Figure 1

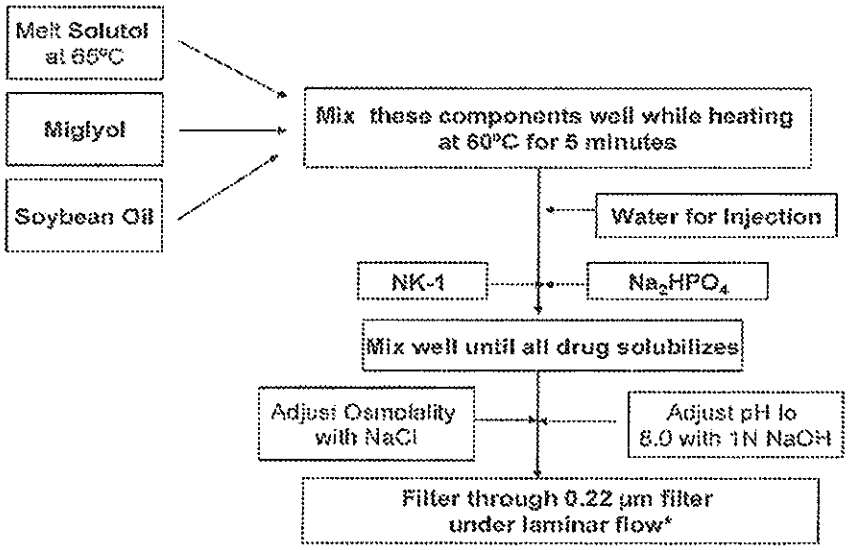

Melt Solutol at 65°C
Migfyol
Soybean Oil
Mix these components well while heating at 60°C for 5 minutes
Water for Injection
NK-1
Na_2HPO_4
Mix well until all drug solubilizes
Adjust Osmolality with NaCl
Adjust pH to 8.0 with 1N NaOH
Filter through 0.22 µm filter under laminar flow*

Figure 2

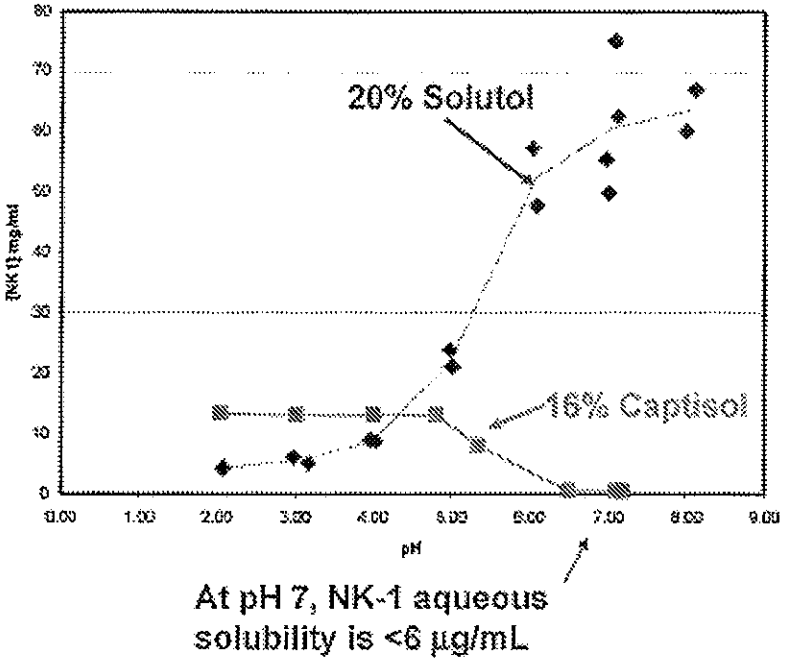

20% Solutol
16% Captisol
pH
At pH 7, NK-1 aqueous solubility is <6 µg/mL

Figure 3

Schematic Representation of the Method for Manufacture NK-1 Emulsion Formulations

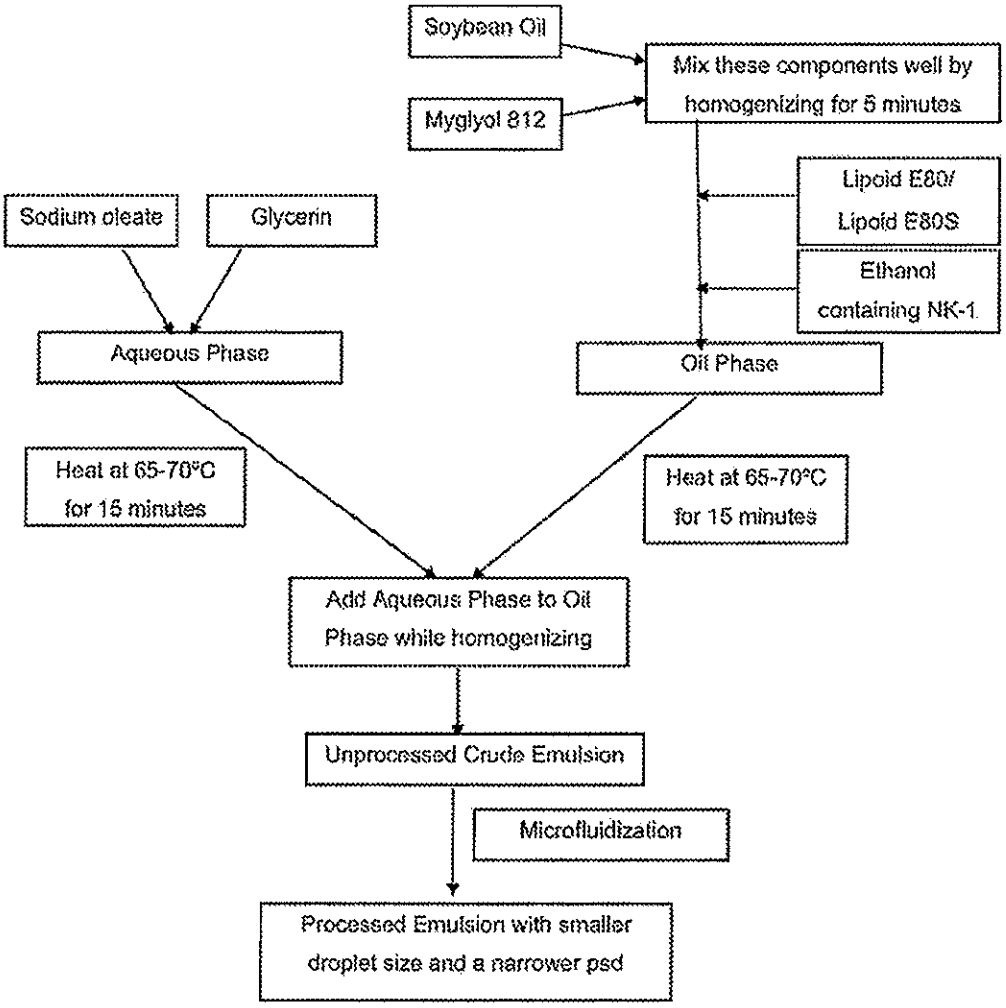


Figure 4

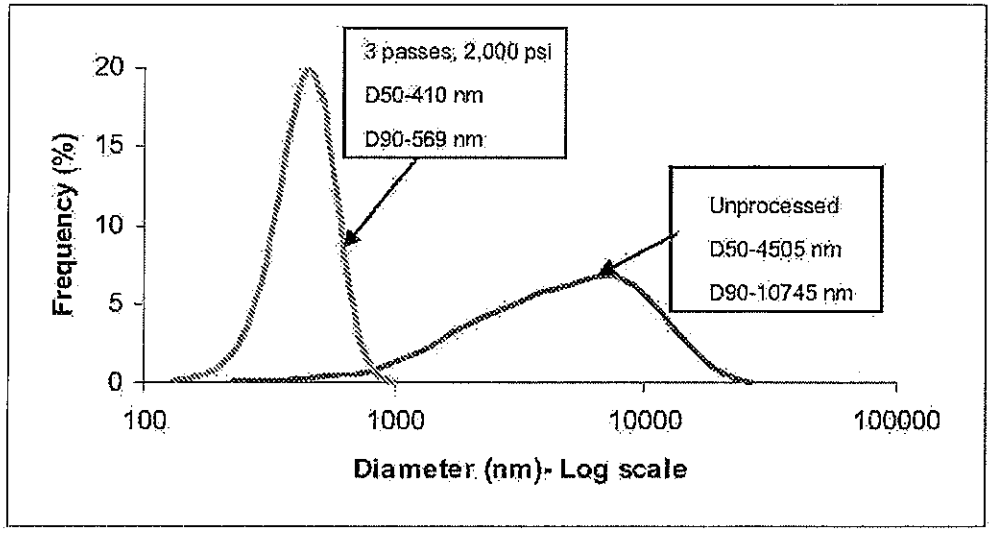

3 passes; 2,000 psi
D50-410 nm
D90-569 nm
Unprocessed
D50-4505 nm
D90-10745 nm
Frequency (%)
20
15
10
5
0
100
1000
10000
100000
Diameter (nm)- Log scale

Figure 5

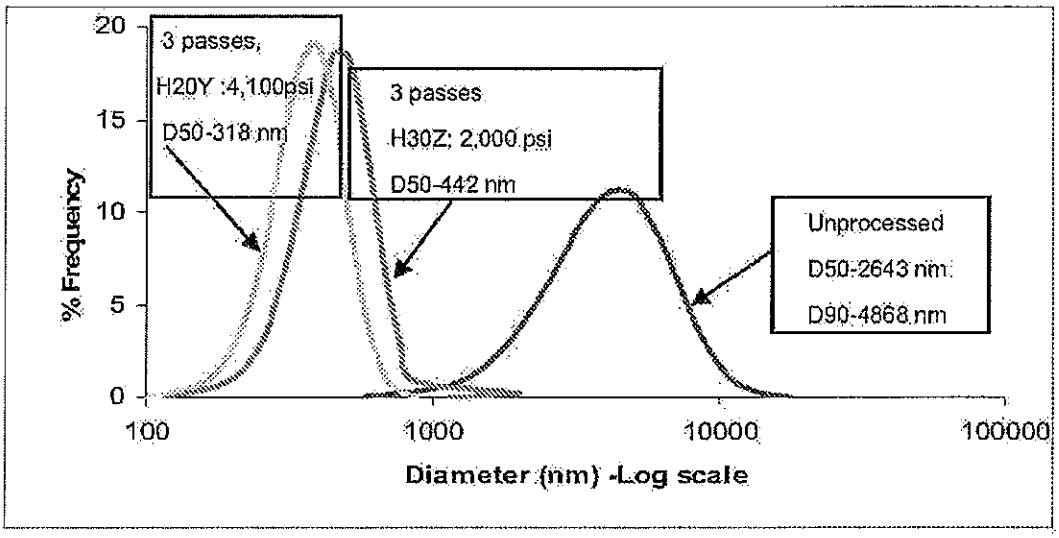

20
15
10
5
0
% Frequency
3 passes,
H20Y :4,100psi
D50-318 nm
3 passes
H30Z: 2,000 psi
D50-442 nm
Unprocessed
D50-2643 nm
D90-4868 nm
100
1000
10000
100000
Diameter (nm) -Log scale

Figure 6

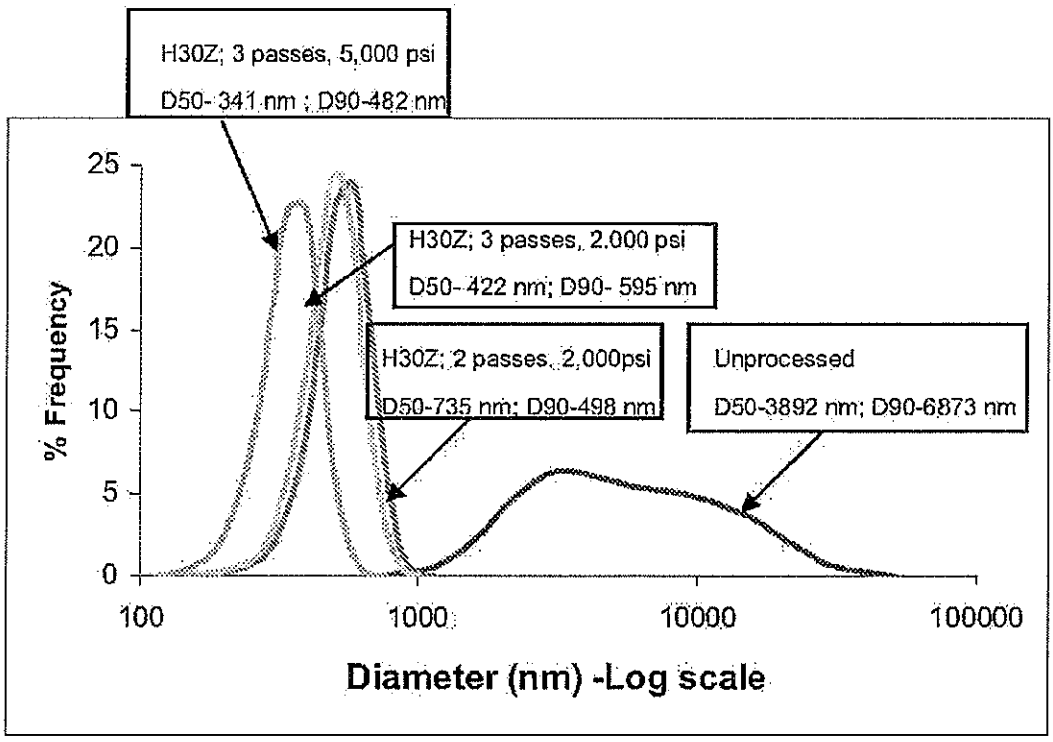

H30Z; 3 passes, 5,000 psi
D50- 341 nm ; D90-482 nm
H30Z; 3 passes, 2,000 psi
D50- 422 nm; D90- 595 nm
H30Z; 2 passes, 2,000psi
D50-735 nm; D90-498 nm
Unprocessed
D50-3892 nm; D90-6873 nm
% Frequency
25
20
15
10
5
0
100
1000
10000
100000
Diameter (nm) -Log scale

Figure 7

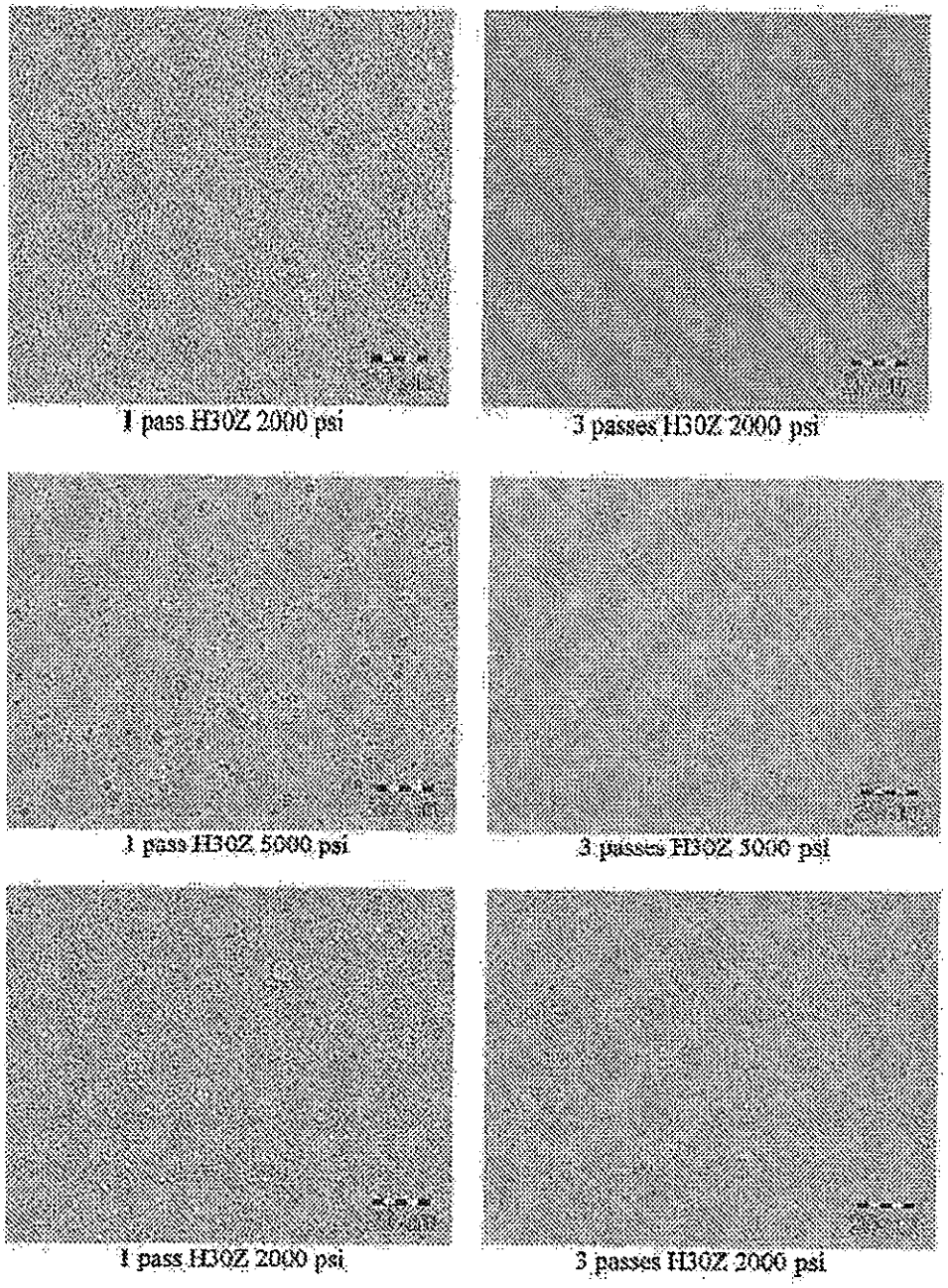

1 pass H30Z 2000 psi
3 passes H30Z 2000 psi
1 pass H30Z 5000 psi
3 passes H30Z 5000 psi
1 pass H30Z 2000 psi
3 passes H30Z 2000 psi

Figure 8

BOL10WSO

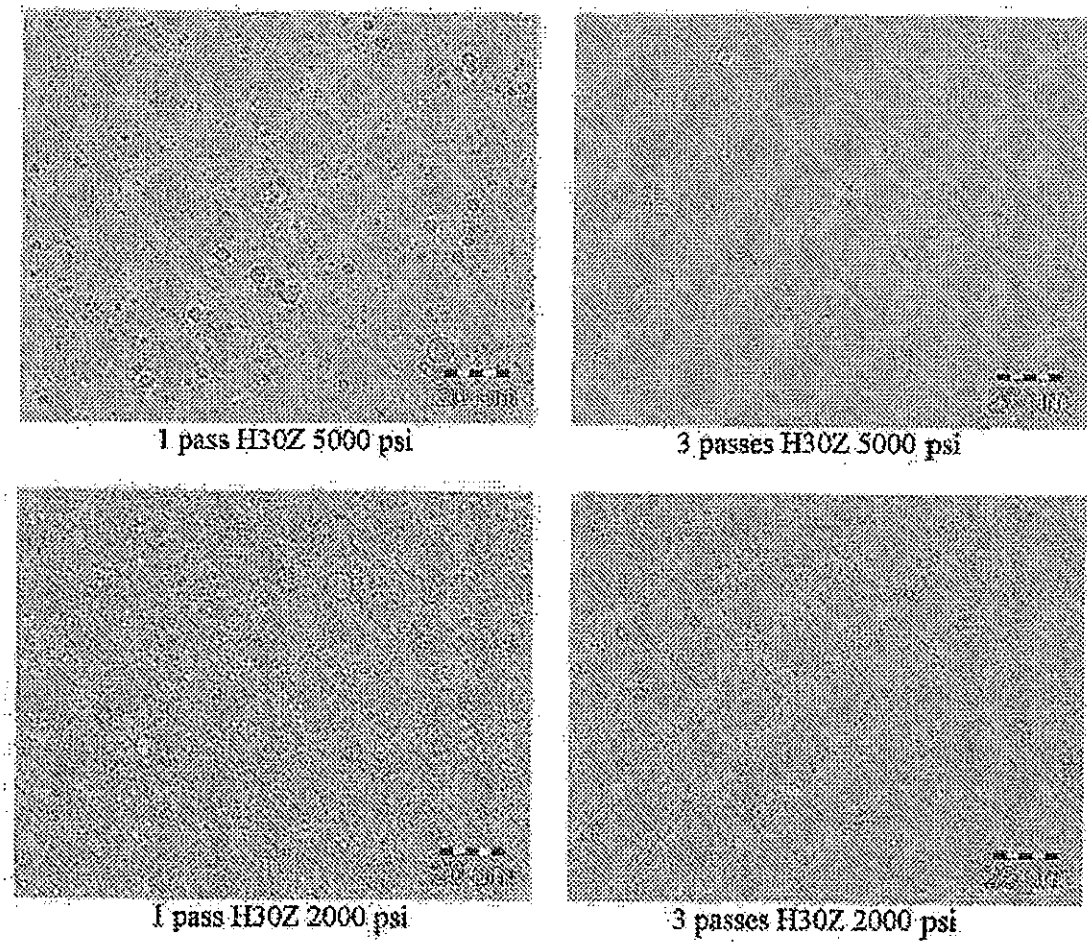


Figure 9

INFSO

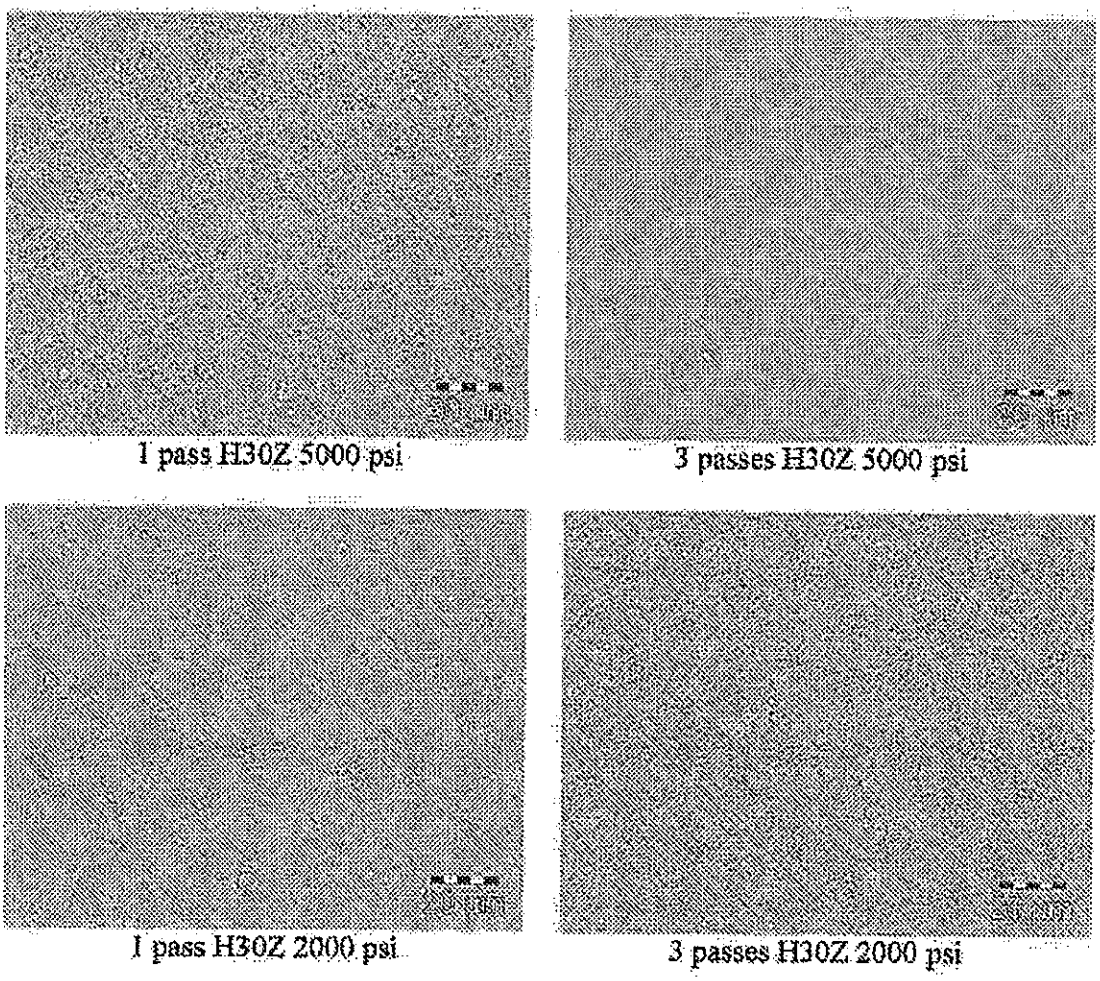


Figure 10

BOL10SO

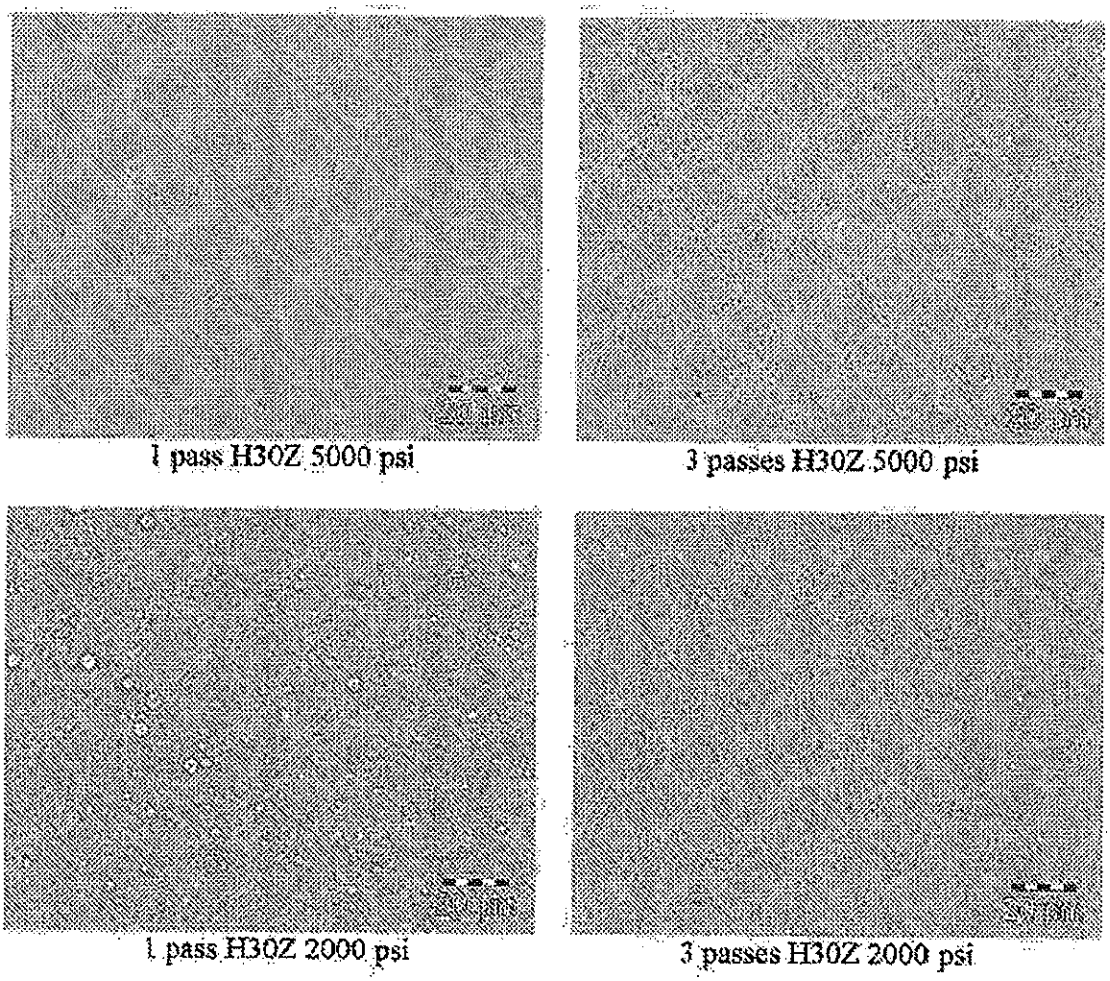


Figure 11

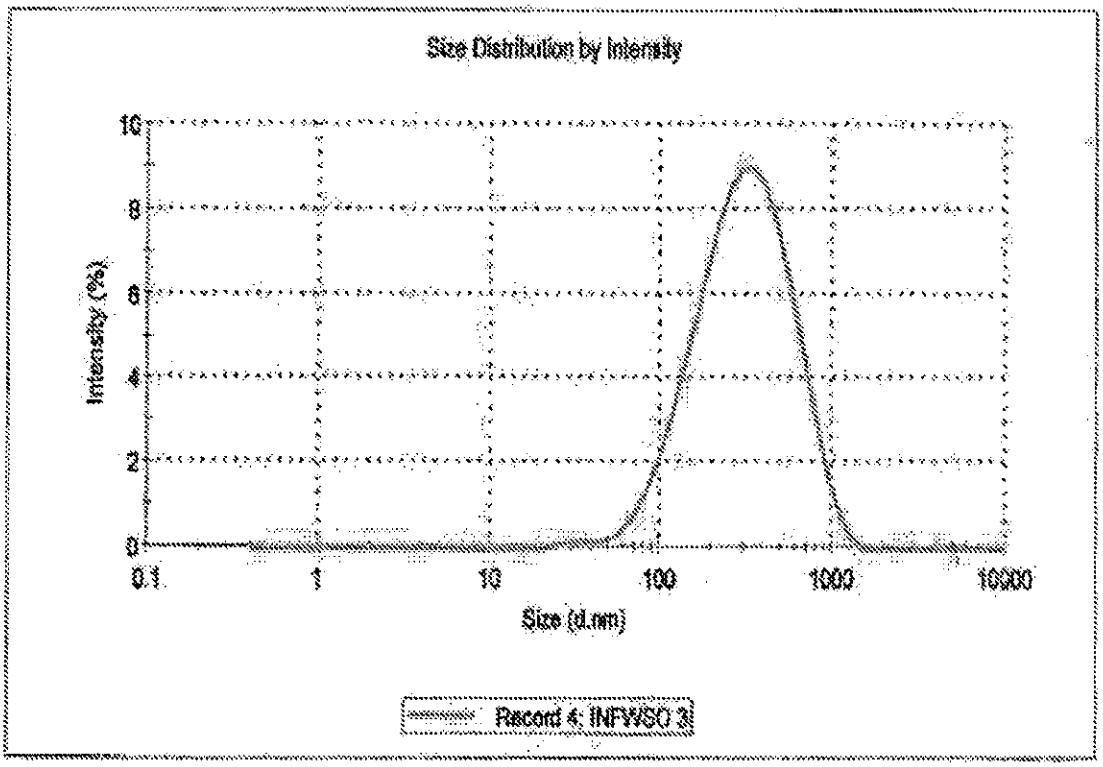

Size Distribution by Intensity
Intensity (%)
10
8
6
4
2
0
0.1
1
10
100
1000
10000
Size (d.nm)
Record 4: INFWSO 3

Figure 12

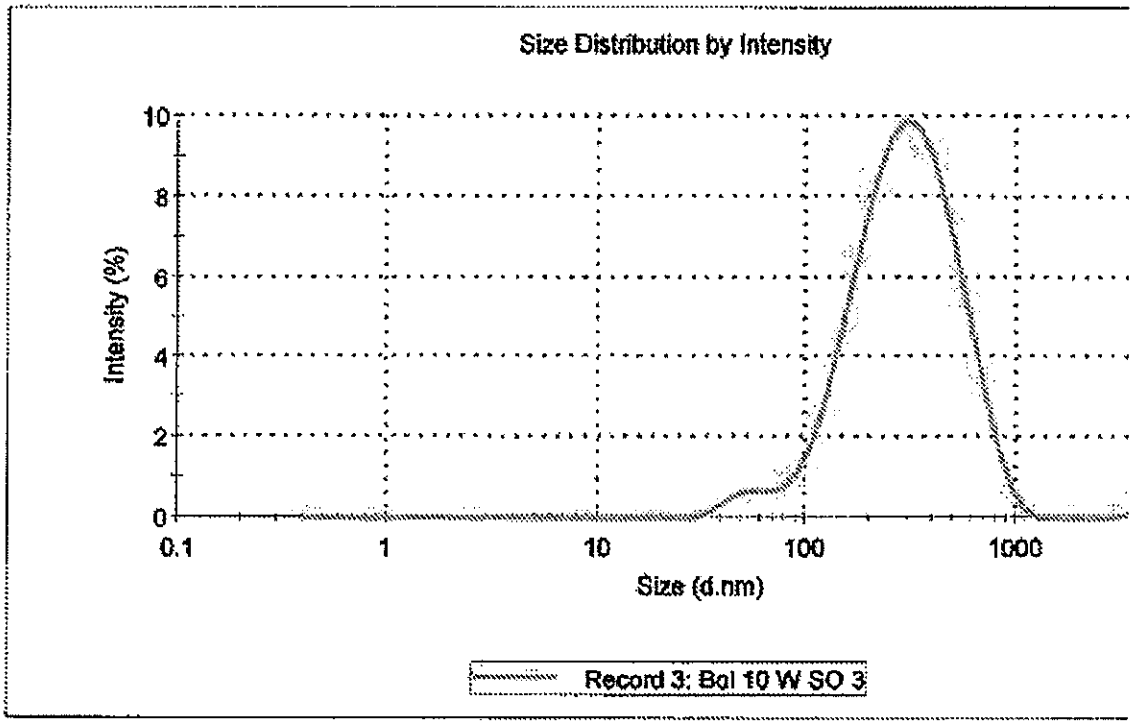
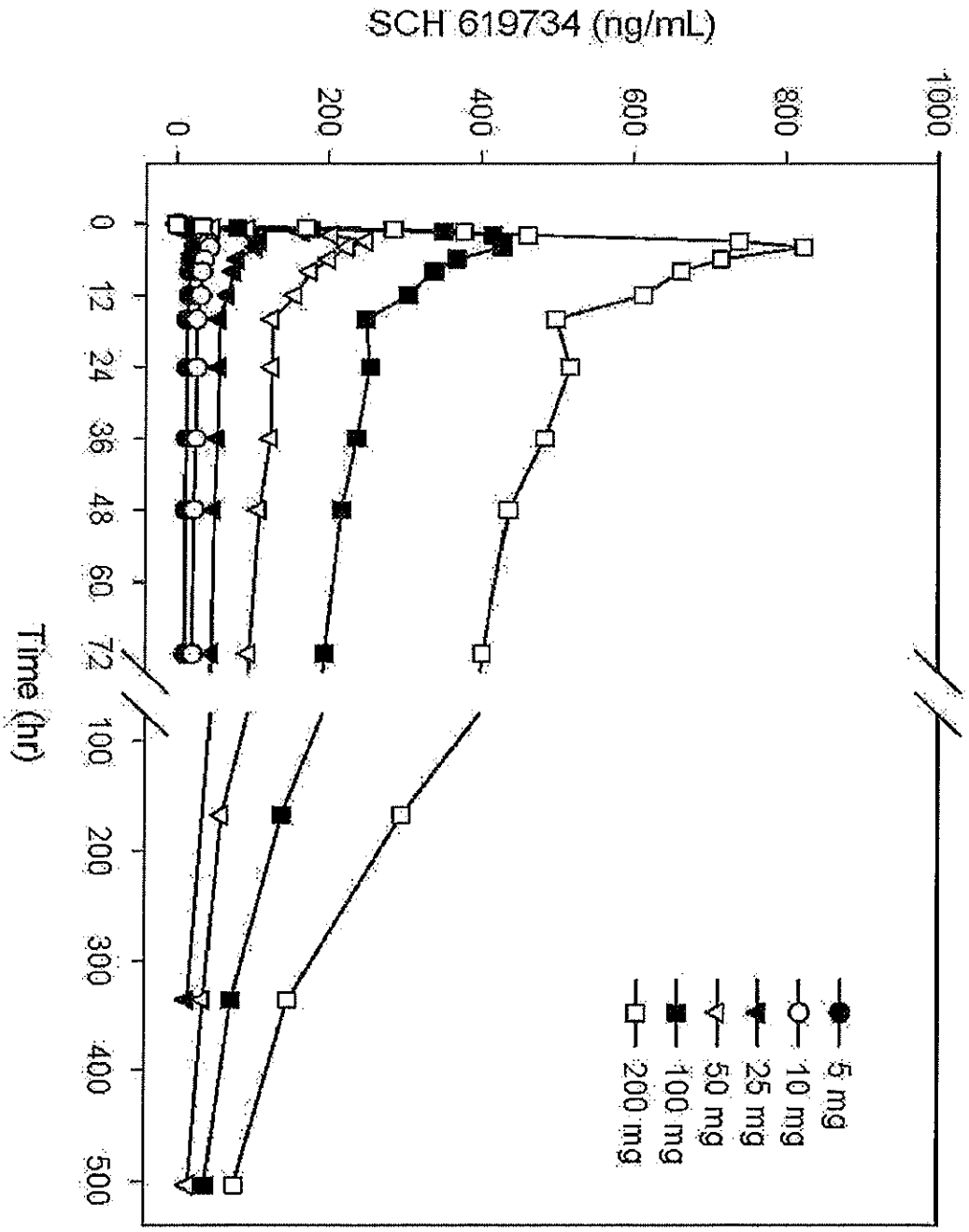

Size Distribution by Intensity
Intensity (%)
10
8
6
4
2
0
0.1
1
10
100
1000
Size (d.nm)
Record 3: Bgl 10 W SO 3

Figure 13


SCH 619734 (ng/mL)
0
200
400
600
800
1000
Time (hr)
0
12
24
36
48
60
72
100
200
300
400
500
5 mg
10 mg
25 mg
50 mg
100 mg
200 mg