FIG. 1

SEQ ID NO: 1: Variable Light Chain of anti-IL5R
DIQMTQSPSSLSASVGDRVTITCGTSEDIINYLNWYQQKPGKAPKLLIYHTSRLQSGVPSR
FSGSGSGTDFTLTISSLQPEDFATYYCQQGYTLPYTFGQGTKVEIK

SEQ ID NO: 2: Light Chain of anti-IL5R
DIQMTQSPSSLSASVGDRVTITCGTSEDIINYLNWYQQKPGKAPKLLIYHTSRLQSGVPSR
FSGSGSGTDFTLTISSLQPEDFATYYCQQGYTLPYTFGQGTKVEIKRTVAAPSVFIFPPSDE
QLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLS
KADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO: 3: Variable Heavy Chain of anti-IL5R
EVQLVQSGAEVKKPGASVKVSCKASGYTFTSYVIHWVRQRPGQGLAWMGYINPYNDG
TKYNERFKGKVTITSDRSTSTVYMELSSLRSEDTAVYLCGREGIRYYGLLGDYWGQGTL
VTVSS

SEQ ID NO: 4: Heavy Chain of anti-IL5R
EVQLVQSGAEVKKPGASVKVSCKASGYTFTSYVIHWVRQRPGQGLAWMGYINPYNDG
TKYNERFKGKVTITSDRSTSTVYMELSSLRSEDTAVYLCGREGIRYYGLLGDYWGQGTL
VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA
VLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAP
ELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYT
LPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKL
TVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 5: VH CDR1 of anti-IL5R
SYVIH

SEQ ID NO: 6: VH CDR2 of anti-IL5R
YINPYNDGTKYNERFKG

SEQ ID NO: 7: VH CDR3 of anti-IL5R
EGIRYYGLLGDY

SEQ ID NO: 8: VL CDR1 of anti-IL5R
GTSEDIINYLN

SEQ ID NO: 9: VL CDR2 of anti-IL5R
HTSRLQS

SEQ ID NO: 10: VL CDR3 of anti-IL5R
QQGYTLPYT

FIG. 2

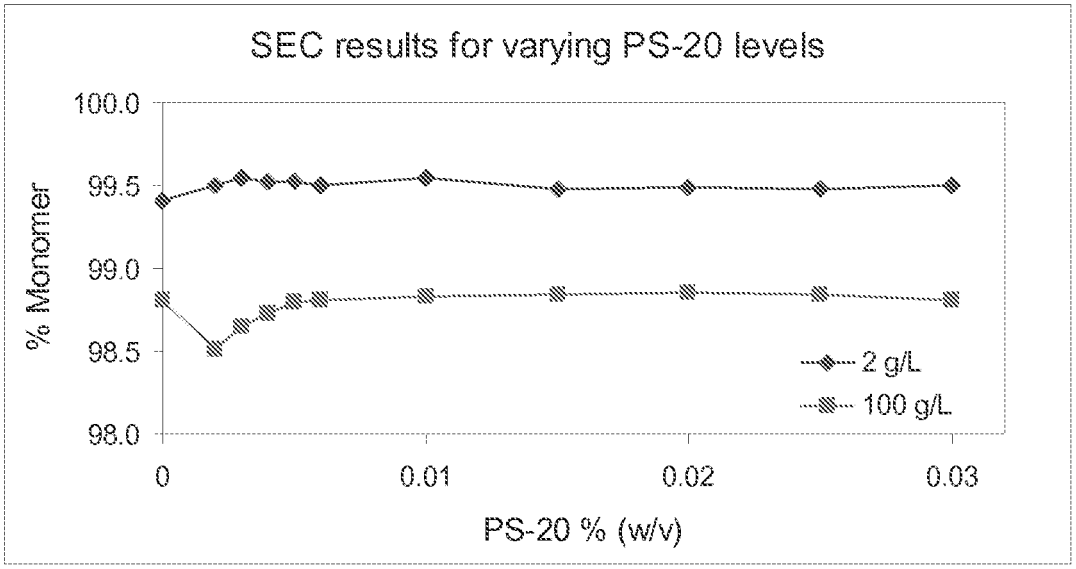

SEC results for varying PS-20 levels
100.0
99.5
99.0
98.5
98.0
% Monomer
0
0.01
0.02
0.03
PS-20 % (w/v)
2 g/L
100 g/L

FIG. 3

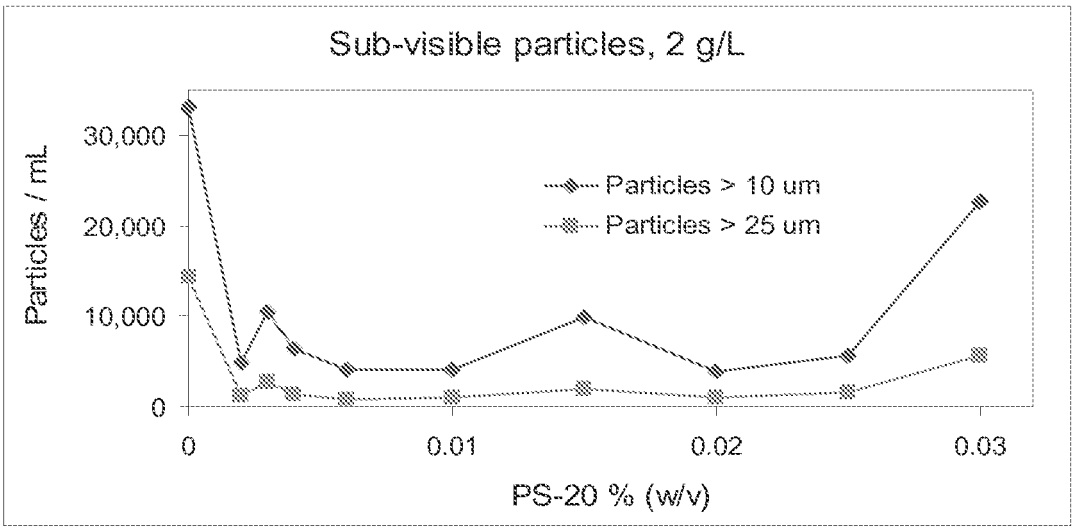

Sub-visible particles, 2 g/L
Particles / mL
30,000
20,000
10,000
0
0
0.01
0.02
0.03
PS-20 % (w/v)
Particles > 10 um
Particles > 25 um

FIG. 4

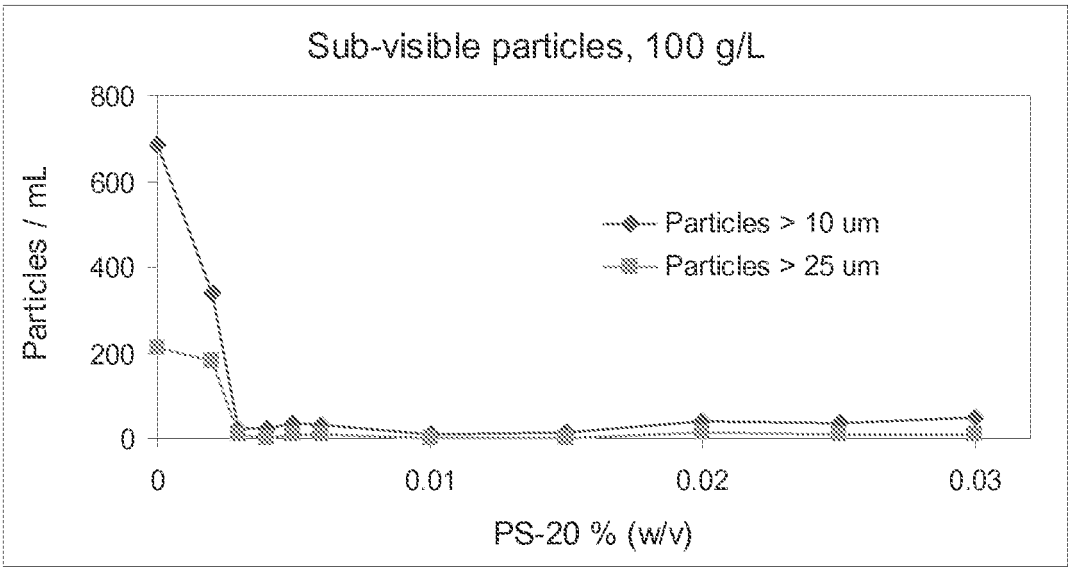

Sub-visible particles, 100 g/L
Particles / mL
800
600
400
200
0
0
0.01
0.02
0.03
PS-20 % (w/v)
Particles > 10 um
Particles > 25 um

FIG. 5

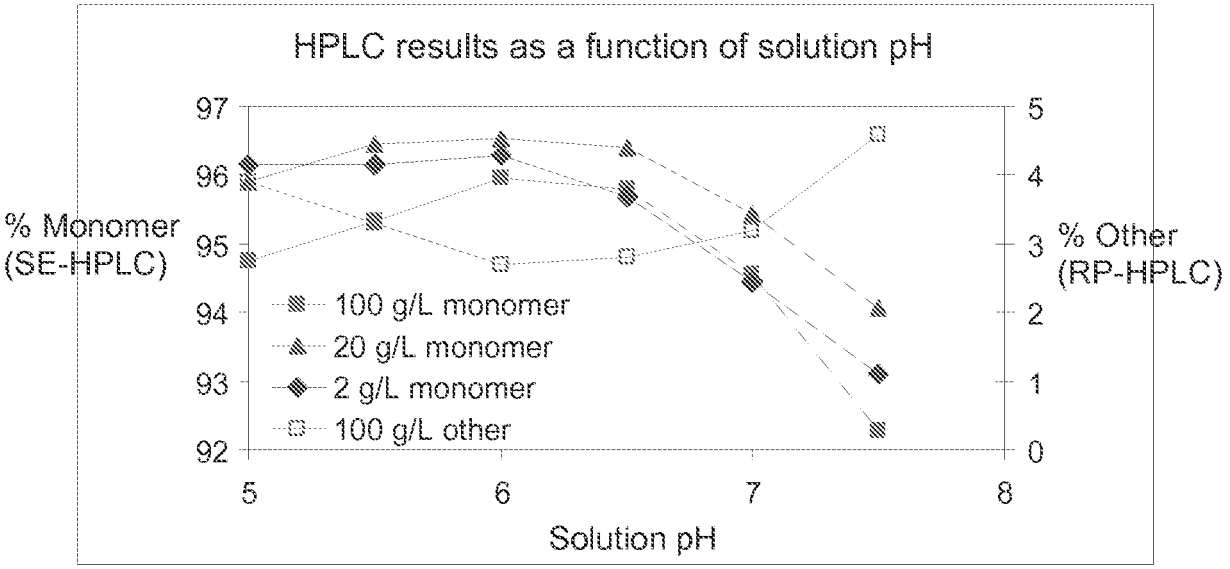

HPLC results as a function of solution pH
% Monomer (SE-HPLC)
% Other (RP-HPLC)
97
96
95
94
93
92
5
4
3
2
1
0
5
6
7
8
Solution pH
100 g/L monomer
20 g/L monomer
2 g/L monomer
100 g/L other

FIG. 6

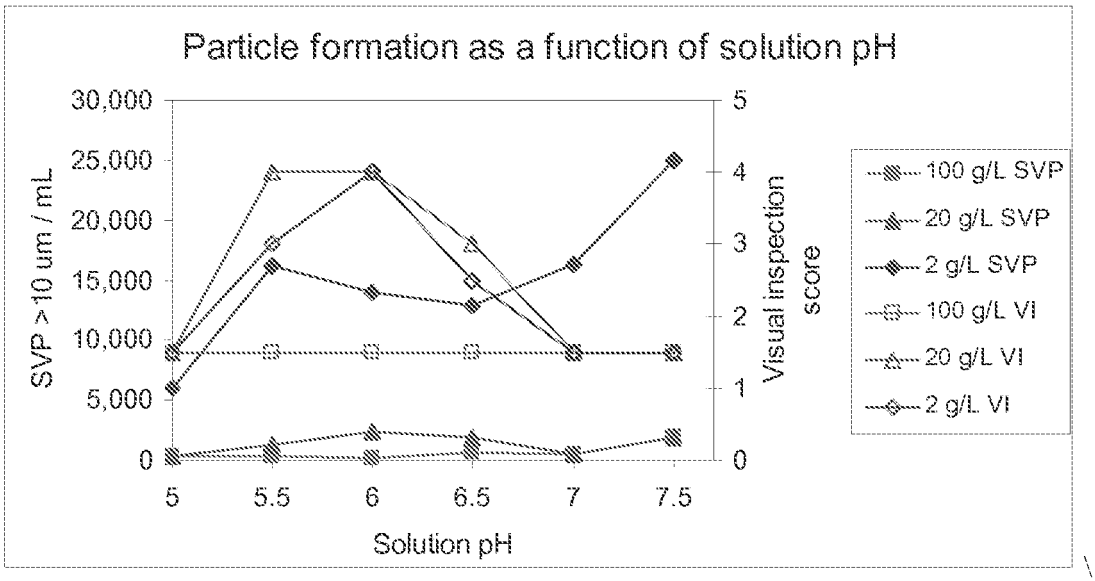

Particle formation as a function of solution pH
SVP >10 um / mL
30,000
25,000
20,000
15,000
10,000
5,000
0
Visual inspection score
5
4
3
2
1
0
5
5.5
6
6.5
7
7.5
Solution pH
100 g/L SVP
20 g/L SVP
2 g/L SVP
100 g/L VI
20 g/L VI
2 g/L VI

FIG. 7

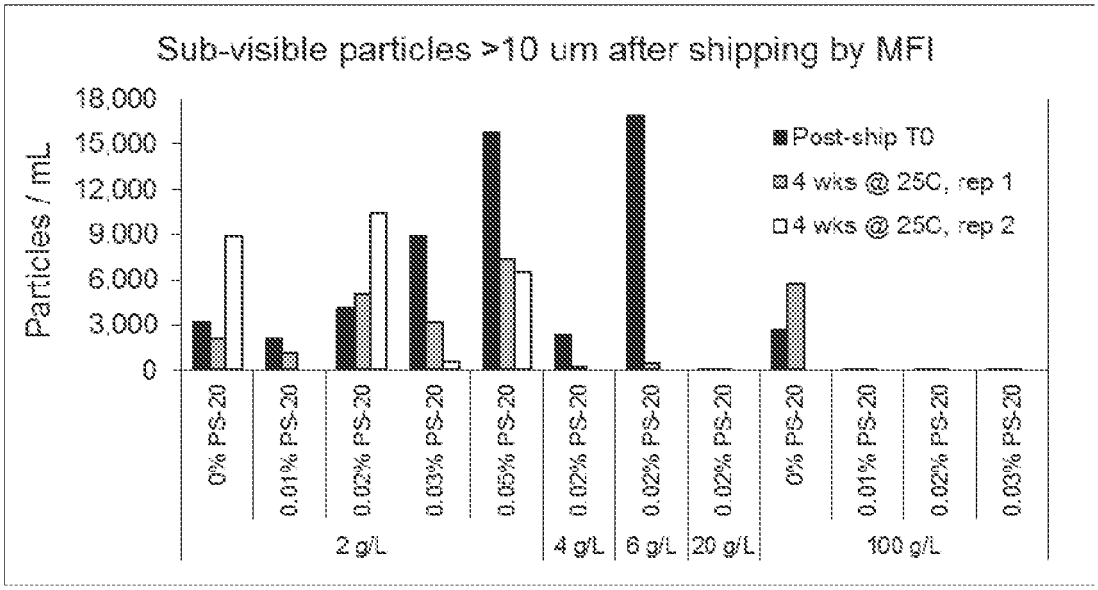

Sub-visible particles >10 um after shipping by MFI
Particles / mL
18,000
15,000
12,000
9,000
6,000
3,000
0
Post-ship T0
4 wks @ 25C, rep 1
4 wks @ 25C, rep 2
0% PS-20
0.01% PS-20
0.02% PS-20
0.03% PS-20
0.05% PS-20
0.02% PS-20
0.02% PS-20
0.02% PS-20
0% PS-20
0.01% PS-20
0.02% PS-20
0.03% PS-20
2 g/L
4 g/L
6 g/L
20 g/L
100 g/L

FIG. 8

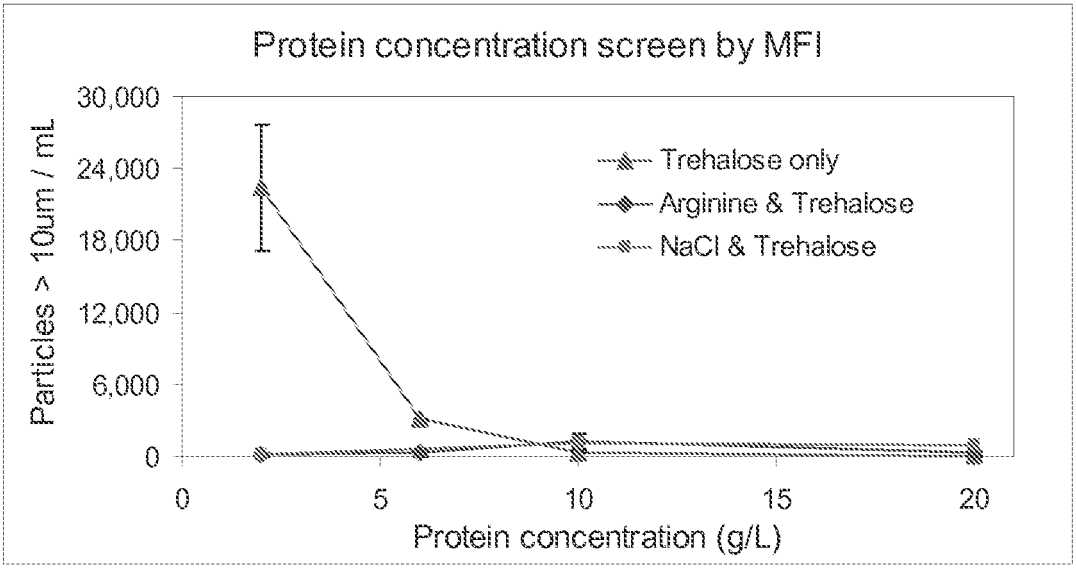

Protein concentration screen by MFI
Particles > 10um / mL
30,000
24,000
18,000
12,000
6,000
0
0
5
10
15
20
Protein concentration (g/L)
Trehalose only
Arginine & Trehalose
NaCl & Trehalose

FIG. 9

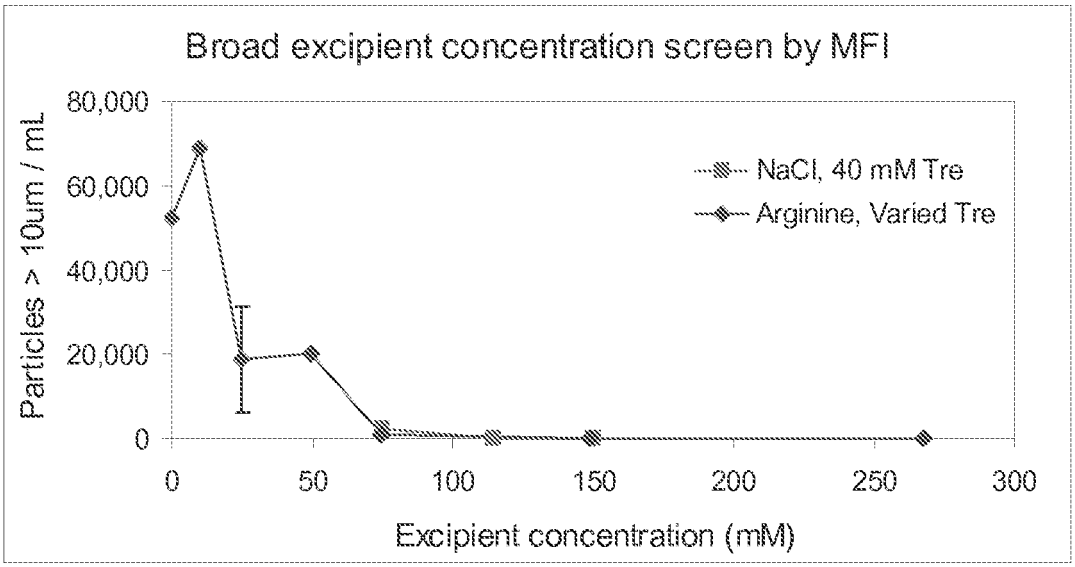

Broad excipient concentration screen by MFI
Particles > 10um / mL
80,000
60,000
40,000
20,000
0
0
50
100
150
200
250
300
Excipient concentration (mM)
NaCl, 40 mM Tre
Arginine, Varied Tre

FIG. 10

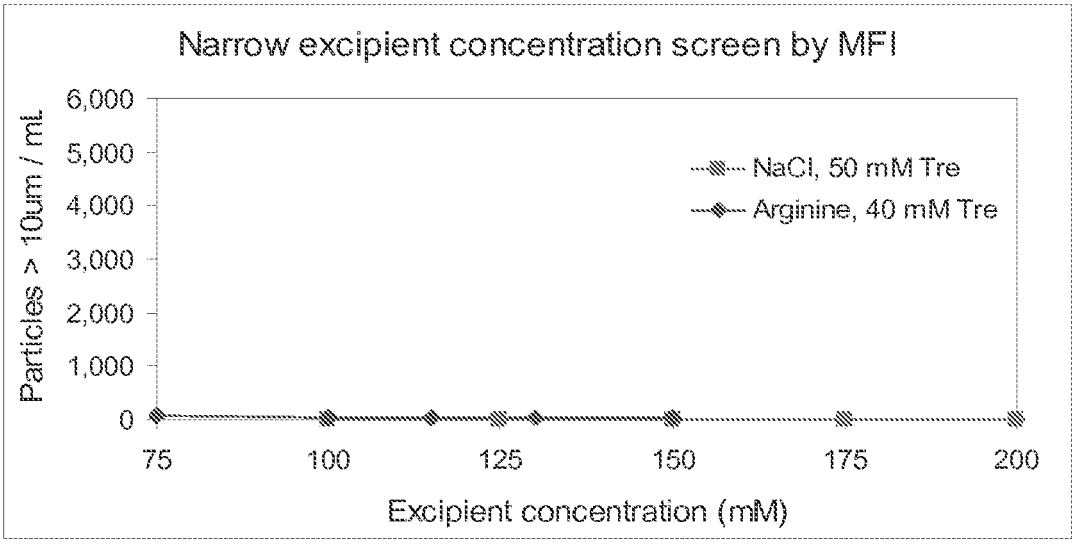

Narrow excipient concentration screen by MFI
Particles > 10um / mL
6,000
5,000
4,000
3,000
2,000
1,000
0
75
100
125
150
175
200
Excipient concentration (mM)
NaCl, 50 mM Tre
Arginine, 40 mM Tre

FIG. 11

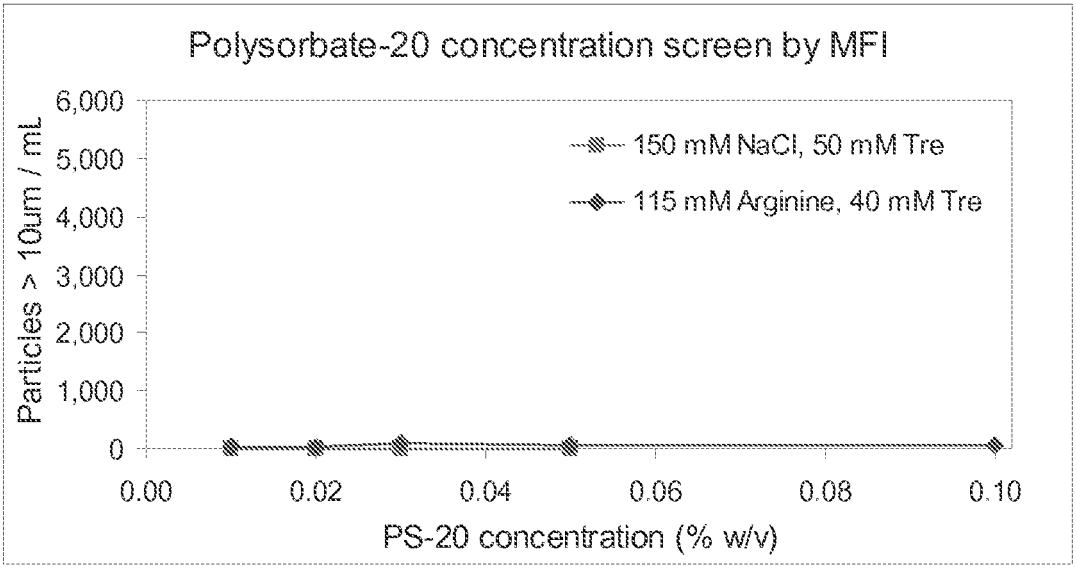
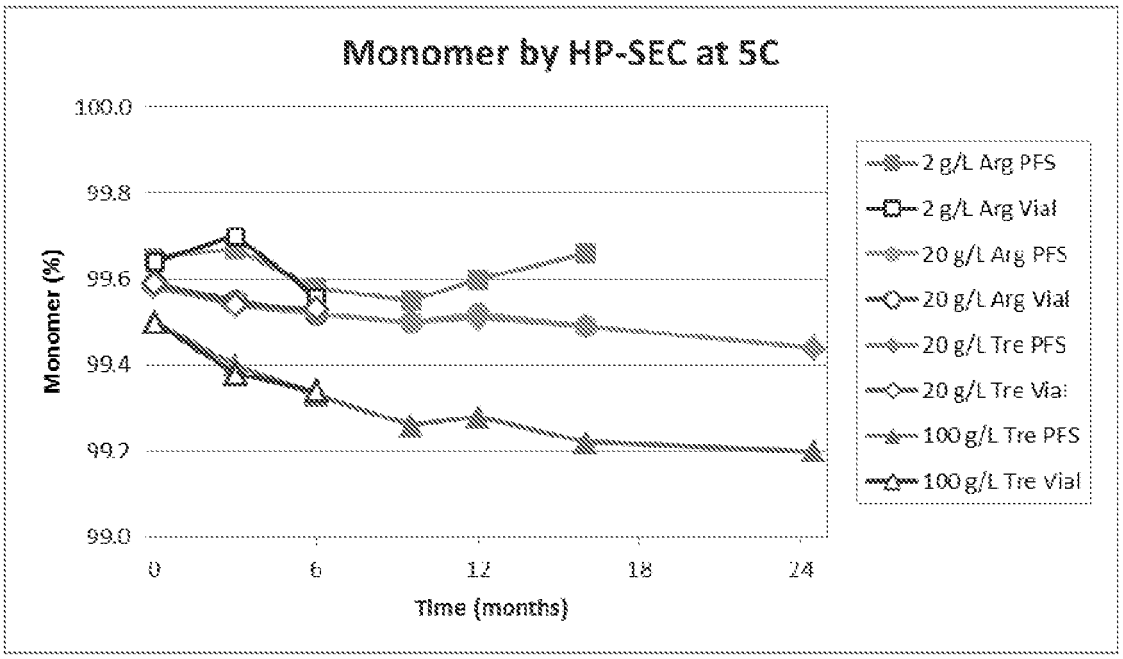

Polysorbate-20 concentration screen by MFI
Particles > 10um / mL
6,000
5,000
4,000
3,000
2,000
1,000
0
0.00
0.02
0.04
0.06
0.08
0.10
PS-20 concentration (% w/v)
150 mM NaCl, 50 mM Tre
115 mM Arginine, 40 mM Tre

FIG. 12

A


Monomer by HP-SEC at 5C
Monomer (%)
100.0
99.8
99.6
99.4
99.2
99.0
0
6
12
18
24
Time (months)
2 g/L Arg PFS
2 g/L Arg Vial
20 g/L Arg PFS
20 g/L Arg Vial
20 g/L Tre PFS
20 g/L Tre Vial
100 g/L Tre PFS
100 g/L Tre Vial

B

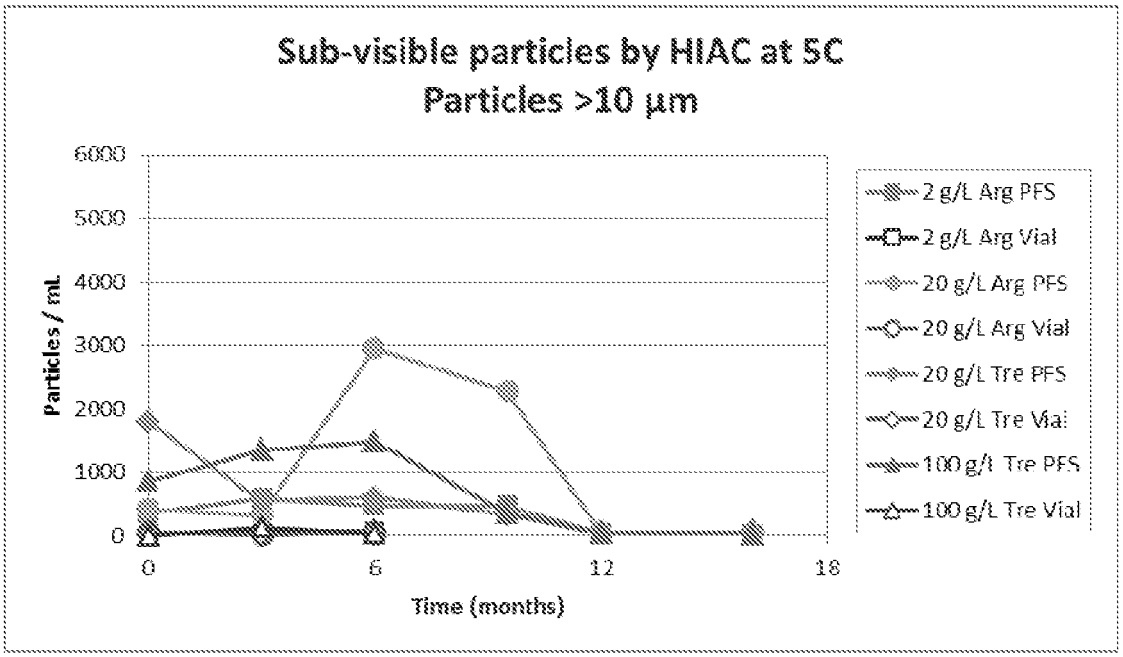

Sub-visible particles by HIAC at 5C
Particles >10 µm
Particles / mL
6000
5000
4000
3000
2000
1000
0
0
6
12
18
Time (months)
2 g/L Arg PFS
2 g/L Arg Vial
20 g/L Arg PFS
20 g/L Arg Vial
20 g/L Tre PFS
20 g/L Tre Vial
100 g/L Tre PFS
100 g/L Tre Vial

FIG. 12 (continued)

C.

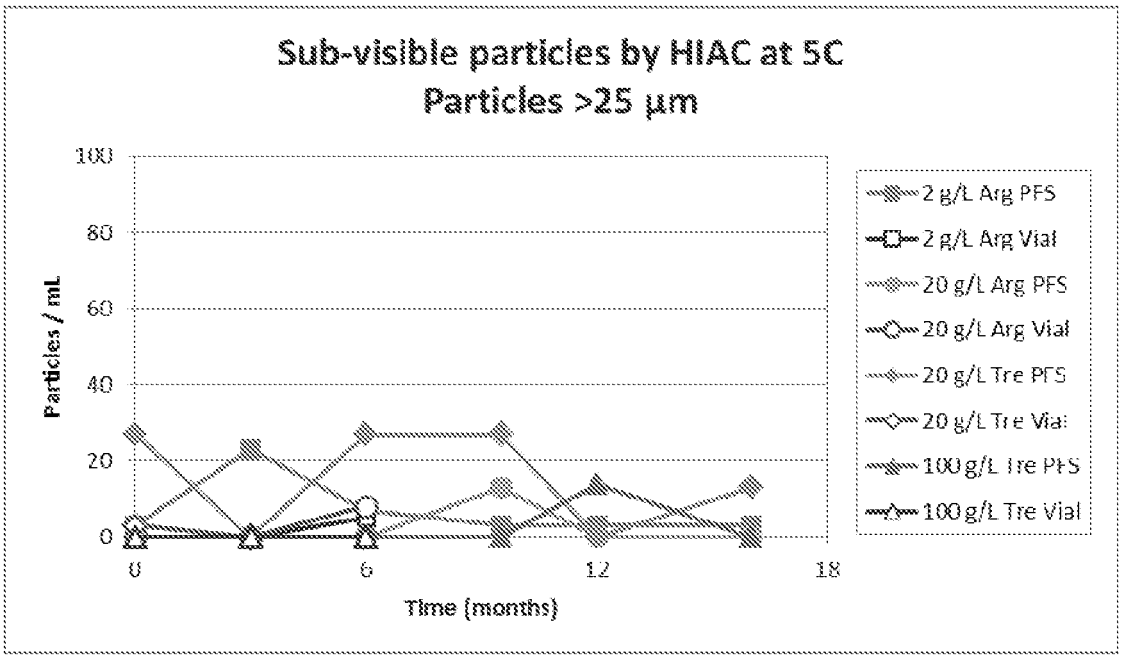


FIG. 13

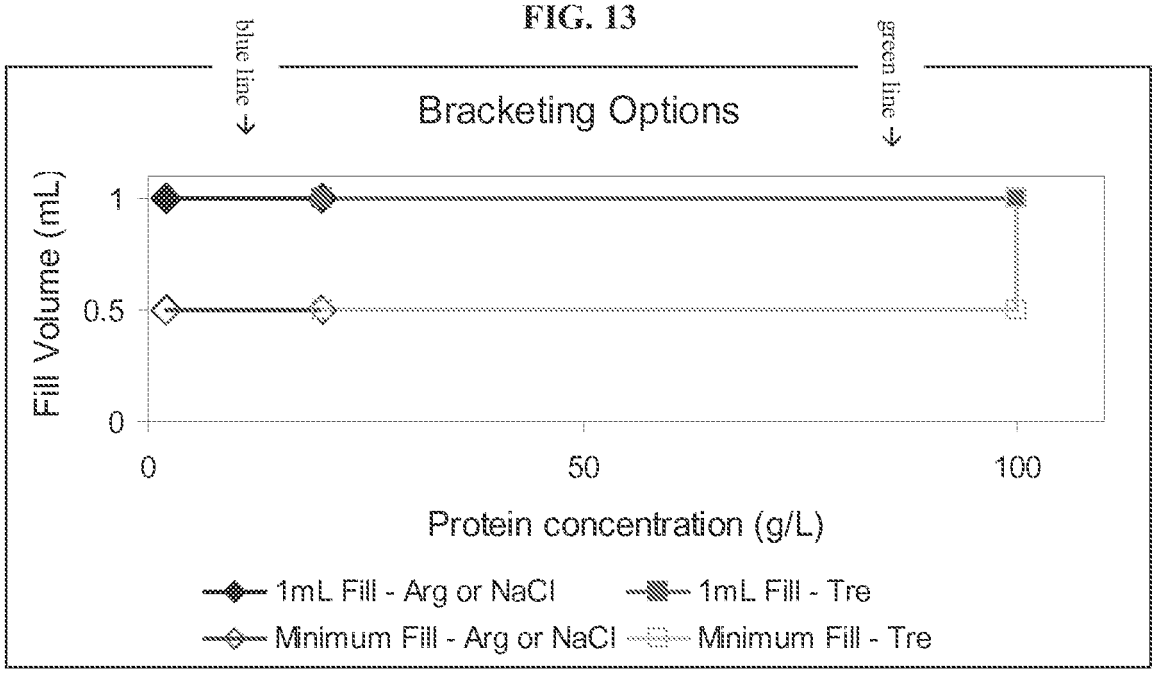

blue line
green line
Bracketing Options
Fill Volume (mL)
1
0.5
0
0
50
100
Protein concentration (g/L)
1mL Fill - Arg or NaCl
1mL Fill - Tre
Minimum Fill - Arg or NaCl
Minimum Fill - Tre

FIG. 14

Formulation	Protein Concentration & Fill Configuration	Visible Particles (worst observation)	Monomer Loss by SEC	Sub-visible particles by HIAC (particles/mL)		Potency
				>10 µm	>25 µm	
130 mM Arginine, 50 mM Trehalose, 20 mM Histidine, 0.02% PS-20, pH 6.0	2 g/L, 1 mL PFS	= STD 0	0.0%/yr	<590	<20	>100%
	2 g/L, 1/2 mL PFS	= STD 0	0.0%/yr	<680	<20	>100%
	2 g/L, 1/2 mL vial	= STD 1	0.0%/yr	<80	<10	>100%
	20 g/L, 1 mL PFS	< STD 4	0.0%/yr	<2010*	<70	>97%
	20 g/L, 1/2 mL PFS	T0 testing only				
	20 g/L g, 1/2 mL vial	= STD 1	0.1%/yr			>100%
250 mM Trehalose, 20 mM Histidine, 0.02% PS-20, pH 6.0	20 g/L, 1 mL PFS	= STD 1	0.0%/yr	<540	<20	>91%
	20 g/L, 1/2 mL PFS	< STD 1	0.1%/yr	<230	<10	>95%
	20 g/L, 1/2 mL vial	= STD 2	0.5 %/yr	<120	<20	>100%
	100 g/L, 1 mL PFS	< STD 3	0.2 %/yr	<1000	<40	>92%
	100 g/L, 1/2 mL PFS	T0 testing only				
	100 g/L, 1/2 mL vial	= STD 1	0.4 %/yr	<100	<30	>99%

*One outlier at 2010 particles/mL. Other 6 measurements <820 particles/mL, including 3 measured later than the outlier.

FIG. 15

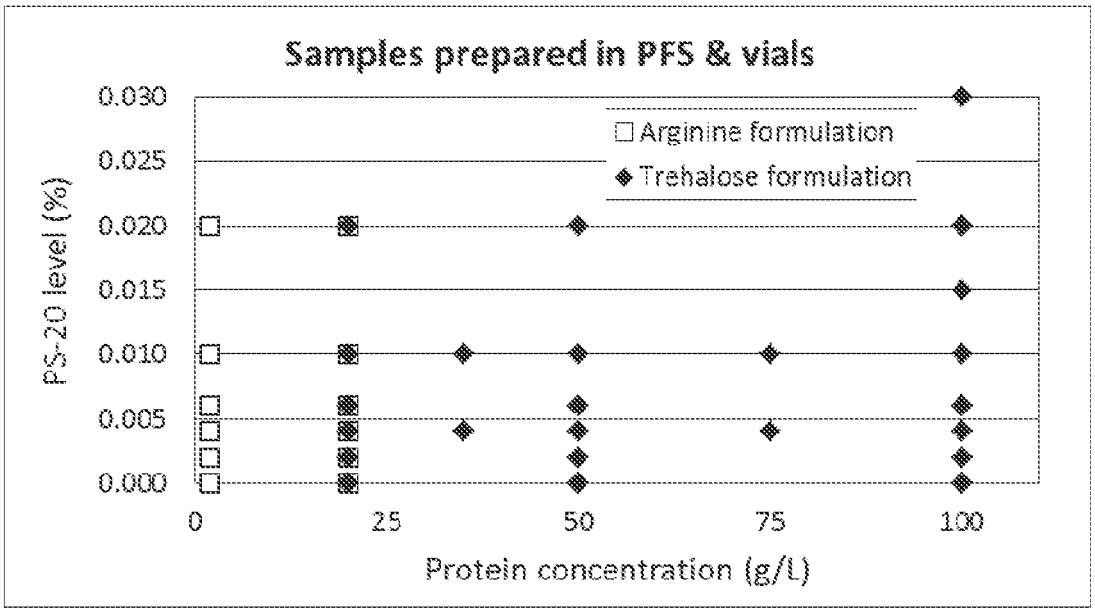

Samples prepared in PFS & vials
PS-20 level (%)
0.030
0.025
0.020
0.015
0.010
0.005
0.000
Arginine formulation
Trehalose formulation
0
25
50
75
100
Protein concentration (g/L)

FIG. 16

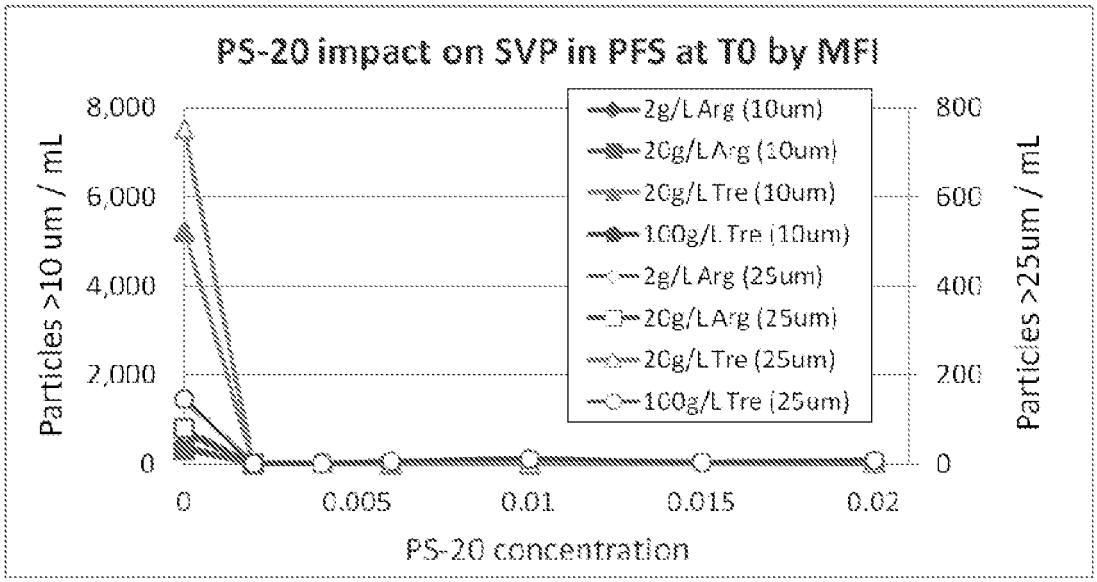
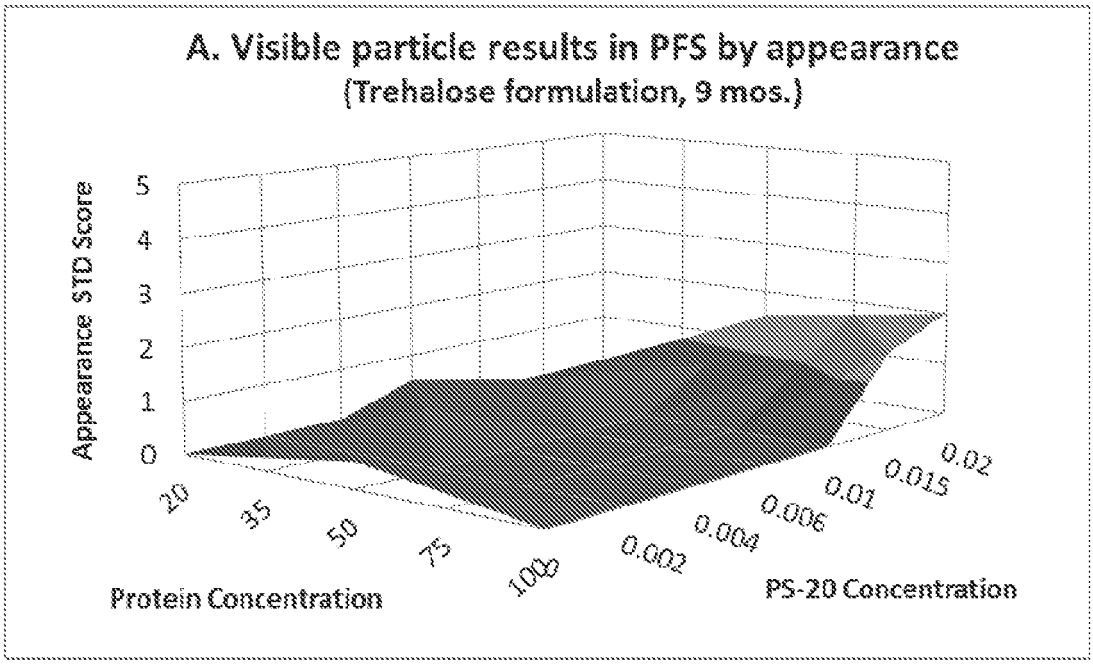
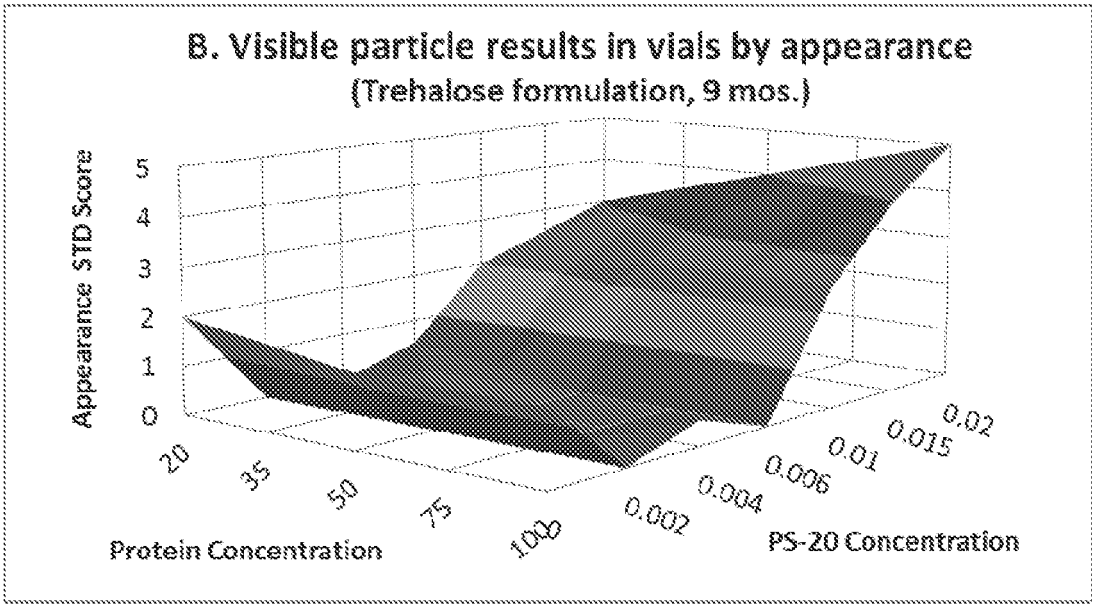

PS-20 impact on SVP in PFS at T0 by MFI
Particles >10 um / mL
Particles >25um / mL
PS-20 concentration
8,000
6,000
4,000
2,000
0
800
600
400
200
0
0
0.005
0.01
0.015
0.02
2g/L Arg (10um)
20g/L Arg (10um)
20g/L Tre (10um)
100g/L Tre (10um)
2g/L Arg (25um)
20g/L Arg (25um)
20g/L Tre (25um)
100g/L Tre (25um)

FIG. 17


A. Visible particle results in PFS by appearance
(Trehalose formulation, 9 mos.)
Appearance STD Score
0
1
2
3
4
5
20
35
50
75
100
Protein Concentration
0.002
0.004
0.006
0.01
0.015
0.02
PS-20 Concentration


B. Visible particle results in vials by appearance
(Trehalose formulation, 9 mos.)
Appearance STD Score
0
1
2
3
4
5
20
35
50
75
100
Protein Concentration
0.002
0.004
0.006
0.01
0.015
0.02
PS-20 Concentration

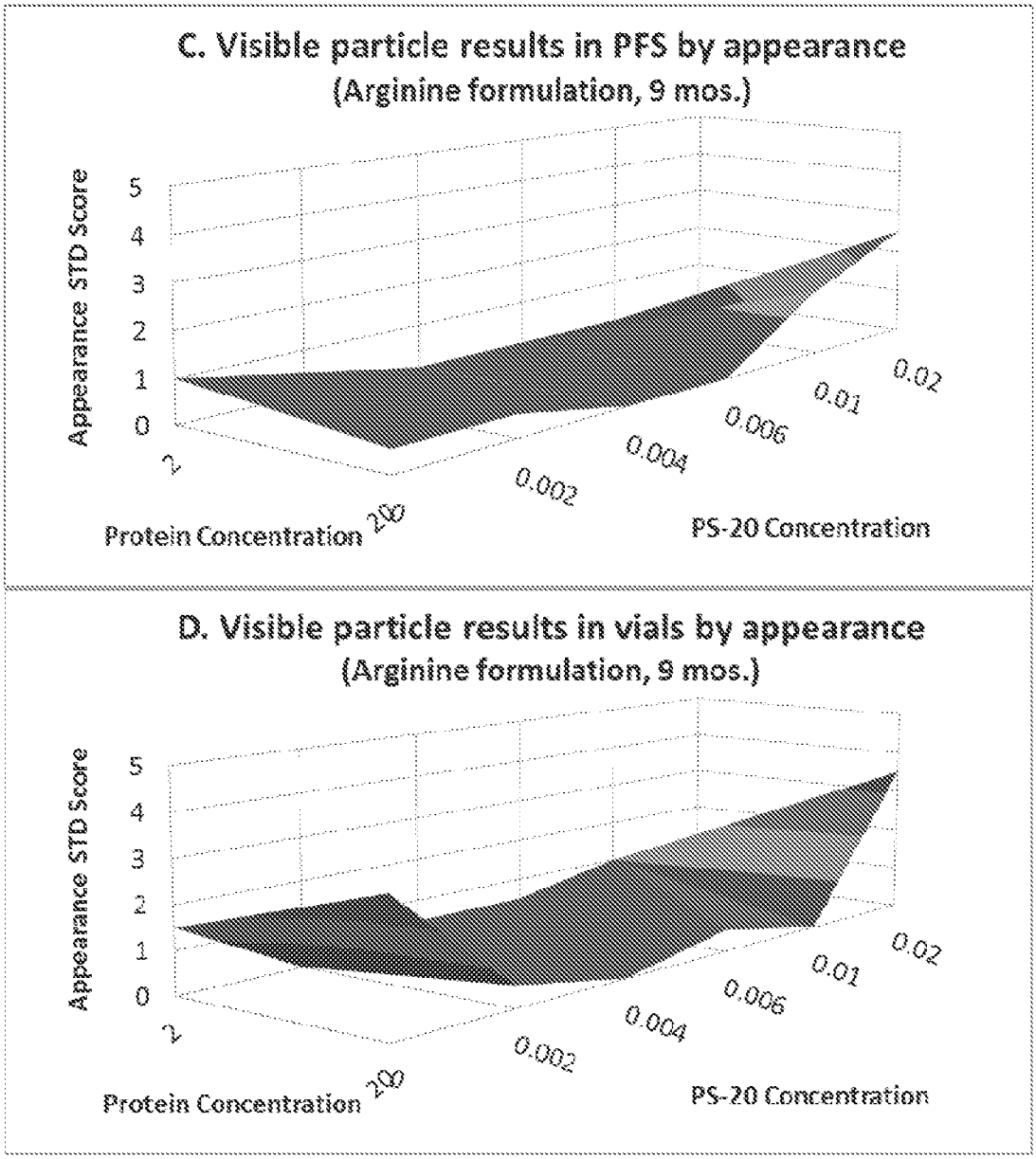

C. Visible particle results in PFS by appearance
(Arginine formulation, 9 mos.)
Appearance STD Score
5
4
3
2
1
0
2
200
Protein Concentration
0.002
0.004
0.006
0.01
0.02
PS-20 Concentration
D. Visible particle results in vials by appearance
(Arginine formulation, 9 mos.)
Appearance STD Score
5
4
3
2
1
0
2
200
Protein Concentration
0.002
0.004
0.006
0.01
0.02
PS-20 Concentration

FIG. 18

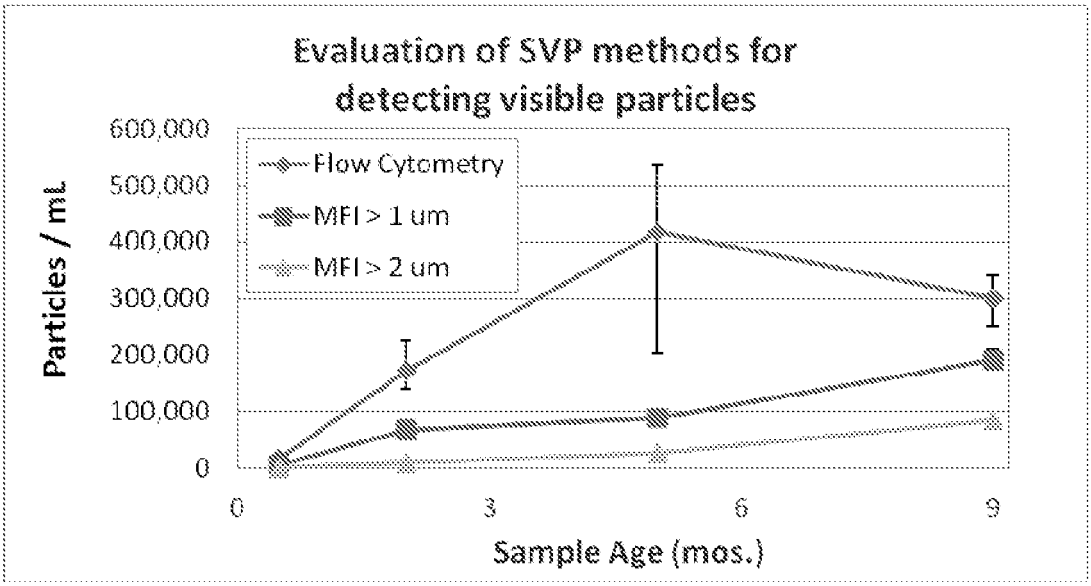

Evaluation of SVP methods for detecting visible particles
Particles / mL
600,000
500,000
400,000
300,000
200,000
100,000
0
Flow Cytometry
MFI > 1 um
MFI > 2 um
0
3
6
9
Sample Age (mos.)

FIG. 19

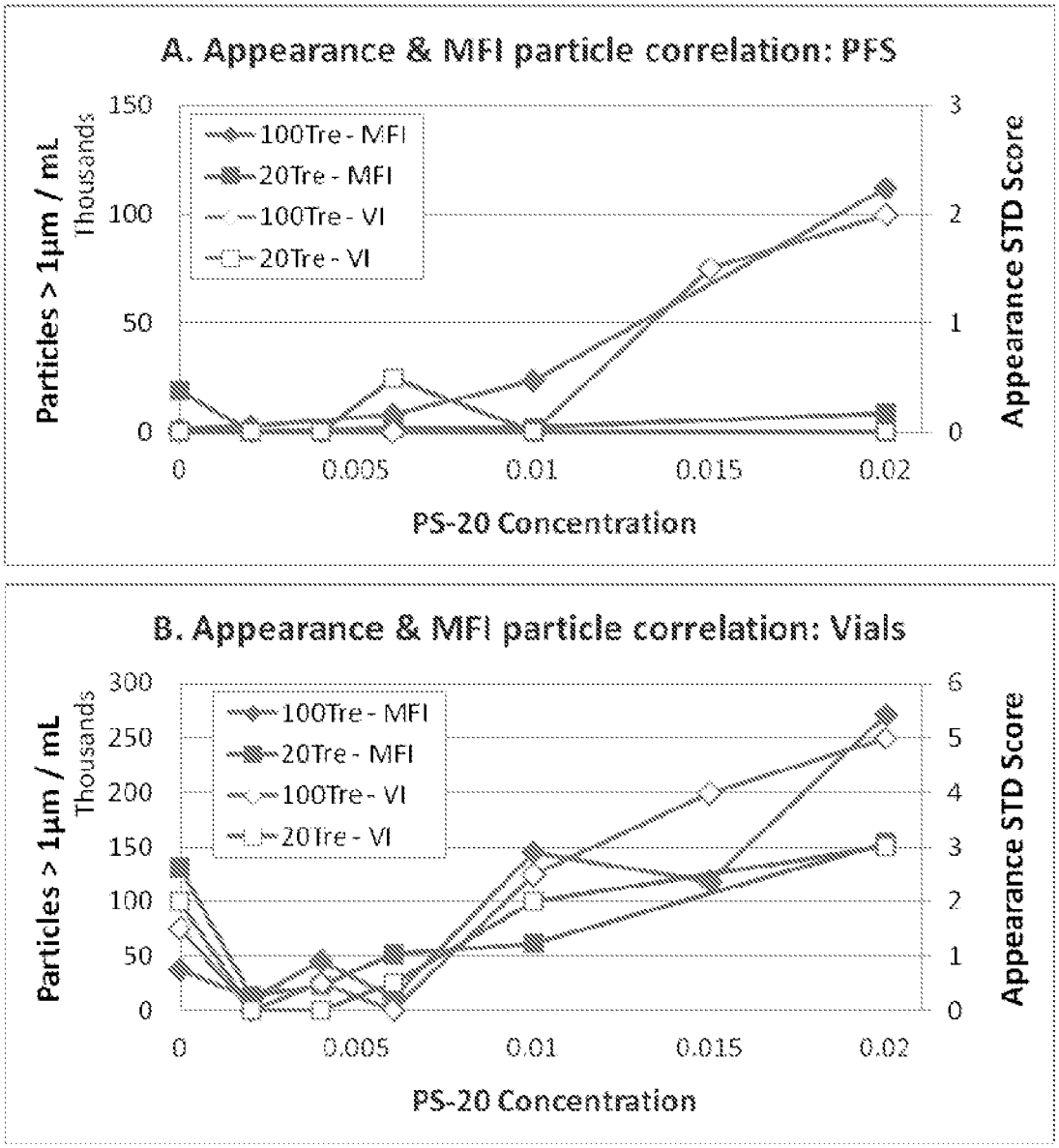

A. Appearance & MFI particle correlation: PFS
Particles > 1µm / mL
Thousands
150
100
50
0
100Tre - MFI
20Tre - MFI
100Tre - VI
20Tre - VI
3
2
1
0
Appearance STD Score
0
0.005
0.01
0.015
0.02
PS-20 Concentration
B. Appearance & MFI particle correlation: Vials
Particles > 1µm / mL
Thousands
300
250
200
150
100
50
0
100Tre - MFI
20Tre - MFI
100Tre - VI
20Tre - VI
6
5
4
3
2
1
0
Appearance STD Score
0
0.005
0.01
0.015
0.02
PS-20 Concentration

FIG. 20

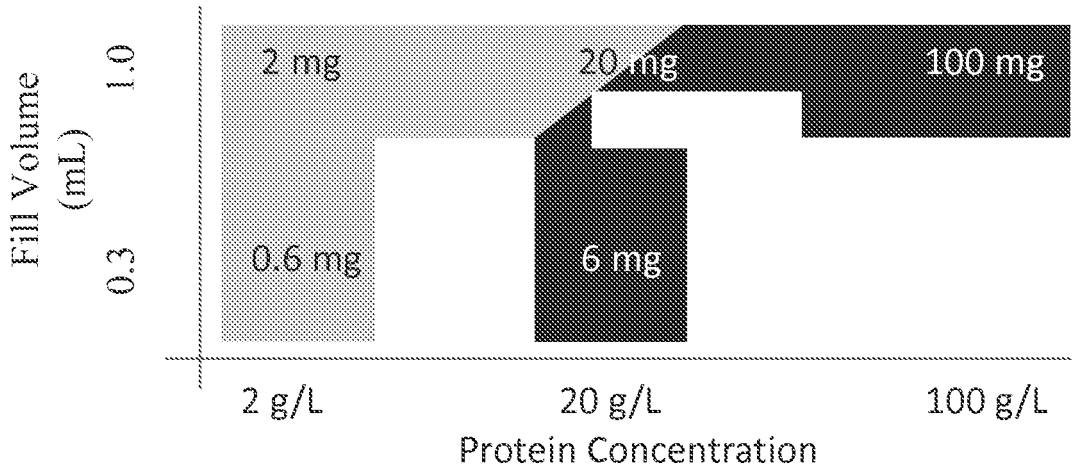

Fill Volume (mL)
1.0
0.3
2 mg
20 mg
100 mg
0.6 mg
6 mg
2 g/L
20 g/L
100 g/L
Protein Concentration

FIG. 21

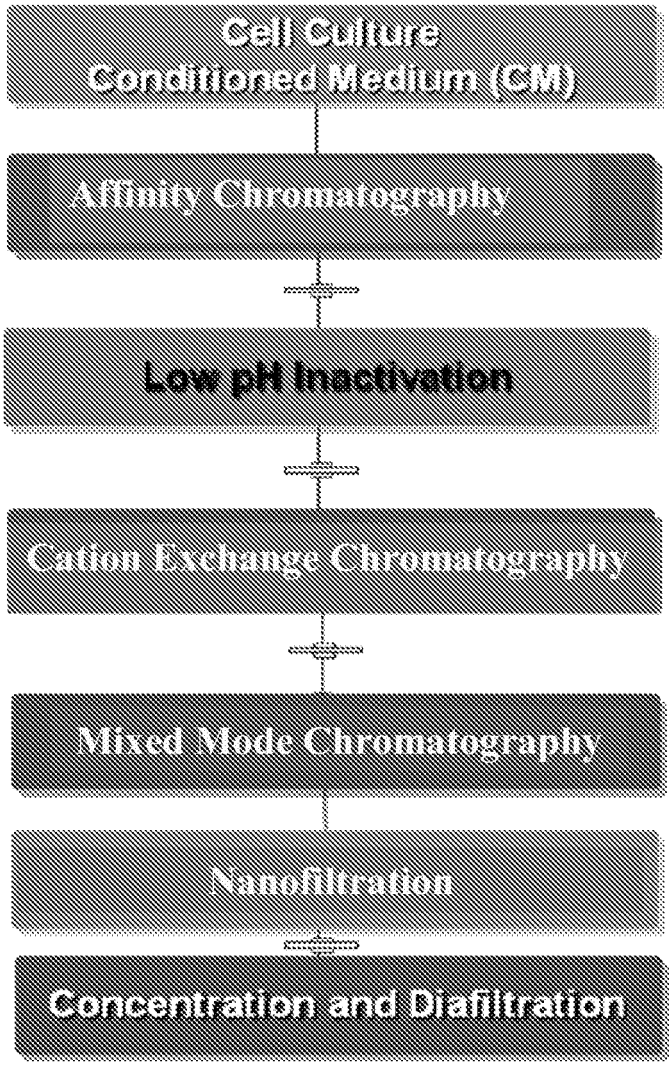

Cell Culture Conditioned Medium (CM)
Affinity Chromatography
Low pH Inactivation
Cation Exchange Chromatography
Mixed Mode Chromatography
Nanofiltration
Concentration and Diafiltration

FIG. 22

