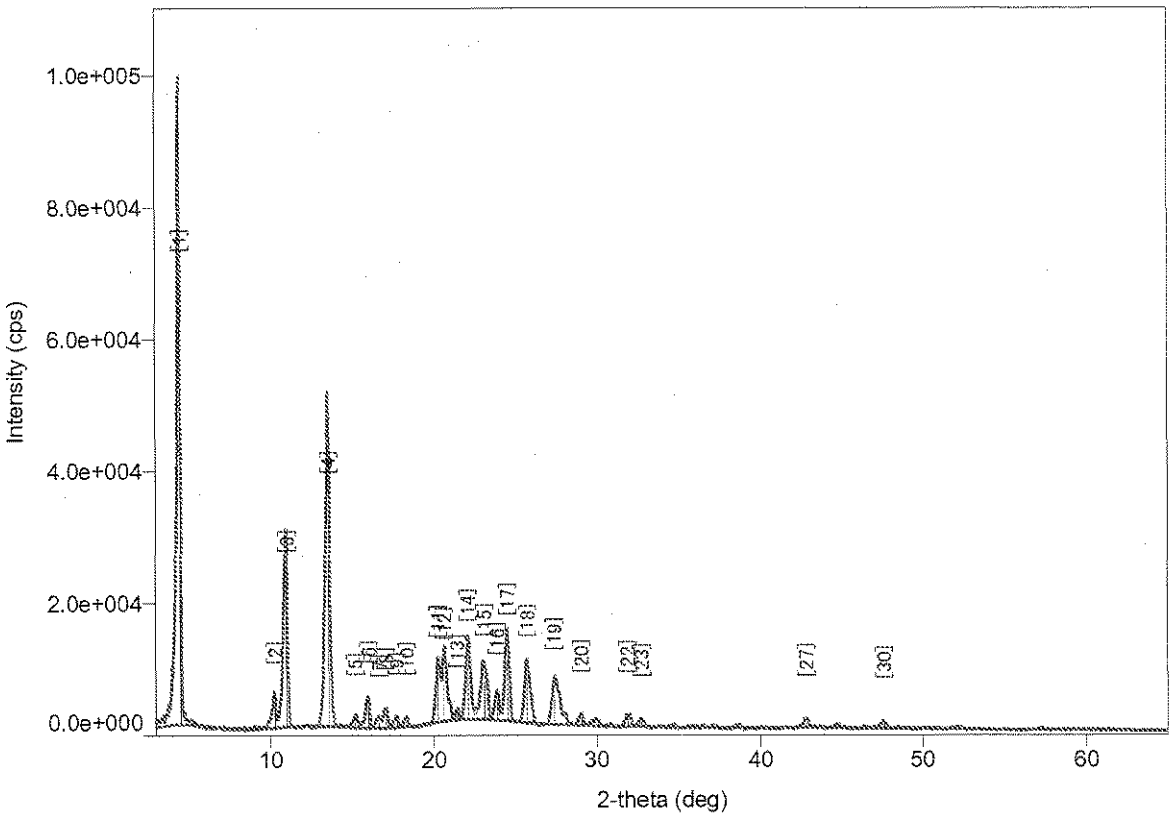

1.0e+005
8.0e+004
6.0e+004
4.0e+004
2.0e+004
0.0e+000
Intensity (cps)
10
20
30
40
50
60
2-theta (deg)
[1]
[2]
[3]
[4]
[5]
[6]
[7]
[8]
[9]
[10]
[11]
[12]
[13]
[14]
[15]
[16]
[17]
[18]
[19]
[20]
[22]
[23]
[27]
[30]

FIGURE 1A

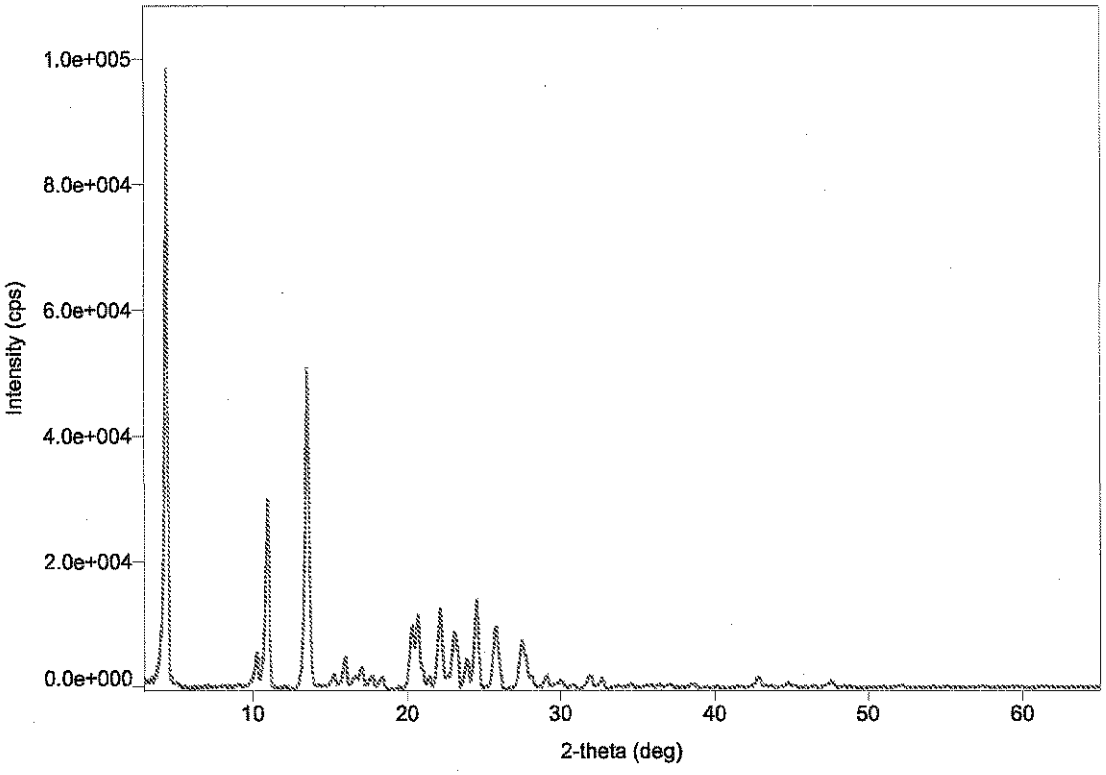
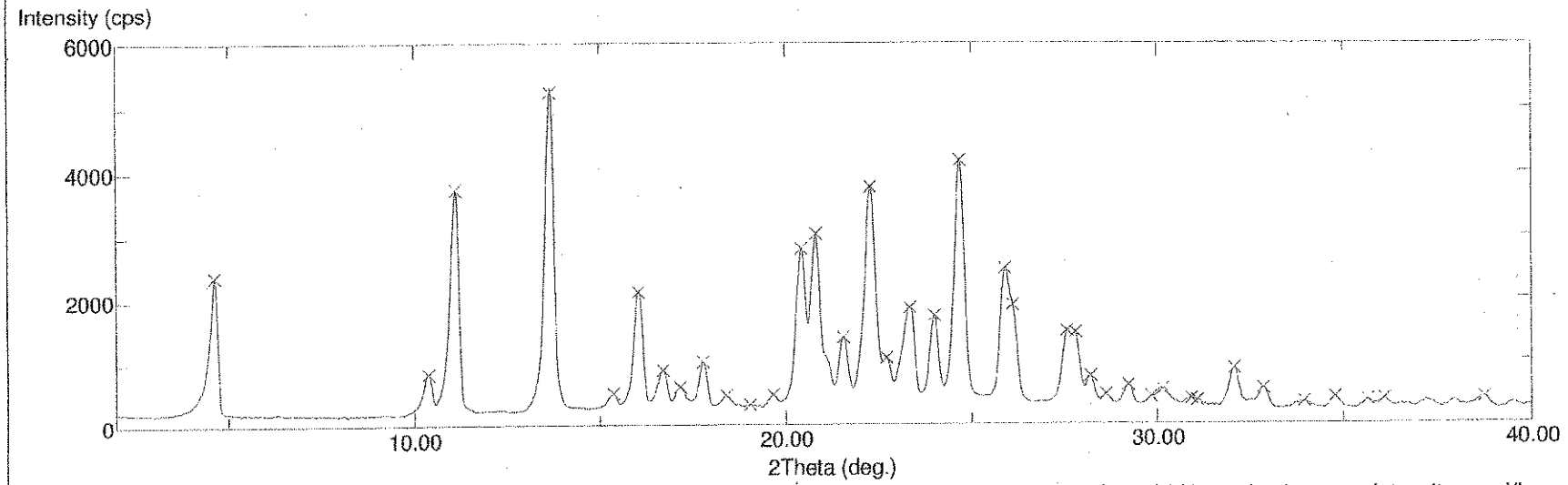

1.0e+005
8.0e+004
6.0e+004
4.0e+004
2.0e+004
0.0e+000
Intensity (cps)
10
20
30
40
50
60
2-theta (deg)

FIGURE 1B

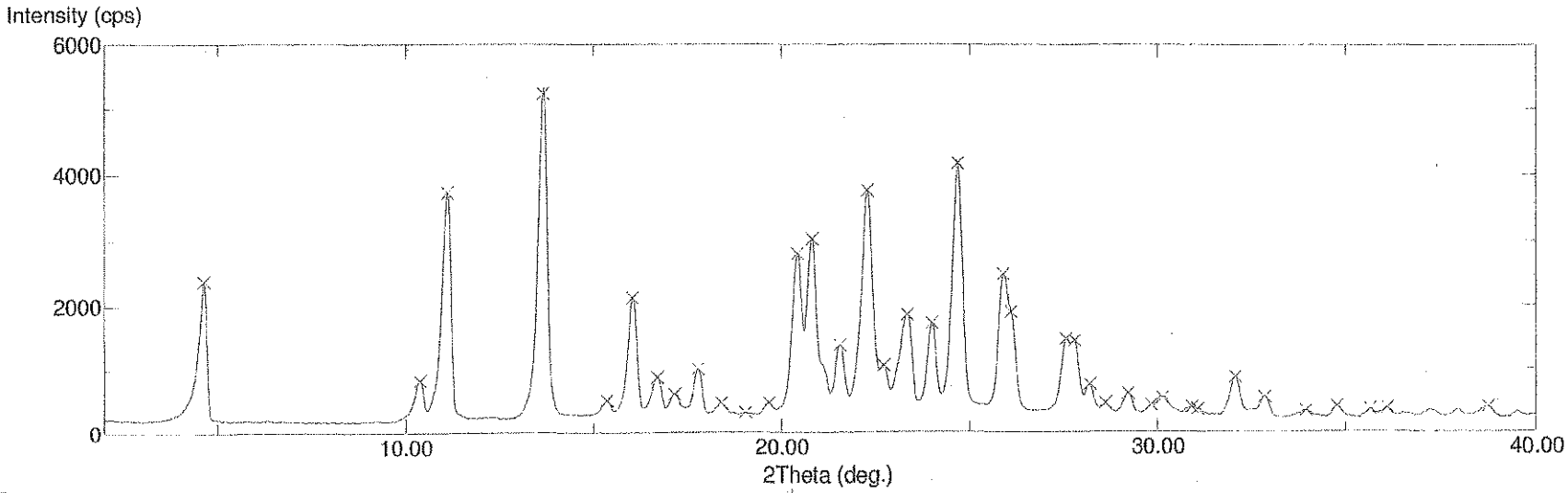
Peak Search



Peak no.	2Theta	Flex Width	d-value	Intensity	I/Io	Peak no.	2Theta	Flex Width	d-value	Intensity	I/Io
1	4.640	0.235	19.0284	2387	46	16	22.280	0.306	3.9868	3762	72
2	10.380	0.259	8.5153	830	16	17	22.720	0.165	3.9106	1057	21
3	11.120	0.282	7.9502	3734	72	18	23.340	0.353	3.8081	1864	36
4	13.660	0.306	6.4771	5236	100	19	24.000	0.282	3.7048	1734	34
5	15.360	0.282	5.7638	511	10	20	24.680	0.306	3.6043	4173	80
6	16.040	0.282	5.5210	2126	41	21	25.900	0.282	3.4372	2490	48
7	16.700	0.282	5.3042	880	17	22	26.100	0.212	3.4113	1904	37
8	17.160	0.282	5.1631	608	12	23	27.560	0.259	3.2338	1479	29
9	17.780	0.259	4.9844	1006	20	24	27.800	0.212	3.2065	1455	28
10	18.400	0.306	4.8178	468	9	25	28.200	0.212	3.1619	759	15
11	19.040	0.212	4.6573	321	7	26	28.620	0.212	3.1164	463	9
12	19.660	0.259	4.5118	473	10	27	29.220	0.282	3.0538	613	12
13	20.420	0.259	4.3456	2809	54	28	29.840	0.212	2.9917	431	9
14	20.820	0.235	4.2630	3031	58	29	30.140	0.329	2.9626	546	11
15	21.560	0.282	4.1183	1388	27	30	30.920	0.329	2.8896	398	8

FIG. 2A

Peak Search



Peak no.	2Theta	Flex Width	d-value	Intensity	I/Io	Peak no.	2Theta	Flex Width	d-value	Intensity	I/Io
31	31.080	0.165	2.8751	368	8						
32	32.080	0.306	2.7878	876	17						
33	32.860	0.282	2.7233	562	11						
34	33.960	0.259	2.6376	344	7						
35	34.780	0.306	2.5773	415	8						
36	35.660	0.212	2.5157	370	8						
37	36.100	0.259	2.4860	387	8						
38	38.760	0.400	2.3213	403	8						

FIG. 2B

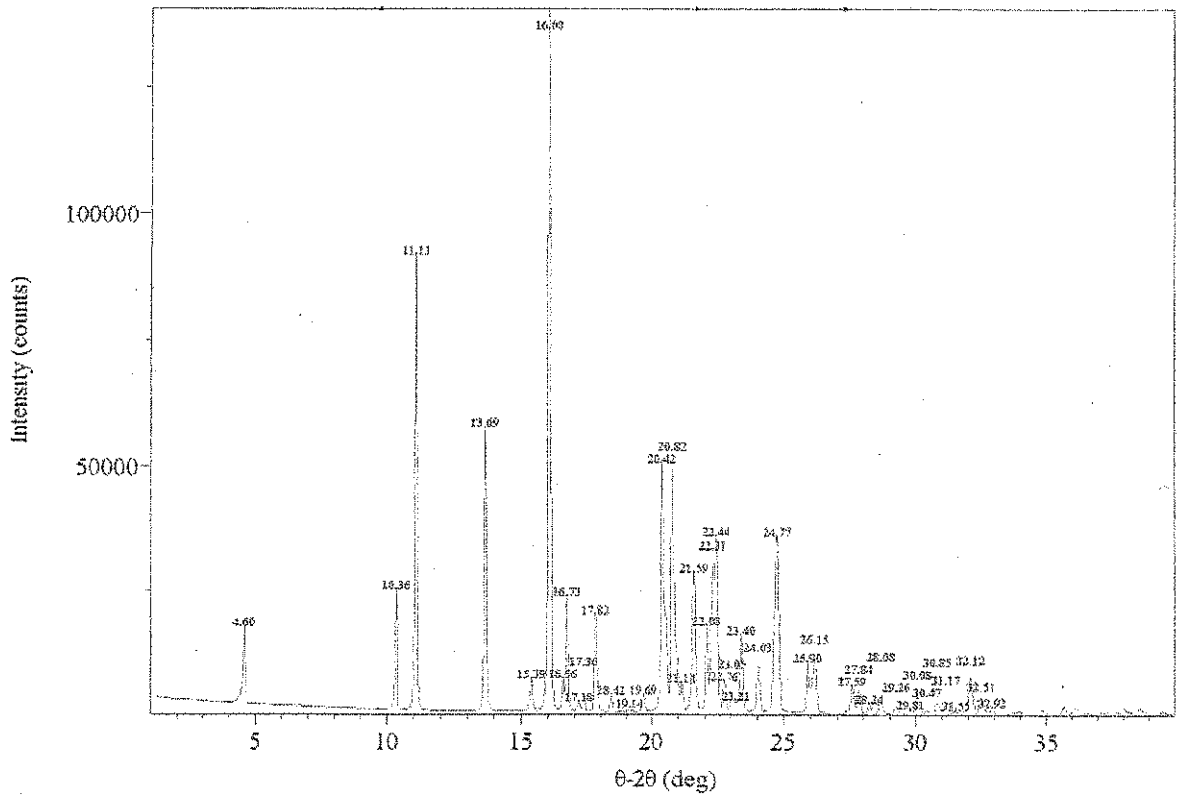


FIG. 3

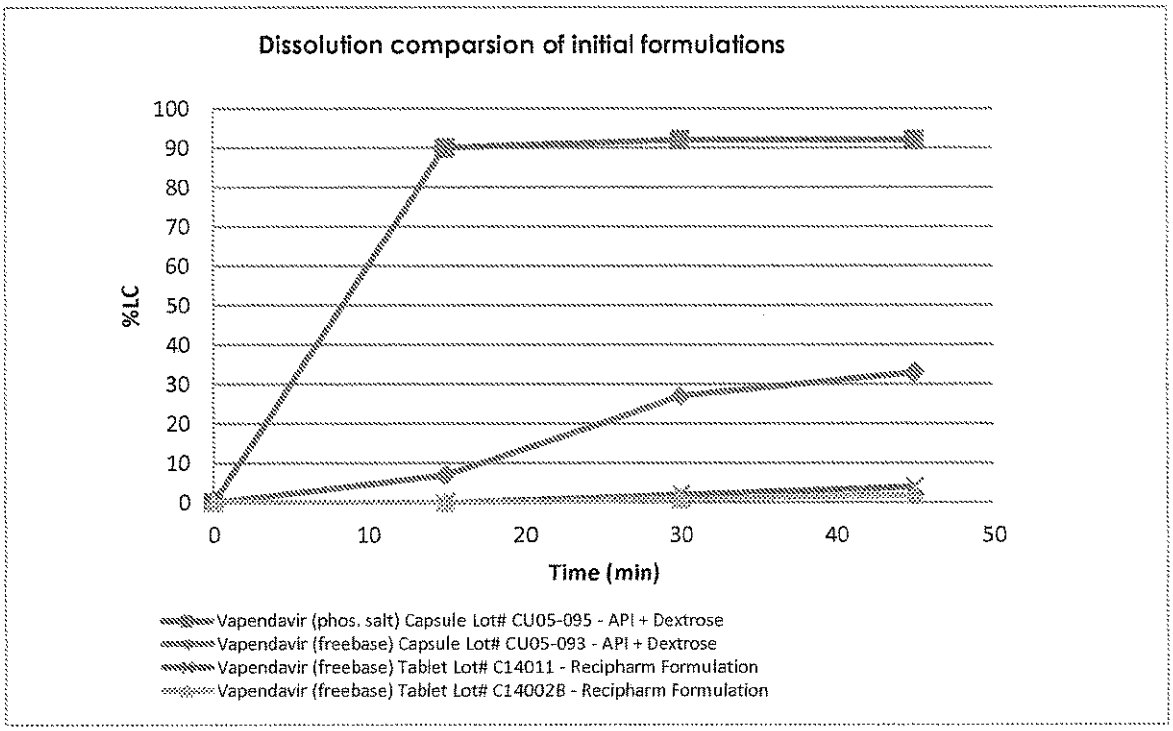

Dissolution comparsion of initial formulations
100
90
80
70
60
50
40
30
20
10
0
%LC
0
10
20
30
40
50
Time (min)
Vapendavir (phos. salt) Capsule Lot# CU05-095 - API + Dextrose
Vapendavir (freebase) Capsule Lot# CU05-093 - API + Dextrose
Vapendavir (freebase) Tablet Lot# C14011 - Recipharm Formulation
Vapendavir (freebase) Tablet Lot# C14002B - Recipharm Formulation

FIGURE 4

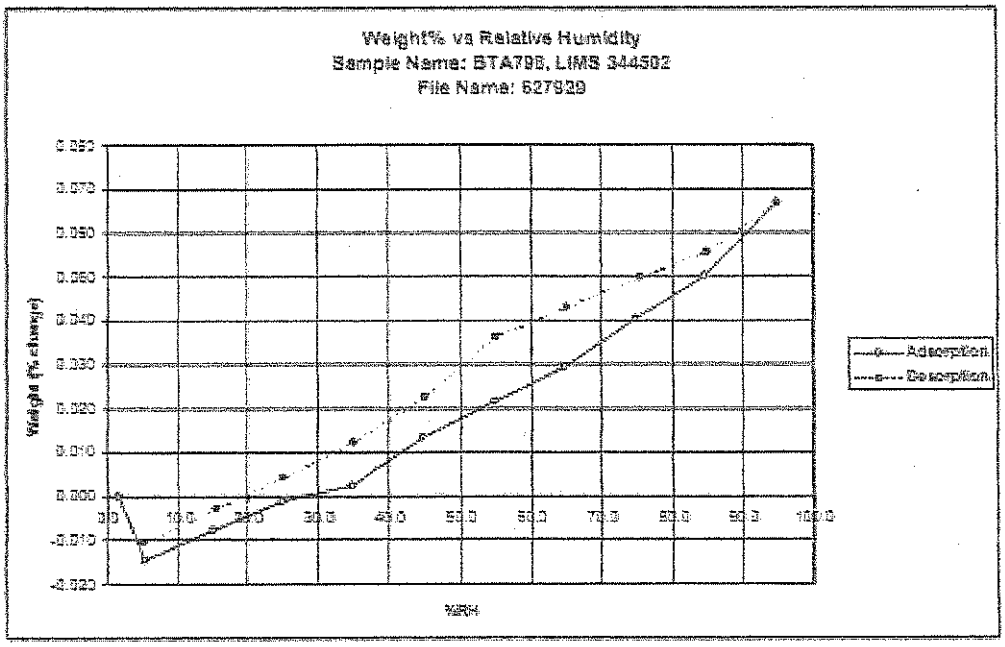

Weight% vs Relative Humidity
Sample Name: BTA798, LIMS 344502
File Name: 627929
Adsorption
Desorption

FIG. 5

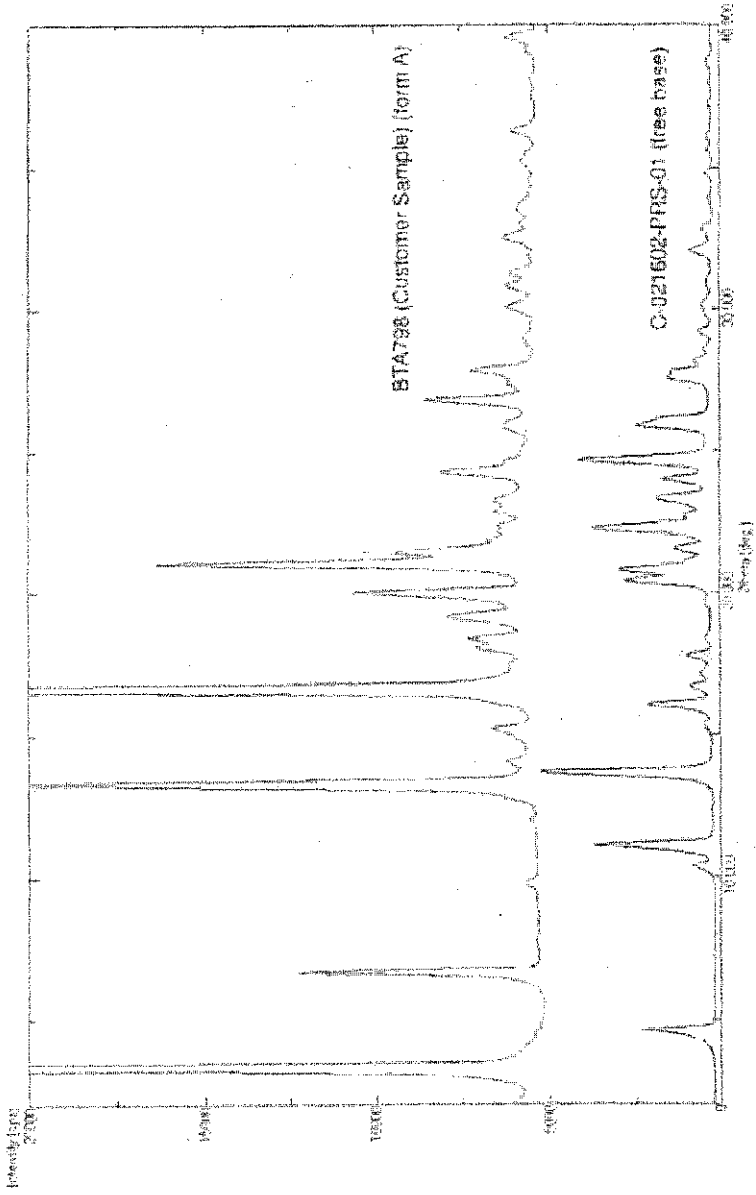
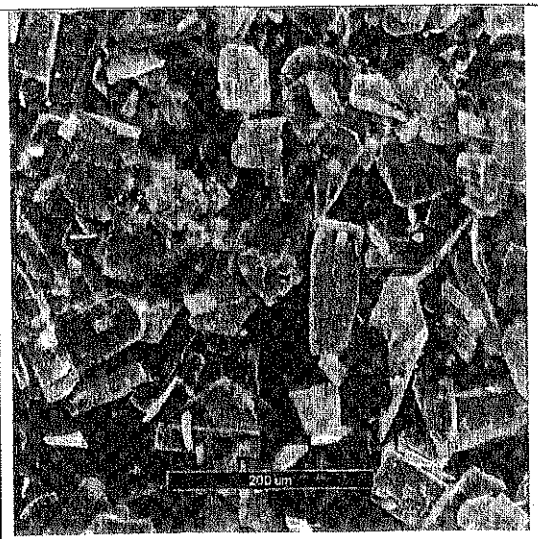
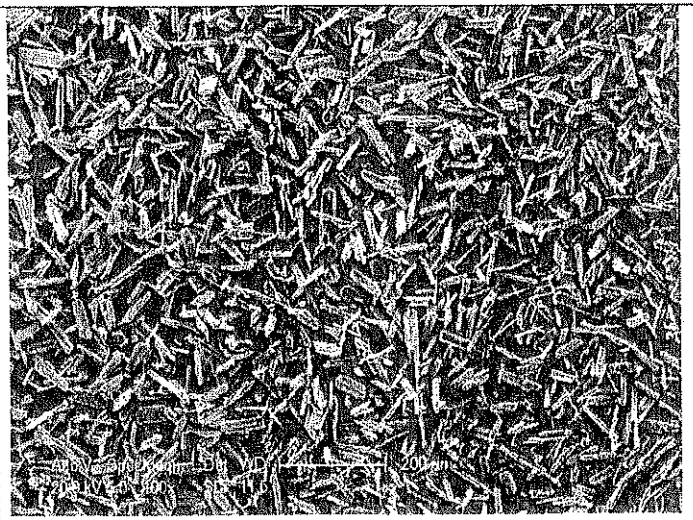


FIG. 6

FIG. 7A

Image of Crystals (obtained using Scanning Electron Microscopy SEM)		

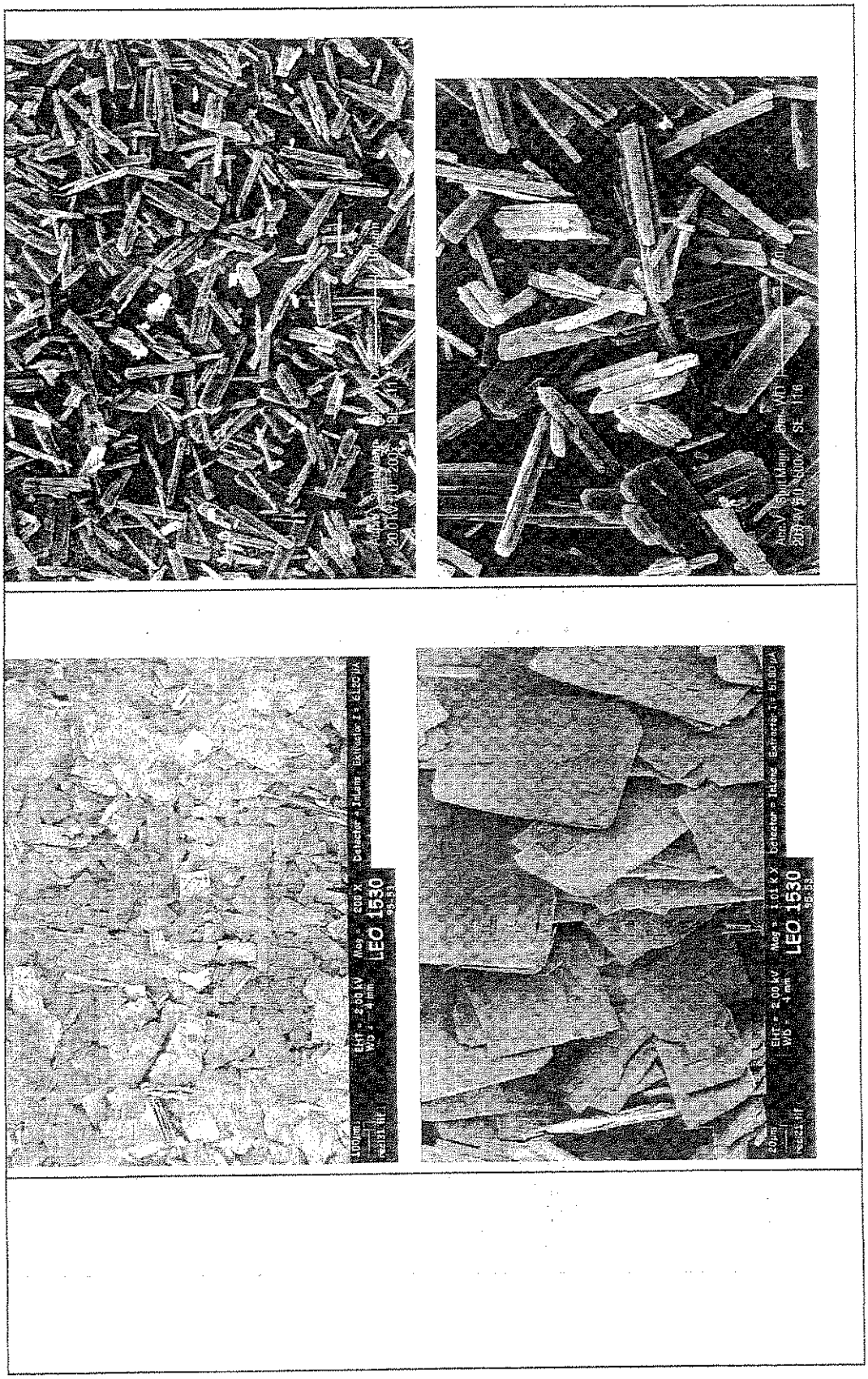


FIG. 7B

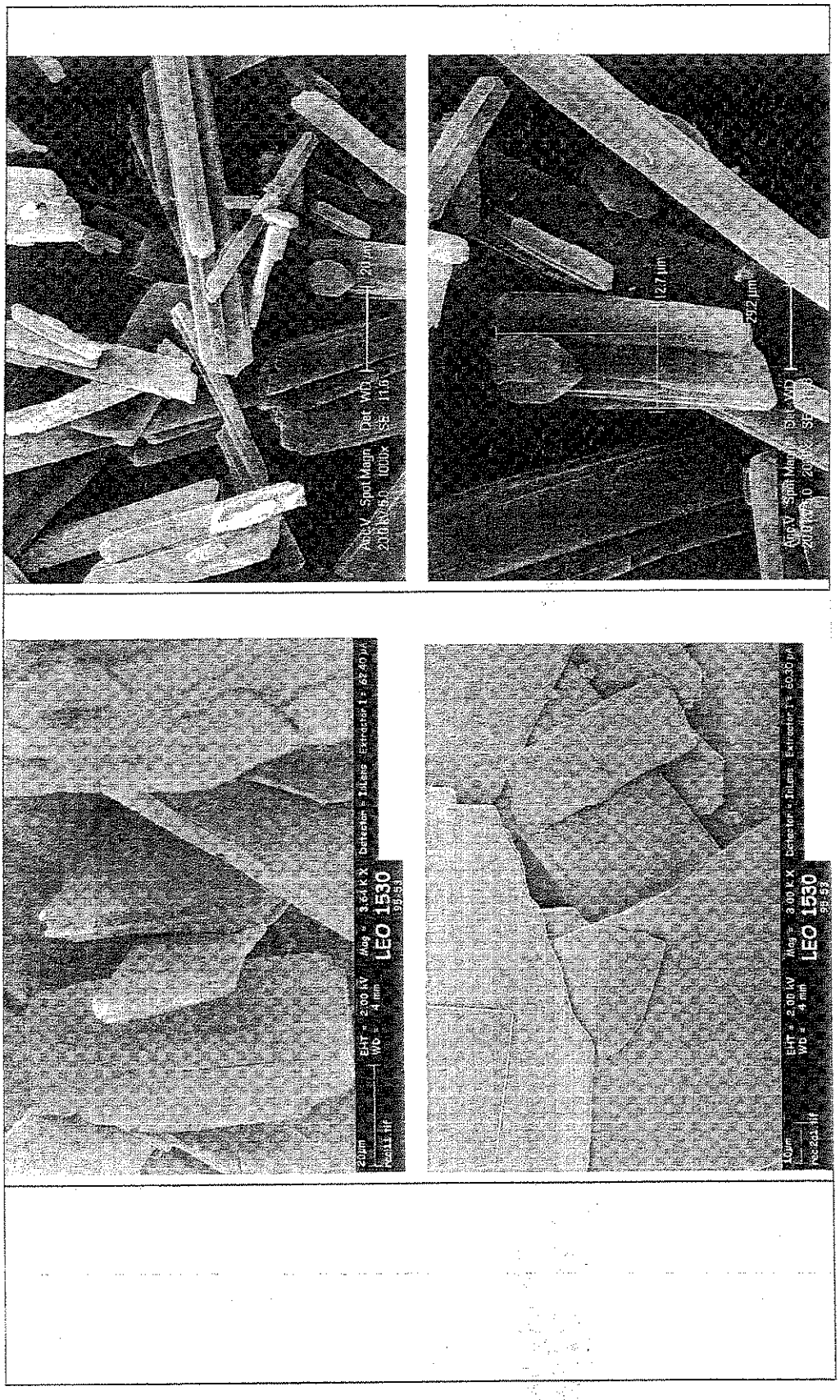


FIG. 7C

Exemplar Tablet Manufacturing Process

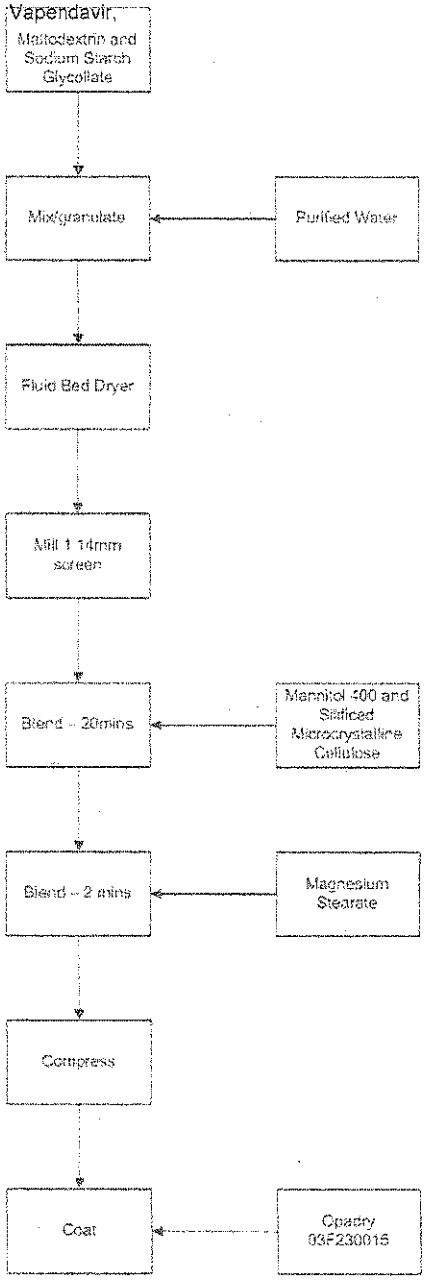


FIG. 8

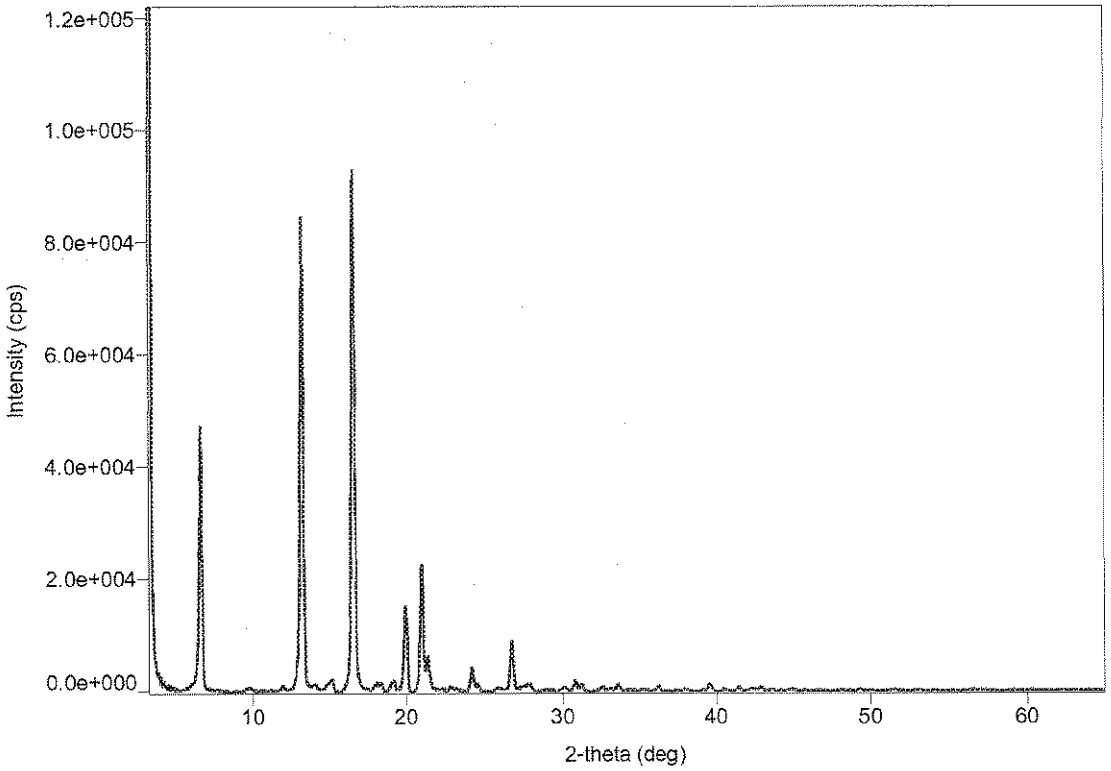

1.2e+005
1.0e+005
8.0e+004
6.0e+004
4.0e+004
2.0e+004
0.0e+000
Intensity (cps)
10
20
30
40
50
60
2-theta (deg)

FIGURE 9

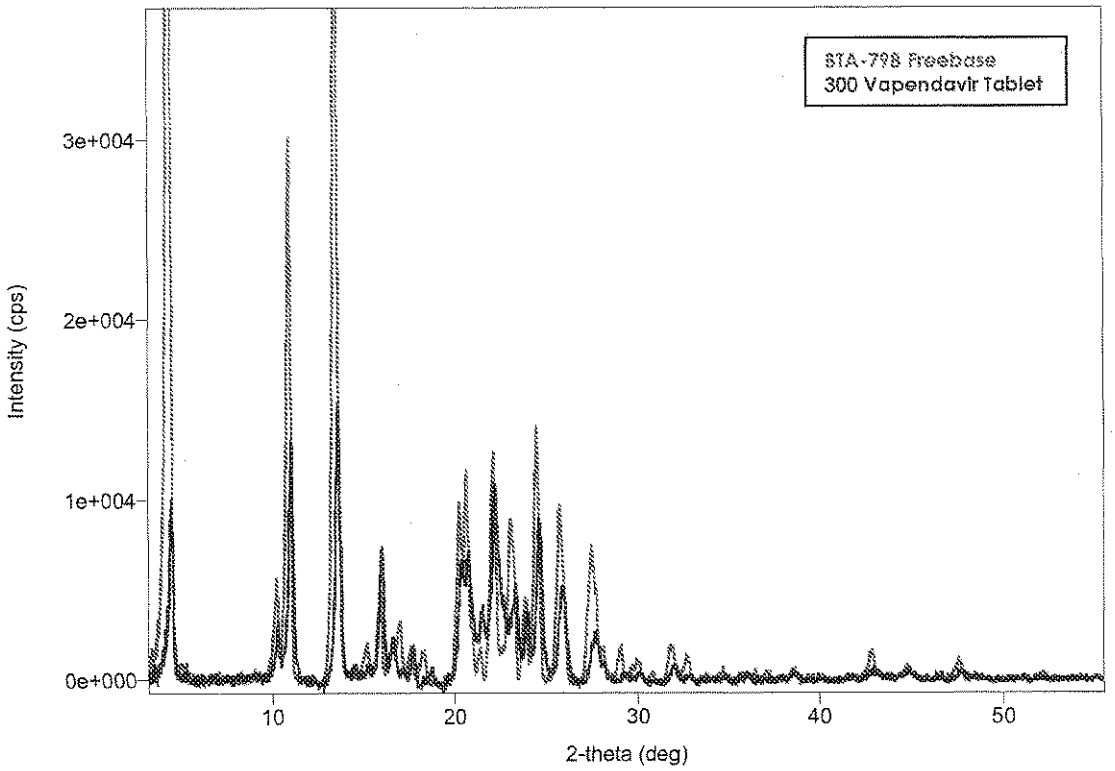

STA-798 Freebase
300 Vapendavir Tablet
Intensity (cps)
3e+004
2e+004
1e+004
0e+000
10
20
30
40
50
2-theta (deg)

FIGURE 10

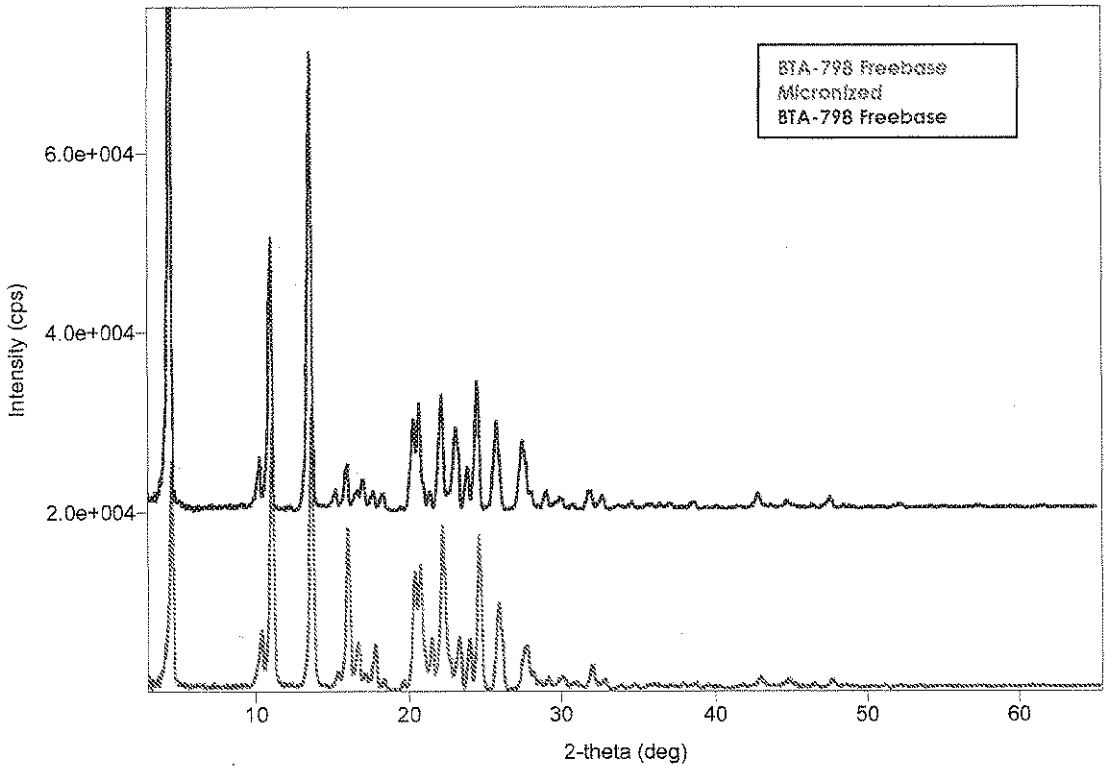

BTA-798 Freebase
Micronized
BTA-798 Freebase
6.0e+004
4.0e+004
2.0e+004
Intensity (cps)
10
20
30
40
50
60
2-theta (deg)

FIGURE 11

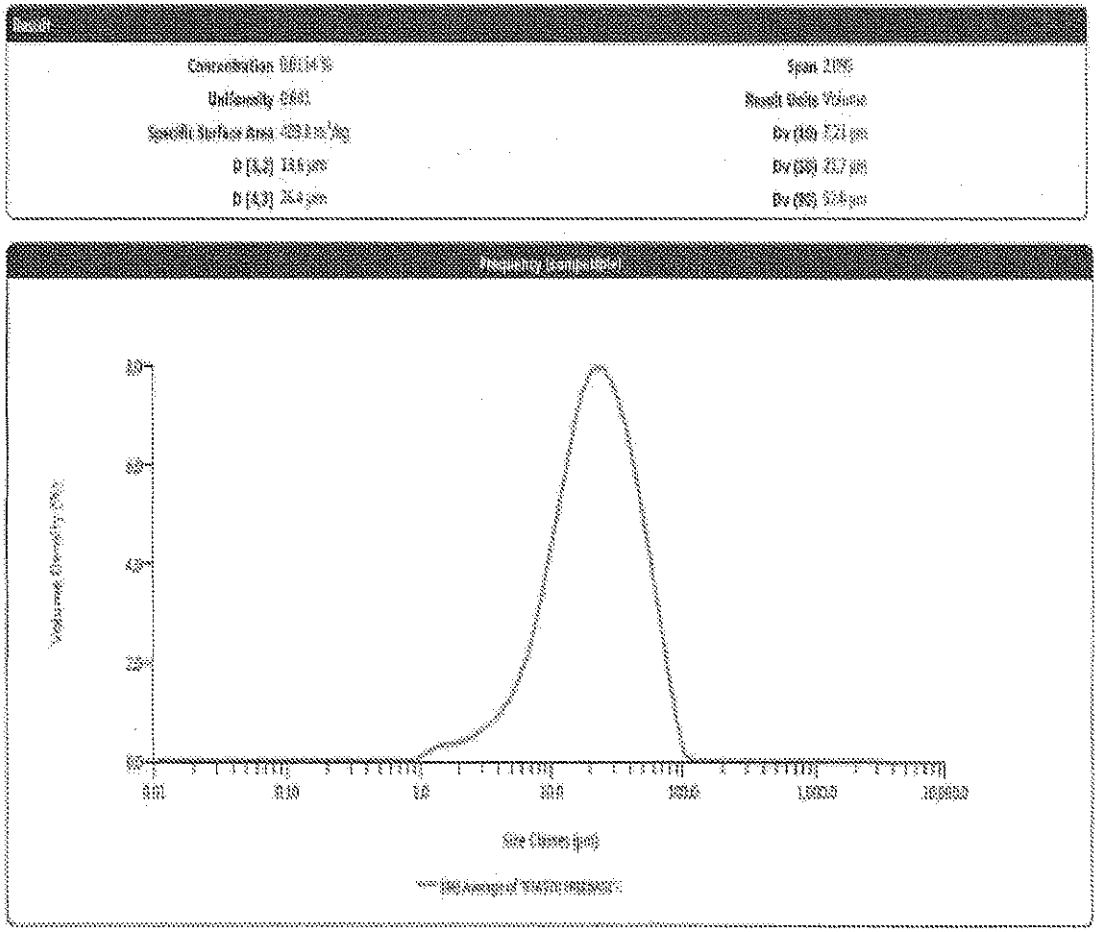


FIGURE 12

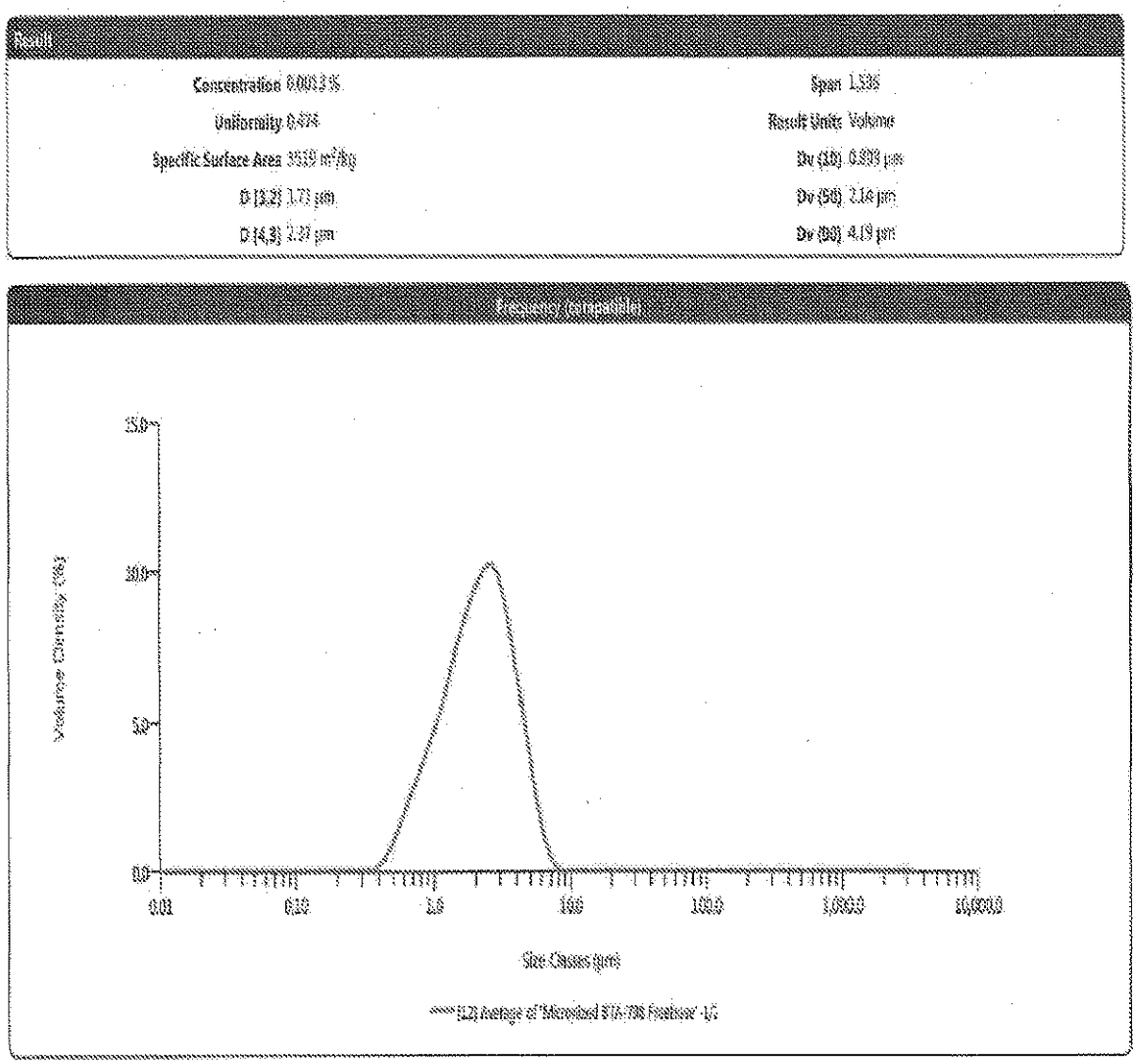

Result
Concentration 0.0013 %
Uniformity 0.474
Specific Surface Area 3519 m²/kg
D [3,2] 1.71 µm
D [4,3] 2.27 µm
Span 1.536
Result Units Volume
Dv (10) 0.803 µm
Dv (50) 2.14 µm
Dv (90) 4.19 µm
Frequency (Cumulative)
Volume Density (%)
Size Classes (µm)

FIGURE 13

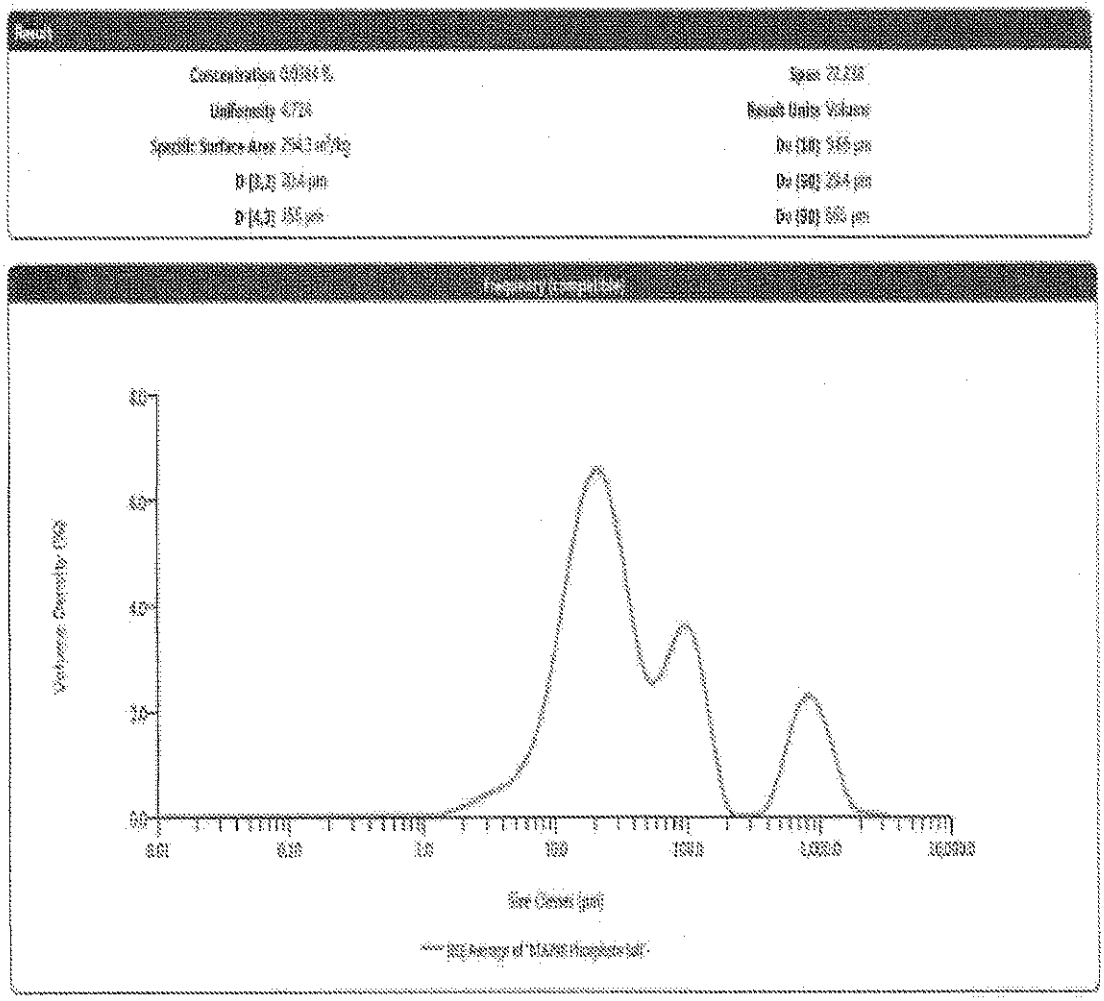


FIGURE 14

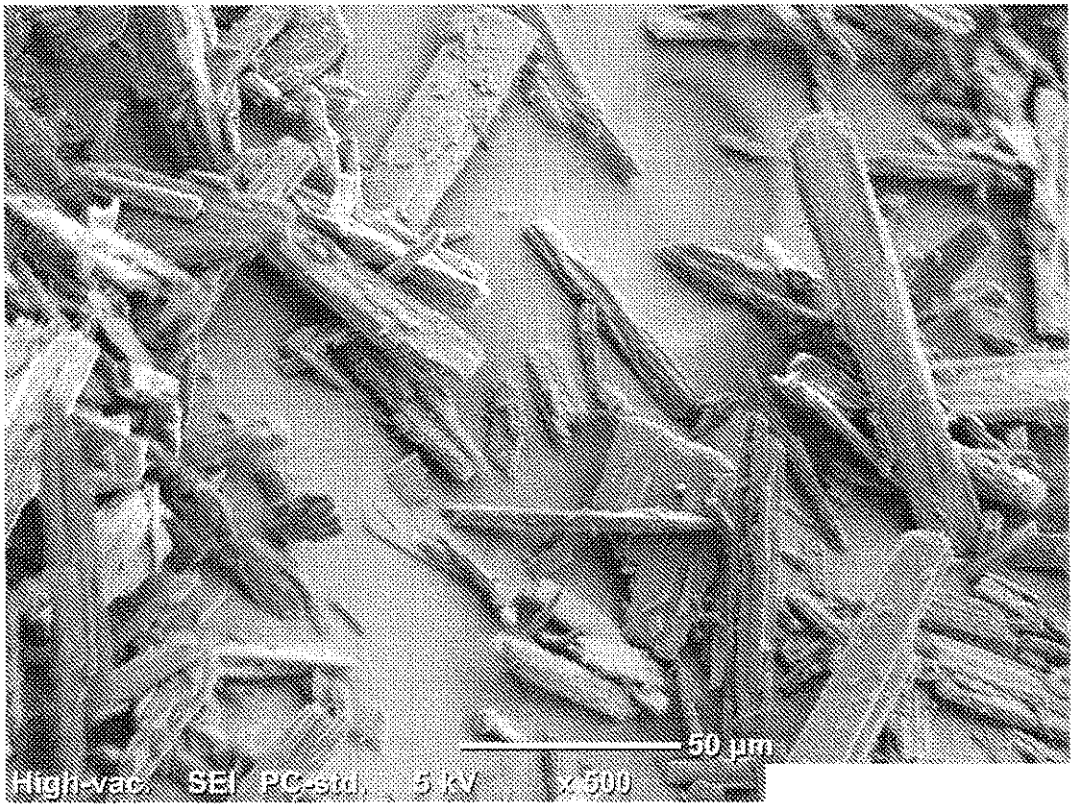


FIGURE 15

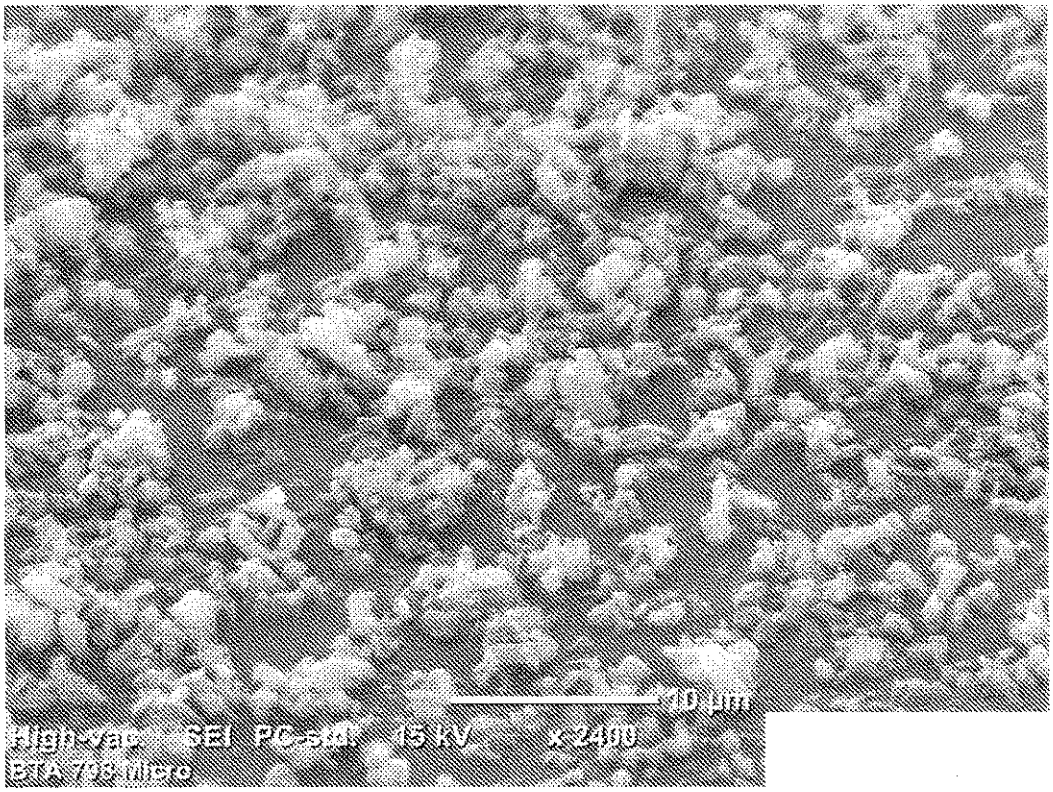


FIGURE 16

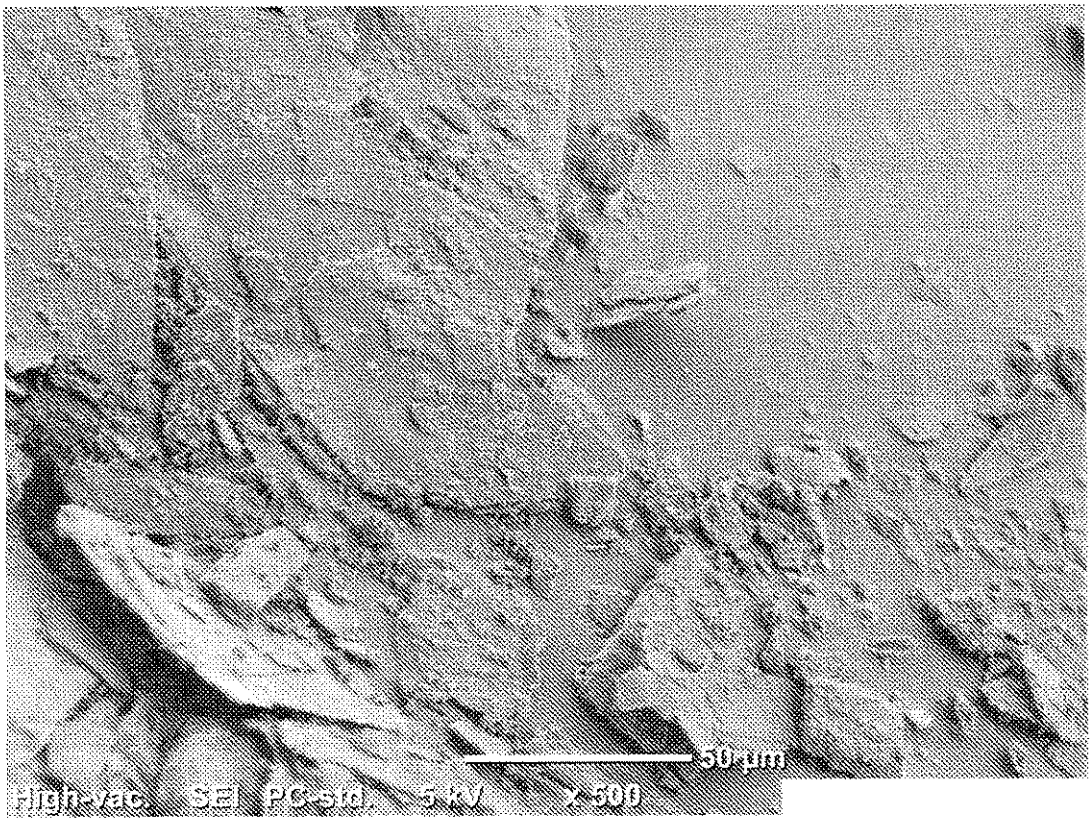


FIGURE 17

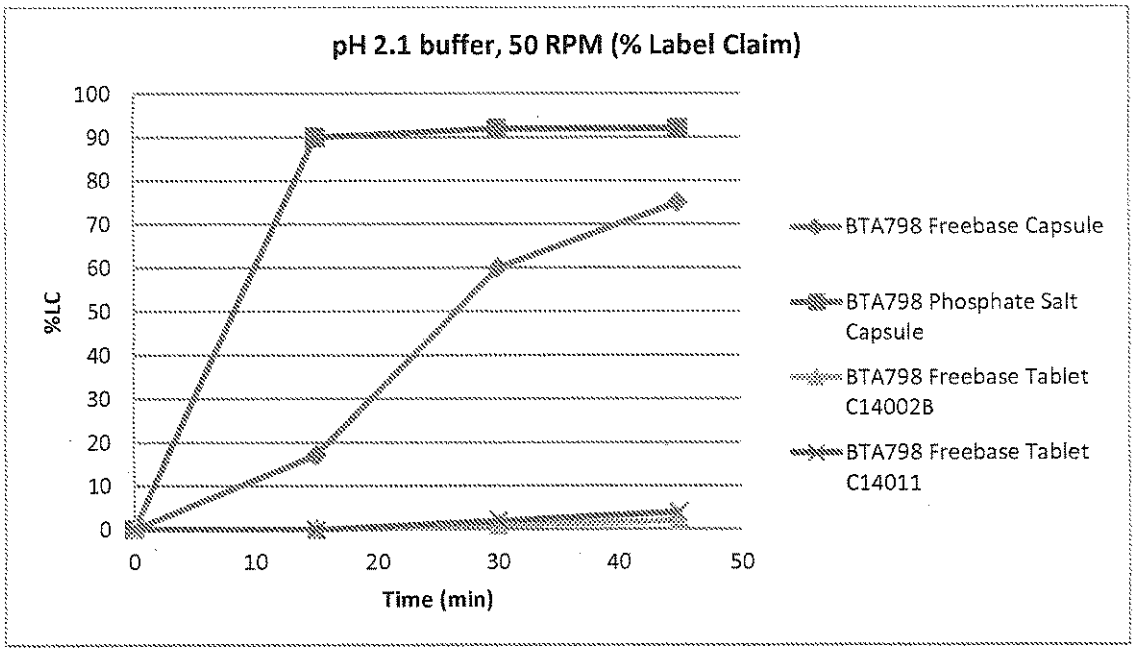


FIGURE 18A

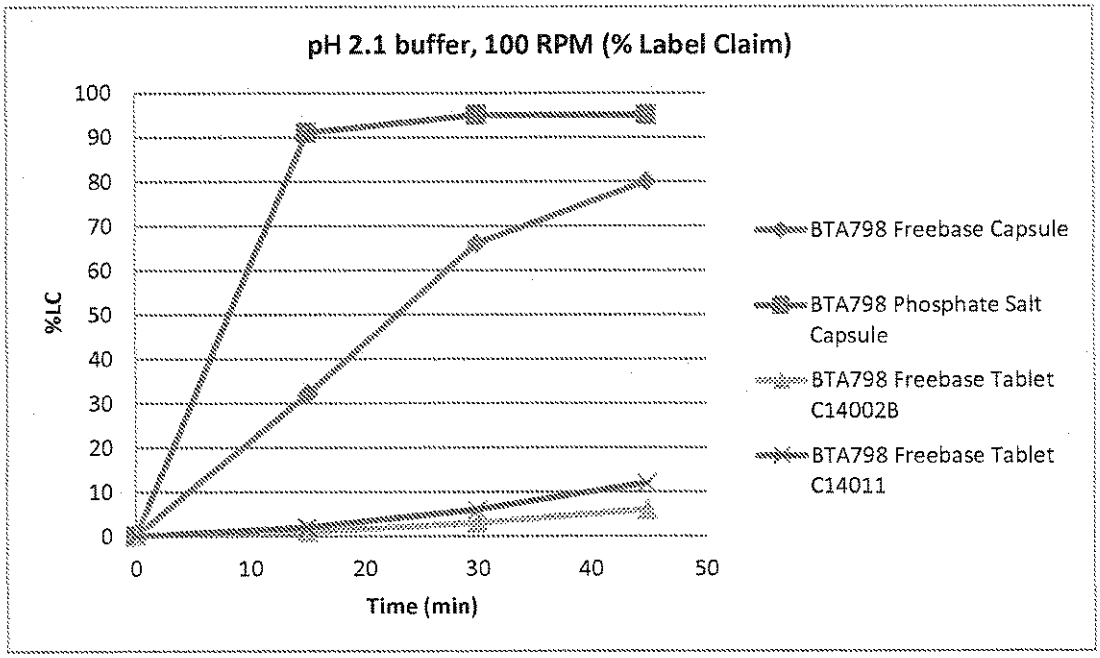


FIGURE 18B

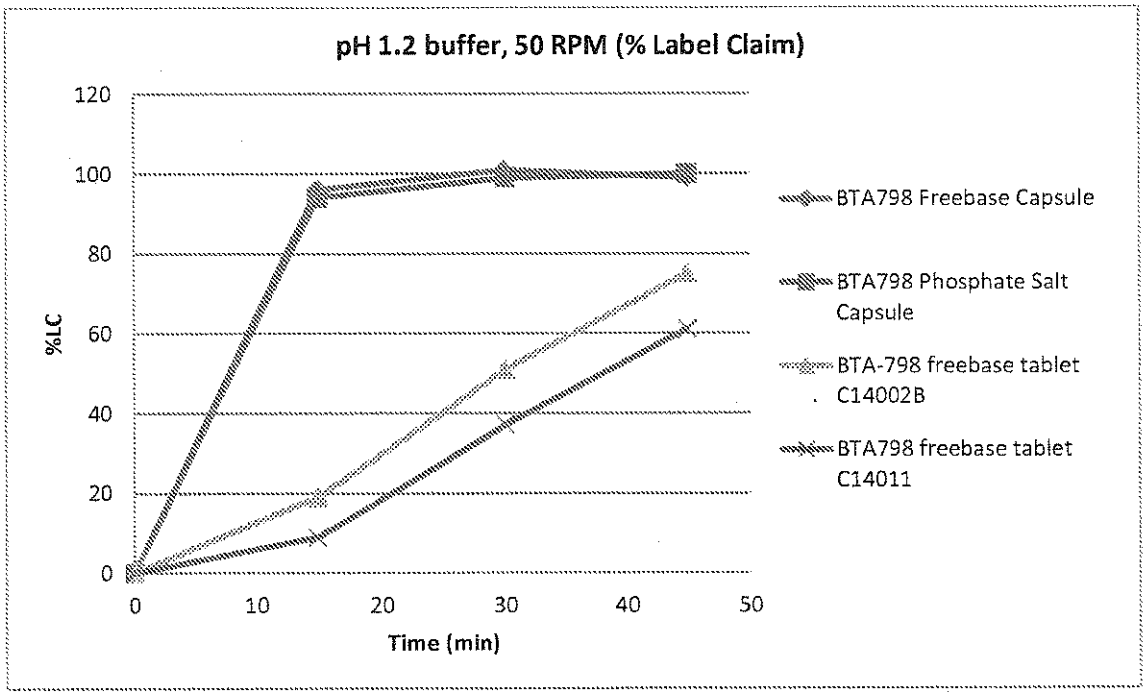


FIGURE 18C

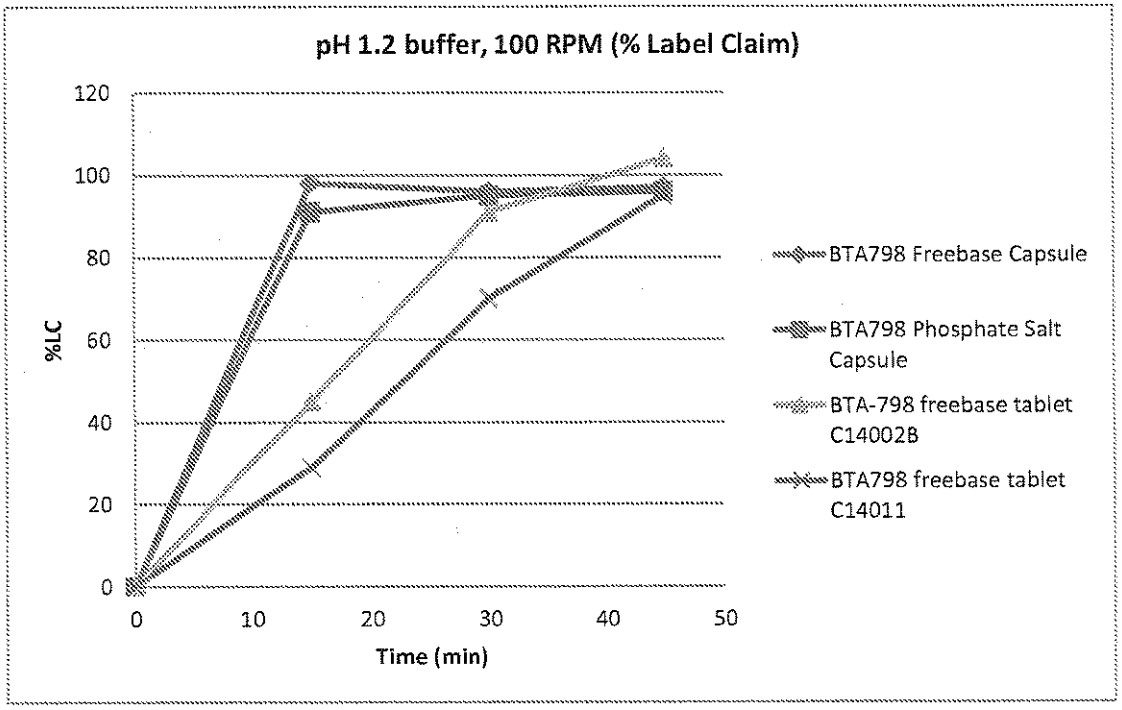
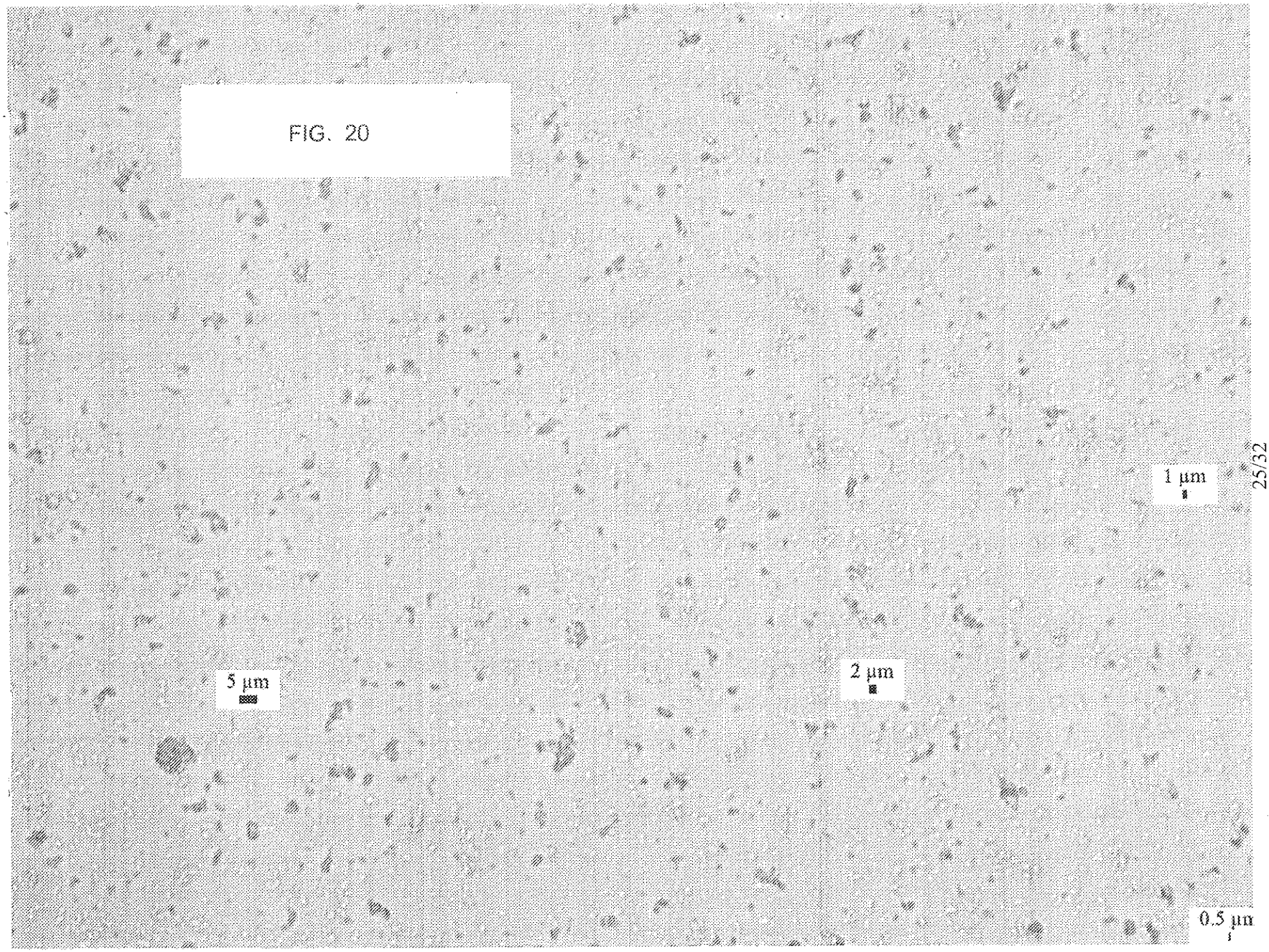


FIGURE 18D

FIG. 19

FIG. 20



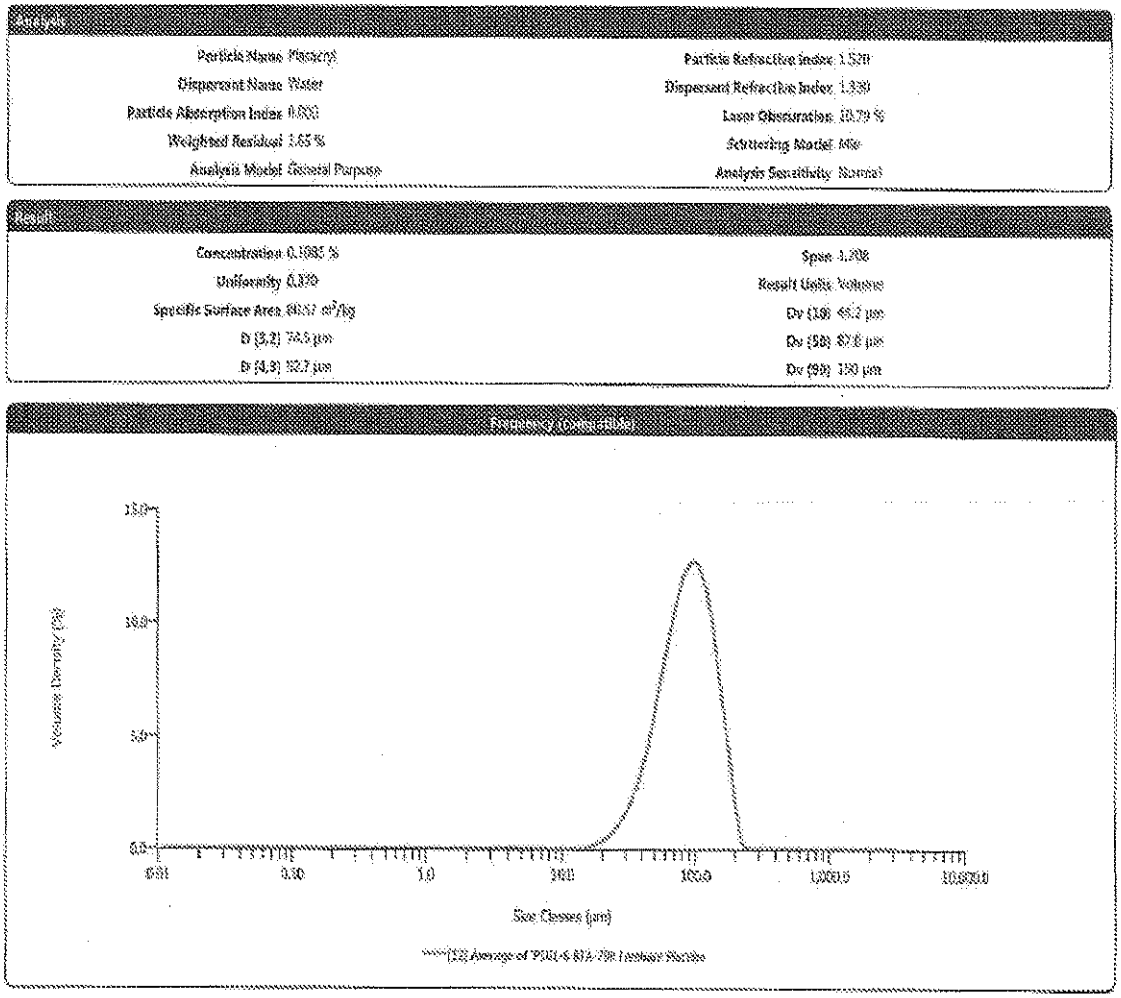

Analysis
Particle Name Plastics
Dispersant Name Water
Particle Absorption Index 0.000
Weighted Residual 1.65 %
Analysis Model General Purpose
Particle Refractive Index 1.520
Dispersant Refractive Index 1.333
Laser Obscuration 10.79 %
Scattering Model Mie
Analysis Sensitivity Normal
Result
Concentration 0.1082 %
Uniformity 0.339
Specific Surface Area 69.57 m²/kg
D (3,2) 74.5 µm
D (4,3) 92.7 µm
Span 1.208
Result Units Volume
Dv (10) 45.2 µm
Dv (50) 87.6 µm
Dv (90) 150 µm
Frequency (Differential)
Volume Density (%)
16.0
8.0
4.0
0.0
0.01
0.10
1.0
10.0
100.0
1,000.0
10,000.0
Size Classes (µm)

FIG. 21

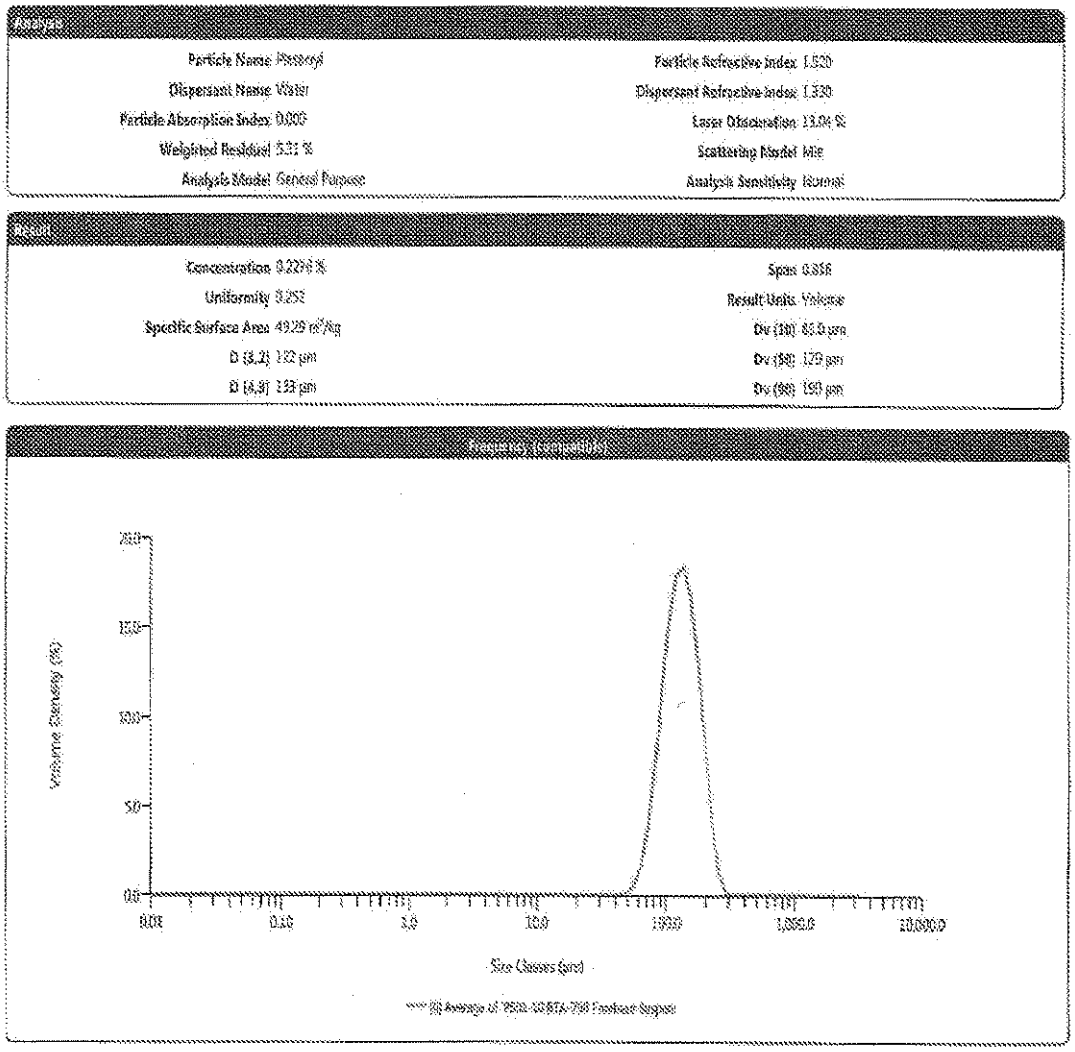

Particle Name: Pinaroyl
Dispersant Name: Water
Particle Absorption Index: 0.000
Weighted Residual: 5.21 %
Analysis Model: General Purpose
Particle Refractive Index: 1.520
Dispersant Refractive Index: 1.330
Laser Obscuration: 13.04 %
Scattering Model: Mie
Analysis Sensitivity: Normal
Result
Concentration: 0.2296 %
Uniformity: 0.252
Specific Surface Area: 49.29 m²/kg
D (3,2): 122 µm
D (4,3): 133 µm
Span: 0.858
Result Units: Volume
Dv (10): 65.0 µm
Dv (50): 129 µm
Dv (90): 193 µm
Volume Density (%)
Size Classes (µm)

FIG. 22

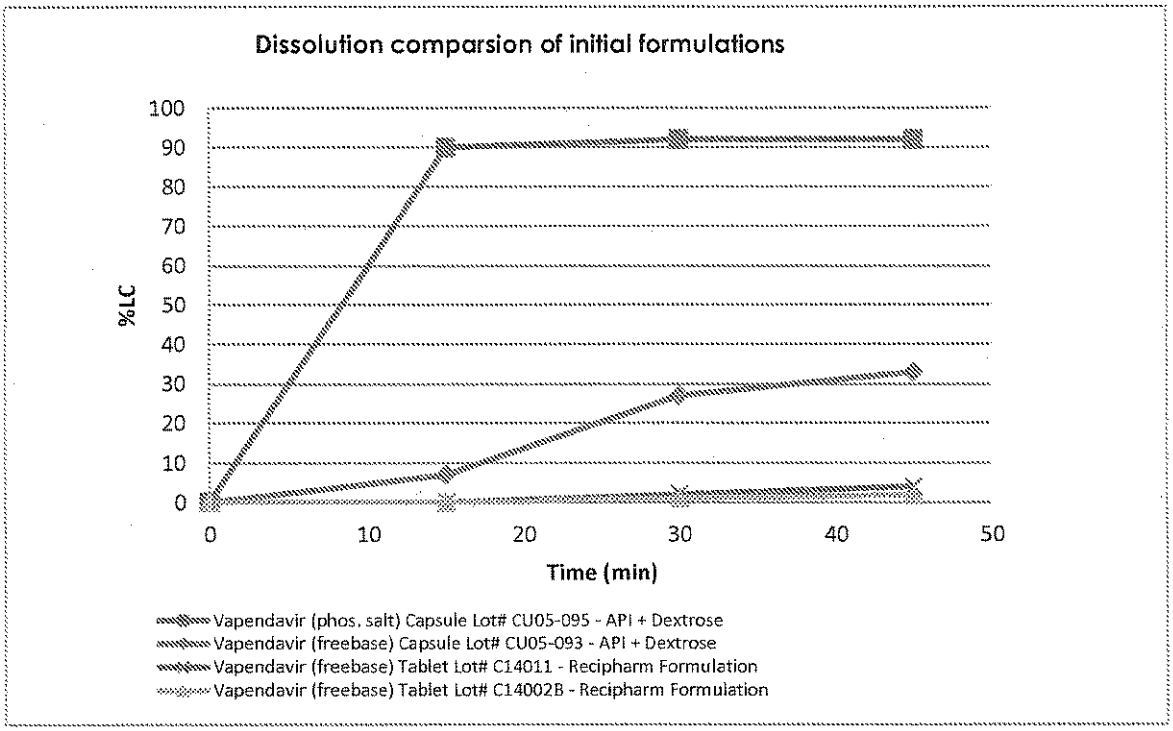

Dissolution comparsion of initial formulations
100
90
80
70
60
50
40
30
20
10
0
%LC
0
10
20
30
40
50
Time (min)
Vapendavir (phos. salt) Capsule Lot# CU05-095 - API + Dextrose
Vapendavir (freebase) Capsule Lot# CU05-093 - API + Dextrose
Vapendavir (freebase) Tablet Lot# C14011 - Recipharm Formulation
Vapendavir (freebase) Tablet Lot# C14002B - Recipharm Formulation

FIG. 23A

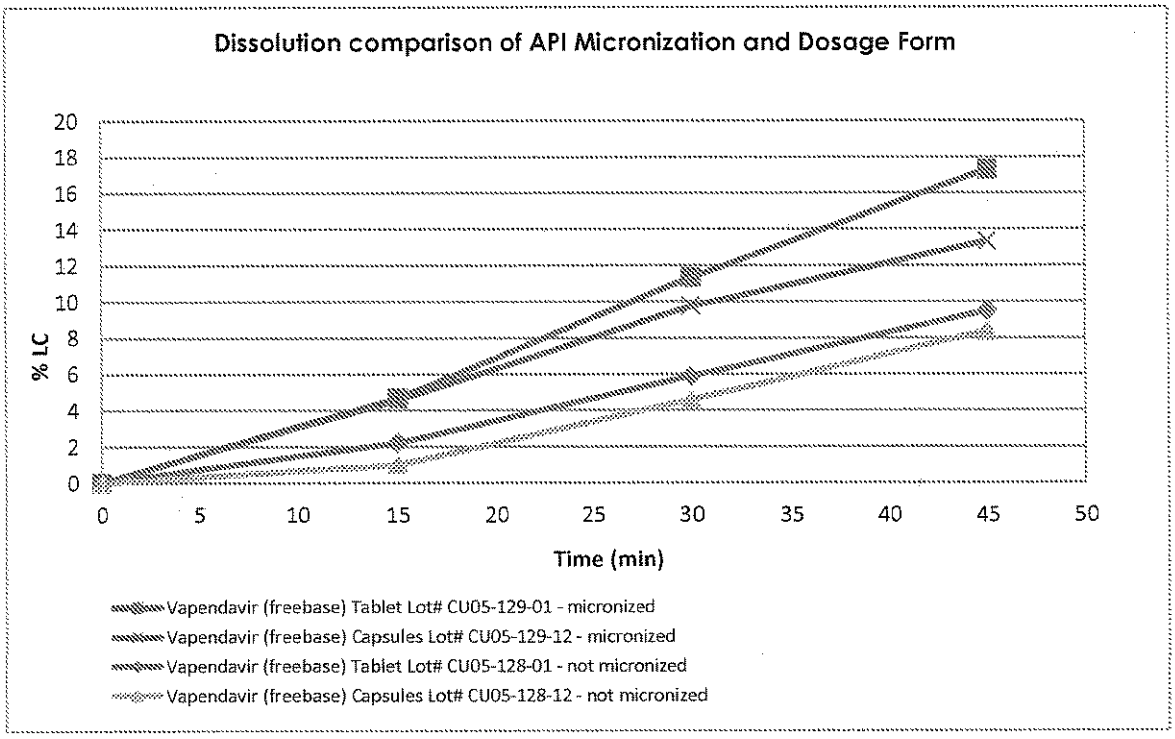

Dissolution comparison of API Micronization and Dosage Form
% LC
20
18
16
14
12
10
8
6
4
2
0
0
5
10
15
20
25
30
35
40
45
50
Time (min)
Vapendavir (freebase) Tablet Lot# CU05-129-01 - micronized
Vapendavir (freebase) Capsules Lot# CU05-129-12 - micronized
Vapendavir (freebase) Tablet Lot# CU05-128-01 - not micronized
Vapendavir (freebase) Capsules Lot# CU05-128-12 - not micronized

FIG. 23B

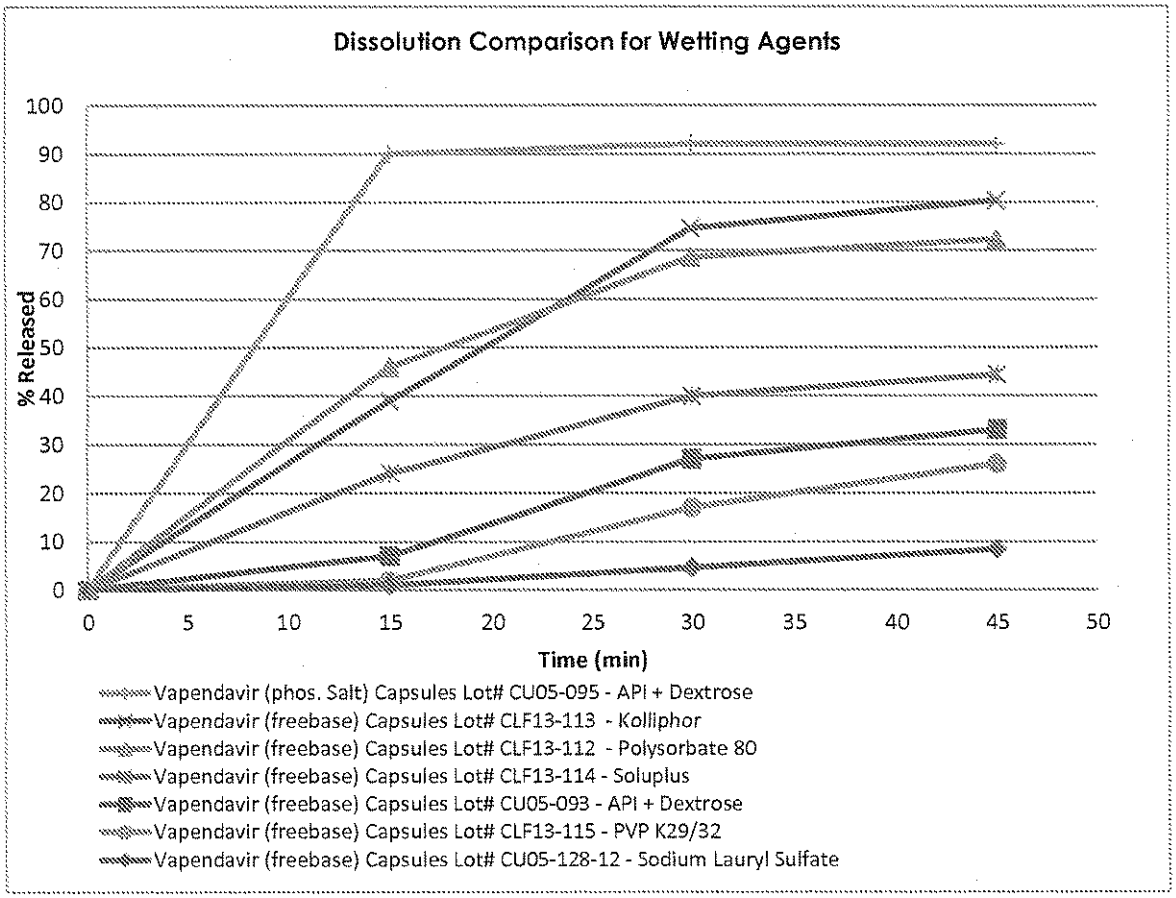

Dissolution Comparison for Wetting Agents
% Released
100
90
80
70
60
50
40
30
20
10
0
0
5
10
15
20
25
30
35
40
45
50
Time (min)
Vapendavir (phos. Salt) Capsules Lot# CU05-095 - API + Dextrose
Vapendavir (freebase) Capsules Lot# CLF13-113 - Kolliphor
Vapendavir (freebase) Capsules Lot# CLF13-112 - Polysorbate 80
Vapendavir (freebase) Capsules Lot# CLF13-114 - Soluplus
Vapendavir (freebase) Capsules Lot# CU05-093 - API + Dextrose
Vapendavir (freebase) Capsules Lot# CLF13-115 - PVP K29/32
Vapendavir (freebase) Capsules Lot# CU05-128-12 - Sodium Lauryl Sulfate

FIG. 24A

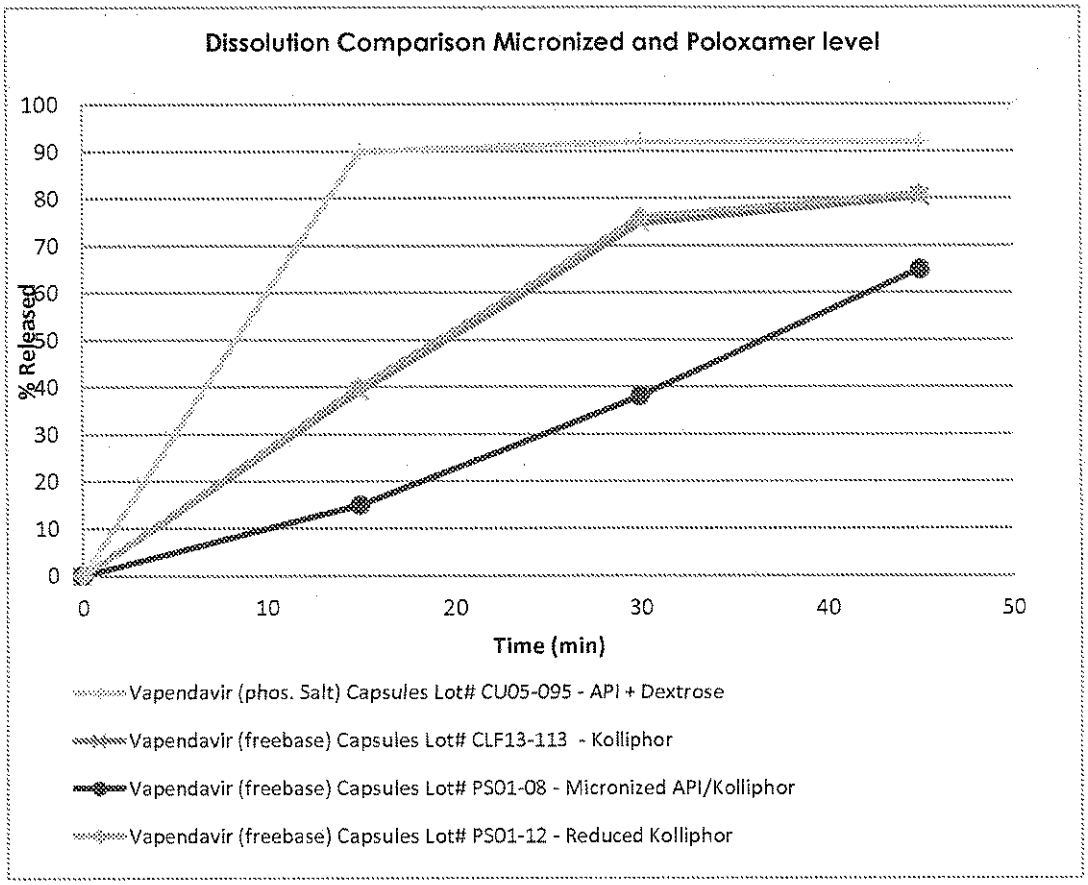

Dissolution Comparison Micronized and Poloxamer level
% Released
100
90
80
70
60
50
40
30
20
10
0
0
10
20
30
40
50
Time (min)
Vapendavir (phos. Salt) Capsules Lot# CU05-095 - API + Dextrose
Vapendavir (freebase) Capsules Lot# CLF13-113 - Kolliphor
Vapendavir (freebase) Capsules Lot# PS01-08 - Micronized API/Kolliphor
Vapendavir (freebase) Capsules Lot# PS01-12 - Reduced Kolliphor

FIG. 24B

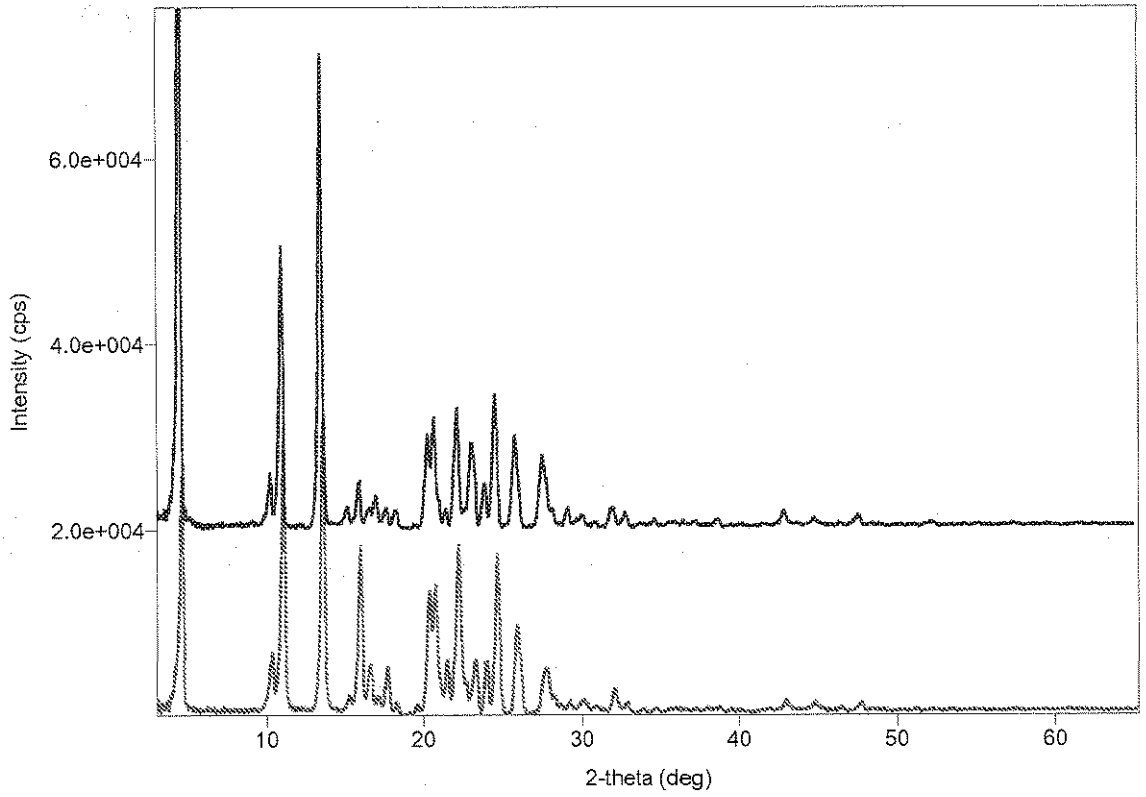

6.0e+004
4.0e+004
2.0e+004
Intensity (cps)
10
20
30
40
50
60
2-theta (deg)
BTA-798 lot # NE-021602Batch – Non-Micronized
BTA-798 lot # NE-021602Batch-Micronized

FIG. 25