FIG. 1

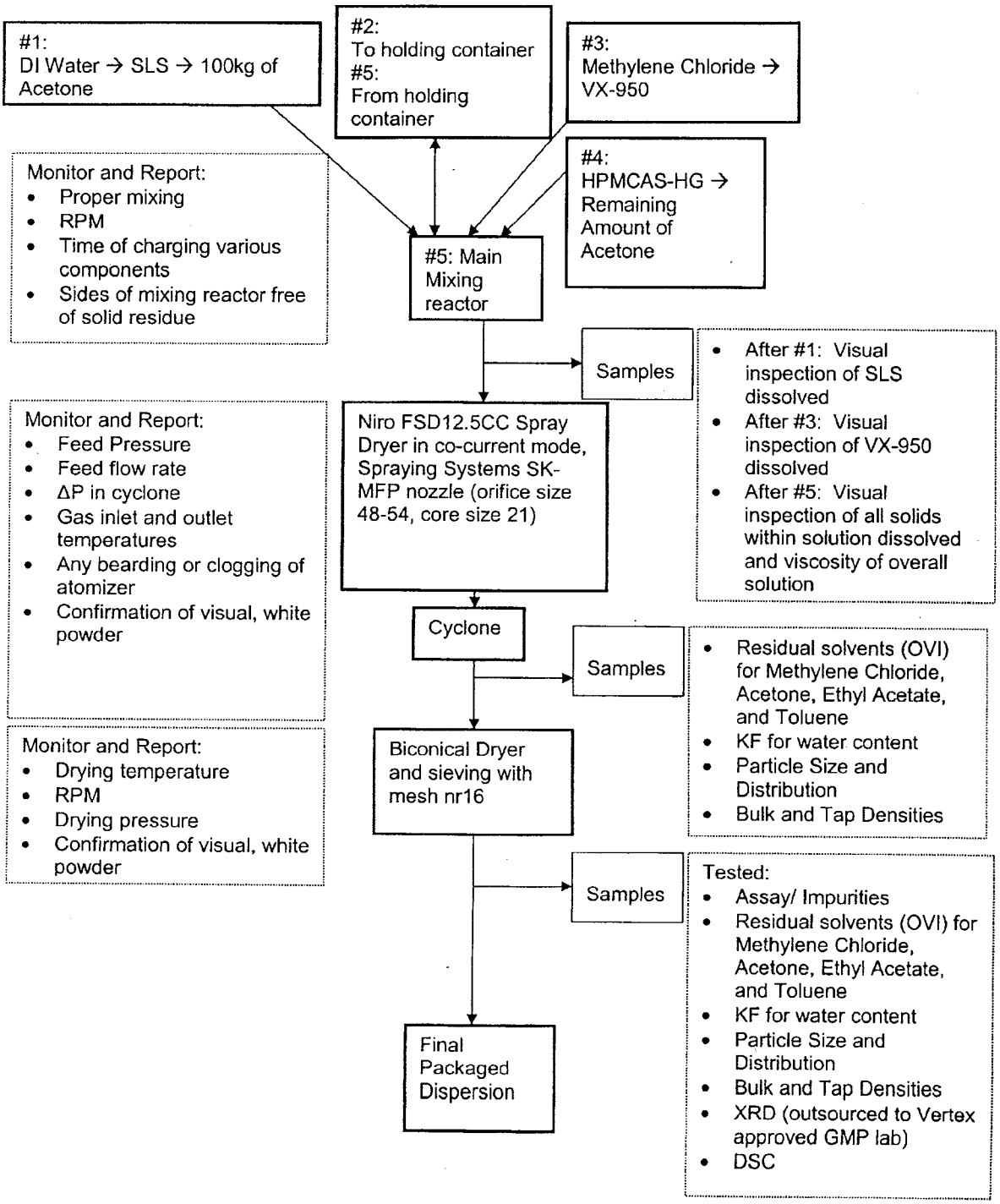

#1:
DI Water → SLS → 100kg of Acetone
#2:
To holding container
#5:
From holding container
#3:
Methylene Chloride → VX-950
#4:
HPMCAS-HG → Remaining Amount of Acetone
Monitor and Report:
• Proper mixing
• RPM
• Time of charging various components
• Sides of mixing reactor free of solid residue
#5: Main Mixing reactor
Samples
• After #1: Visual inspection of SLS dissolved
• After #3: Visual inspection of VX-950 dissolved
• After #5: Visual inspection of all solids within solution dissolved and viscosity of overall solution
Monitor and Report:
• Feed Pressure
• Feed flow rate
• ΔP in cyclone
• Gas inlet and outlet temperatures
• Any bearding or clogging of atomizer
• Confirmation of visual, white powder
Niro FSD12.5CC Spray Dryer in co-current mode, Spraying Systems SK-MFP nozzle (orifice size 48-54, core size 21)
Cyclone
Samples
• Residual solvents (OVI) for Methylene Chloride, Acetone, Ethyl Acetate, and Toluene
• KF for water content
• Particle Size and Distribution
• Bulk and Tap Densities
Monitor and Report:
• Drying temperature
• RPM
• Drying pressure
• Confirmation of visual, white powder
Biconical Dryer and sieving with mesh nr16
Samples
Tested:
• Assay/ Impurities
• Residual solvents (OVI) for Methylene Chloride, Acetone, Ethyl Acetate, and Toluene
• KF for water content
• Particle Size and Distribution
• Bulk and Tap Densities
• XRD (outsourced to Vertex approved GMP lab)
• DSC
Final Packaged Dispersion

FIG. 2

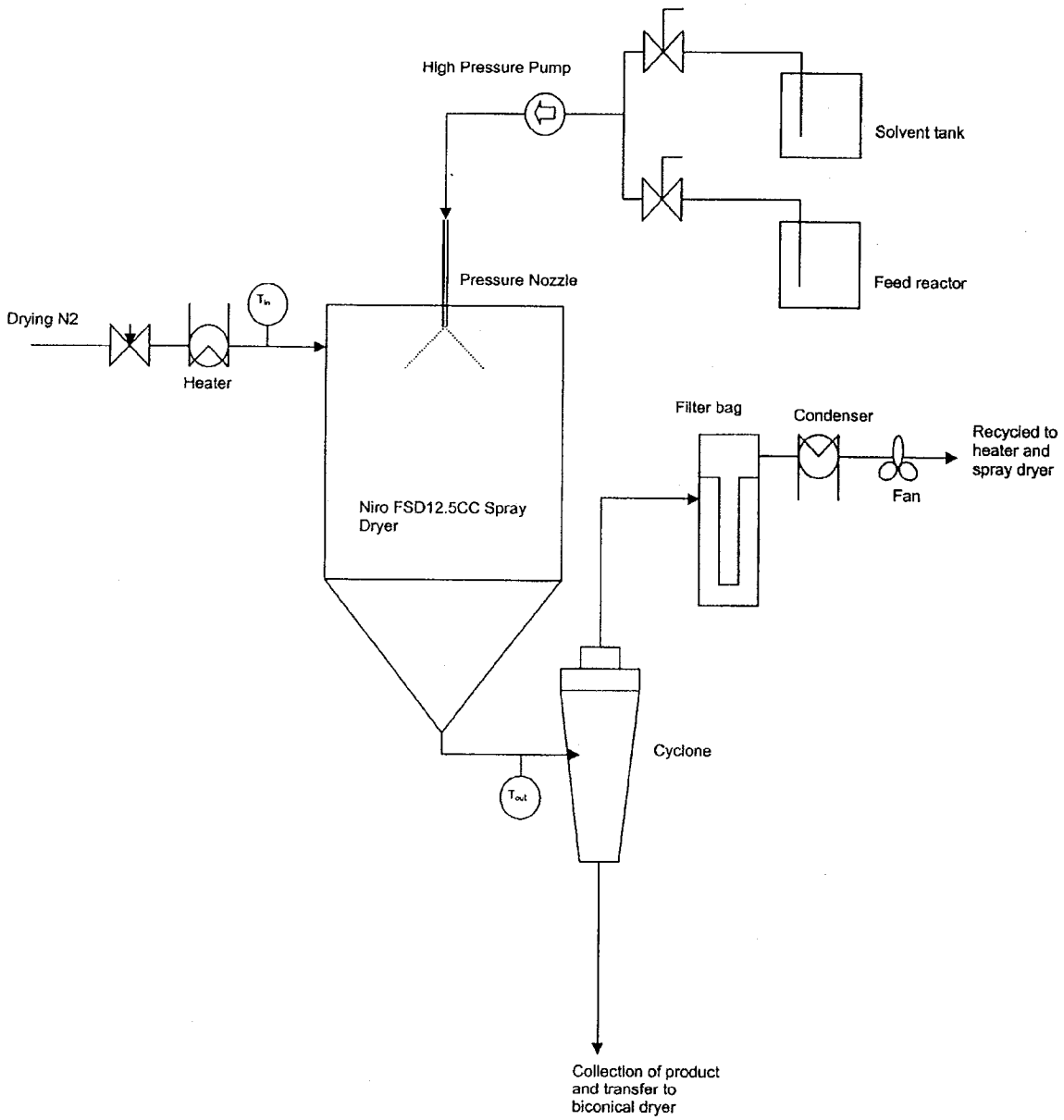
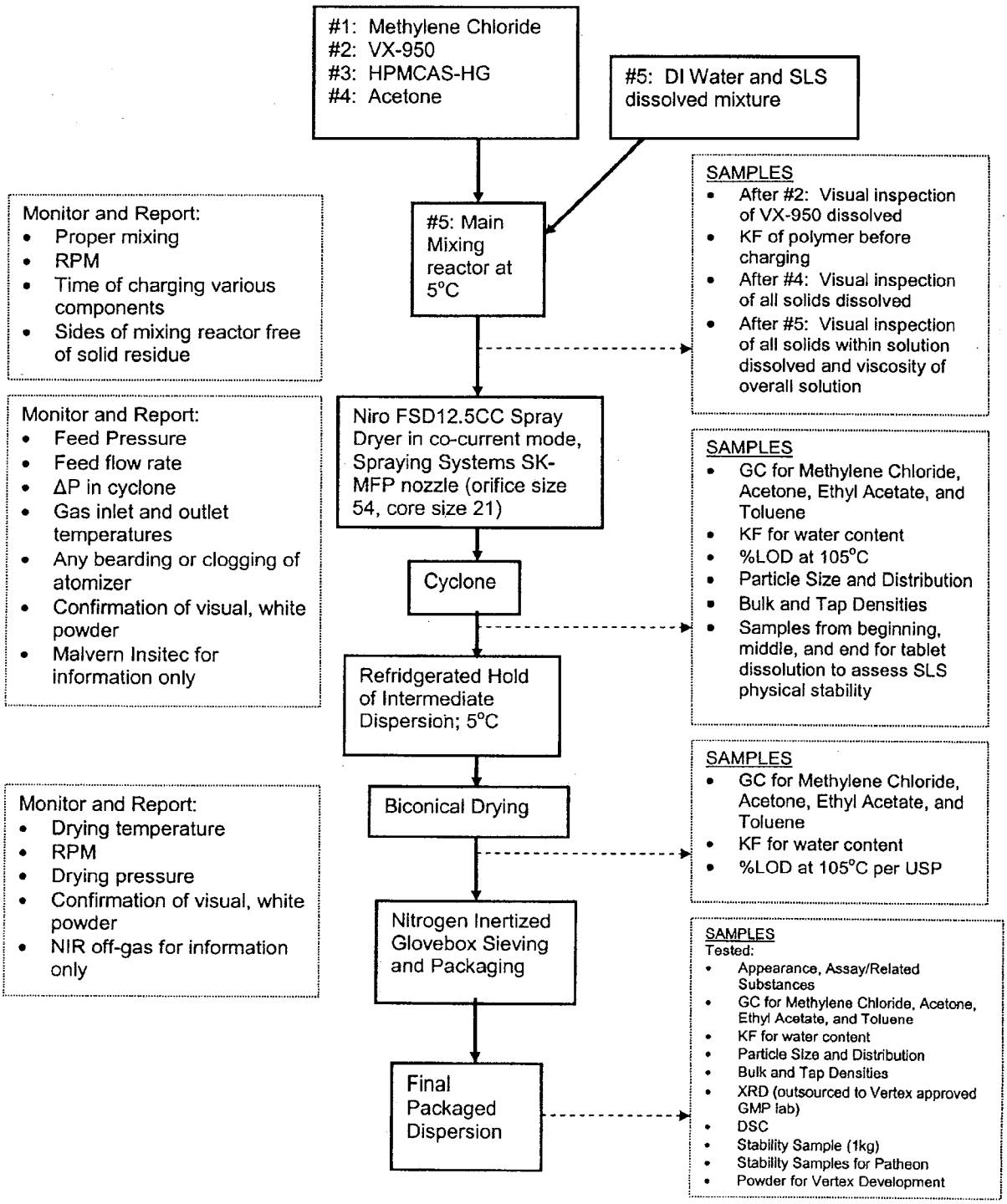

High Pressure Pump
Solvent tank
Feed reactor
Pressure Nozzle
Drying N2
Heater
Filter bag
Condenser
Recycled to heater and spray dryer
Fan
Niro FSD12.5CC Spray Dryer
Cyclone
Collection of product and transfer to biconical dryer

FIG. 3

°C	bar	cmH_2O	°C	SS SK-MFP	wt%	microns		g/cc	g/cc	%	kg/hr	%w/w	ppm	ppm
Outlet Temperature	**Feed Pressure**	**Cyclone Pressure**	**Condenser Setpoint Temp**	**Nozzle**	**Solids Loading**	**PS**	**span**	**bulk density**	**tap density**	**LOD**	**Solution Feedrate**	**KF**	**DCM**	**Acetone**
30	40	12	-3	50/21	17	106.2	1.52	0.4	0.5	10.03	183	0.63	108628	29701
50	20	12	-3	50/21	17	80.88	1.98	0.23	0.27	7.02	130	1.36	59090	21140
50	40	12	-3	54/21	17	58.96	1.96	0.22	0.28	6.28	142	0.63	49452	14469
30	20	12	-3	54/21	17	93.84	1.87	0.35	0.45	10.27	103	1.04	45626	11640
40	30	12	-3	54/21	17	75.5	1.86	0.31	0.38	8.1	124	0.67	60395	16483
40	30	12	-3	54/21	17	78.75	1.72	0.3	0.38	8.68	124	0.63	68464	21373
40	30	12	-3	54/21	12	66.71	1.74	0.33	0.43	7.26	124	0.74	55802	127
40	30	12	-3	54/21	12	63.09	1.8	0.34	0.44	8.09	124	0.74	54704	14323
50	20	12	-3	54/21	12	64.98	1.84	0.25	0.32	6.59	99	0.55	23645	7310
30	40	12	-3	54/21	12	66.51	1.71	0.39	0.51	9.89	142	0.85	42078	9485
30	20	12	-3	50/21	12	86.71	2.06	0.4	0.53	11.3	183	0.63	80579	19275
50	40	12	-3	50/21	12	52.8	2.11	0.25	0.32	6.42	185	0.63	20805	6340
30	30	12	-3	54/21	17	95.53	1.59	0.35	0.46	10.41	103	.	99084	28431
30	40	12	-10	52/21	15	95.26	1.45	0.34	0.45	8.96	160	0.71	52975	24399
40	30	12	-10	52/21	15	89.89	1.71	0.28	0.36	7.01	137	0.6	41192	21435
30	30	12	-10	52/21	13	114.29	1.5	0.33	0.41	10.51	136	0.57	55576	31638
40	40	12	-10	52/21	13	94.09	1.68	0.27	0.34	8.2	155	0.43	41051	26826
30	50	12	-10	54/21	15	71.81	1.56	0.34	0.47	8.32	155	.	43413	13946
30	30	12	-10	54/21	15	83.31	1.55	0.34	0.44	6.98	123	.	60819	21951
26	50	12	-10	54/21	15	68.75	1.63	0.37	.	10.02	155	.	53482	16955
26	30	12	-10	54/21	15	86.91	1.52	0.4	0.54	10.78	122	.	79148	27092
28	40	12	-10	54/21	15	75.17	1.65	0.37	0.48	8.67	141	.	69673	21067
40	25	10	-10	52/21	20	110.61	1.87	0.27	0.33	8.7	132	.	.	.
40	50	10	-10	52/21	20	93.05	1.91	0.25	0.31	7.96	180	.	.	.

30	50	10	-10	52/21	20	102.8	1.74	0.33	0.42	7.43	184	.	.	.
30	25	10	-10	52/21	20	146.58	1.86	0.33	0.41	9.6	133	.	.	.
27	70	10	-10	56/21	20	78.18	1.69	0.35	0.46	8.6	150	.	80368	10511
40	25	10	-10	52/21	17	102.27	1.71	0.26	0.31	8.93	130	.	.	.
40	50	10	-10	52/21	17	85.48	1.75	0.27	0.35	9.22	184	.	.	.
30	50	10	-10	52/21	17	104.95	1.51	0.31	0.41	11.4	185	.	.	.
30	25	10	-10	52/21	17	111.22	1.71	0.31	0.4	10.38	131	.	.	.
27	60	10	-10	54/21	17	86.14	1.68	0.33	0.47	10.63	170	.	75835	31366
40	25	10	-10	52/21	15	79.57	1.77	0.26	0.33	9.41	130	.	.	.
40	50	10	-10	52/21	15	67.06	1.79	0.26	0.34	5.94	183	.	.	.
30	50	10	-10	52/21	15	84.18	1.56	0.31	0.43	10.36	183	.	.	.
30	25	10	-10	52/21	15	96.86	1.62	0.31	0.4	10.98	130	.	.	.
23	60	10	-10	54/21	15	110.61	1.87	0.27	0.48	8.7	132	.	69444	27689
23	65	10	-10	54/21	17	93.62	1.34	0.34	0.45	8.5	178	.	.	.
23	65	10	-3	54/21	17	93.42	1.4	0.4	0.5	10.38	178	.	.	.
22	65	10	-10	56/21	17	63.52	1.56	0.36	0.49	6.96	146	.	.	.
22	65	10	-3	56/21	17	50.81	1.85	0.39	0.54	8.81	146	.	.	.

FIG. 4


#1: Methylene Chloride
#2: VX-950
#3: HPMCAS-HG
#4: Acetone
#5: DI Water and SLS dissolved mixture
#5: Main Mixing reactor at 5°C
Monitor and Report:
• Proper mixing
• RPM
• Time of charging various components
• Sides of mixing reactor free of solid residue
SAMPLES
• After #2: Visual inspection of VX-950 dissolved
• KF of polymer before charging
• After #4: Visual inspection of all solids dissolved
• After #5: Visual inspection of all solids within solution dissolved and viscosity of overall solution
Niro FSD12.5CC Spray Dryer in co-current mode, Spraying Systems SK-MFP nozzle (orifice size 54, core size 21)
Monitor and Report:
• Feed Pressure
• Feed flow rate
• ΔP in cyclone
• Gas inlet and outlet temperatures
• Any bearding or clogging of atomizer
• Confirmation of visual, white powder
• Malvern Insitec for information only
Cyclone
SAMPLES
• GC for Methylene Chloride, Acetone, Ethyl Acetate, and Toluene
• KF for water content
• %LOD at 105°C
• Particle Size and Distribution
• Bulk and Tap Densities
• Samples from beginning, middle, and end for tablet dissolution to assess SLS physical stability
Refridgerated Hold of Intermediate Dispersion; 5°C
Biconical Drying
Monitor and Report:
• Drying temperature
• RPM
• Drying pressure
• Confirmation of visual, white powder
• NIR off-gas for information only
SAMPLES
• GC for Methylene Chloride, Acetone, Ethyl Acetate, and Toluene
• KF for water content
• %LOD at 105°C per USP
Nitrogen Inertized Glovebox Sieving and Packaging
Final Packaged Dispersion
SAMPLES
Tested:
• Appearance, Assay/Related Substances
• GC for Methylene Chloride, Acetone, Ethyl Acetate, and Toluene
• KF for water content
• Particle Size and Distribution
• Bulk and Tap Densities
• XRD (outsourced to Vertex approved GMP lab)
• DSC
• Stability Sample (1kg)
• Stability Samples for Patheon
• Powder for Vertex Development