

HMWS Evolution Over 12 Weeks of Storage at 5°C

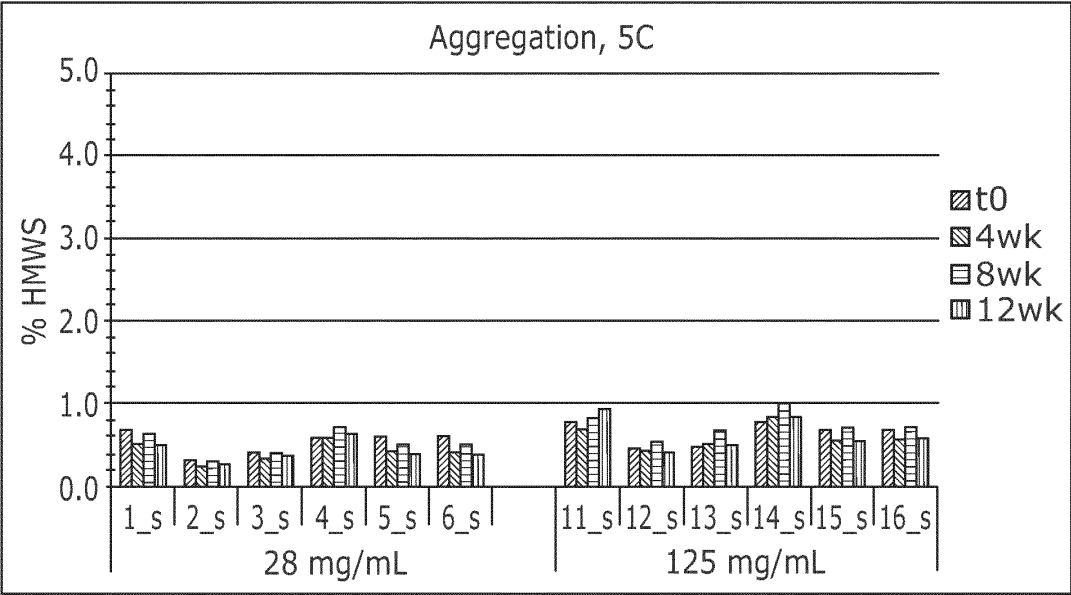


FIG. 1A

HMWS Evolution Over 12 Weeks of Storage at 25°C

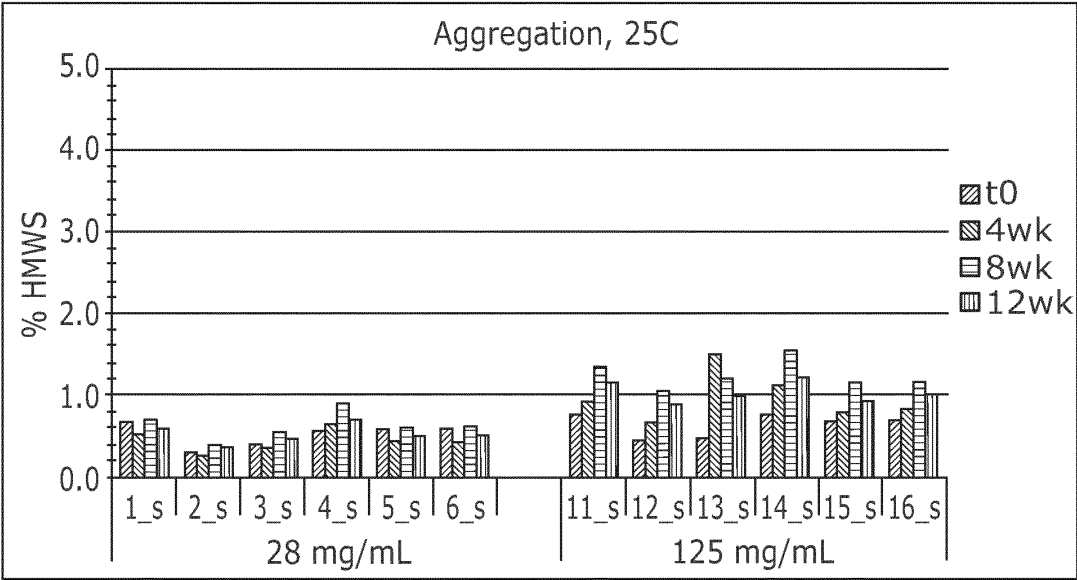


FIG. 1B

HMWS Evolution Over 12 Weeks of Storage at 40°C

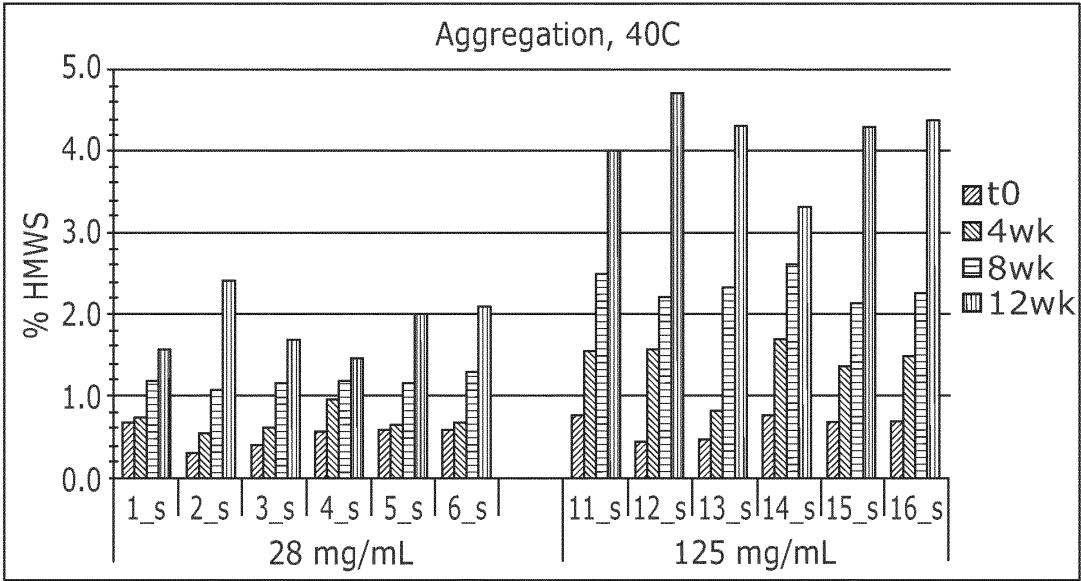


FIG. 1C

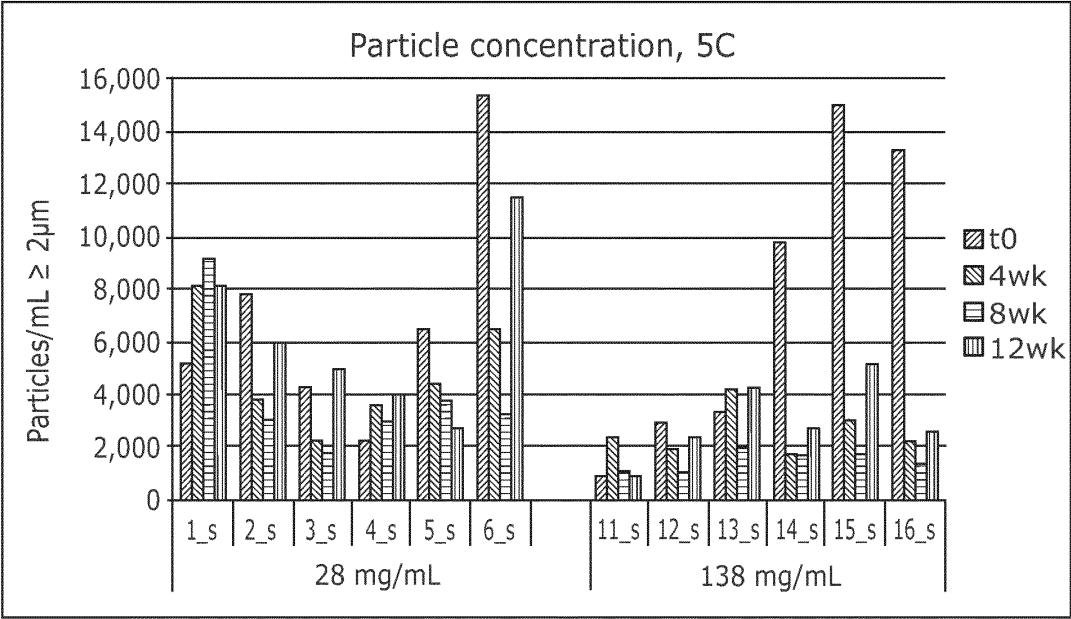


FIG. 2A

Evolution of $\geq 2\mu\text{m}$ subvisible particles in buffer formulations over 12 weeks of storage at 5° C, 25° C, and 40° C.

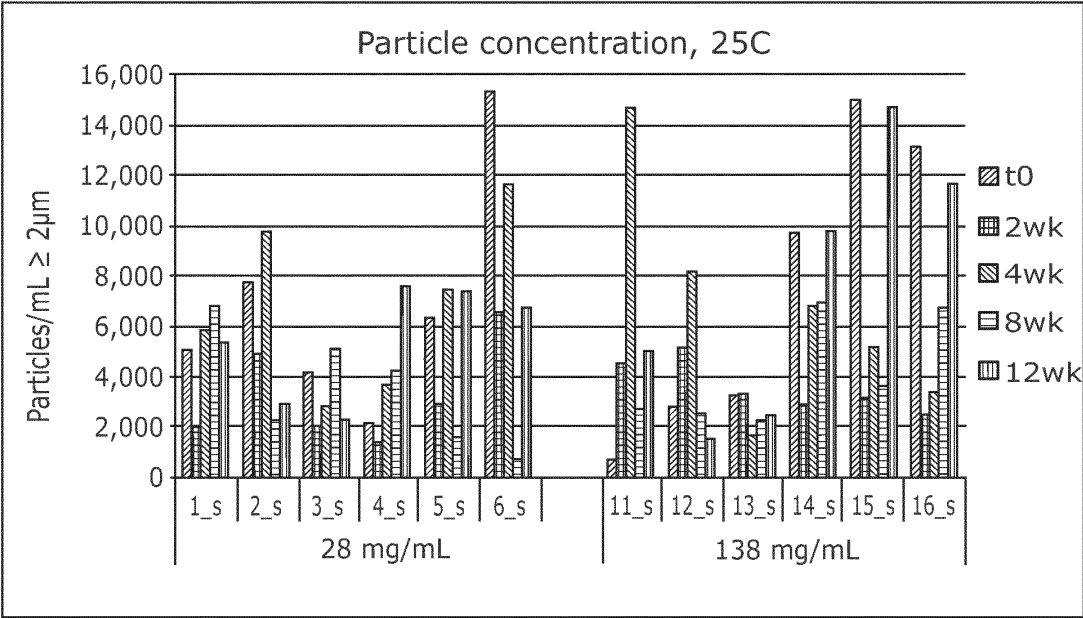


FIG. 2B

Evolution of $\geq 2\mu\text{m}$ subvisible particles in buffer formulations over 12 weeks of storage at 5° C, 25° C, and 40° C.

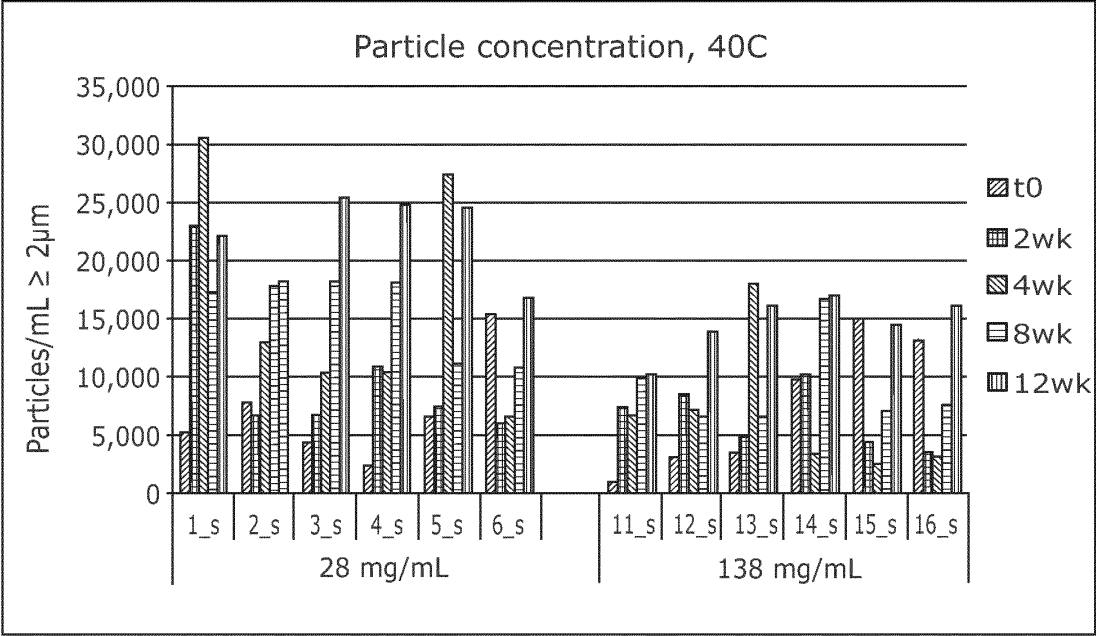


FIG. 2C

Evolution of $\geq 2\mu\text{m}$ subvisible particles in buffer formulations over 12 weeks of storage at 5° C, 25° C, and 40° C.

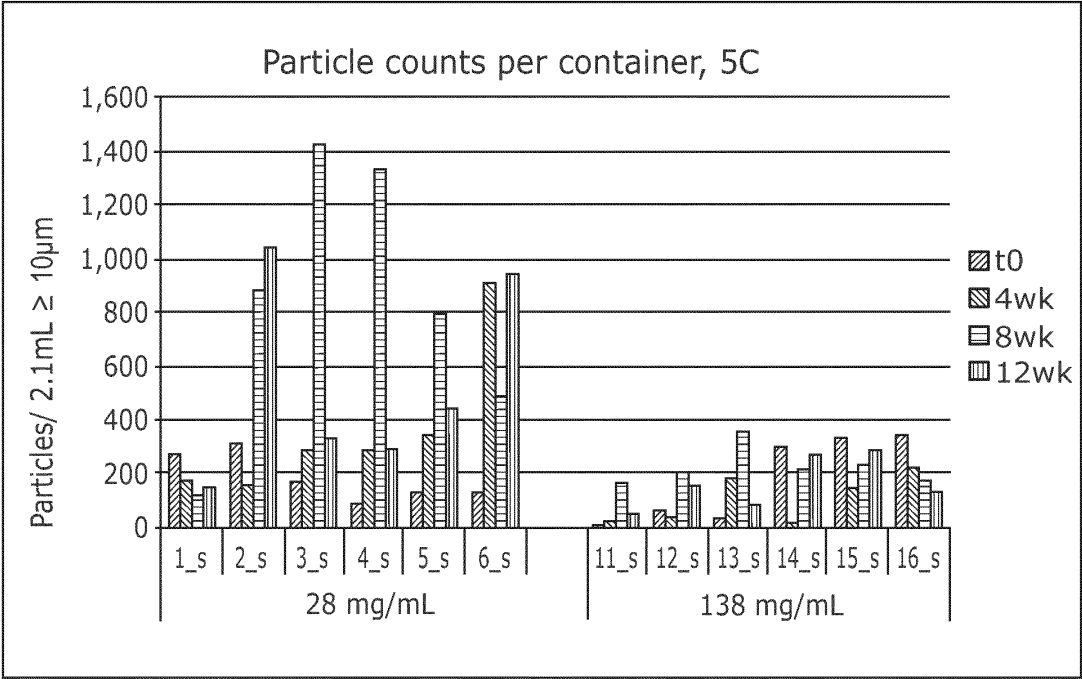


FIG. 3A

Evolution of $\geq 10\mu\text{m}$ subvisible particles in buffer formulations over 12 weeks of storage at 5° C, 25° C, and 40° C.

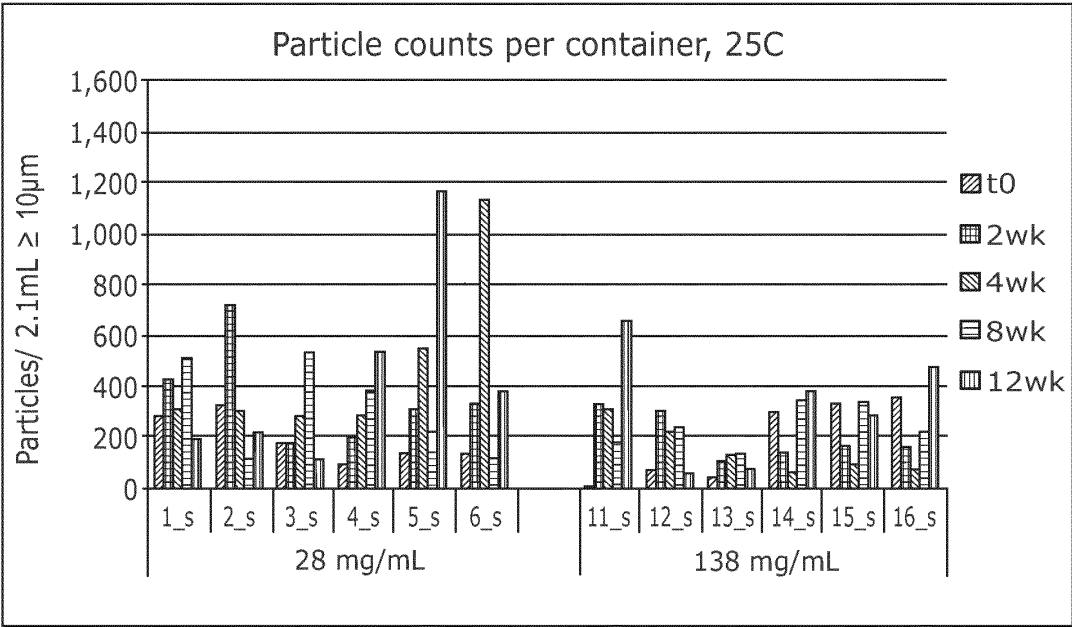


FIG. 3B

Evolution of $\geq 10\mu\text{m}$ subvisible particles in buffer formulations over 12 weeks of storage at 5° C, 25° C, and 40° C.

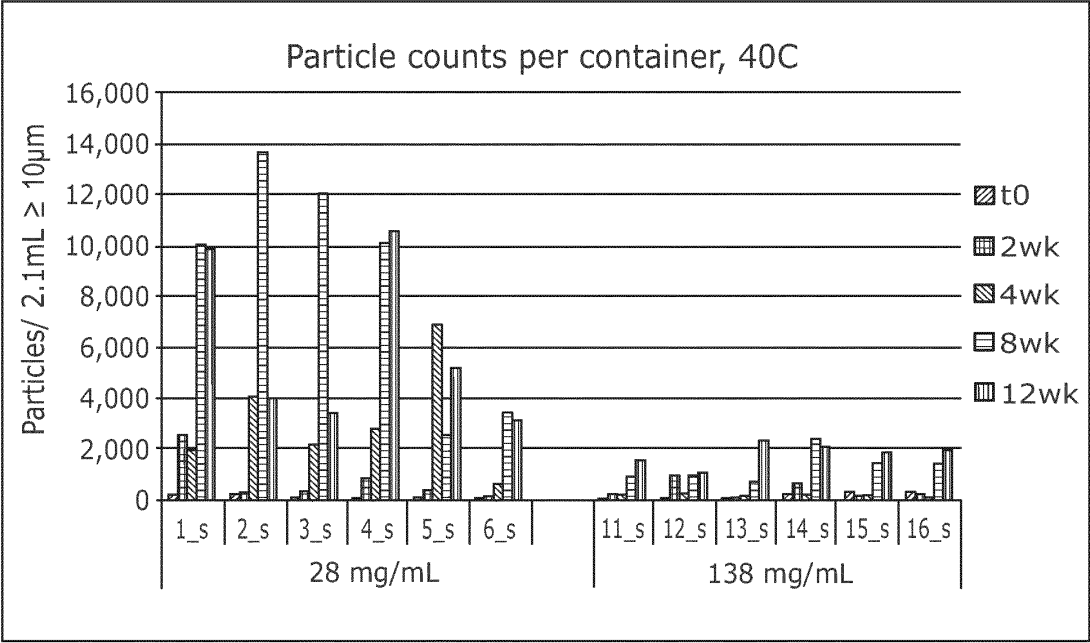


FIG. 3C

Evolution of $\geq 10\ \mu\text{m}$ subvisible particles in buffer formulations over 12 weeks of storage at 5° C, 25° C, and 40° C.

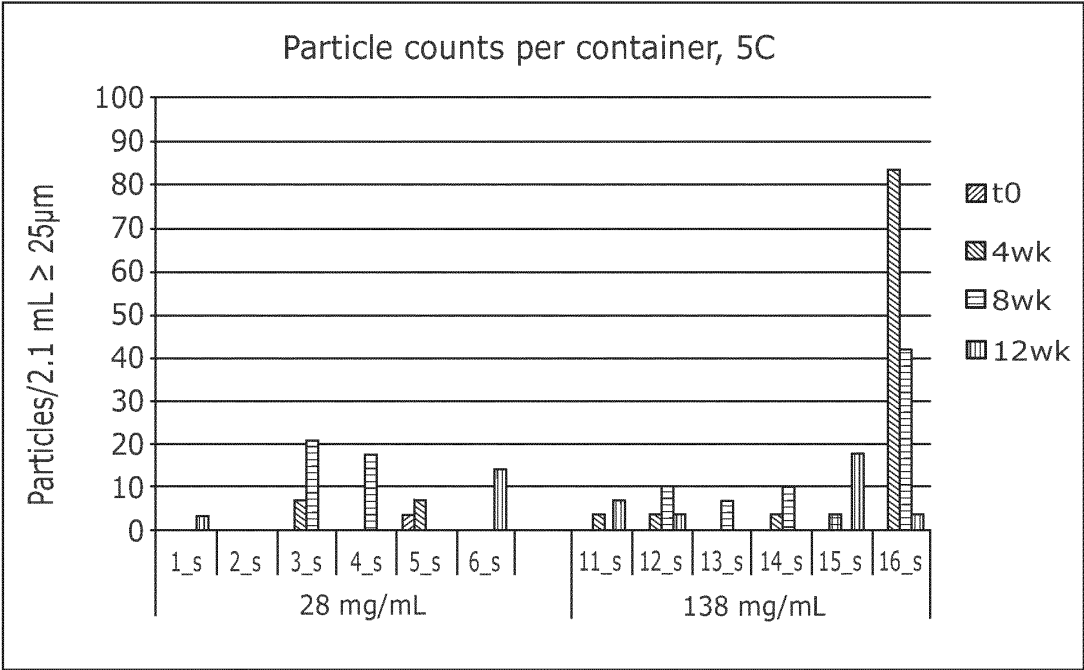


FIG. 4A

Evolution of $\geq 25\mu\text{m}$ subvisible particles in formulations over 12 weeks of storage at 5° C, 25° C, and 40° C.

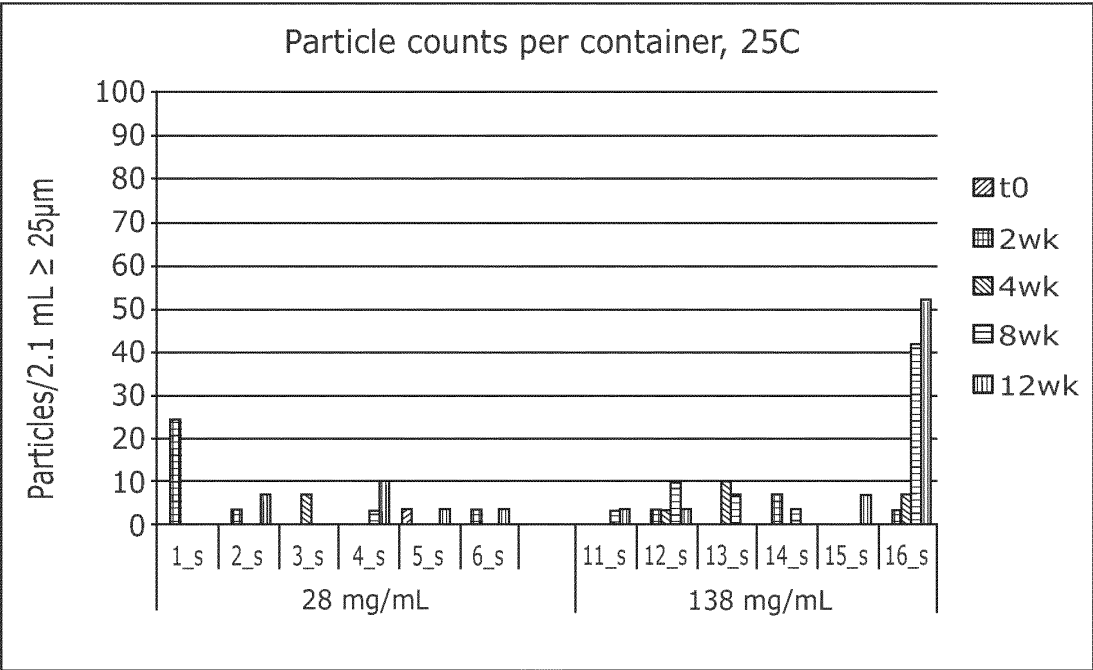


FIG. 4B

Evolution of $\geq 25\mu\text{m}$ subvisible particles in formulations over 12 weeks of storage at 5° C, 25° C, and 40° C.

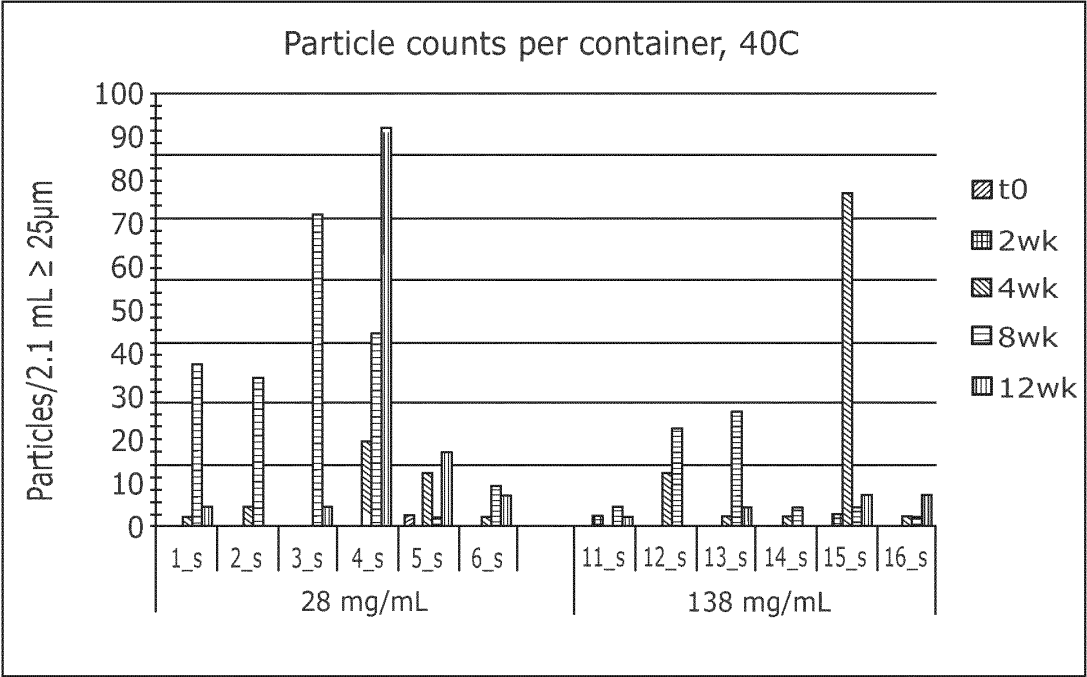


FIG. 4C

Evolution of $\geq 25\mu\text{m}$ subvisible particles in formulations over 12 weeks of storage at 5° C, 25° C, and 40° C.

Turbidity at t0 and after 12 weeks weeks of storage at 5° C, 25° C, and 40° C.

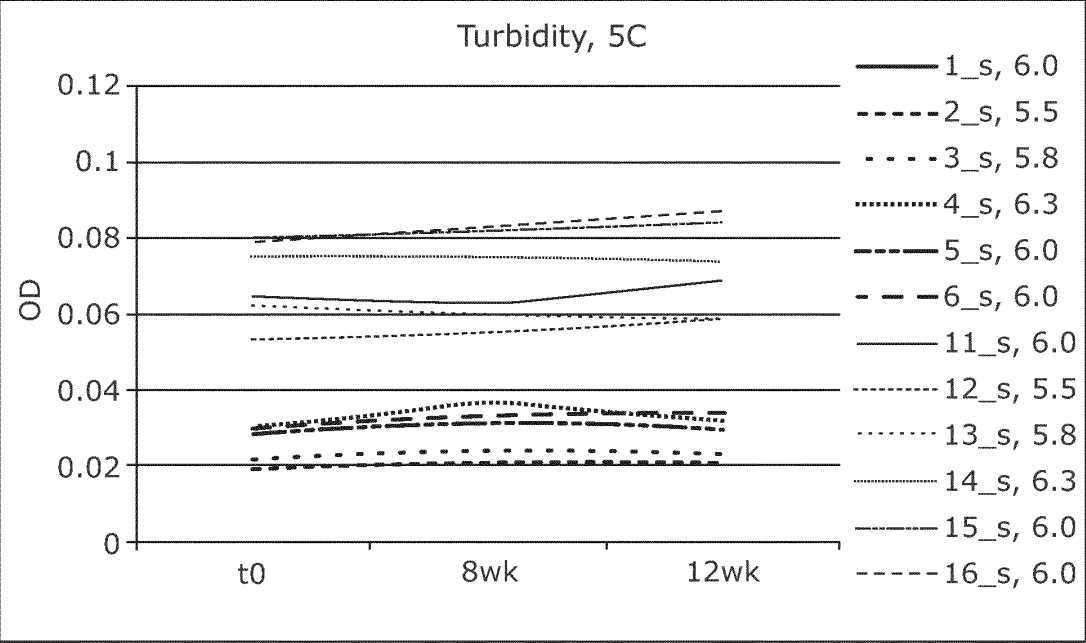


FIG. 5A

Turbidity at t0 and after 12 weeks weeks of storage at 5° C, 25° C, and 40° C.

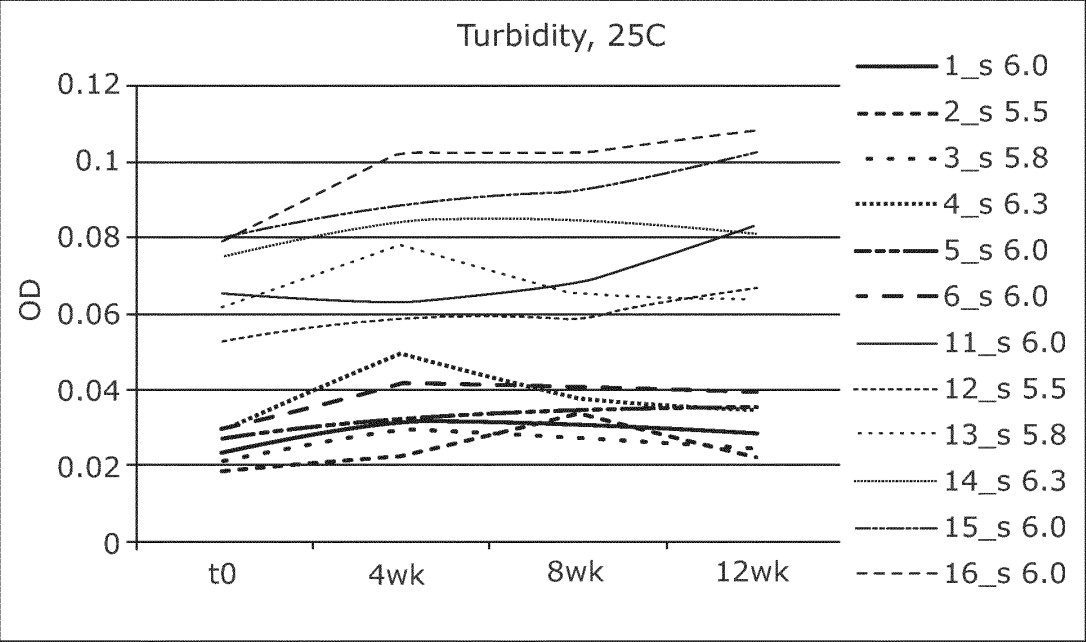


FIG. 5B

Turbidity at t0 and after 12 weeks weeks of storage at 5° C, 25° C, and 40° C.

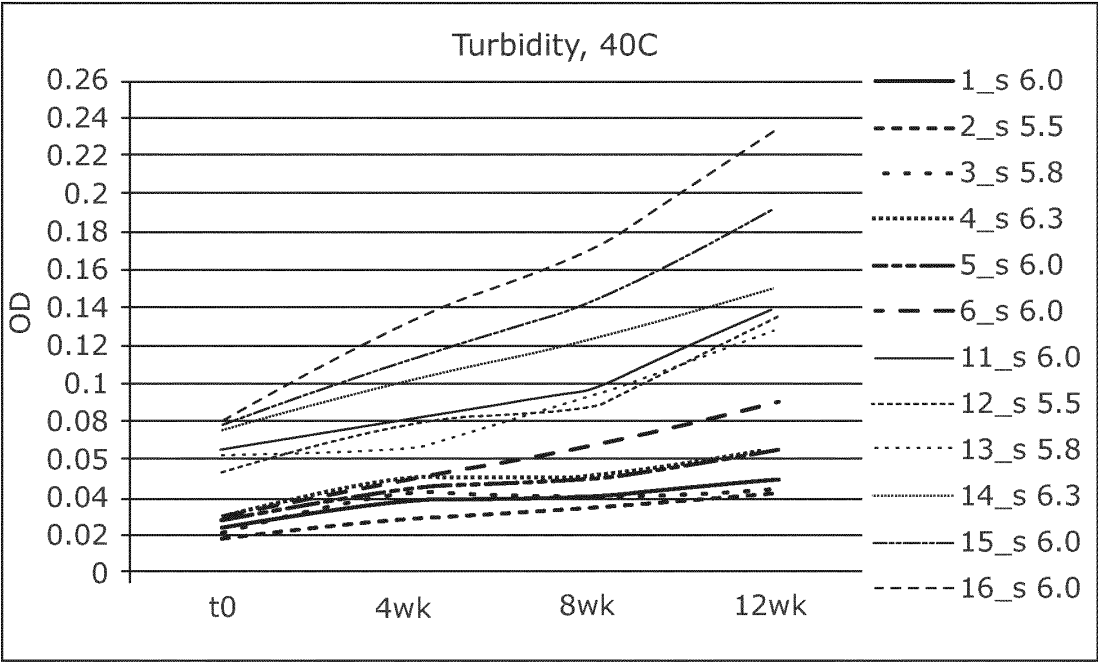


FIG. 5C

PURITY AND FRAGMENTATION BY CAPILLARY ELECTROPHORESIS

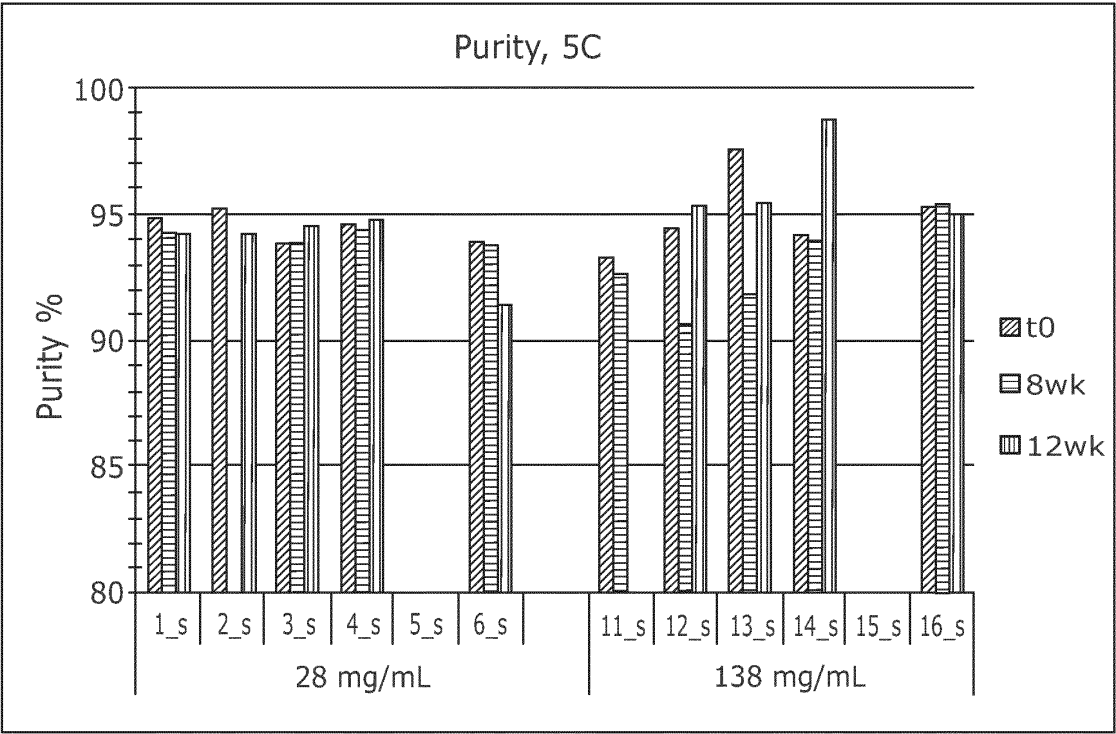


FIG. 6A

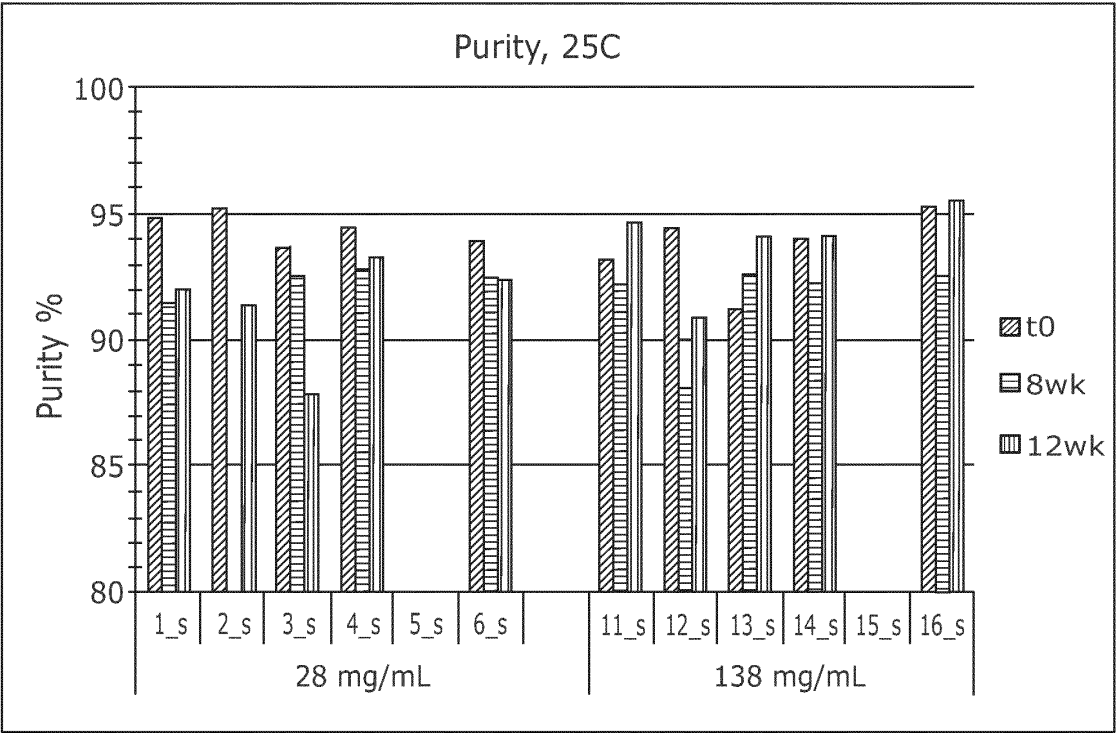


FIG. 6B

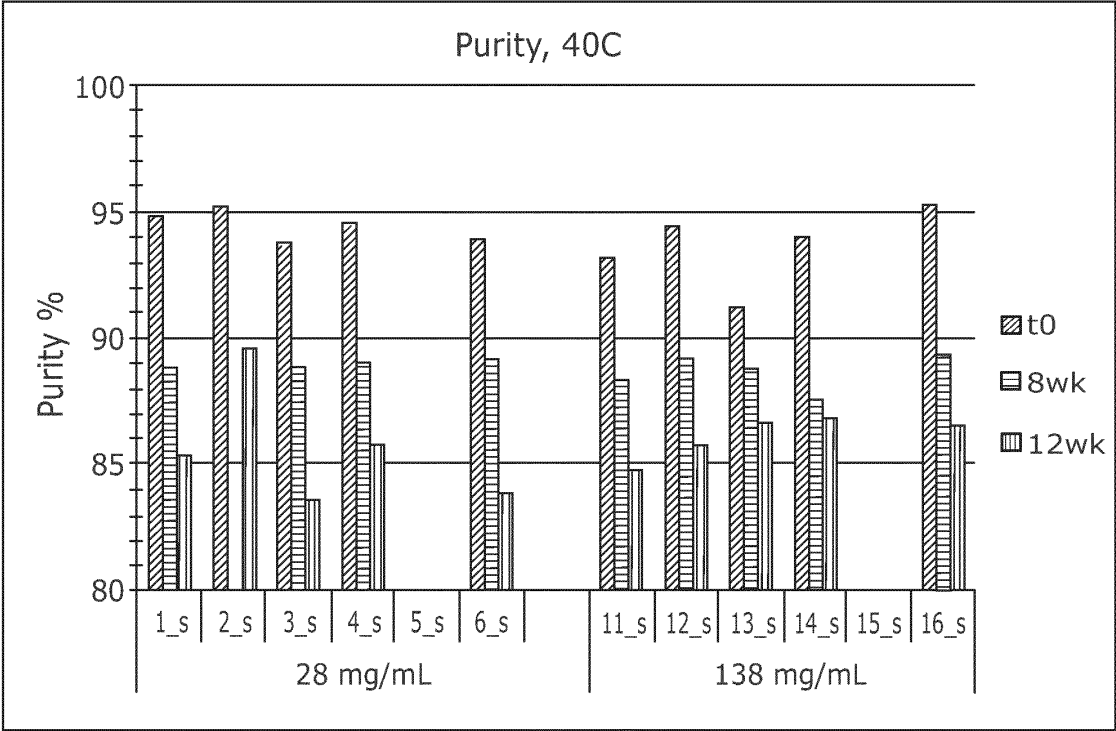


FIG. 6C

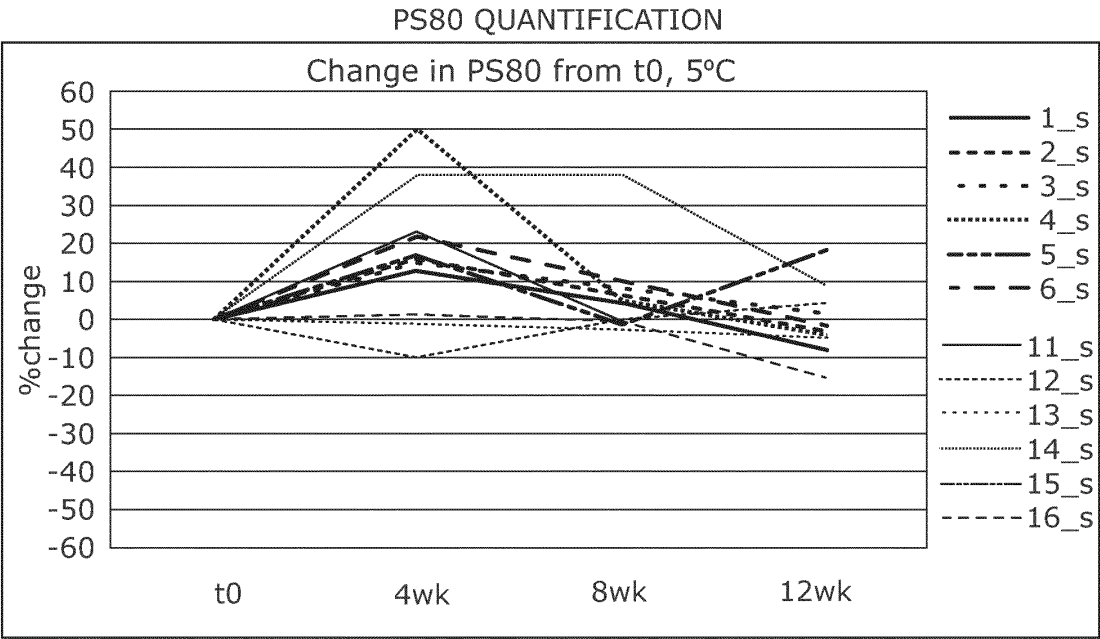


FIG. 7A

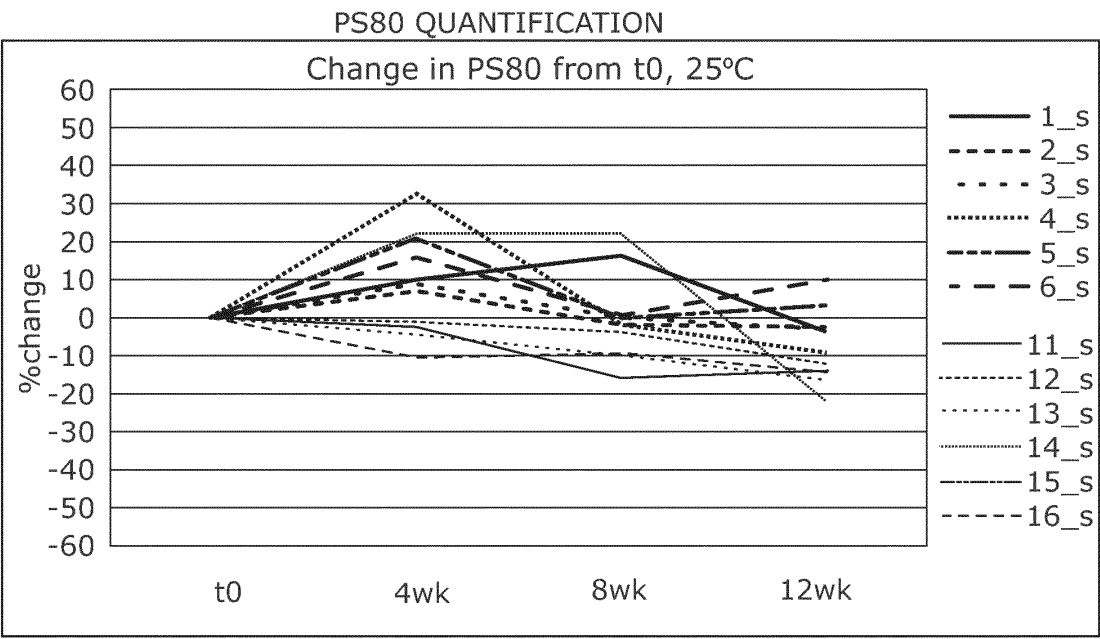


FIG. 7B

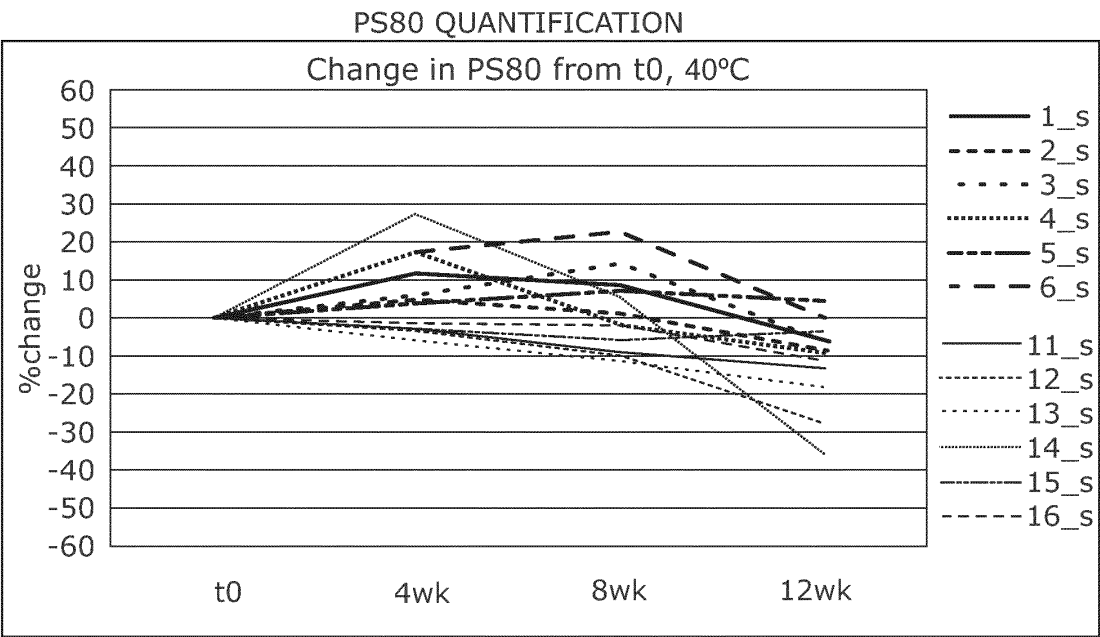


FIG. 7C

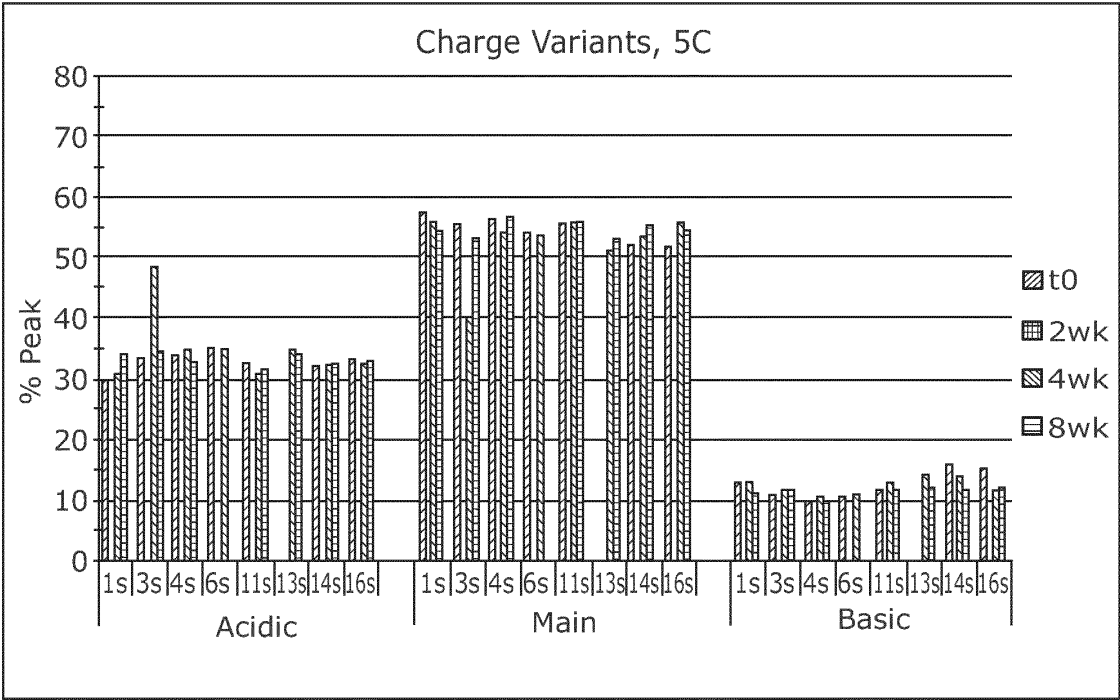


FIG. 8A

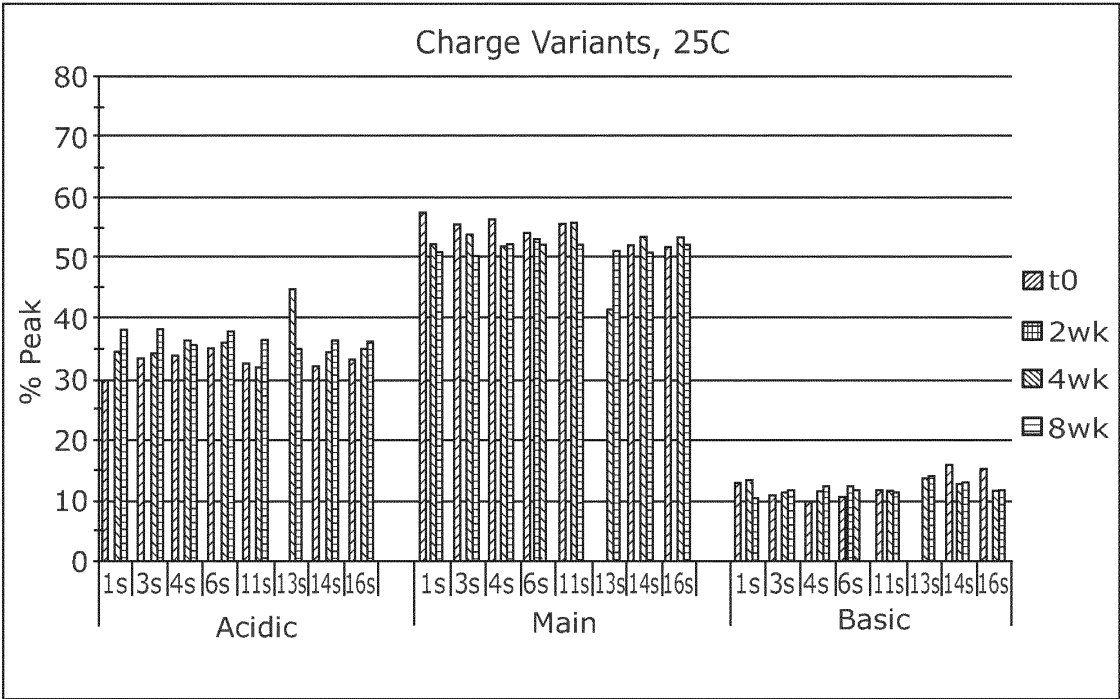


FIG. 8B

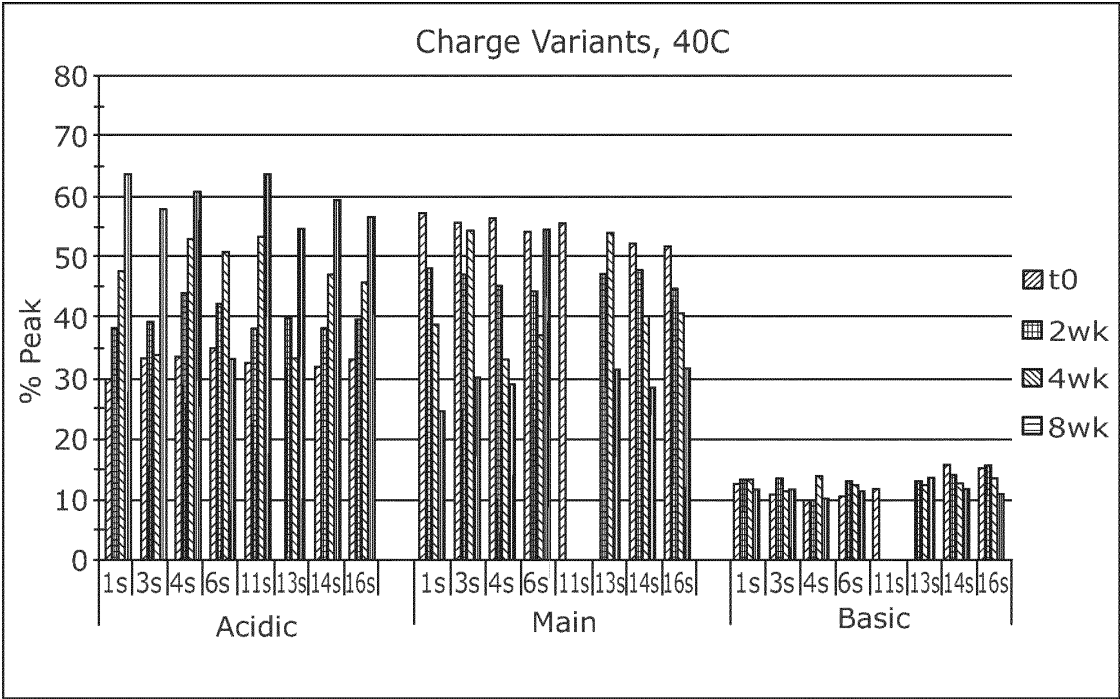


FIG. 8C

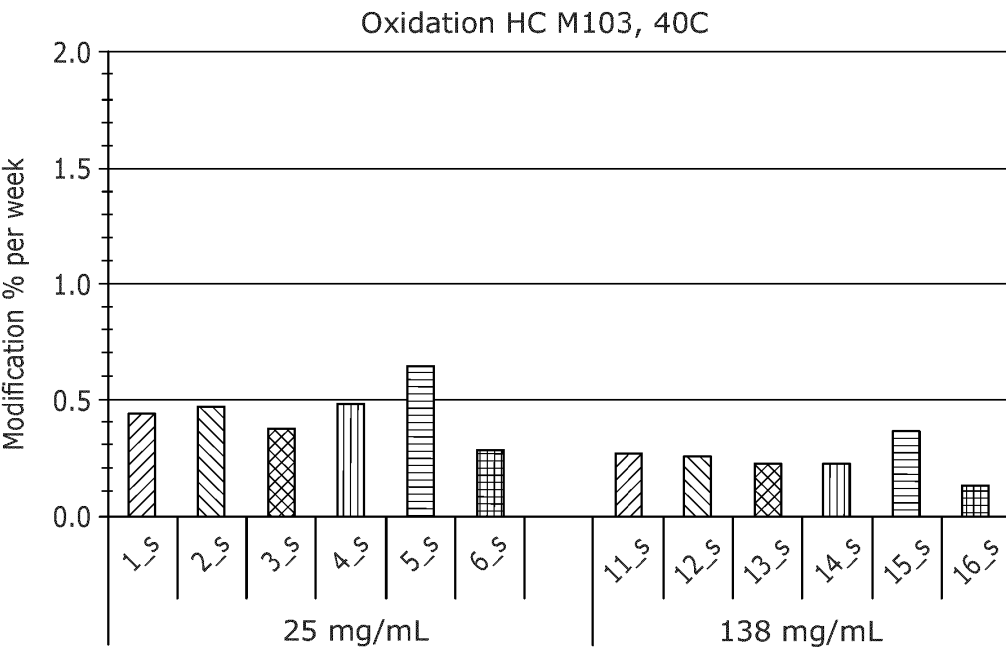


FIG. 9

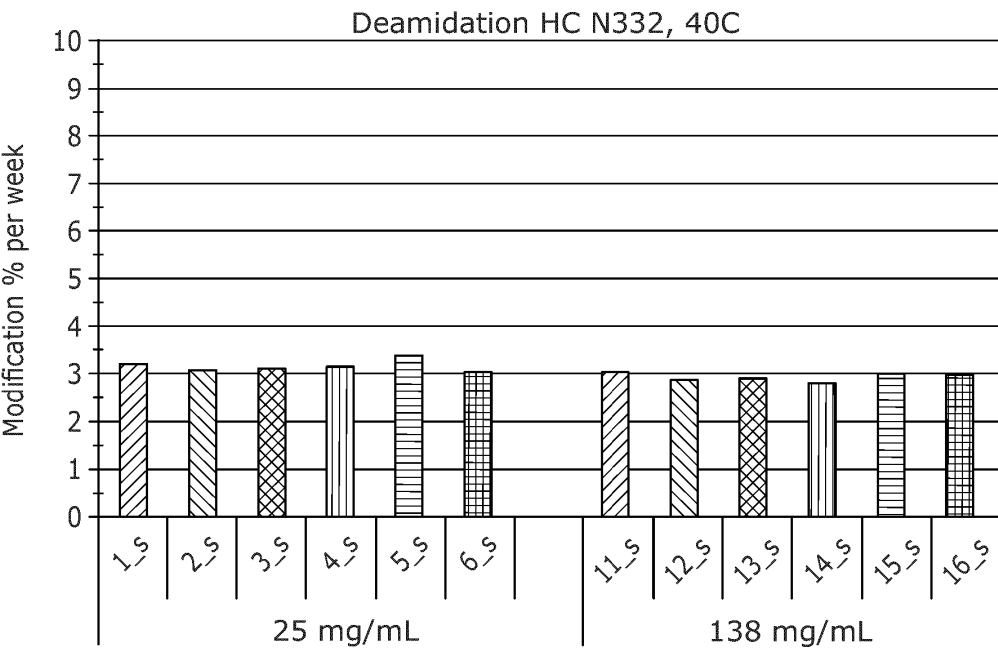


FIG. 10

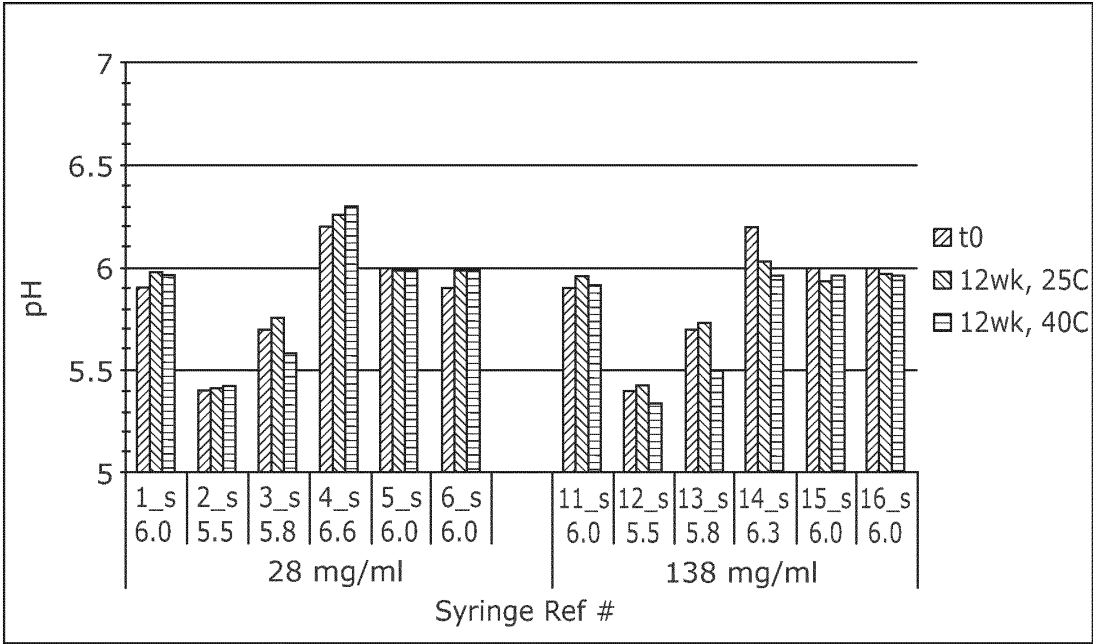


FIG. 11

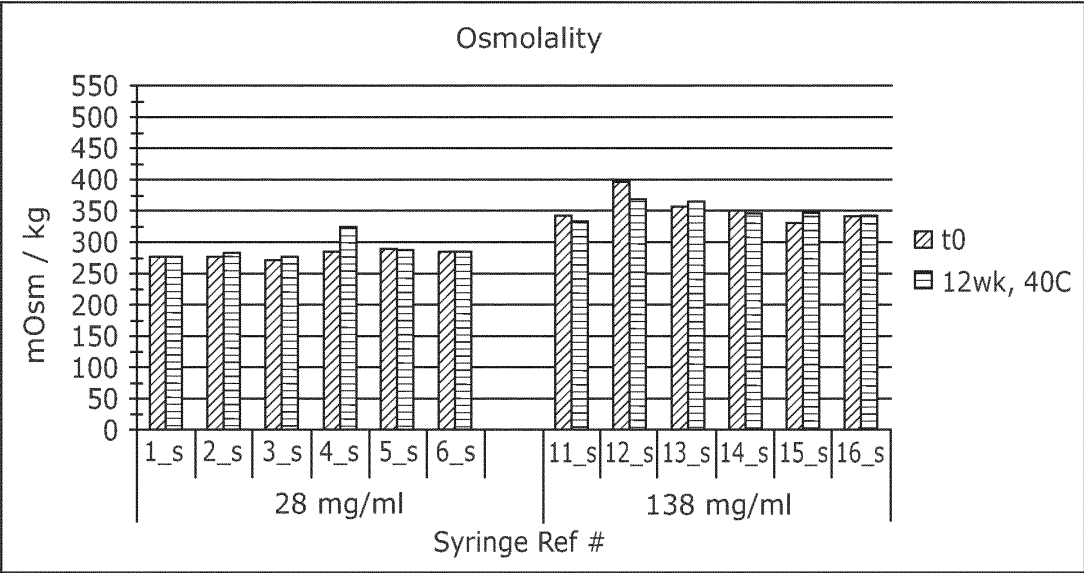


FIG. 12

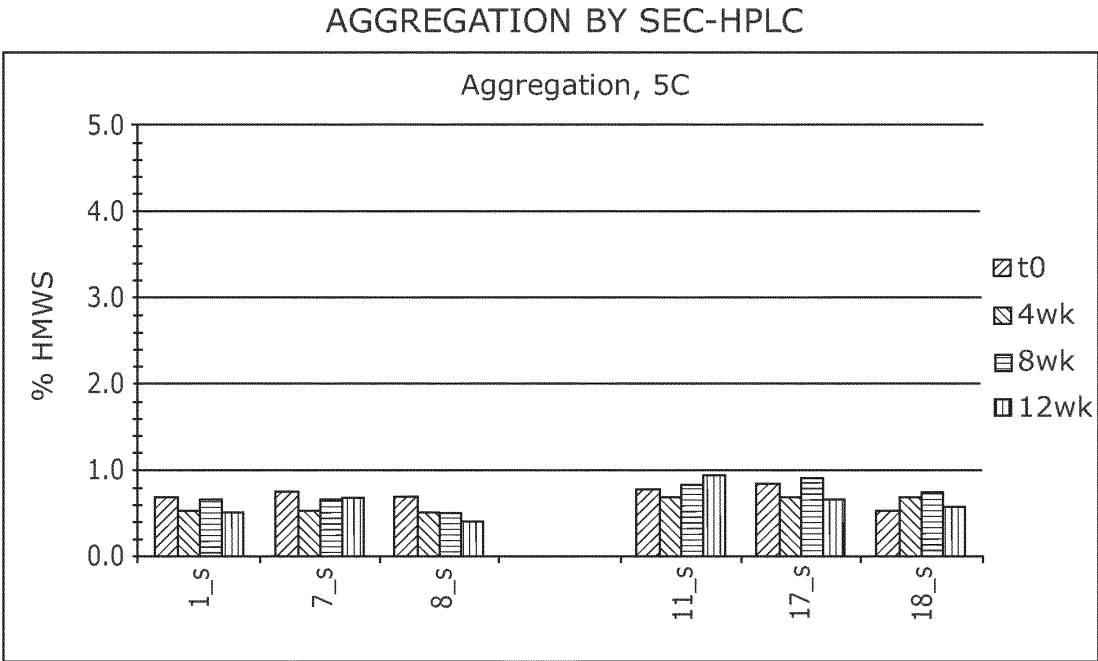


FIG. 13A

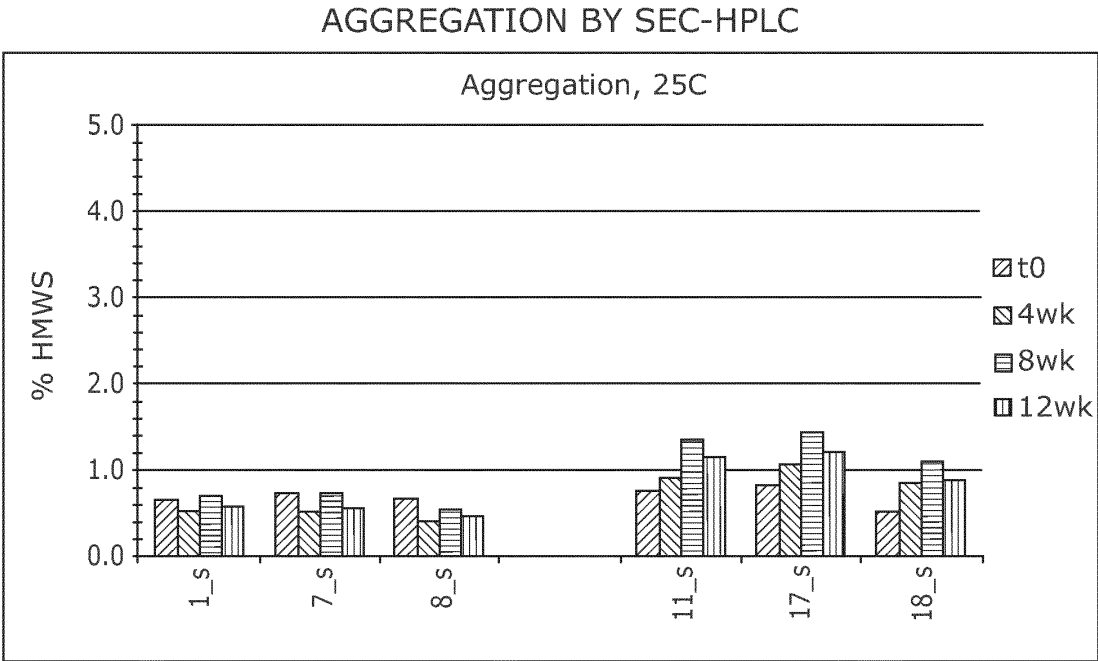


FIG. 13B

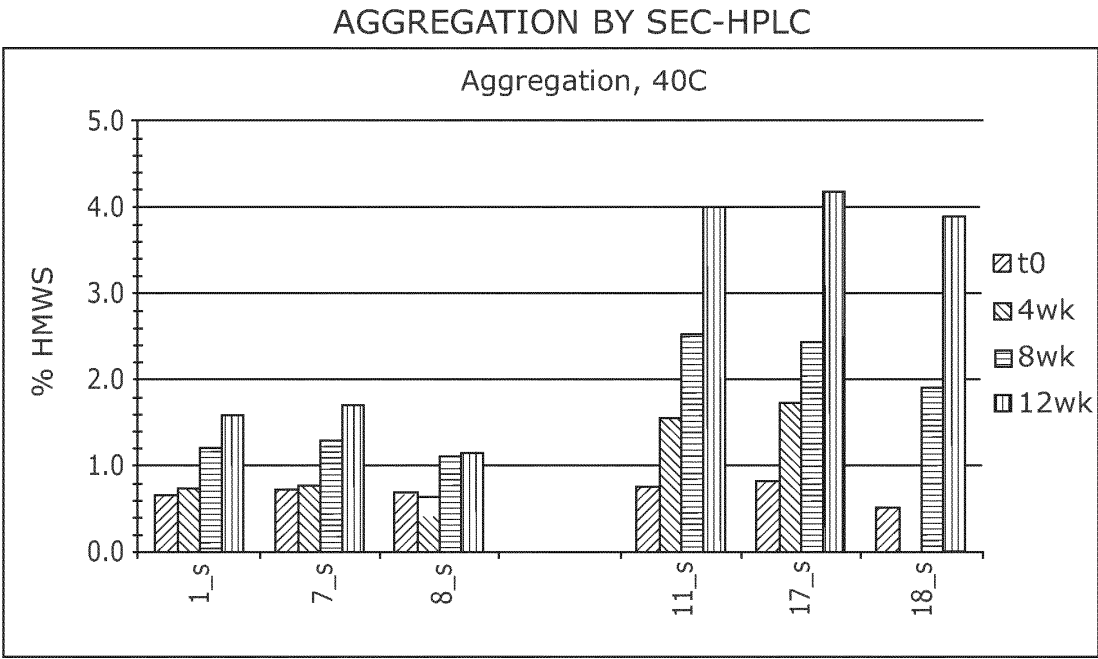


FIG. 13C

Evolution of $\geq 2\mu\text{m}$ subvisible particles in histidine-stabilizer formulations over 12 weeks of storage at 5° C, 25° C, and 40° C

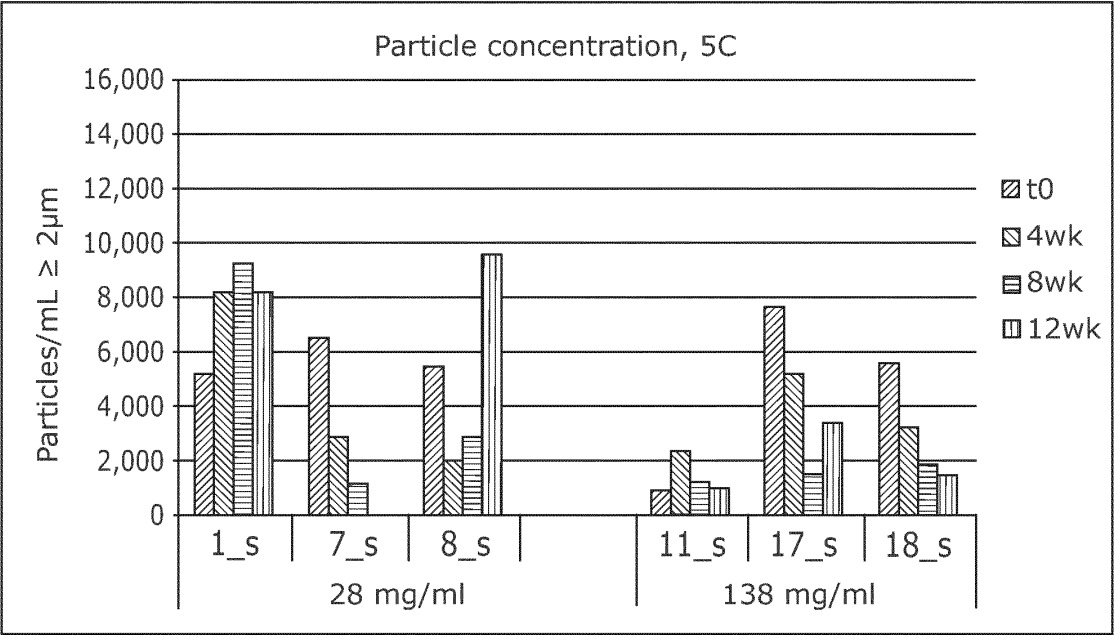


FIG. 14A

Evolution of $\geq 2\mu\text{m}$ subvisible particles in histidine-stabilizer formulations over 12 weeks of storage at 5° C, 25° C, and 40° C

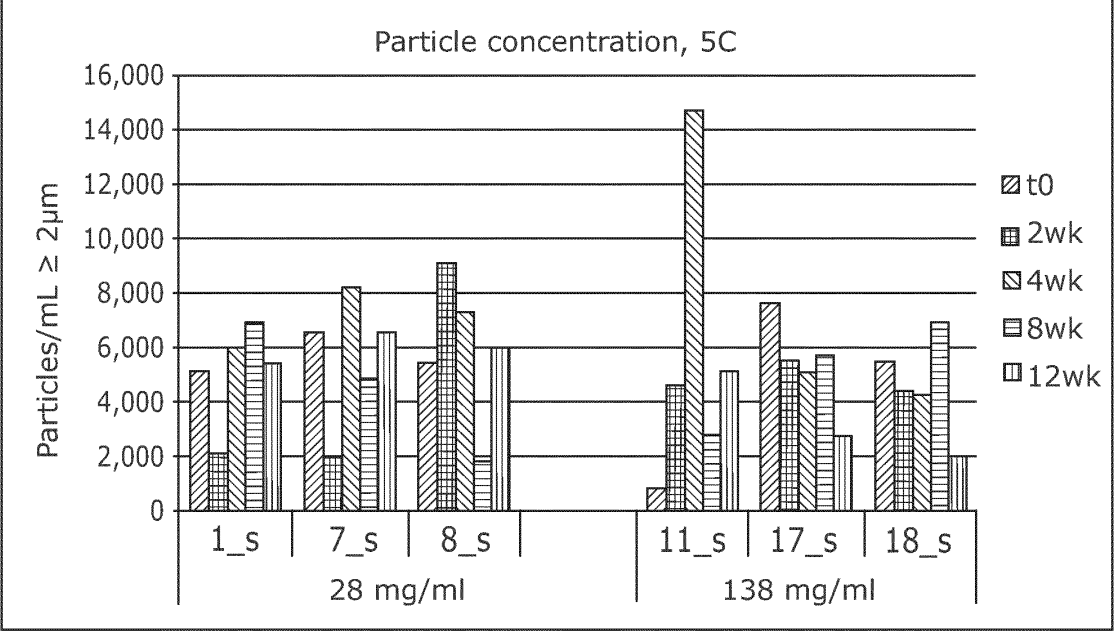


FIG. 14B

Evolution of $\geq 2\mu\text{m}$ subvisible particles in histidine-stabilizer formulations over 12 weeks of storage at 5° C, 25° C, and 40° C

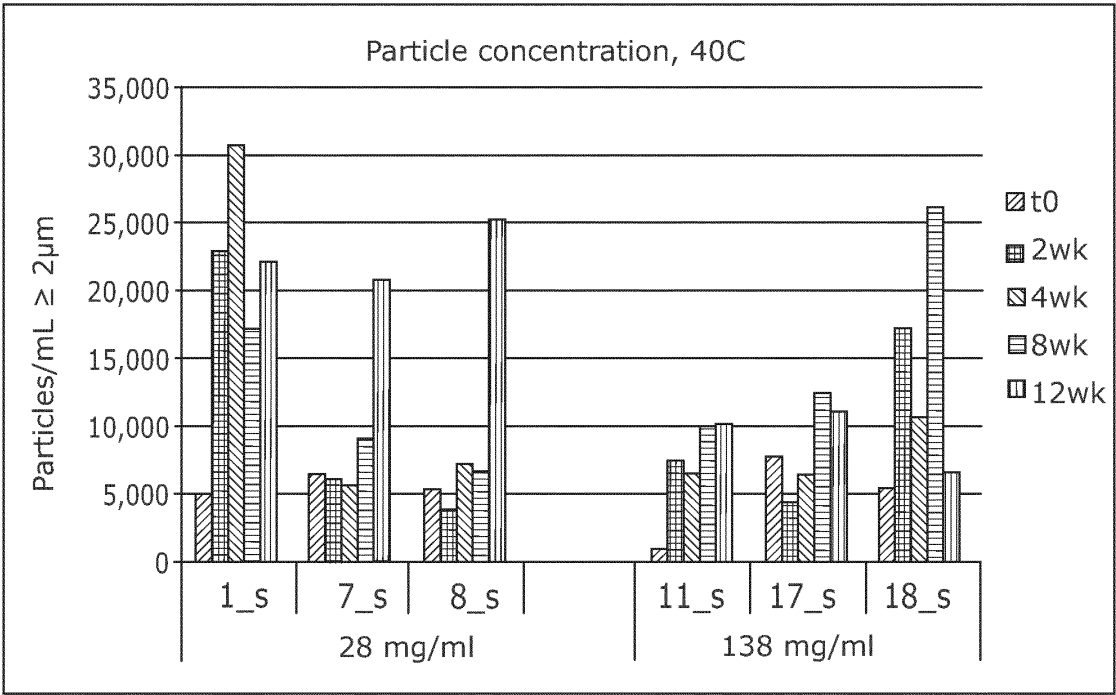


FIG. 14C

Evolution of $\geq 10\mu\text{m}$ subvisible particles in histidine-stabilizer formulations over 12 weeks of storage at 5° C, 25° C, and 40° C

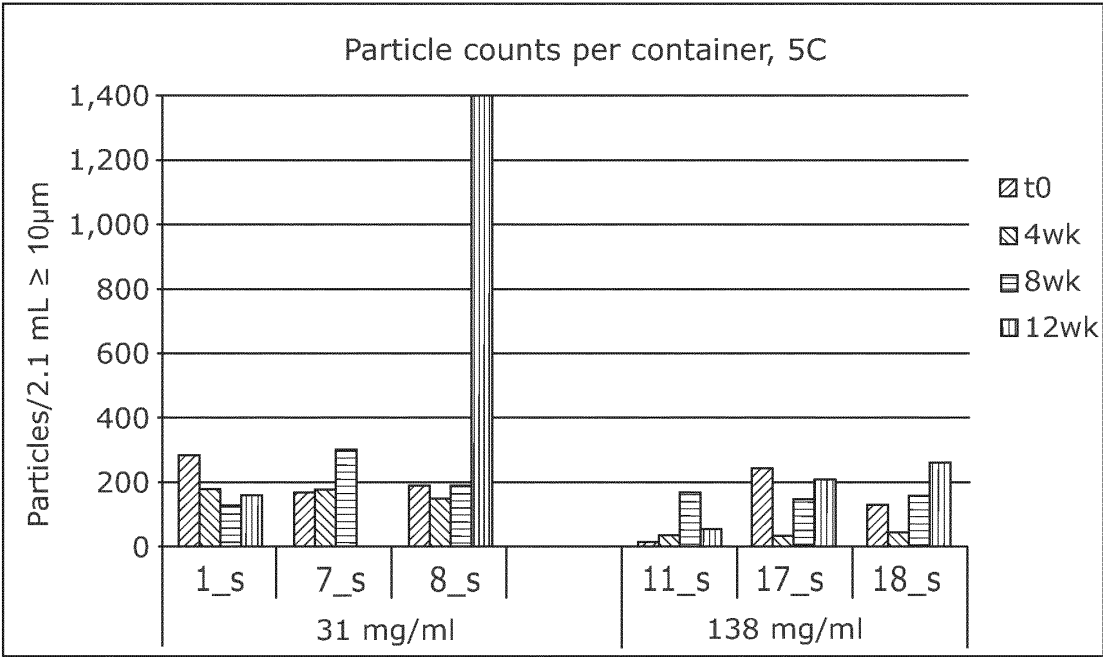


FIG. 15A

Evolution of $\geq 10\mu\text{m}$ subvisible particles in histidine-stabilizer formulations over 12 weeks of storage at 5° C, 25° C, and 40° C

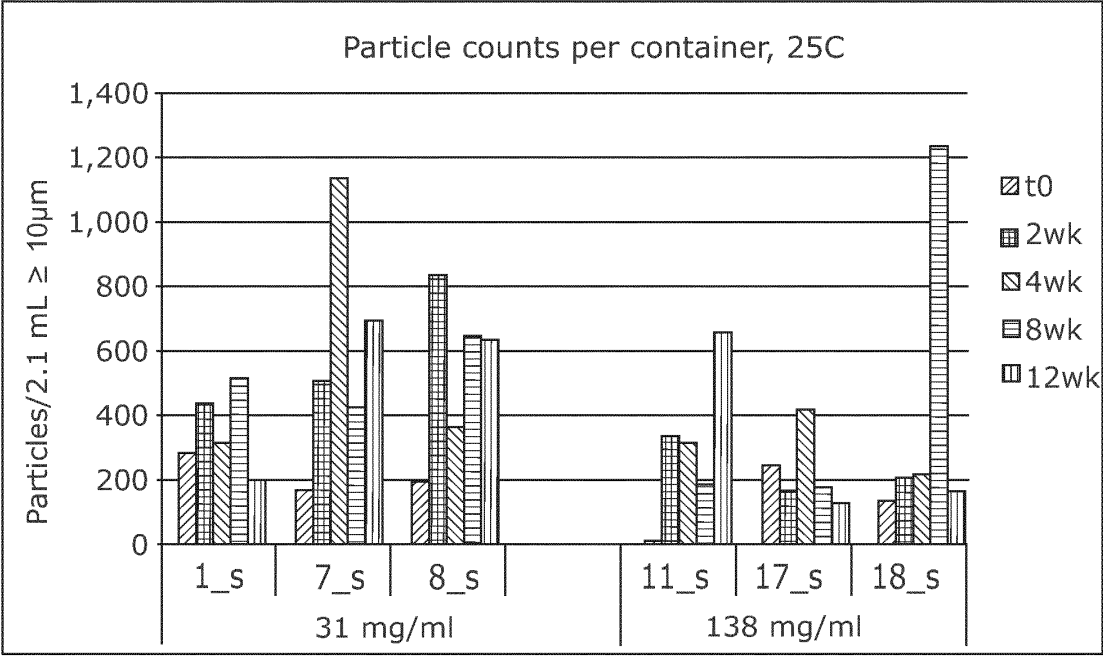


FIG. 15B

Evolution of $\geq 10\mu\text{m}$ subvisible particles in histidine-stabilizer formulations over 12 weeks of storage at 5° C, 25° C, and 40° C

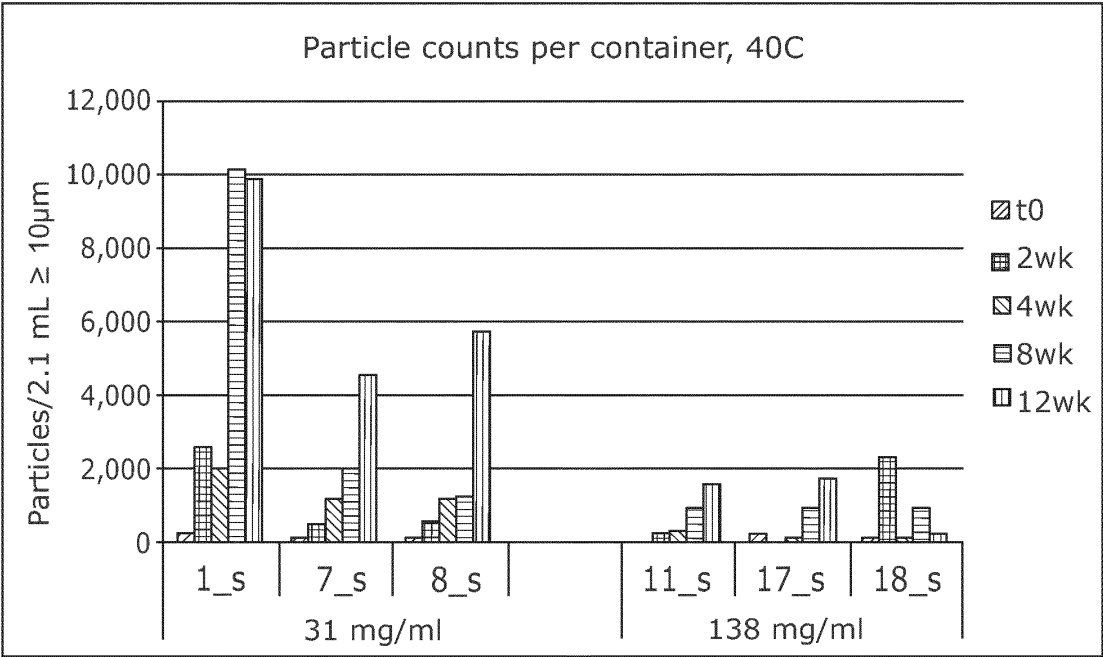


FIG. 15C

Evolution of $\geq 25\mu\text{m}$ subvisible particles in histidine-stabilizer formulations over 12 weeks of storage at 5° C, 25° C, and 40° C

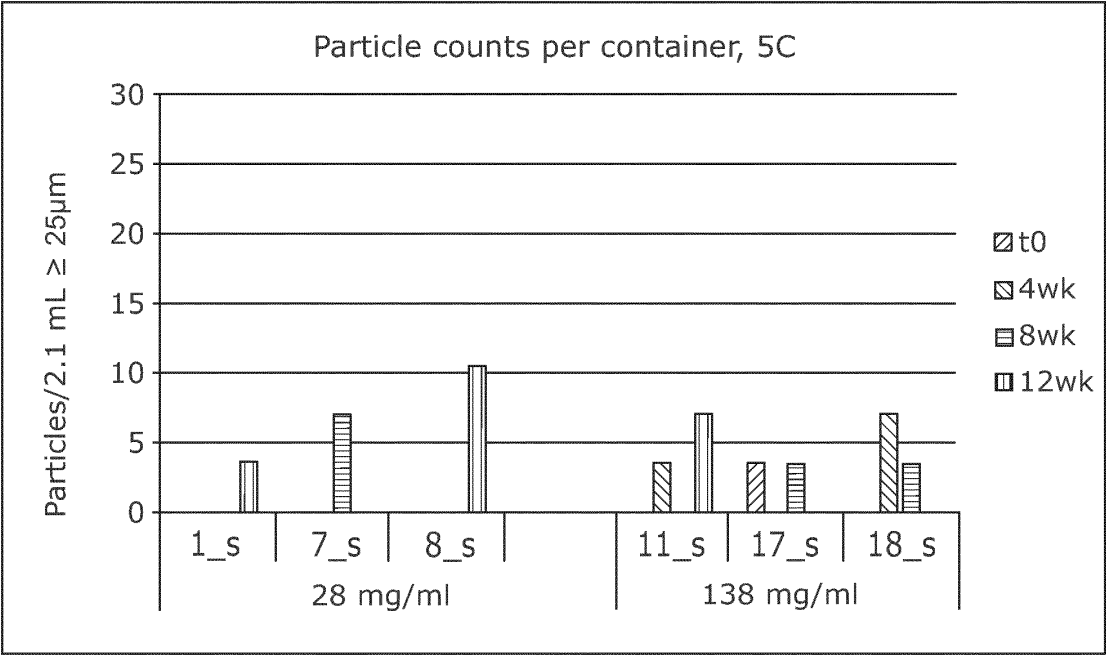


FIG. 16A

Evolution of $\geq 25\mu\text{m}$ subvisible particles in histidine-stabilizer formulations over 12 weeks of storage at 5° C, 25° C, and 40° C

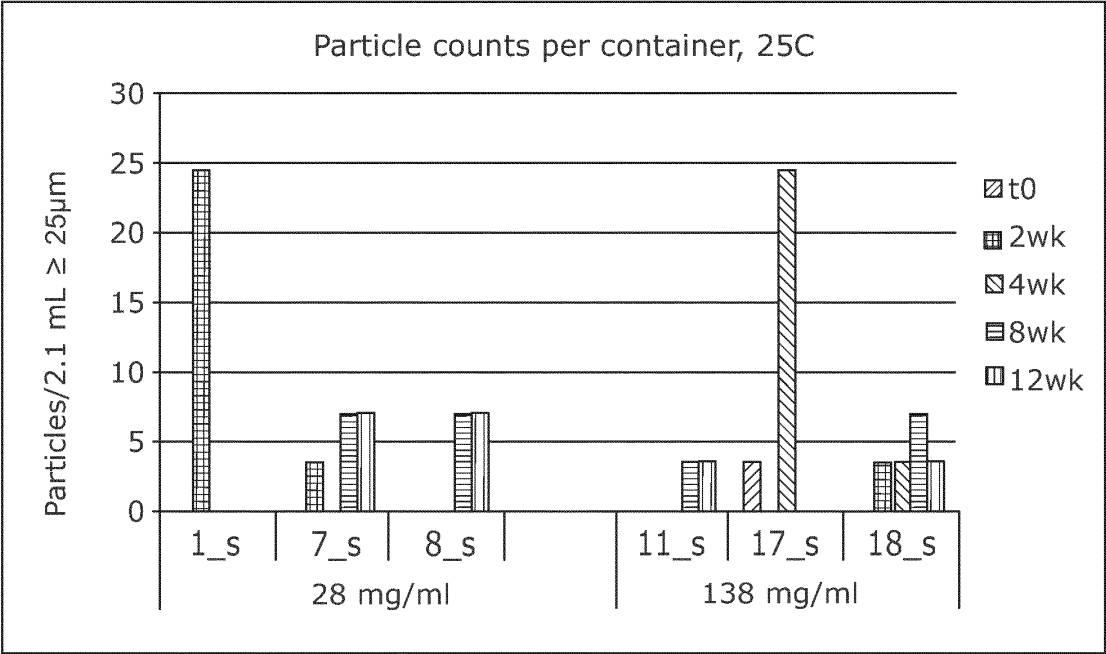


FIG. 16B

Evolution of $\geq 25\mu\text{m}$ subvisible particles in histidine-stabilizer formulations over 12 weeks of storage at 5° C, 25° C, and 40° C

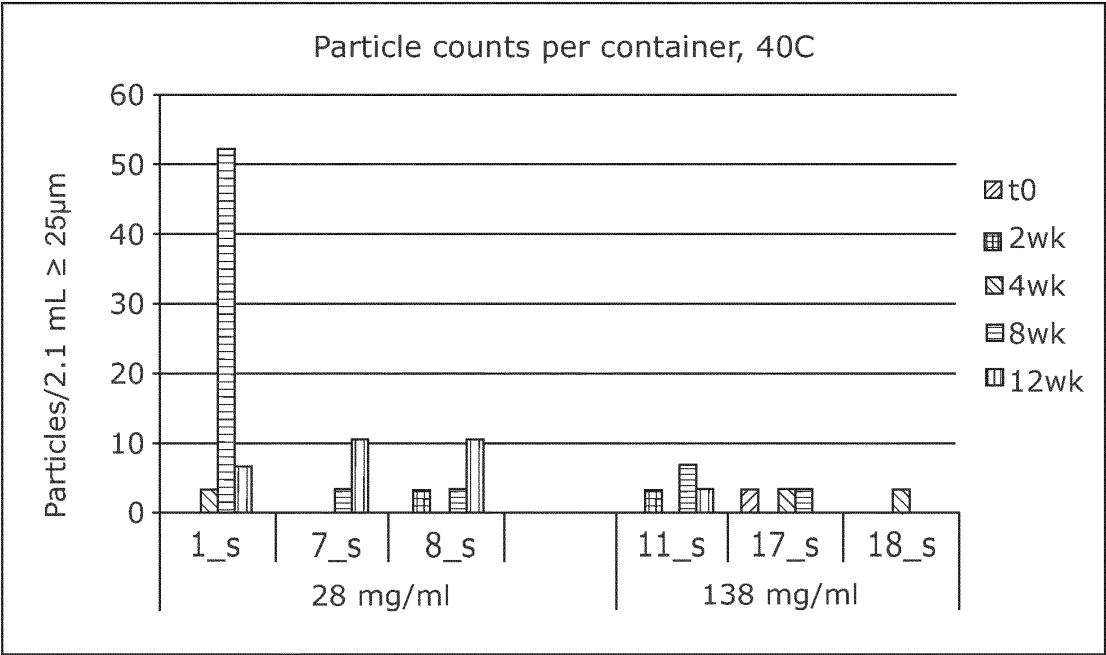


FIG. 16C

Turbidity at t0 and after 12 weeks of storage at 5° C, 25° C, and 40° C

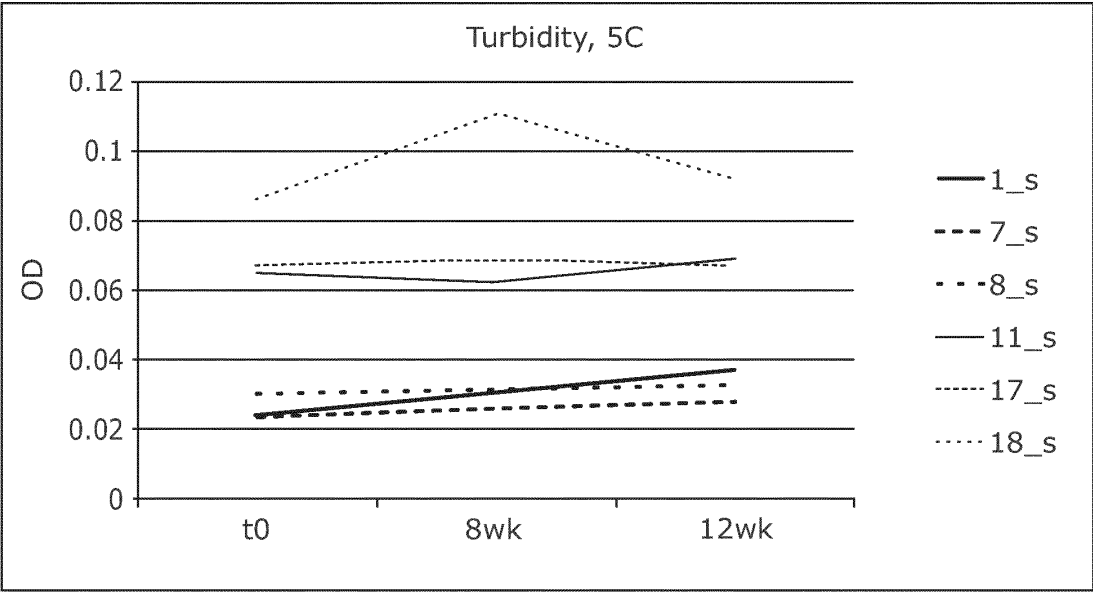


FIG. 17A

Turbidity at t0 and after 12 weeks of storage at 5° C, 25° C, and 40° C

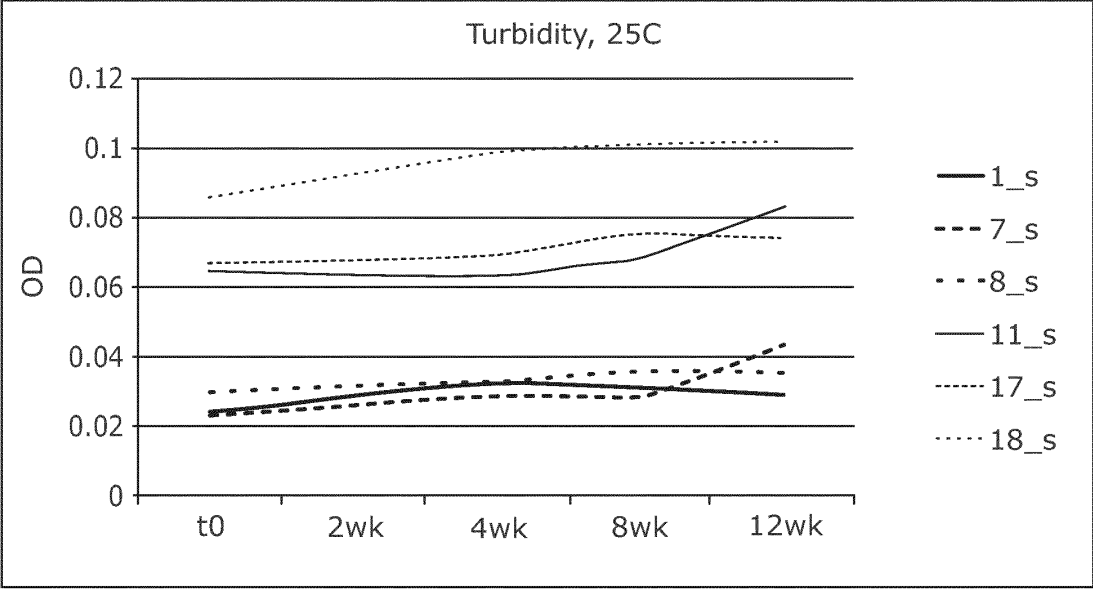


FIG. 17B

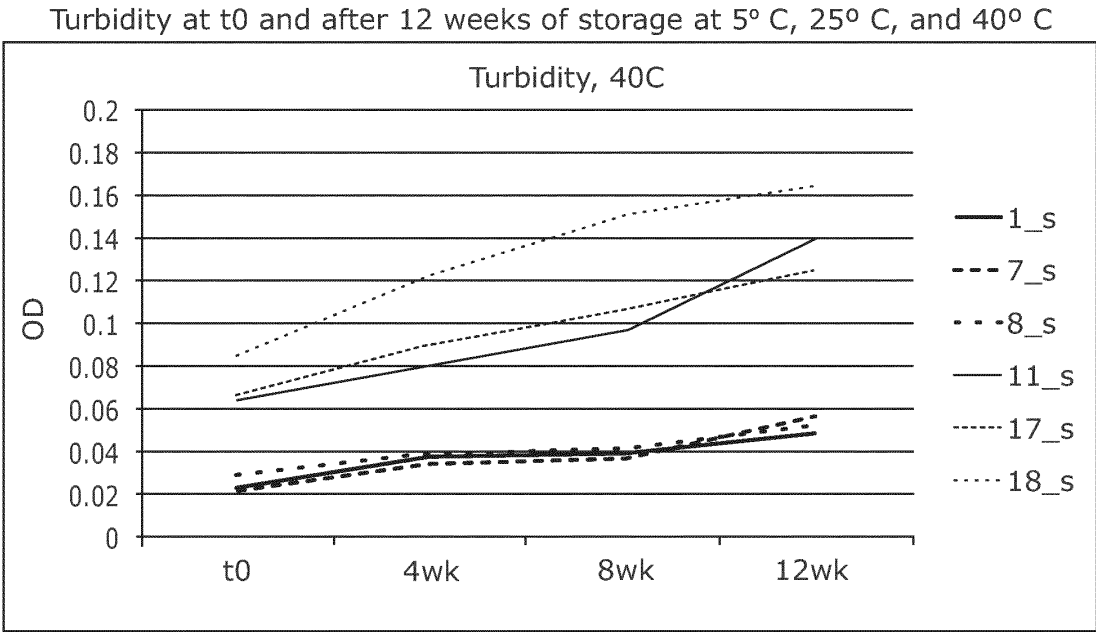


FIG. 17C

PS80 quantification after 12 weeks of storage at 5° C, 25° C, and 40° C

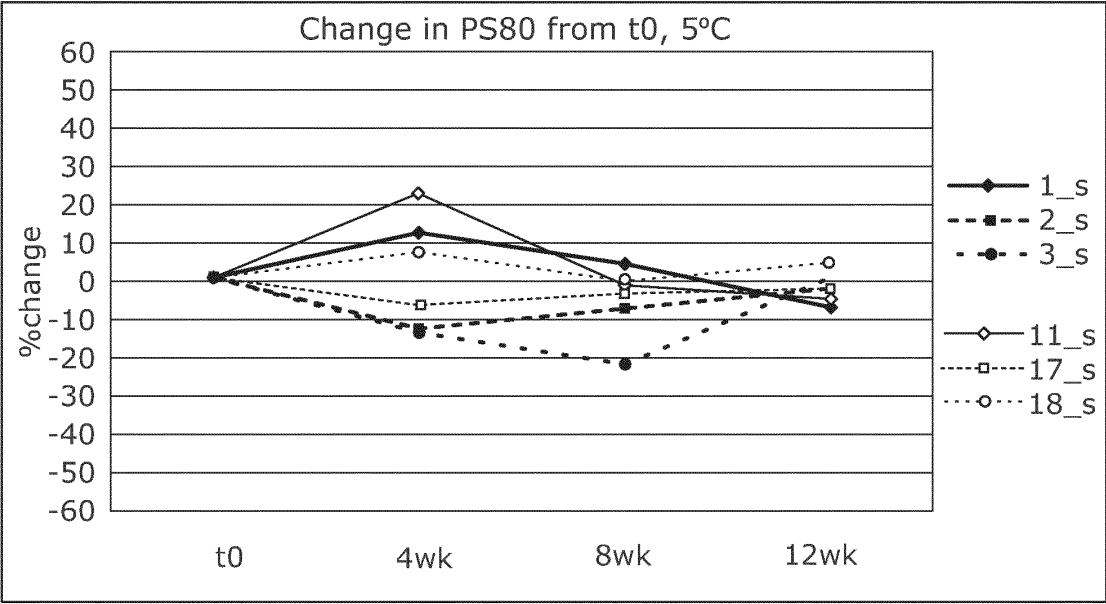


FIG. 18A

PS80 quantification after 12 weeks of storage at 5° C, 25° C, and 40° C

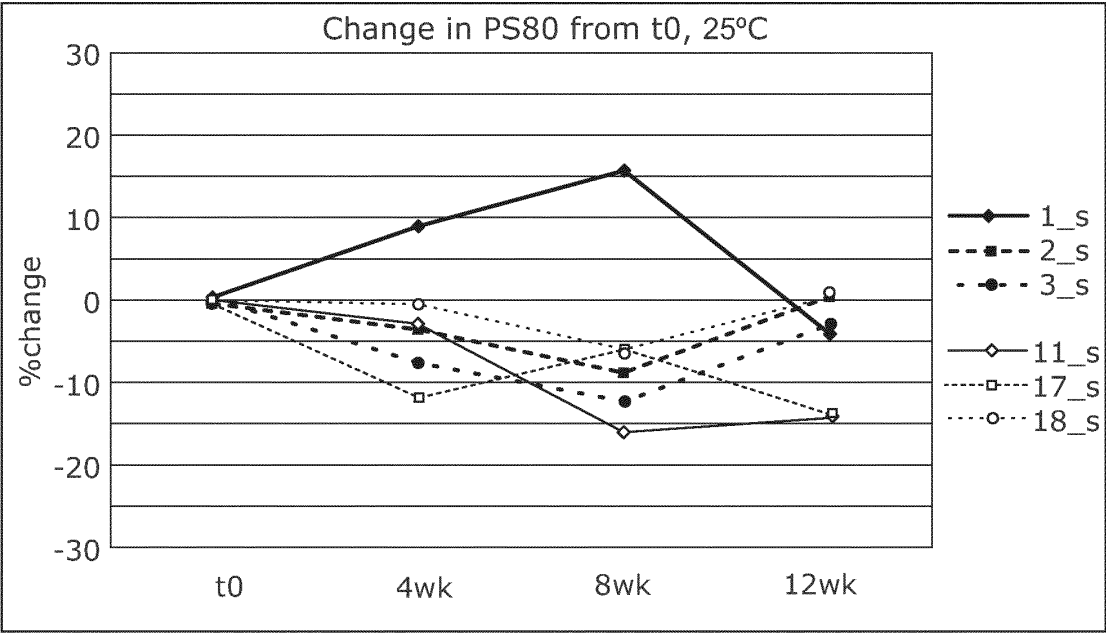


FIG. 18B

PS80 quantification after 12 weeks of storage at 5° C, 25° C, and 40° C

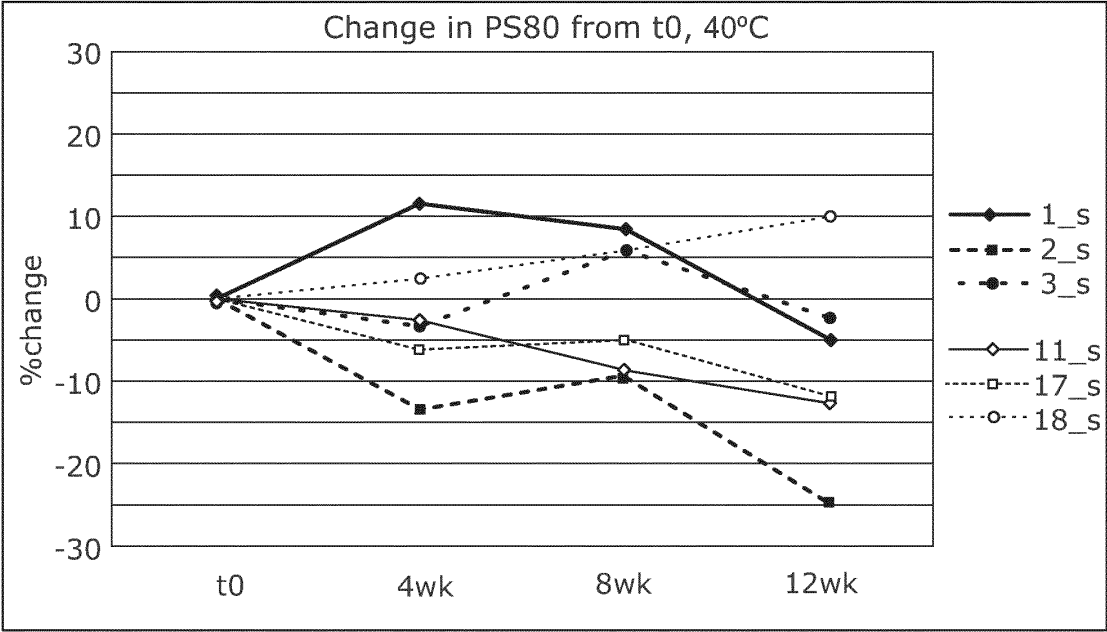


FIG. 18C

HMWS evolution in Ompi and BD syringes over 12 weeks of storage at 5 °C, 25 °C, and 40 °C

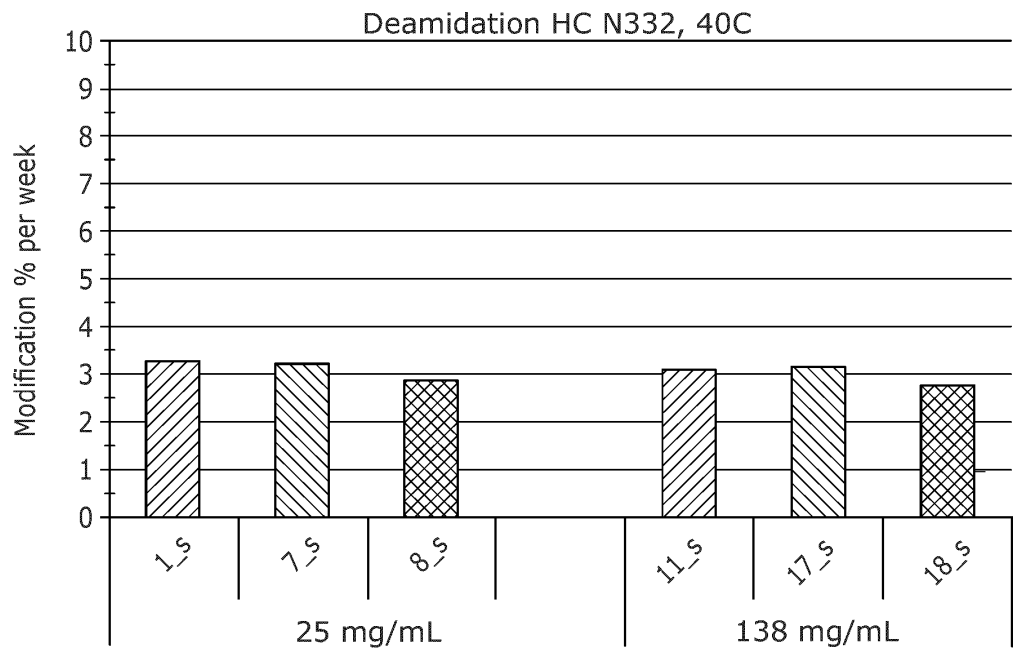


FIG. 19

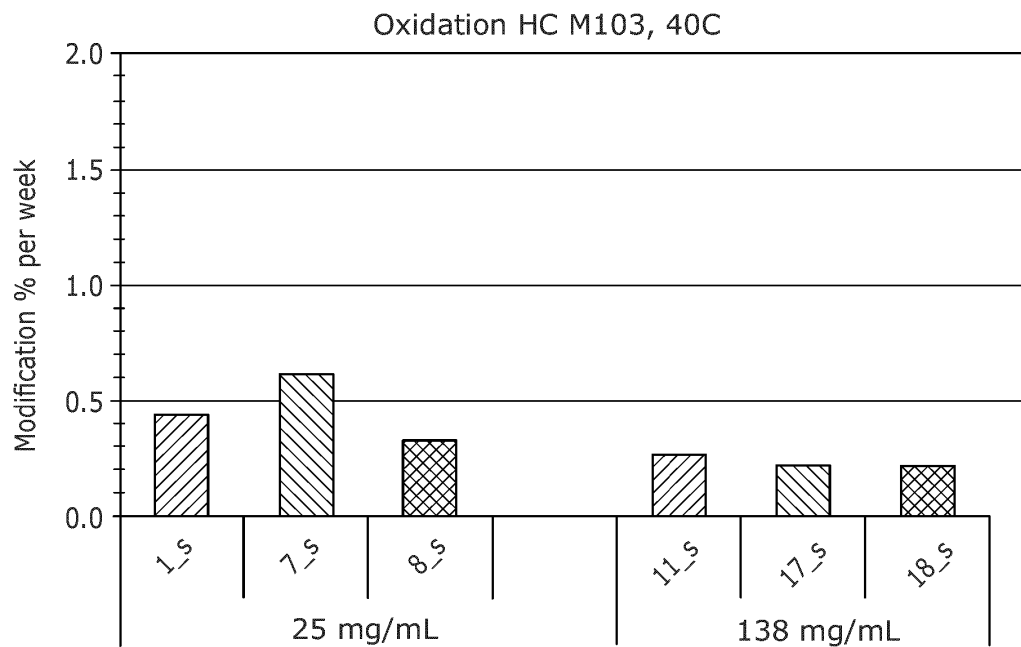


FIG. 20

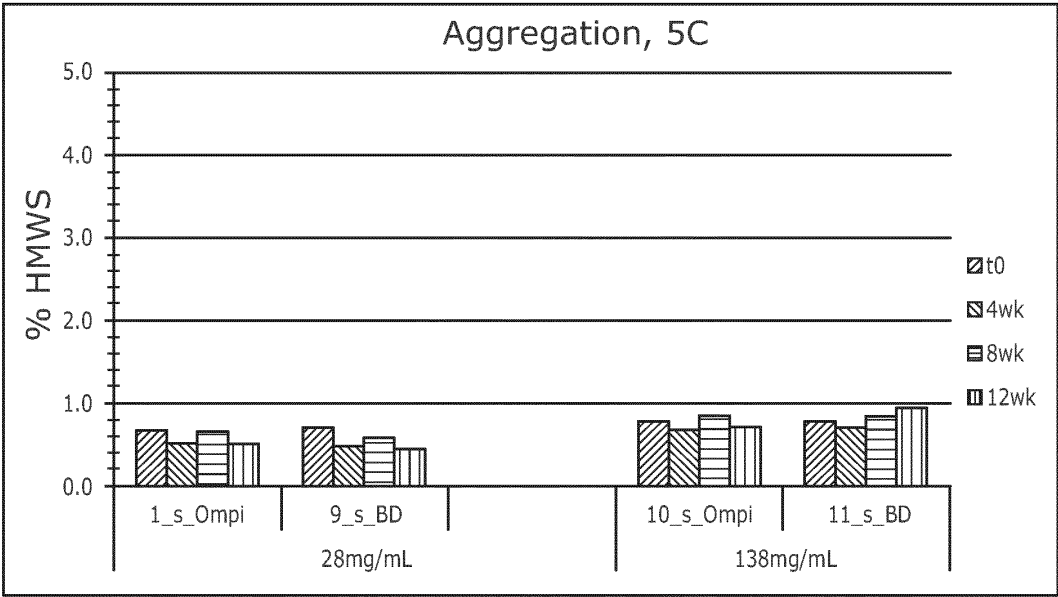


FIG. 21A

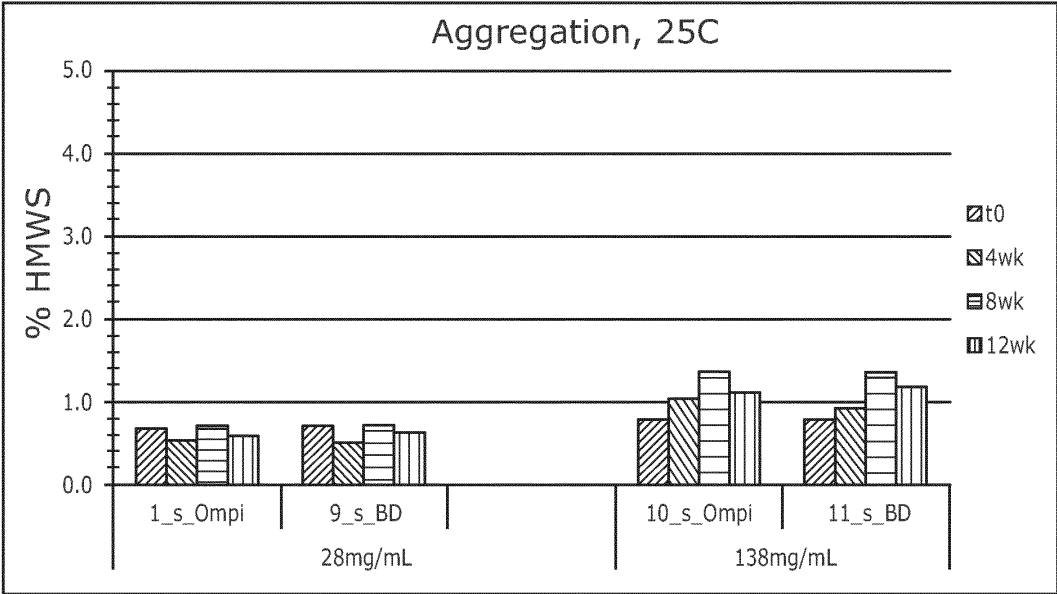


FIG. 21B

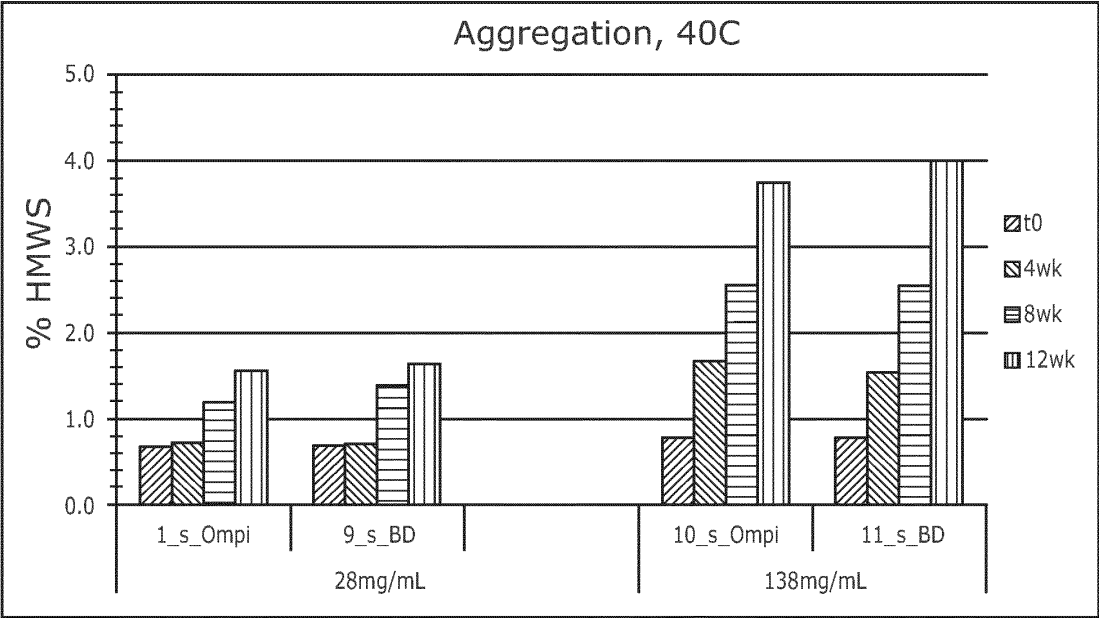


FIG. 21C

subvisible particles $\geq 2 \mu\text{m}$ in Ompi and BD syringes
over 12 weeks of storage at 5° C, 25° C, and 40° C

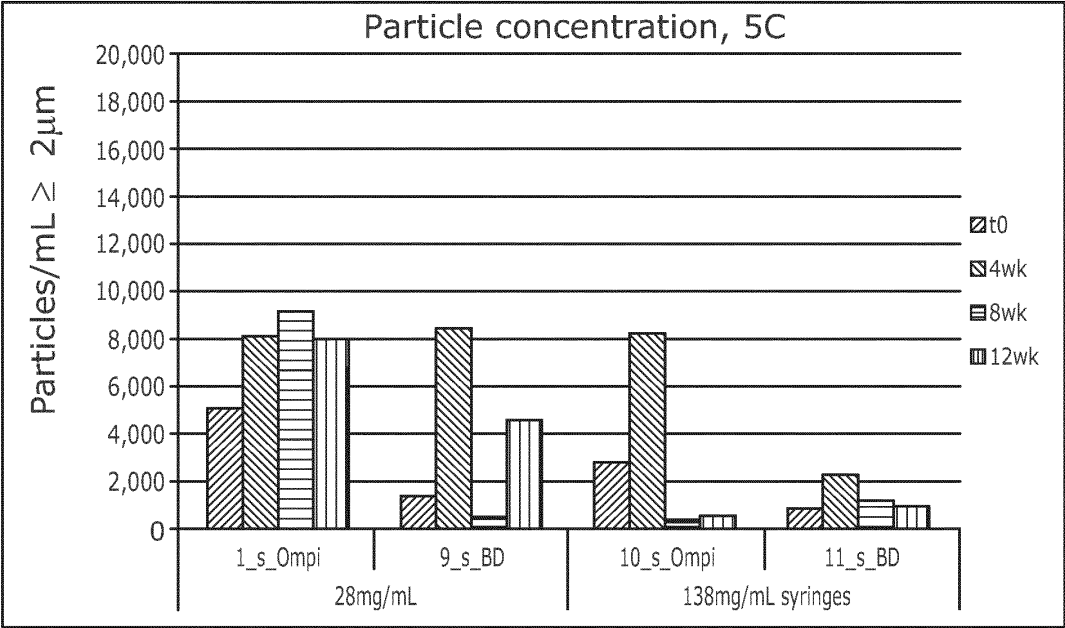


FIG. 22A

subvisible particles $\geq 2 \mu\text{m}$ in Ompi and BD syringes
over 12 weeks of storage at 5° C, 25° C, and 40° C

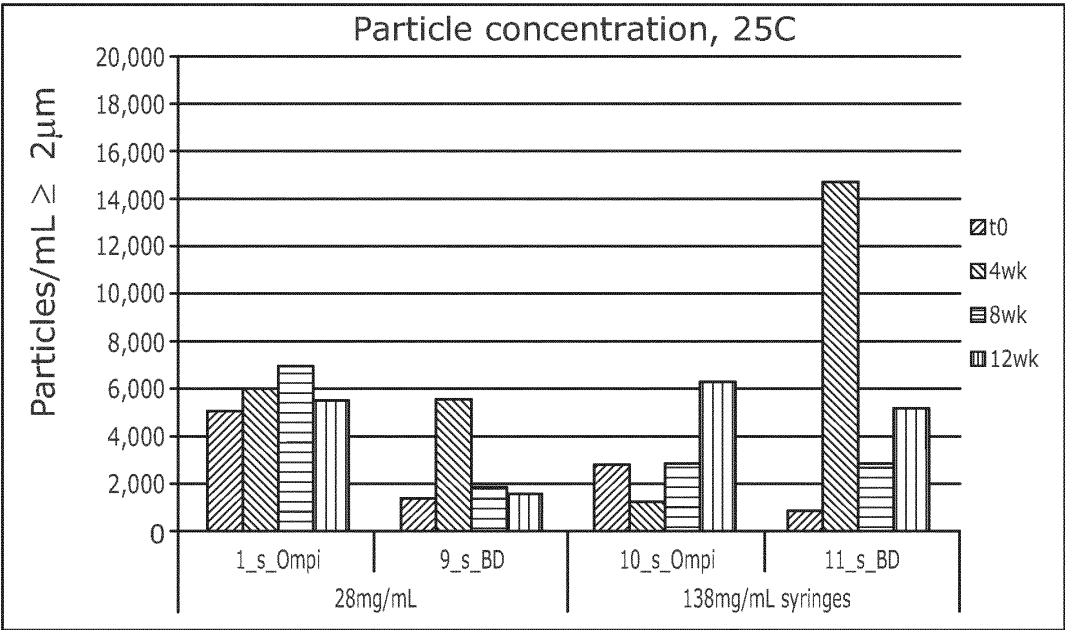


FIG. 22B

subvisible particles $\geq 2 \mu\text{m}$ in Ompi and BD syringes
over 12 weeks of storage at 5° C, 25° C, and 40° C

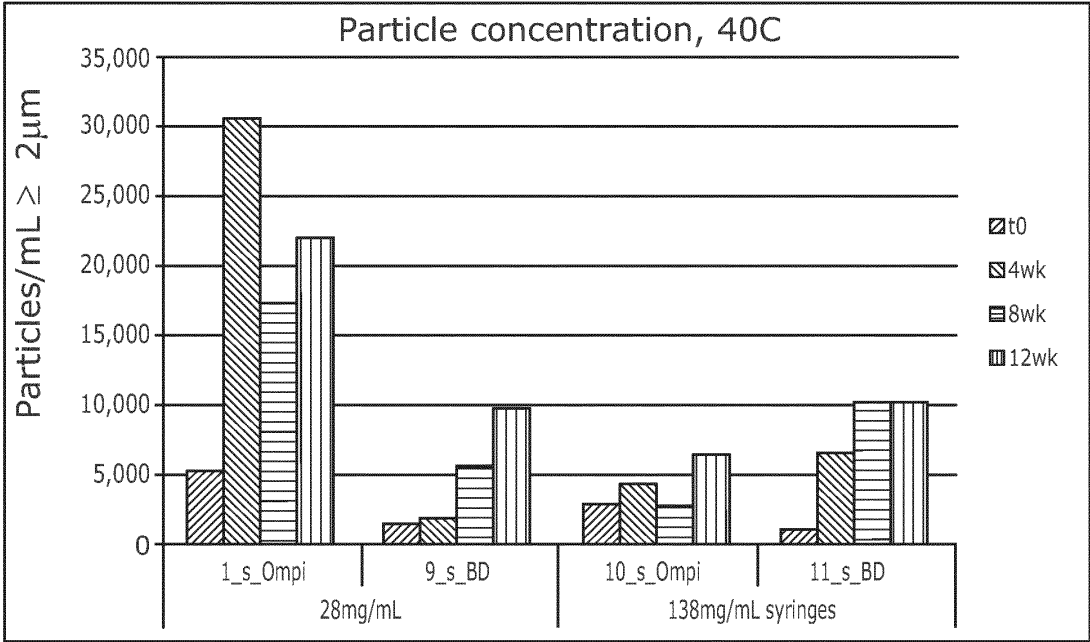


FIG. 22C

subvisible particles $\geq 10\ \mu\text{m}$ in Ompi and BD syringes
over 12 weeks of storage at 5° C, 25° C, and 40° C

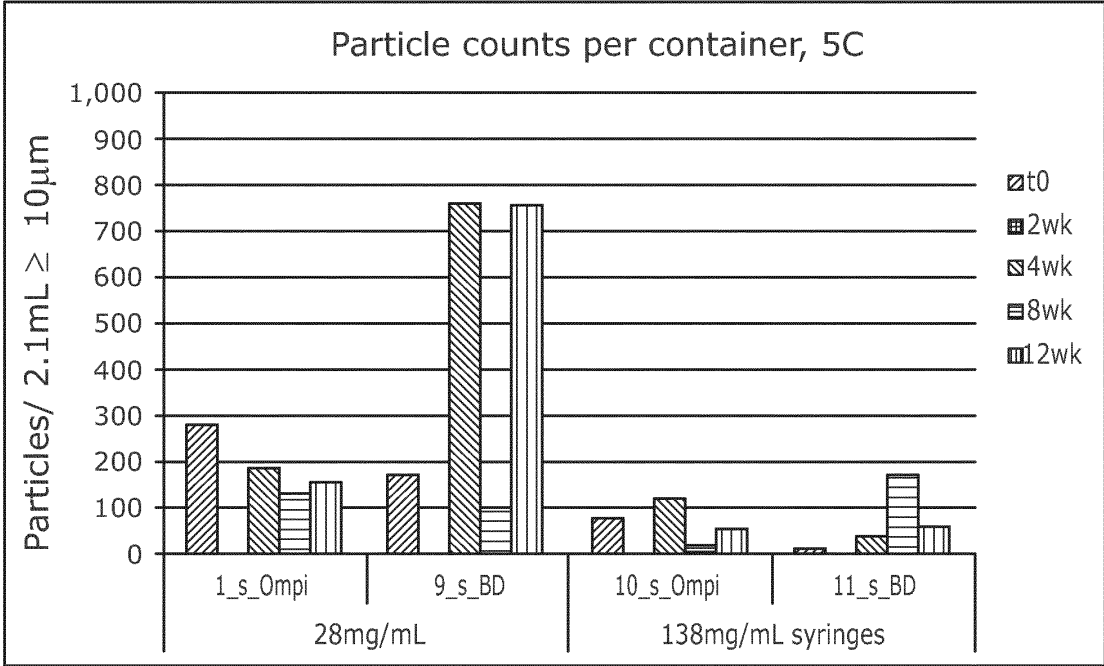


FIG. 23A

subvisible particles $\geq 10\ \mu\text{m}$ in Ompi and BD syringes
over 12 weeks of storage at 5° C, 25° C, and 40° C

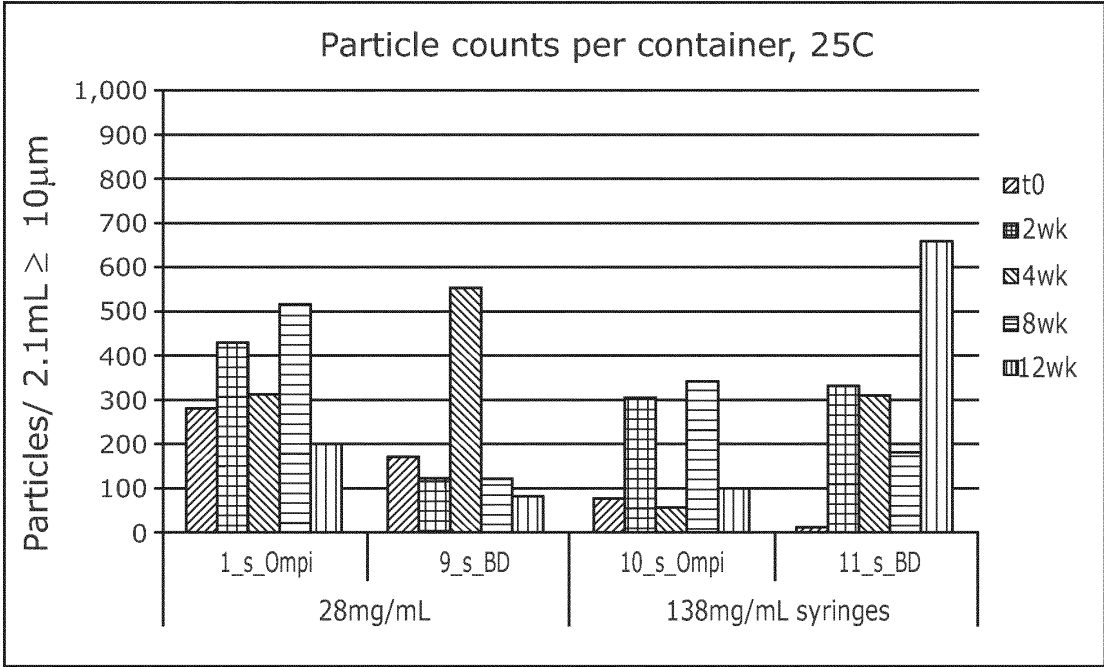


FIG. 23B

subvisible particles $\geq 10 \mu\text{m}$ in Ompi and BD syringes
over 12 weeks of storage at 5° C, 25° C, and 40° C

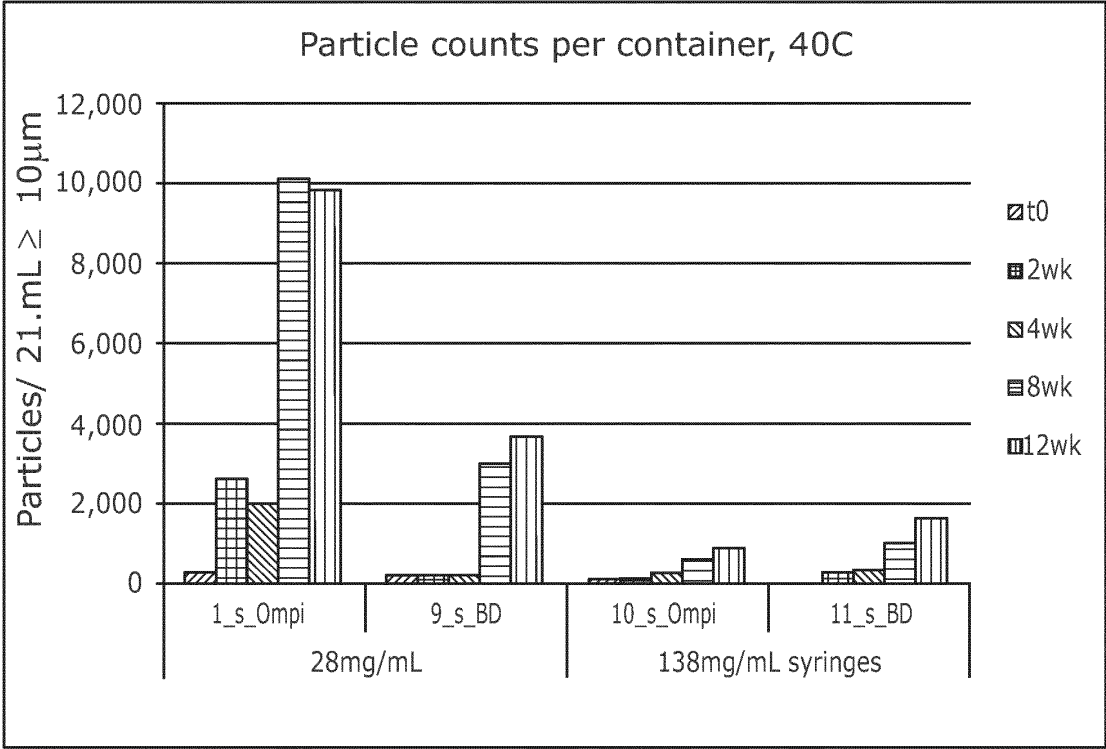


FIG. 23C

subvisible particles $\geq 25 \mu\text{m}$ in Ompi and BD syringes
over 12 weeks of storage at 5° C, 25° C, and 40° C

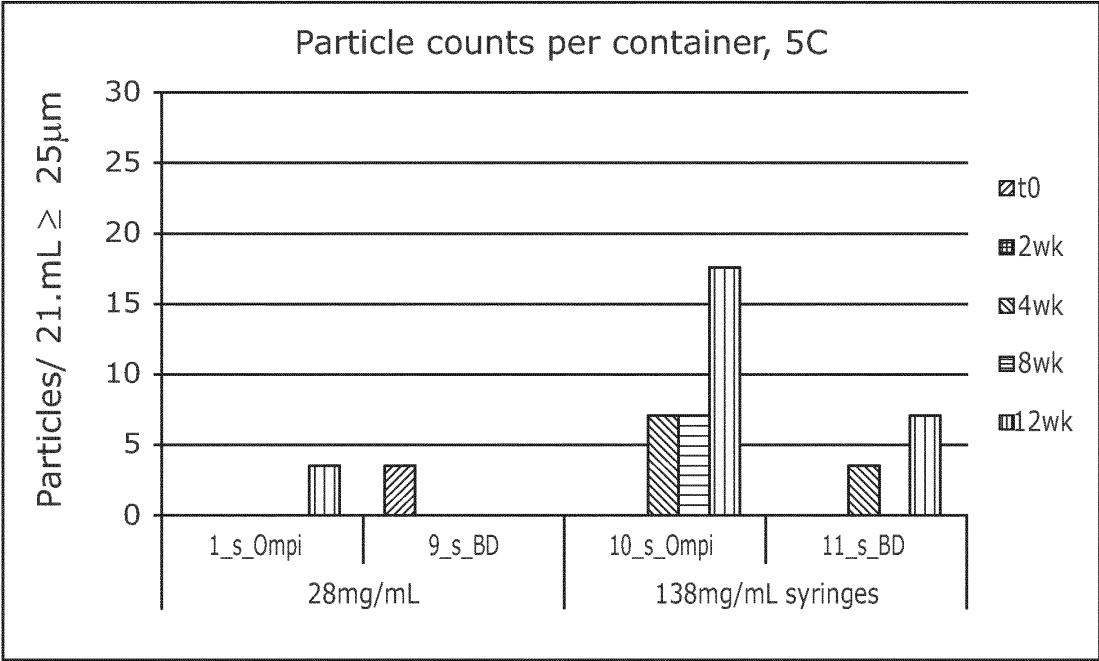


FIG. 24A

subvisible particles $\geq 25 \mu\text{m}$ in Ompi and BD syringes
over 12 weeks of storage at 5° C, 25° C, and 40° C

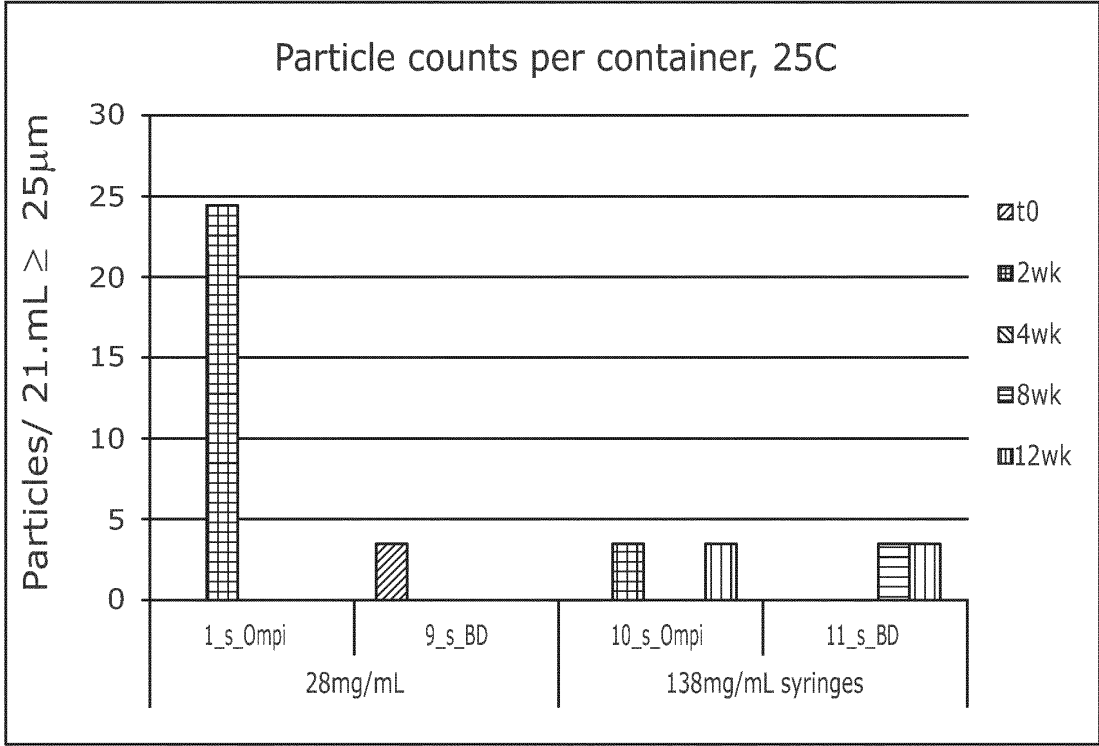


FIG. 24B

subvisible particles $\geq 25 \mu\text{m}$ in Ompi and BD syringes
over 12 weeks of storage at 5° C, 25° C, and 40° C

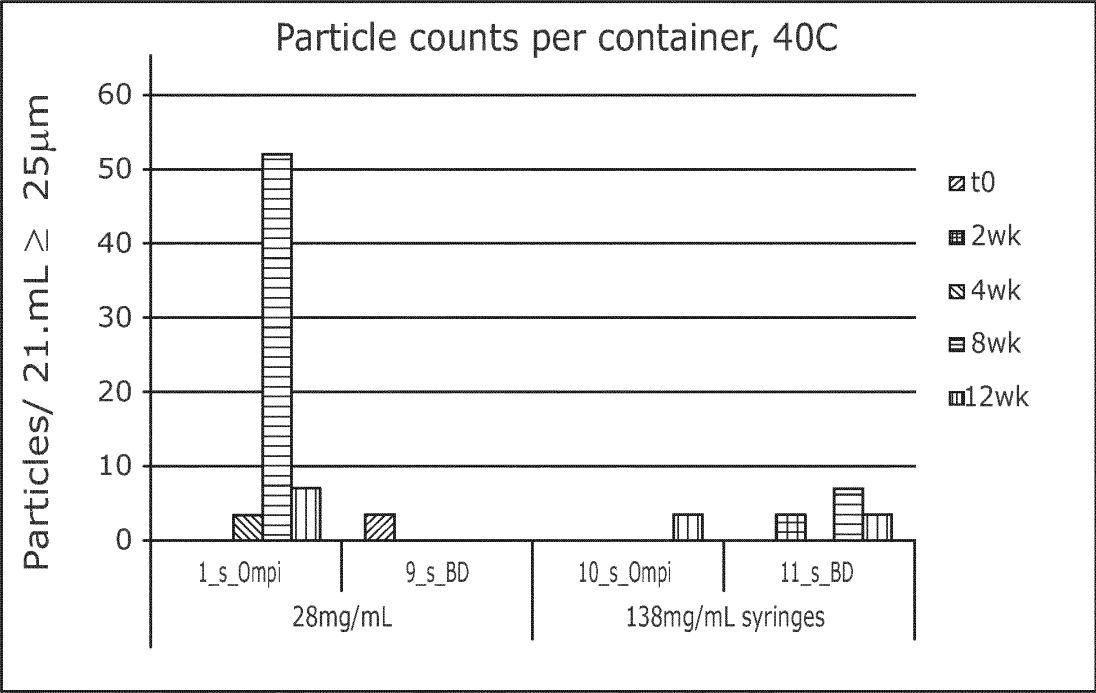


FIG. 24C

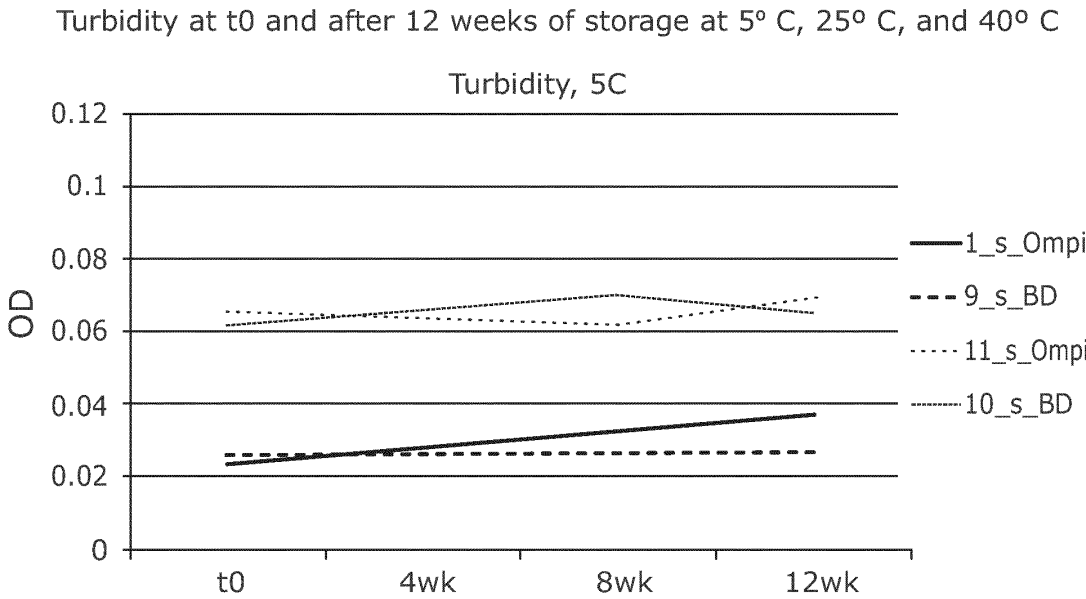


FIG. 25A

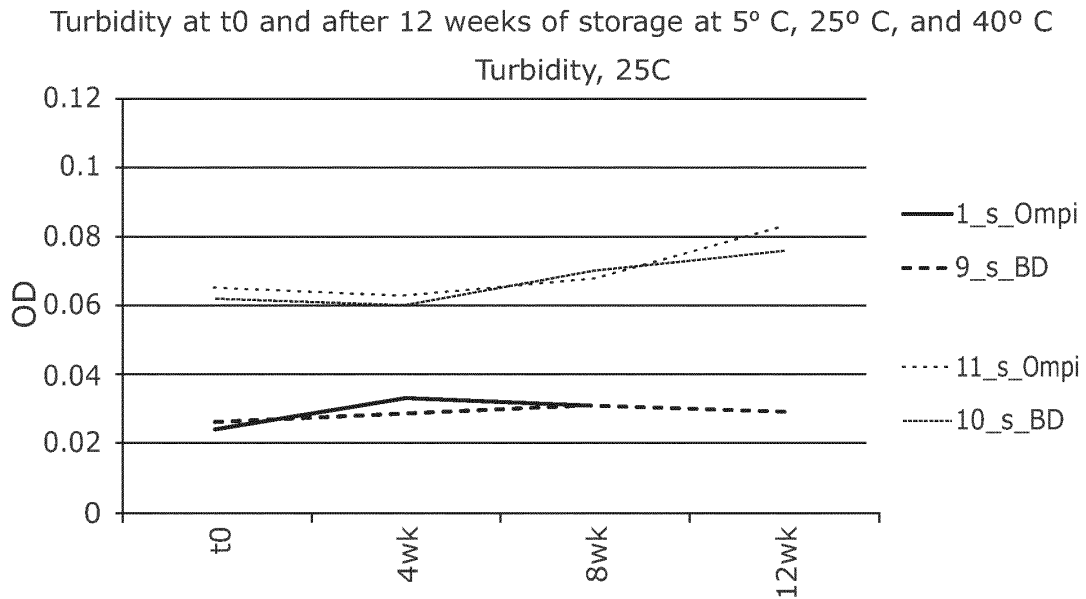


FIG. 25B

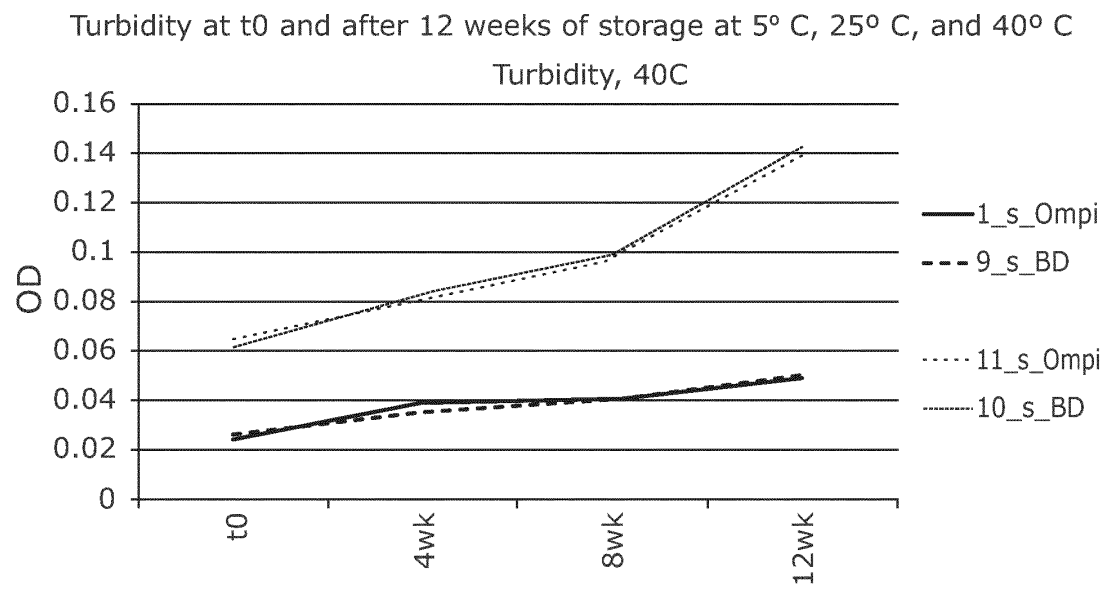


FIG. 25C

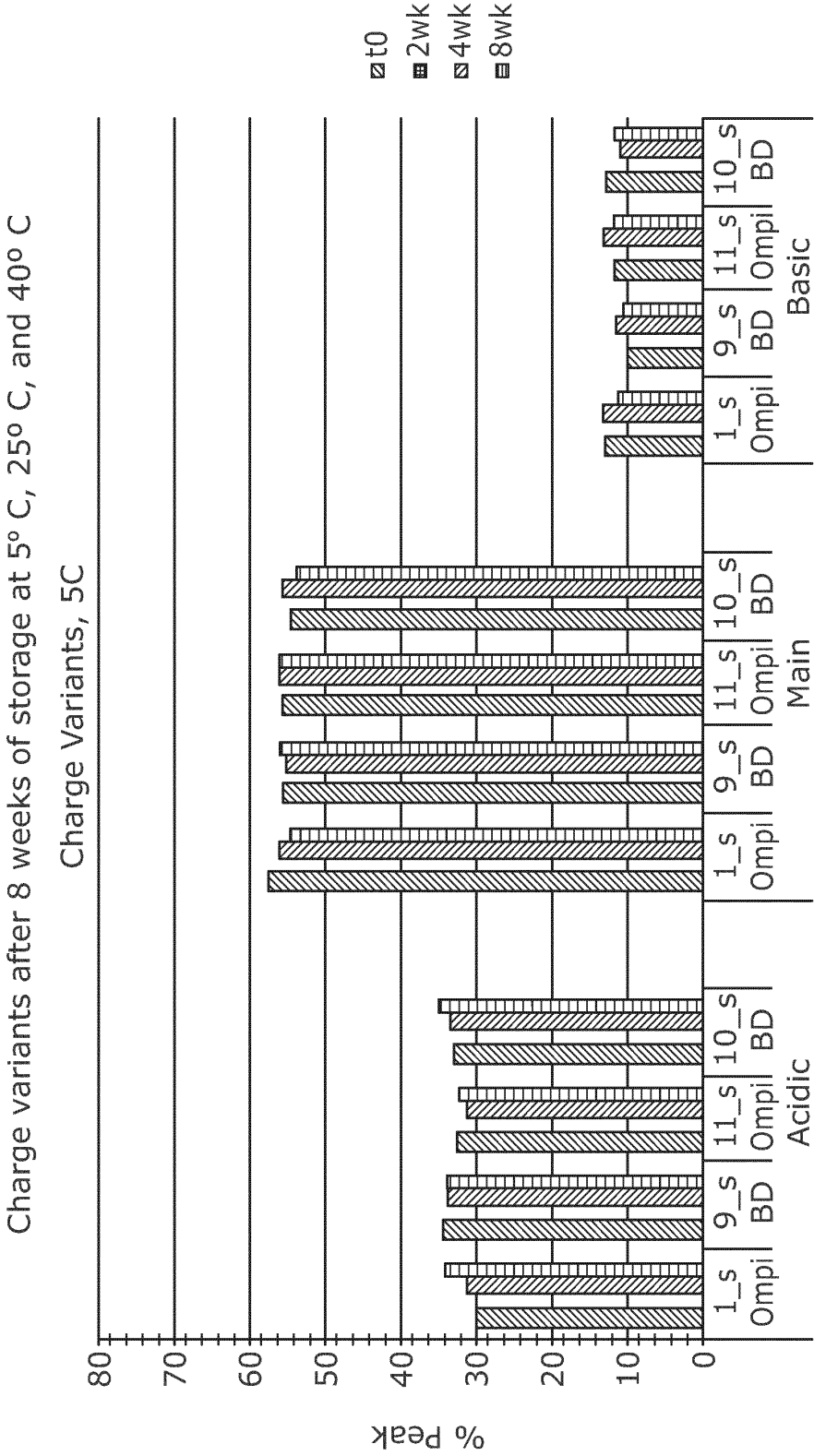


FIG. 26A

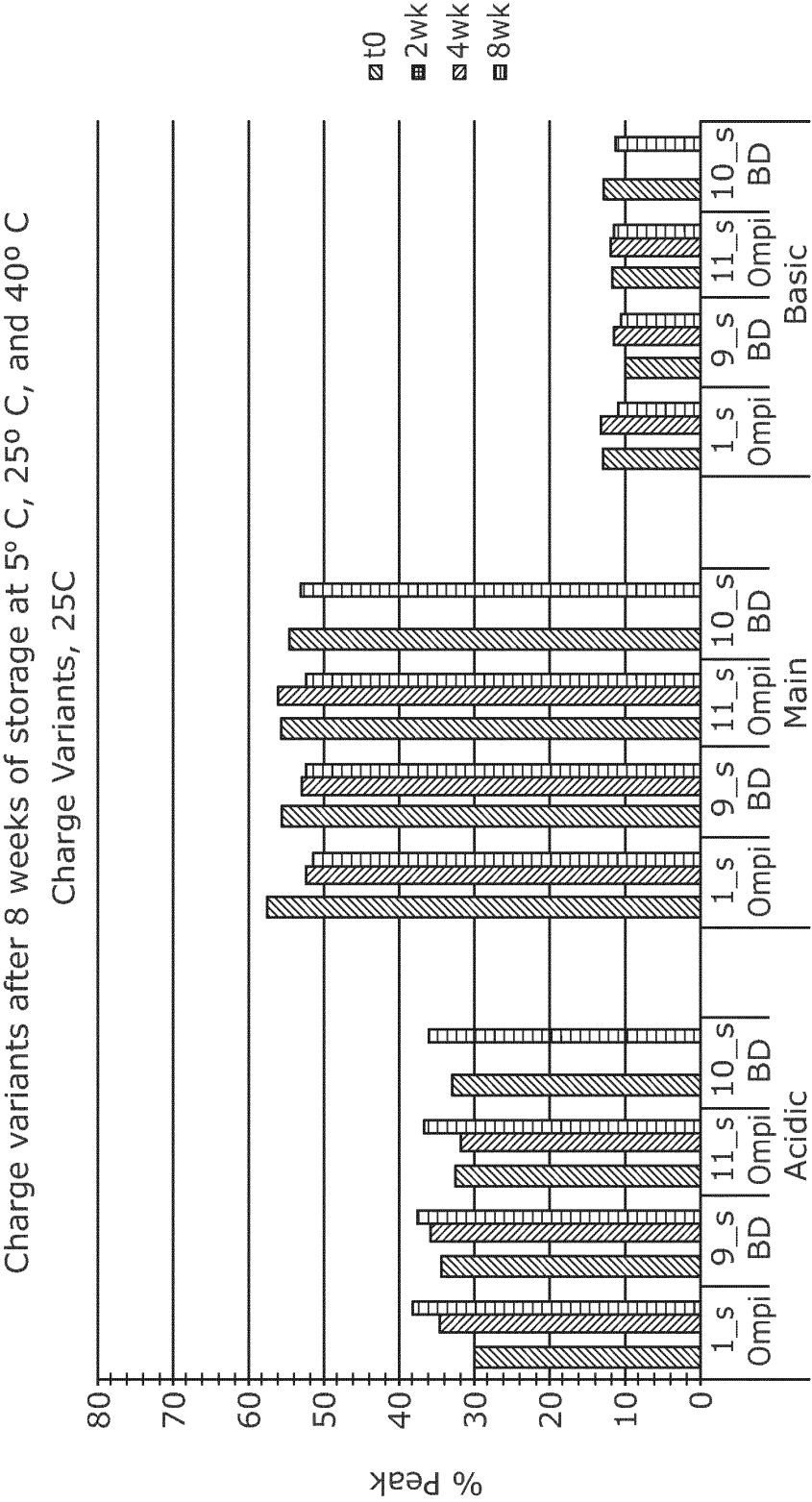


FIG. 26B

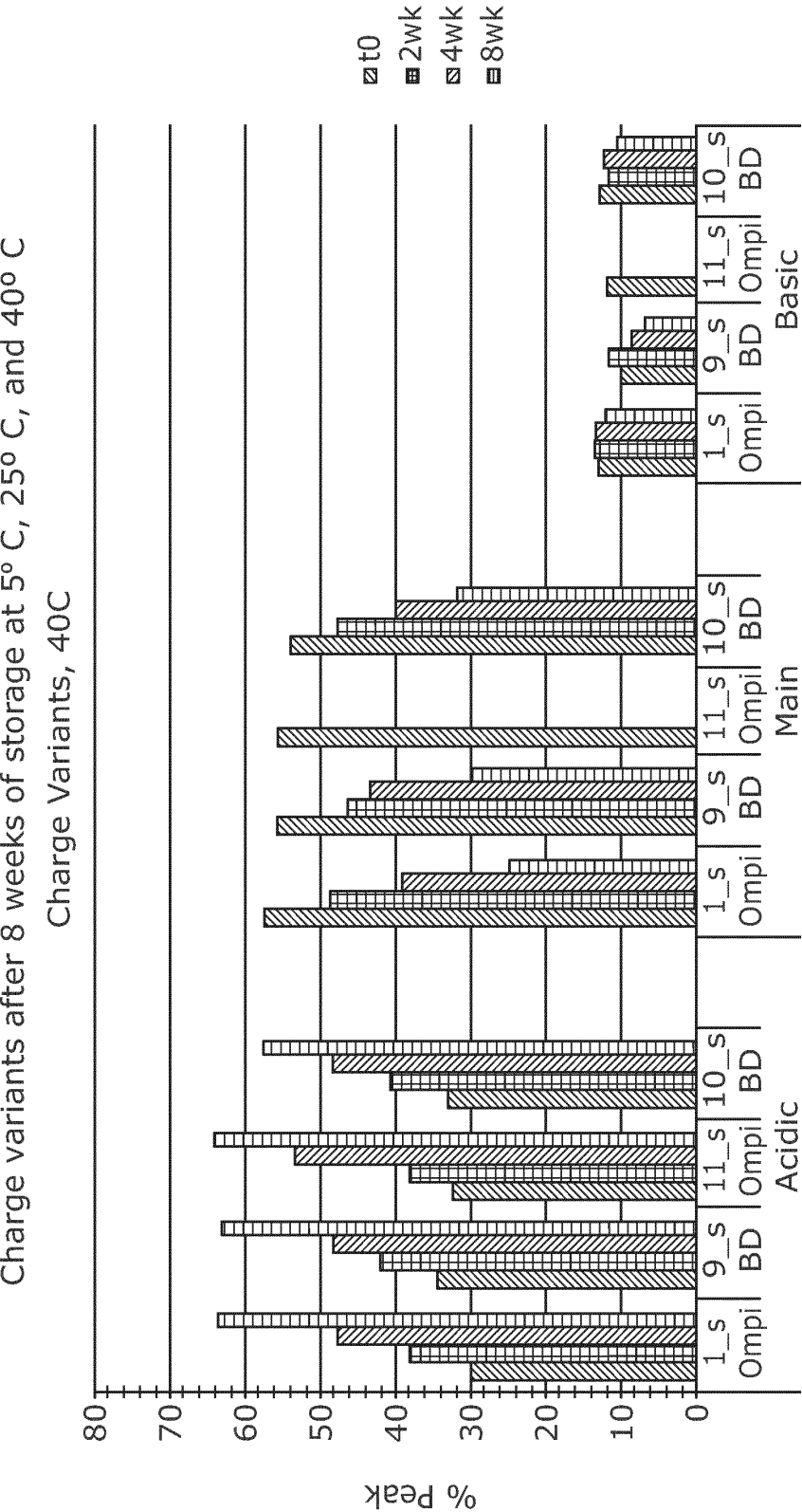


FIG. 26C

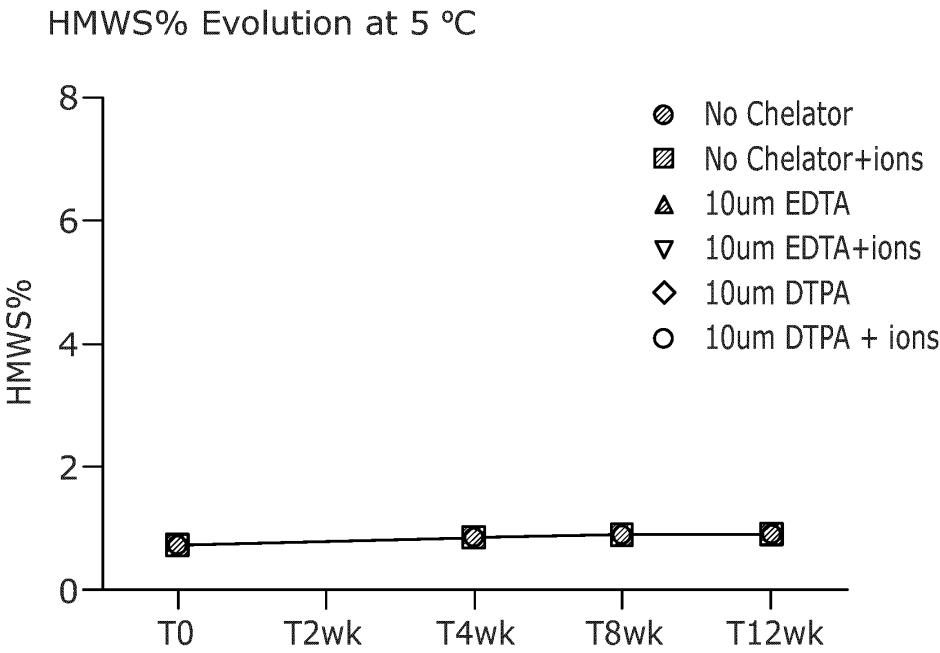


FIG. 27A

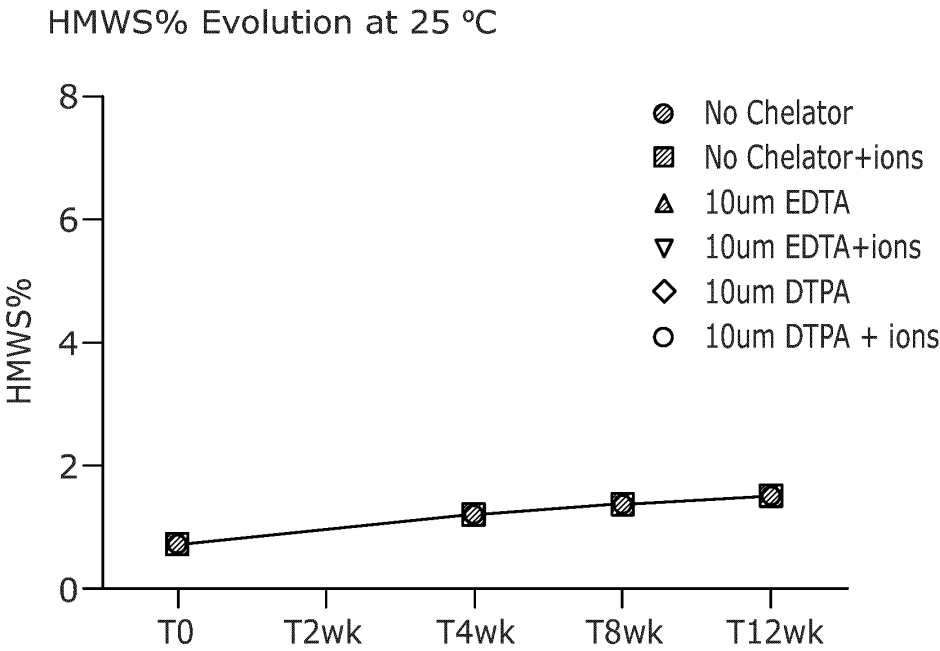


FIG. 27B

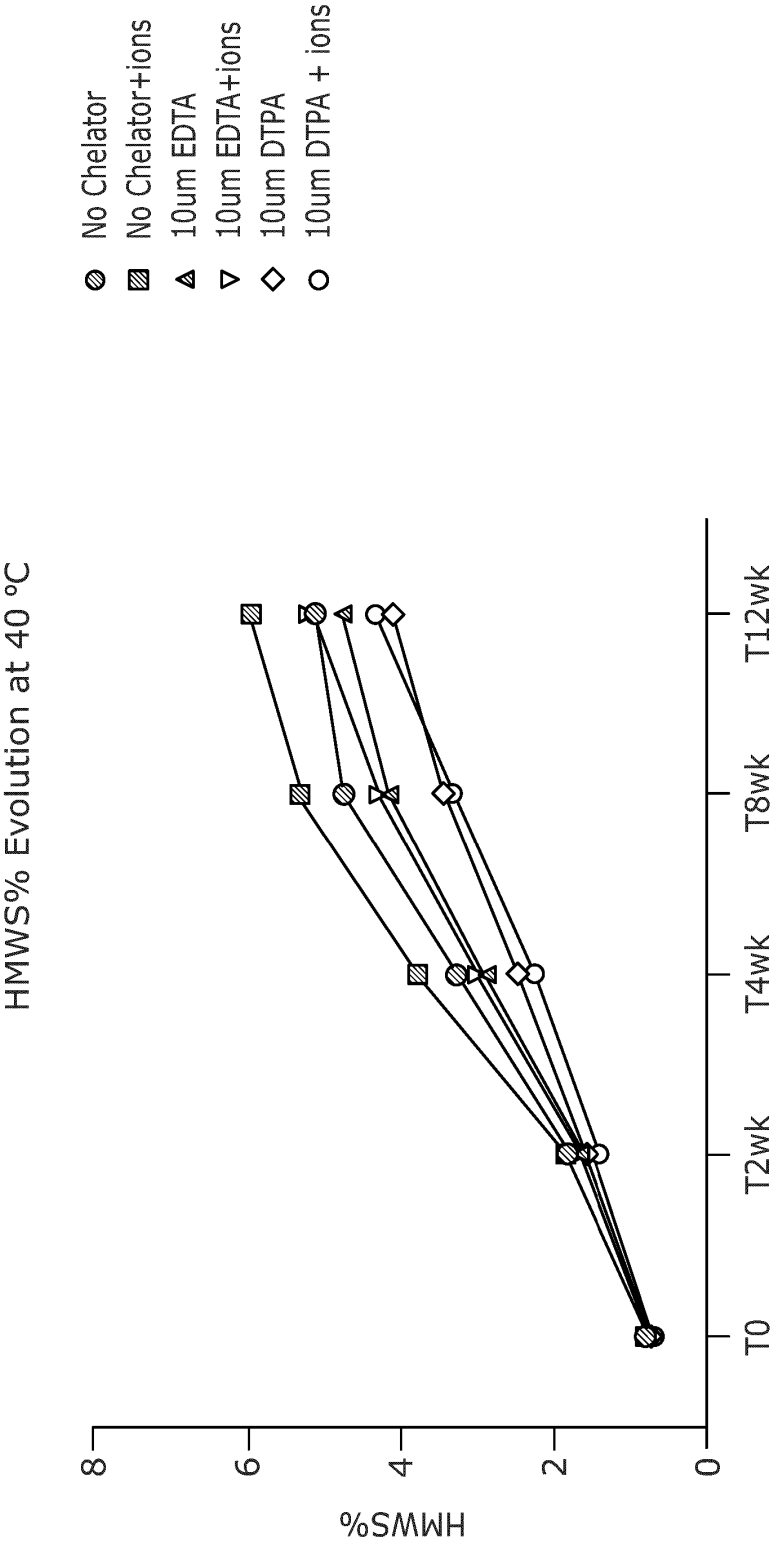


FIG. 27C

No PS80 degradation observed even without chelator

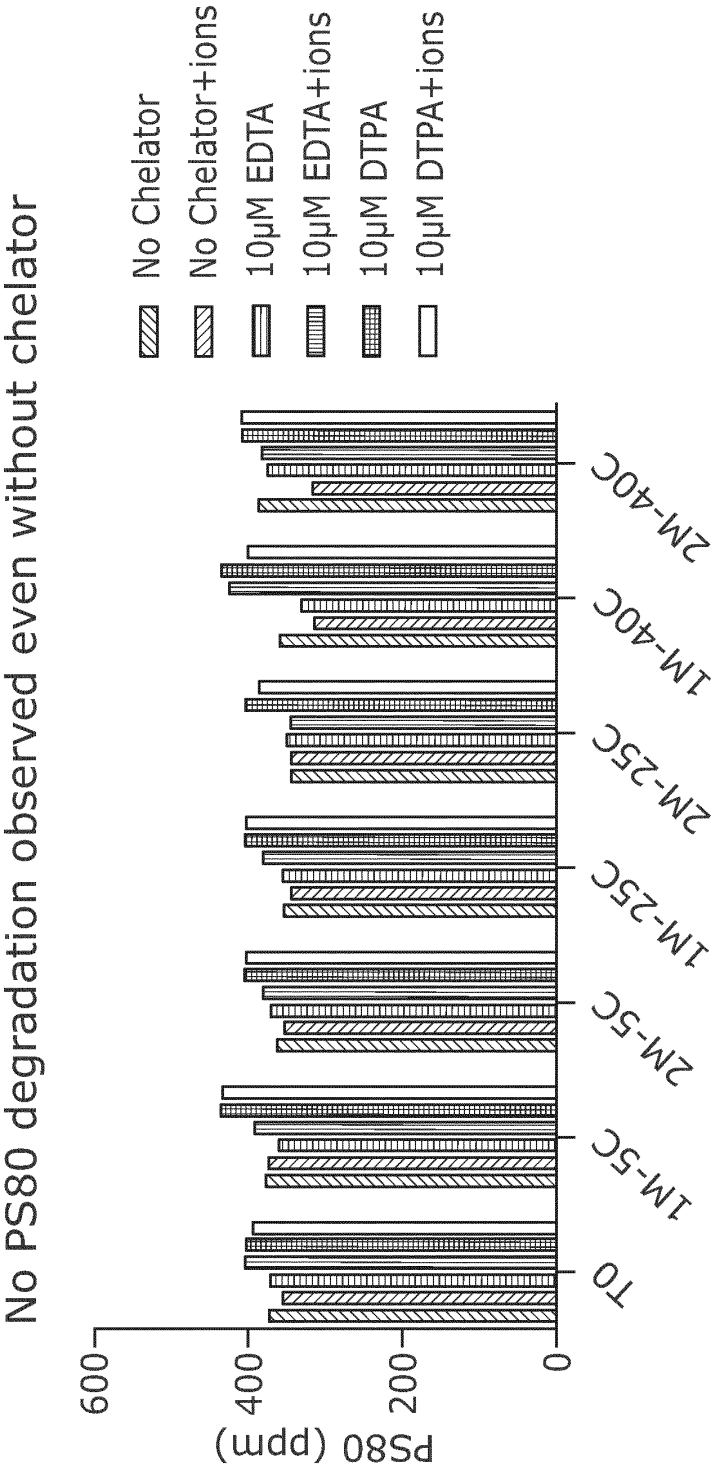


FIG. 28A

PS80 Loss in formulations over 3 months of storage at 5 °C
(Dotted line indicates the method variability)

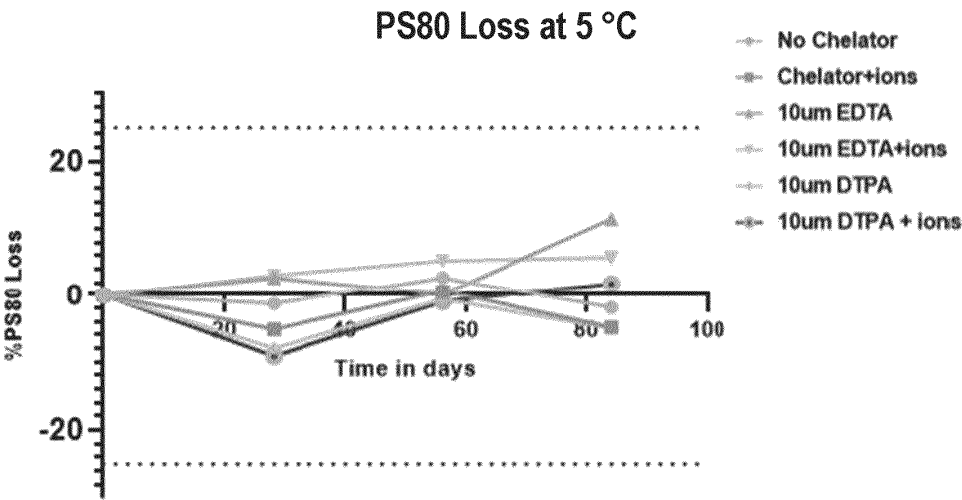


FIG. 28B

PS80 Loss in formulations over 3 months of storage at 25 °C
(Dotted line indicates the method variability)

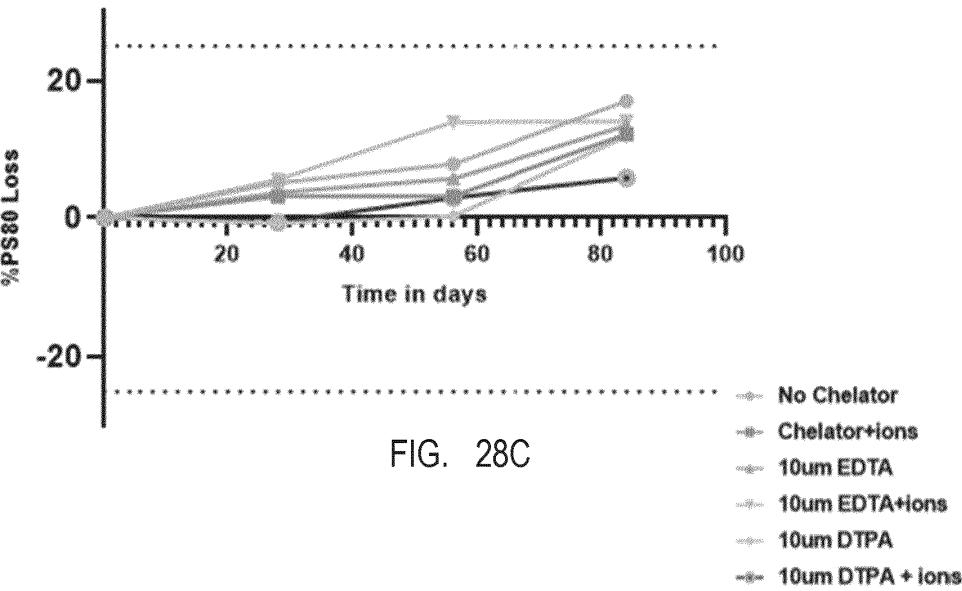


FIG. 28C

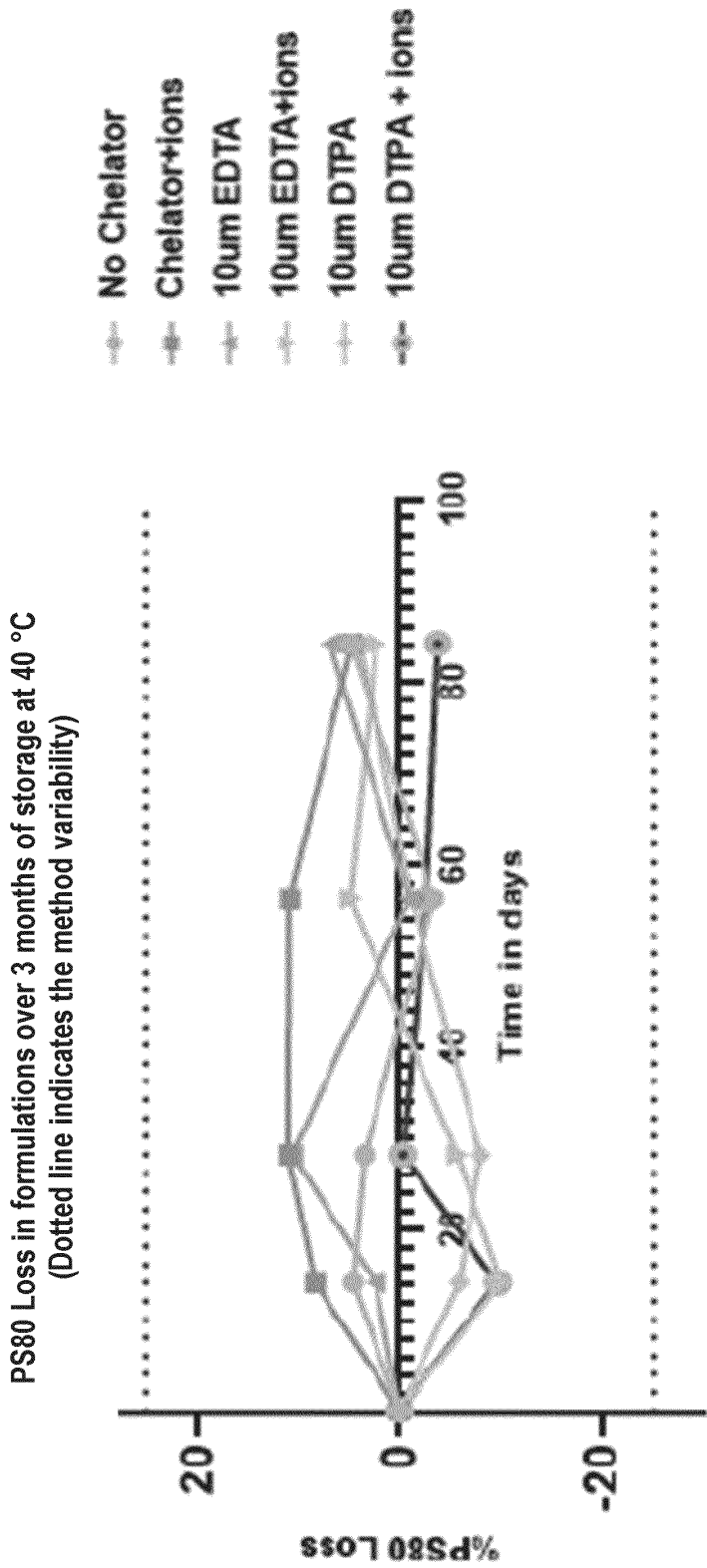


FIG. 28D

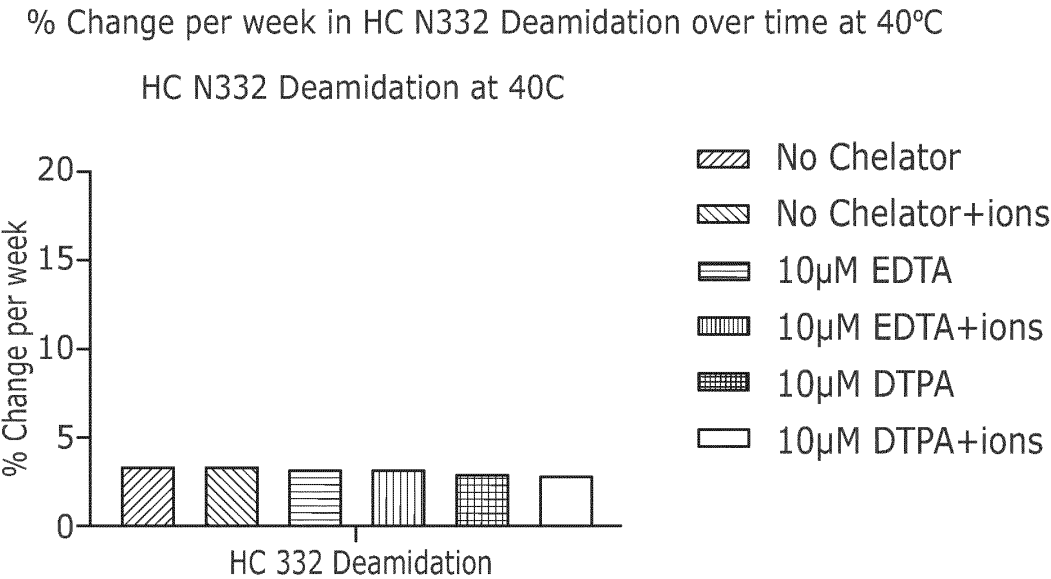


FIG. 29

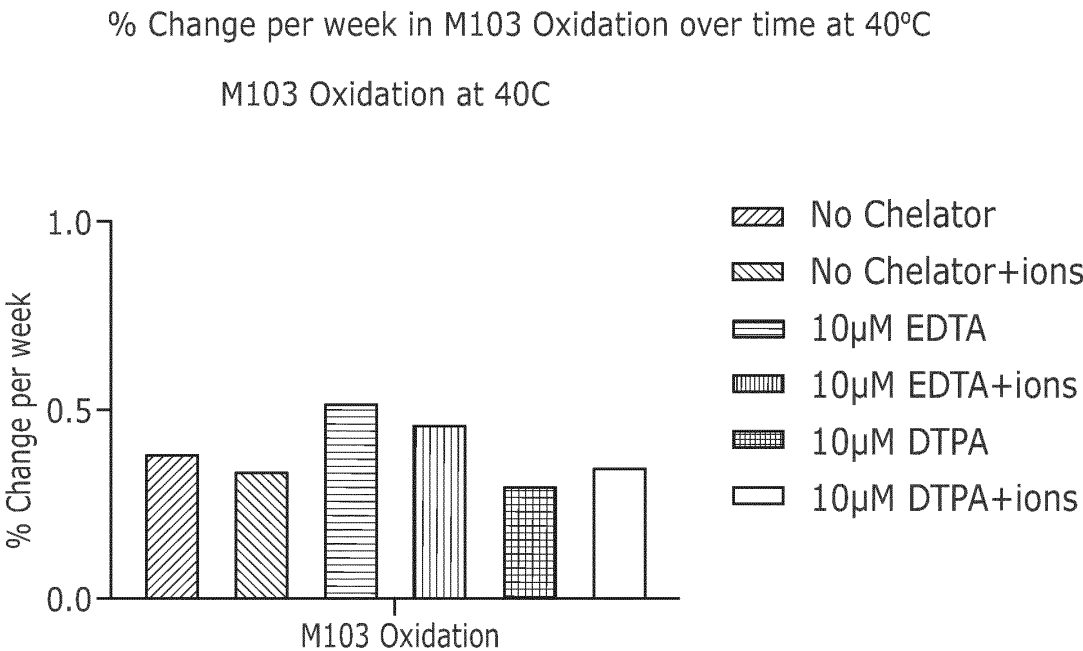


FIG. 30

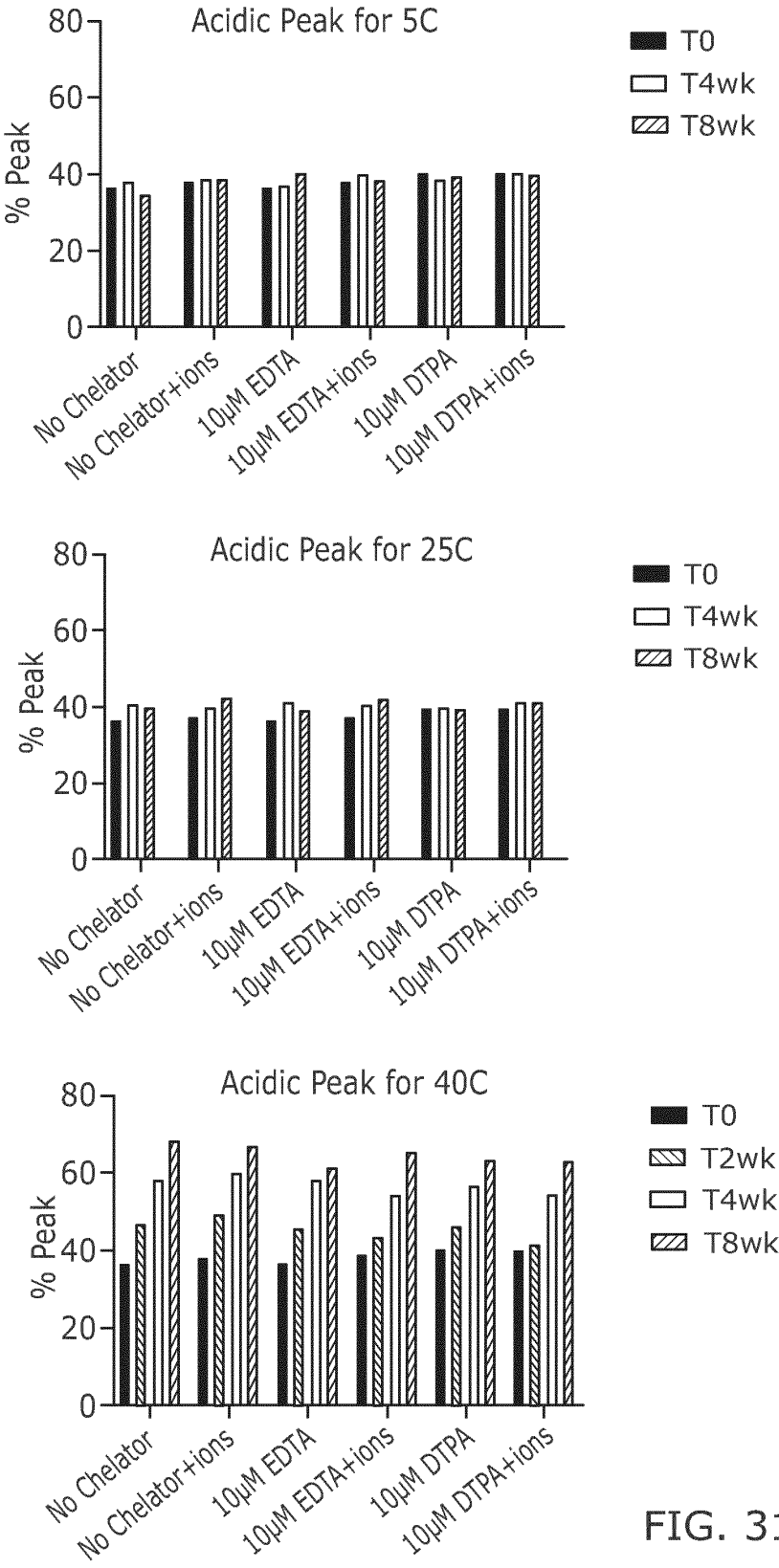


FIG. 31A

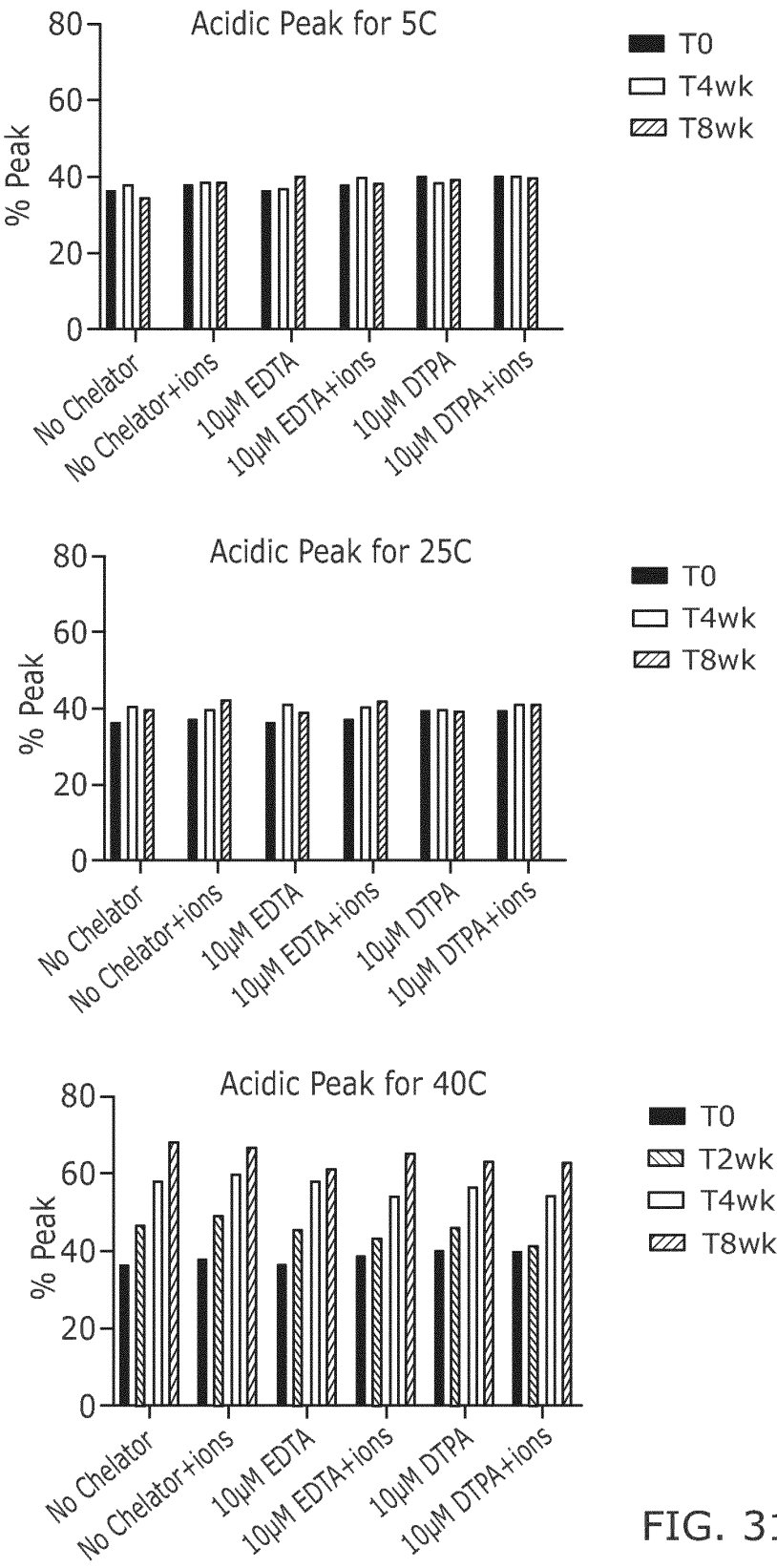


FIG. 31B

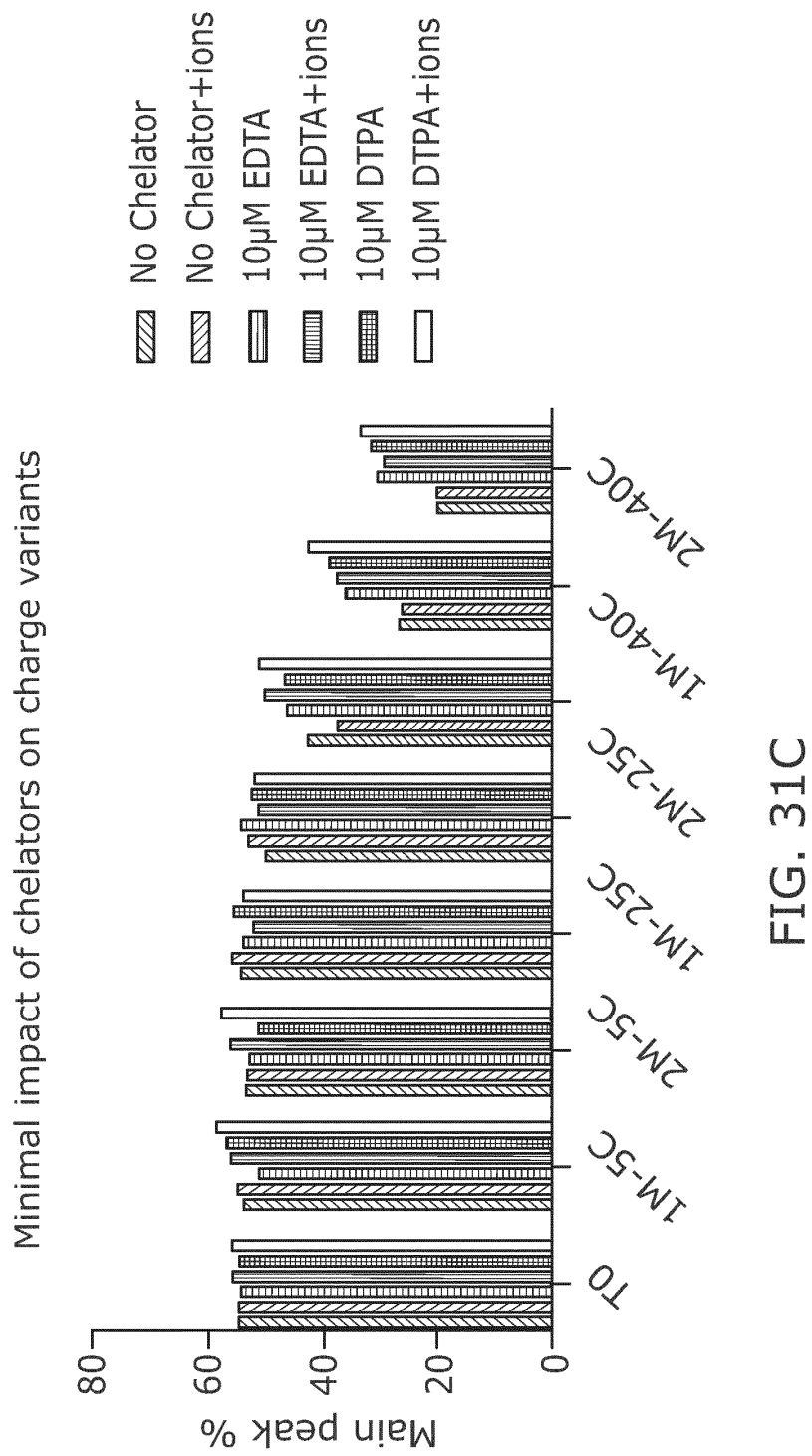


FIG. 31C

HMWS evolution for 31 mg/mL formulations over
the duration of the wrist-action study

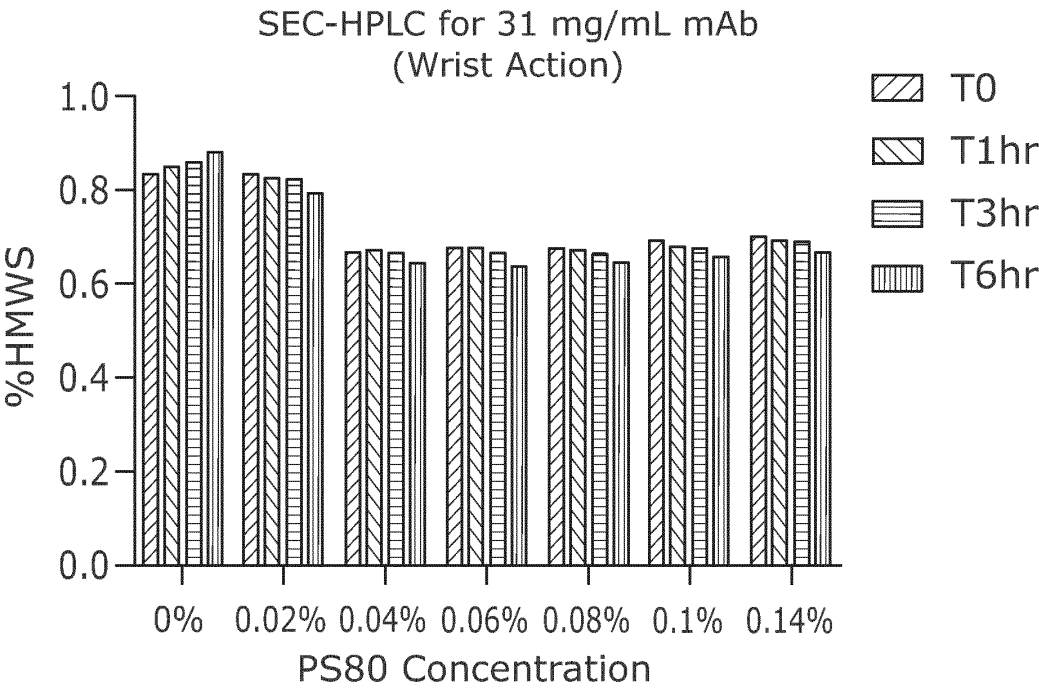


FIG. 32A

HMWS evolution for 31 mg/mL and 125 mg/mL formulations over the duration of the wrist-action study

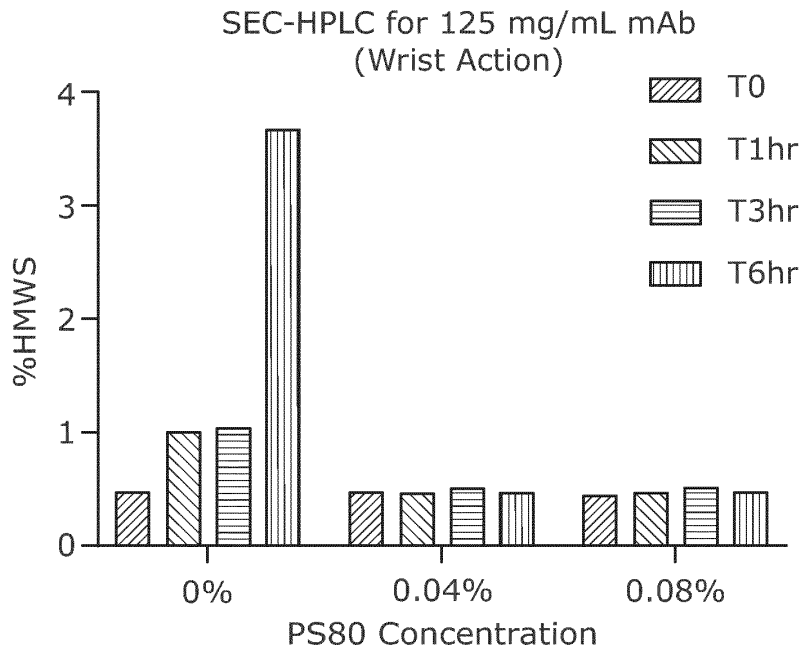


FIG. 32B

HMWS evolution for 31 mg/mL and 125 mg/mL formulations over the duration of the wrist-action study

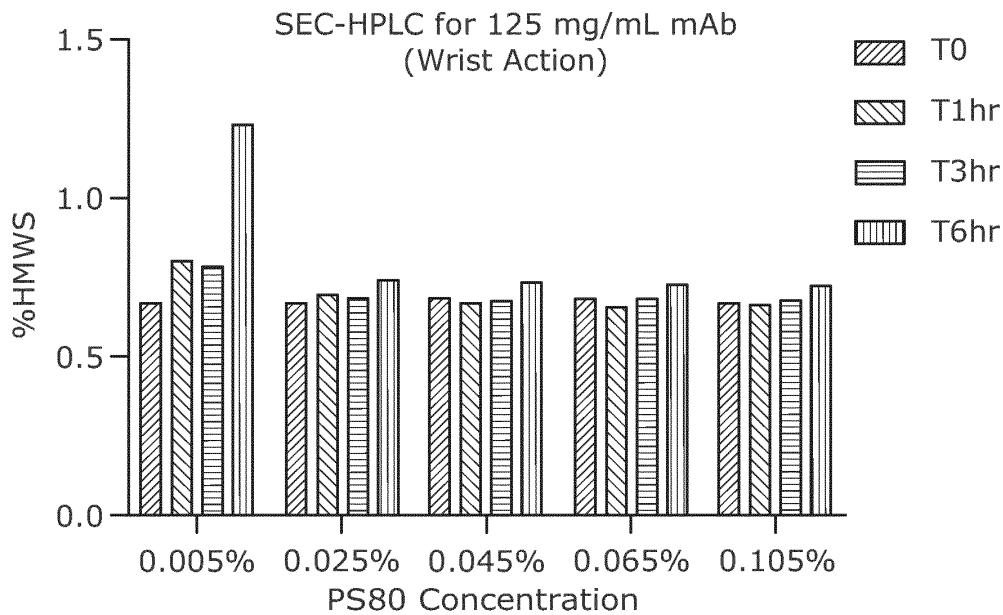


FIG. 32C

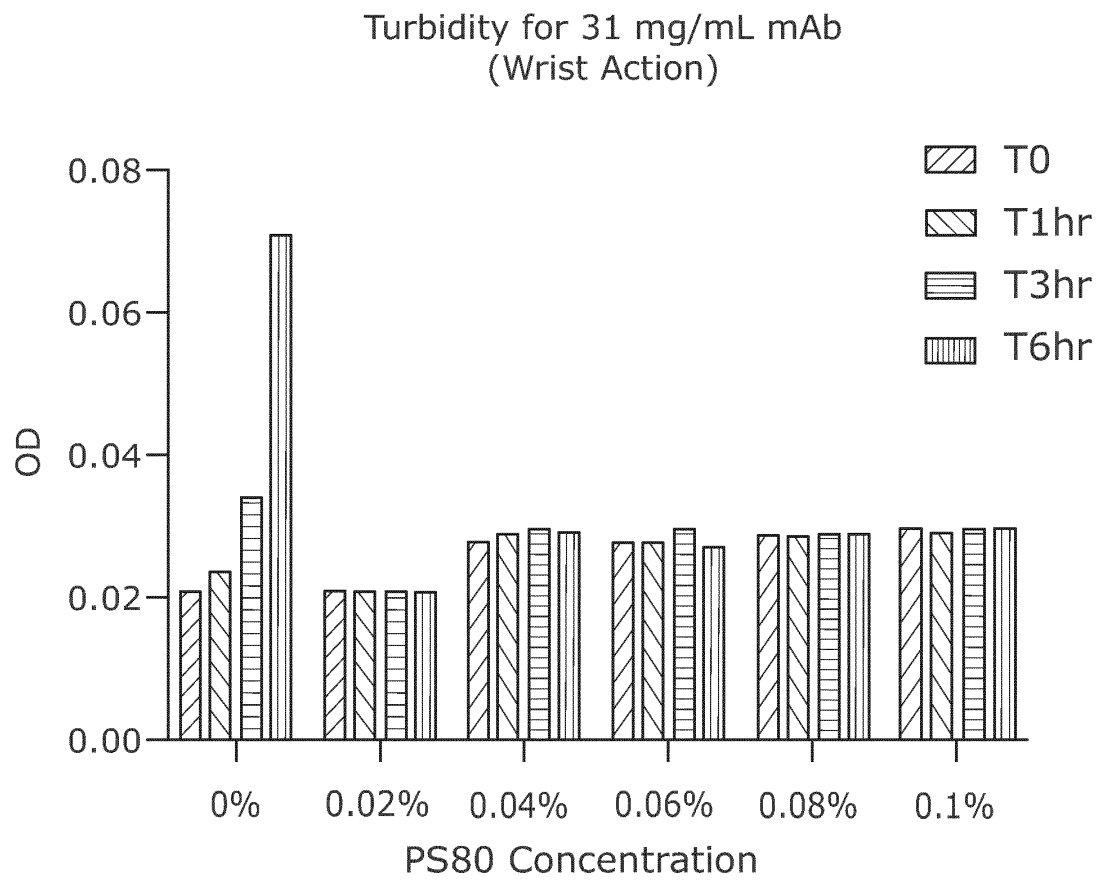


FIG. 33A

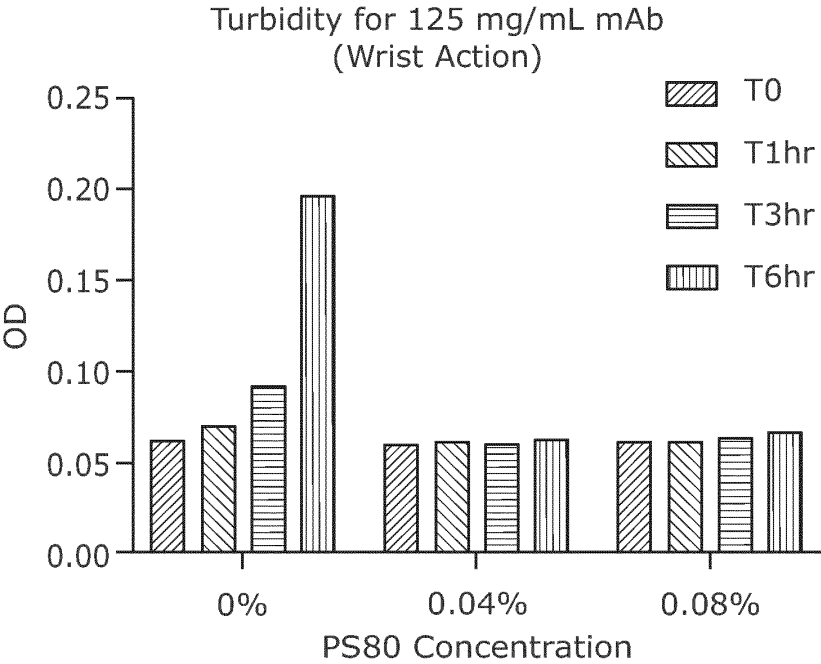


FIG. 33B

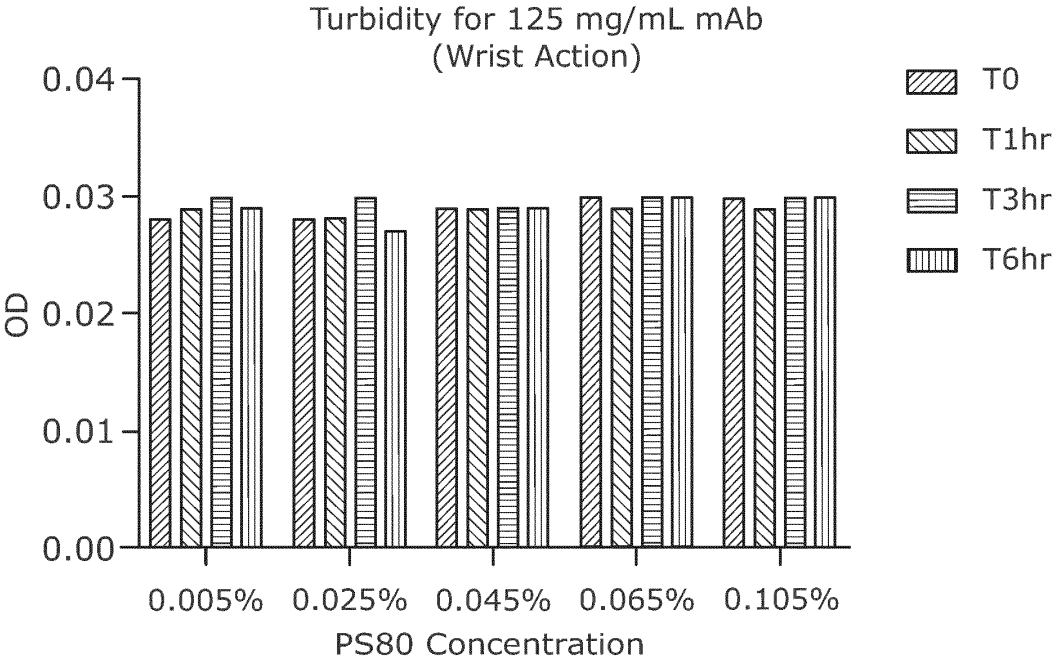


FIG. 33C

HIAC data for 31 mg/mL and 125 mg/mL formulations
for the duration of the wrist-action study

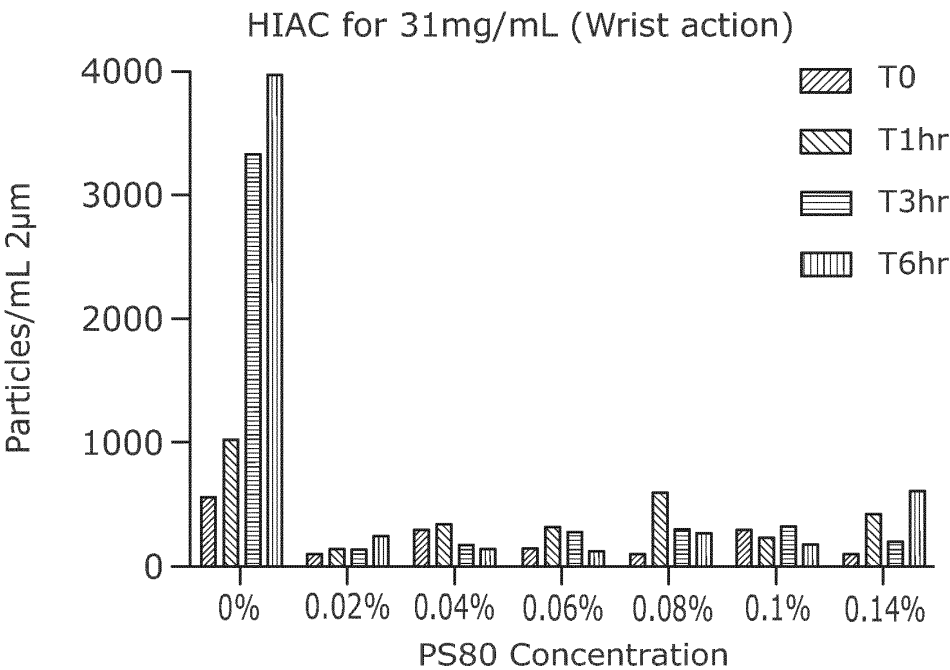


FIG. 34A

HIAC data for 31 mg/mL and 125 mg/mL formulations
for the duration of the wrist-action study

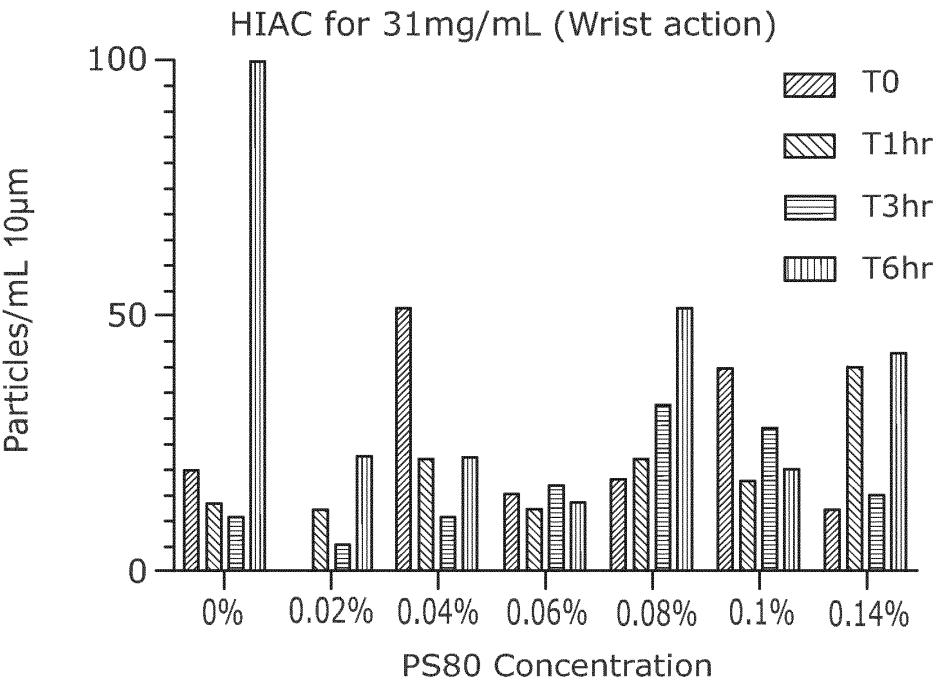


FIG. 34B

HIAC data for 31 mg/mL and 125 mg/mL formulations
for the duration of the wrist-action study

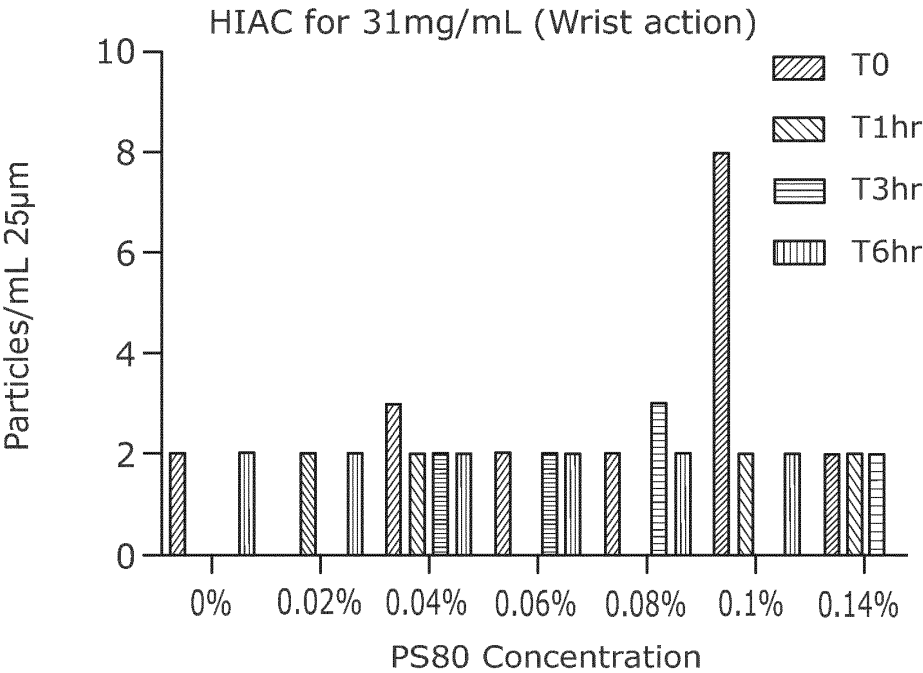


FIG. 34C

HIAC data for 31 mg/mL and 125 mg/mL formulations
for the duration of the wrist-action study

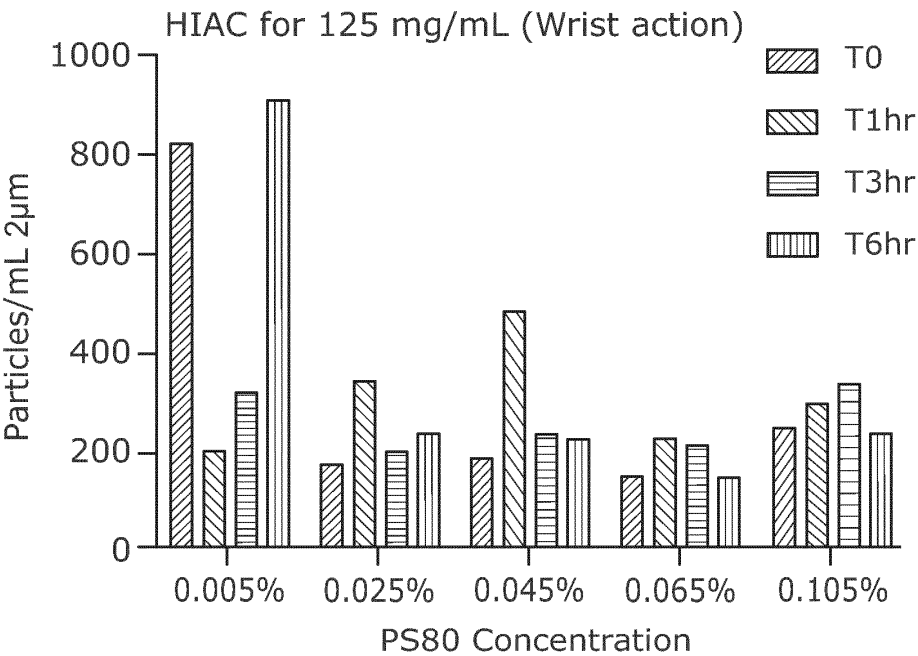


FIG. 34D

HIAC data for 31 mg/mL and 125 mg/mL formulations
for the duration of the wrist-action study

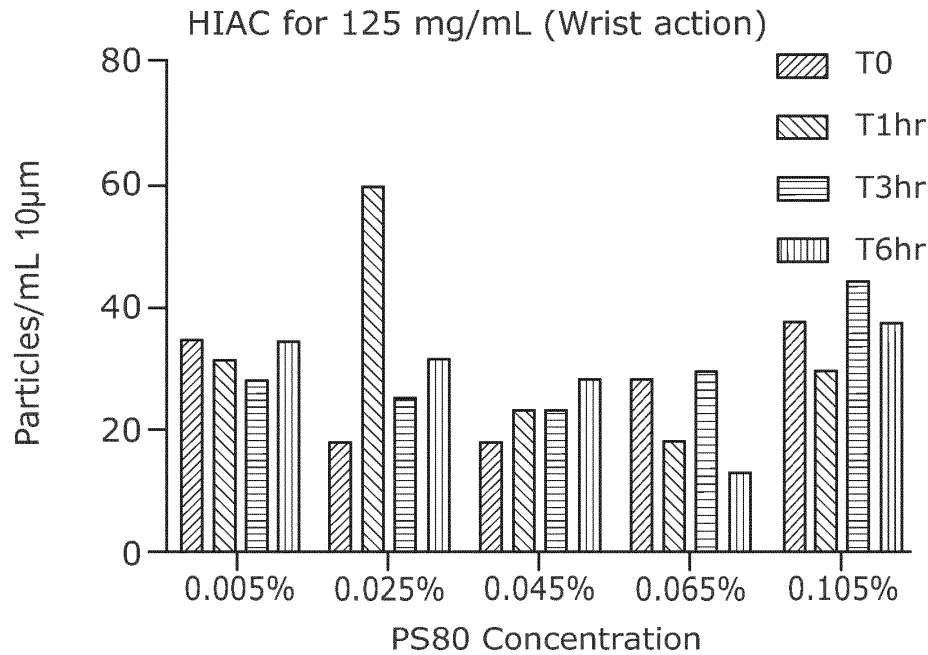


FIG. 34E

HIAC data for 31 mg/mL and 125 mg/mL formulations
for the duration of the wrist-action study

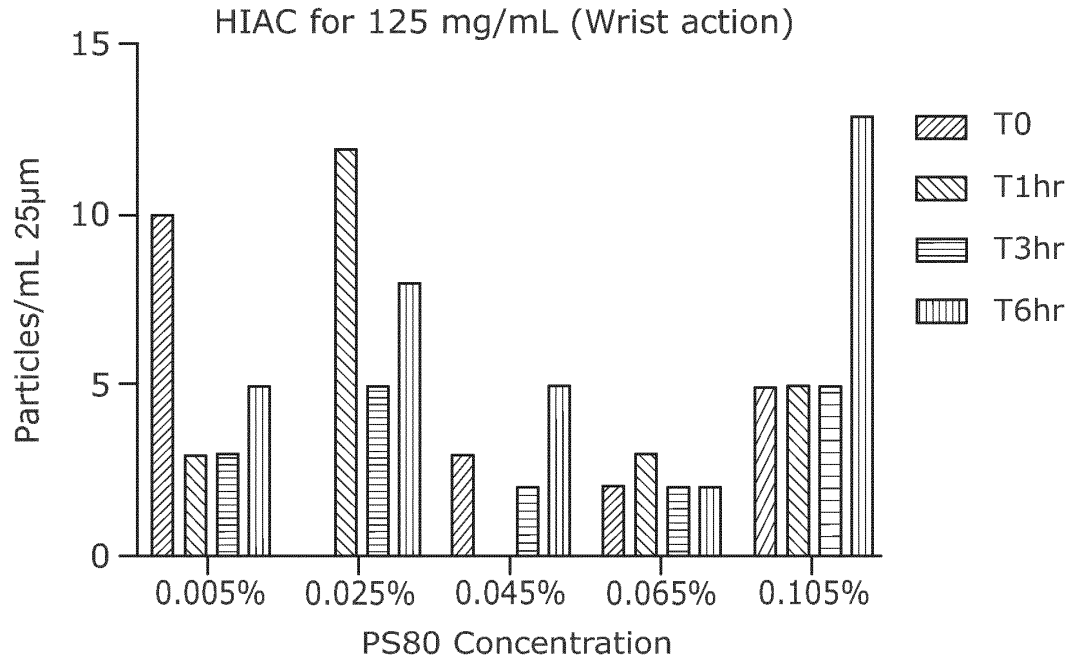


FIG. 34F

HIAC data for 31 mg/mL and 125 mg/mL formulations
for the duration of the orbital-shaking study

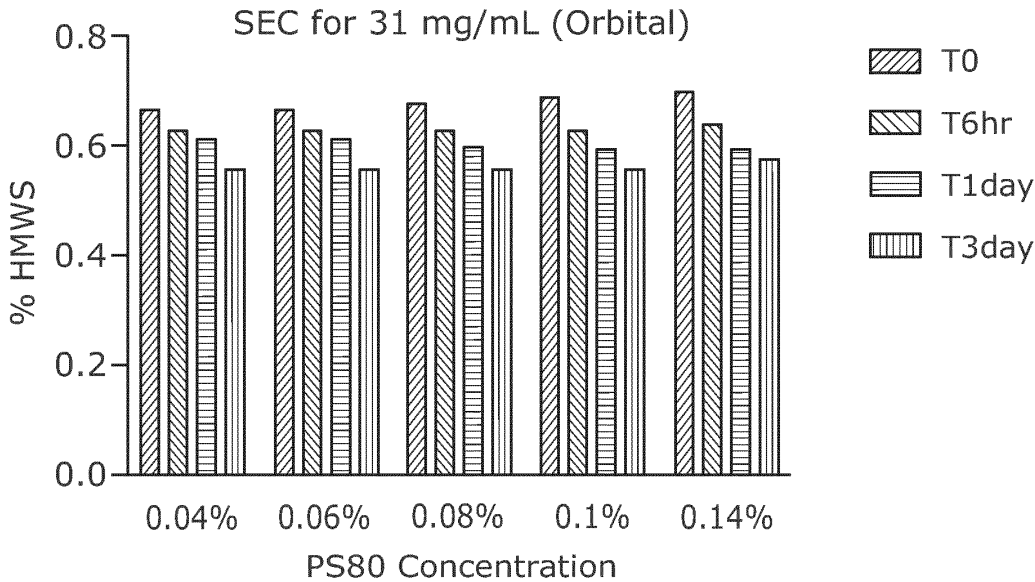


FIG. 35A

HIAC data for 31 mg/mL and 125 mg/mL formulations
for the duration of the orbital-shaking study

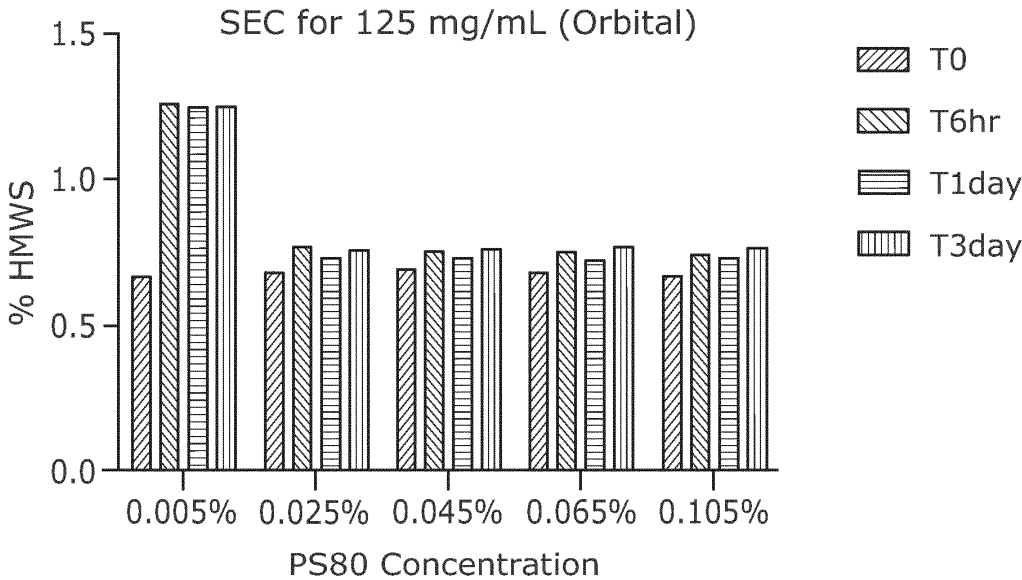
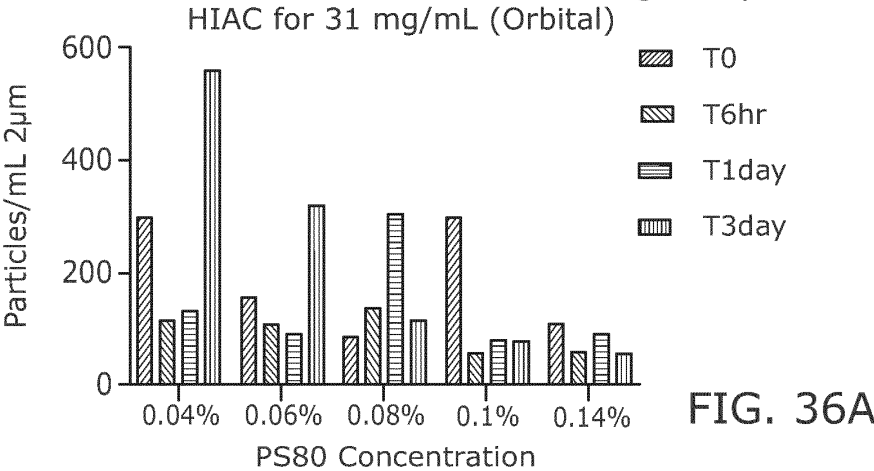
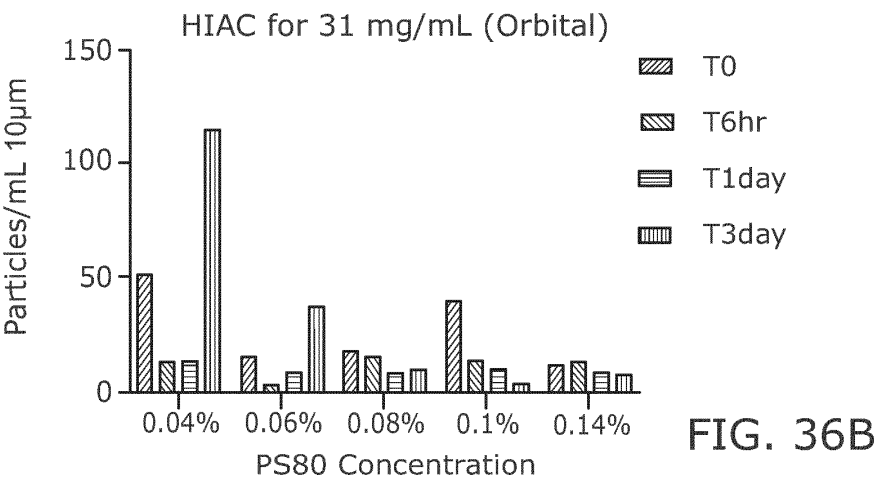


FIG. 35B

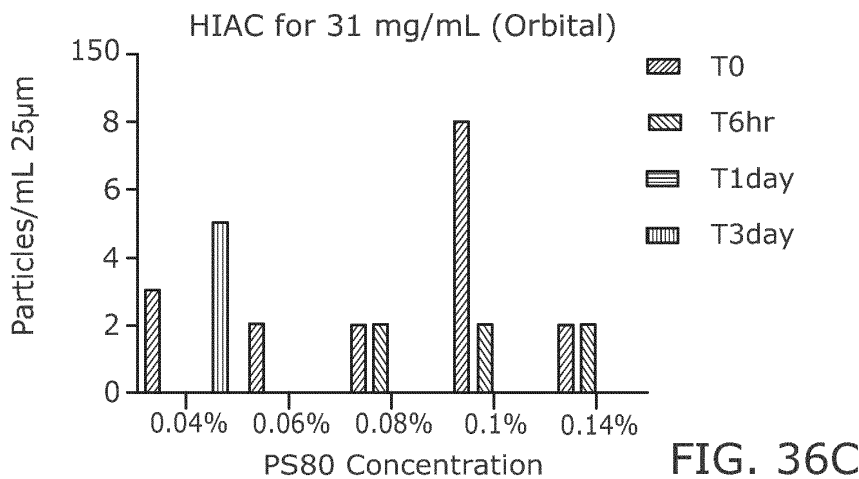
HMWS for 31 mg/mL and 125 mg/mL formulations
for the duration of the orbital-shaking study



HMWS for 31 mg/mL and 125 mg/mL formulations
for the duration of the orbital-shaking study



HMWS for 31 mg/mL and 125 mg/mL formulations
for the duration of the orbital-shaking study



HMWS for 31 mg/mL and 125 mg/mL formulations
for the duration of the orbital-shaking study

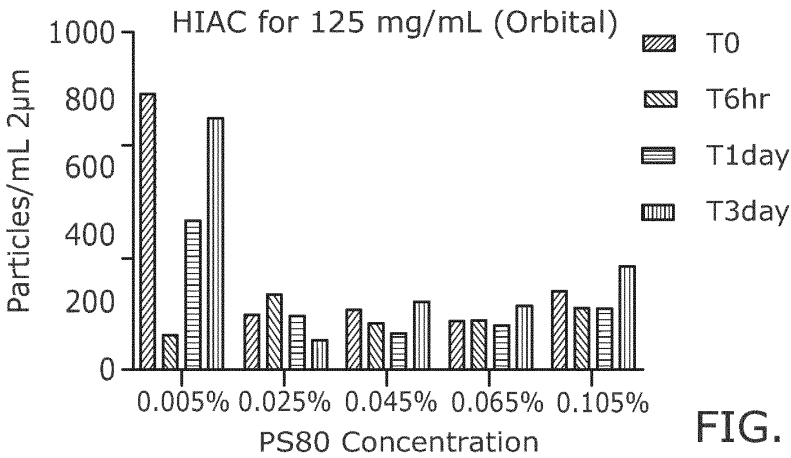


FIG. 36D

HMWS for 31 mg/mL and 125 mg/mL formulations
for the duration of the orbital-shaking study

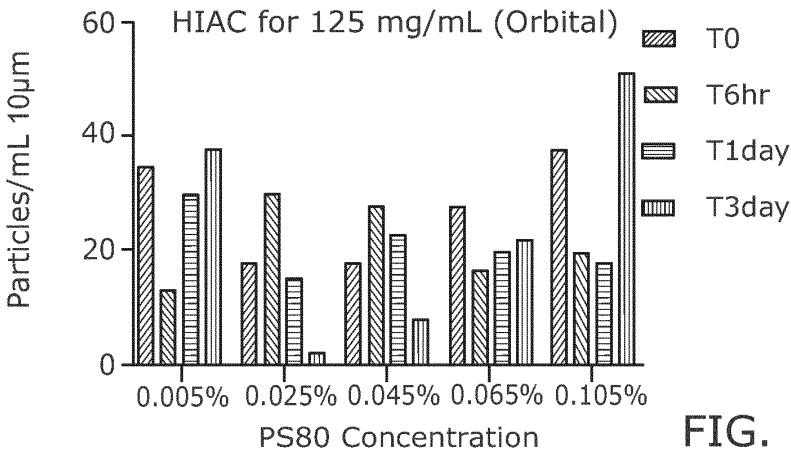


FIG. 36E

HMWS for 31 mg/mL and 125 mg/mL formulations
for the duration of the orbital-shaking study

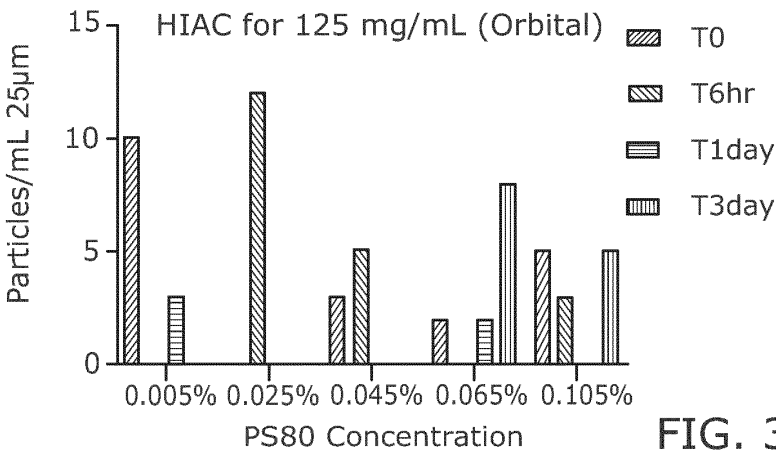


FIG. 36F

Turbidity for 31 mg/mL and 125 mg/mL formulations over the duration of the study with wrist-action and silicone oil

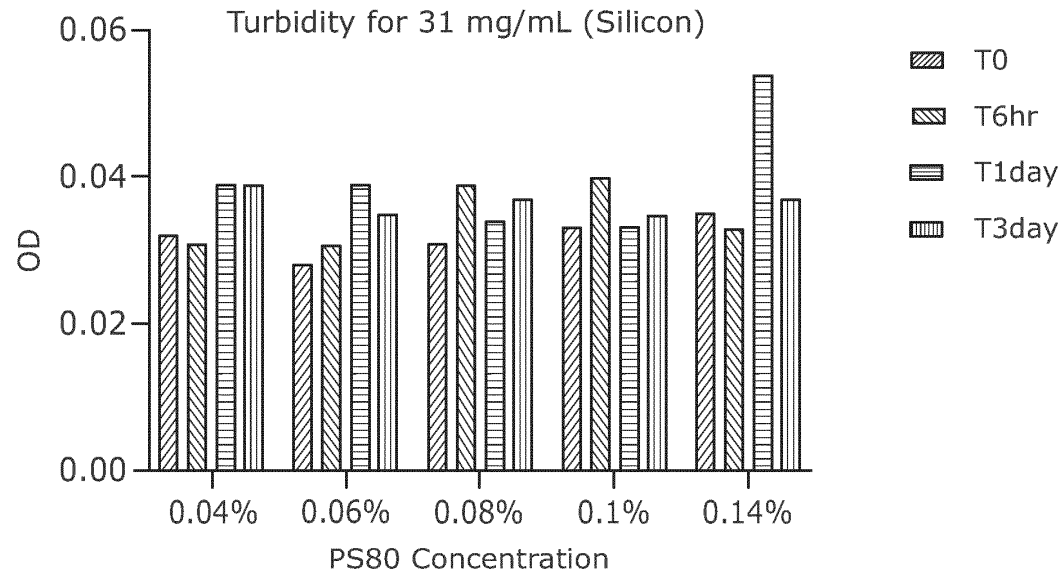


FIG. 37A

Turbidity for 31 mg/mL and 125 mg/mL formulations over the duration of the study with wrist-action and silicone oil

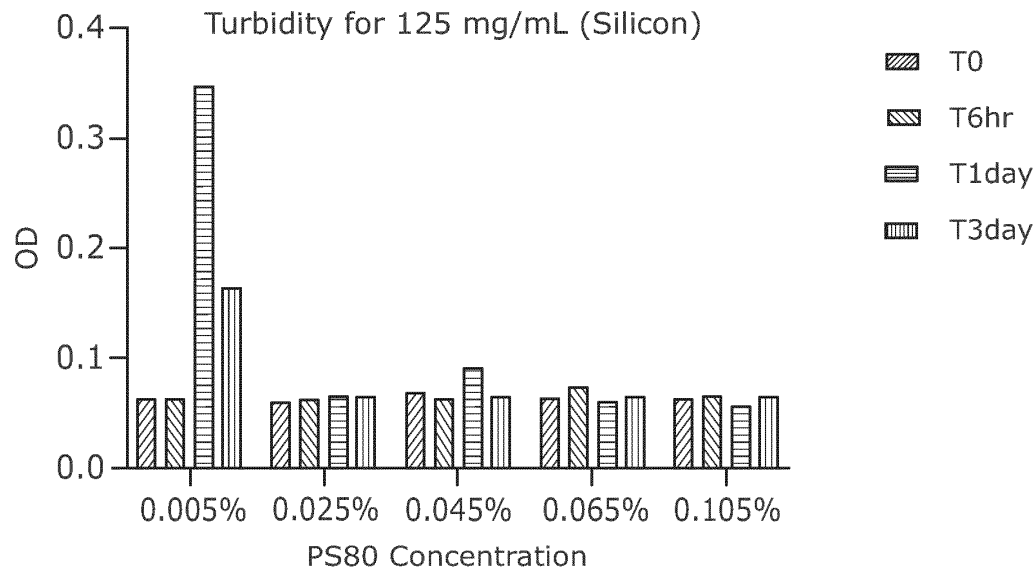


FIG. 37B

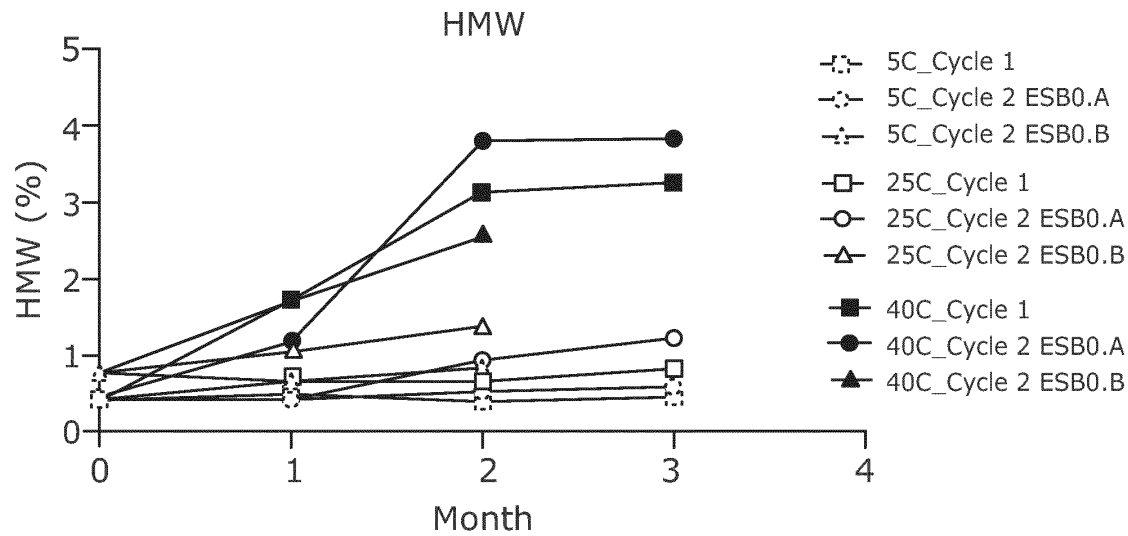


FIG. 38

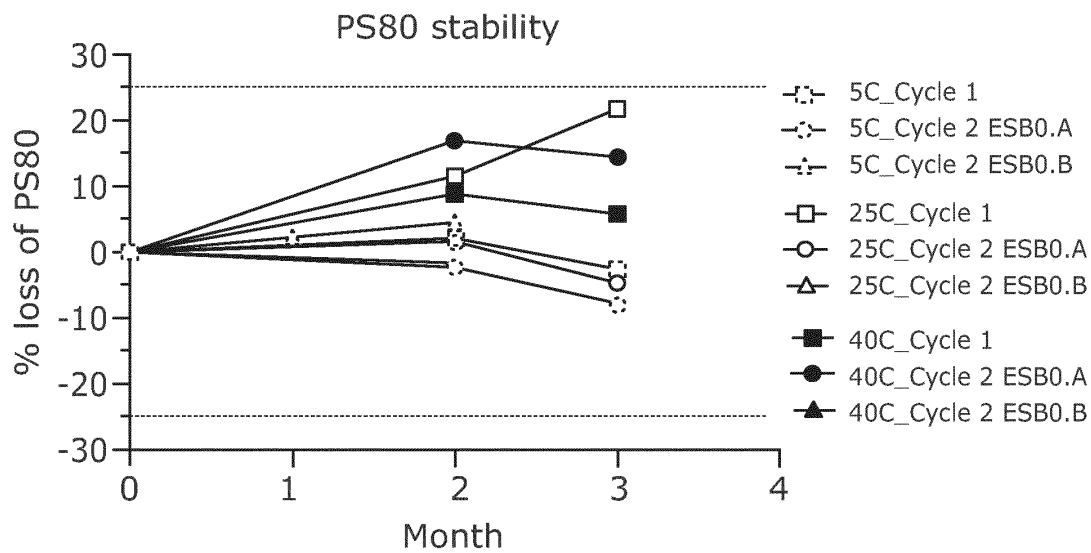


FIG. 39

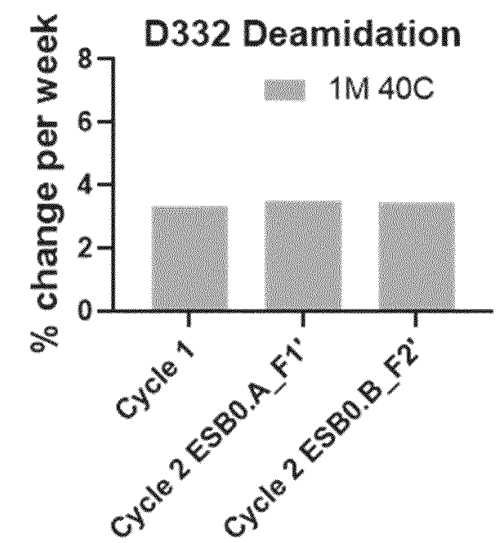


FIG. 40

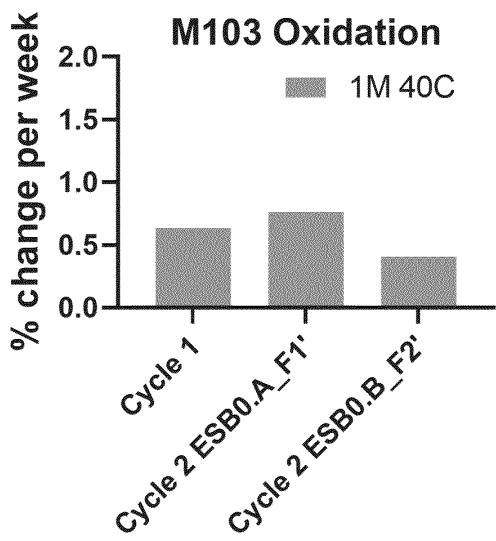


FIG. 41

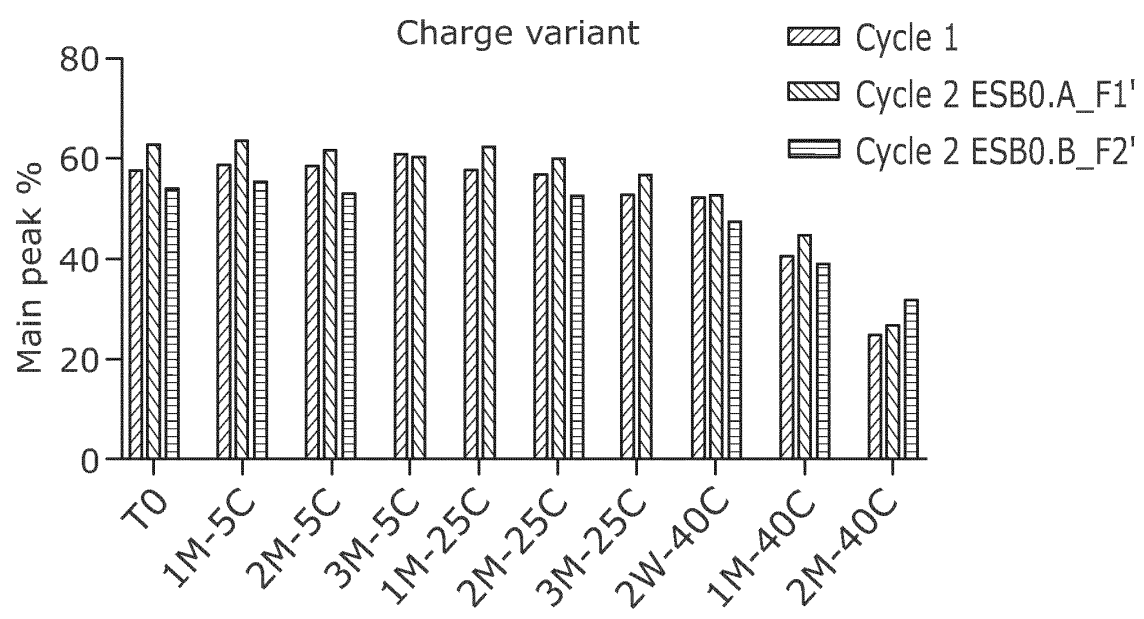


FIG. 42

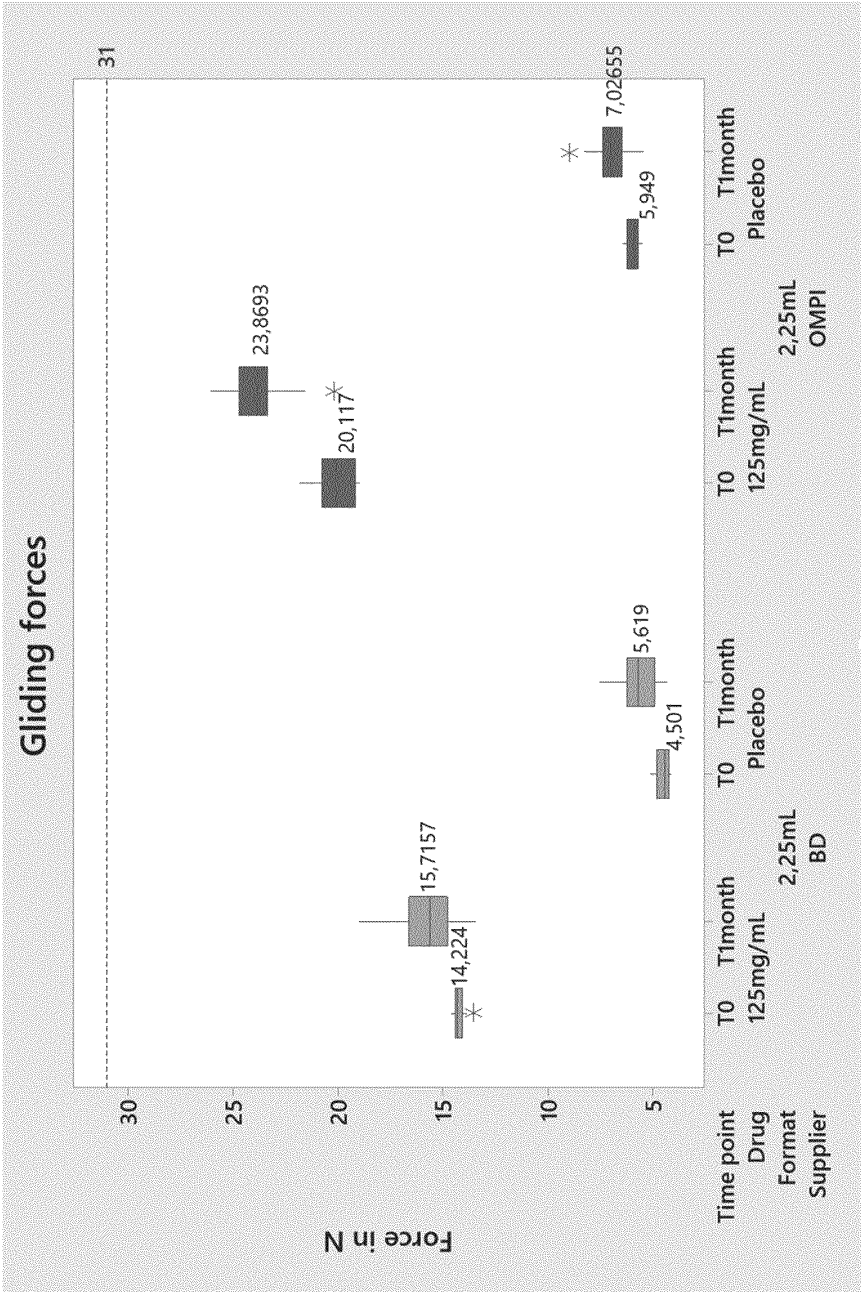
Stability Results: Heatmap

		Cycle 1**					Cycle 2_ESB0.B**				
		125 mg/mL					28 mg/mL				
		5°C-3M	25°C-3M	40°C-3M	Freeze-thaw		5°C-2M	25°C-2M	40°C-2M	5°C-2M	25°C-2M
											40°C-2M
											1M at -30°C
											Freeze-thaw
General product attributes	Attributes										
	F1 Specifications										
	Visible particles	Practically free from particles									
PS 80	Concentration	± 10%									
	% w/vol	Report results									
	HMWS	<5%									
Physical stability	HIAC	Particles ≥10 µm: ≤ 6000 per container									
		Particles ≥25 µm: ≤ 600 per container									
	Purity by CE-SDS (NR)***	≥85%									
Chemical stability	Charge variant by cIEF	Report results									
	D332										
	Deamidation M103										
		No SPEC									
		Oxidation									

* 0.01% decrease observed in GMP stability data. No significant decrease has been observed so far in internal assessment to date.
** Primary containers for Cycle 1 are 6R vials; Primary containers for Cycle 2_ESB0.B are BD 2.25 mL PFS
*** Data pending

FIG. 43

Gliding forces for 2,25mL BD and Ompi PFS



BD 2,25mL is selected for clinical activities based on gliding forces results

FIG. 44

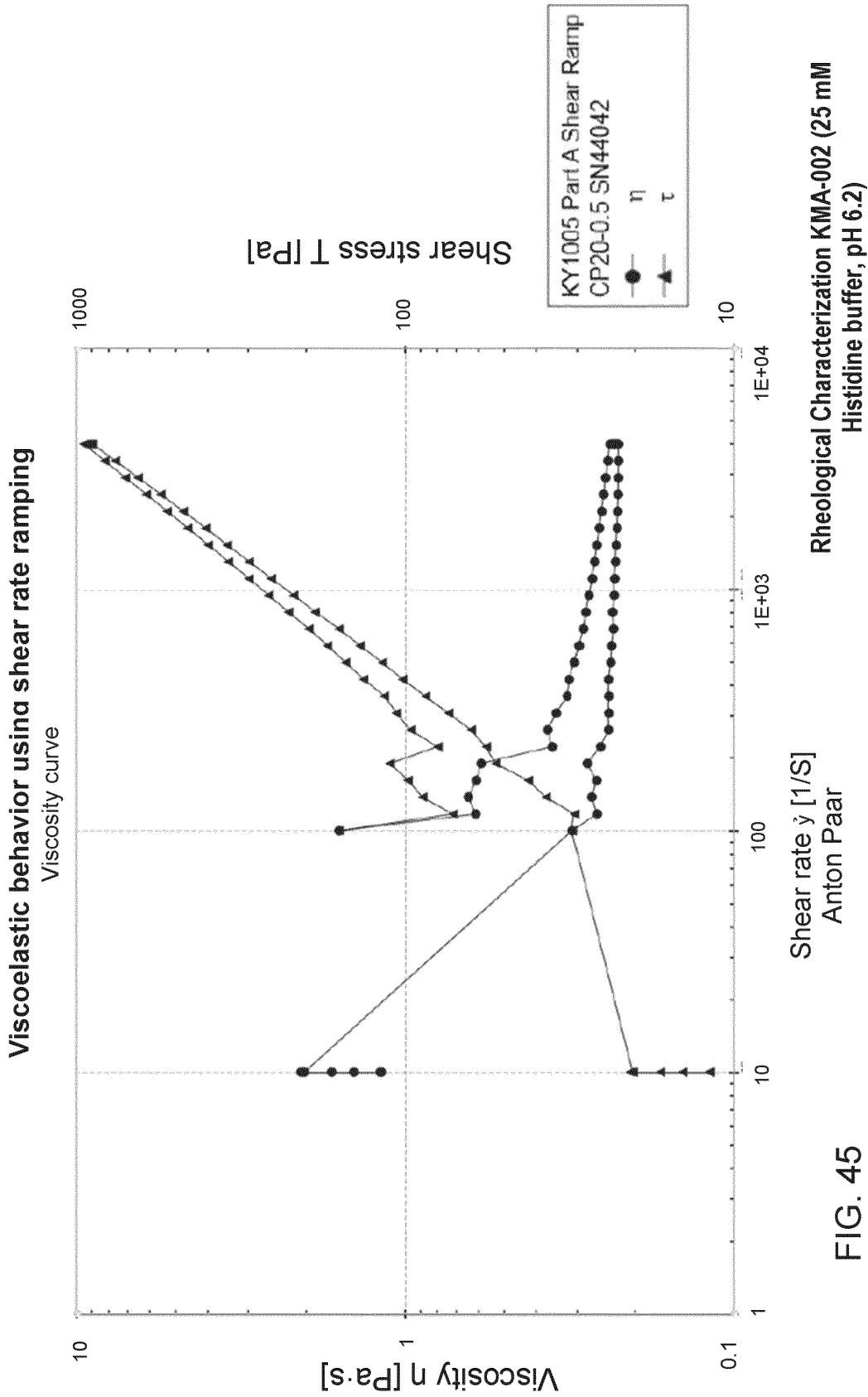


FIG. 45

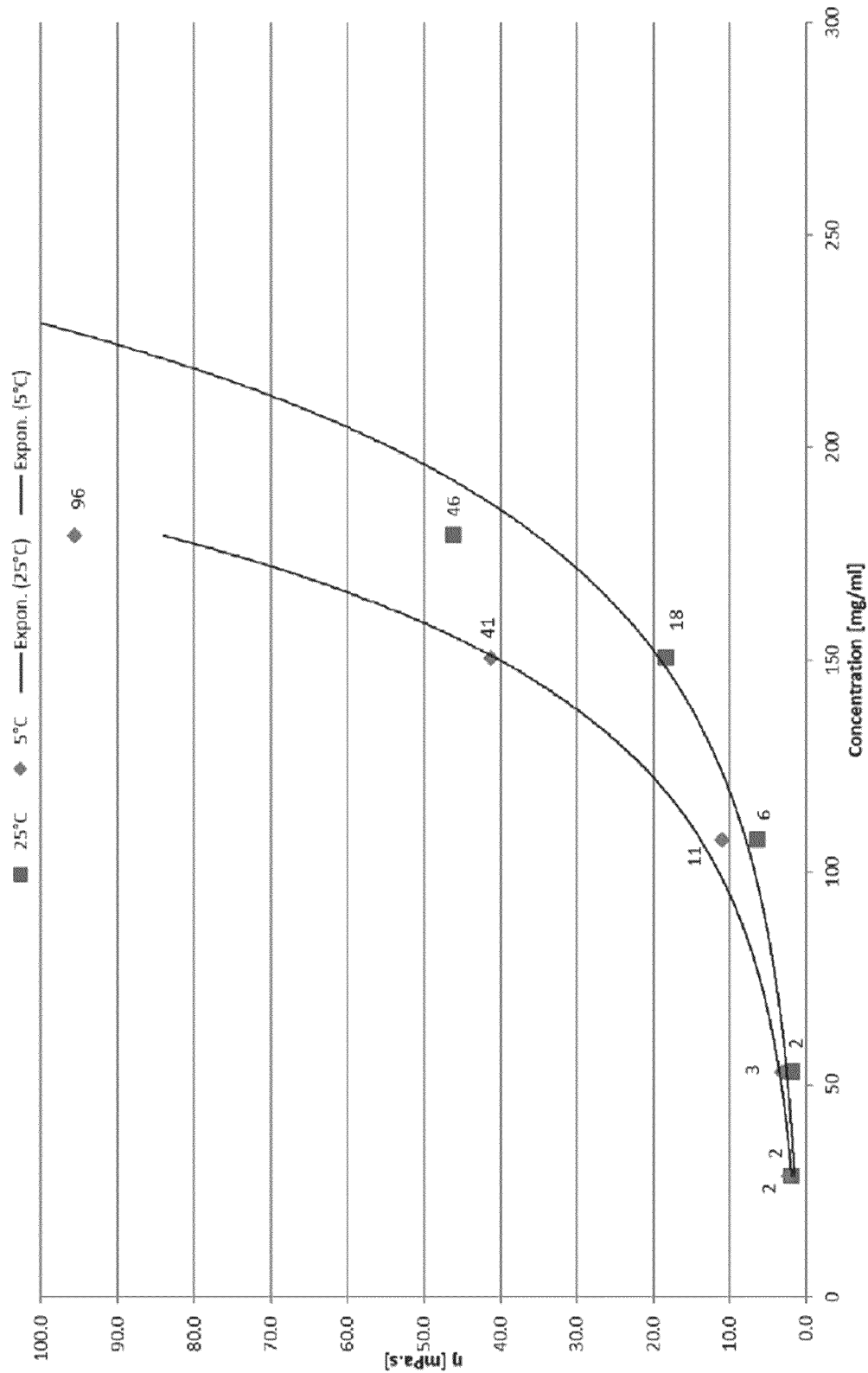


FIG. 46

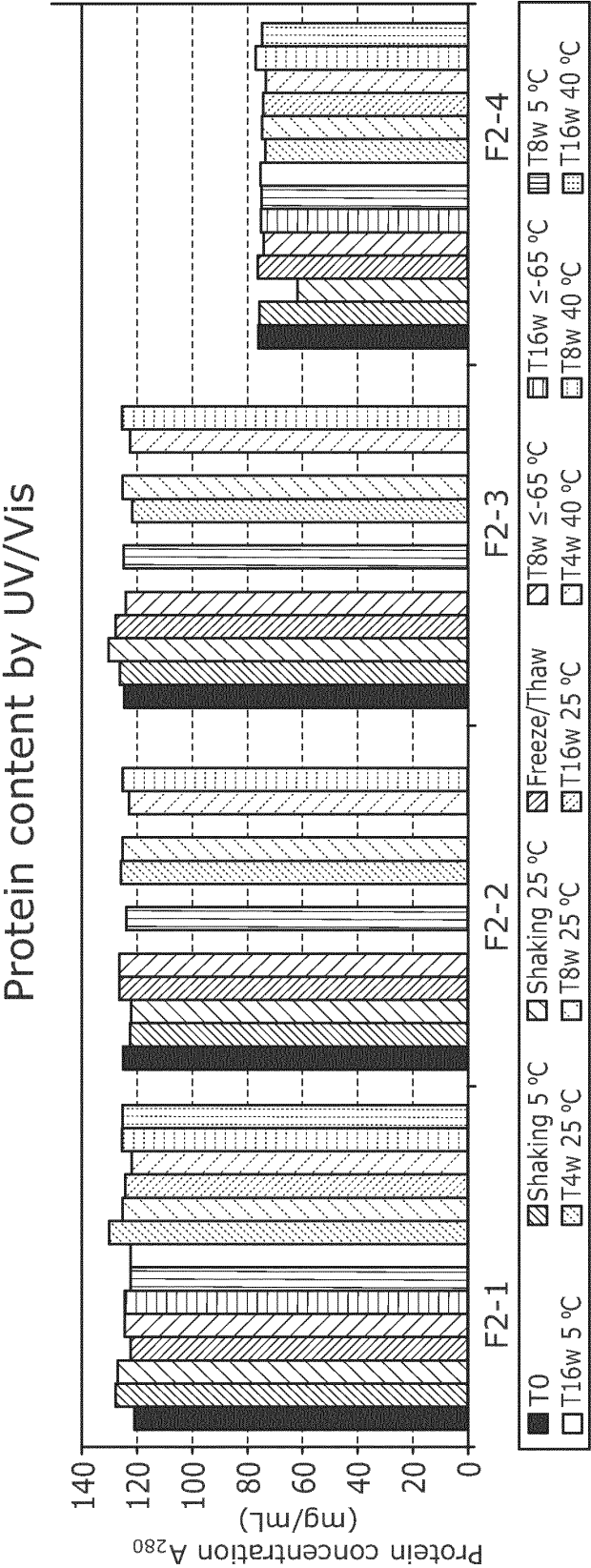


FIG. 47

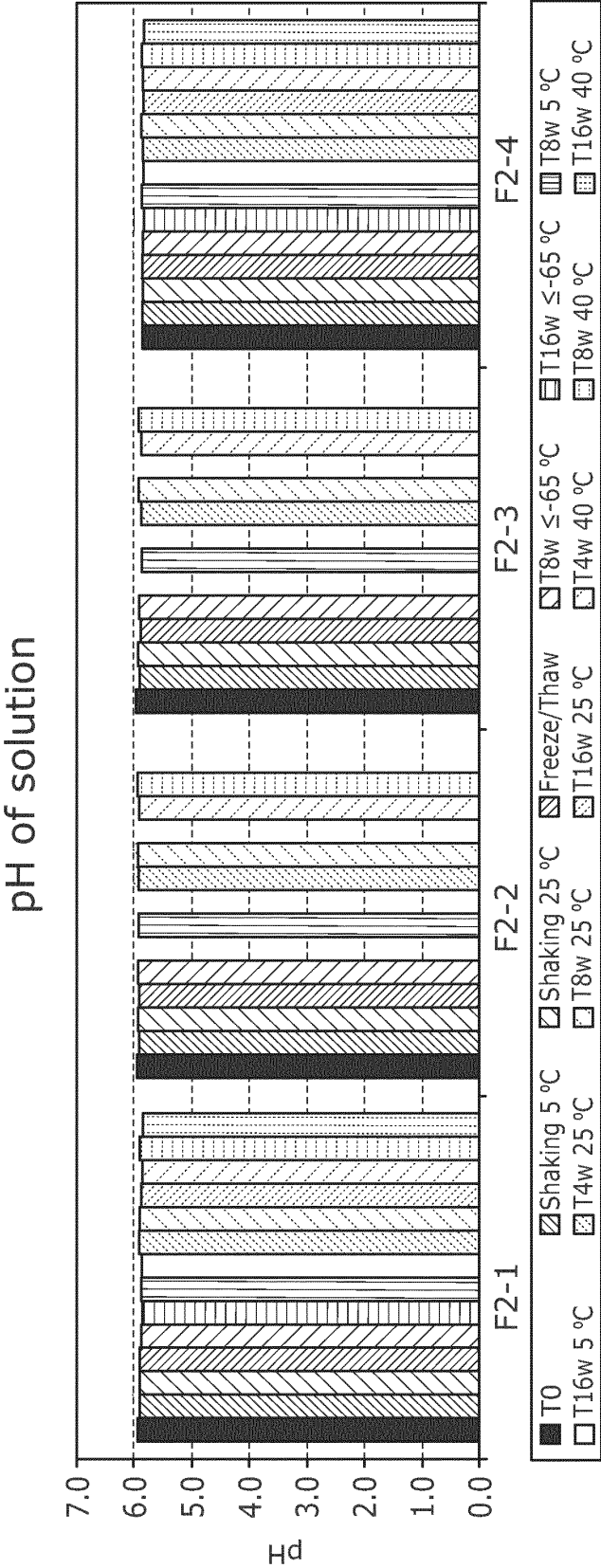


FIG. 48

Surfactant content by fluorescent micelle assay

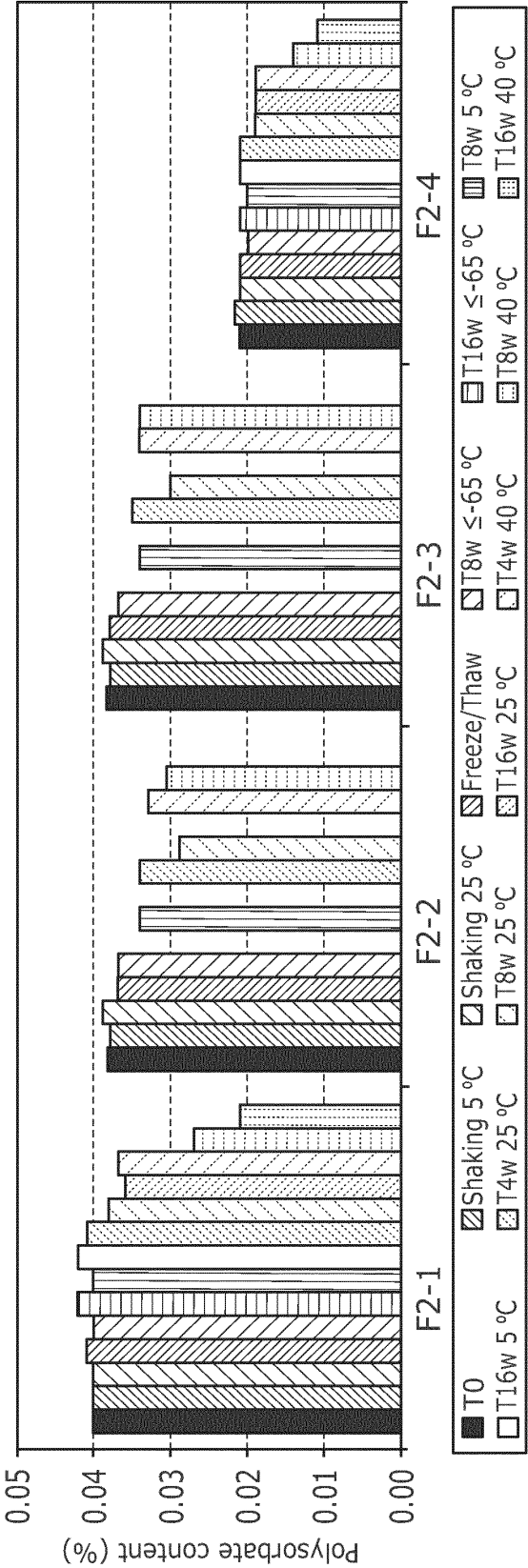


FIG. 49

Clarity and opalescence of solution (turbidity)

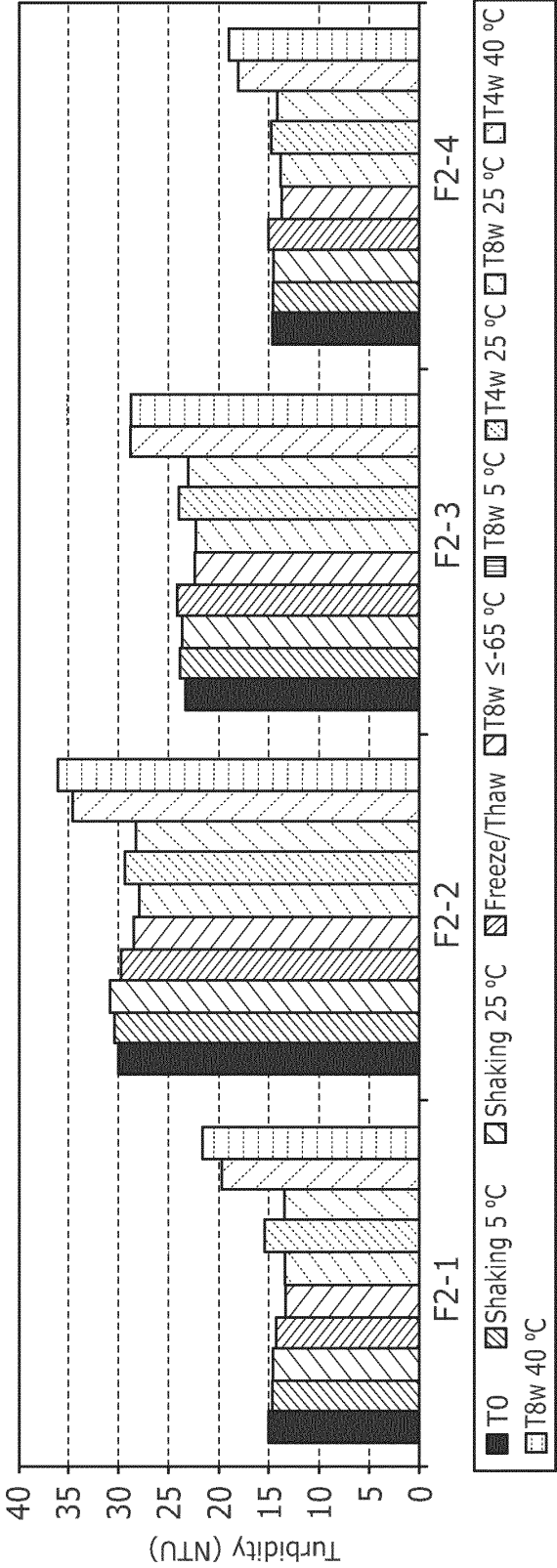


FIG. 50

Purity by size exclusion chromatography (SE-HPLC): Main peak Species

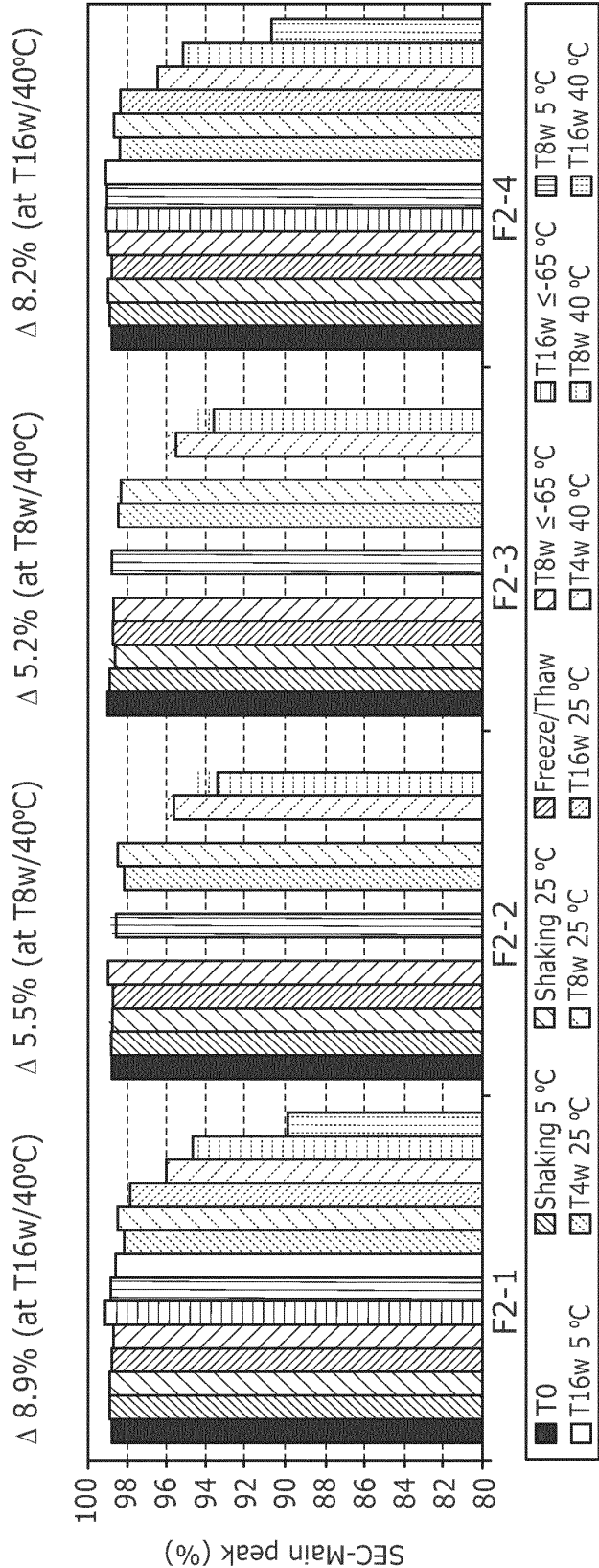


FIG. 51A

Purity by size exclusion chromatography (SE-HPLC): High Molecular Weight (HMWS) Species

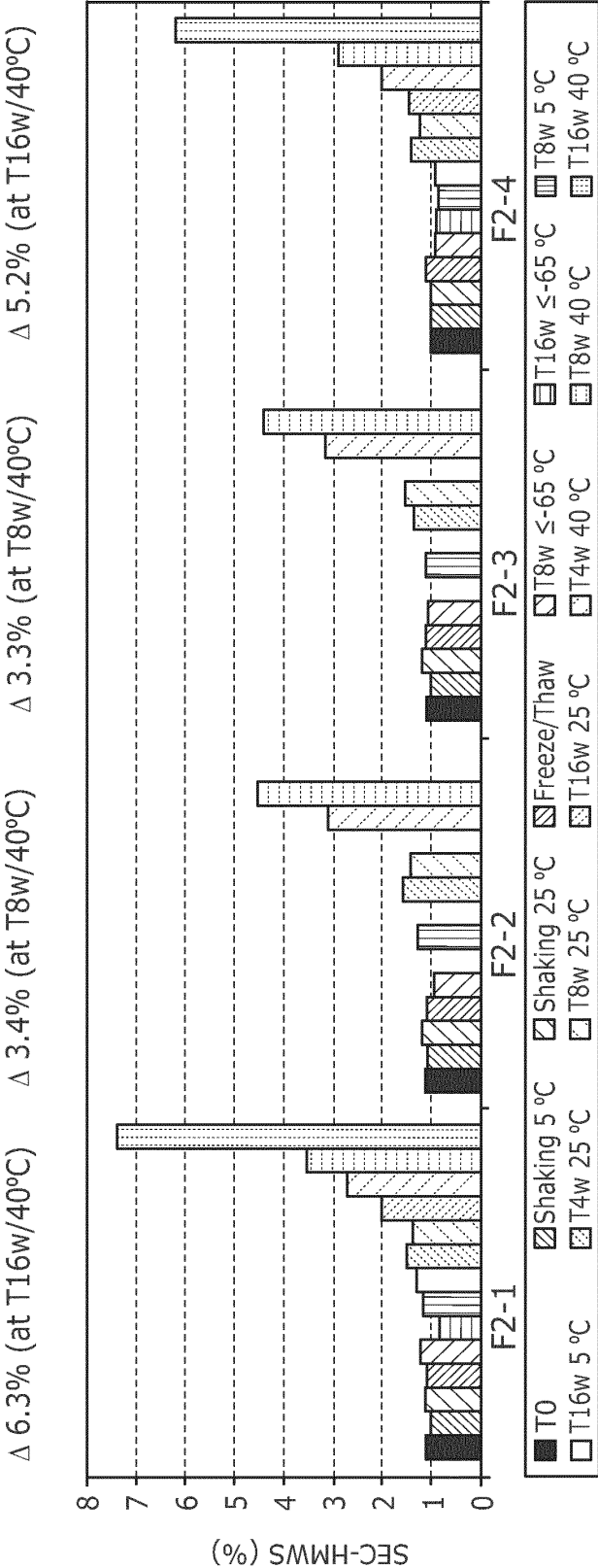


FIG. 51B

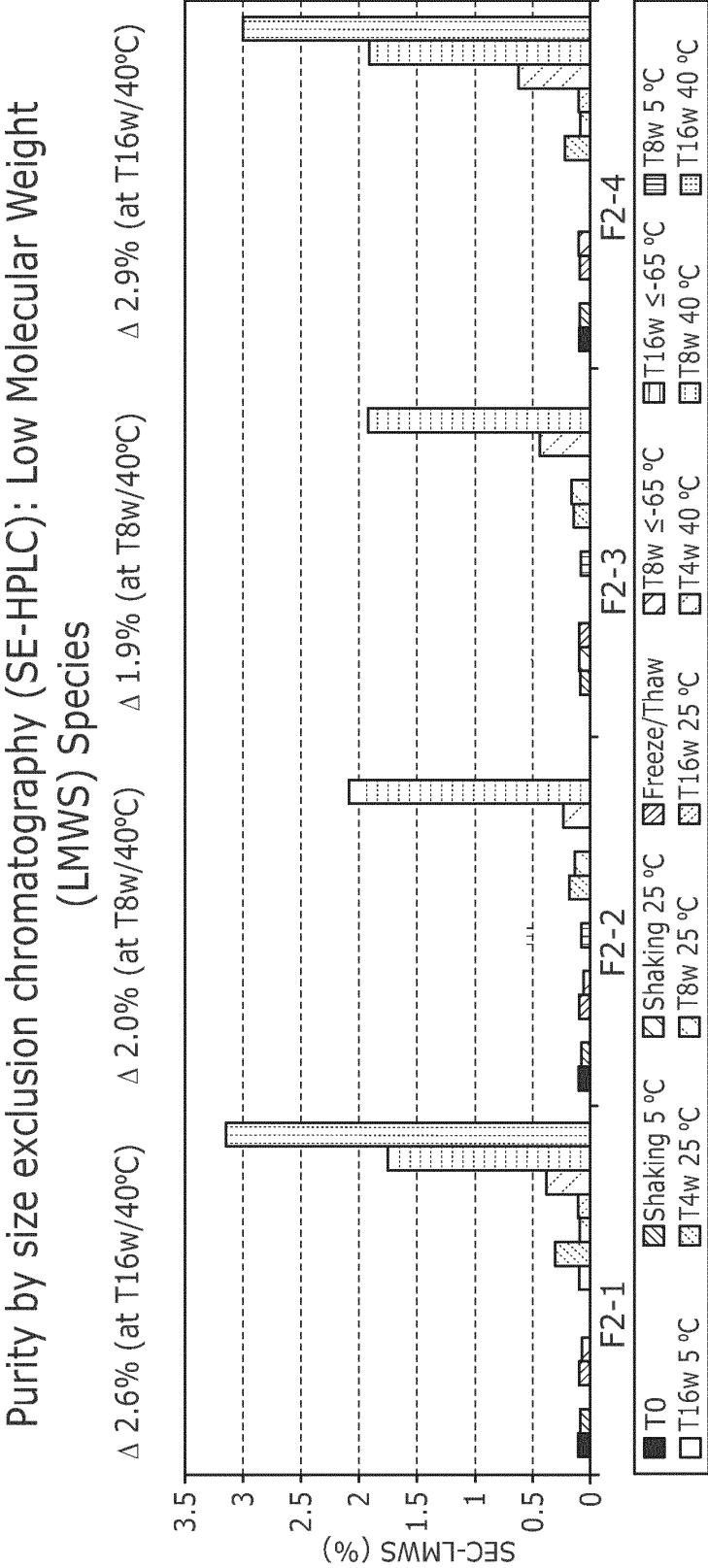


FIG. 51C

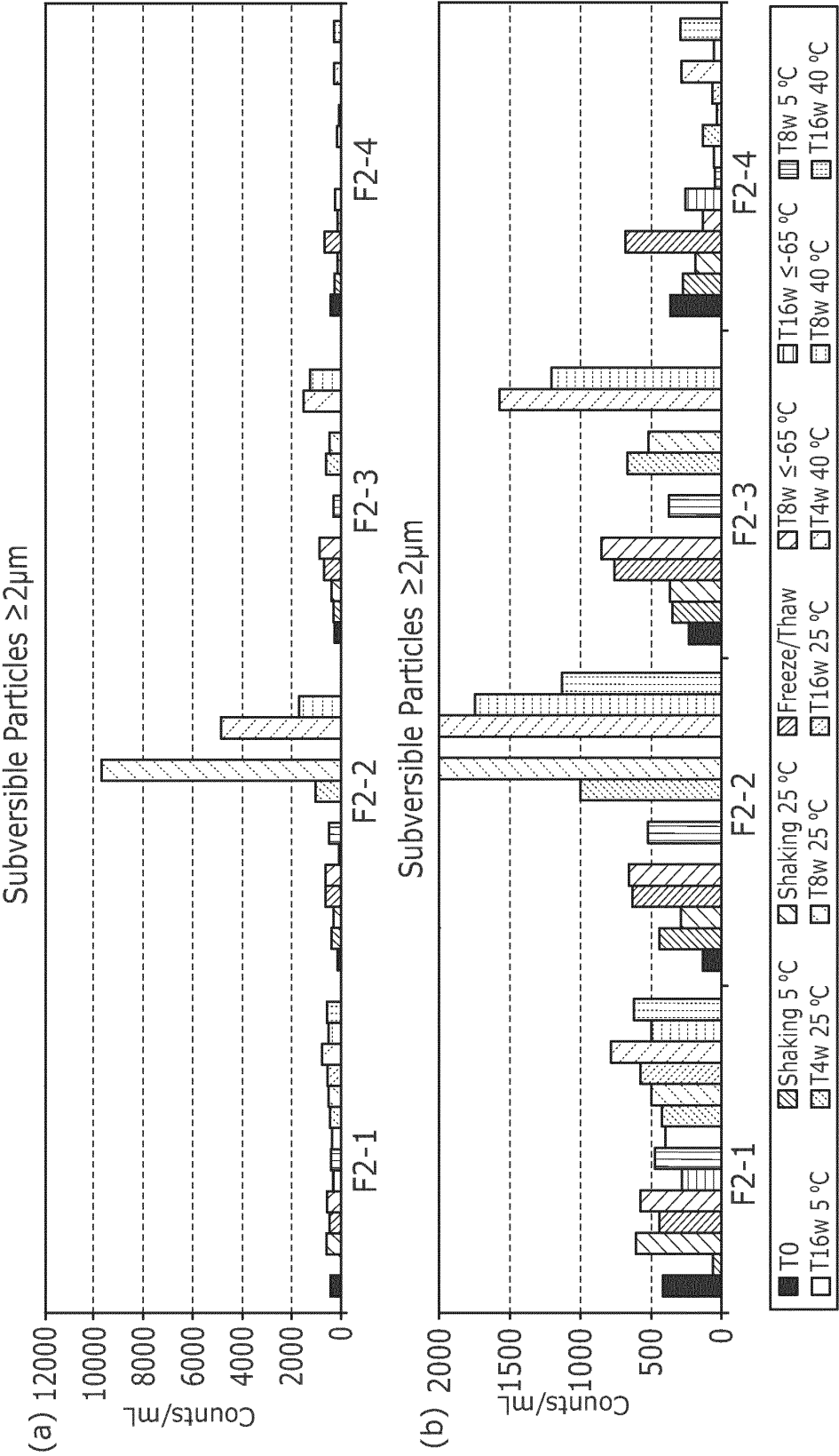


FIG. 52A

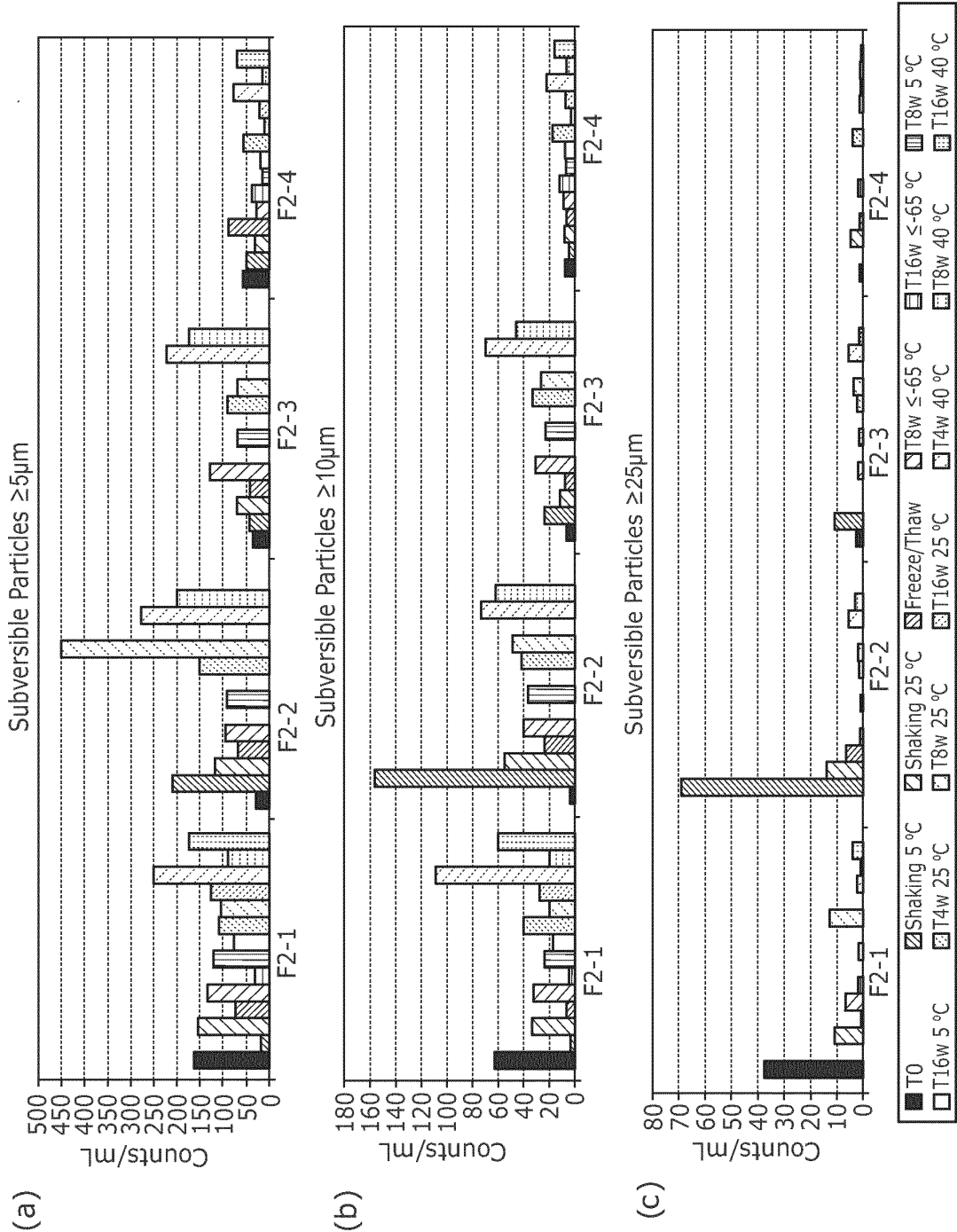


FIG. 52B

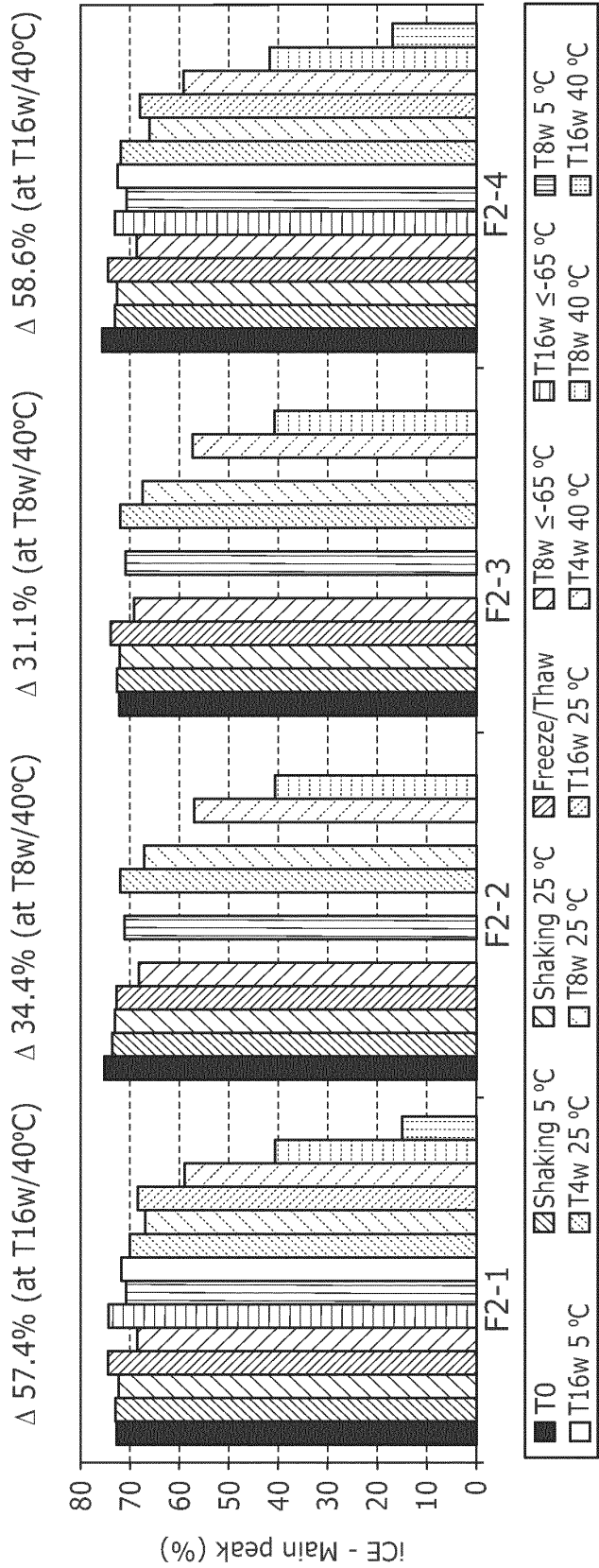


FIG. 53A

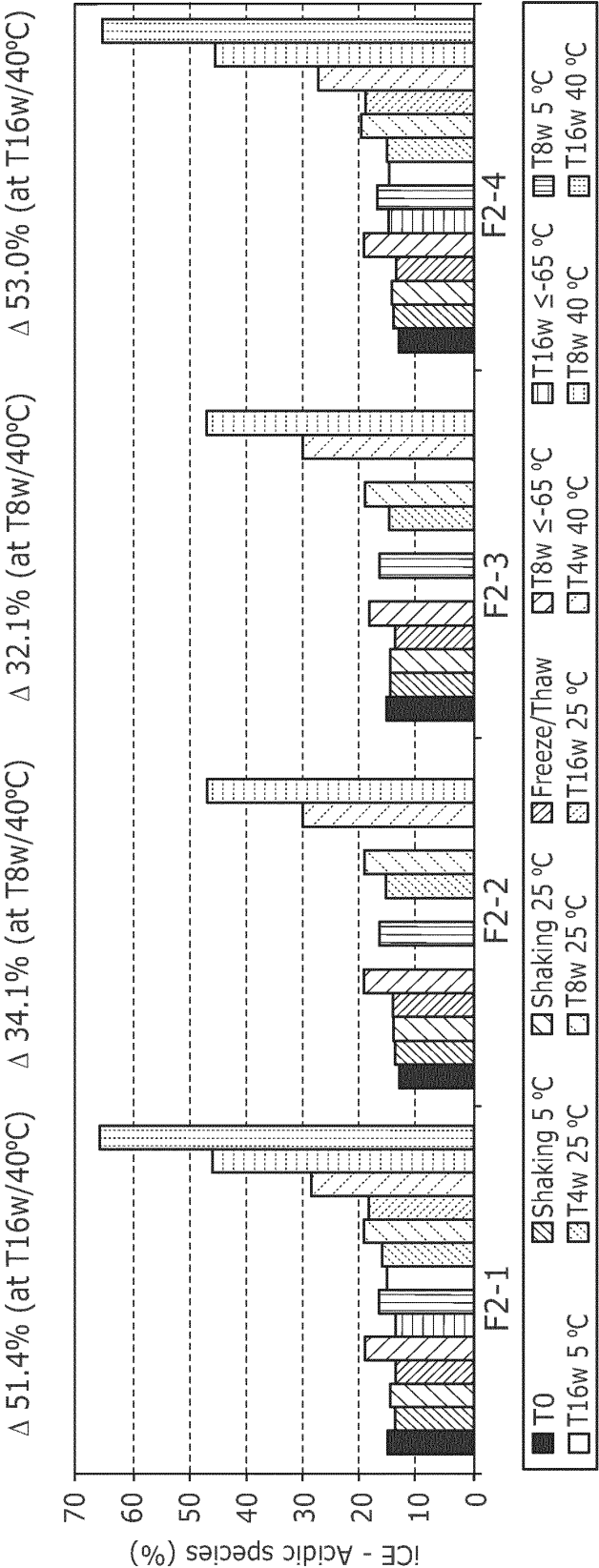


FIG. 53B

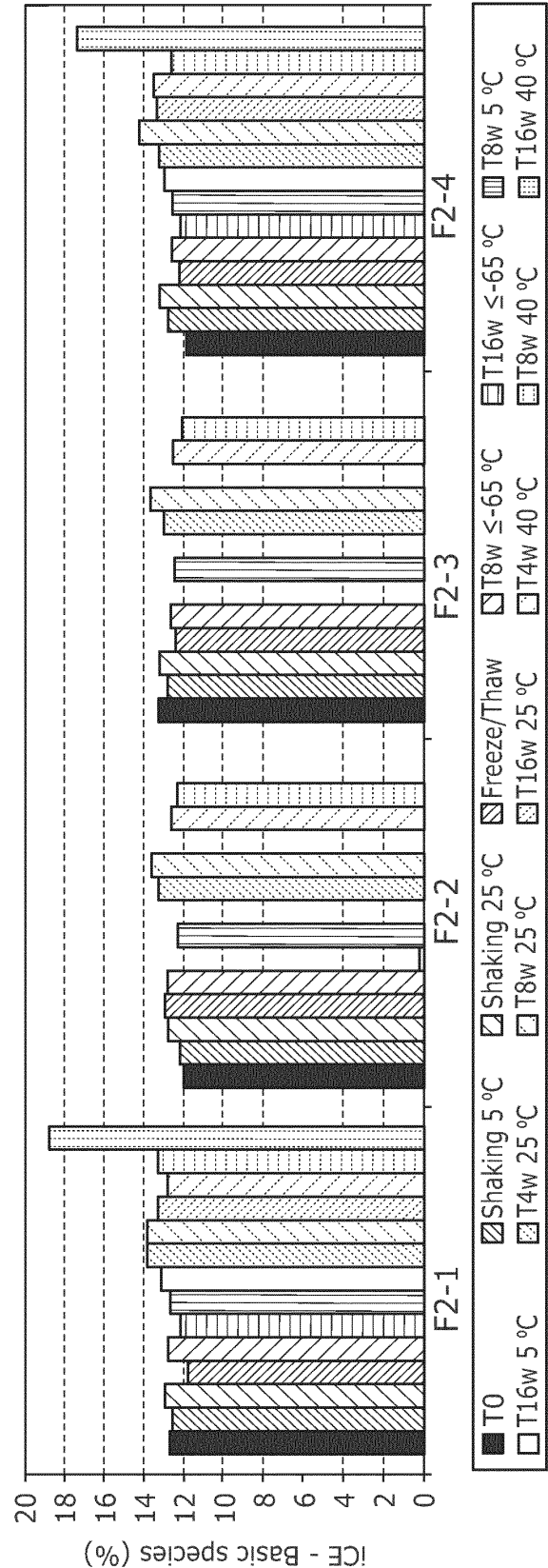


FIG. 53C