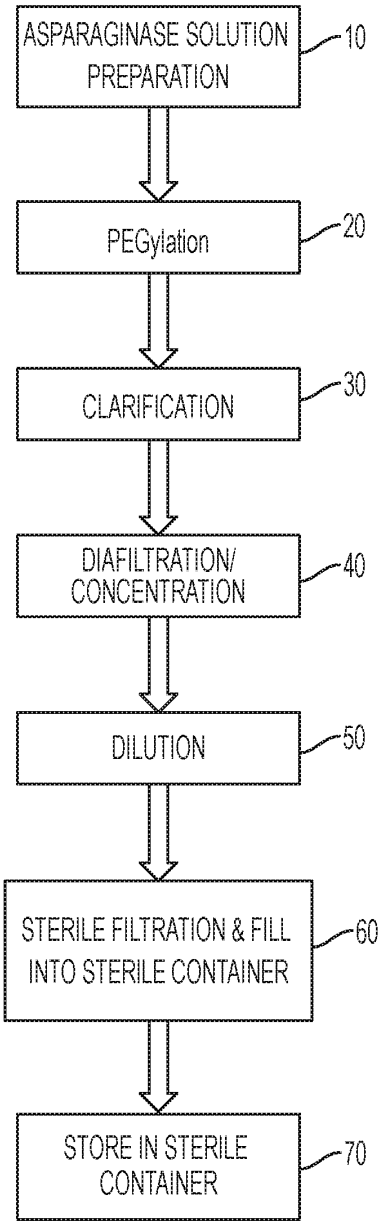

ASPARAGINASE SOLUTION PREPARATION
10
PEGylation
20
CLARIFICATION
30
DIAFILTRATION/ CONCENTRATION
40
DILUTION
50
STERILE FILTRATION & FILL INTO STERILE CONTAINER
60
STORE IN STERILE CONTAINER
70

FIG. 1

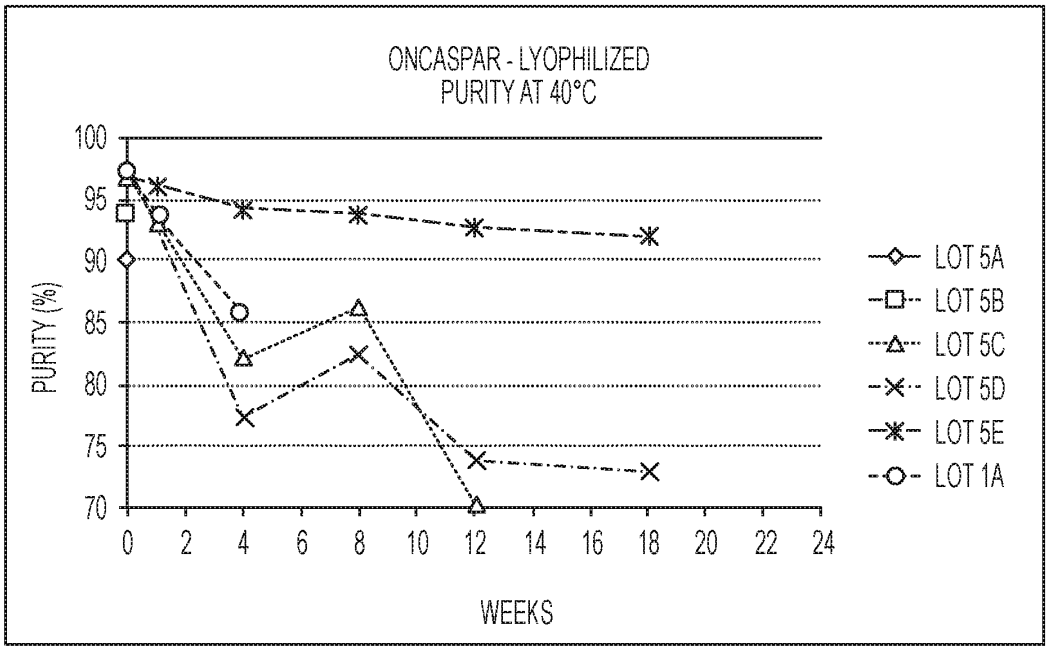

ONCASPAR - LYOPHILIZED
PURITY AT 40°C
PURITY (%)
100
95
90
85
80
75
70
0
2
4
6
8
10
12
14
16
18
20
22
24
WEEKS
LOT 5A
LOT 5B
LOT 5C
LOT 5D
LOT 5E
LOT 1A

FIG. 2

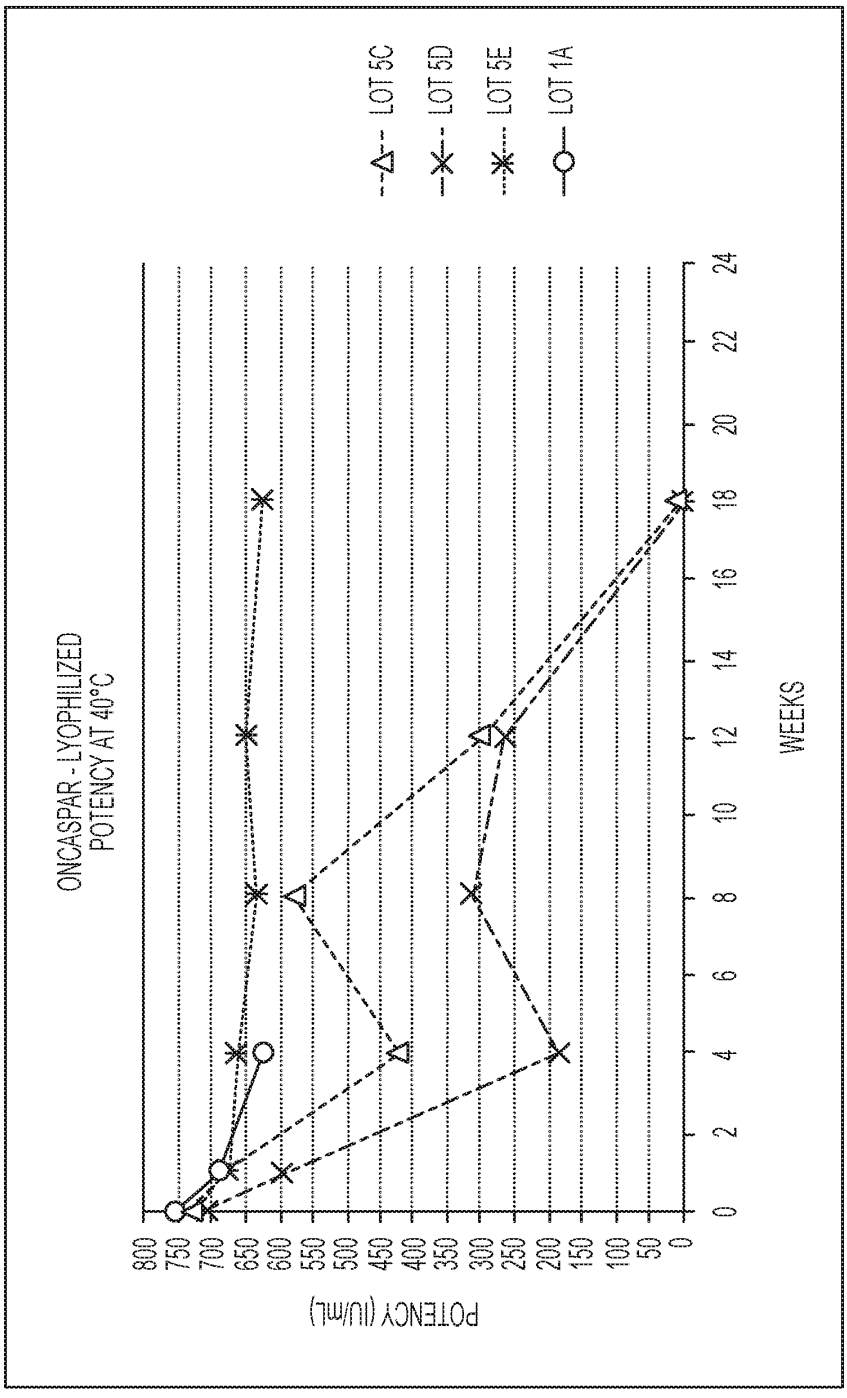

ONCASPAR - LYOPHILIZED
POTENCY AT 40°C
LOT 5C
LOT 5D
LOT 5E
LOT 1A
POTENCY (IU/mL)
800
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
WEEKS
0
2
4
6
8
10
12
14
16
18
20
22
24

FIG. 3

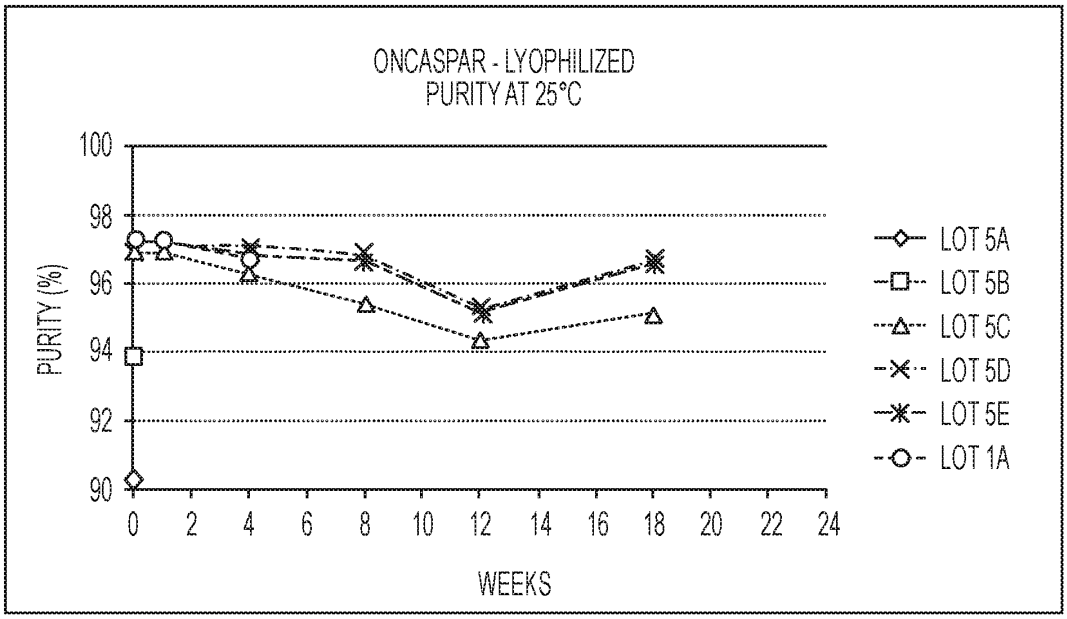

ONCASPAR - LYOPHILIZED
PURITY AT 25°C
PURITY (%)
100
98
96
94
92
90
0
2
4
6
8
10
12
14
16
18
20
22
24
WEEKS
LOT 5A
LOT 5B
LOT 5C
LOT 5D
LOT 5E
LOT 1A

FIG. 4

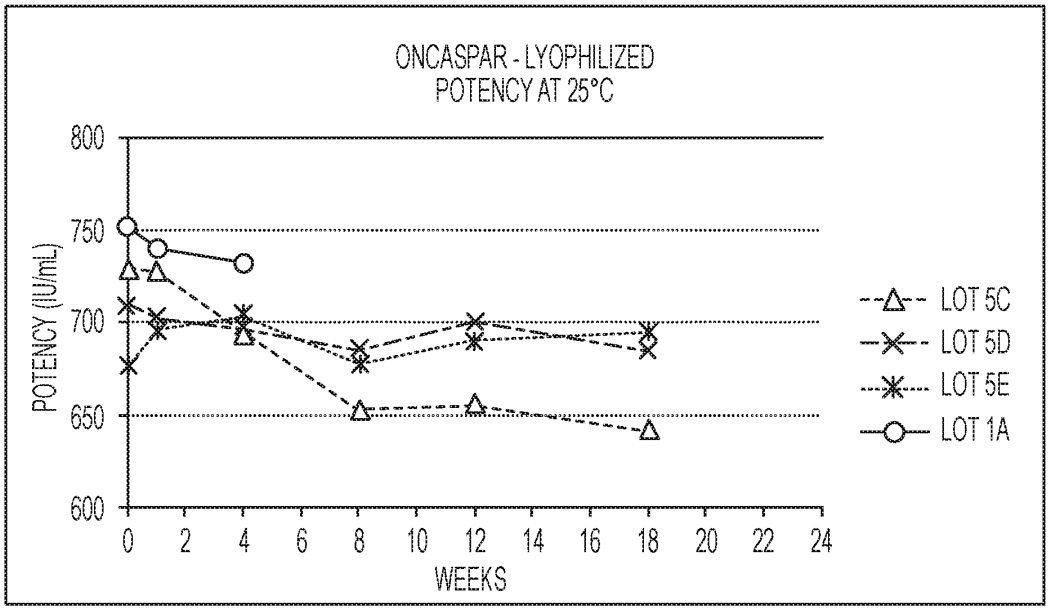

ONCASPAR - LYOPHILIZED
POTENCY AT 25°C
POTENCY (IU/mL)
800
750
700
650
600
0
2
4
6
8
10
12
14
16
18
20
22
24
WEEKS
LOT 5C
LOT 5D
LOT 5E
LOT 1A

FIG. 5

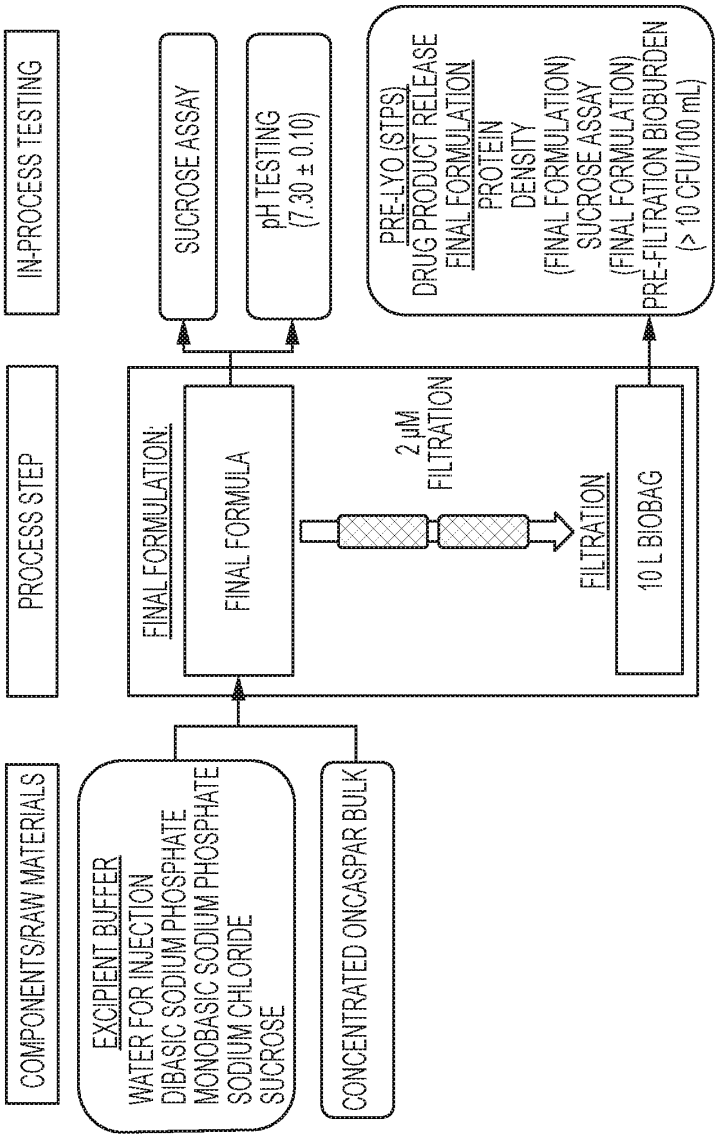

COMPONENTS/RAW MATERIALS
PROCESS STEP
IN-PROCESS TESTING
EXCIPIENT BUFFER
WATER FOR INJECTION
DIBASIC SODIUM PHOSPHATE
MONOBASIC SODIUM PHOSPHATE
SODIUM CHLORIDE
SUCROSE
CONCENTRATED ONCASPAR BULK
FINAL FORMULATION:
FINAL FORMULA
2 µM FILTRATION
FILTRATION
10 L BIOBAG
SUCROSE ASSAY
pH TESTING (7.30 ± 0.10)
PRE-LYO (STPS)
DRUG PRODUCT RELEASE
FINAL FORMULATION
PROTEIN
DENSITY
(FINAL FORMULATION)
SUCROSE ASSAY
(FINAL FORMULATION)
PRE-FILTRATION BIOBURDEN
(> 10 CFU/100 mL)

FIG. 6

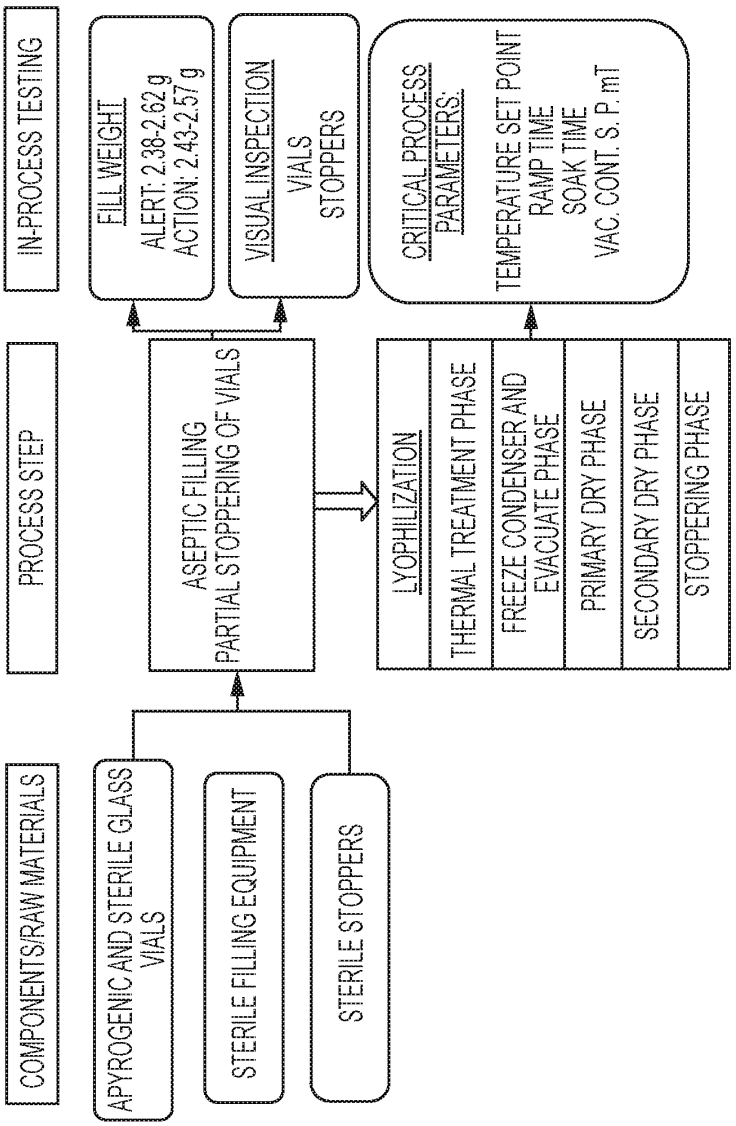

COMPONENTS/RAW MATERIALS
PROCESS STEP
IN-PROCESS TESTING
APYROGENIC AND STERILE GLASS VIALS
STERILE FILLING EQUIPMENT
STERILE STOPPERS
ASEPTIC FILLING
PARTIAL STOPPERING OF VIALS
FILL WEIGHT
ALERT: 2.38-2.62 g
ACTION: 2.43-2.57 g
VISUAL INSPECTION
VIALS
STOPPERS
LYOPHILIZATION
THERMAL TREATMENT PHASE
FREEZE CONDENSER AND EVACUATE PHASE
PRIMARY DRY PHASE
SECONDARY DRY PHASE
STOPPERING PHASE
CRITICAL PROCESS PARAMETERS:
TEMPERATURE SET POINT
RAMP TIME
SOAK TIME
VAC. CONT. S. P. mT

FIG. 7

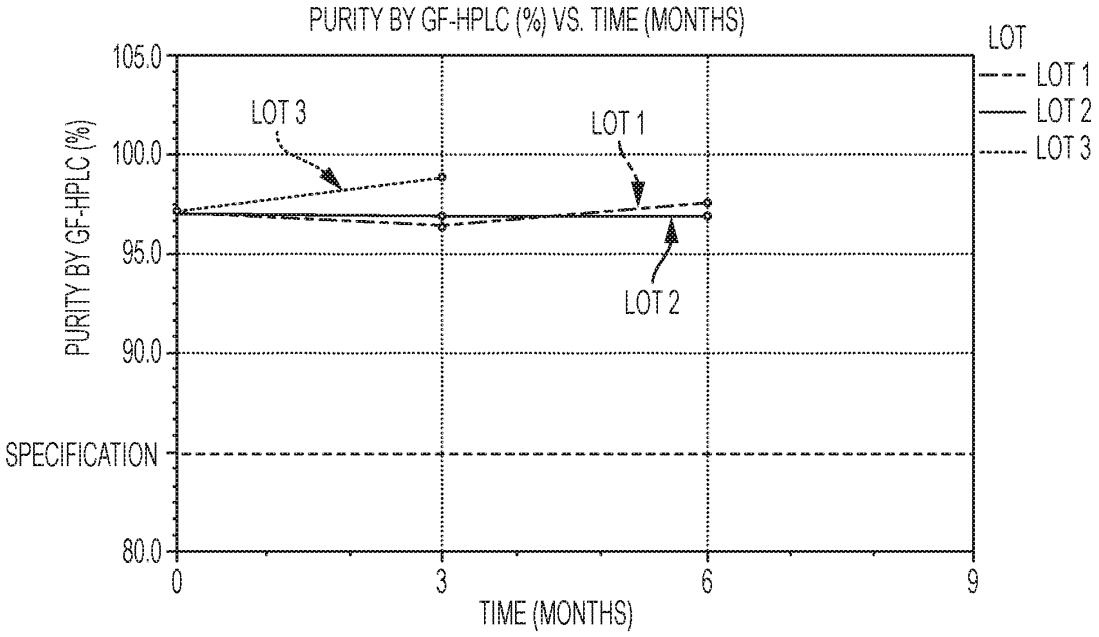

PURITY BY GF-HPLC (%) VS. TIME (MONTHS)
PURITY BY GF-HPLC (%)
105.0
100.0
95.0
90.0
SPECIFICATION
80.0
0
3
6
9
TIME (MONTHS)
LOT 3
LOT 1
LOT 2
LOT
LOT 1
LOT 2
LOT 3

FIG. 8

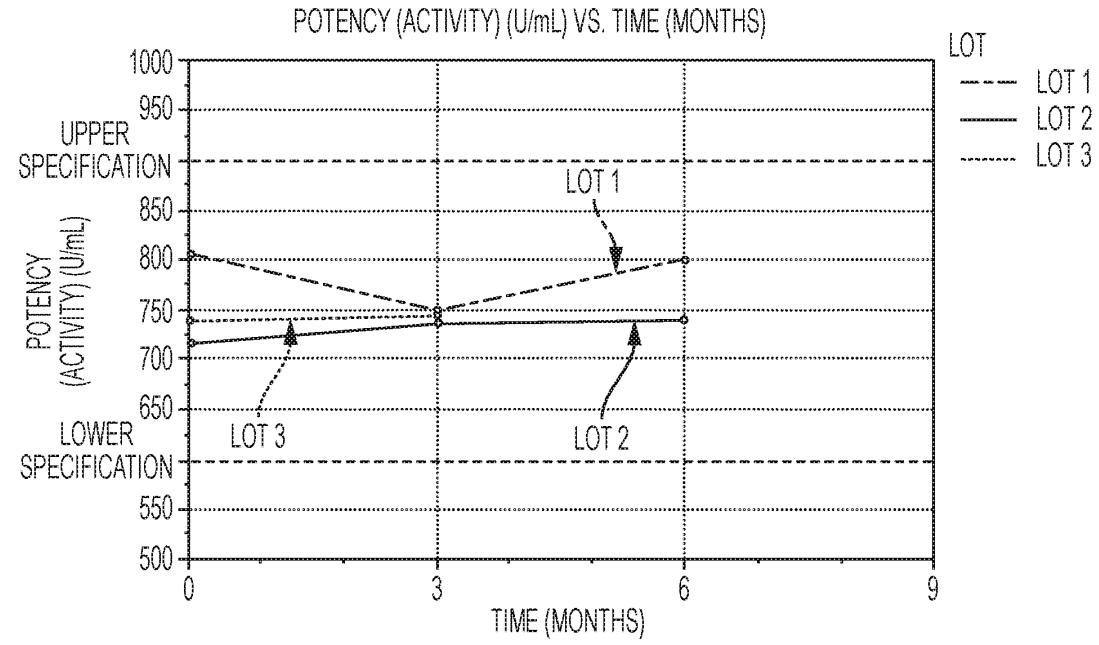

POTENCY (ACTIVITY) (U/mL) VS. TIME (MONTHS)
POTENCY (ACTIVITY) (U/mL)
1000
950
UPPER SPECIFICATION
850
800
750
700
650
LOWER SPECIFICATION
550
500
0
3
6
9
TIME (MONTHS)
LOT 1
LOT 3
LOT 2
LOT
LOT 1
LOT 2
LOT 3

FIG. 9

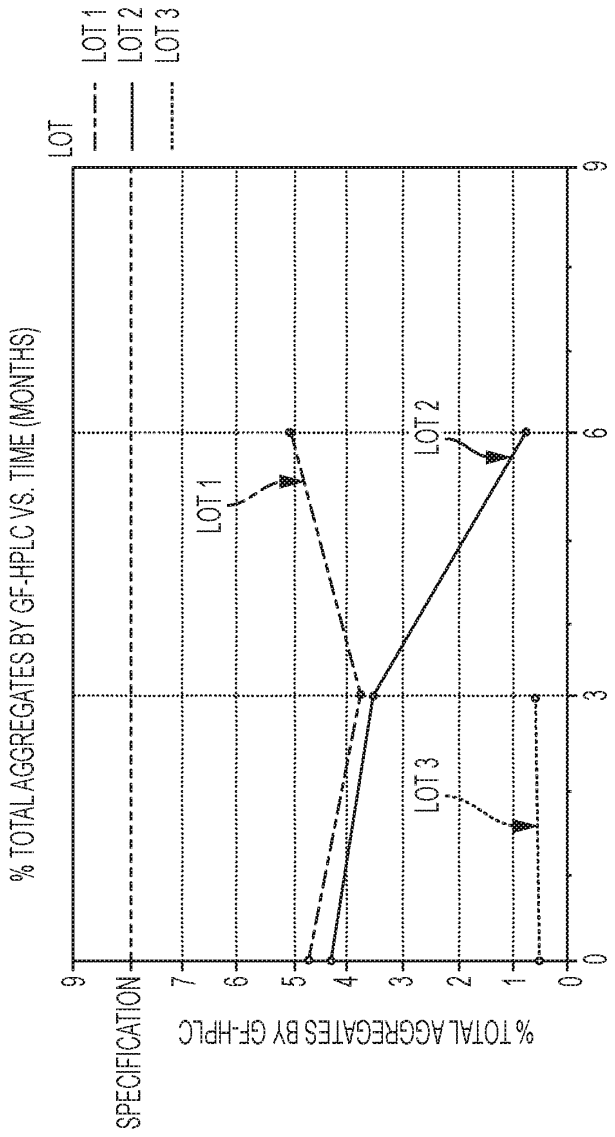

% TOTAL AGGREGATES BY GF-HPLC VS. TIME (MONTHS)
LOT
LOT 1
LOT 2
LOT 3
% TOTAL AGGREGATES BY GF-HPLC
SPECIFICATION
TIME (MONTHS)
0
1
2
3
4
5
6
7
9
0
3
6
9

FIG. 10

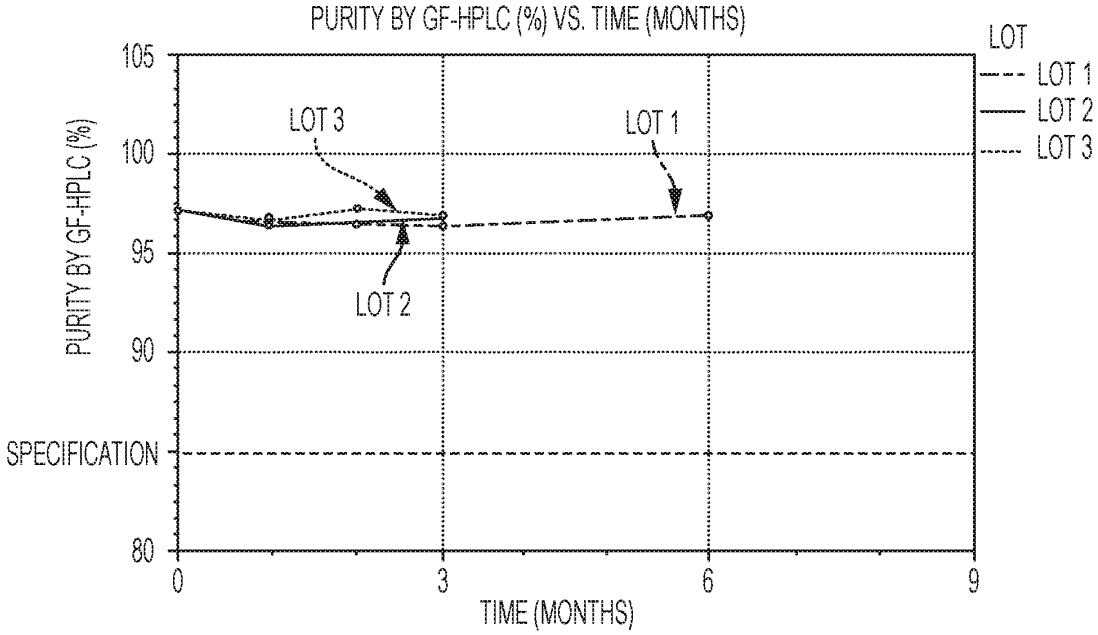

PURITY BY GF-HPLC (%) VS. TIME (MONTHS)
PURITY BY GF-HPLC (%)
105
100
95
90
SPECIFICATION
80
0
3
6
9
TIME (MONTHS)
LOT 3
LOT 1
LOT 2
LOT
LOT 1
LOT 2
LOT 3

FIG. 11

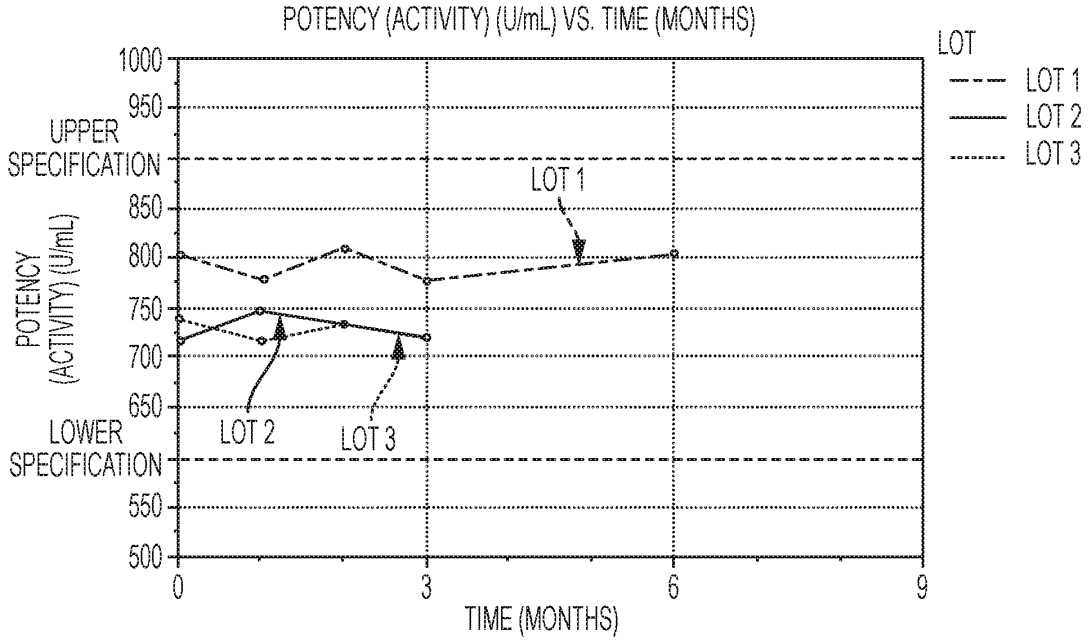

POTENCY (ACTIVITY) (U/mL) VS. TIME (MONTHS)
POTENCY (ACTIVITY) (U/mL)
1000
950
UPPER SPECIFICATION
850
800
750
700
650
LOWER SPECIFICATION
550
500
0
3
6
9
TIME (MONTHS)
LOT 1
LOT 2
LOT 3
LOT
LOT 1
LOT 2
LOT 3

FIG. 12

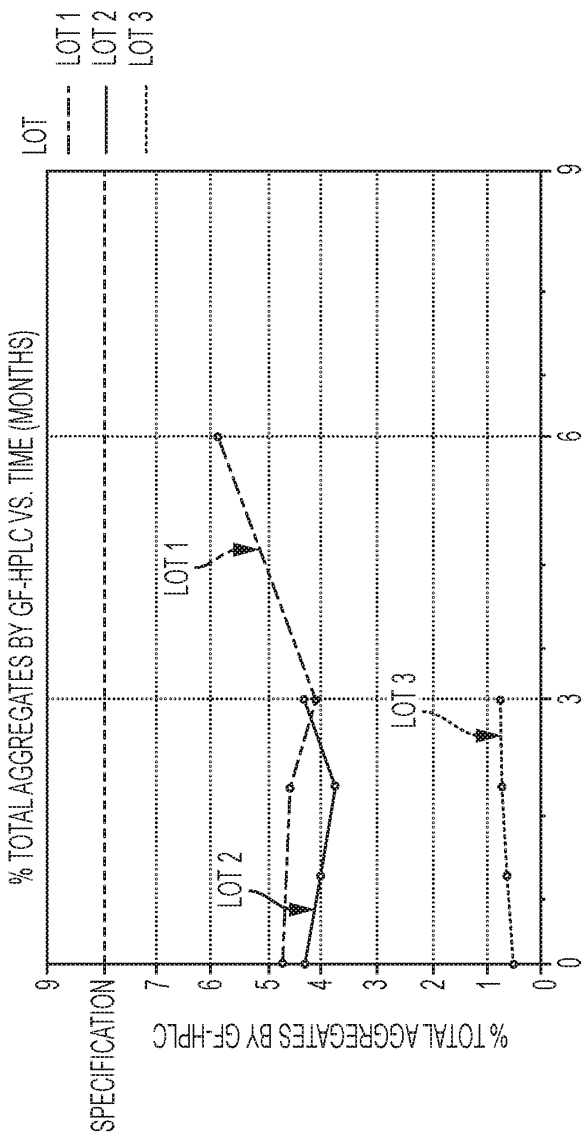

% TOTAL AGGREGATES BY GF-HPLC VS. TIME (MONTHS)
LOT
LOT 1
LOT 2
LOT 3
SPECIFICATION
% TOTAL AGGREGATES BY GF-HPLC
TIME (MONTHS)
0
1
2
3
4
5
6
7
9
3
6
9

FIG. 13

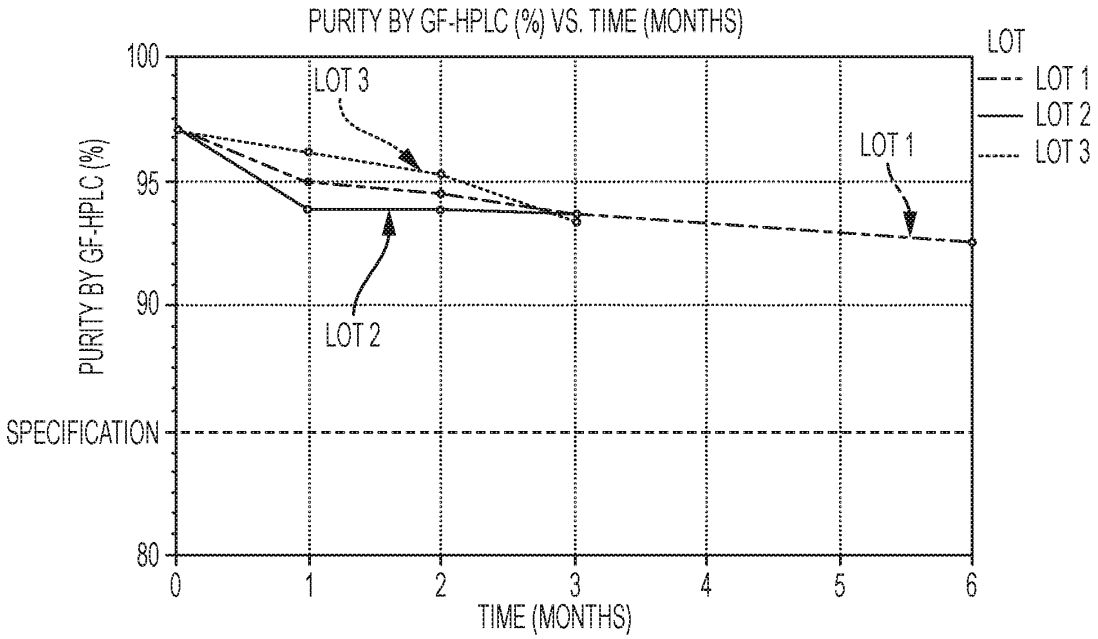

PURITY BY GF-HPLC (%) VS. TIME (MONTHS)
PURITY BY GF-HPLC (%)
100
95
90
SPECIFICATION
80
0
1
2
3
4
5
6
TIME (MONTHS)
LOT 3
LOT 2
LOT 1
LOT
LOT 1
LOT 2
LOT 3

FIG. 14

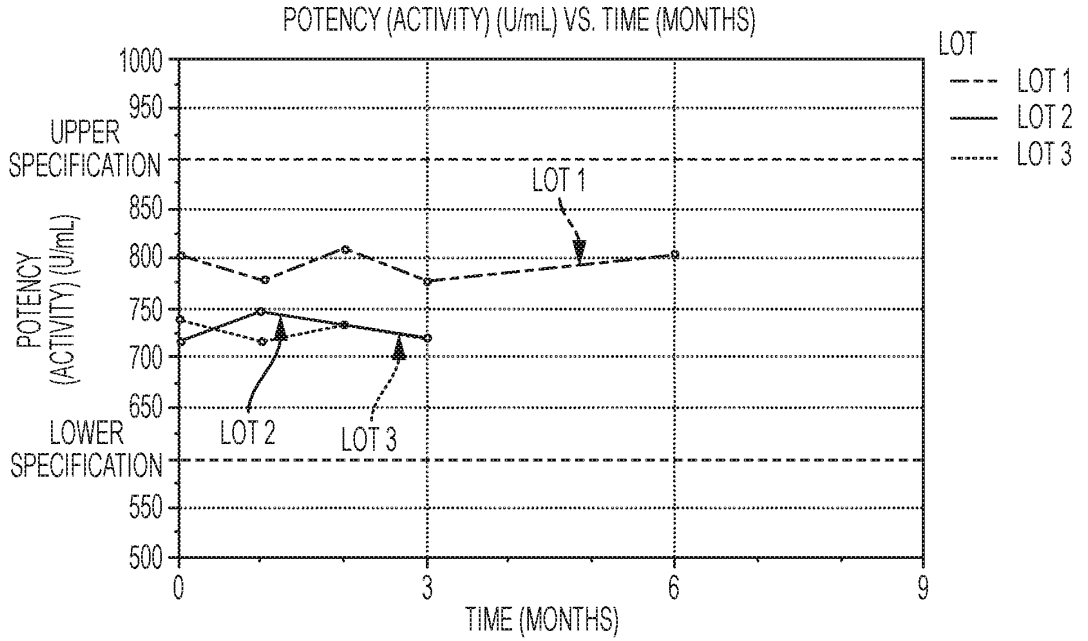

POTENCY (ACTIVITY) (U/mL) VS. TIME (MONTHS)
POTENCY (ACTIVITY) (U/mL)
1000
950
UPPER SPECIFICATION
850
800
750
700
650
LOWER SPECIFICATION
550
500
0
3
6
9
TIME (MONTHS)
LOT 1
LOT 2
LOT 3
LOT
LOT 1
LOT 2
LOT 3

FIG. 15

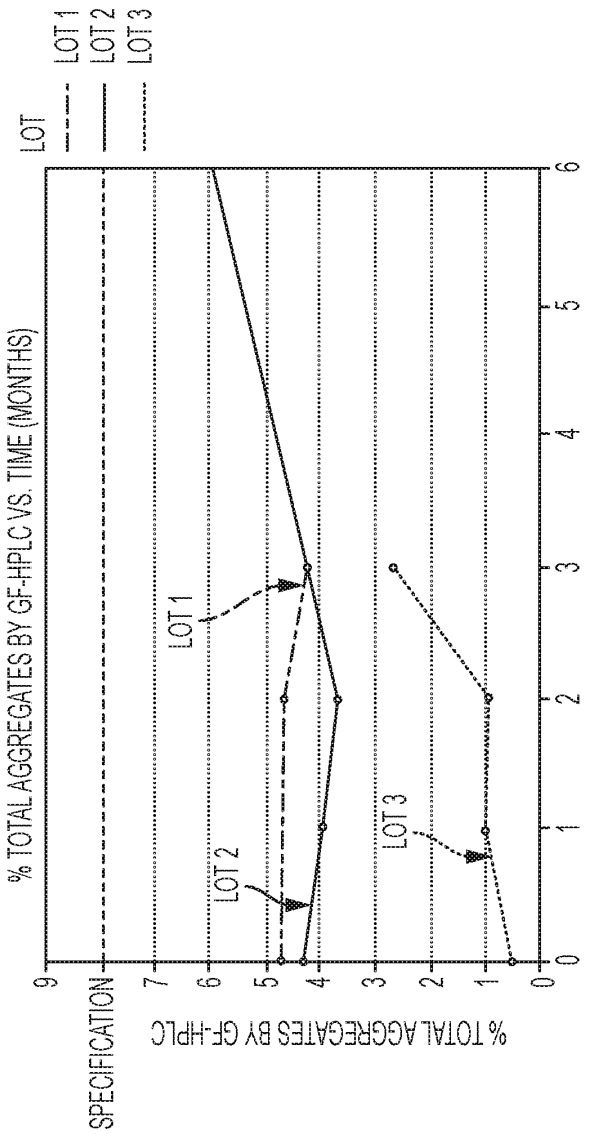

% TOTAL AGGREGATES BY GF-HPLC VS. TIME (MONTHS)
LOT
LOT 1
LOT 2
LOT 3
SPECIFICATION
% TOTAL AGGREGATES BY GF-HPLC
TIME (MONTHS)
0
1
2
3
4
5
6
7
9

FIG. 16