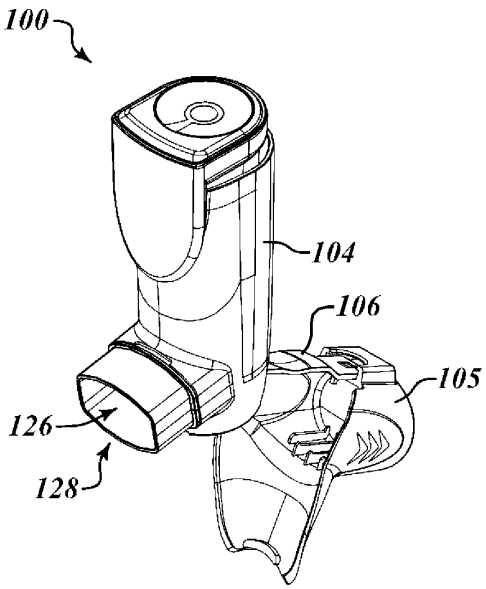

100
104
106
105
126
128

FIG.1

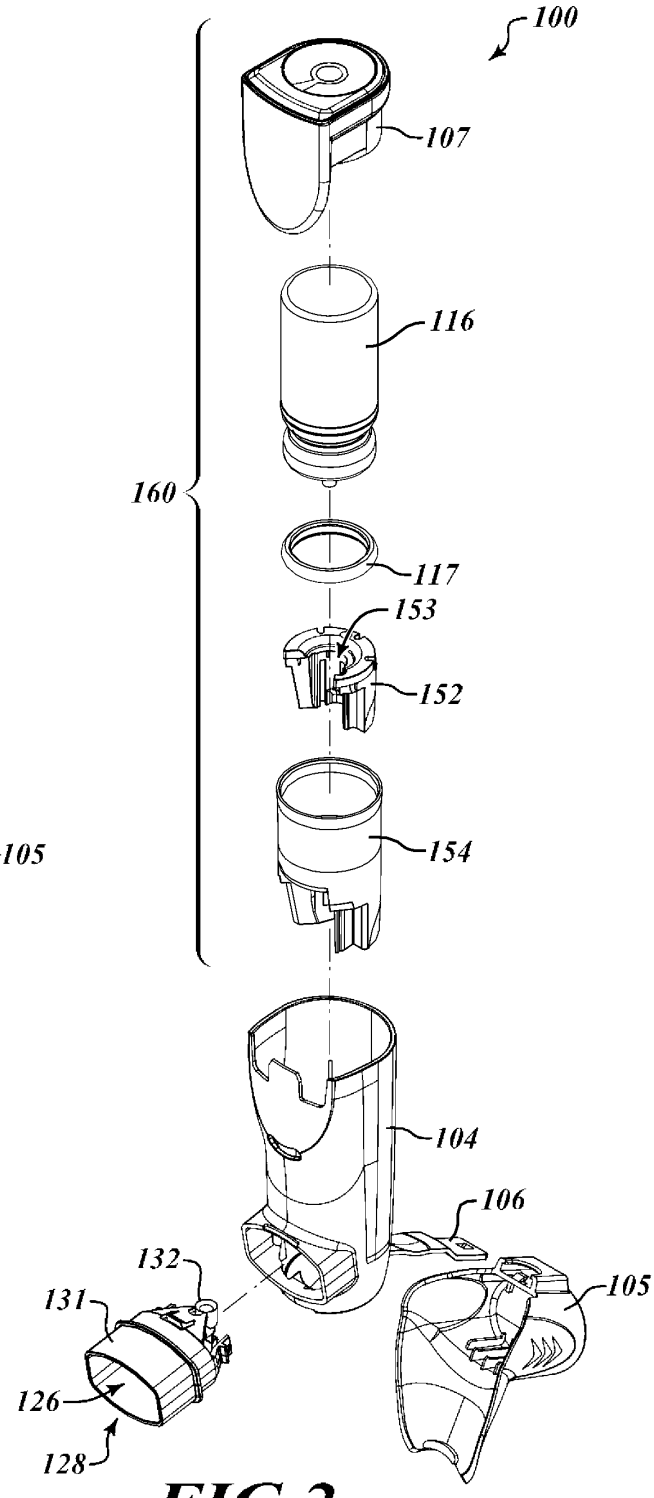

100
107
116
160
117
153
152
154
104
106
132
131
105
126
128

FIG.2

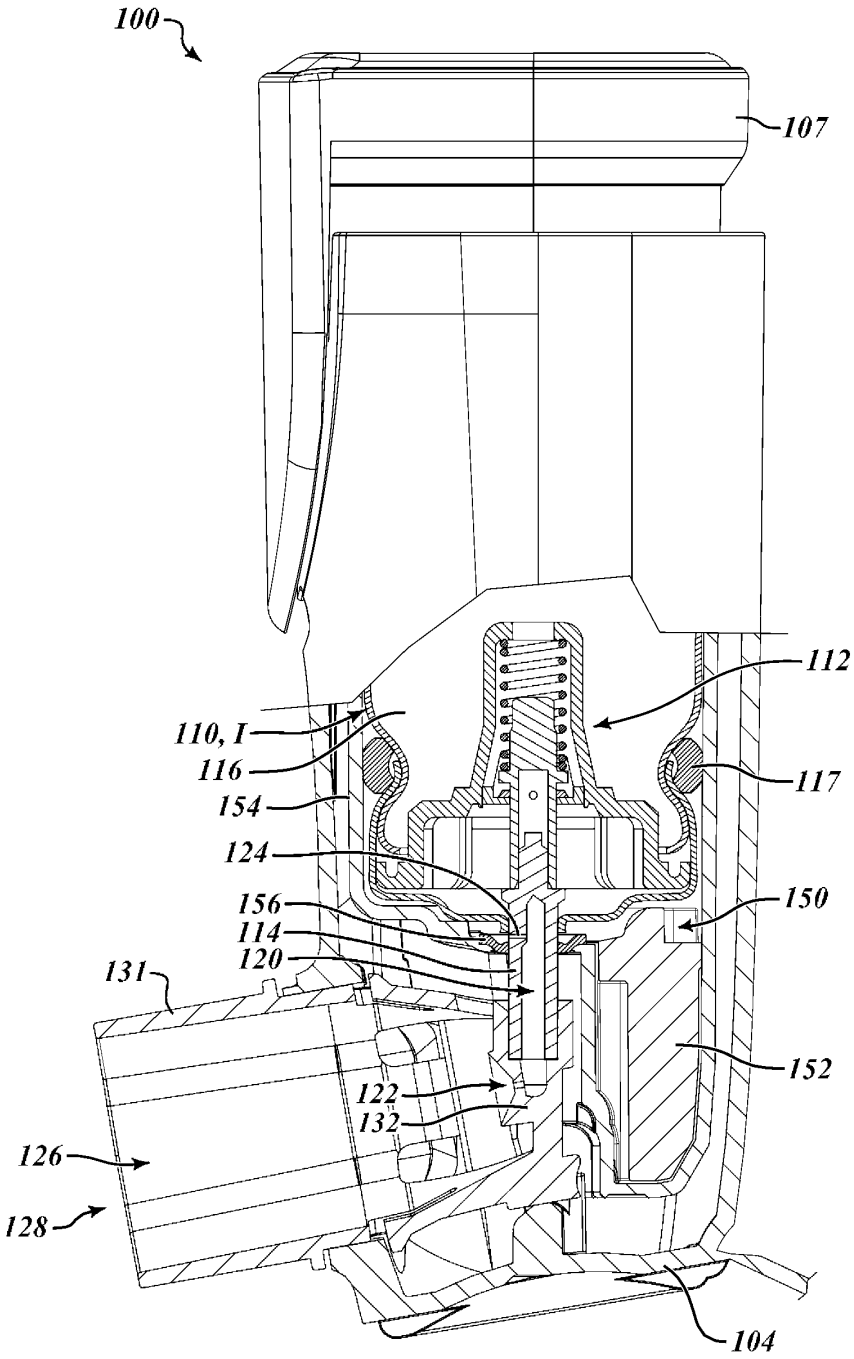

100
107
112
110, I
116
154
124
156
114
120
131
150
117
152
122
132
126
128
104

FIG.3A

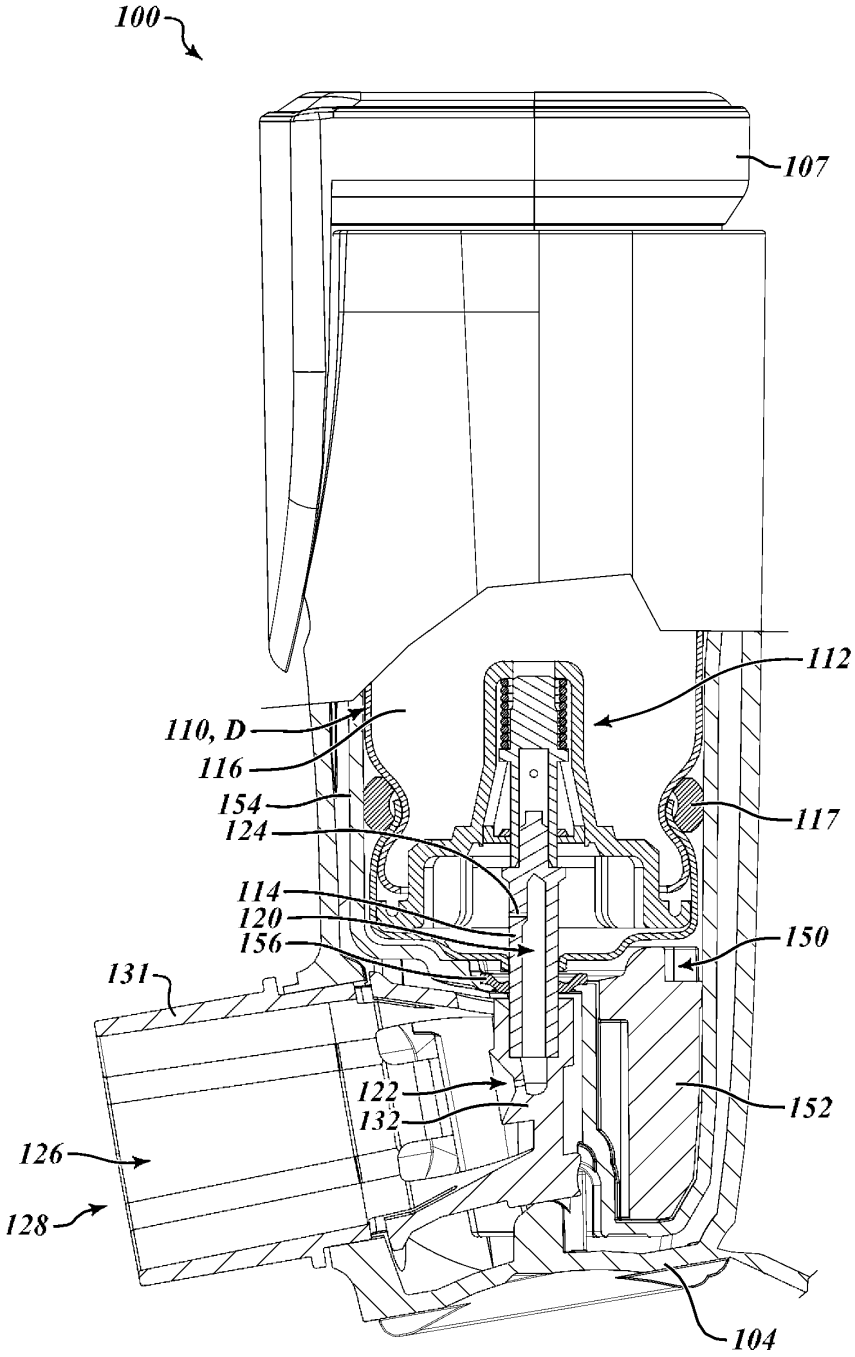

100
107
112
110, D
116
154
124
117
114
120
156
150
131
122
132
152
126
128
104

FIG.3B

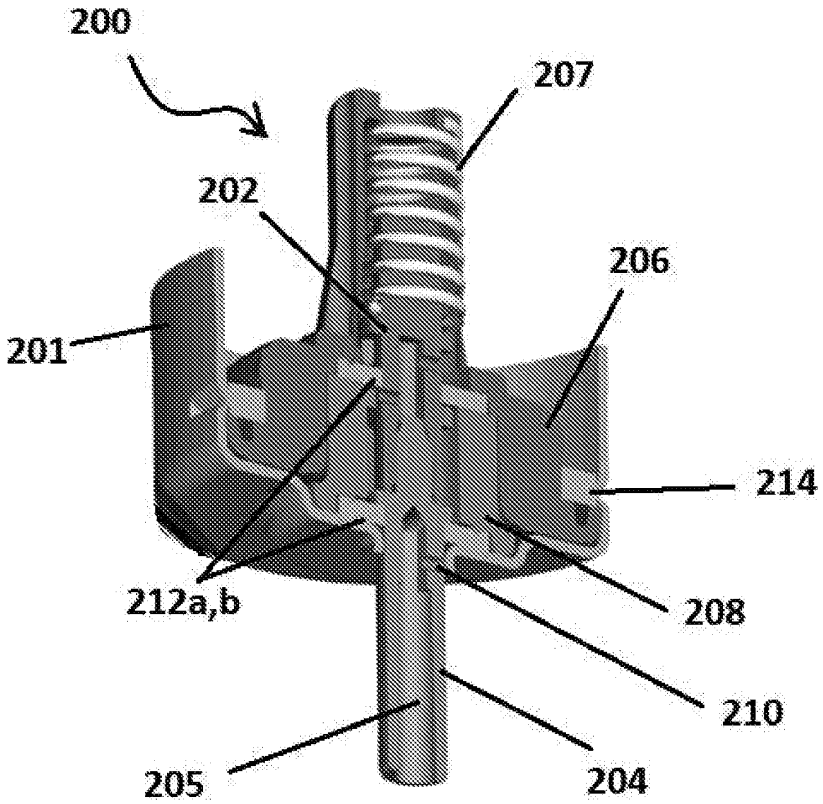


FIG. 4

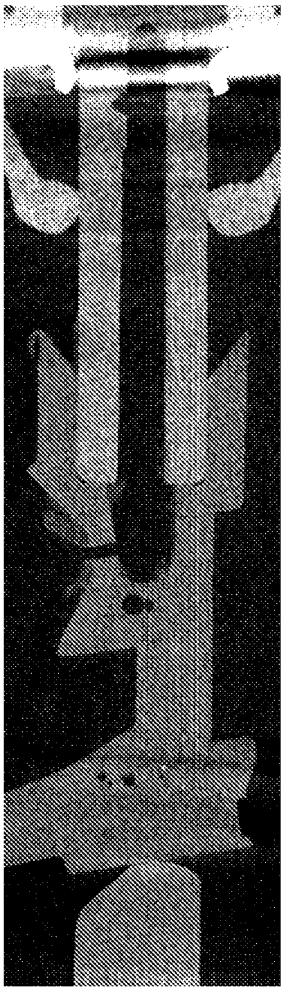


FIG. 5

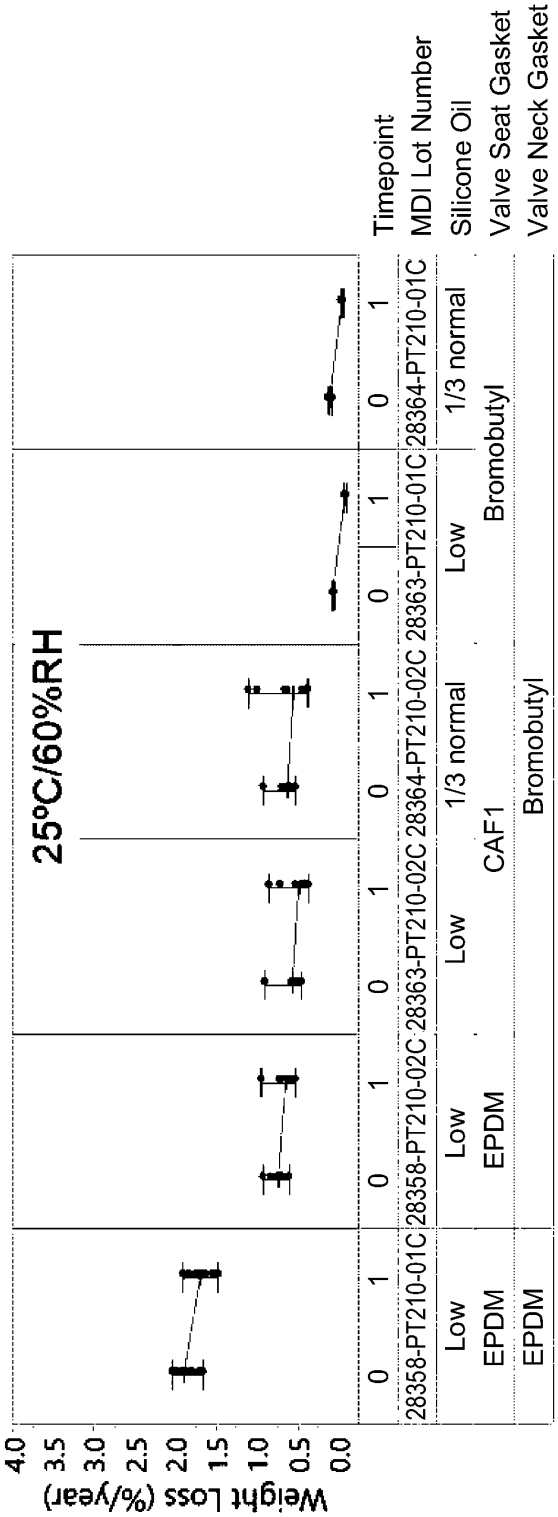

25ºC/60%RH
Weight Loss (%/year)
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Timepoint
MDI Lot Number
Silicone Oil
Valve Seat Gasket
Valve Neck Gasket
0
1
28358-PT210-01C
28358-PT210-02C
28363-PT210-02C
28364-PT210-02C
28363-PT210-01C
28364-PT210-01C
Low
1/3 normal
EPDM
CAF1
Bromobutyl

FIG. 6

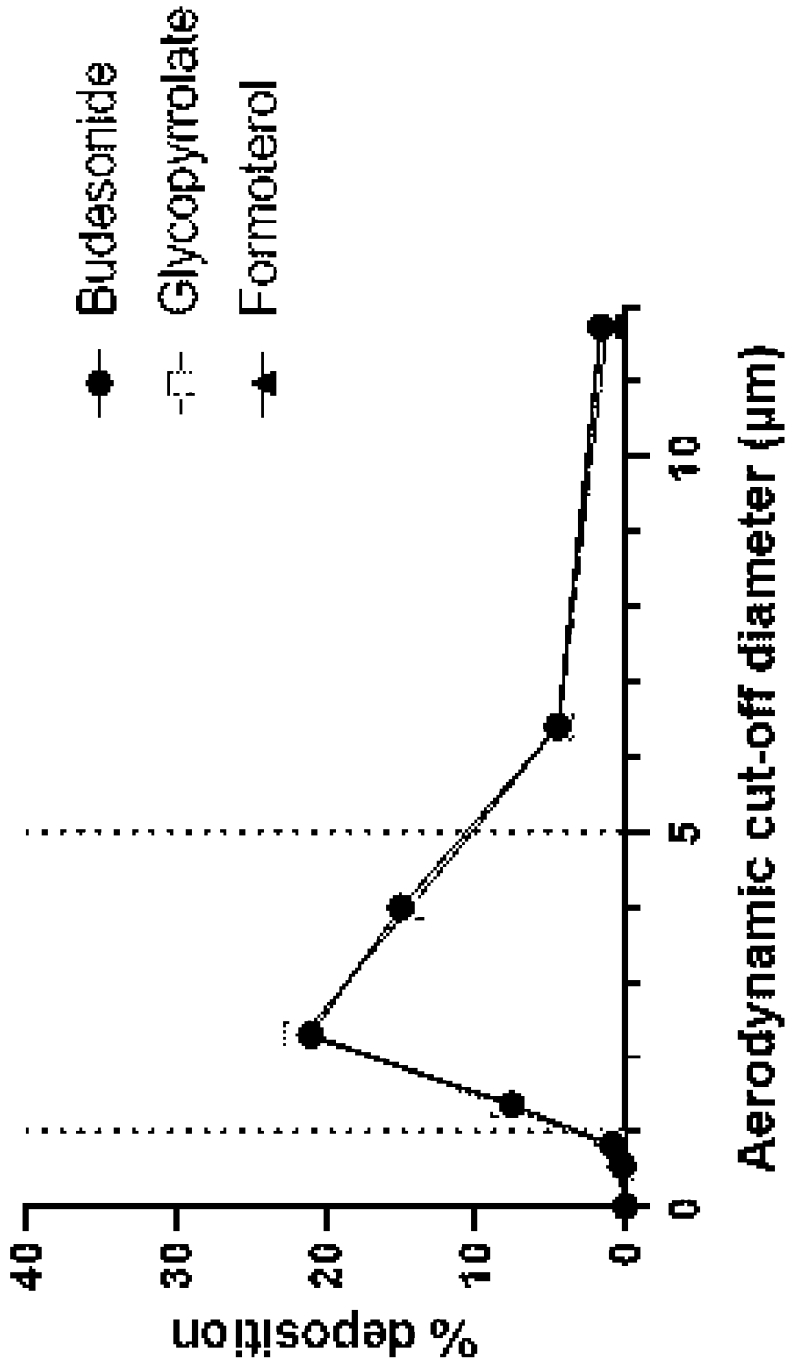

Budesonide
Glycopyrrolate
Formoterol
% deposition
40
30
20
10
0
0
5
10
Aerodynamic cut-off diameter (µm)

FIG.7

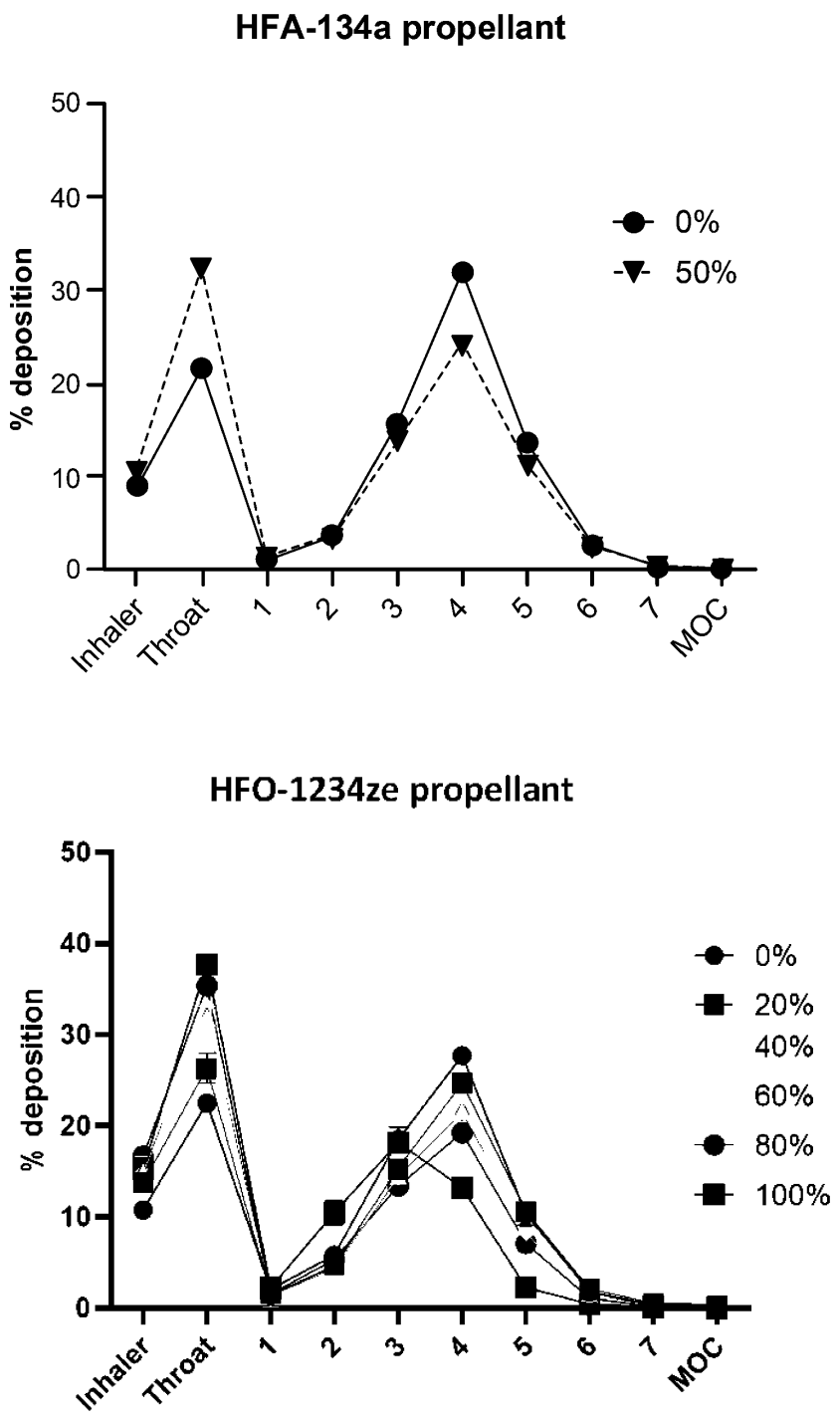

HFA-134a propellant
% deposition
50
40
30
20
10
0
0%
50%
Inhaler
Throat
1
2
3
4
5
6
7
MOC
HFO-1234ze propellant
% deposition
50
40
30
20
10
0
0%
20%
40%
60%
80%
100%
Inhaler
Throat
1
2
3
4
5
6
7
MOC

FIG. 8

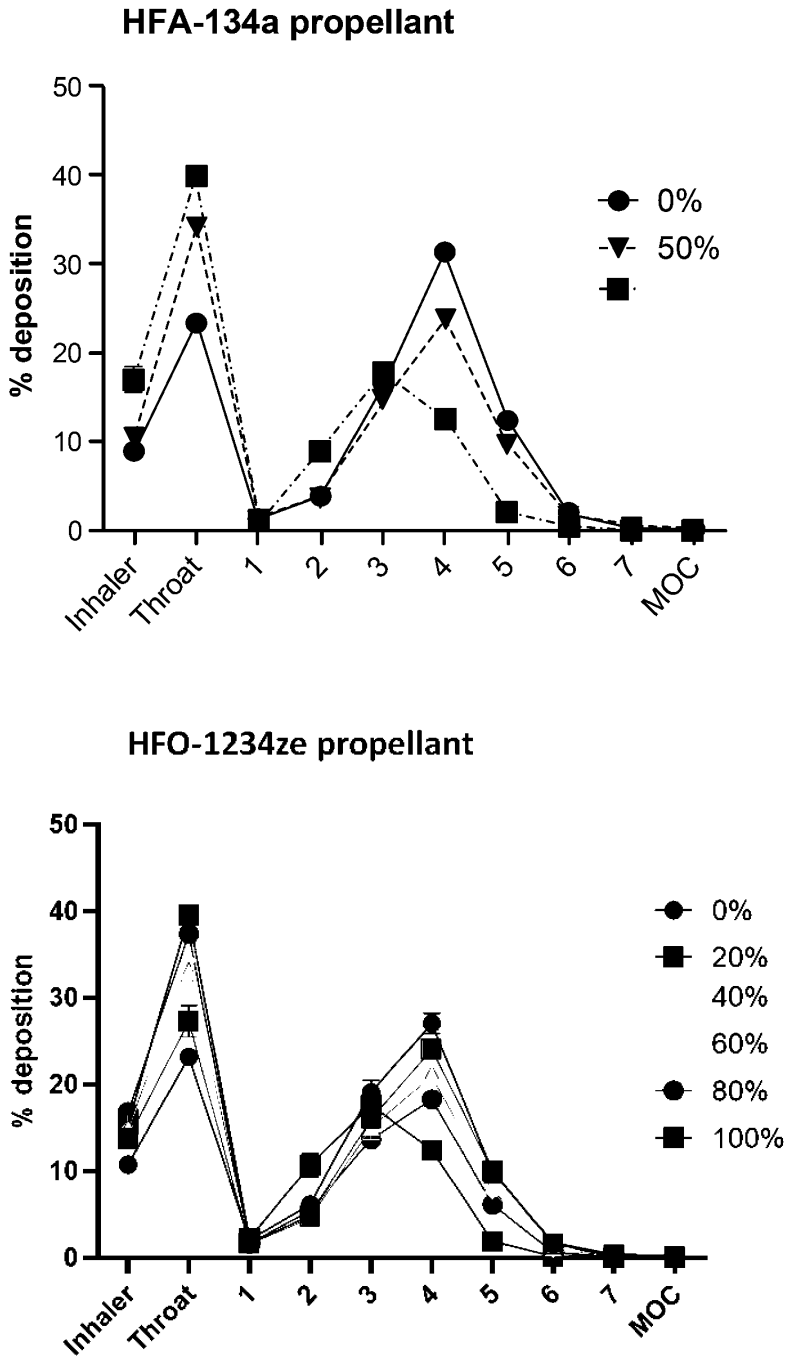

HFA-134a propellant
% deposition
50
40
30
20
10
0
0%
50%
Inhaler
Throat
1
2
3
4
5
6
7
MOC
HFO-1234ze propellant
% deposition
50
40
30
20
10
0
0%
20%
40%
60%
80%
100%
Inhaler
Throat
1
2
3
4
5
6
7
MOC

FIG. 9

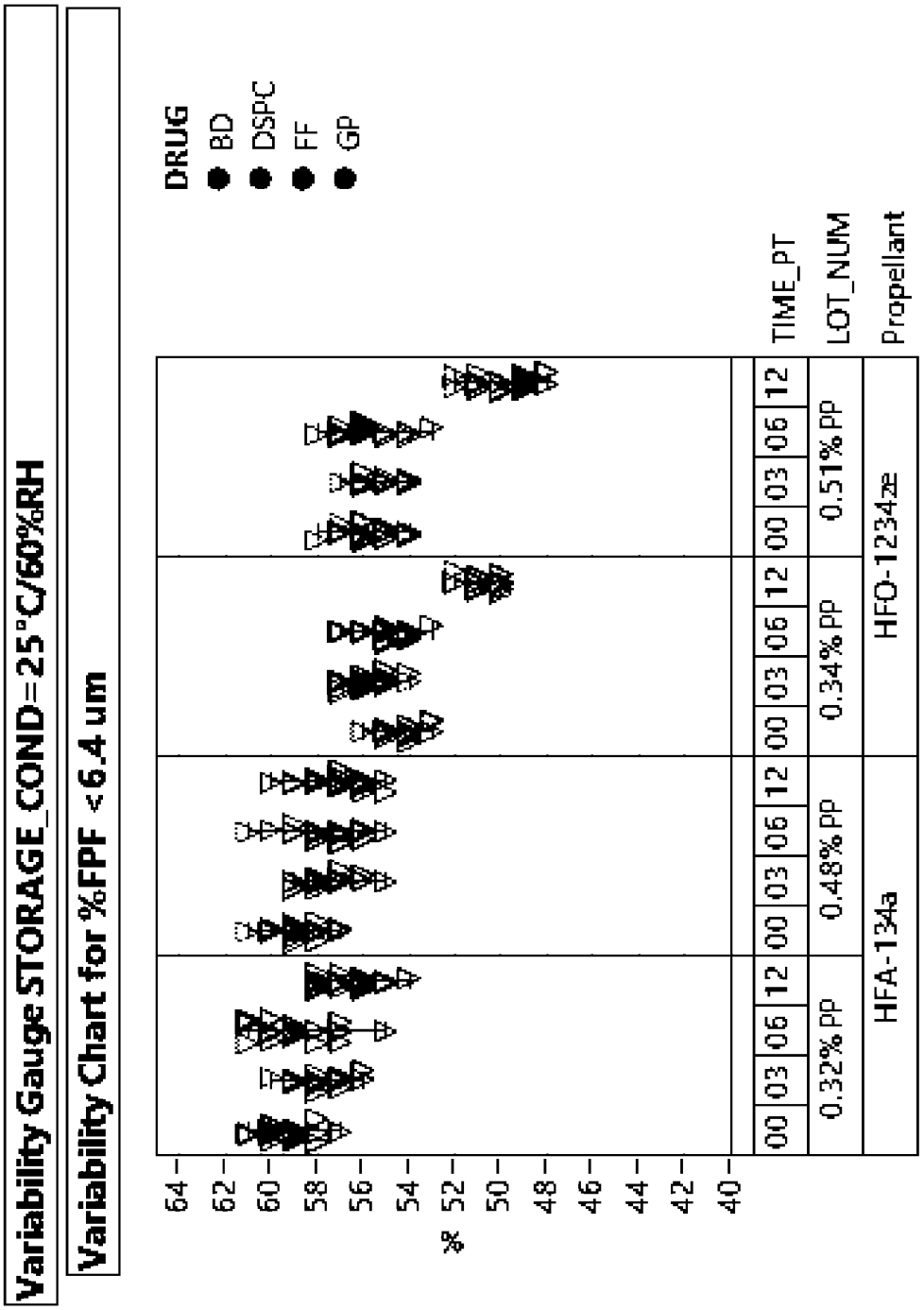

Variability Gauge STORAGE_COND=25°C/60%RH
Variability Chart for %FPF <6.4 um
DRUG
BD
DSPC
FF
GP
%
64
62
60
58
56
54
52
50
48
46
44
42
40
TIME_PT
LOT_NUM
Propellant
00 03 06 12 00 03 06 12 00 03 06 12
0.32% PP
0.48% PP
0.34% PP
0.51% PP
HFA-134a
HFO-1234ze

FIG. 10A

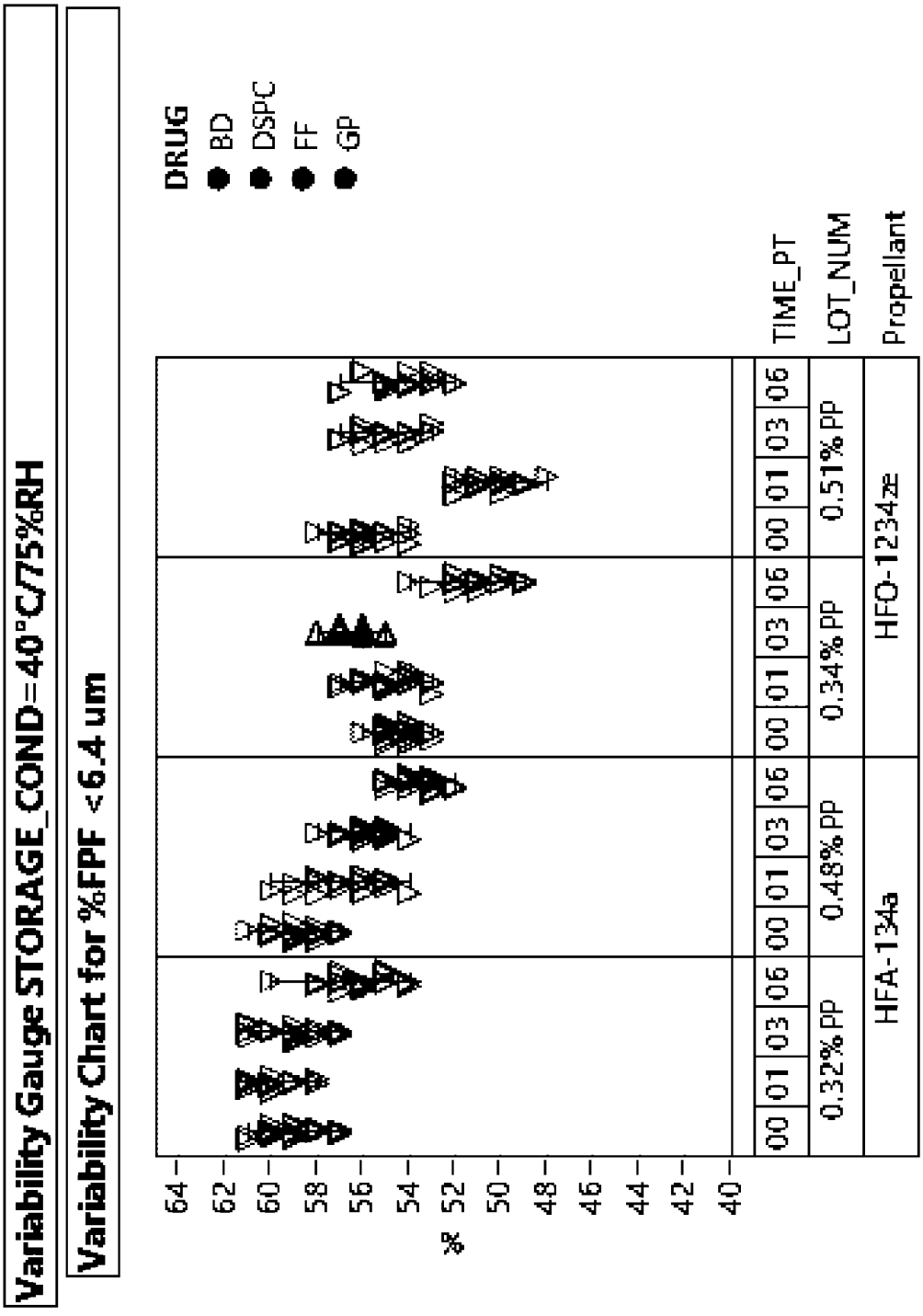

Variability Gauge STORAGE_COND=40°C/75%RH
Variability Chart for %FPF <6.4 um
DRUG
BD
DSPC
FF
GP
%
64
62
60
58
56
54
52
50
48
46
44
42
40
TIME_PT
LOT_NUM
Propellant
00 01 03 06 00 01 03 06 00 01 03 06 00 01 03 06
0.32% PP
0.48% PP
0.34% PP
0.51% PP
HFA-134a
HFO-1234ze

FIG. 10B

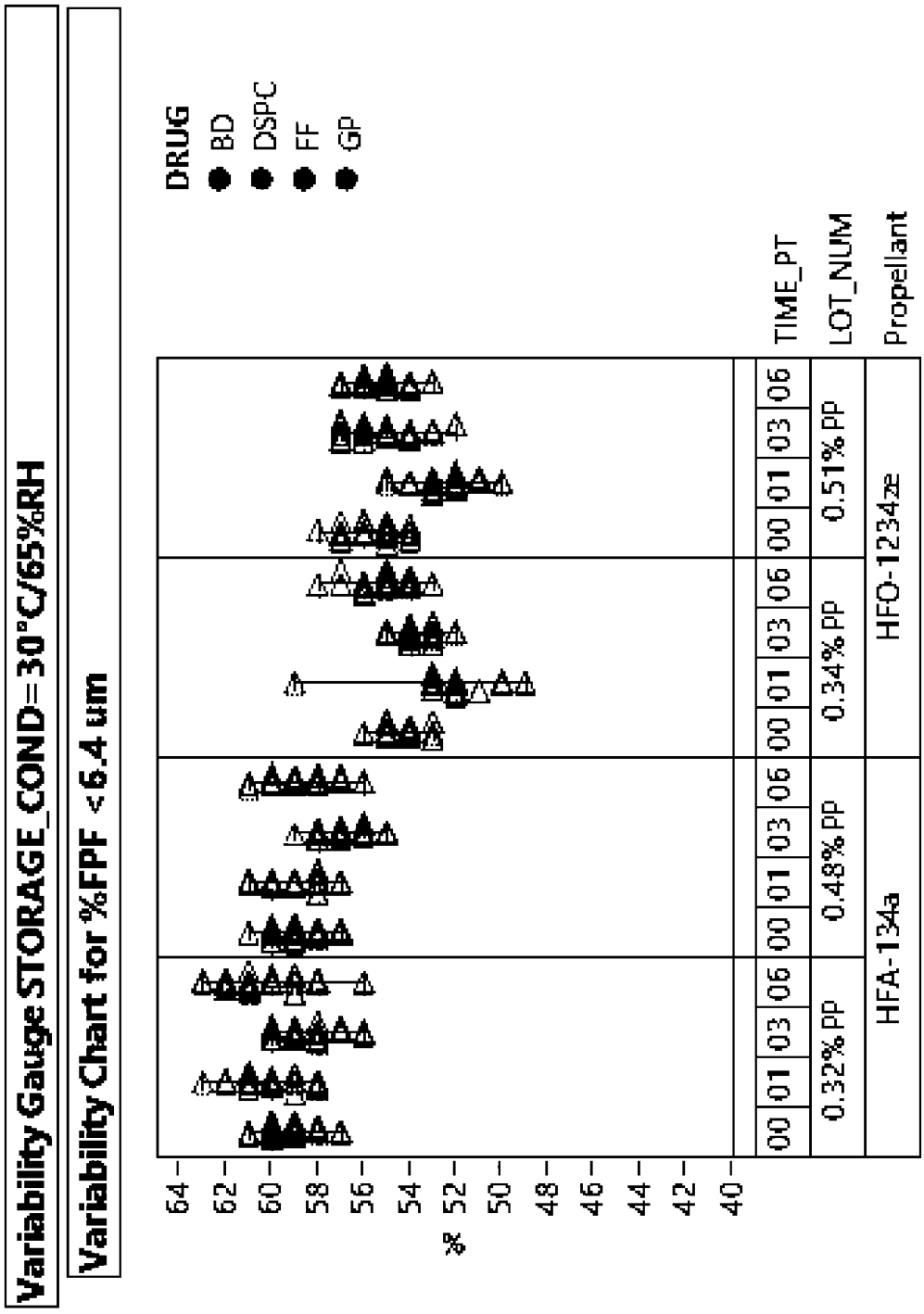

Variability Gauge STORAGE_COND=30°C/65%RH
Variability Chart for %FPF <6.4 um
DRUG
BD
DSPC
FF
GP
%
64
62
60
58
56
54
52
50
48
46
44
42
40
TIME_PT
LOT_NUM
Propellant
00 01 03 06 00 01 03 06 00 01 03 06 00 01 03 06
0.32% PP
0.48% PP
0.34% PP
0.51% PP
HFA-134a
HFO-1234ze

FIG. 10C

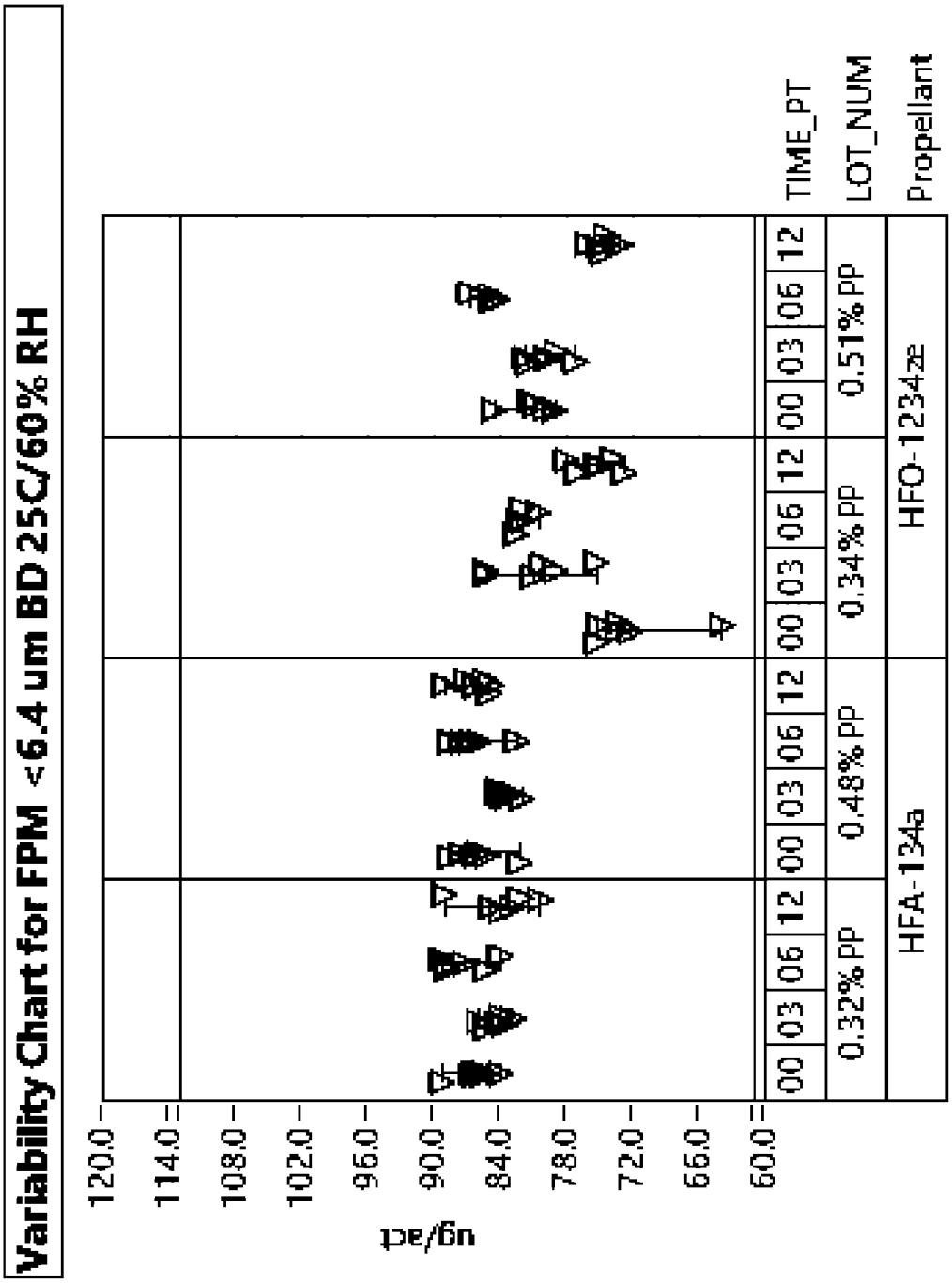

Variability Chart for FPM <6.4 um BD 25C/60% RH
ug/act
120.0
114.0
108.0
102.0
96.0
90.0
84.0
78.0
72.0
66.0
60.0
TIME_PT
LOT_NUM
Propellant
00 03 06 12 00 03 06 12 00 03 06 12
0.32% PP
0.48% PP
0.34% PP
0.51% PP
HFA-134a
HFO-1234ze

FIG. 11A

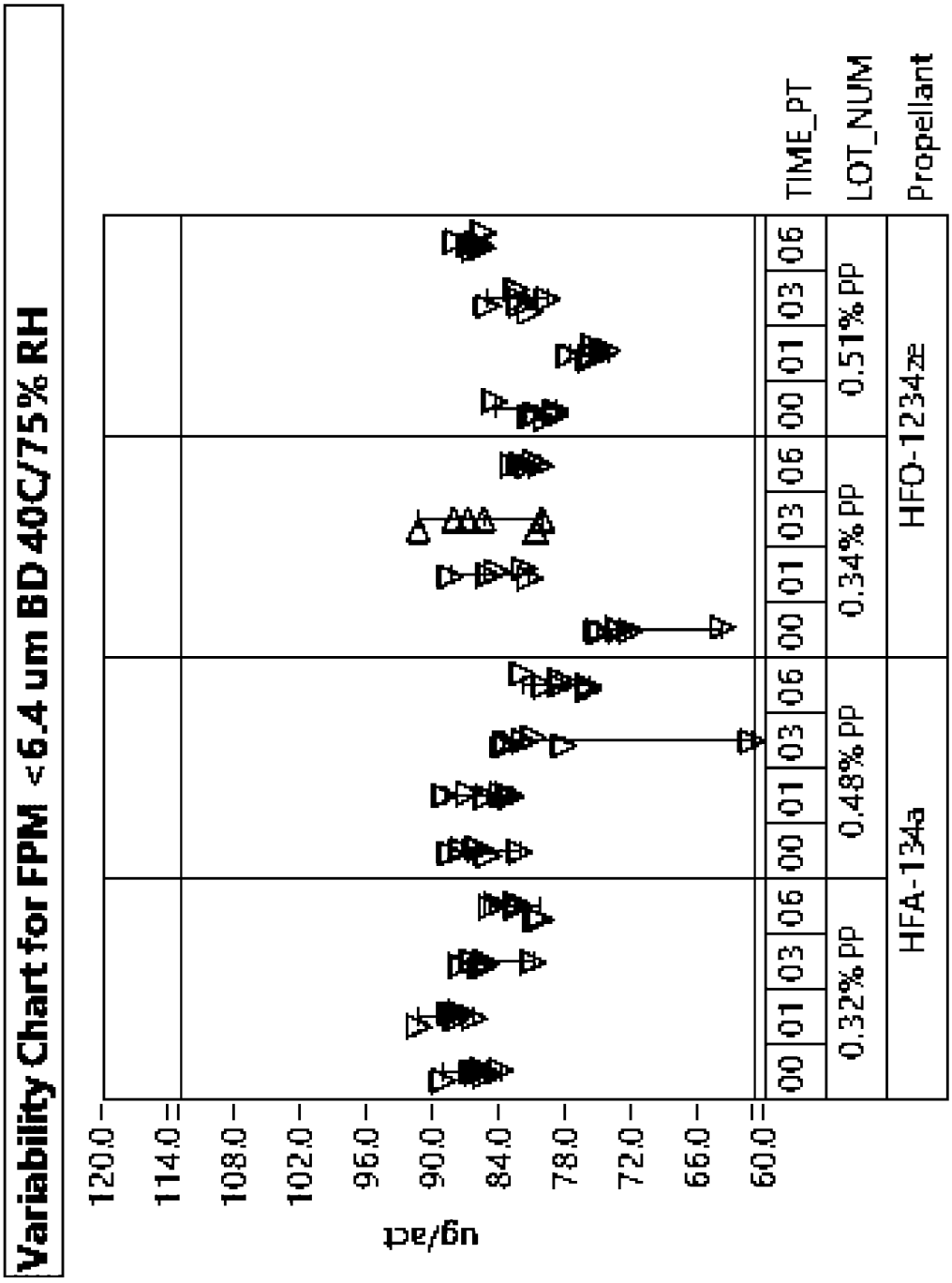

Variability Chart for FPM <6.4 um BD 40C/75% RH
ug/act
120.0
114.0
108.0
102.0
96.0
90.0
84.0
78.0
72.0
66.0
60.0
TIME_PT
LOT_NUM
Propellant
00 01 03 06 00 01 03 06 00 01 03 06 00 01 03 06
0.32% PP
0.48% PP
0.34% PP
0.51% PP
HFA-134a
HFO-1234ze

FIG. 11B

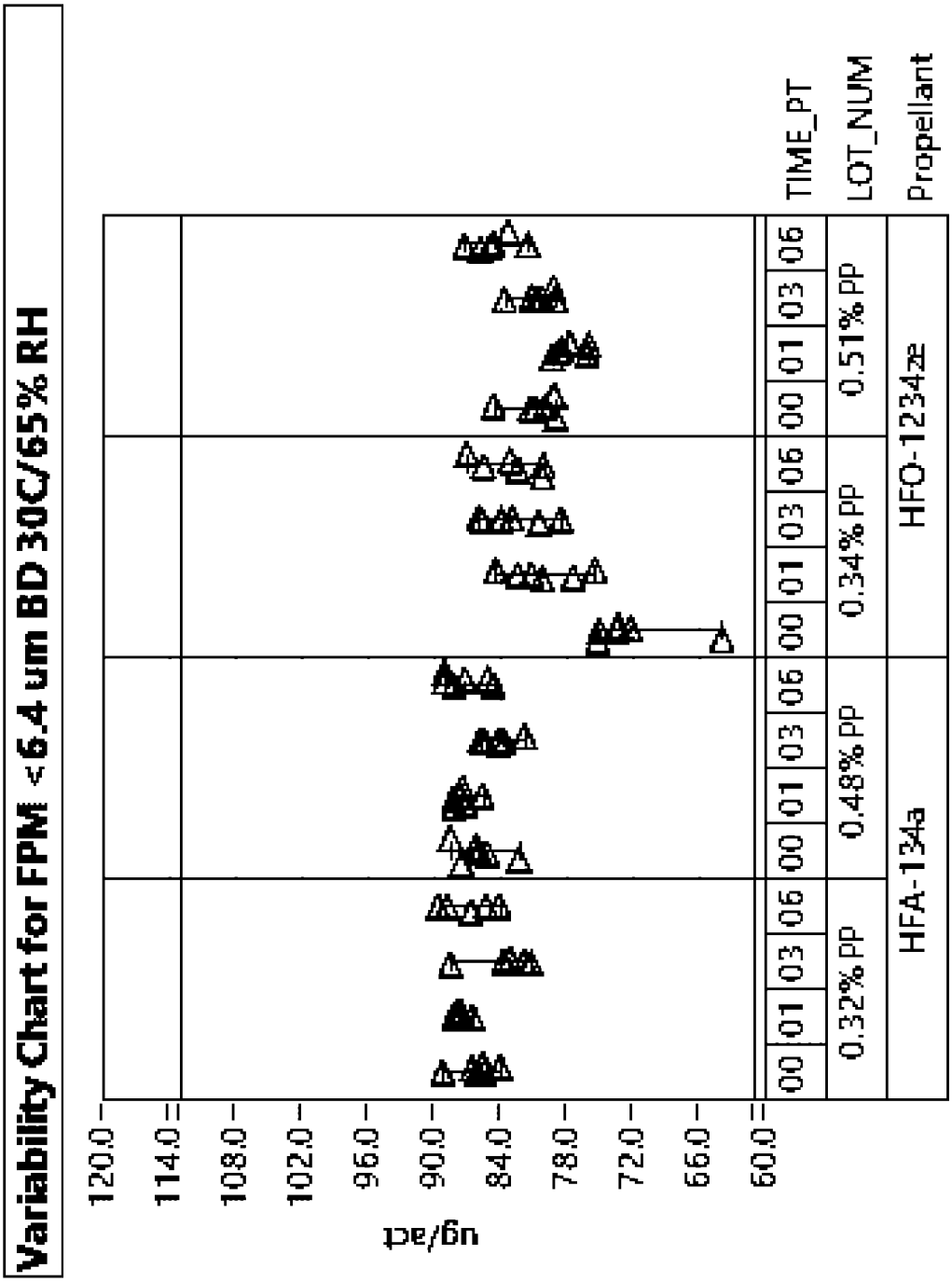

Variability Chart for FPM ≤6.4 um BD 30C/65% RH
ug/act
120.0
114.0
108.0
102.0
96.0
90.0
84.0
78.0
72.0
66.0
60.0
TIME_PT
LOT_NUM
Propellant
00 01 03 06
0.32% PP
0.48% PP
0.34% PP
0.51% PP
HFA-134a
HFO-1234ze

FIG. 11C

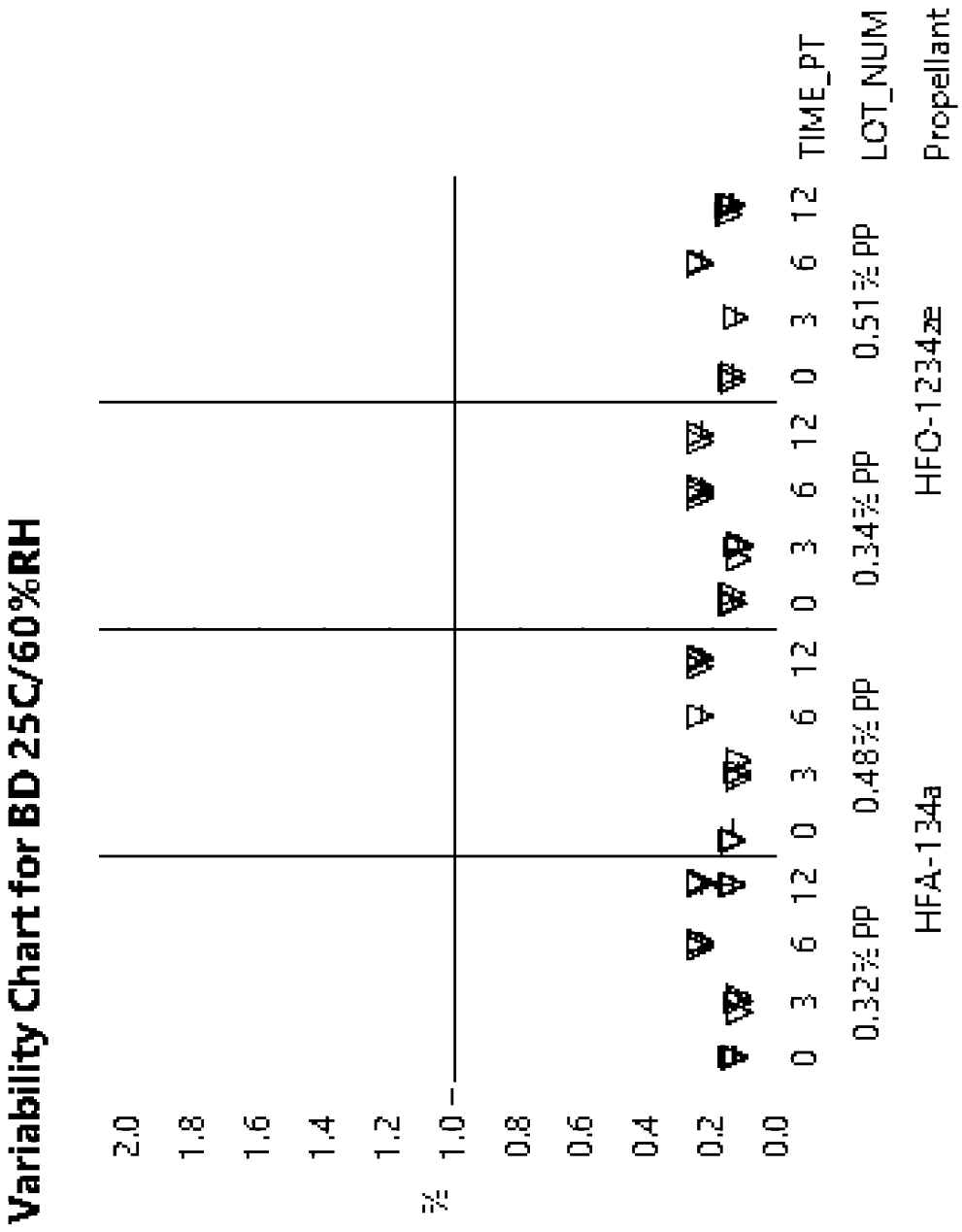

Variability Chart for BD 25C/60%RH
%
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0 3 6 12 0 3 6 12 0 3 6 12 0 3 6 12
TIME_PT
0.32% PP
0.48% PP
0.34% PP
0.51% PP
LOT_NUM
HFA-134a
HFO-1234ze
Propellant

FIG. 12A

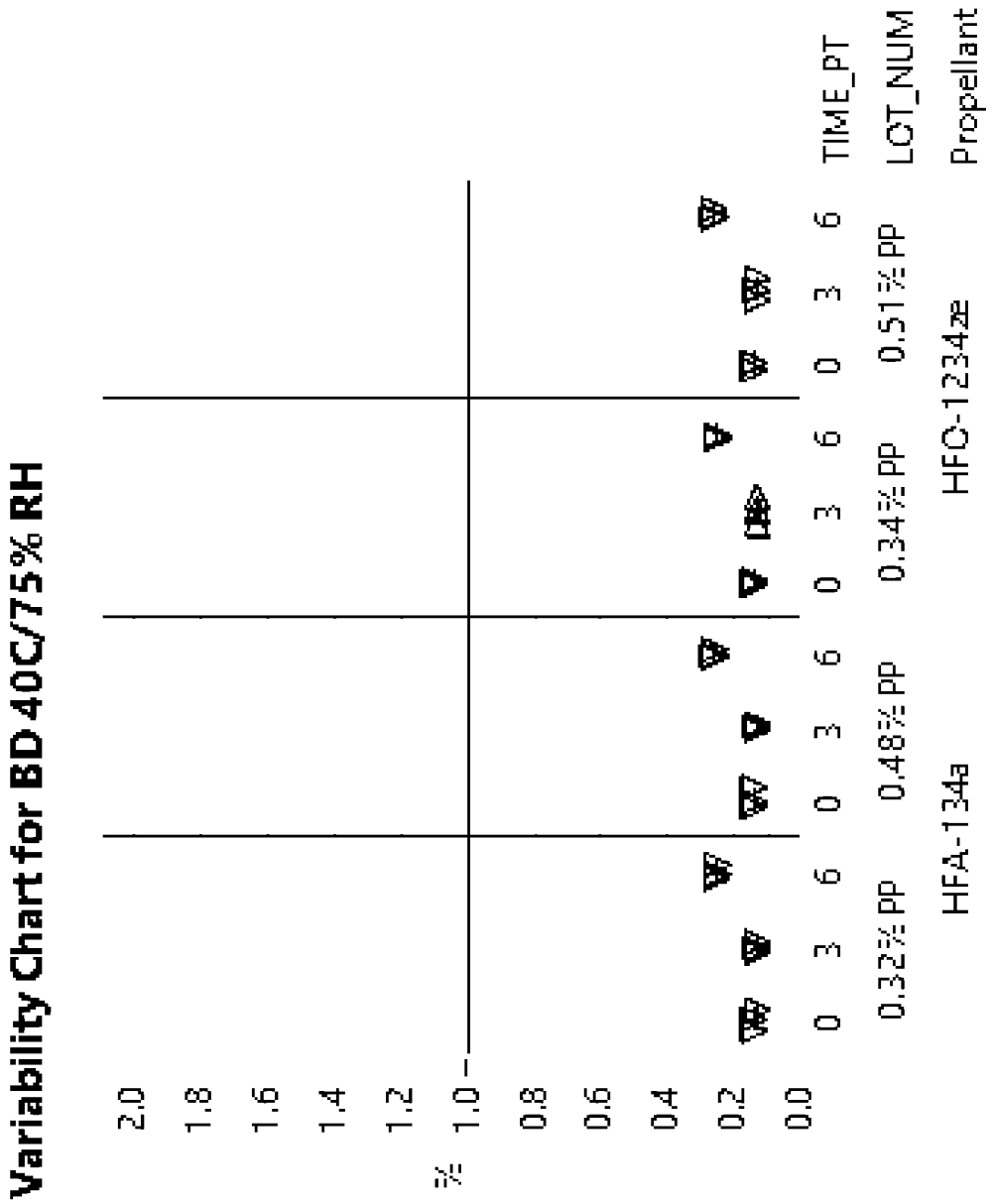

Variability Chart for BD 40C/75% RH
%
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0 3 6 0 3 6 0 3 6 0 3 6
0.32% PP
0.48% PP
0.34% PP
0.51% PP
HFA-134a
HFO-1234ze
TIME_PT
LOT_NUM
Propellant

FIG. 12B

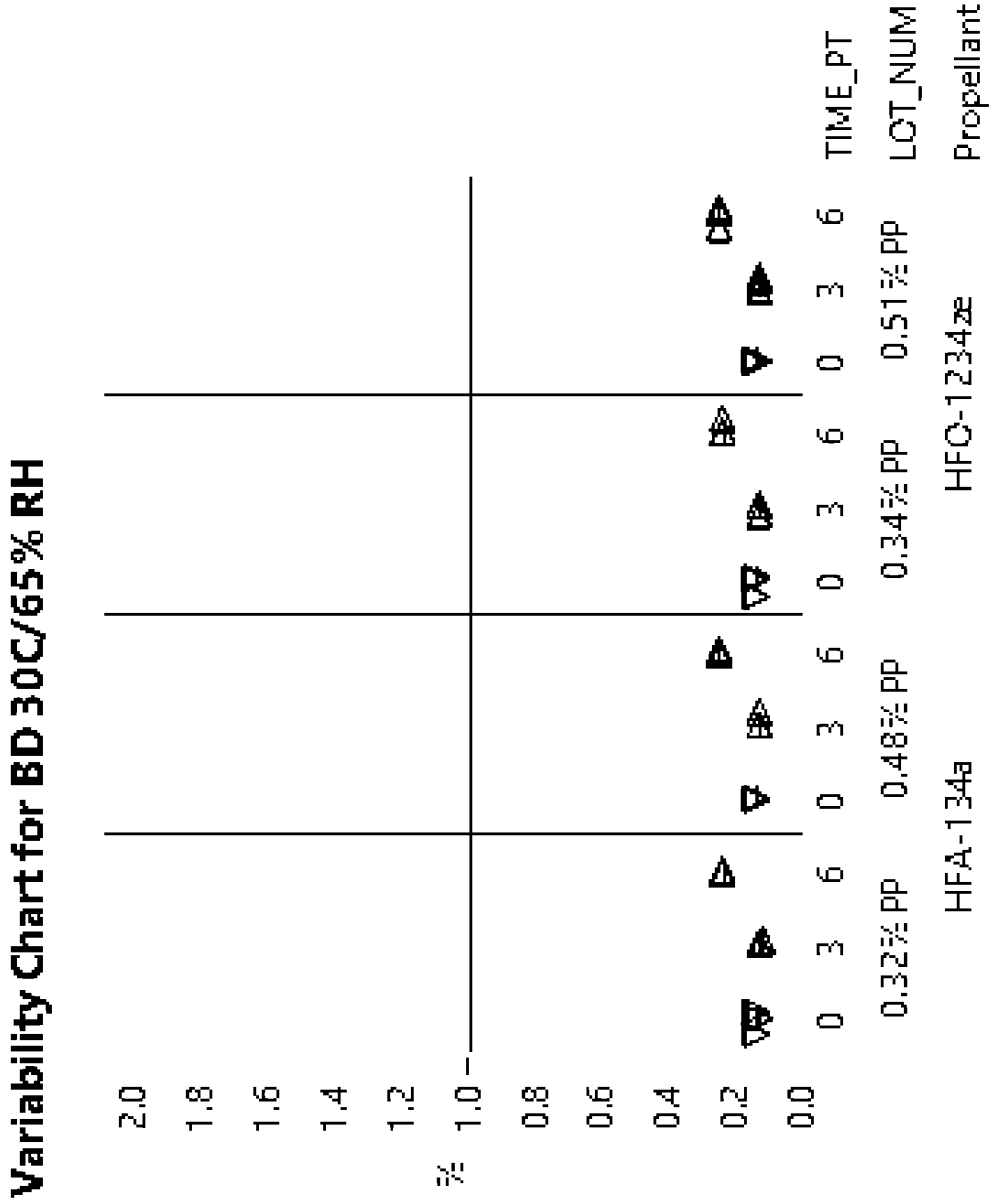

Variability Chart for BD 30C/65% RH
%
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0 3 6 0 3 6 0 3 6 0 3 6
0.32% PP
0.48% PP
0.34% PP
0.51% PP
TIME_PT
LOT_NUM
HFA-134a
HFO-1234ze
Propellant

FIG. 12C

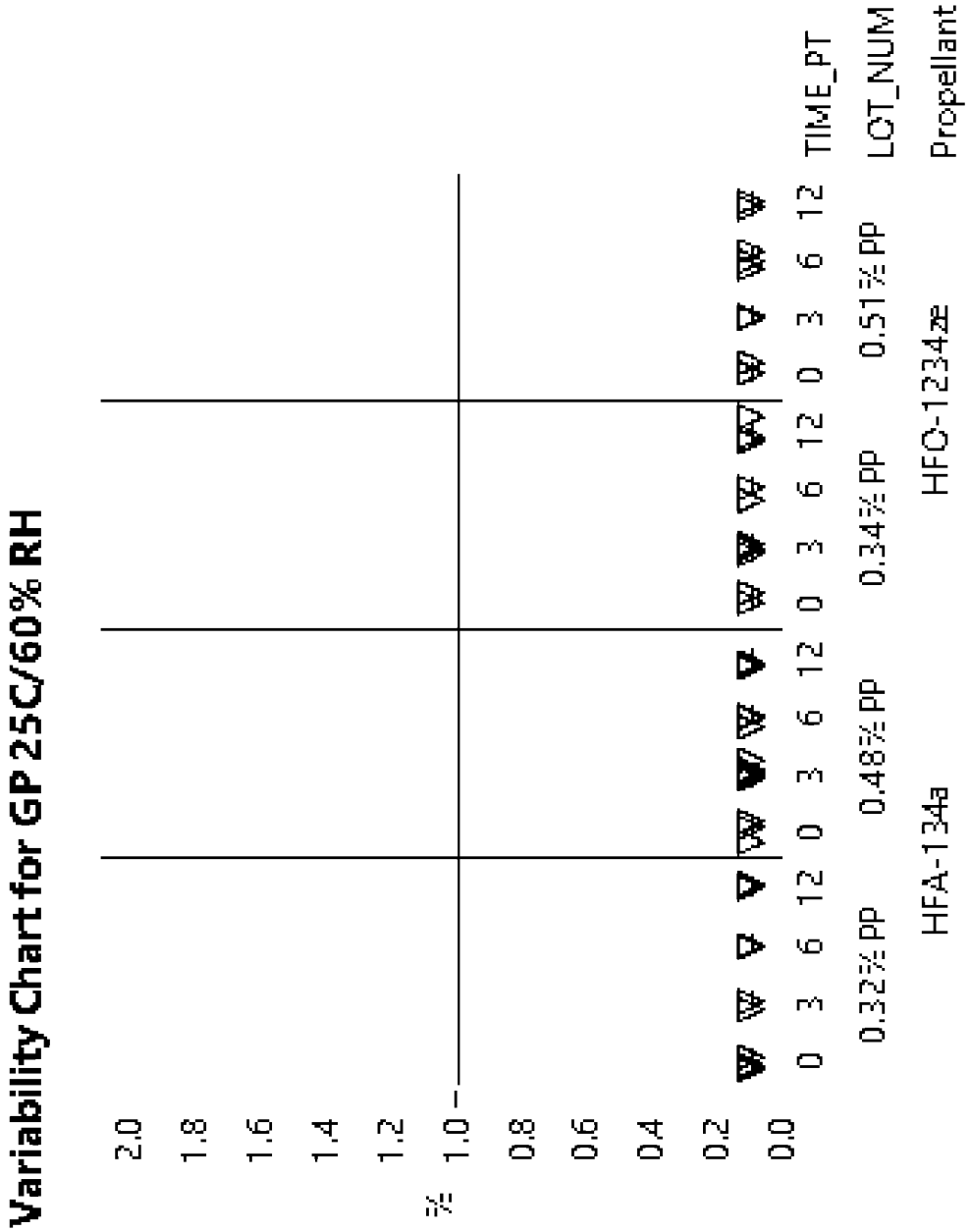

Variability Chart for GP 25C/60% RH
%
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0 3 6 12 0 3 6 12 0 3 6 12 0 3 6 12
TIME_PT
0.32% PP
0.48% PP
0.34% PP
0.51% PP
LOT_NUM
HFA-134a
HFO-1234ze
Propellant

FIG. 13A

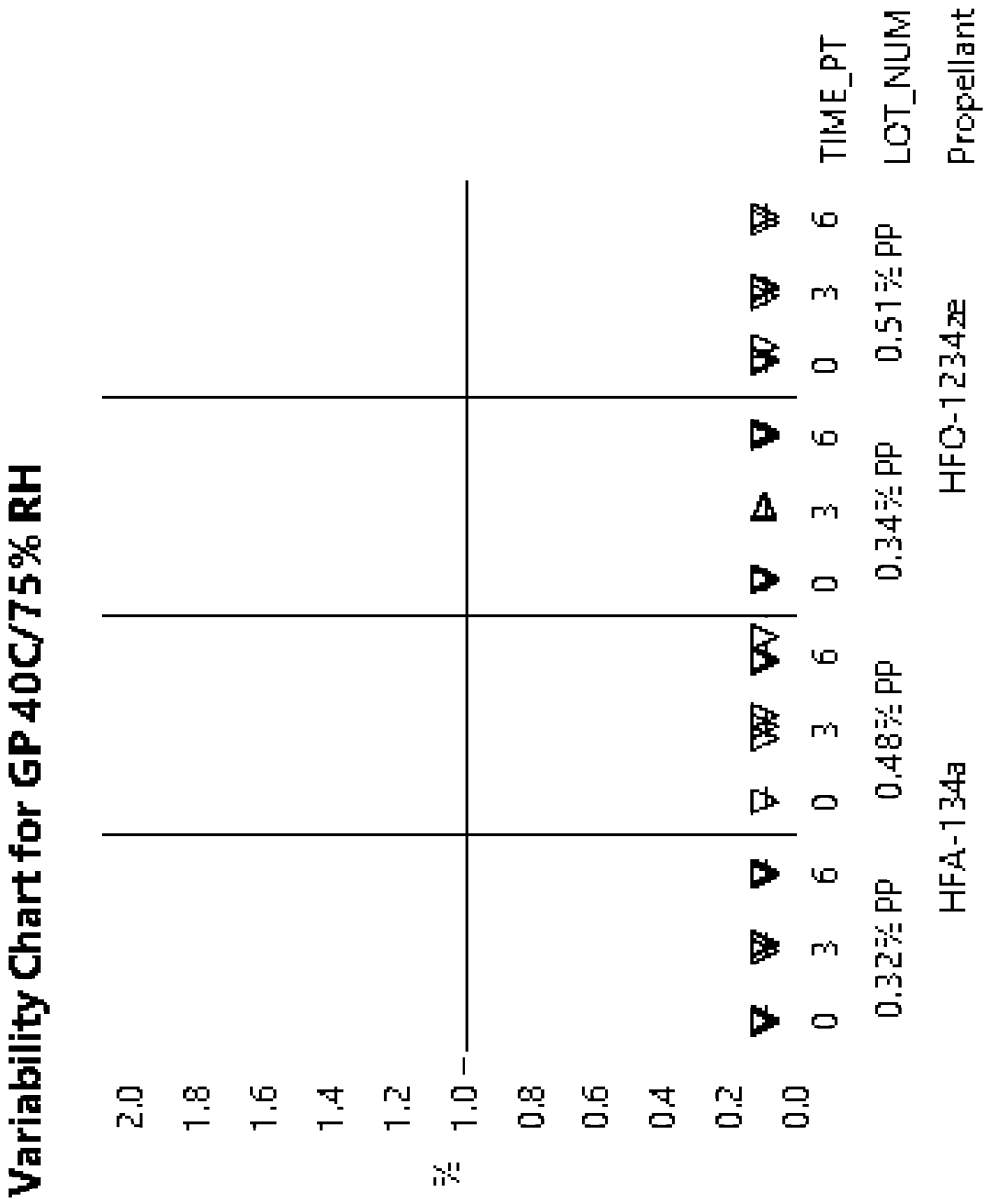

Variability Chart for GP 40C/75% RH
%
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0 3 6 0 3 6 0 3 6 0 3 6
0.32% PP
0.48% PP
0.34% PP
0.51% PP
HFA-134a
HFO-1234ze
TIME_PT
LOT_NUM
Propellant

FIG. 13B

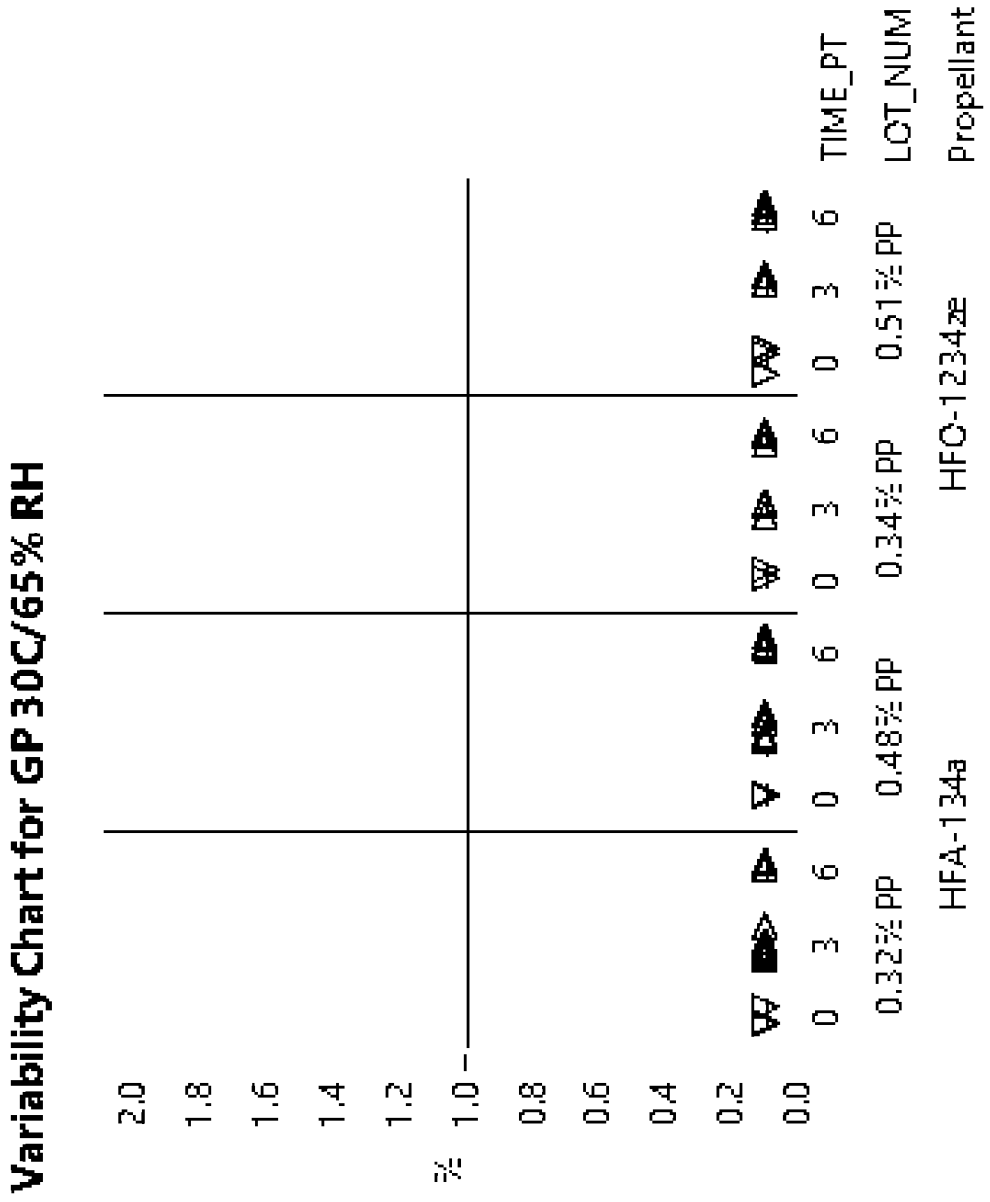

Variability Chart for GP 30C/65% RH
%
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0 3 6 0 3 6 0 3 6 0 3 6
0.32% PP 0.48% PP 0.34% PP 0.51% PP
HFA-134a HFO-1234ze
TIME_PT
LOT_NUM
Propellant

FIG. 13C

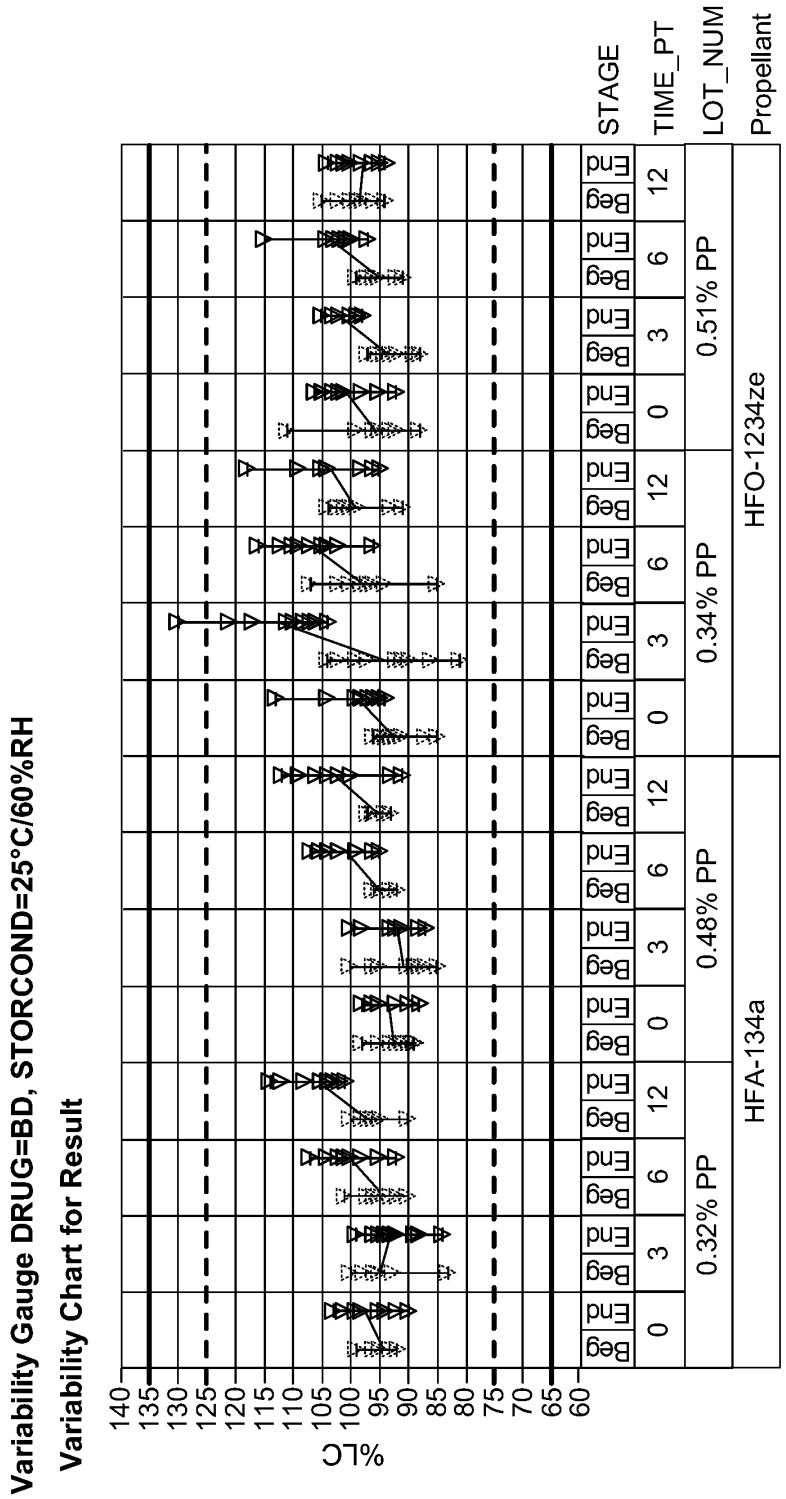

Variability Gauge DRUG=BD, STORCOND=25°C/60%RH
Variability Chart for Result
%LC
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
STAGE
TIME_PT
LOT_NUM
Propellant
Beg
End
0
3
6
12
0.32% PP
0.48% PP
0.34% PP
0.51% PP
HFA-134a
HFO-1234ze

FIG. 14A

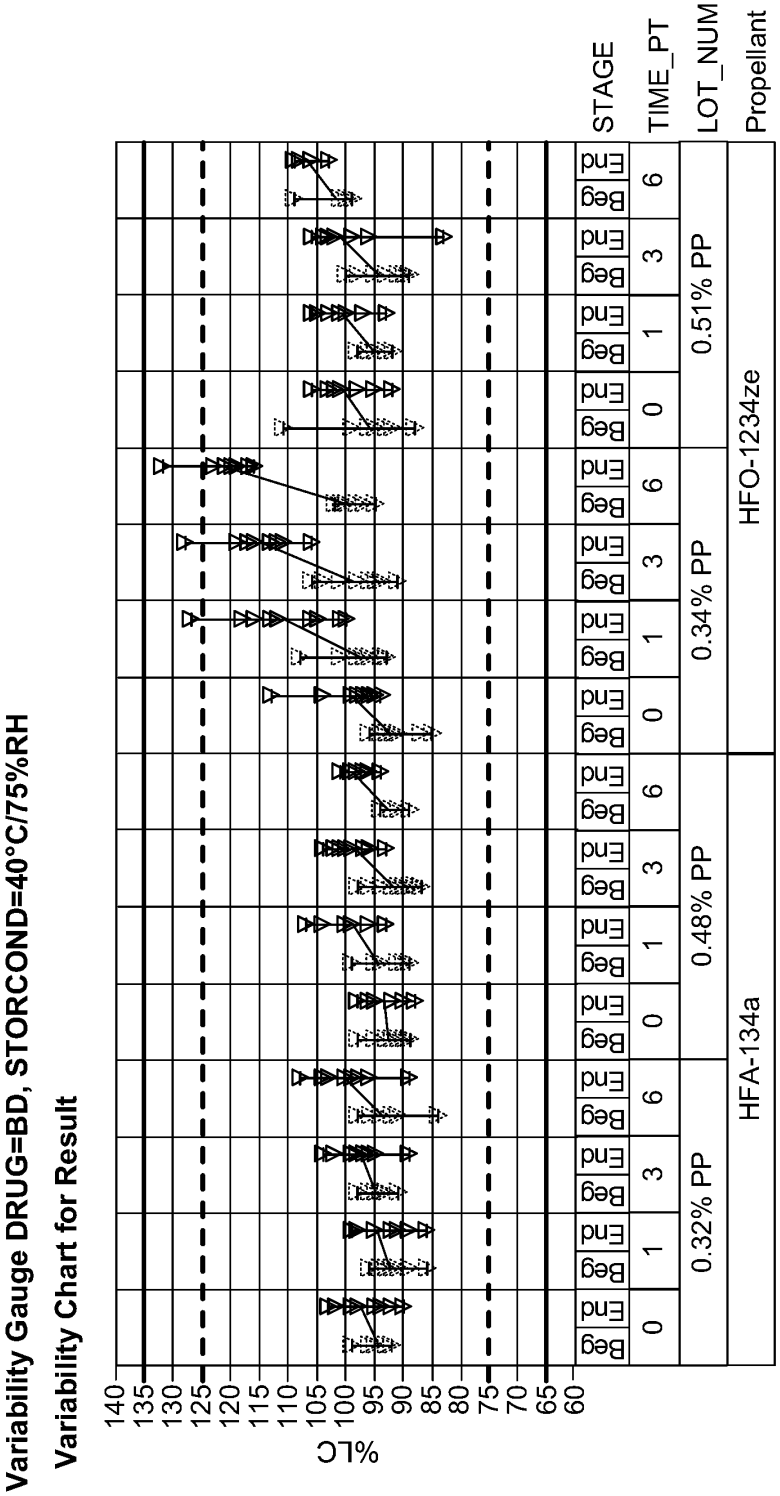

Variability Gauge DRUG=BD, STORCOND=40°C/75%RH
Variability Chart for Result
%LC
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
STAGE
TIME_PT
LOT_NUM
Propellant
Beg
End
0
1
3
6
0.32% PP
0.48% PP
0.34% PP
0.51% PP
HFA-134a
HFO-1234ze

FIG. 14B

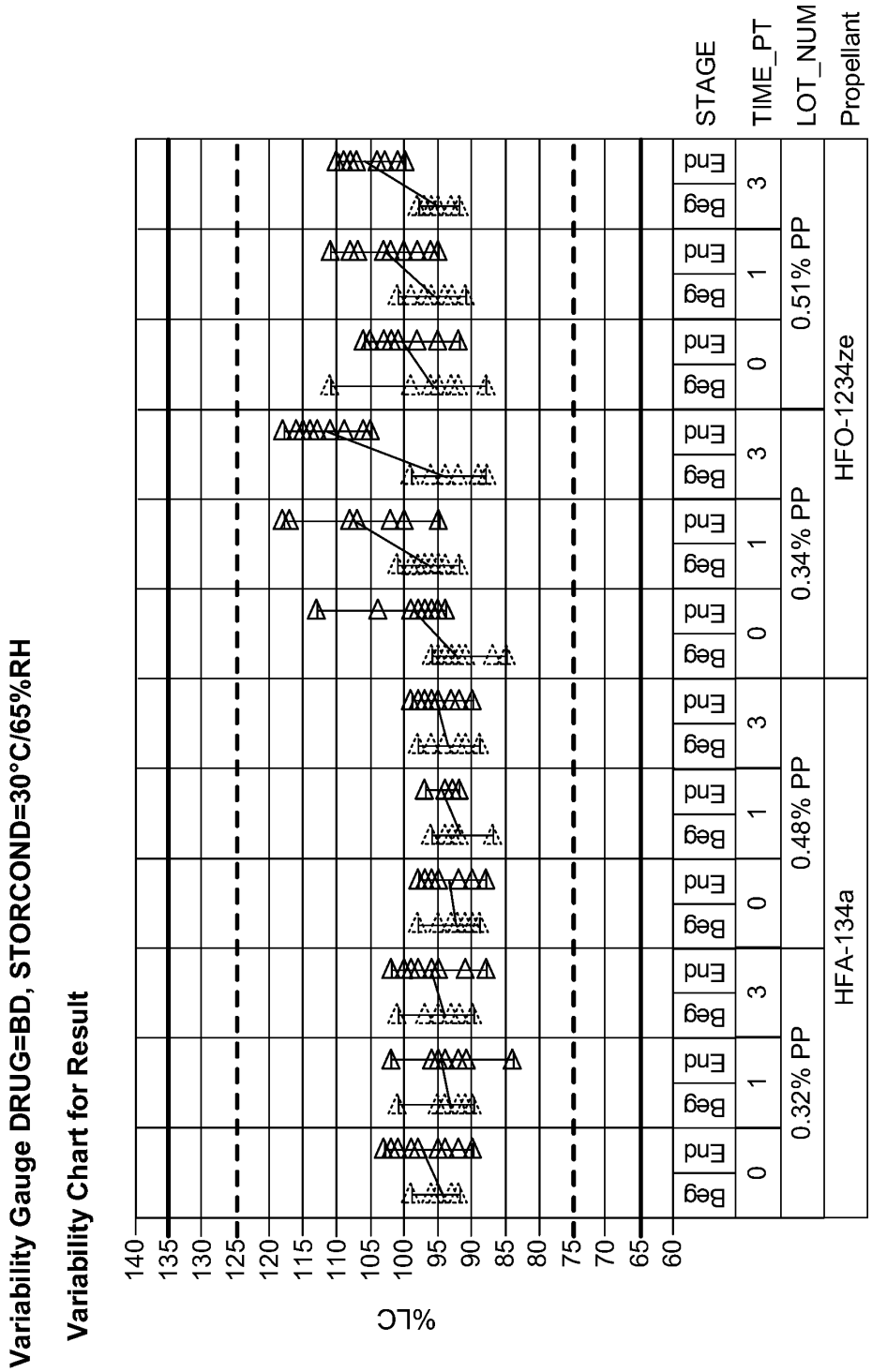

Variability Gauge DRUG=BD, STORCOND=30°C/65%RH
Variability Chart for Result
%LC
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
STAGE
TIME_PT
LOT_NUM
Propellant
Beg
End
0
1
3
0.32% PP
0.48% PP
0.34% PP
0.51% PP
HFA-134a
HFO-1234ze

FIG. 14C

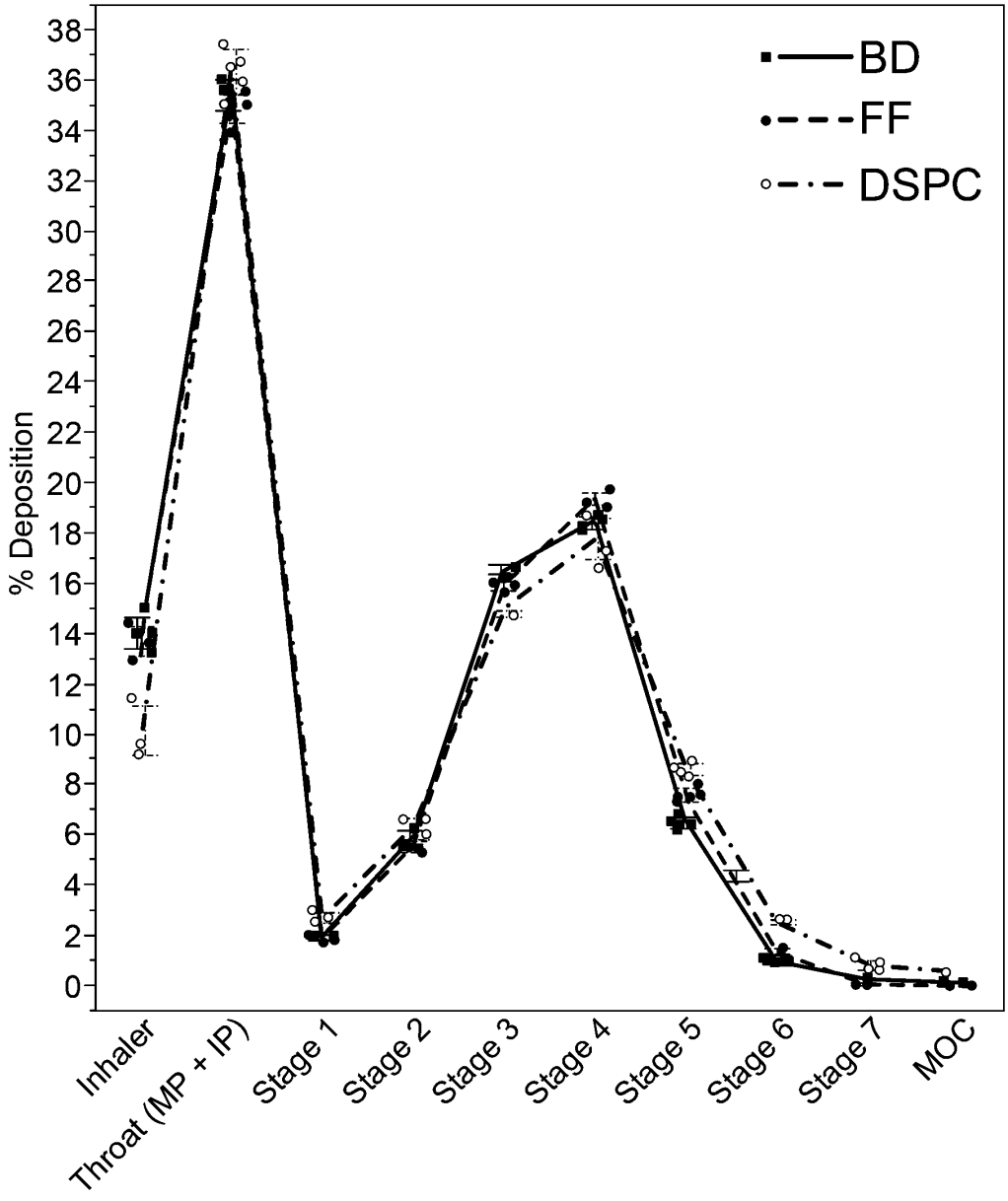

BD
FF
DSPC
% Deposition
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
38
Inhaler
Throat (MP + IP)
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Stage 6
Stage 7
MOC

FIG. 15

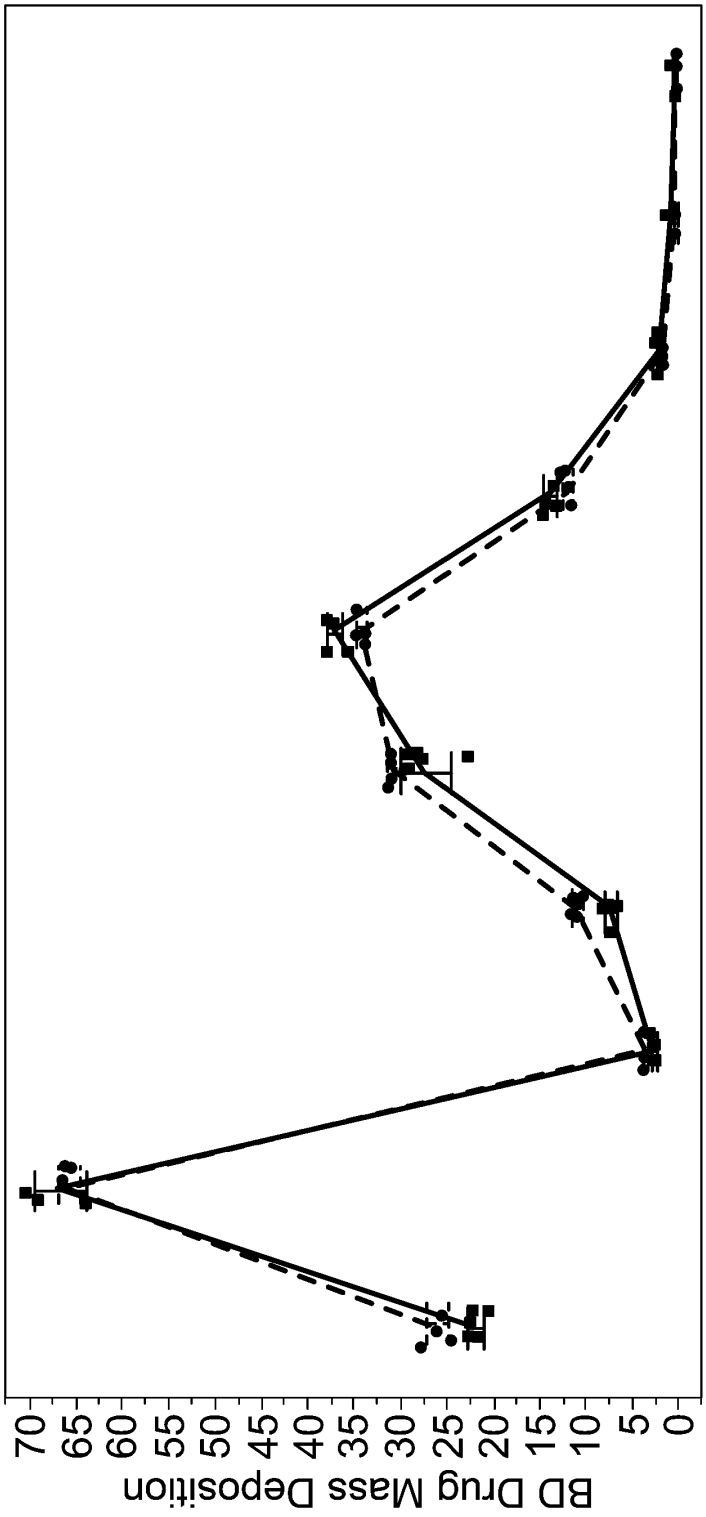

BD Drug Mass Deposition
0
5
10
15
20
25
30
35
40
45
50
55
60
65
70
Inhaler
Throat (MP + IP)
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Stage 6
Stage 7
MOC

FIG. 16

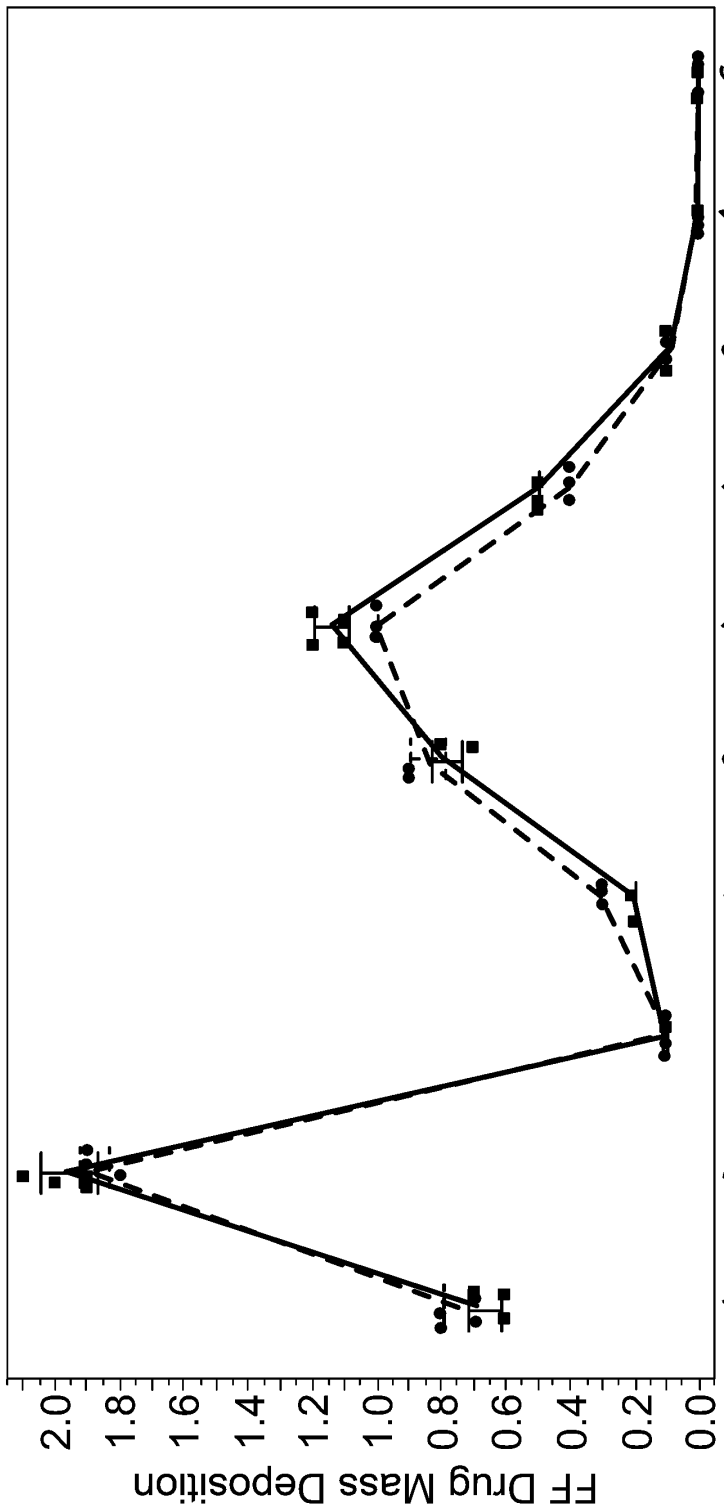

FF Drug Mass Deposition
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8
2.0
Inhaler
Throat (MP + IP)
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Stage 6
Stage 7
MOC

FIG. 17

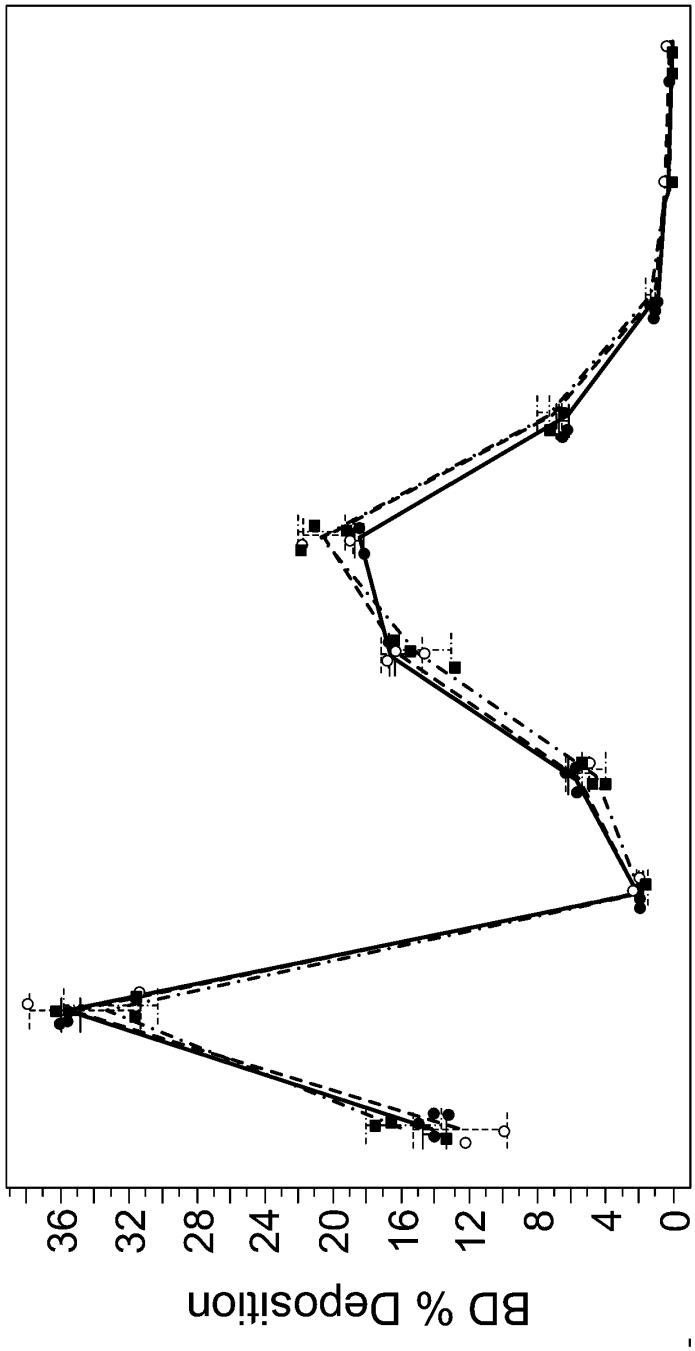

BD % Deposition
0
4
8
12
16
20
24
28
32
36
Inhaler
Throat (MP + IP)
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Stage 6
Stage 7
MOC

FIG. 18

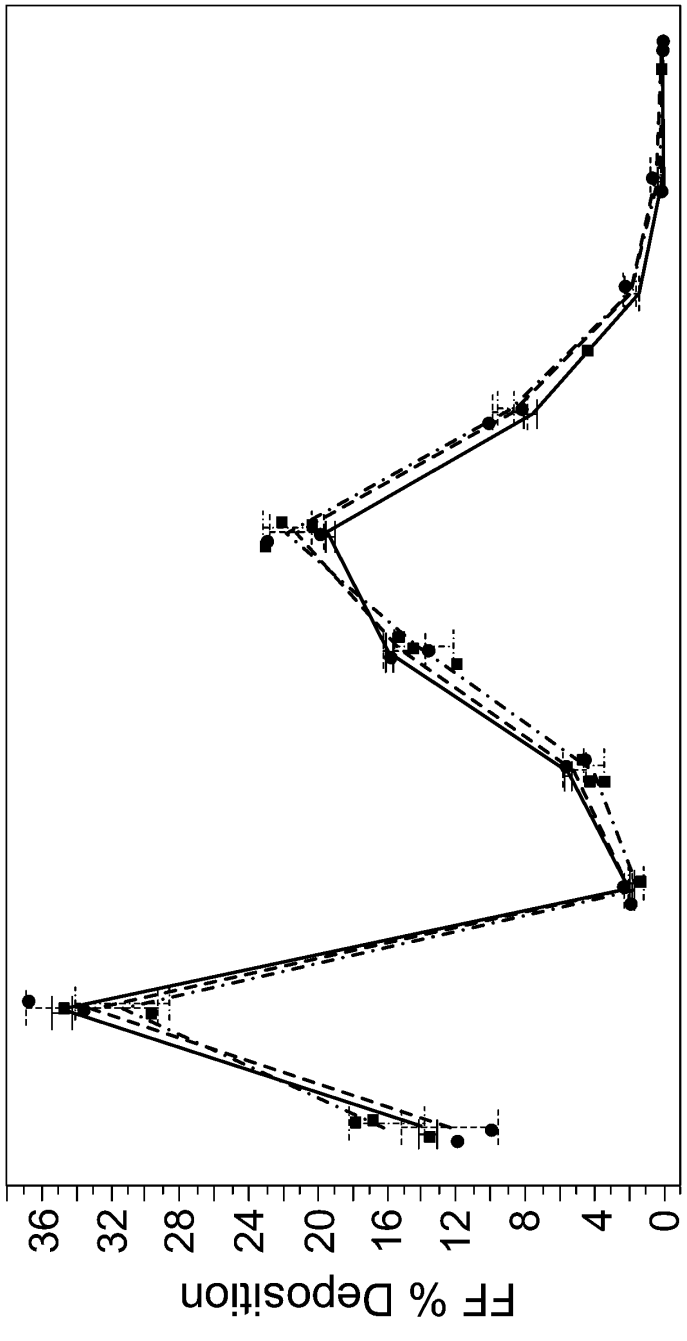

FF % Deposition
0
4
8
12
16
20
24
28
32
36
Inhaler
Throat (MP + IP)
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Stage 6
Stage 7
MOC

FIG. 19

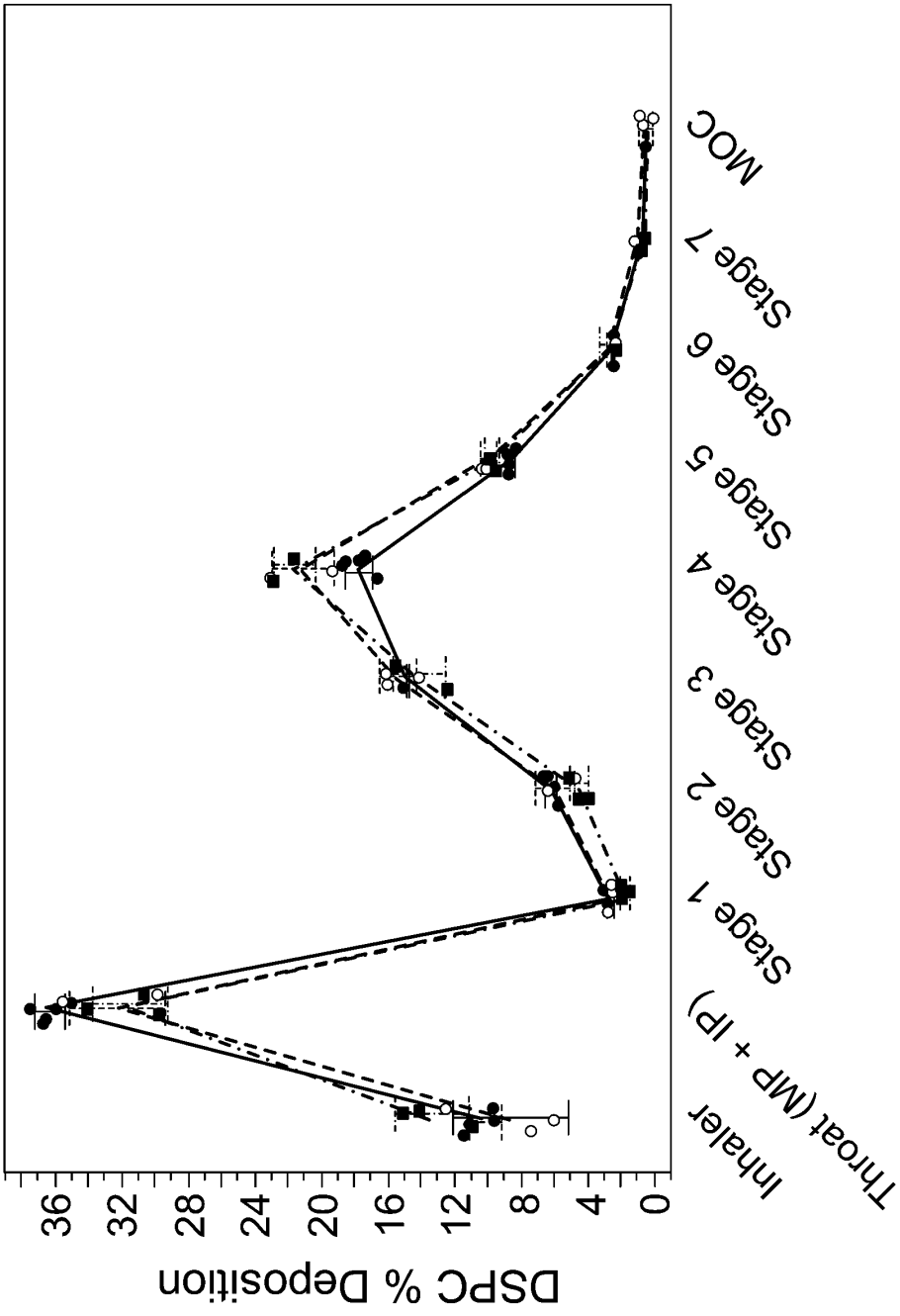

DSPC % Deposition
0
4
8
12
16
20
24
28
32
36
Inhaler
Throat (MP + IP)
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Stage 6
Stage 7
MOC

FIG. 20

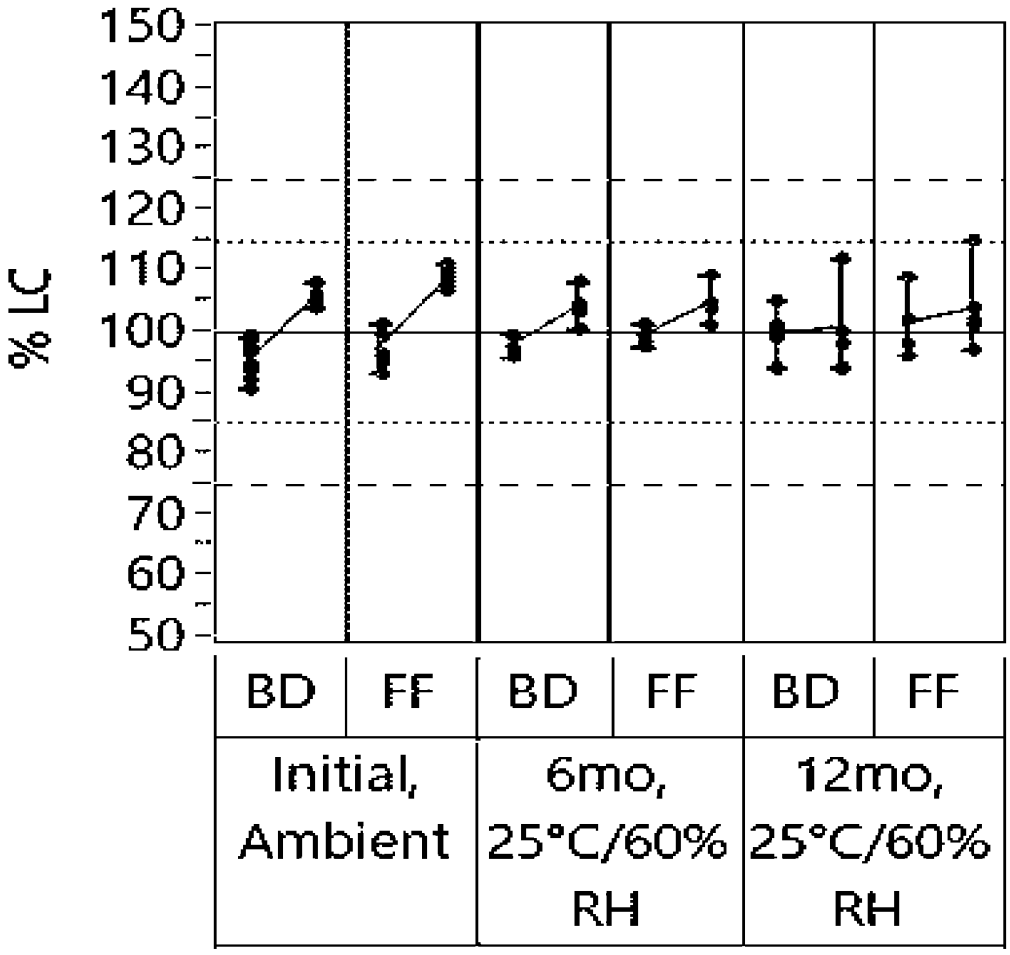

150
140
130
120
110
100
90
80
70
60
50
% LC
BD
FF
BD
FF
BD
FF
Initial, Ambient
6mo, 25°C/60% RH
12mo, 25°C/60% RH

FIG. 21

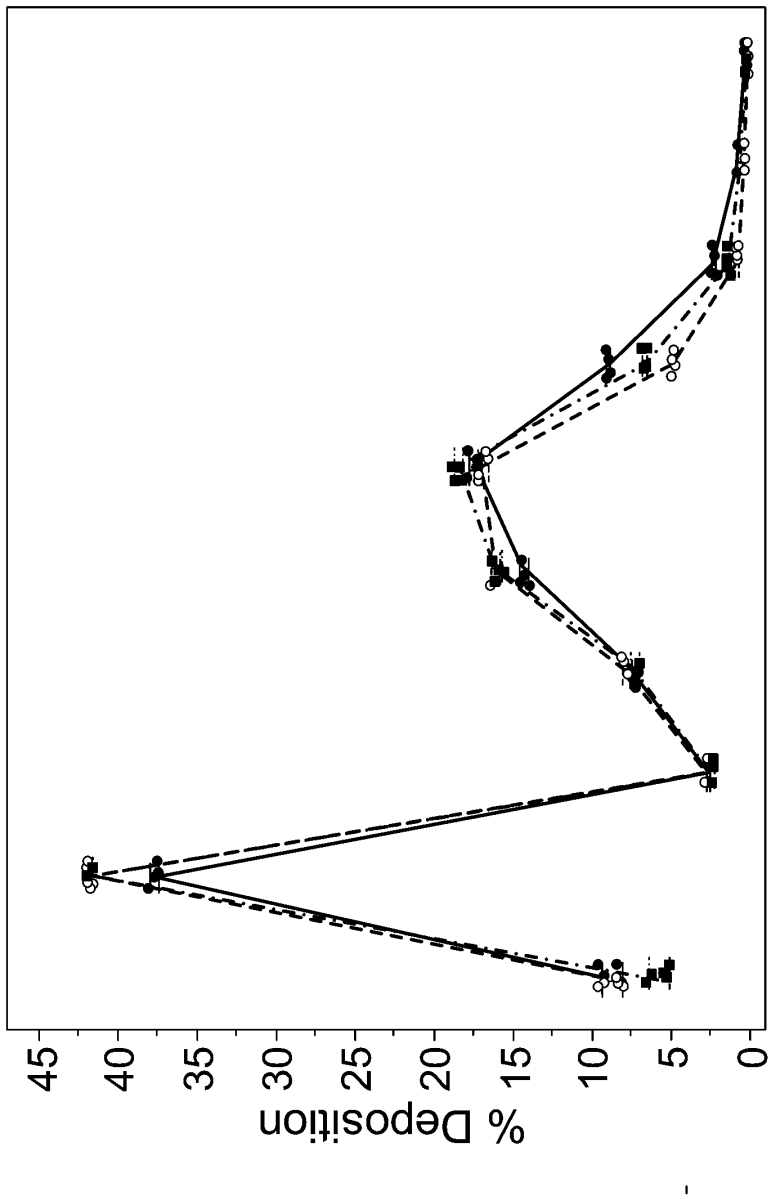

% Deposition
0
5
10
15
20
25
30
35
40
45
Inhaler
Throat (MP + IP)
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Stage 6
Stage 7
MOC

FIG. 22

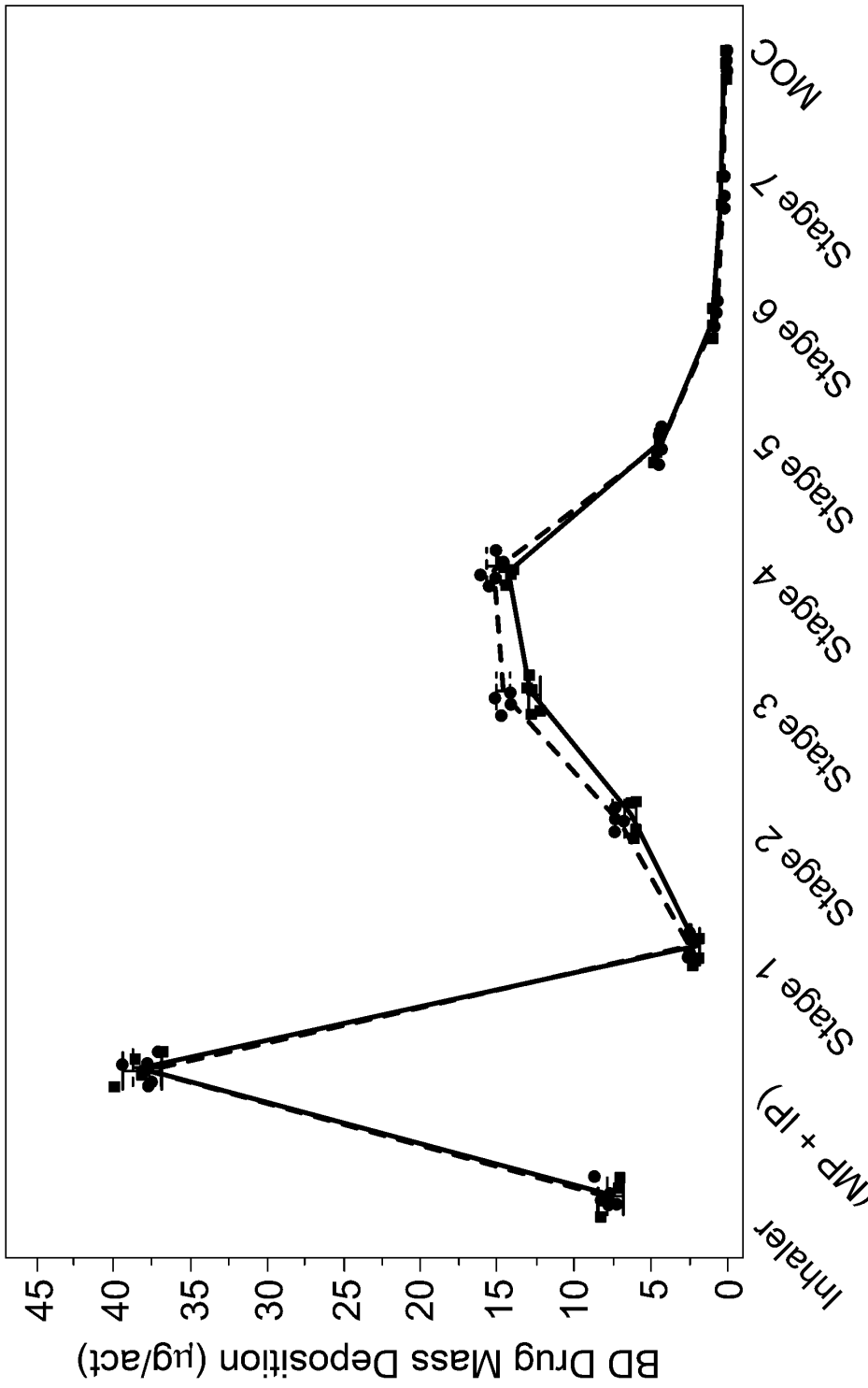

BD Drug Mass Deposition (μg/act)
0
5
10
15
20
25
30
35
40
45
Inhaler
Throat (MP + IP)
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Stage 6
Stage 7
MOC

FIG. 23

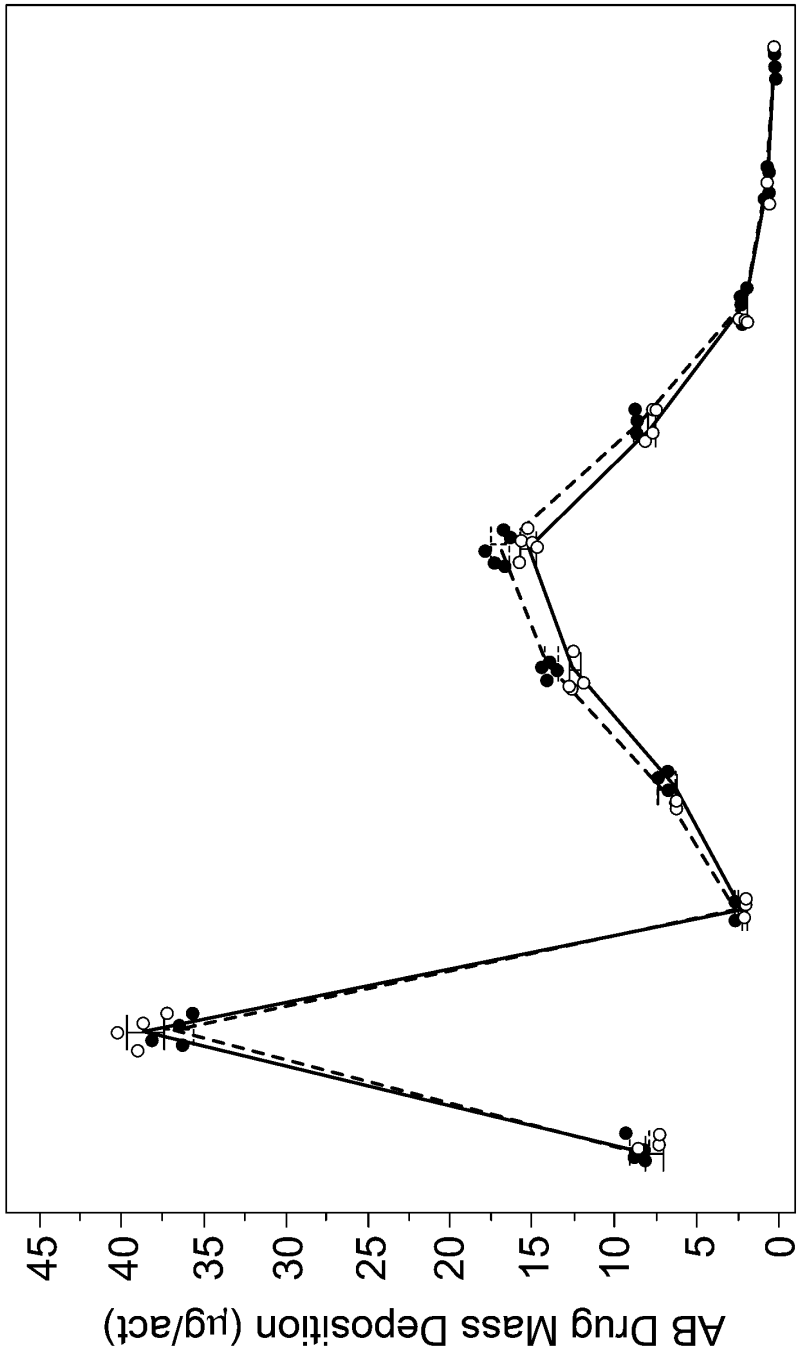

AB Drug Mass Deposition (µg/act)
0
5
10
15
20
25
30
35
40
45
Inhaler
Throat (MP + IP)
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Stage 6
Stage 7
MOC

FIG. 24

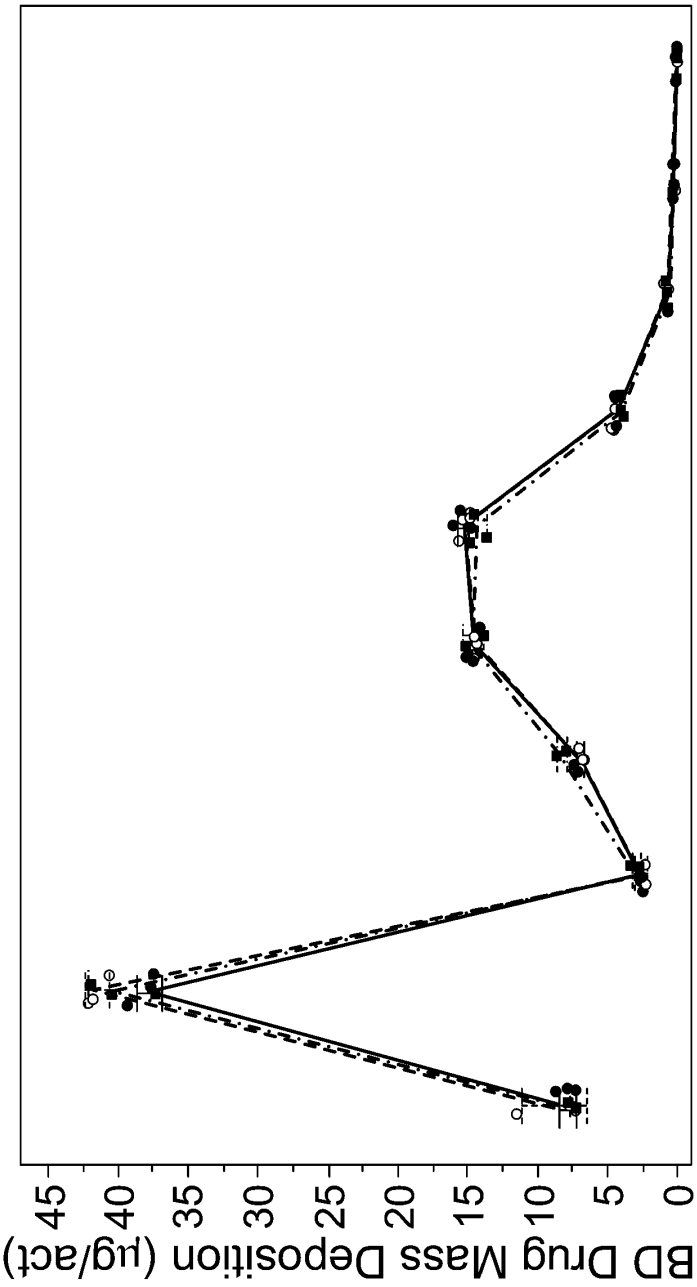

BD Drug Mass Deposition (µg/act)
0
5
10
15
20
25
30
35
40
45
Inhaler
Throat (MP + IP)
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Stage 6
Stage 7
MOC

FIG. 25

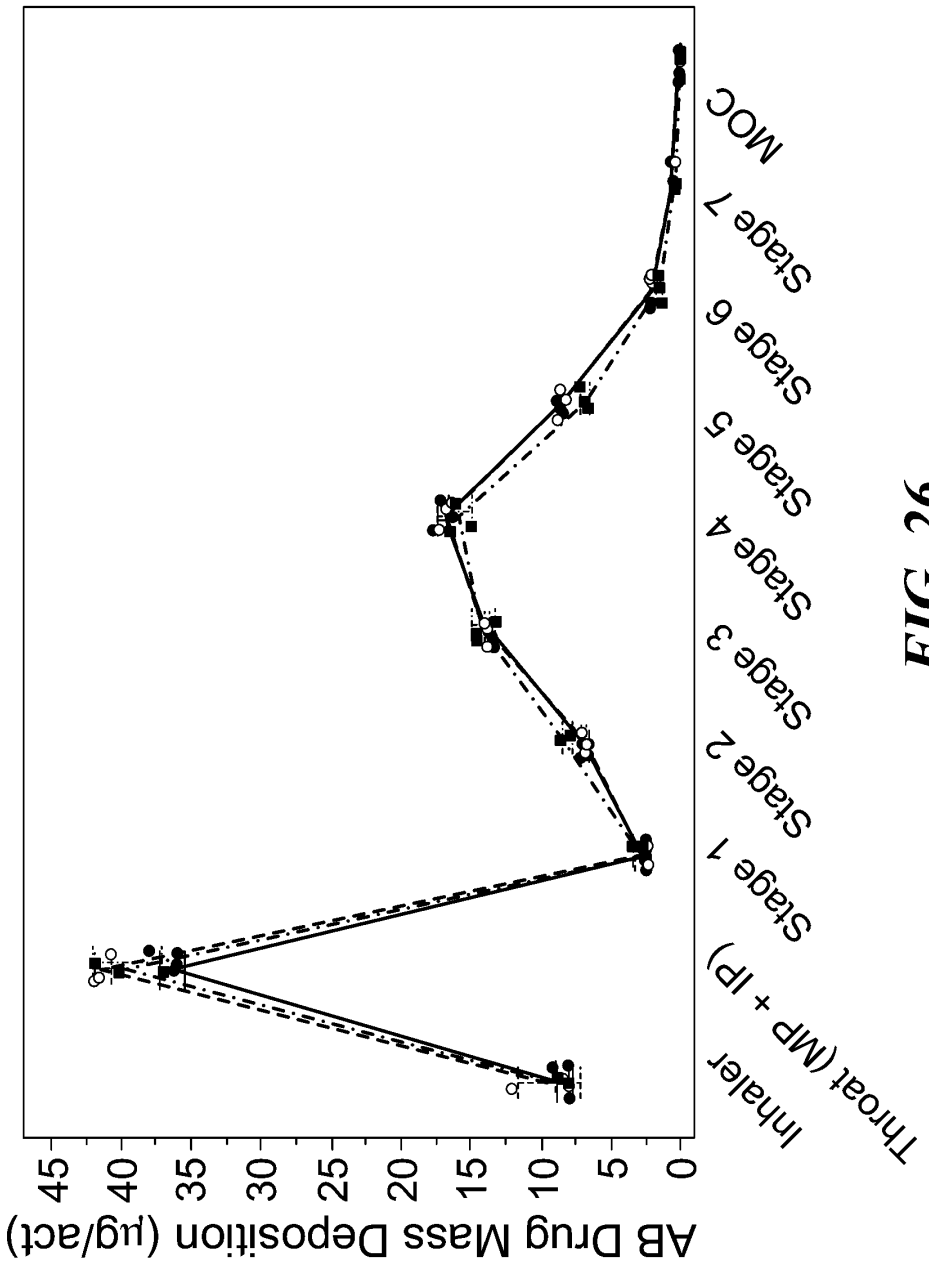

AB Drug Mass Deposition (µg/act)
0
5
10
15
20
25
30
35
40
45
Inhaler
Throat (MP + IP)
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Stage 6
Stage 7
MOC

FIG. 26

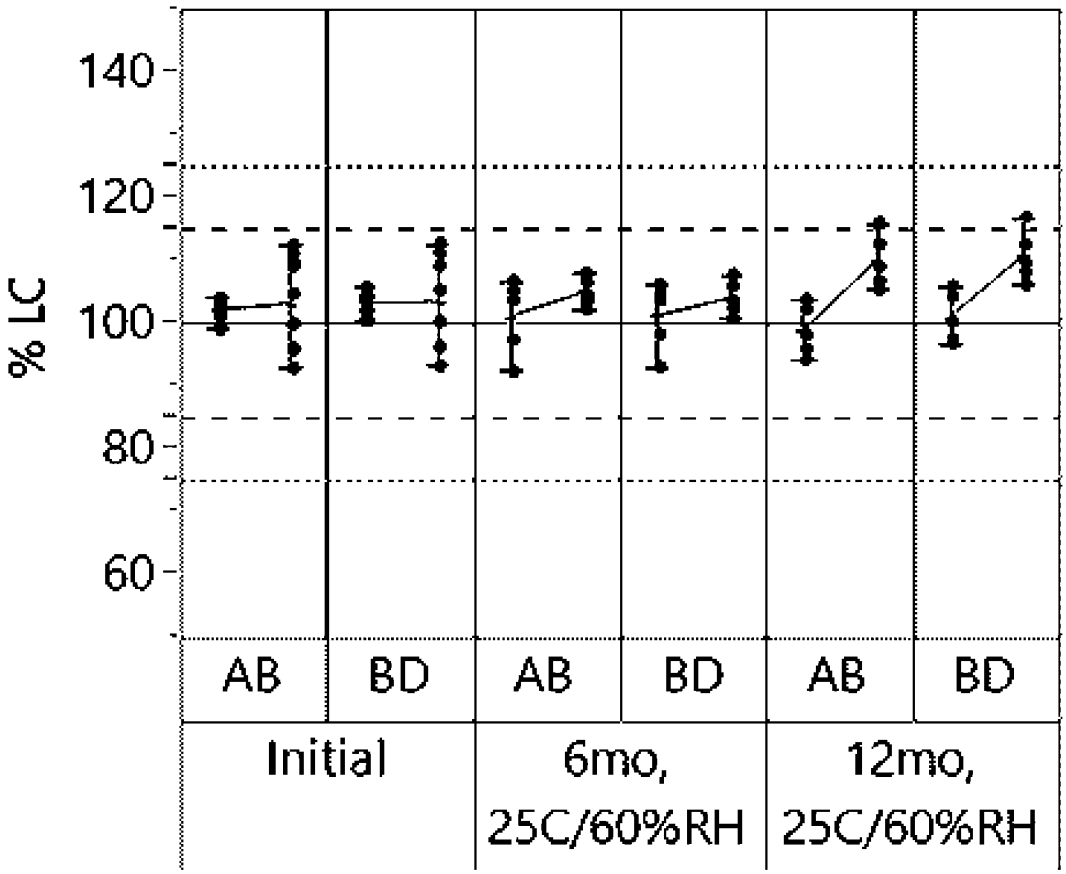

140
120
100
80
60
% LC
AB
BD
AB
BD
AB
BD
Initial
6mo,
25C/60%RH
12mo,
25C/60%RH

FIG. 27

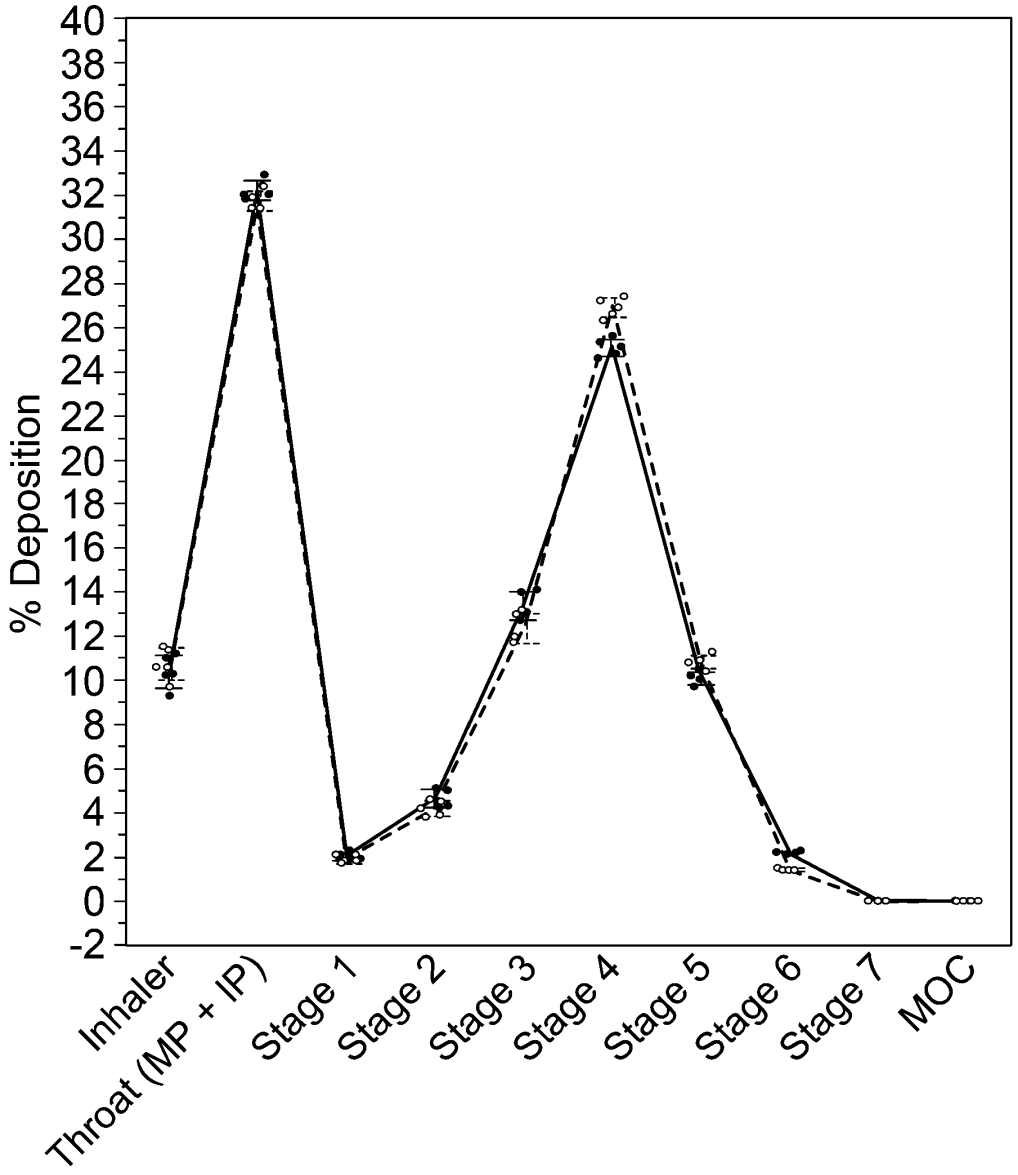

% Deposition
40
38
36
34
32
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
-2
Inhaler
Throat (MP + IP)
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Stage 6
Stage 7
MOC

FIG. 28

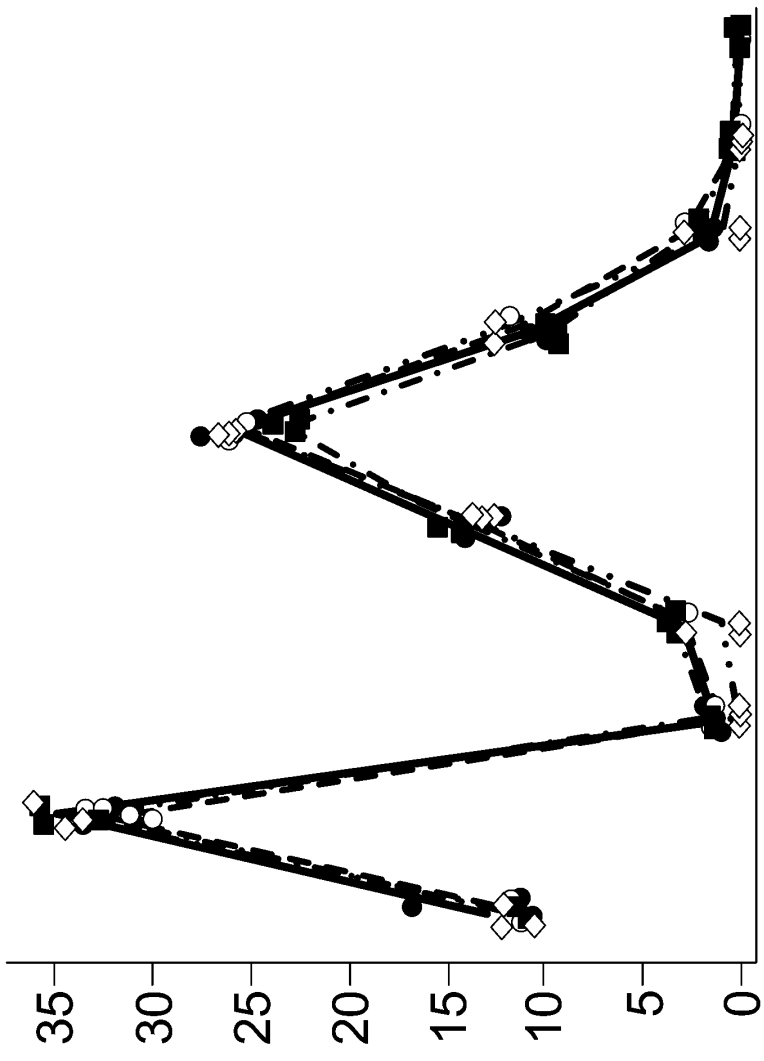


FIG. 29

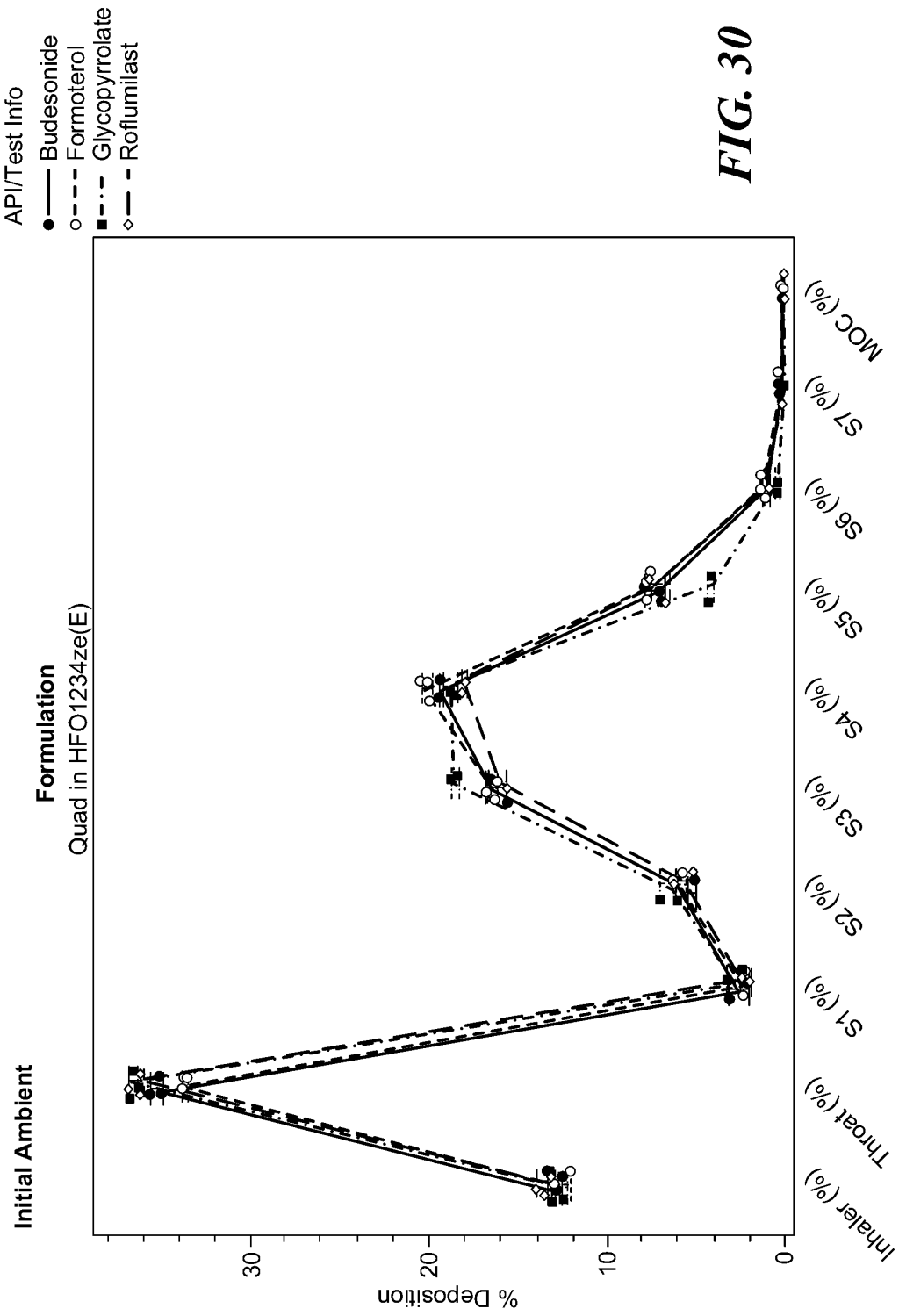

API/Test Info
Budesonide
Formoterol
Glycopyrrolate
Roflumilast
Formulation
Quad in HFO1234ze(E)
Initial Ambient
% Deposition
0
10
20
30
Inhaler (%)
Throat (%)
S1 (%)
S2 (%)
S3 (%)
S4 (%)
S5 (%)
S6 (%)
S7 (%)
MOC (%)

FIG. 30

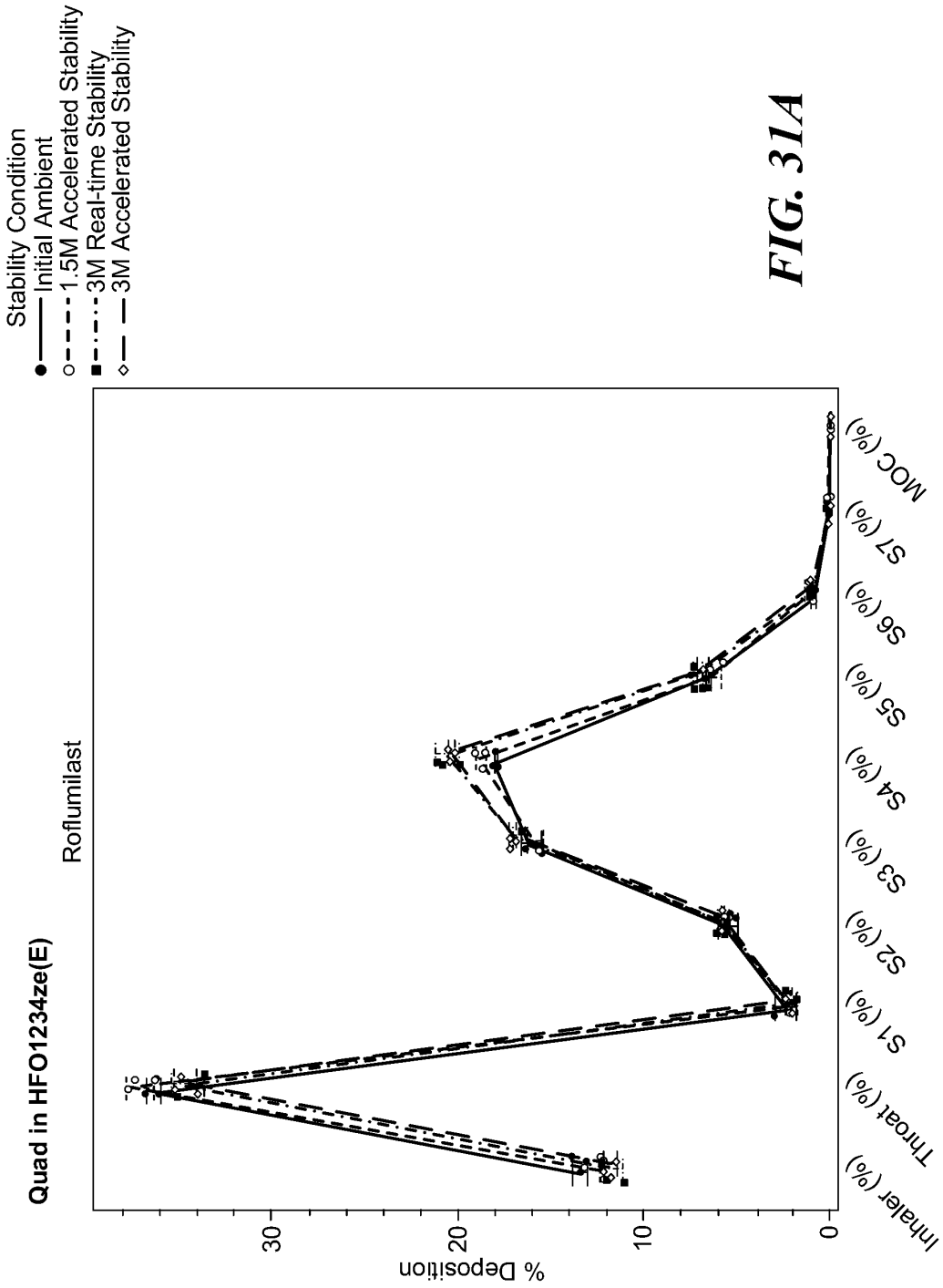

Stability Condition
Initial Ambient
1.5M Accelerated Stability
3M Real-time Stability
3M Accelerated Stability
Quad in HFO1234ze(E)
Roflumilast
% Deposition
0
10
20
30
Inhaler (%)
Throat (%)
S1 (%)
S2 (%)
S3 (%)
S4 (%)
S5 (%)
S6 (%)
S7 (%)
MOC (%)

FIG. 31A

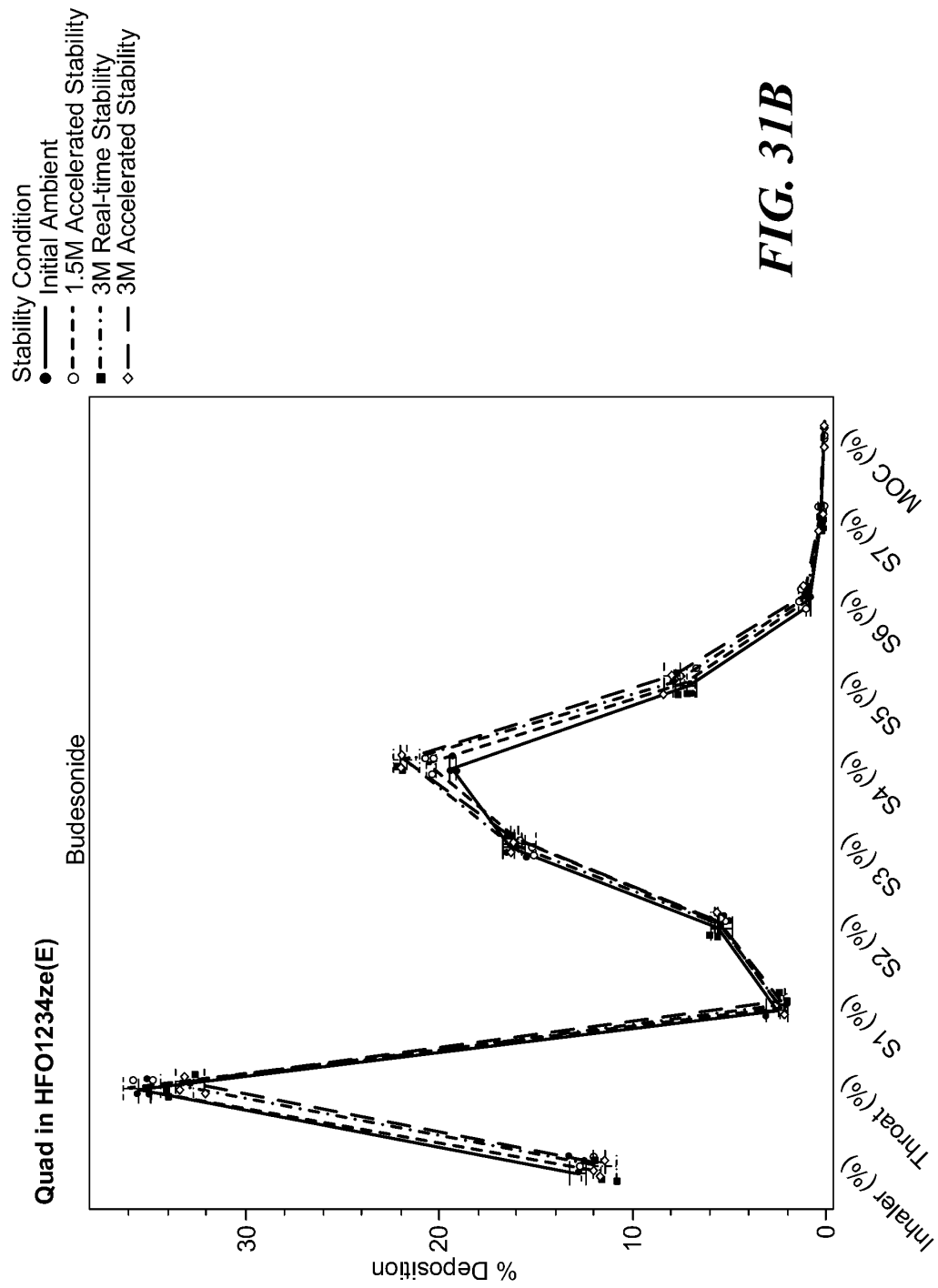

Stability Condition
Initial Ambient
1.5M Accelerated Stability
3M Real-time Stability
3M Accelerated Stability
Quad in HFO1234ze(E)
Budesonide
% Deposition
0
10
20
30
Inhaler (%)
Throat (%)
S1 (%)
S2 (%)
S3 (%)
S4 (%)
S5 (%)
S6 (%)
S7 (%)
MOC (%)

FIG. 31B

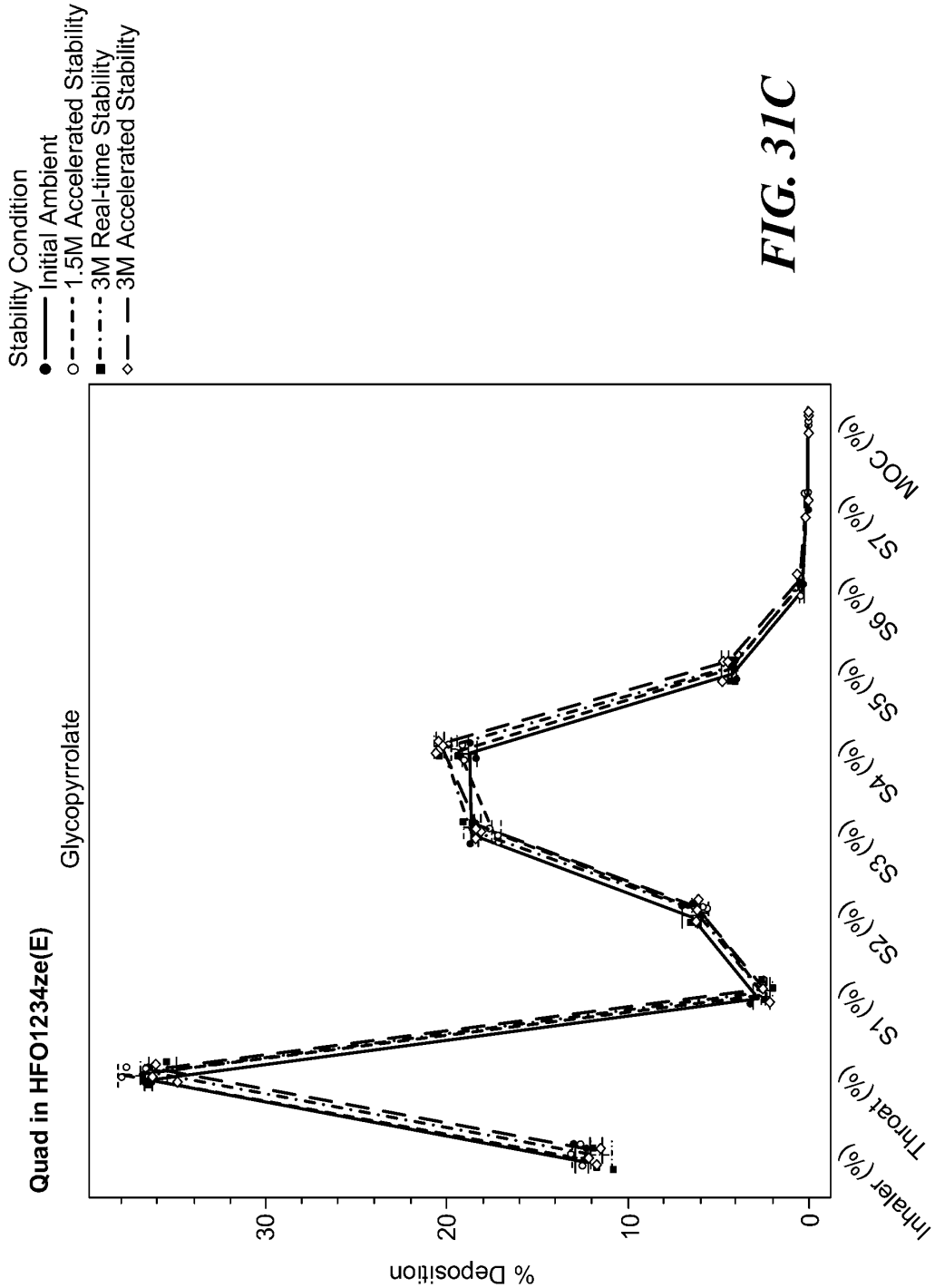

Stability Condition
Initial Ambient
1.5M Accelerated Stability
3M Real-time Stability
3M Accelerated Stability
Quad in HFO1234ze(E)
Glycopyrrolate
% Deposition
0
10
20
30
Inhaler (%)
Throat (%)
S1 (%)
S2 (%)
S3 (%)
S4 (%)
S5 (%)
S6 (%)
S7 (%)
MOC (%)

FIG. 31C

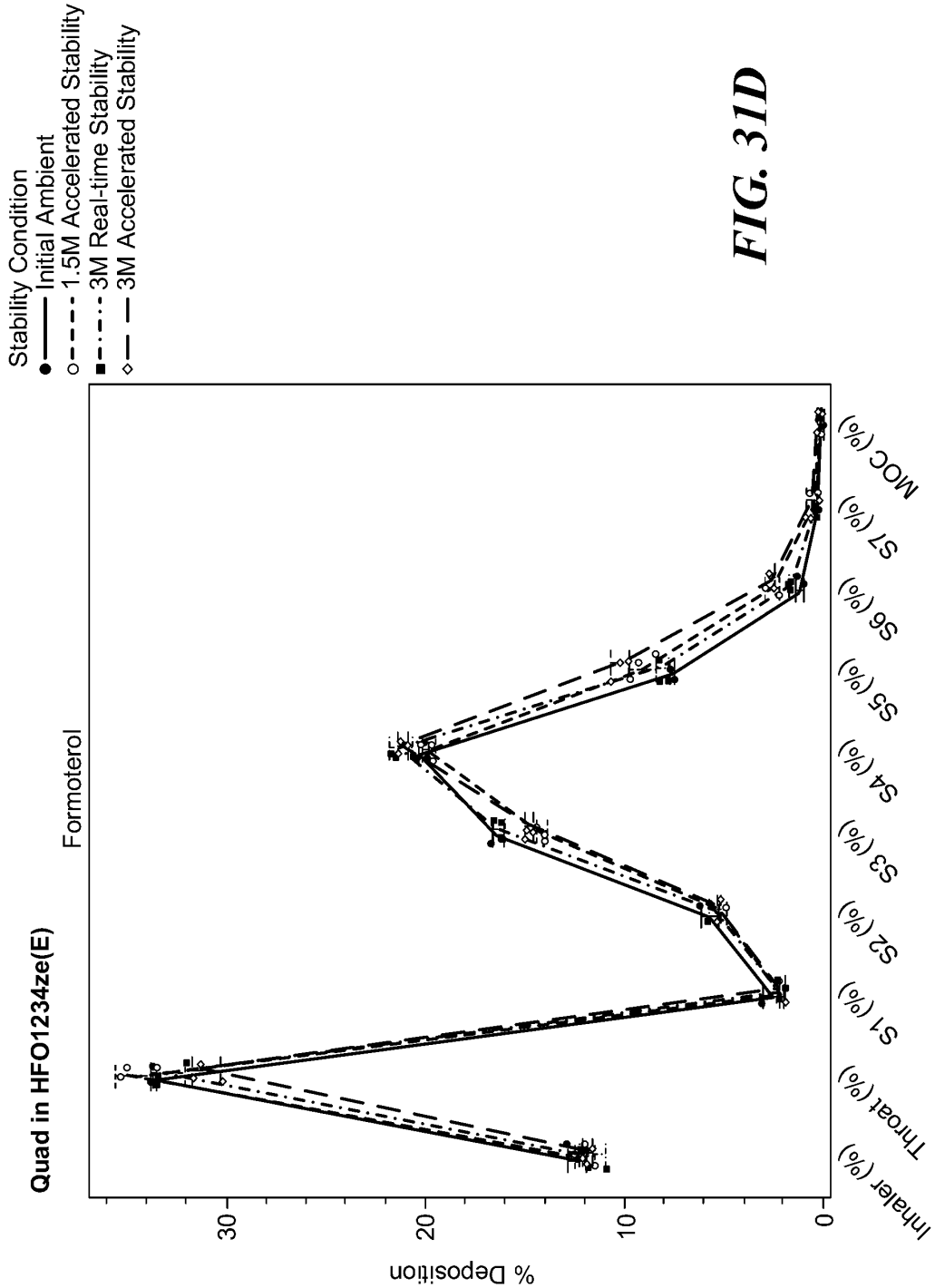

Stability Condition
Initial Ambient
1.5M Accelerated Stability
3M Real-time Stability
3M Accelerated Stability
Quad in HFO1234ze(E)
Formoterol
% Deposition
0
10
20
30
Inhaler (%)
Throat (%)
S1 (%)
S2 (%)
S3 (%)
S4 (%)
S5 (%)
S6 (%)
S7 (%)
MOC (%)

FIG. 31D

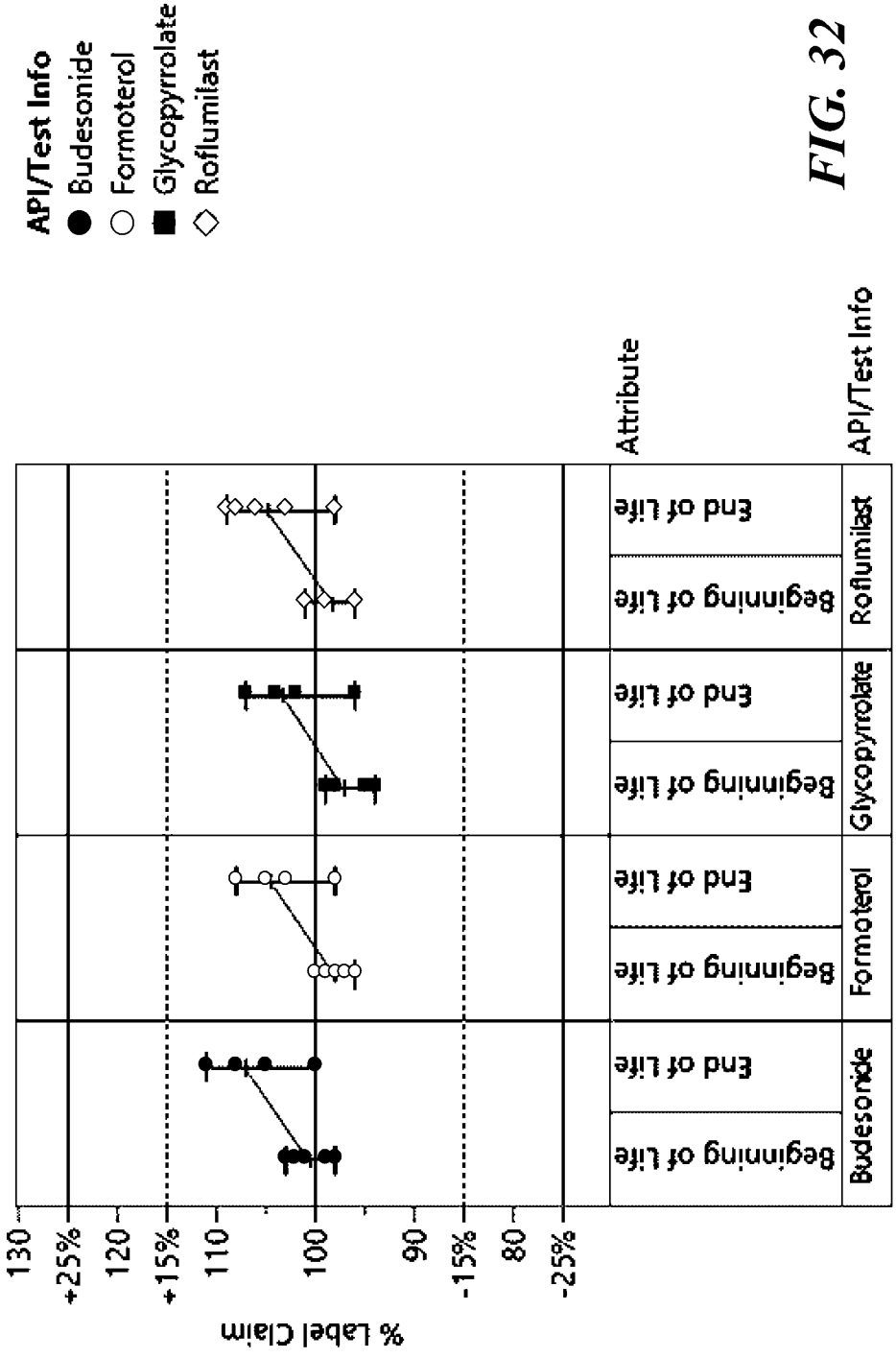

API/Test Info
Budesonide
Formoterol
Glycopyrrolate
Roflumilast
% Label Claim
130
+25%
120
+15%
110
100
90
-15%
80
-25%
Attribute
API/Test Info
Budesonide
Formoterol
Glycopyrrolate
Roflumilast
Beginning of Life
End of Life

FIG. 32

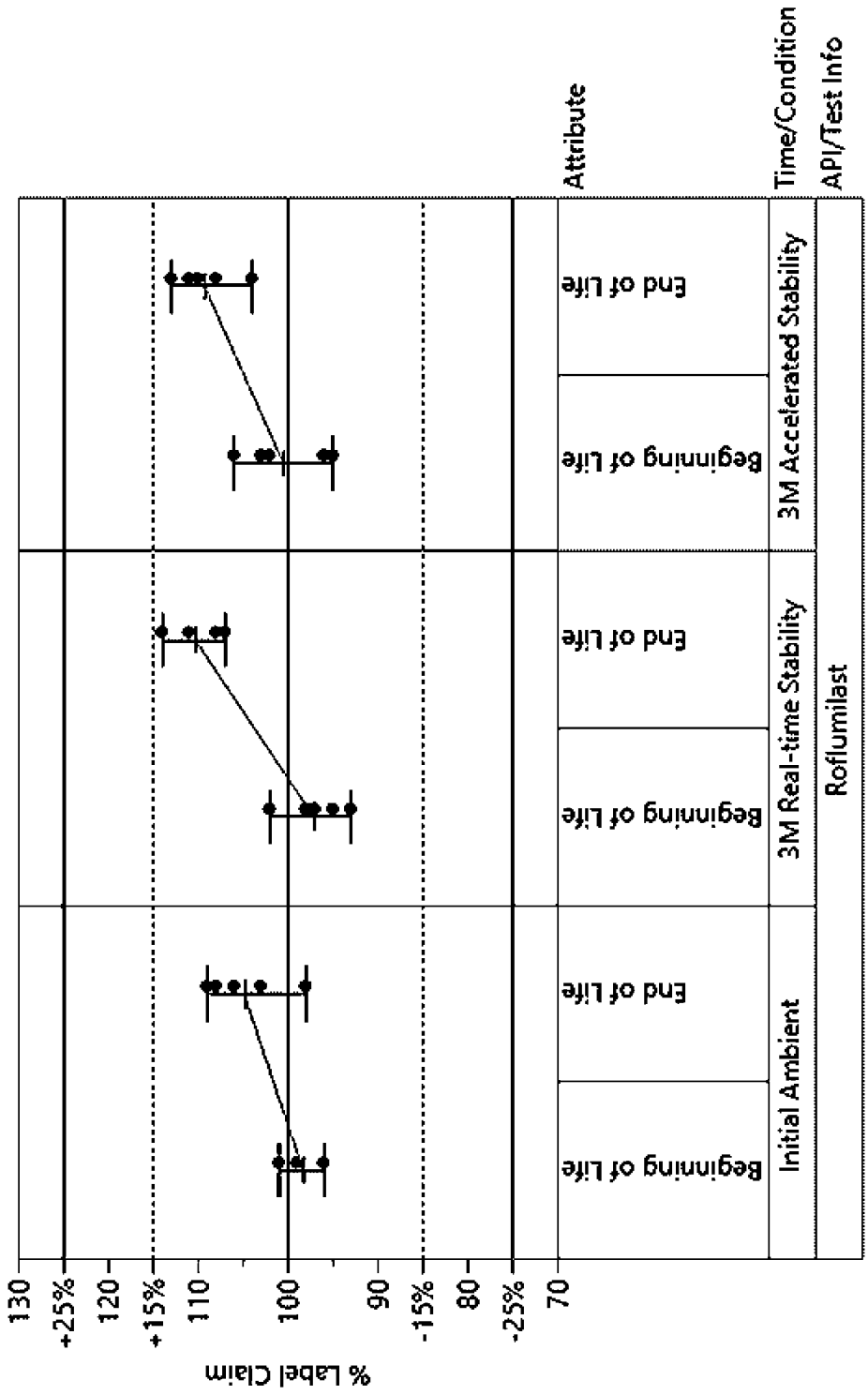

% Label Claim
130
+25%
120
+15%
110
100
90
-15%
80
-25%
70
Attribute
Time/Condition
API/Test Info
Beginning of Life
End of Life
Beginning of Life
End of Life
Beginning of Life
End of Life
Initial Ambient
3M Real-time Stability
3M Accelerated Stability
Roflumilast

FIG. 33A

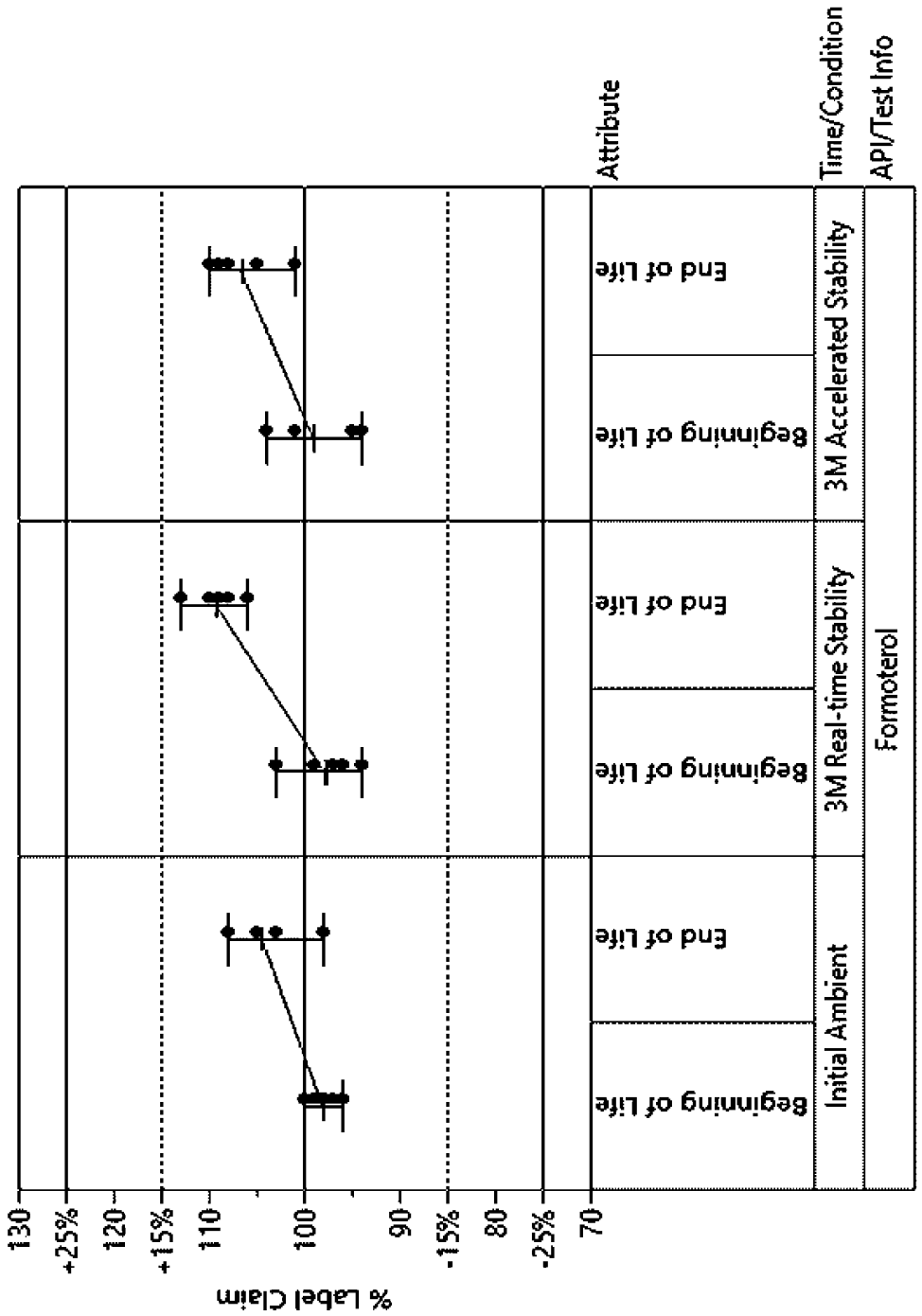

% Label Claim
130
+25%
120
+15%
110
100
90
-15%
80
-25%
70
Attribute
Time/Condition
API/Test Info
Beginning of Life
End of Life
Beginning of Life
End of Life
Beginning of Life
End of Life
Initial Ambient
3M Real-time Stability
3M Accelerated Stability
Formoterol

FIG. 33B

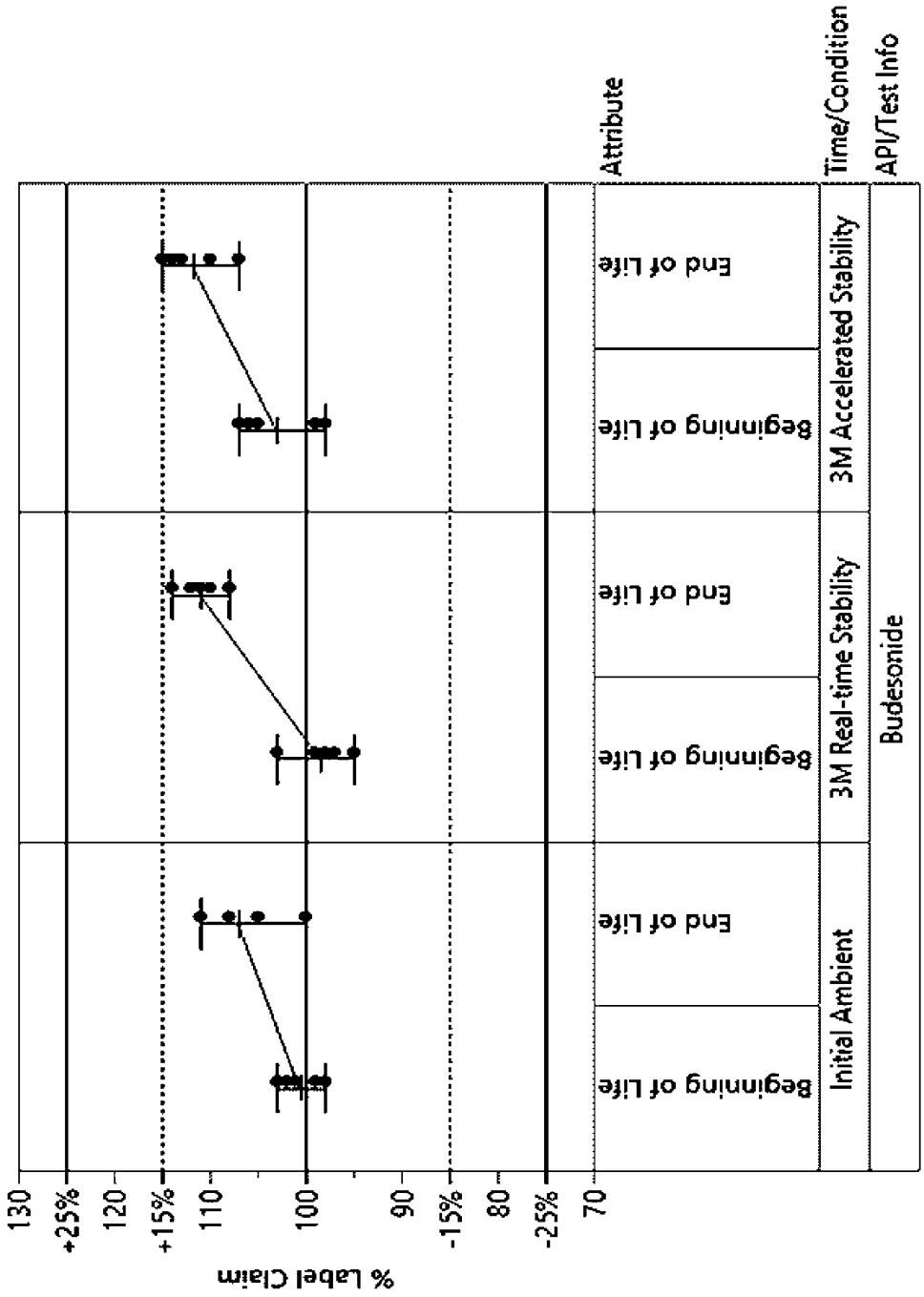

% Label Claim
130
+25%
120
+15%
110
100
90
-15%
80
-25%
70
Attribute
Time/Condition
API/Test Info
Beginning of Life
End of Life
Beginning of Life
End of Life
Beginning of Life
End of Life
Initial Ambient
3M Real-time Stability
3M Accelerated Stability
Budesonide

FIG. 33C

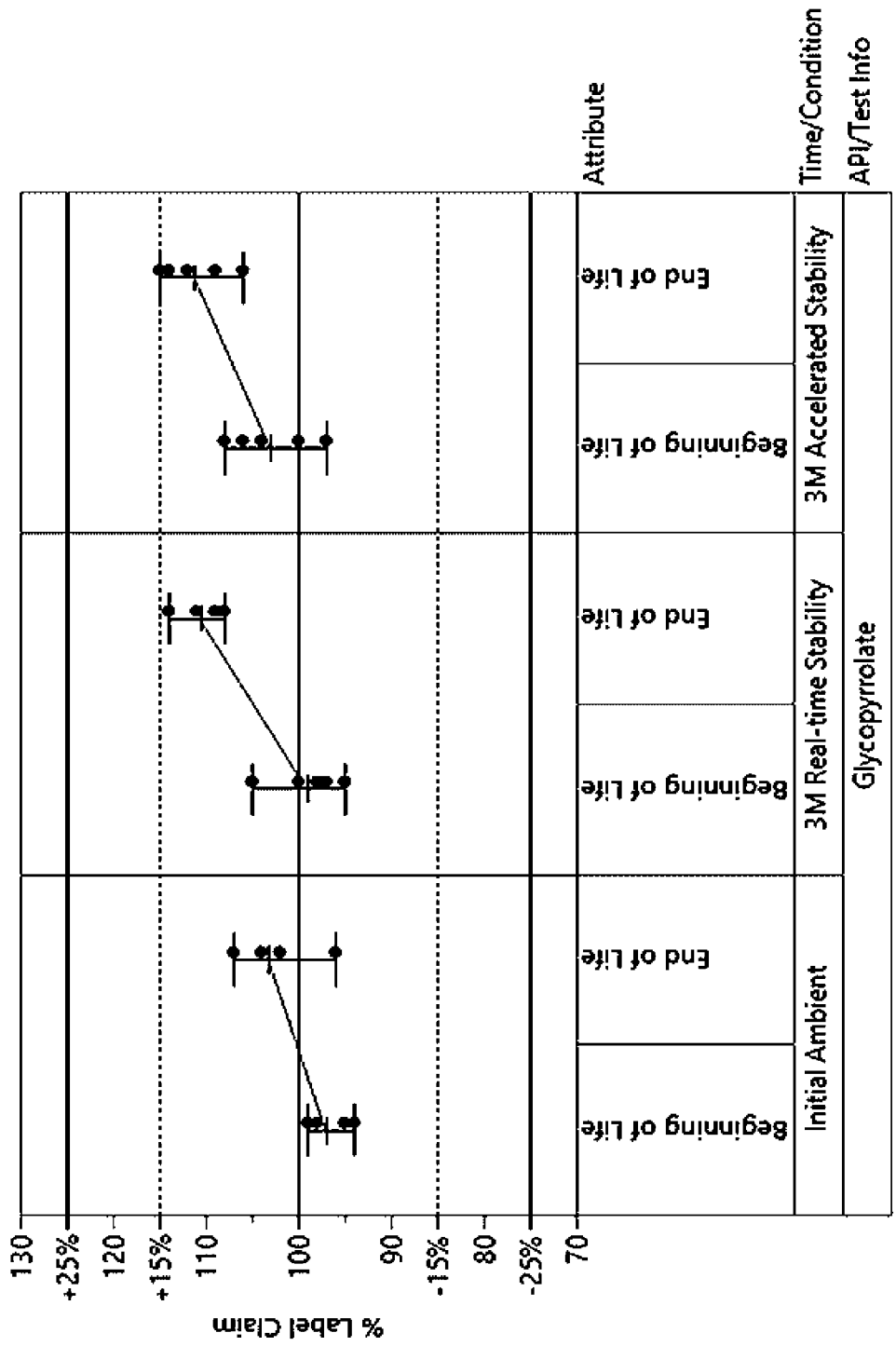

% Label Claim
130
+25%
120
+15%
110
100
90
-15%
80
-25%
70
Attribute
Time/Condition
API/Test Info
Initial Ambient
3M Real-time Stability
3M Accelerated Stability
Glycopyrrolate
Beginning of Life
End of Life
Beginning of Life
End of Life
Beginning of Life
End of Life

FIG. 33D

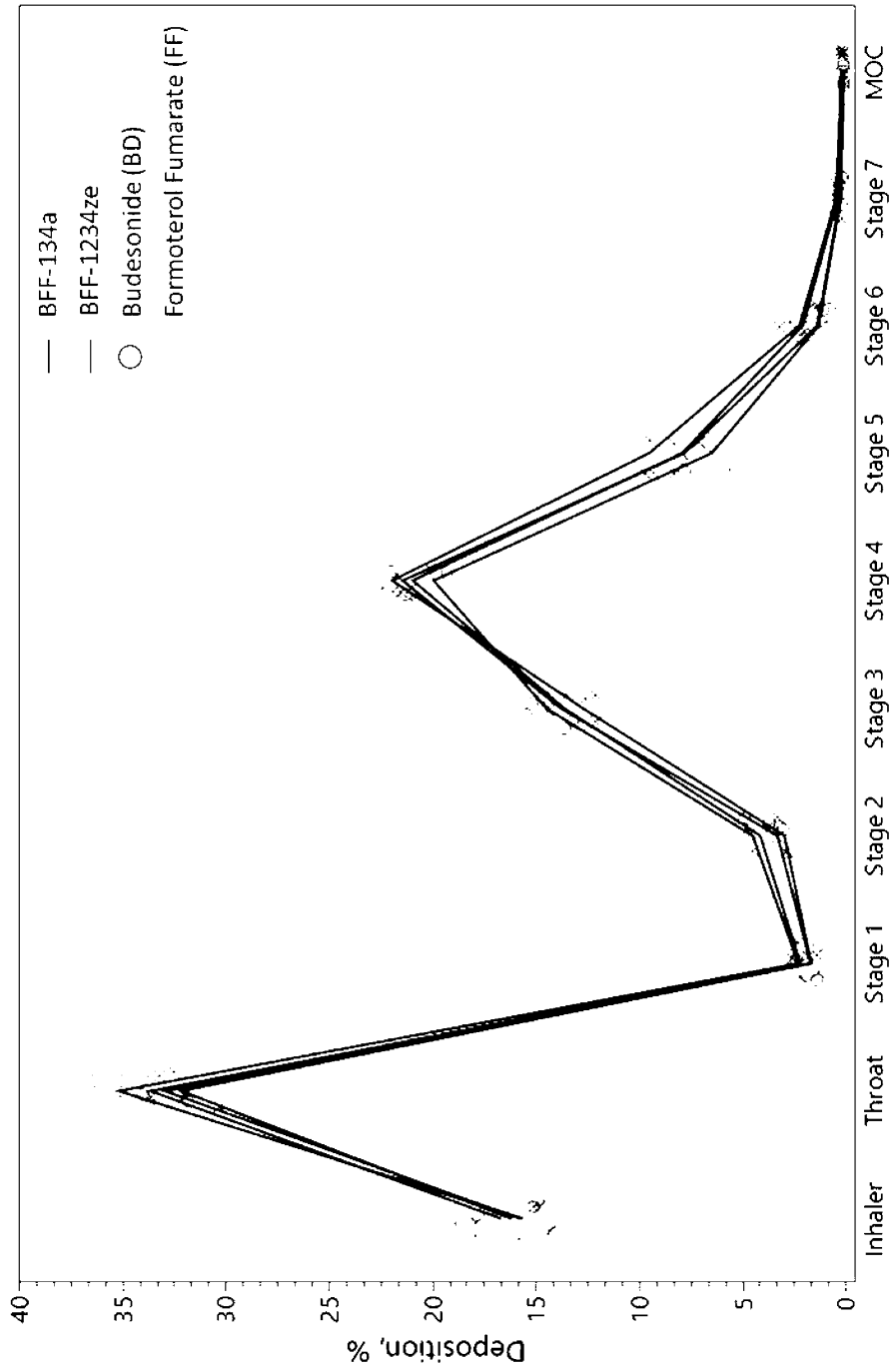

BFF-134a
BFF-1234ze
Budesonide (BD)
Formoterol Fumarate (FF)
Deposition, %
0
5
10
15
20
25
30
35
40
Inhaler
Throat
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Stage 6
Stage 7
MOC

FIG. 34

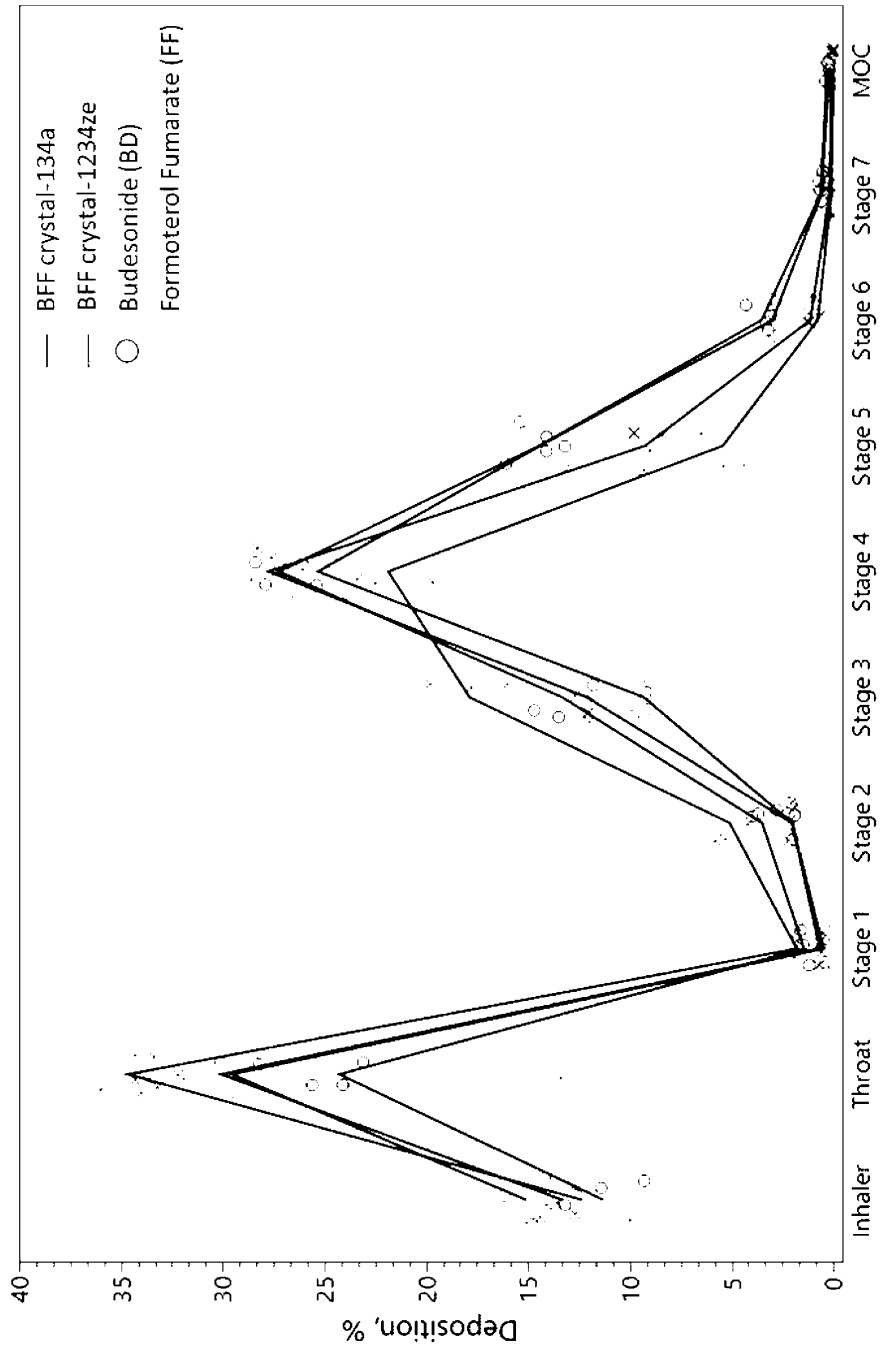

BFF crystal-134a
BFF crystal-1234ze
Budesonide (BD)
Formoterol Fumarate (FF)
Deposition, %
0
5
10
15
20
25
30
35
40
Inhaler
Throat
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Stage 6
Stage 7
MOC

FIG. 35

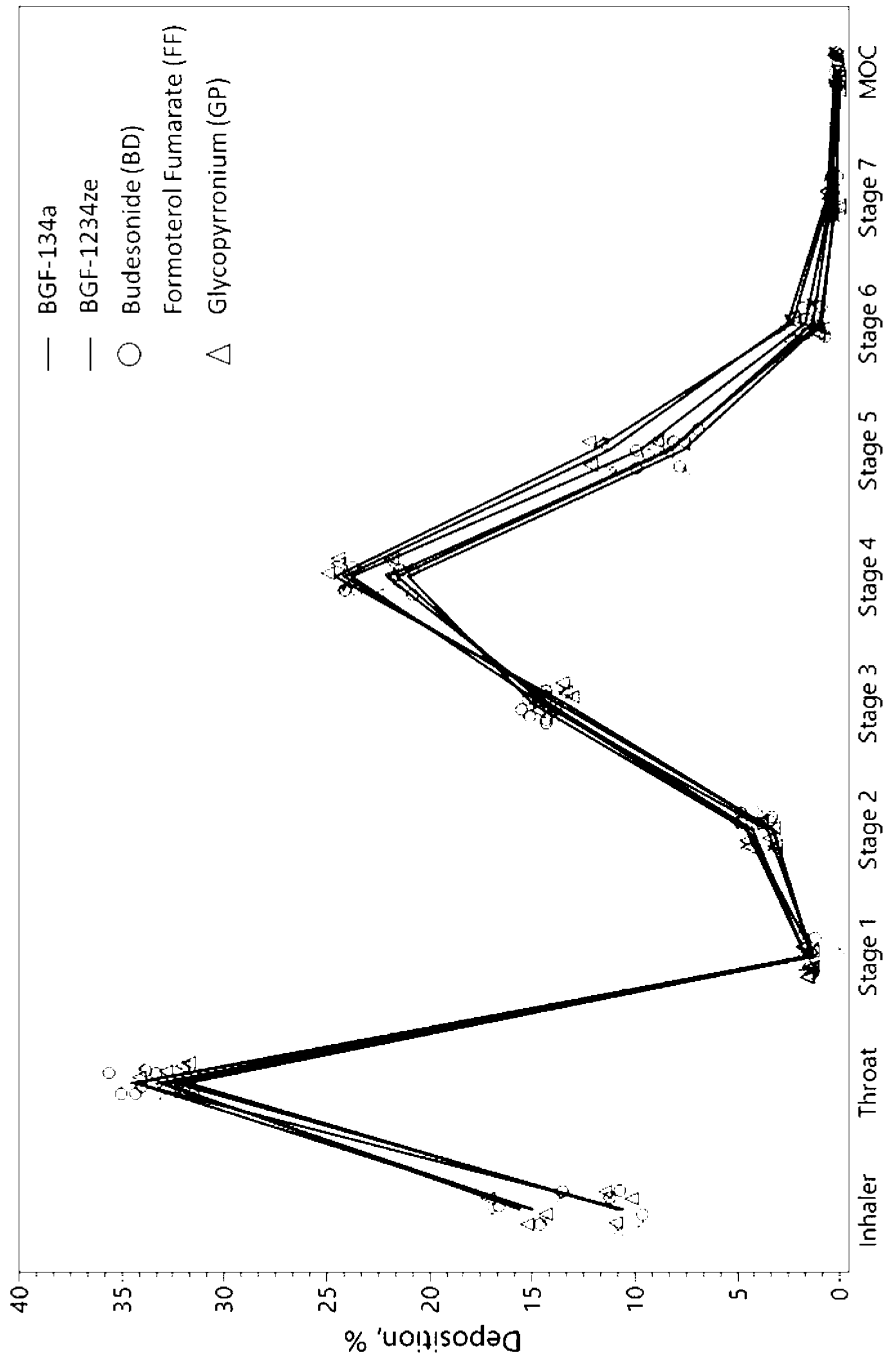

BGF-134a
BGF-1234ze
Budesonide (BD)
Formoterol Fumarate (FF)
Glycopyrronium (GP)
Deposition, %
0
5
10
15
20
25
30
35
40
Inhaler
Throat
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Stage 6
Stage 7
MOC

FIG. 36

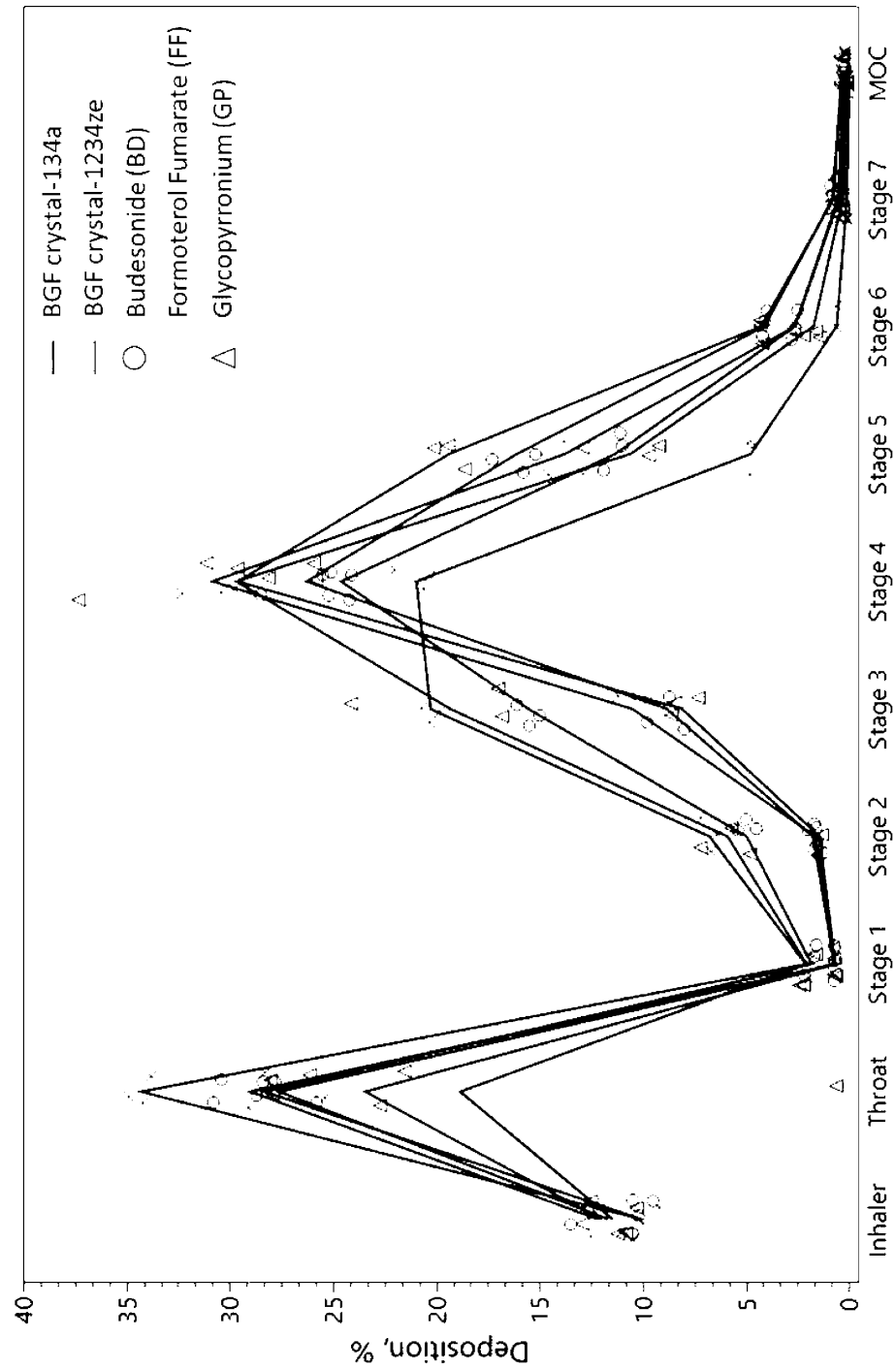

BGF crystal-134a
BGF crystal-1234ze
Budesonide (BD)
Formoterol Fumarate (FF)
Glycopyrronium (GP)
Deposition, %
0
5
10
15
20
25
30
35
40
Inhaler
Throat
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Stage 6
Stage 7
MOC

FIG. 37