FIG. 1: Formulations

Formulation	CYT002-NicQß	pH	Polysorbate 20	Sodium phosphate	Potassium phosphate	Histidine/ HistidineHCl	Sodium succinate	Trehalose dihydrate	Mannitol	Sodium chloride
	[mg/ml]		[%]	[mM]	[mM]		[mM]	[%]	[%]	[mM]
F29RL	0.2	6.2	0.005	20	0	0	0	10	0	0
F49RL	0.6	6.2	0.005	20	0	0	0	10	0	0
F10RL	1.0	6.2	0.005	20	0	0	0	10	0	0
F 48RL	2.0	6.2	0.005	20	0	0	0	10	0	0
F16RL	1.0	6.2	0.005	0	20	0	0	10	0	0
F08RL	1.0	6.2	0.005	0	20	0	0	10	0	30
F39RL	1.0	6.2	0.005	0	20	0	0	10	0	60
F37RL	1.0	6.2	0.005	0	20	0	0	10	0	90
F38RL	1.0	6.2	0.005	0	20	0	0	10	0	150
F40RL	1.0	6.2	0.005	20	0	0	0	5	0	0
F41RL	1.0	6.2	0.005	20	0	0	0	7.5	0	0
F01RL	0.2	6.2	0.005	10	0	0	0	10	0	30
F22RL	0.2	6.2	0.0	10	0	0	0	10	0	30
F19RL	1.0	6.2	0.01	0	20	0	0	10	0	0
F34RL	1.0	6.2	0.005	0	0	20	0	10	0	0
F30RL	1.0	6.2	0.005	0	20	0	0	1.0	4.0	0
F32RL	1.0	6.2	0.005	0	20	0	0	1.3	5.3	0
F42RL	1.0	6.2	0.005	20	0	0	0	1.1	4.4	0
F35RL	1.0	5.8	0.005	20	0	0	0	10	0	0
F15RL	1.0	6.2	0.005	0	0	0	20	10	0	0
F54RL	1.0	6.2	0.005	20	0	0	0	0	5.0	0

FIG. 2: Results

Formulation	Water content	Osmolarity	Increased amount of sum of oligomers and aggregates after lyophilization (AF4)	Dynamic Light Scattering (DLS)*	
	[%]	[mosm/kg]	[%]	PI	Main peak [%]
F29RL	0.5	307	0.0	0.19	98.6
F49RL	0.6	310	0.7	0.15	99.3
F10RL	0.5	318	0.1	0.16	99.1
F48RL	0.5	302	1.0	0.13	99.8
F16RL	0.3	301	0.0	0.20	99.2
F08RL	0.6	331	0.3	0.20	99.3
F39RL	0.7	369	0.0	0.15	99.1
F37RL	0.9	417	2.8	0.16	99.8
F38RL	1.2	483	3.5	0.18	99.1
F40RL	0.4	169	0.0	0.18	99.6
F41RL	0.4	230	0.0	0.19	99.5
F01RL	0.7	n/a	0.0	0.13	100.0
F22RL	0.8	n/a	5.5	0.35	98.5
F19RL	0.2	295	0.0	0.19	99.3
F34RL	0.4	281	0.0	0.18	99.6
F30RL	0.1	258	0.0	0.18	99.6
F32RL	0.1	327	0.0	0.19	99.5
F42RL[#]	0.2	320	0.4	0.15	99.0
F42RL[°]	0.2	328	1.1	0.11	99.9
F35RL	0.5	314	0.0	0.16	96.0
F15RL	0.7	n.a	3.0	0.12	99.9
F54RL	0.3	336	6.4	0.16	99.6

* as determined by using the volume conversion model [#] produced without annealing step [°] produced with annealing step

FIG. 3 Stability test

Formulation	Storage temperature	Water content [%]			Increased amount of sum of oligomers and aggregates as determined by AF4 [%]			DLS						Content of free nicotine derivatives [% of total]			
								PI			Main peak* [%]						
		6 wks	15 wks	25 wks	6 wks	15 wks	25 wks	6 wks	15 wks	25 wks	6 wks	15 wks	25 wks	0 wks	6 wks	15 wks	25 wks
F42RL#	2-8°C	0.1	0.1	n/a	1.4	1.8	n/a	0.145	0.148	n/a	99.2	99.5	n/a	0	0	0	n/a
	25 °C	0.2	0.3	n/a	0.8	2.1	n/a	0.147	0.149	n/a	99.8	99.3	n/a		0	0.5	n/a
	40 °C	0.5	0.9	n/a	1.3	1.1	n/a	0.143	0.146	n/a	99.2	99.6	n/a		0.6	1.4	n/a
F42RL°	2-8°C	0.5	n/a	n/a	3.9	n/a	n/a	0.116	n/a	n/a	99.9	n/a	n/a	0.8	1.0	n/a	n/a
	25 °C	0.7	n/a	n/a	3.6	n/a	n/a	0.120	n/a	n/a	99.5	n/a	n/a		1.1	n/a	n/a
	40 °C	0.8	n/a	n/a	4.1	n/a	n/a	0.128	n/a	n/a	99.5	n/a	n/a		1.7	n/a	n/a
F10RL	2-8°C	0.6	0.5	0.7	1.1	2.1	3.0	0.155	0.153	0.155	99.0	98.6	98.6	0	0	0	0.1
	25 °C	0.6	0.7	0.8	1.3	1.1	2.8	0.155	0.153	0.164	98.9	98.9	98.9		0	0.4	0.5
	40 °C	0.9	1.2	1.6	1.6	1.6	2.1	0.153	0.155	0.168	99.4	99.3	98.8		0.7	1.1	1.1
F35RL	2-8°C	0.6	0.5	0.5	1.5	1.5	3.0	0.162	0.162	0.174	98.7	99.5	99.6	0	0	0	0
	25 °C	0.6	0.6	0.7	1.4	1.7	1.9	0.161	0.168	0.163	99.1	98.7	99.4		0	0.4	0.4
	40 °C	0.8	1.2	1.4	1.6	2.5	2.4	0.161	0.157	0.186	99.5	99.5	99.3		0.6	0.9	1.0
F16RL	2-8°C	0.5	0.4	n/a	0.4	1.1	n/a	0.149	0.146	n/a	99.4	99.1	n/a	0	0	0	n/a
	25 °C	0.6	0.7	n/a	0.1	0.9	n/a	0.173	0.149	n/a	99.4	98.8	n/a		0	0.5	n/a
	40 °C	0.8	1.1	n/a	0.3	0.9	n/a	0.144	0.148	n/a	99.4	99.1	n/a		0.7	1.1	n/a
F54RL	2-8°C	0.5	n/a	n/a	6.7	n/a	n/a	0.177	n/a	n/a	99.7	n/a	n/a	0.8	0.8	n/a	n/a
	25 °C	0.6	n/a	n/a	14.4	n/a	n/a	0.179	n/a	n/a	100	n/a	n/a		1.1	n/a	n/a
	40 °C	0.8	n/a	n/a	28.0	n/a	n/a	0.239	n/a	n/a	100	n/a	n/a		4.2	n/a	n/a

Results of the five formulations at day 0 were shown in Figure 2.
* as determined by using the volume conversion model # produced without annealing step ° produced with annealing step