



*FIG. 47B*

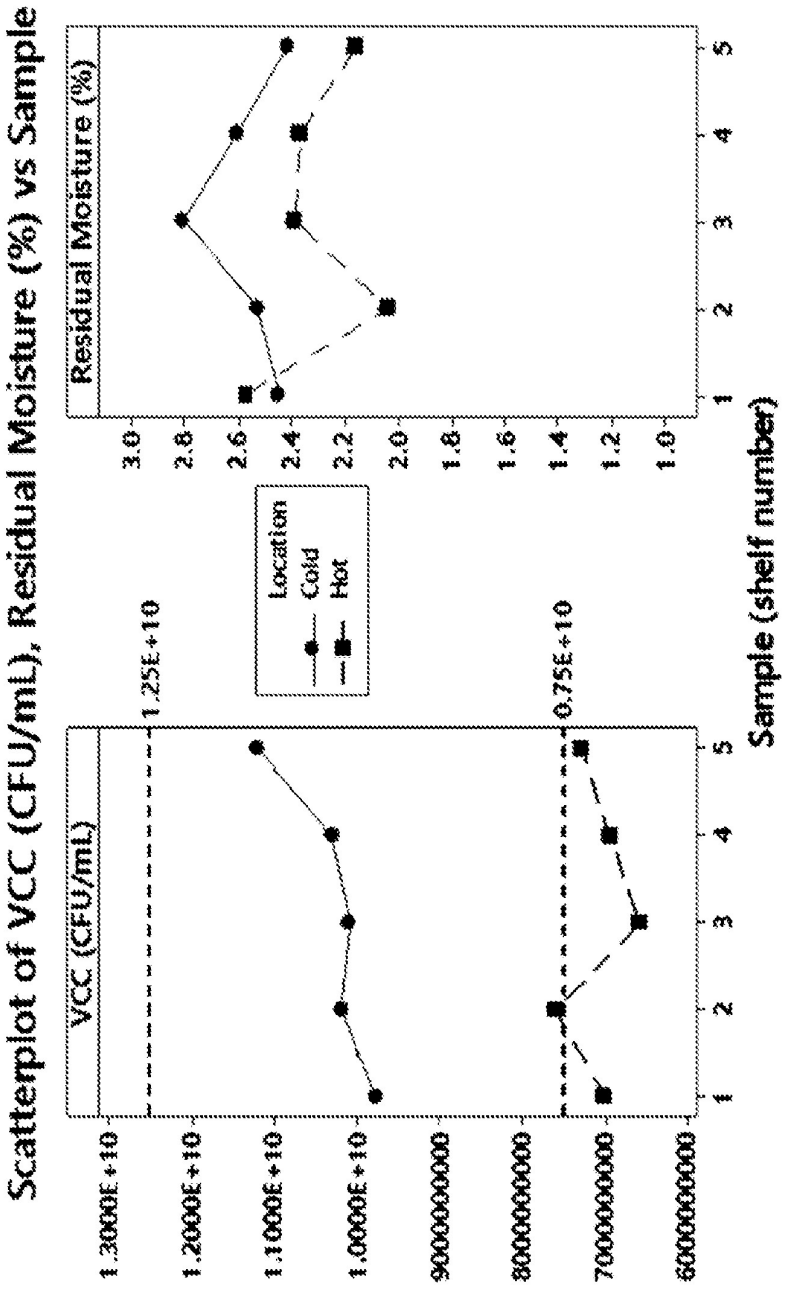

Scatterplot of VCC (CFU/mL), Residual Moisture (%) vs Sample
VCC (CFU/mL)
Residual Moisture (%)
1.25E+10
0.75E+10
Location
Cold
Hot
Sample (shelf number)

*FIG. 48*

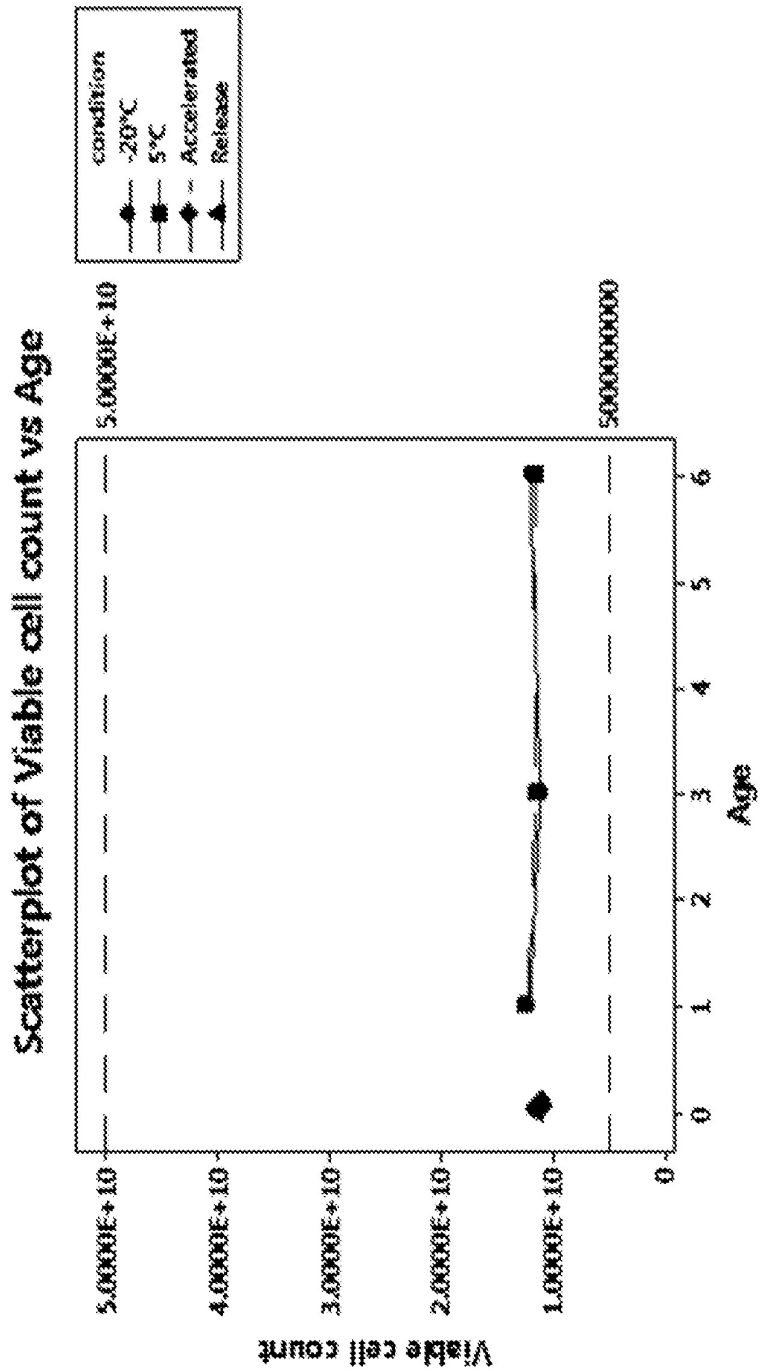

Scatterplot of Viable cell count vs Age
condition
-20°C
5°C
Accelerated
Release
5.0000E+10
5000000000
Viable cell count
5.0000E+10
4.0000E+10
3.0000E+10
2.0000E+10
1.0000E+10
0
0
1
2
3
4
5
6
Age

*FIG. 49*

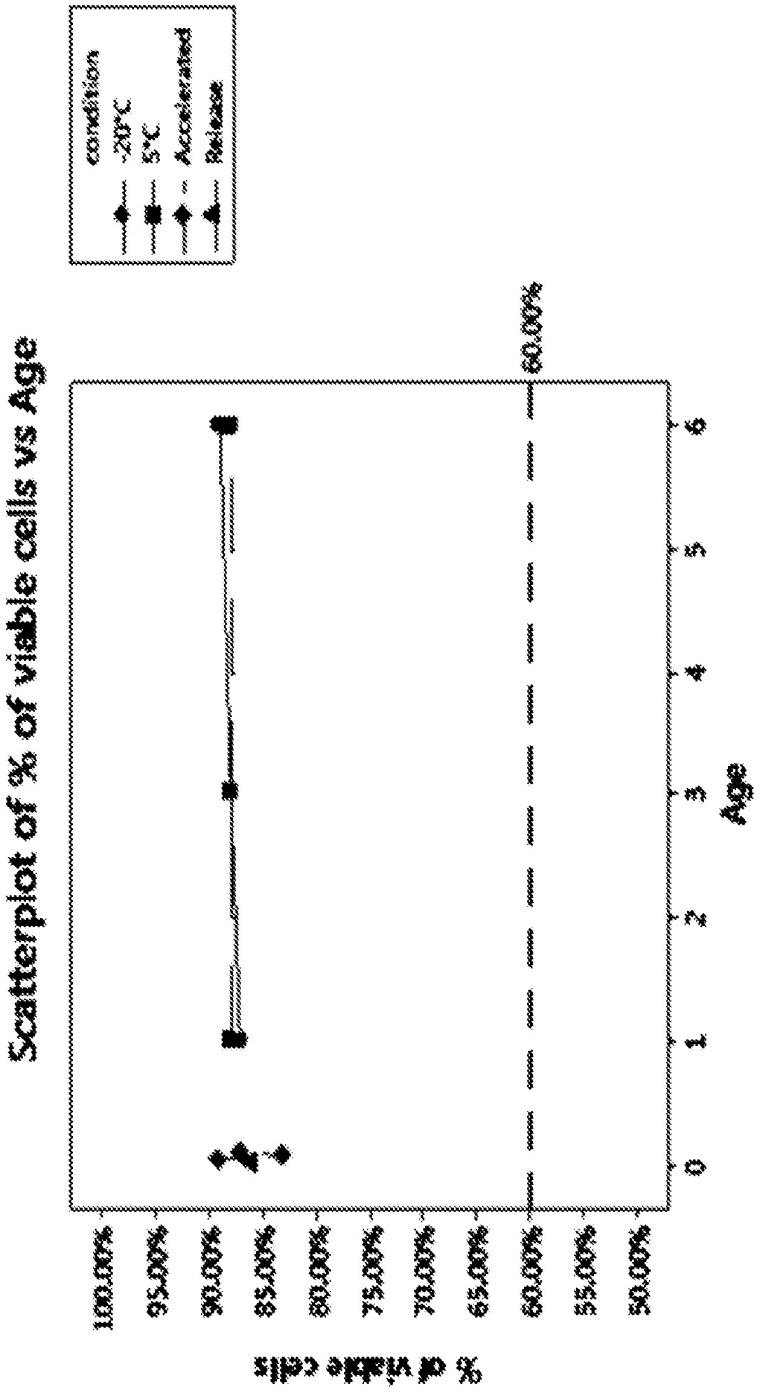

Scatterplot of % of viable cells vs Age
condition
-20°C
5°C
Accelerated
Release
% of viable cells
Age
100.00%
95.00%
90.00%
85.00%
80.00%
75.00%
70.00%
65.00%
60.00%
55.00%
50.00%
0
1
2
3
4
5
6

*FIG. 50*

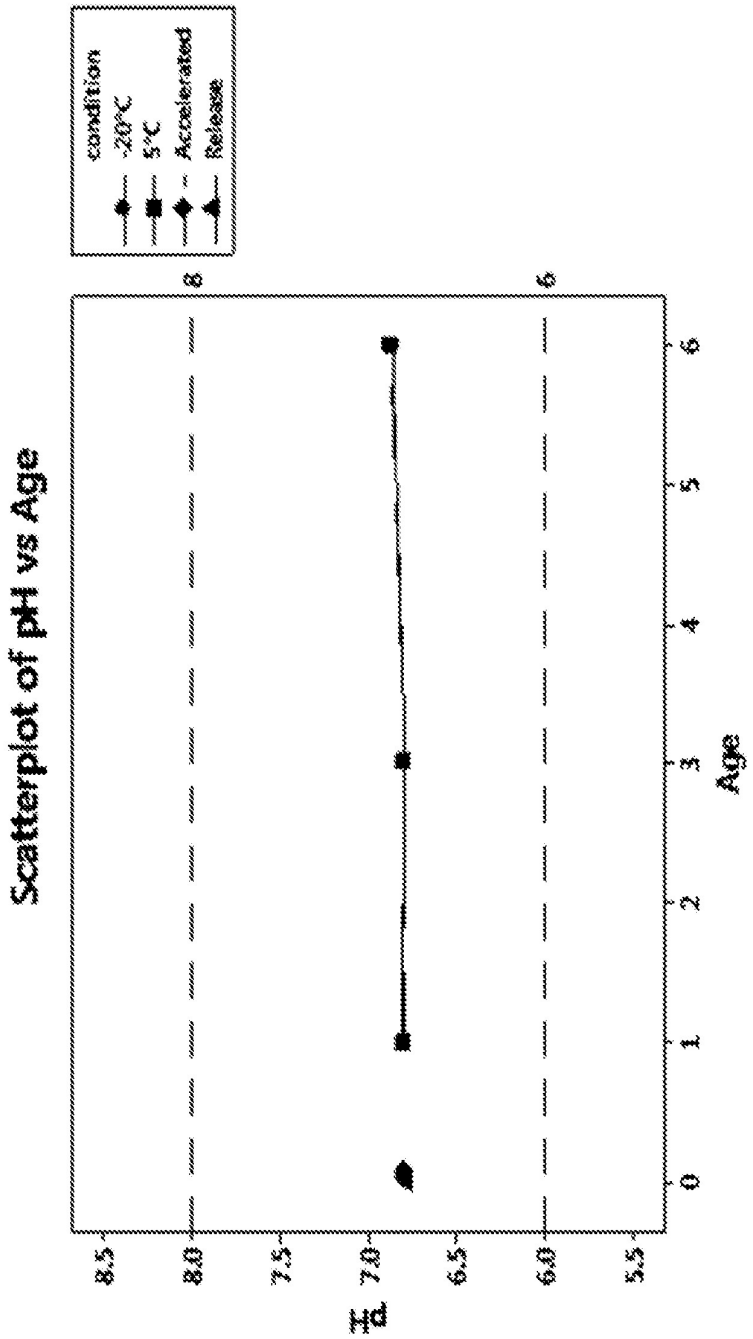

Scatterplot of pH vs Age
condition
-20°C
5°C
Accelerated
Release
pH
Age
8.5
8.0
7.5
7.0
6.5
6.0
5.5
0
1
2
3
4
5
6
8
6

*FIG. 51*

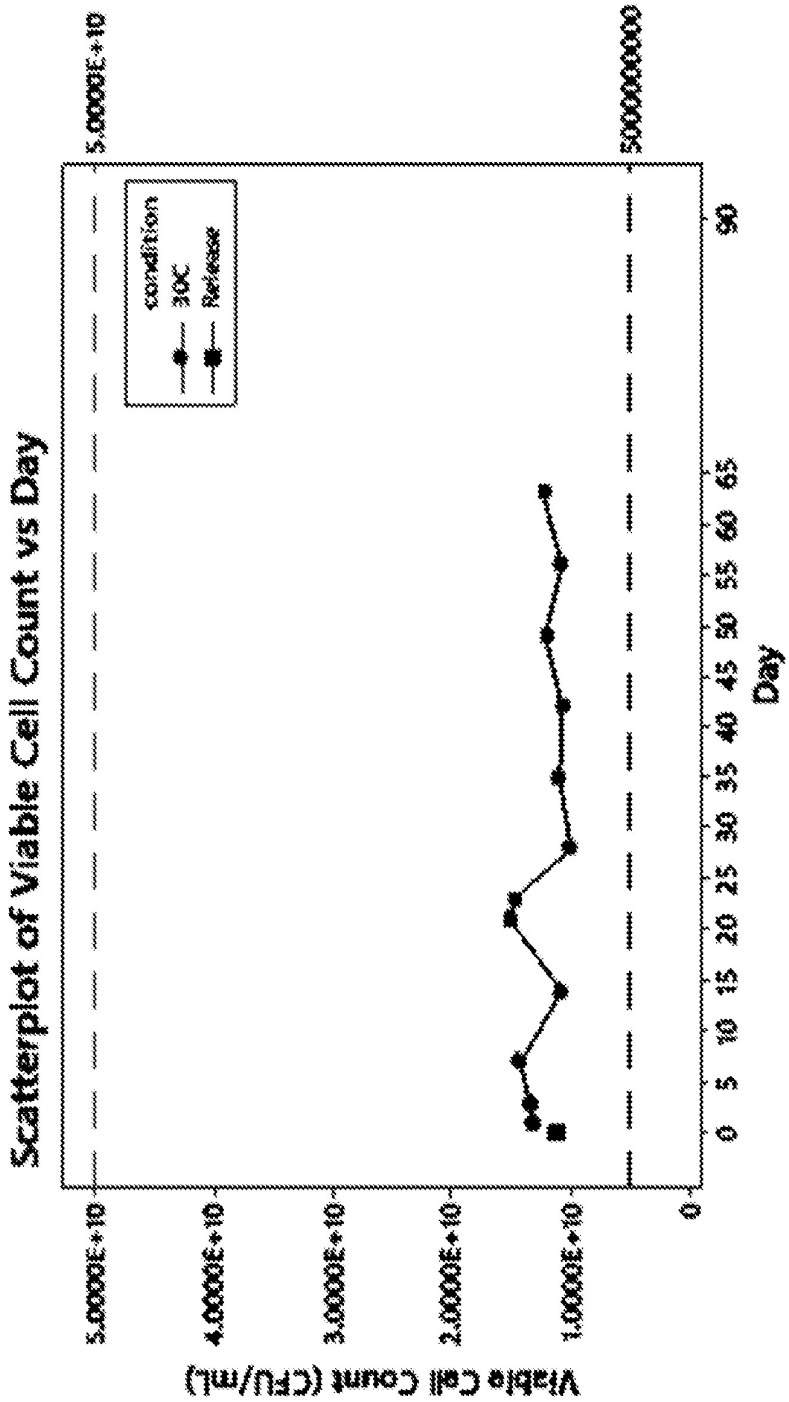

Scatterplot of Viable Cell Count vs Day
condition
30C
Release
Viable Cell Count (CFU/mL)
5.0000E+10
4.0000E+10
3.0000E+10
2.0000E+10
1.0000E+10
0
5000000000
0
5
10
15
20
25
30
35
40
45
50
55
60
65
90
Day

*FIG. 52*

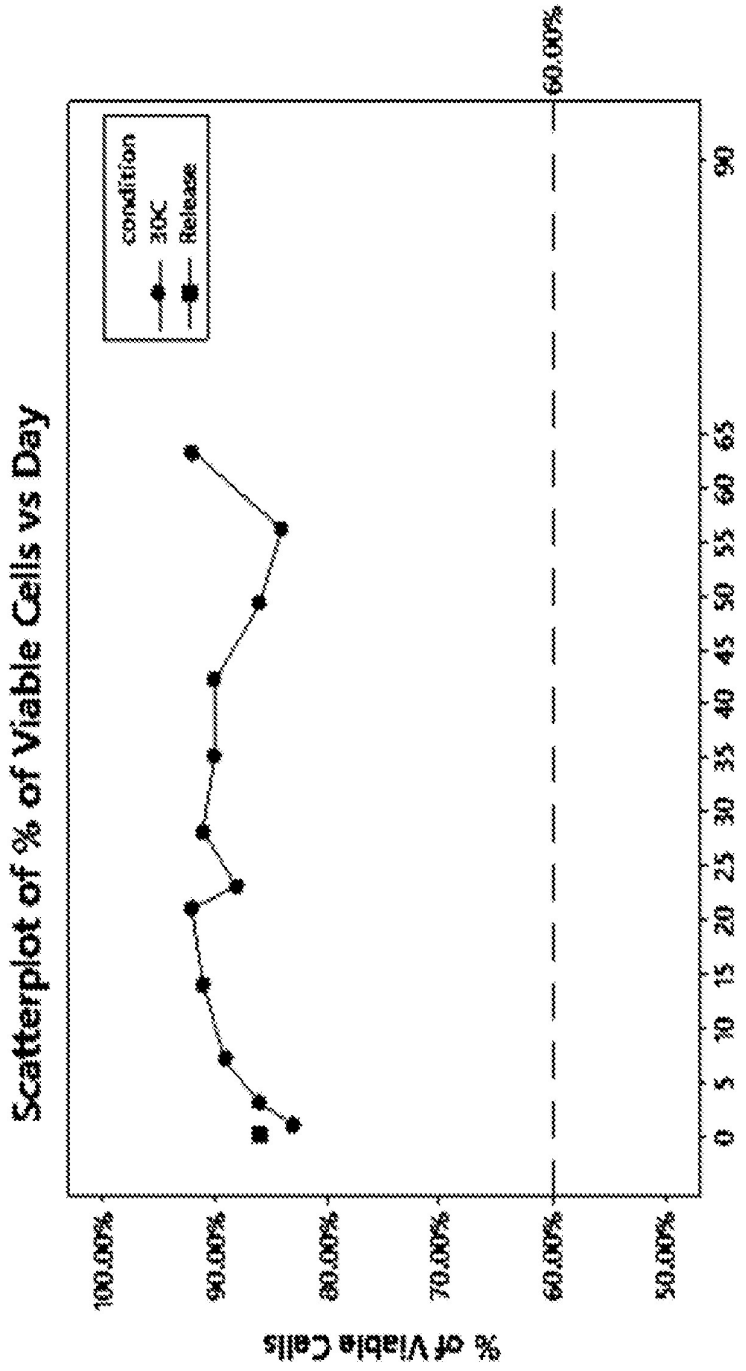

Scatterplot of % of Viable Cells vs Day
condition
30C
Release
% of Viable Cells
100.00%
90.00%
80.00%
70.00%
60.00%
50.00%
0
5
10
15
20
25
30
35
40
45
50
55
60
65
90
Day
60.00%

*FIG. 53*

**Treatment schedule:**

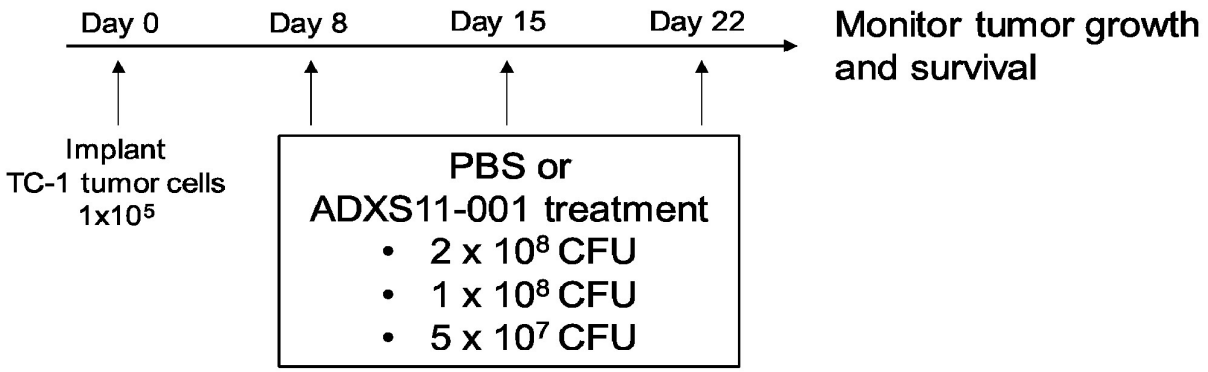



*FIG. 54*

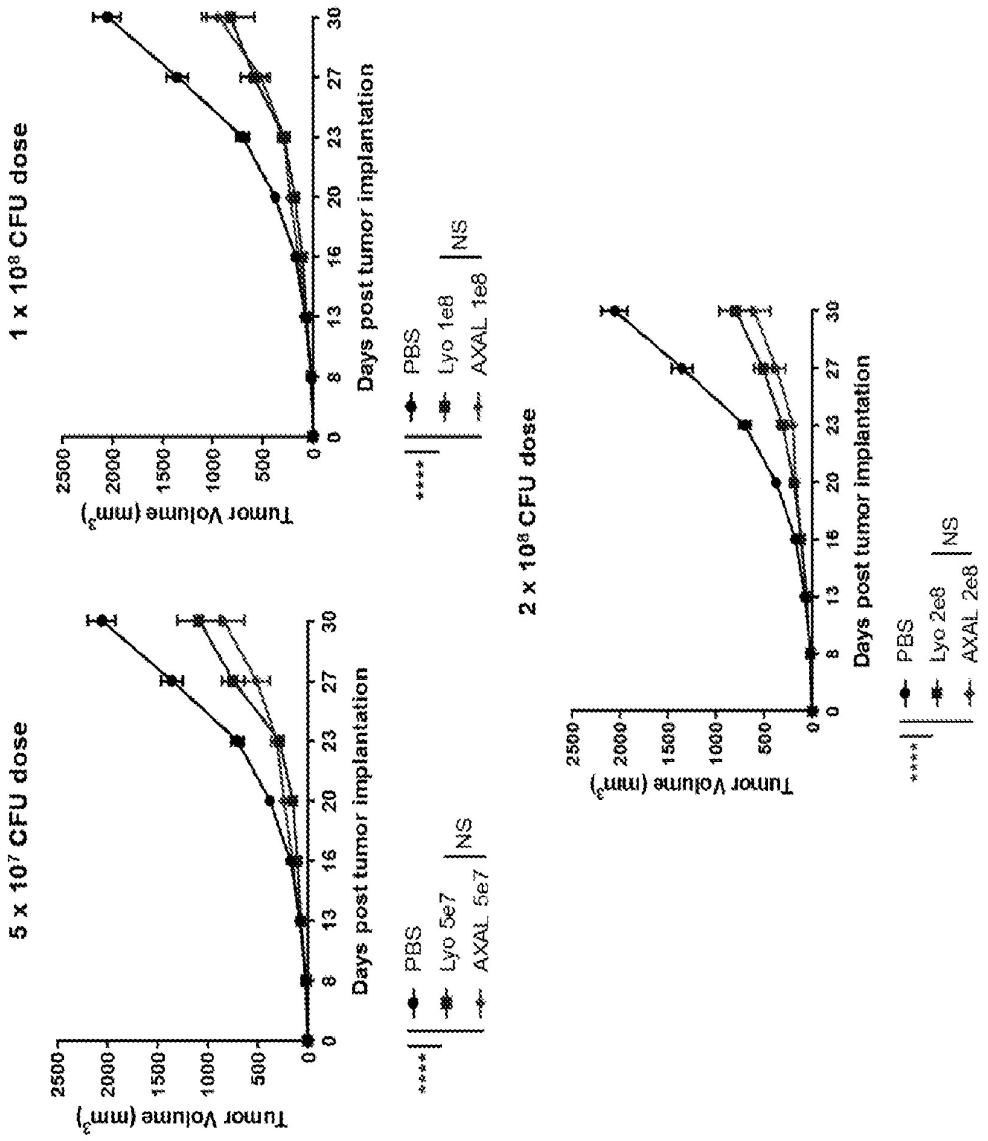

5 x 10^7 CFU dose
1 x 10^8 CFU dose
2 x 10^8 CFU dose
Tumor Volume (mm^3)
Days post tumor implantation
PBS
Lyo 5e7
AXAL 5e7
Lyo 1e8
AXAL 1e8
Lyo 2e8
AXAL 2e8
****
NS

*FIG. 55*

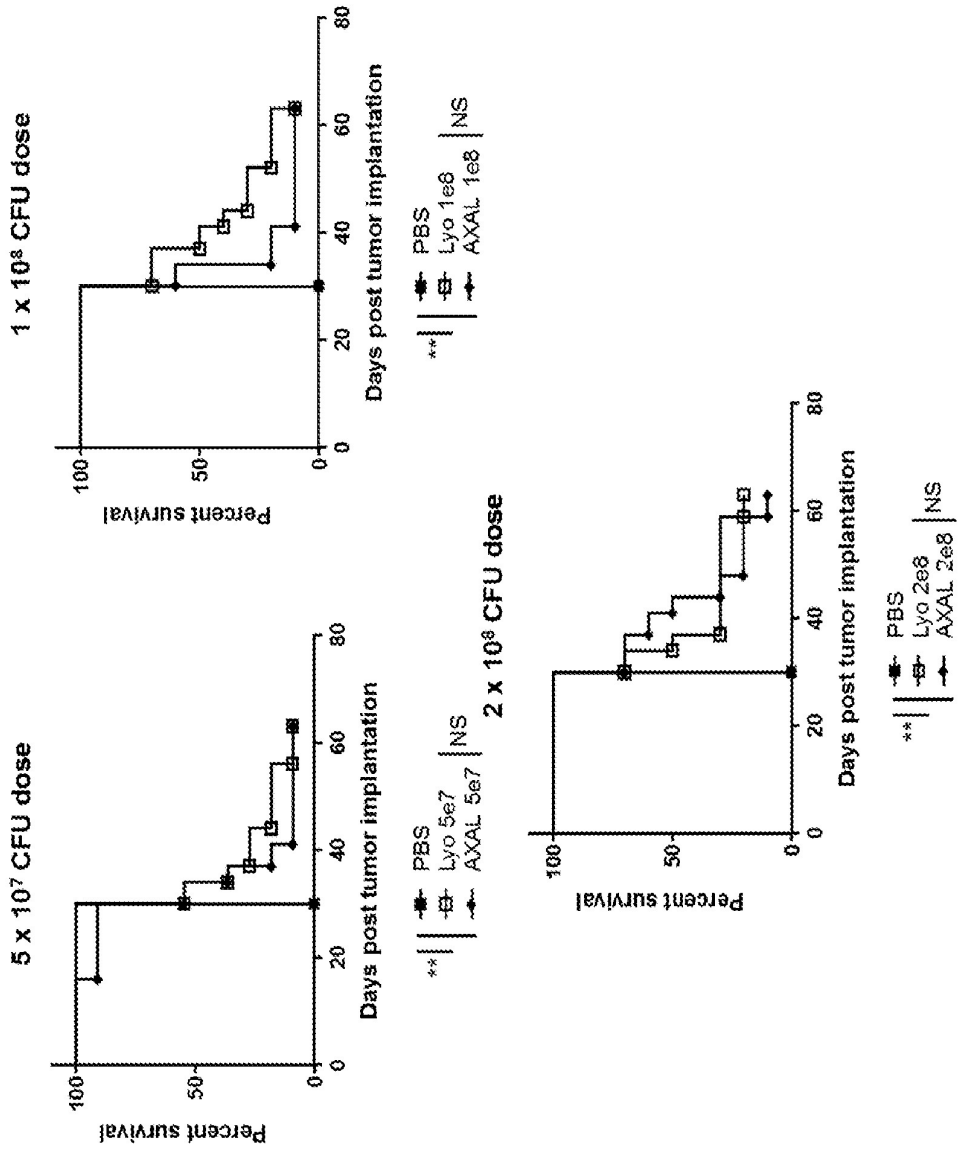

5 x 10^7 CFU dose
1 x 10^8 CFU dose
2 x 10^8 CFU dose
Percent survival
Days post tumor implantation
PBS
Lyo 5e7
AXAL 5e7
Lyo 1e8
AXAL 1e8
Lyo 2e8
AXAL 2e8
**
NS

*FIG. 56*

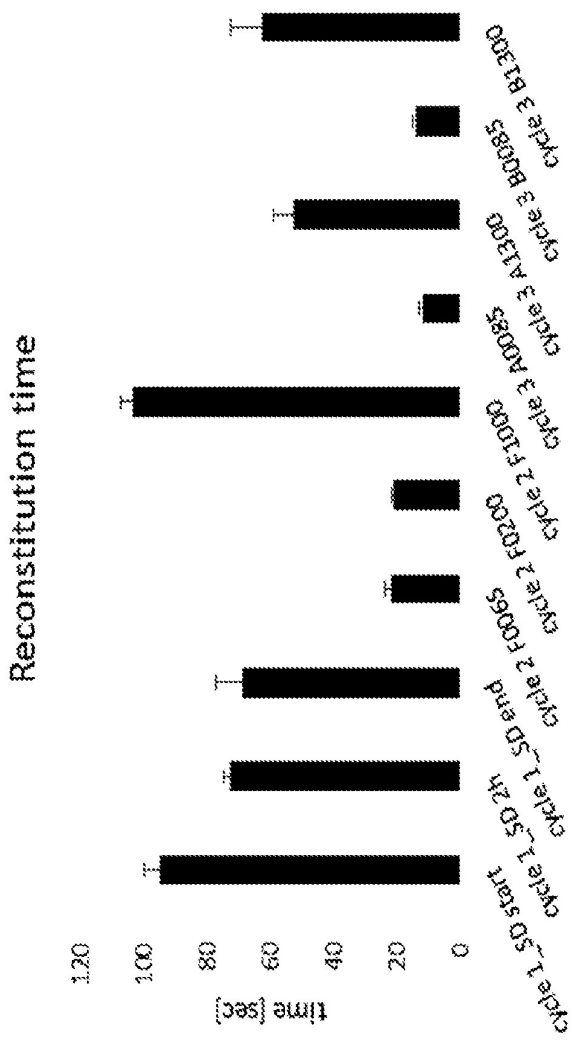

Reconstitution time
time [sec]
0
20
40
60
80
100
120
cycle 1_SD start
cycle 1_SD 2h
cycle 1_SD end
cycle 2 F0065
cycle 2 F0200
cycle 2 F1000
cycle 3 A0085
cycle 3 A1300
cycle 3 B0085
cycle 3 B1300

*FIG. 57*

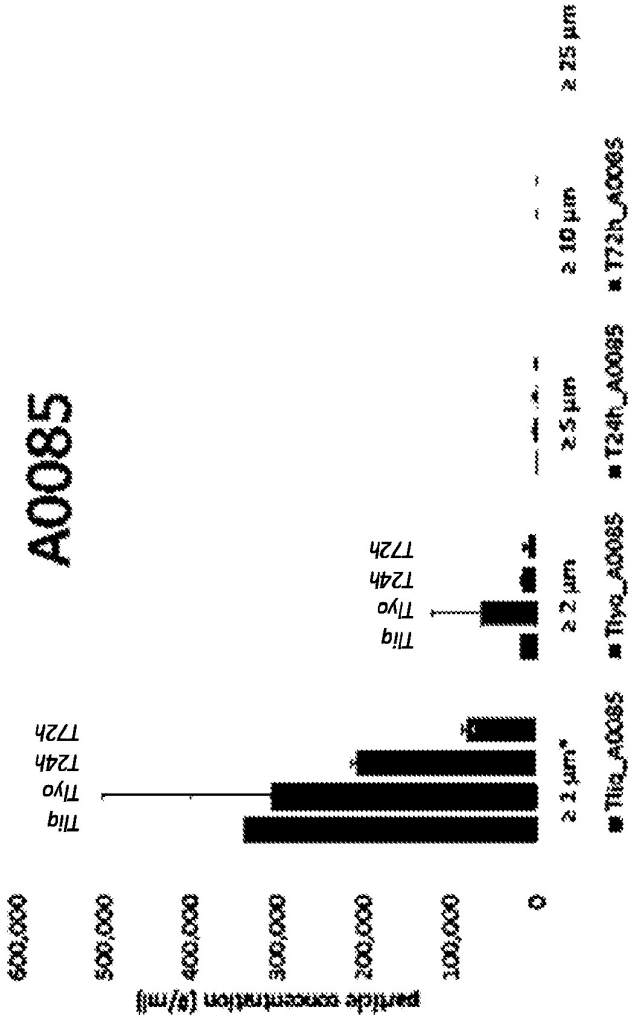

MFI - WP7 - cycle 3
A0085
particle concentration (#/ml)
600,000
500,000
400,000
300,000
200,000
100,000
0
T1iq
T1yo
T24h
T72h
≥ 1 µm*
≥ 2 µm
≥ 5 µm
≥ 10 µm
≥ 25 µm
T1iq_A0085
T1yo_A0085
T24h_A0085
T72h_A0085

*FIG. 58A*

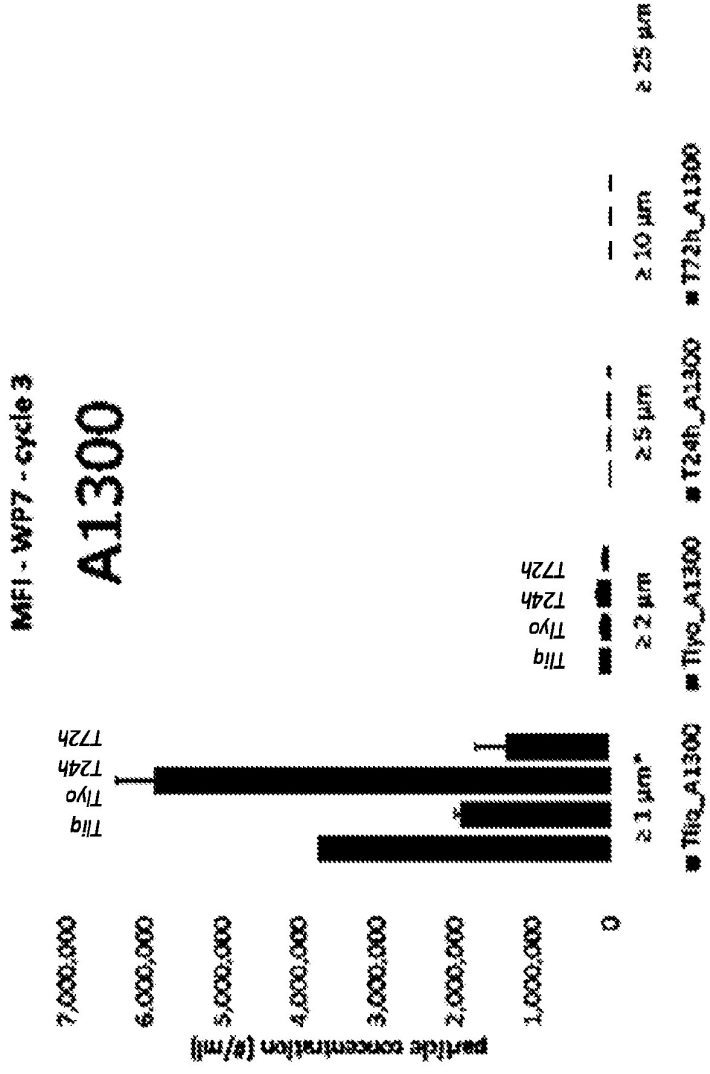

MFI - WP7 - cycle 3
A1300
particle concentration (#/ml)
7,000,000
6,000,000
5,000,000
4,000,000
3,000,000
2,000,000
1,000,000
0
≥ 1 µm*
≥ 2 µm
≥ 5 µm
≥ 10 µm
≥ 25 µm
T1q_A1300
T1yo_A1300
T24h_A1300
T72h_A1300
T1q
T1yo
T24h
T72h

*FIG. 58B*

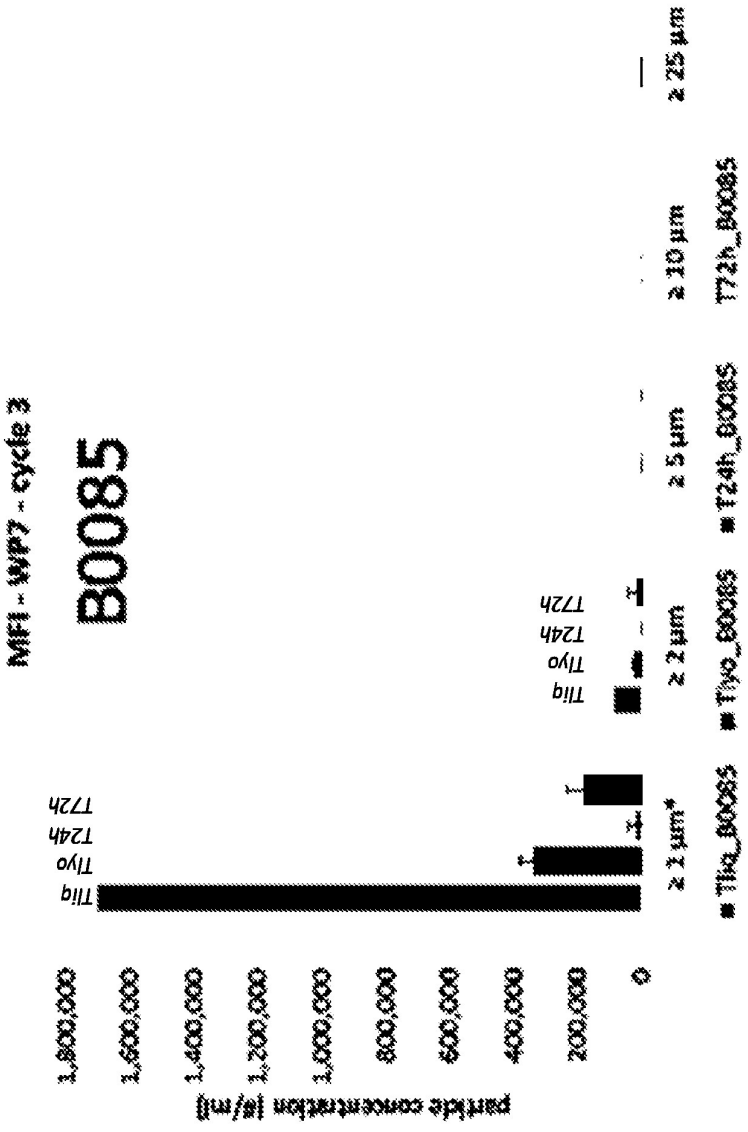

MFI - WP7 - cycle 3
B0085
particle concentration [#/ml]
1,800,000
1,600,000
1,400,000
1,200,000
1,000,000
800,000
600,000
400,000
200,000
0
T1iq
T1yo
T24h
T72h
≥ 2 µm*
≥ 2 µm
≥ 5 µm
≥ 10 µm
≥ 25 µm
T1iq_B0085
T1yo_B0085
T24h_B0085
T72h_B0085

*FIG. 58C*

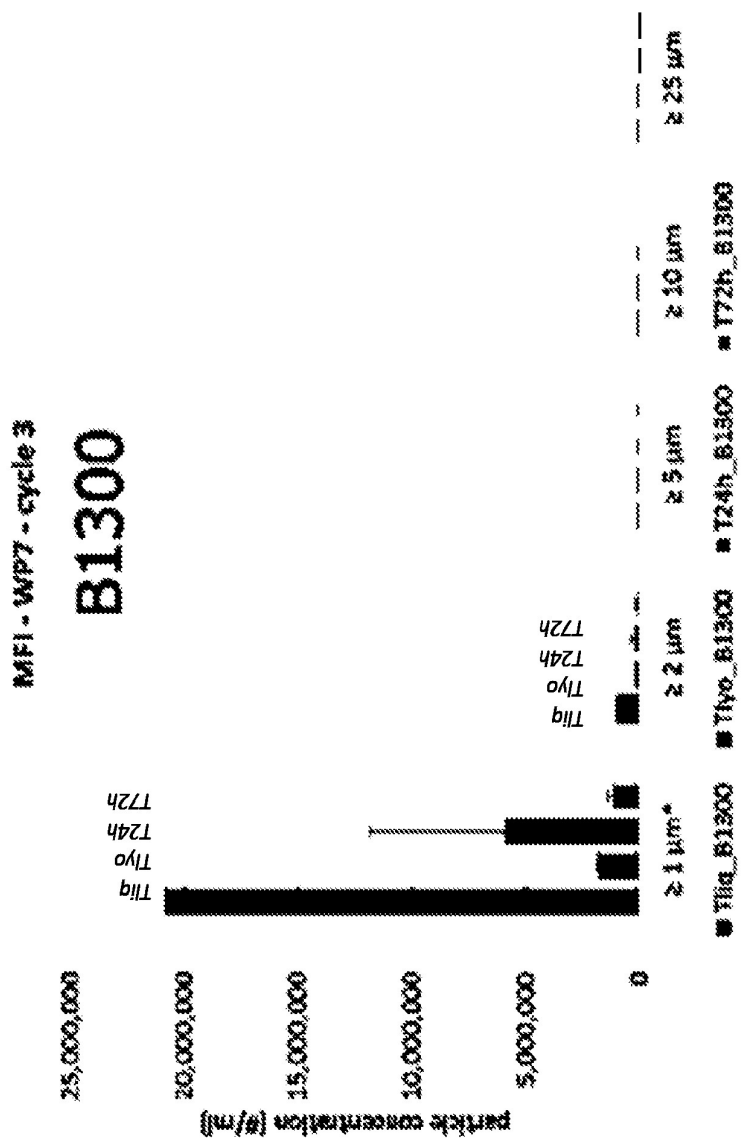

MFI - WP7 - cycle 3
B1300
particle concentration (#/ml)
25,000,000
20,000,000
15,000,000
10,000,000
5,000,000
0
T1ia
T1yo
T24h
T72h
≥ 1 µm*
≥ 2 µm
≥ 5 µm
≥ 10 µm
≥ 25 µm
T1ia_B1300
T1yo_B1300
T24h_B1300
T72h_B1300

*FIG. 58D*

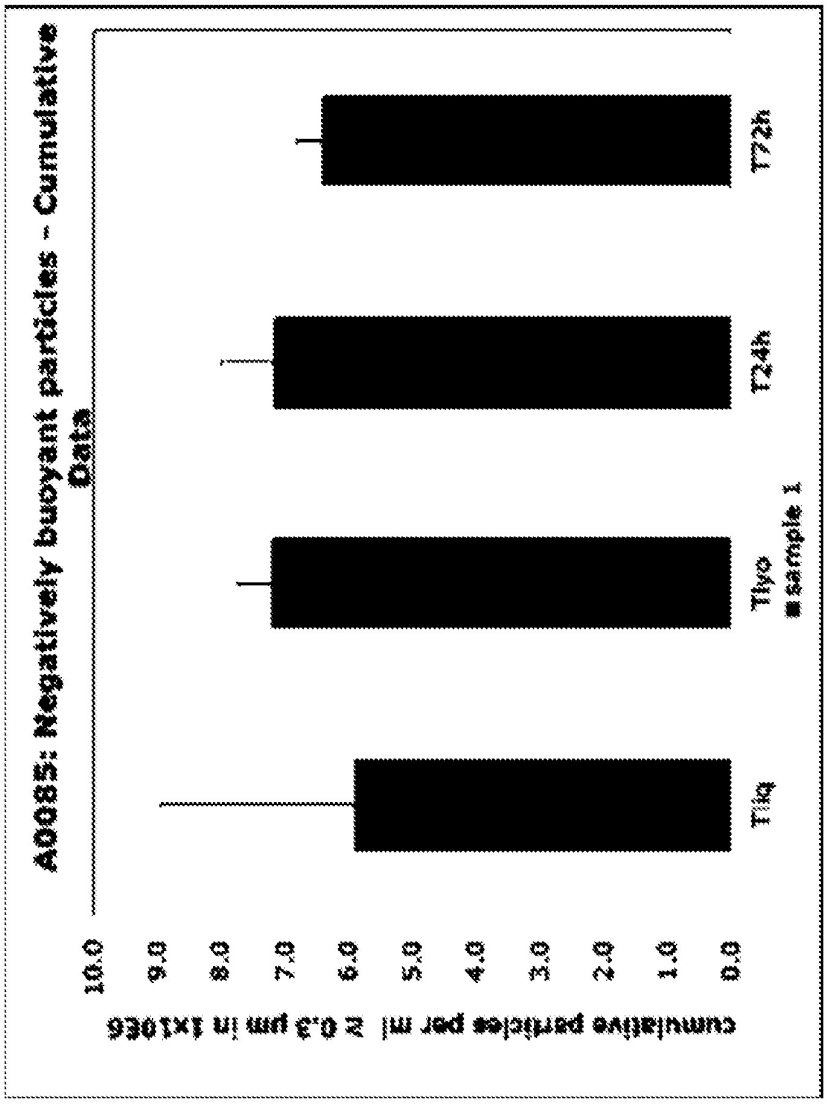

A0085: Negatively buoyant particles - Cumulative Data
cumulative particles per ml N 0.3 µm in 1x10E6
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
T=q
T=yo
T24h
T72h
sample 1

*FIG. 59A*

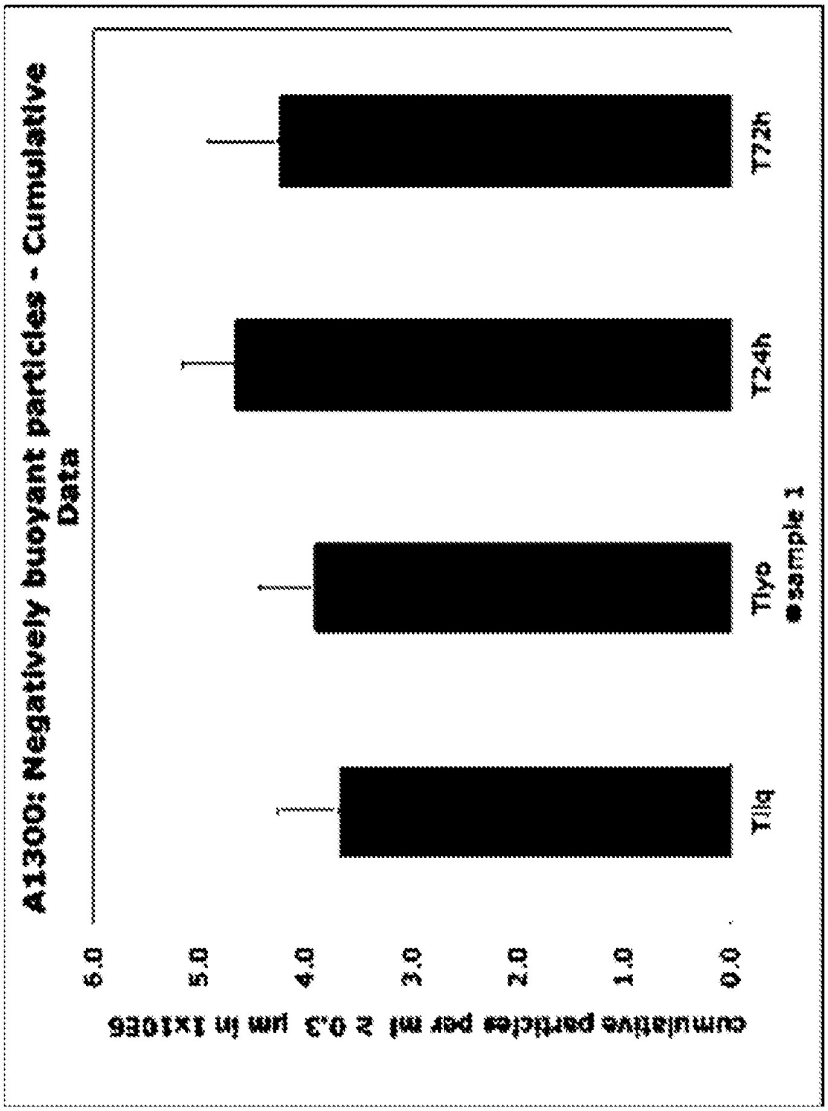

A1300: Negatively buoyant particles - Cumulative Data
cumulative particles per ml ≥ 0.3 µm in 1x10E6
6.0
5.0
4.0
3.0
2.0
1.0
0.0
Tliq
Tlyo
T24h
T72h
sample 1

*FIG. 59B*

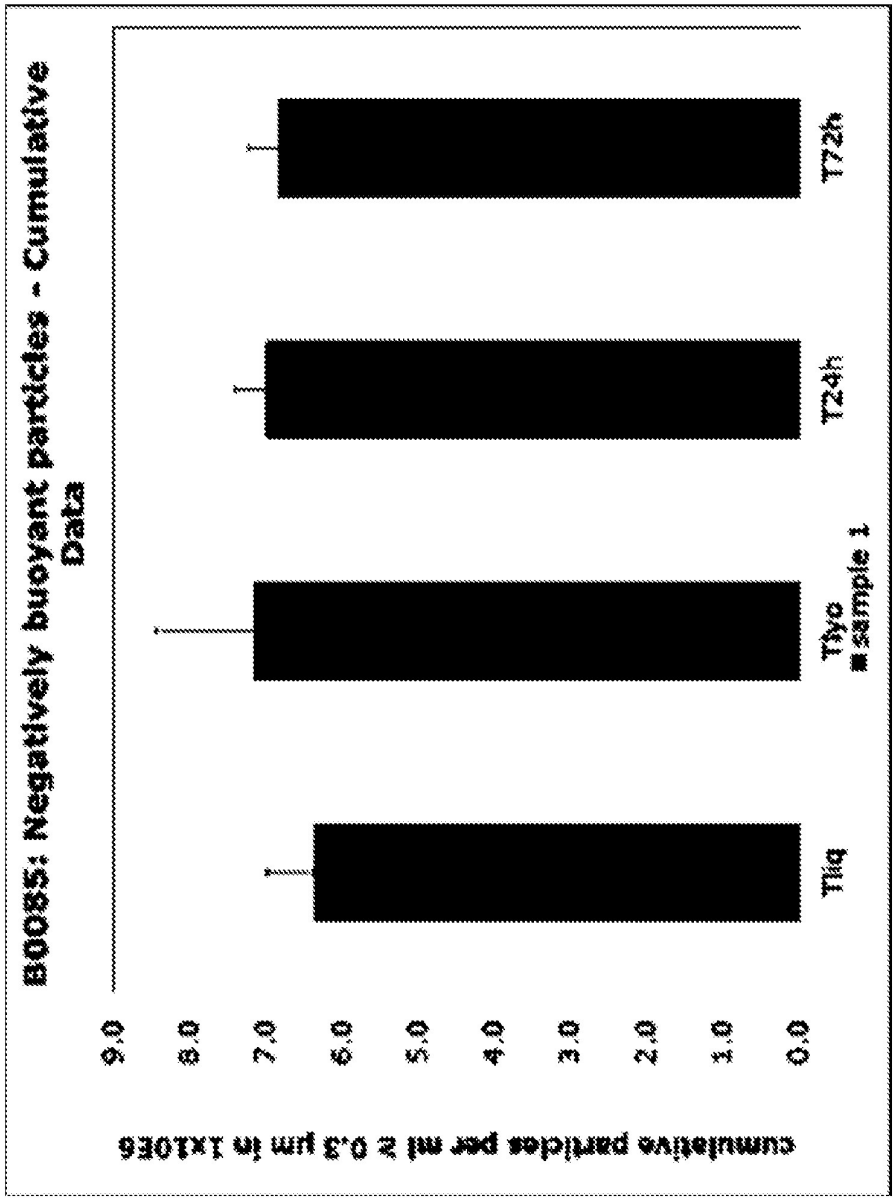

B0085: Negatively buoyant particles - Cumulative Data
cumulative particles per ml ≥ 0.3 µm in 1x10E6
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
Tliq
T0yo
sample 1
T24h
T72h

*FIG. 59C*

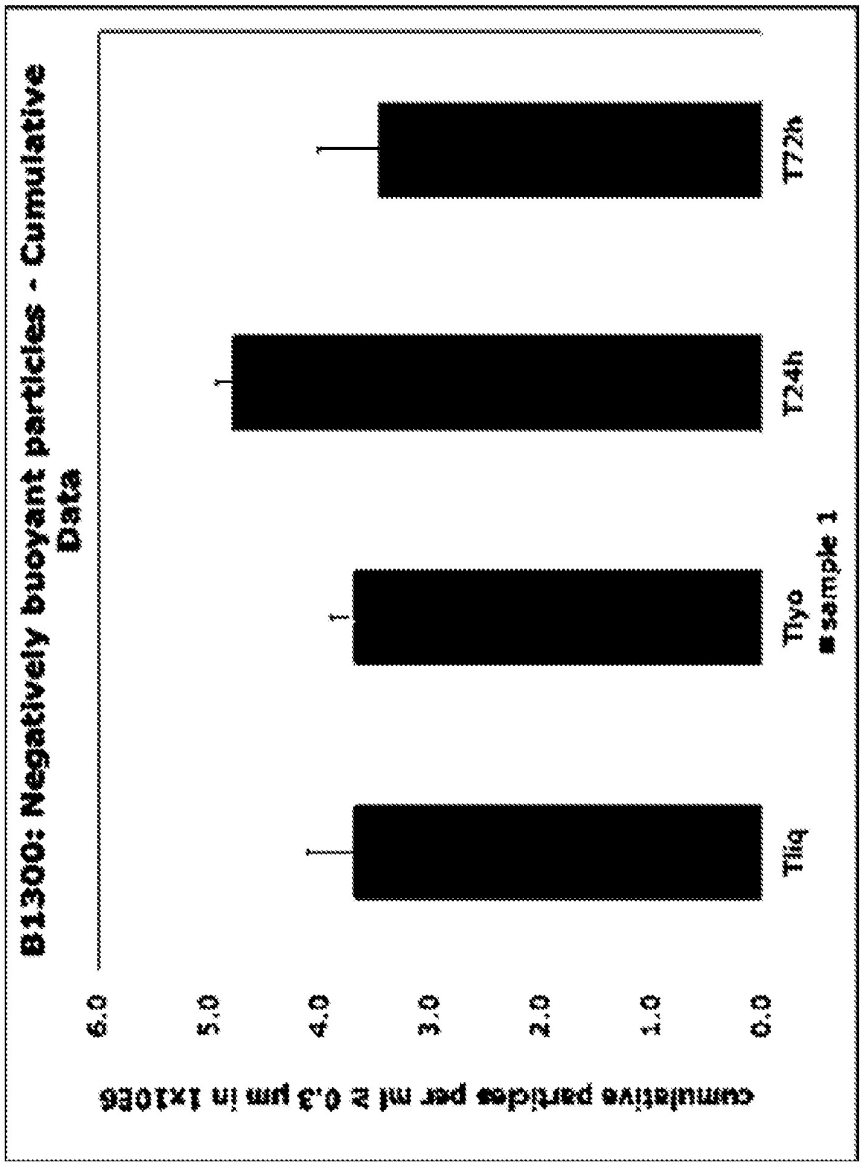

B1300: Negatively buoyant particles - Cumulative Data
cumulative particles per ml ≥ 0.3 µm in 1x10E6
6.0
5.0
4.0
3.0
2.0
1.0
0.0
Tliq
Tlyo
T24h
T72h
sample 1

*FIG. 59D*

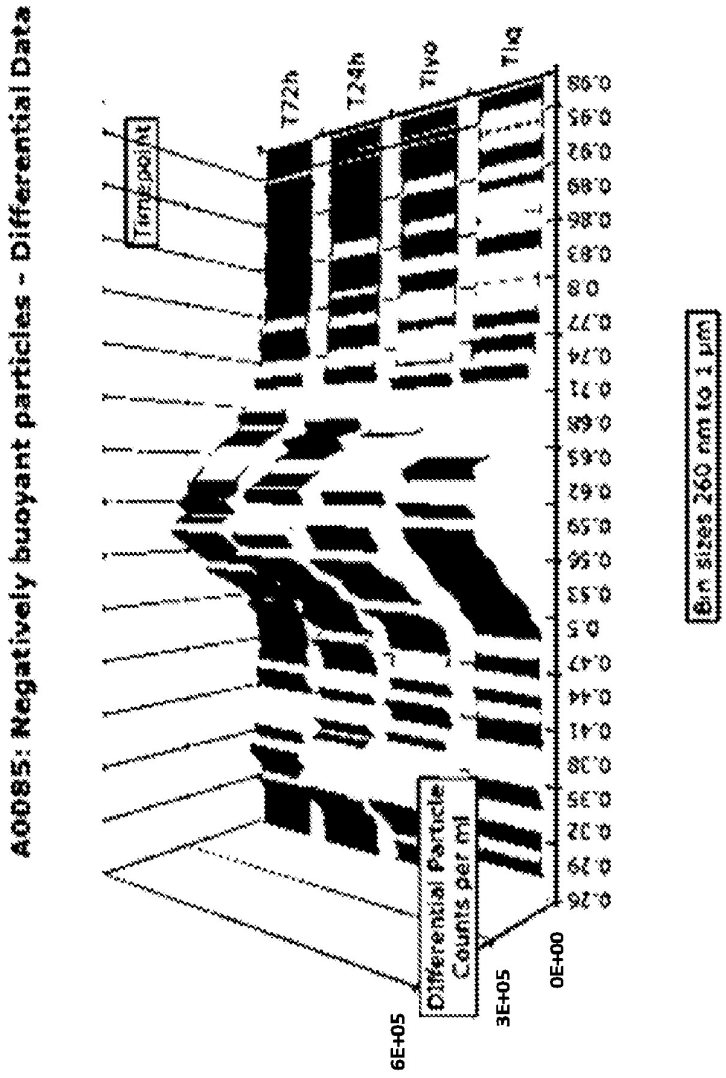

A0085: Negatively buoyant particles - Differential Data
Timepoint
T72h
T24h
T1yo
T1q
Differential Particle Counts per ml
6E+05
3E+05
0E+00
0.26
0.29
0.32
0.35
0.38
0.41
0.44
0.47
0.5
0.53
0.56
0.59
0.62
0.65
0.68
0.71
0.74
0.77
0.8
0.83
0.86
0.89
0.92
0.95
0.98
Bin sizes 260 nm to 1 µm

*FIG. 60A*

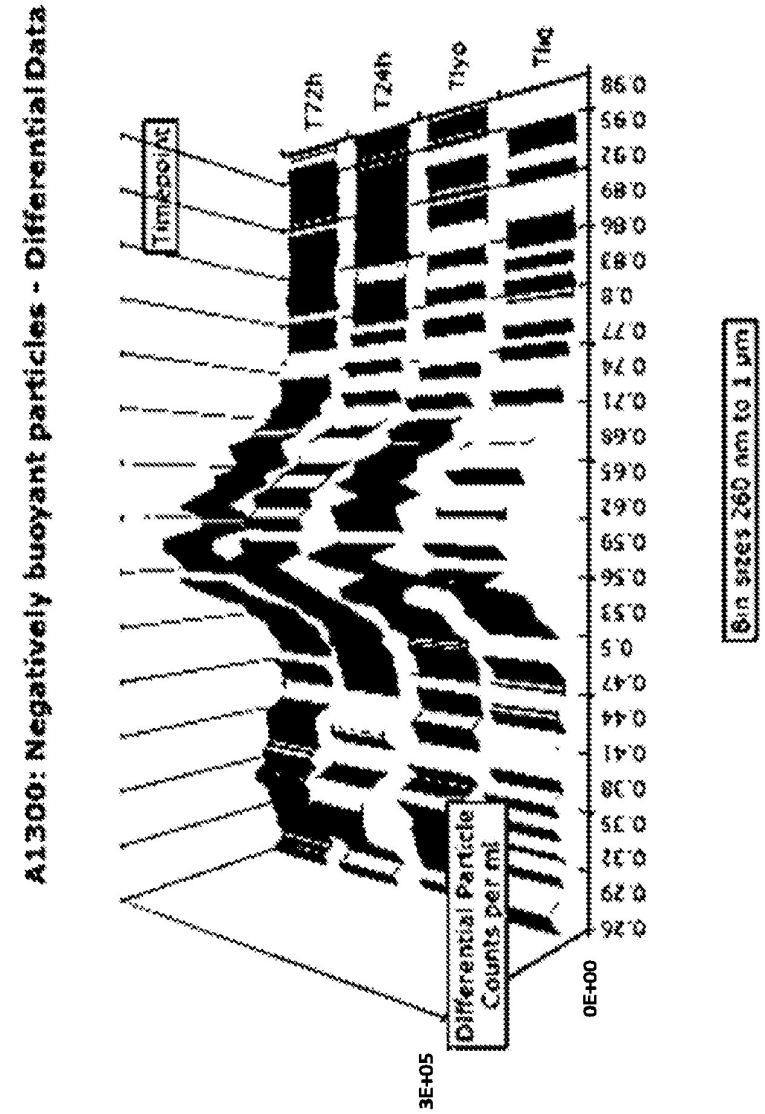

A1300: Negatively buoyant particles - Differential Data
Timepoint
T72h
T24h
T1yo
T1wo
Differential Particle Counts per ml
3E+05
0E+00
0.26
0.29
0.32
0.35
0.38
0.41
0.44
0.47
0.5
0.53
0.56
0.59
0.62
0.65
0.68
0.71
0.74
0.77
0.8
0.83
0.86
0.89
0.92
0.95
0.98
Bin sizes 260 nm to 1 µm

*FIG. 60B*

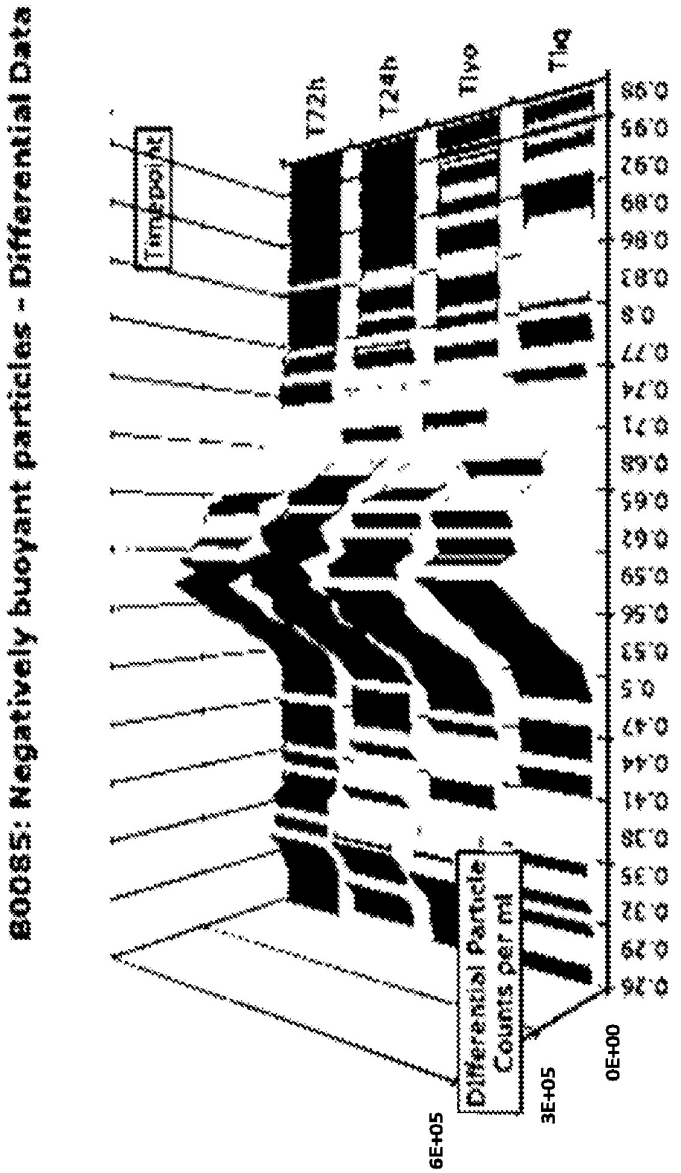

80085: Negatively buoyant particles - Differential Data
Time point
T72h
T24h
T1yo
T1q
Differential Particle Counts per ml
6E+05
3E+05
0E+00
0.26
0.29
0.32
0.35
0.38
0.41
0.44
0.47
0.5
0.53
0.56
0.59
0.62
0.65
0.68
0.71
0.74
0.77
0.8
0.83
0.86
0.89
0.92
0.95
0.98
Bin sizes 260 nm to 1 µm

*FIG. 60C*

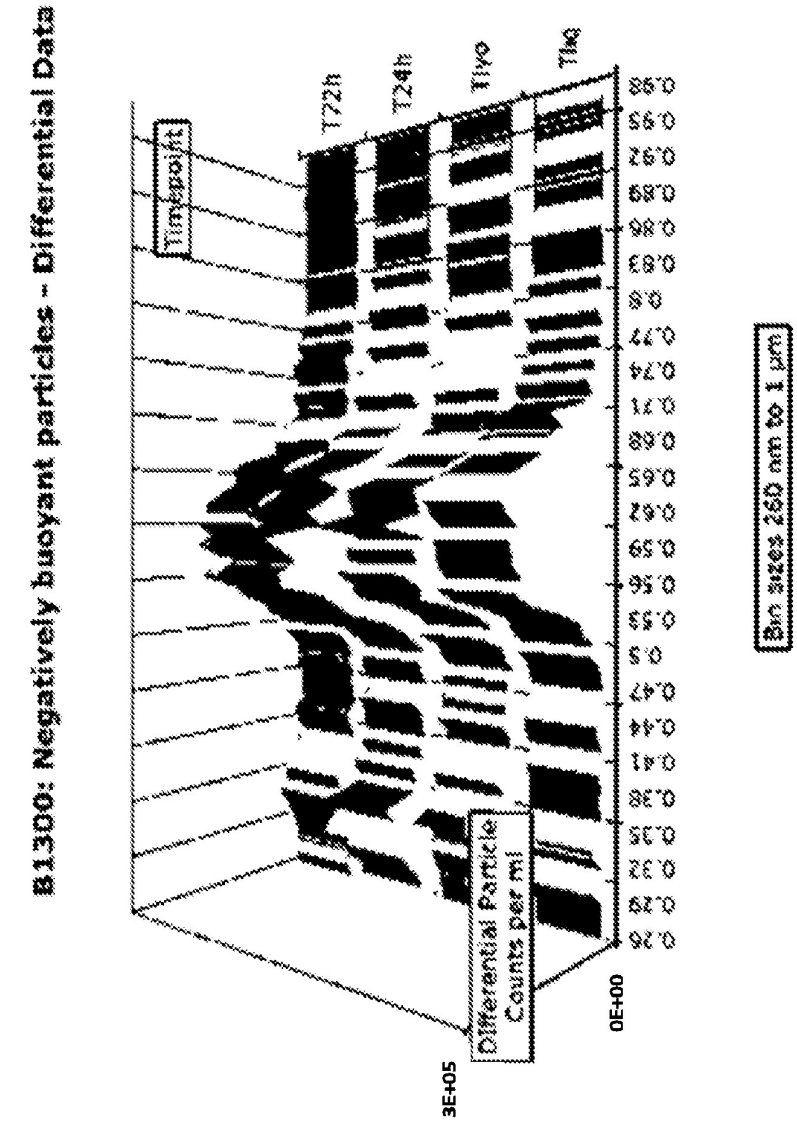

B1300: Negatively buoyant particles - Differential Data
Timepoint
T72h
T24h
T1yo
T1wo
Differential Particle Counts per ml
3E+05
0E+00
0.26
0.29
0.32
0.35
0.38
0.41
0.44
0.47
0.5
0.53
0.56
0.59
0.62
0.65
0.68
0.71
0.74
0.77
0.8
0.83
0.86
0.89
0.92
0.95
0.98
Bin sizes 260 nm to 1 µm

*FIG. 60D*

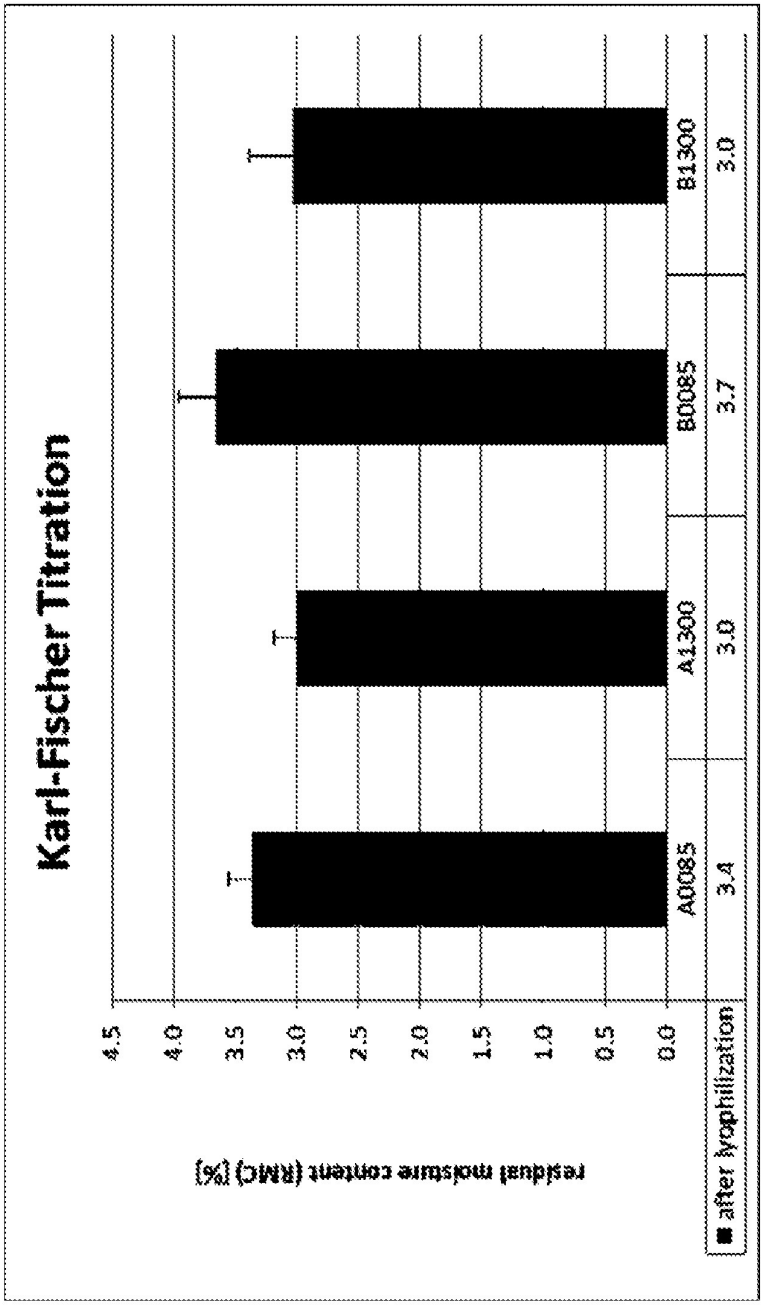

Karl-Fischer Titration
residual moisture content (RMC) [%]
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
A0085
A1300
B0085
B1300
after lyophilization
3.4
3.0
3.7
3.0

*FIG. 61*

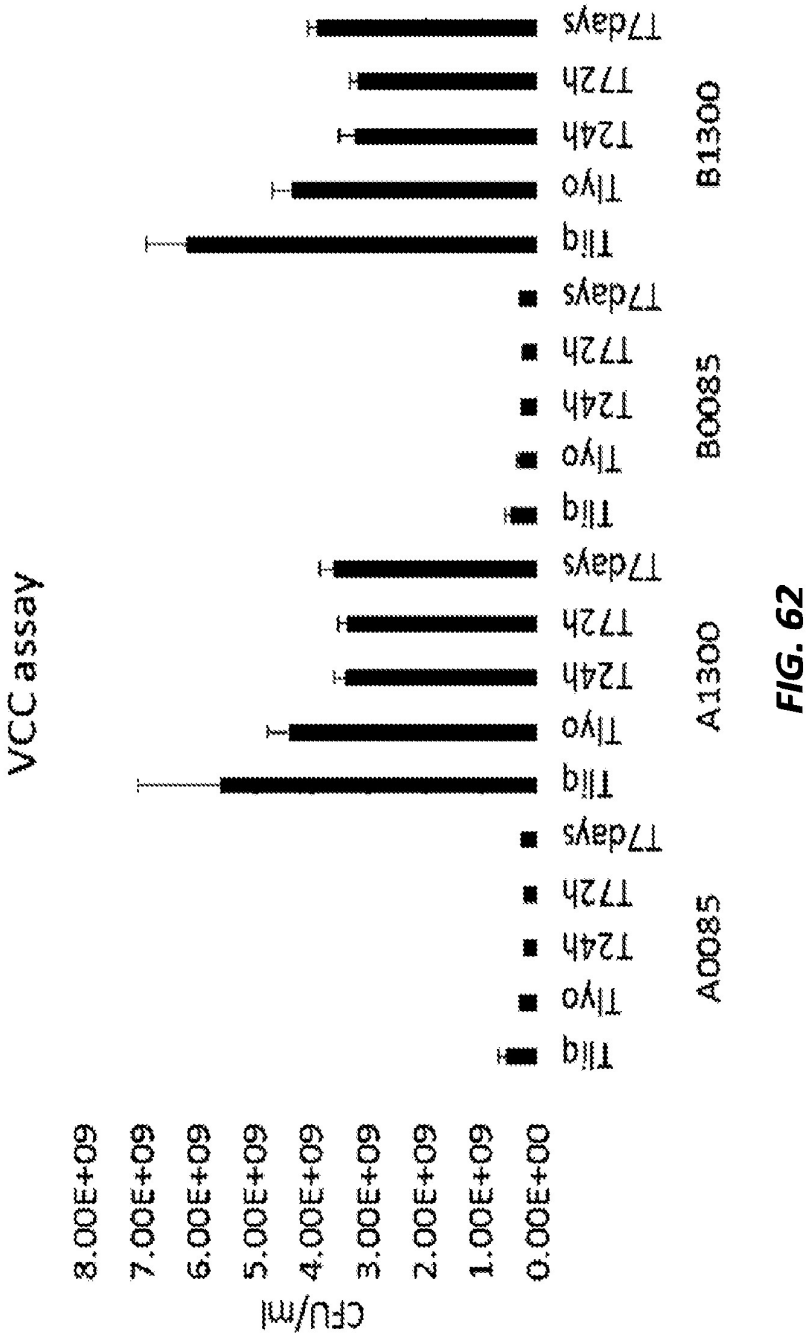

VCC assay
CFU/ml
8.00E+09
7.00E+09
6.00E+09
5.00E+09
4.00E+09
3.00E+09
2.00E+09
1.00E+09
0.00E+00
T0
Tiyo
T24h
T72h
T7days
A0085
B0085
A1300
B1300

*FIG. 62*

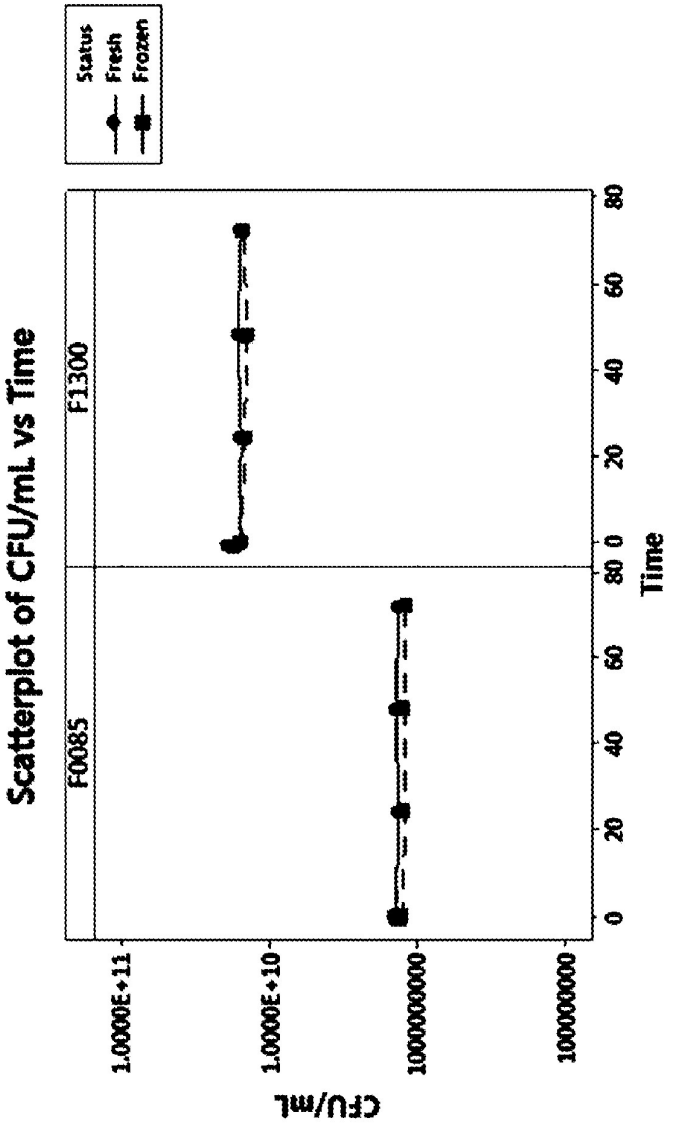

Scatterplot of CFU/mL vs Time
F0085
F1300
Status
Fresh
Frozen
CFU/mL
1.0000E+11
1.0000E+10
1000000000
100000000
0
20
40
60
80
Time
Panel variable: WP8 Lot

FIG. 63A

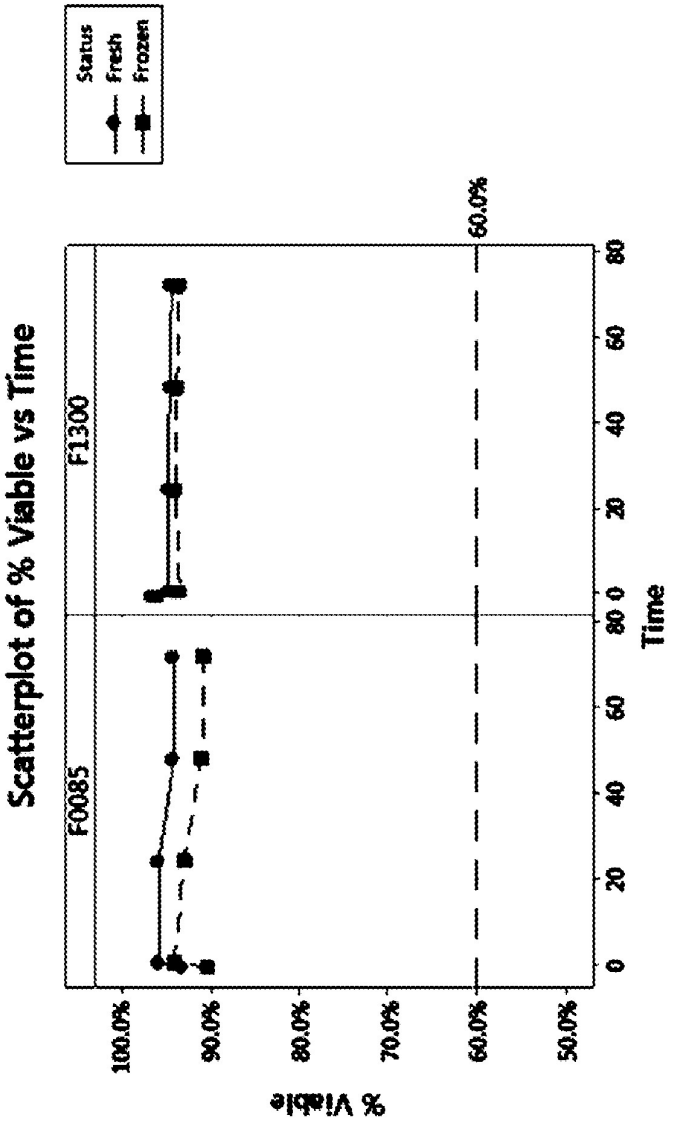

Scatterplot of % Viable vs Time
Status
Fresh
Frozen
F0085
F1300
60.0%
% Viable
100.0%
90.0%
80.0%
70.0%
60.0%
50.0%
0
20
40
60
80
0
20
40
60
80
Time
Panel variable: WP8 Lot

FIG. 63B

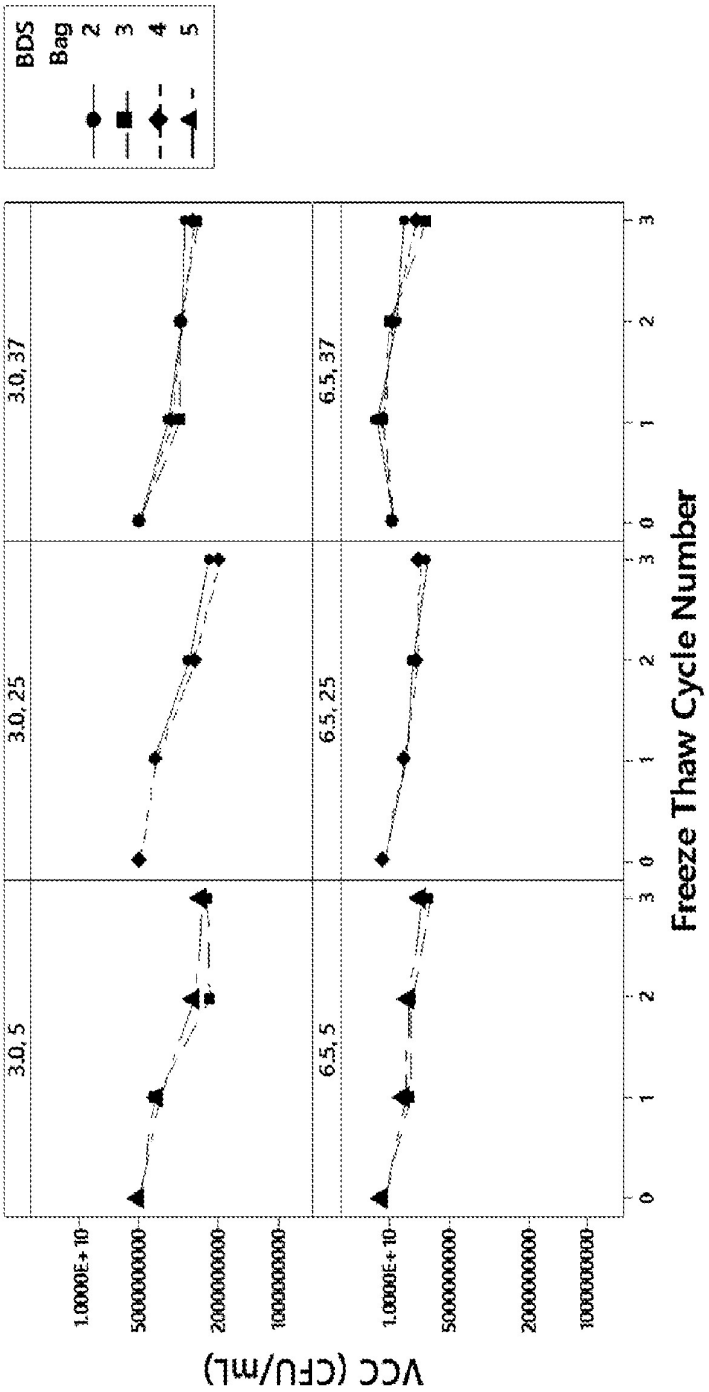

BDS
Bag
2
3
4
5
3.0, 5
3.0, 25
3.0, 37
6.5, 5
6.5, 25
6.5, 37
VCC (CFU/mL)
1.0000E+10
5000000000
2000000000
1000000000
0
1
2
3
Freeze Thaw Cycle Number

*FIG. 64*

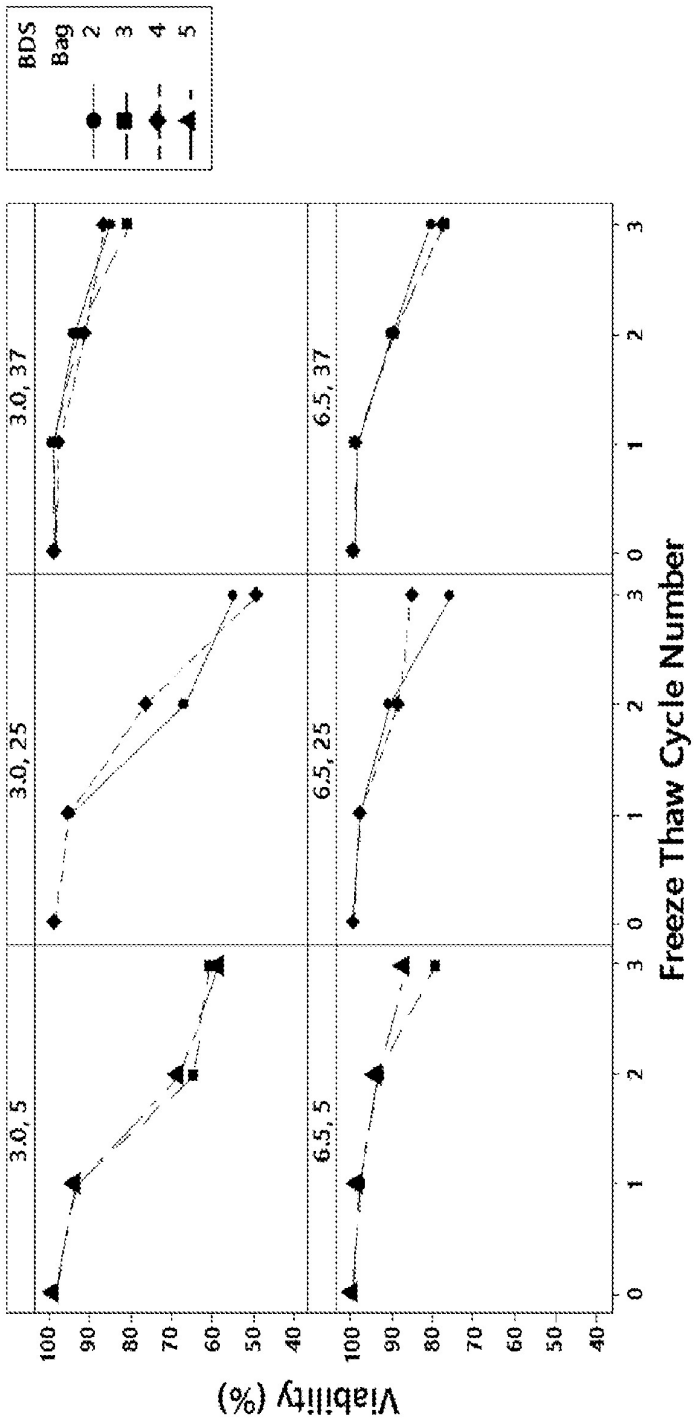

BDS
Bag
2
3
4
5
3.0, 5
3.0, 25
3.0, 37
6.5, 5
6.5, 25
6.5, 37
Viability (%)
100
90
80
70
60
50
40
0
1
2
3
Freeze Thaw Cycle Number

*FIG. 65*