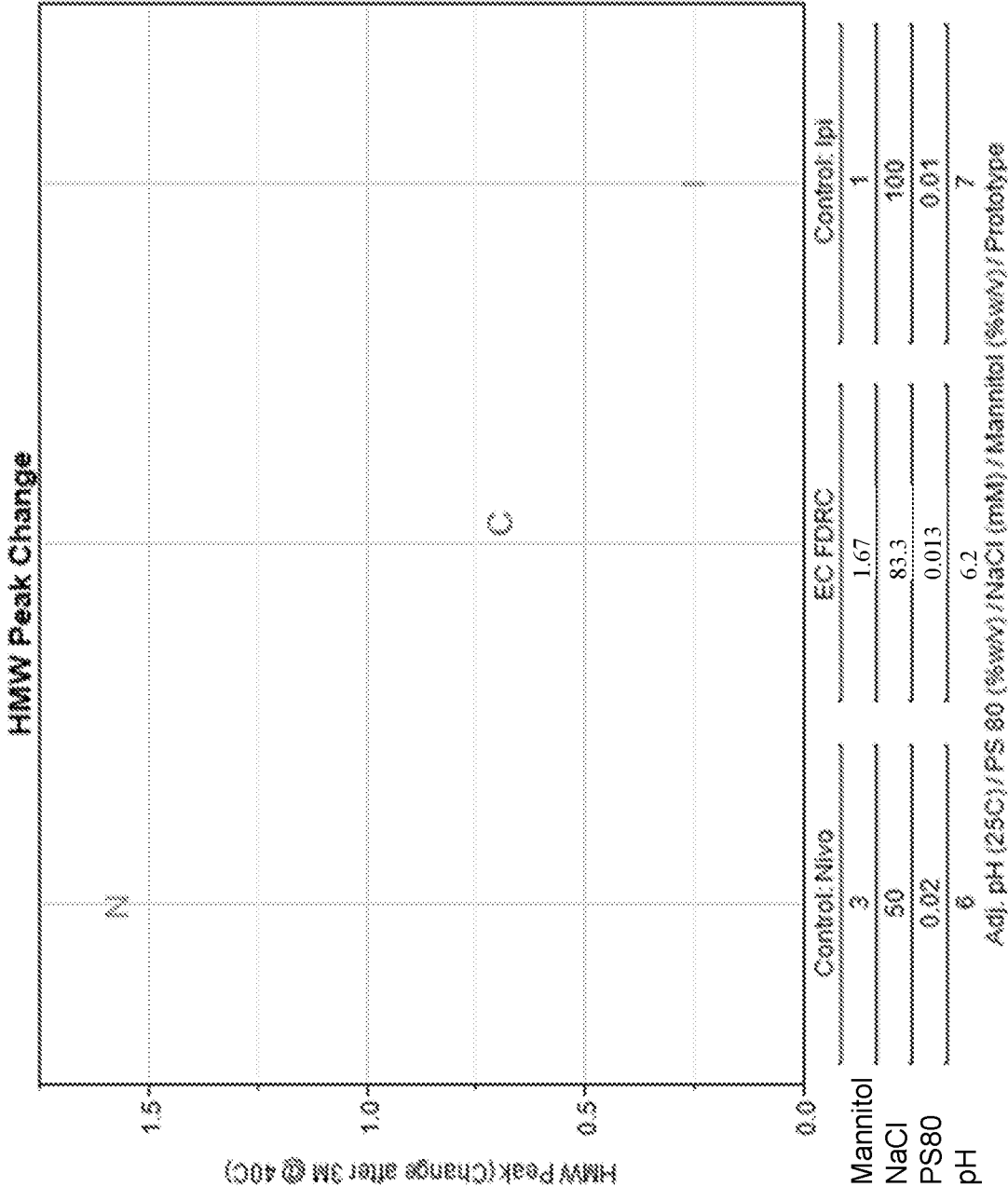


Fig. 1: Commercial Formulations of Ipilimumab and Nivolumab

Ipilimumab Composition	DS	DP	Nivolumab Composition	DS	DP
Type	IgG1; Mol. Wt.: 147,991 Daltons		Type	IgG4; Mol. Wt.: 143,567 Daltons	
pl:	8.7-8.8		pl:	8.0-8.1	
BMS-734016	5 mg/ml	5 mg/ml	BMS-936558	20 mg/ml	10 mg/ml
Tris HCl, USP	20 mM	20 mM	Sodium Citrate Dihydrate, USP	20mM	20mM
pH	7.0	7.0	pH	6.0	6.0
Sodium Chloride, USP	100 mM	100 mM	Sodium Chloride, USP	50 mM	50 mM
Mannitol (%w/v), USP	1.0 %	1.0%	Mannitol (%w/v), USP	3.0 %	3.0 %
Pentetic Acid (DTPA), USP	100 µM	100 µM	Pentetic Acid (DTPA), USP	20 µM	20 µM
Polysorbate 80, NF	0.01 %	0.01%	Polysorbate 80, NF	0.04 %	0.02 %
Strengths (fill volumes): 50 mg (10 mL in a 10 mL vial) and 200 mg (40 mL in a 50 mL vial) DP Unit Ops: Fill, Finish			Strength (fill volume): 100 mg (10 mL in a 10 mL vial) DP Unit Ops: Dilute, Fill, Finish		

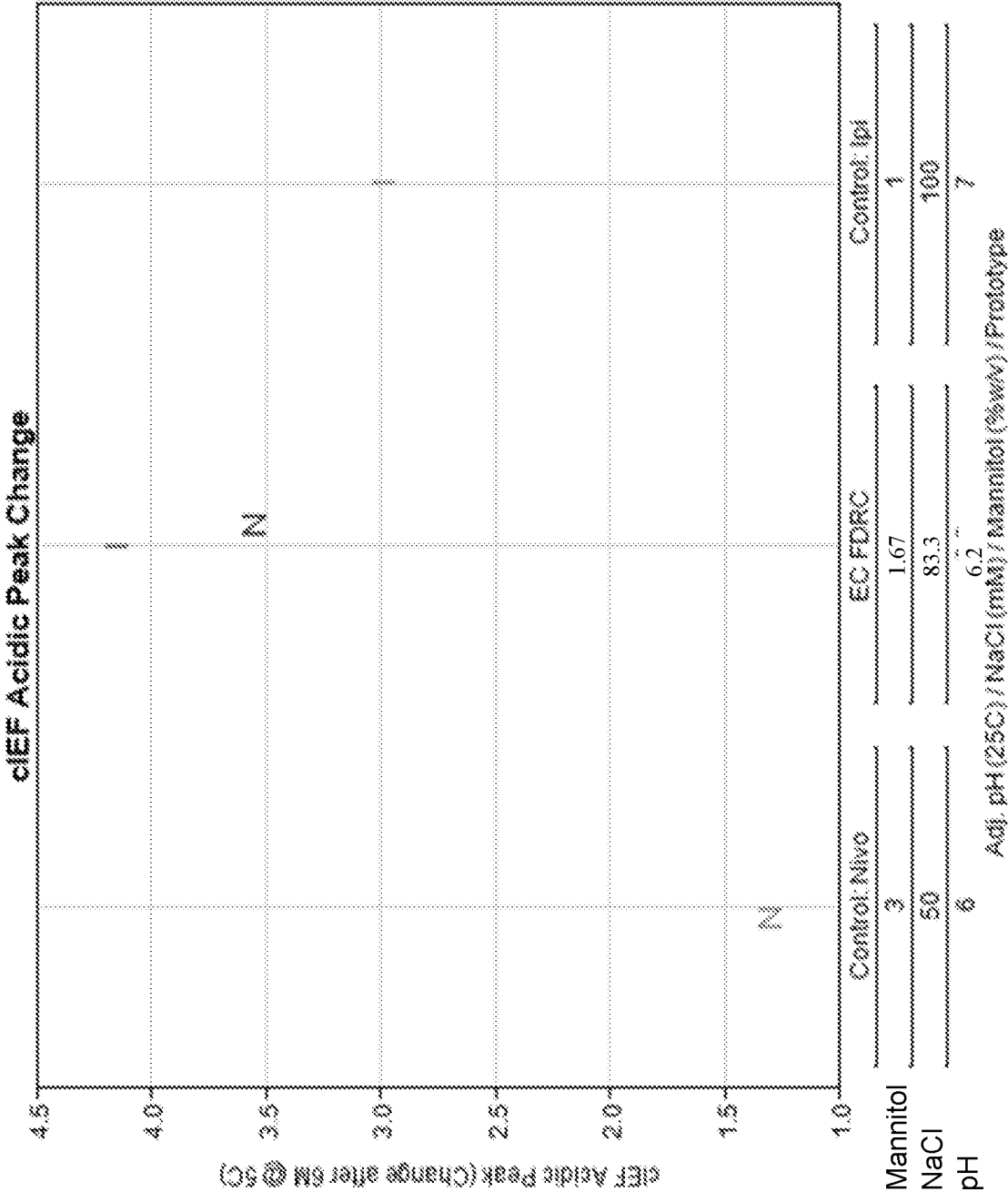
DS: Drug Substance; DP: Drug Product

Fig. 2A: 1:1 Ratio Fixed Dosing Formulation for Nivolumab and Ipilimumab
HMW Profile Change (3M at 40°C)



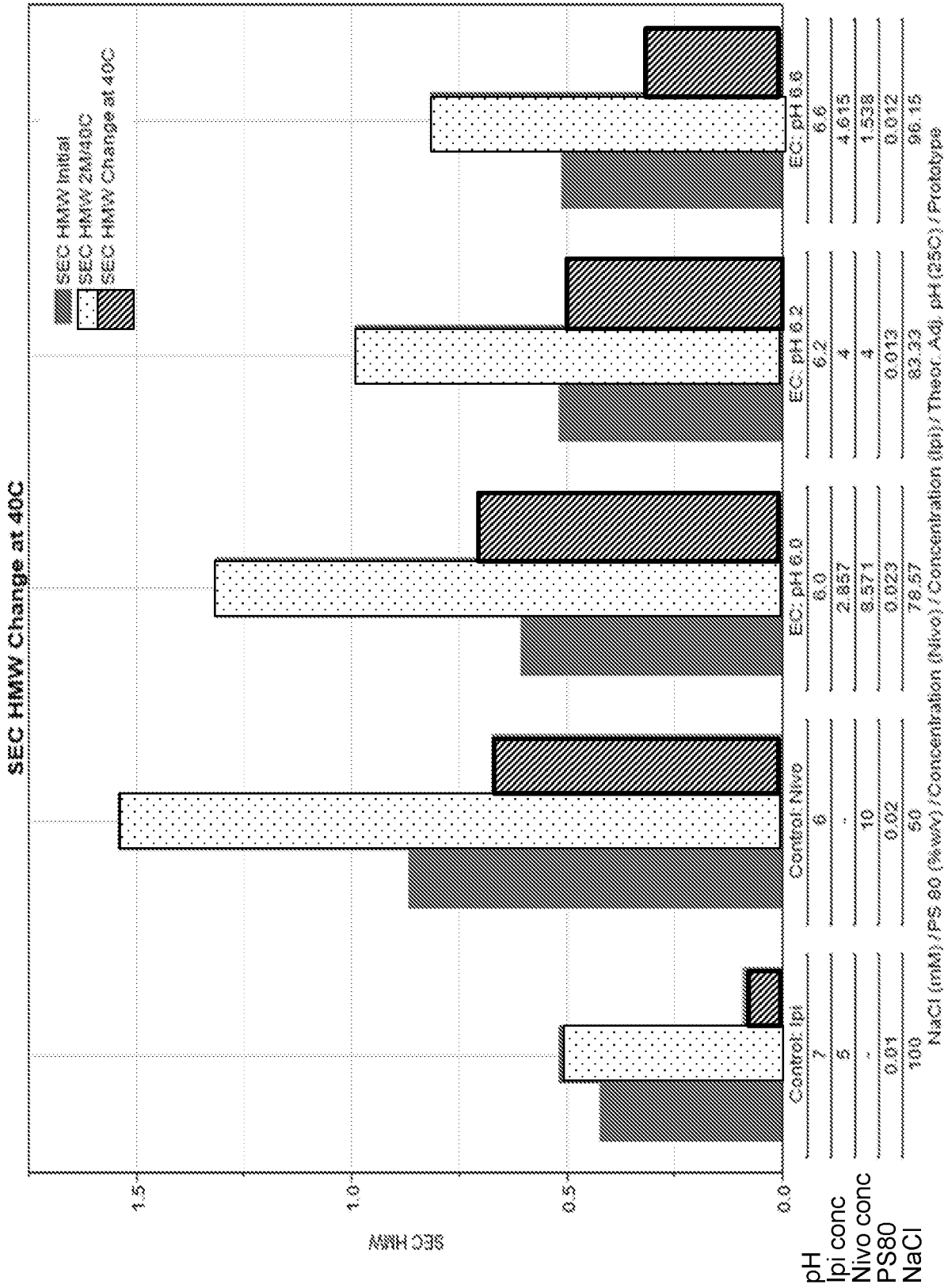
N: Nivolumab HMW Peak; C: Combined HMW Peak; I: Ipilimumab HMW Peak

Fig. 2B: 1:1 Ratio Fixed Dosing Formulation for for Nivolumab and Ipilimumab
Charge Profile Change (cIEF) (6M at 5°C)



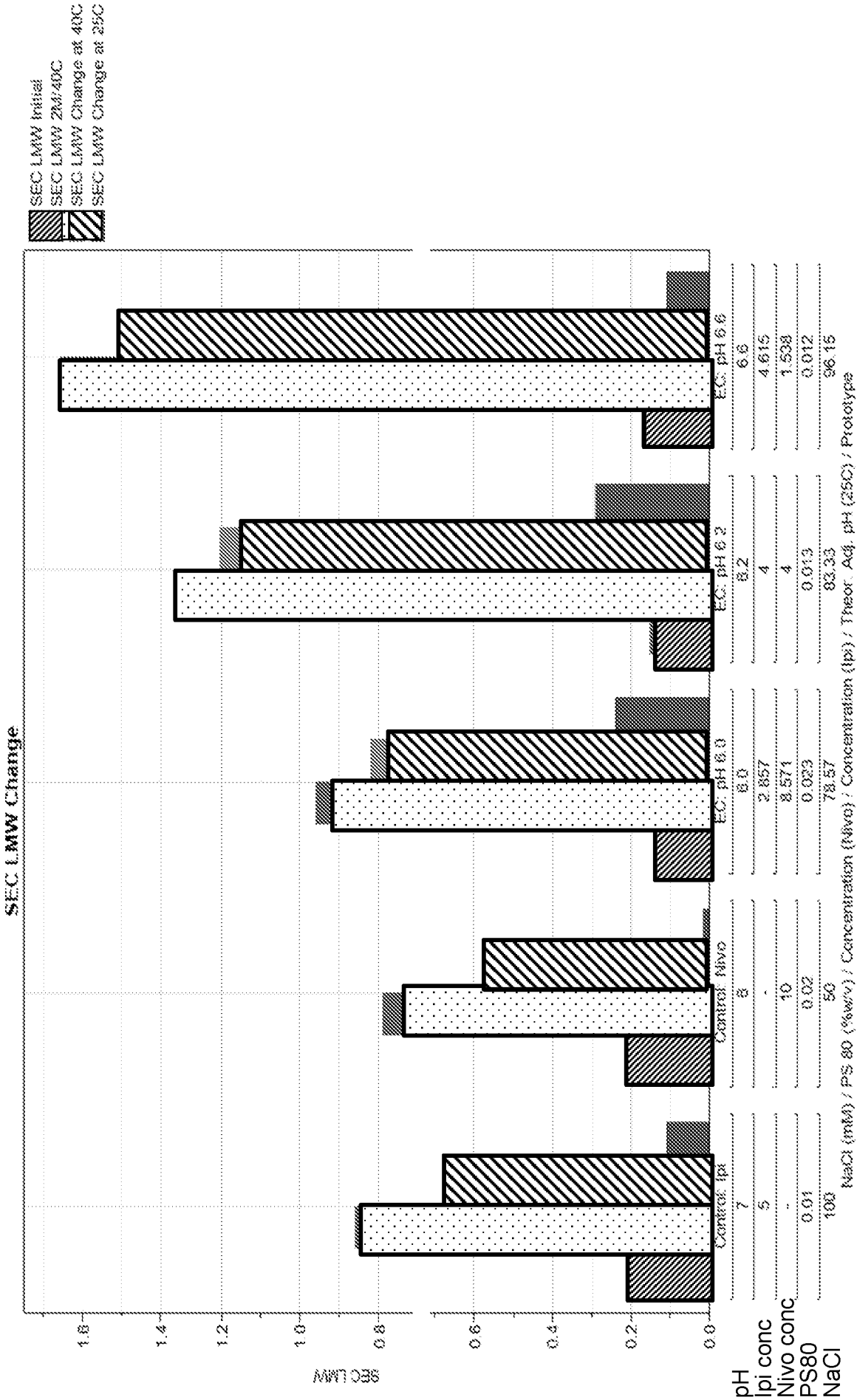
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Fig. 3A: 1:3, 1:1, or 3:1 Ratio Fixed Dosing Formulations
for Nivolumab and Ipilimumab: HMW Profile Change (2M at 40°C)



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Fig. 3B: 1:3, 1:1, or 3:1 Fixed Dosing Formulations
for Nivolumab and Ipilimumab: LMW Profile Change (2M at 40°C and 3M at 25°C)



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Fig. 4A: 1:3, 1:1, or 3:1 Ratio Fixed Dosing Formulations
for Nivolumab and Ipilimumab: cIEF Acidic Peak Change (3M at 25°C)

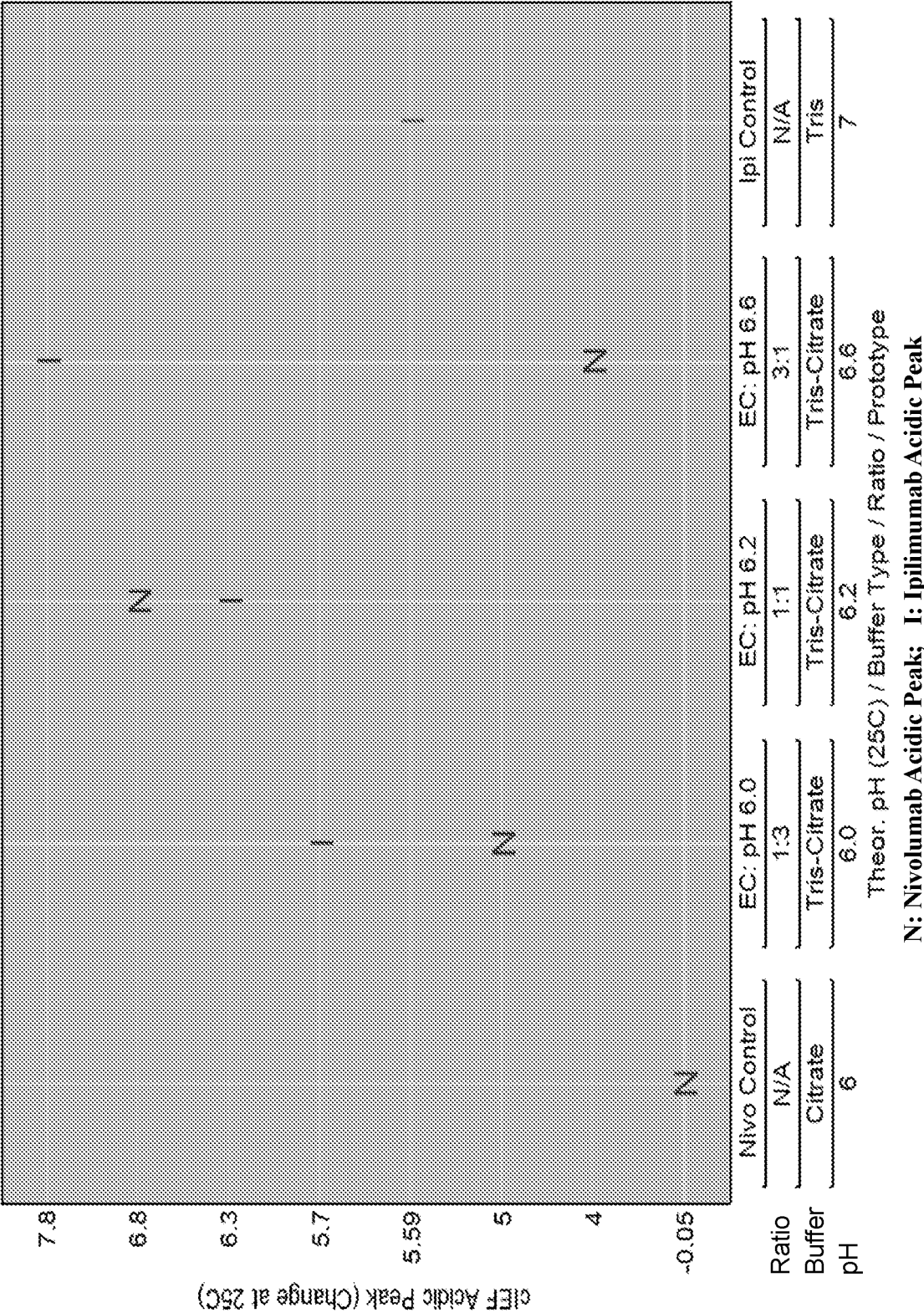
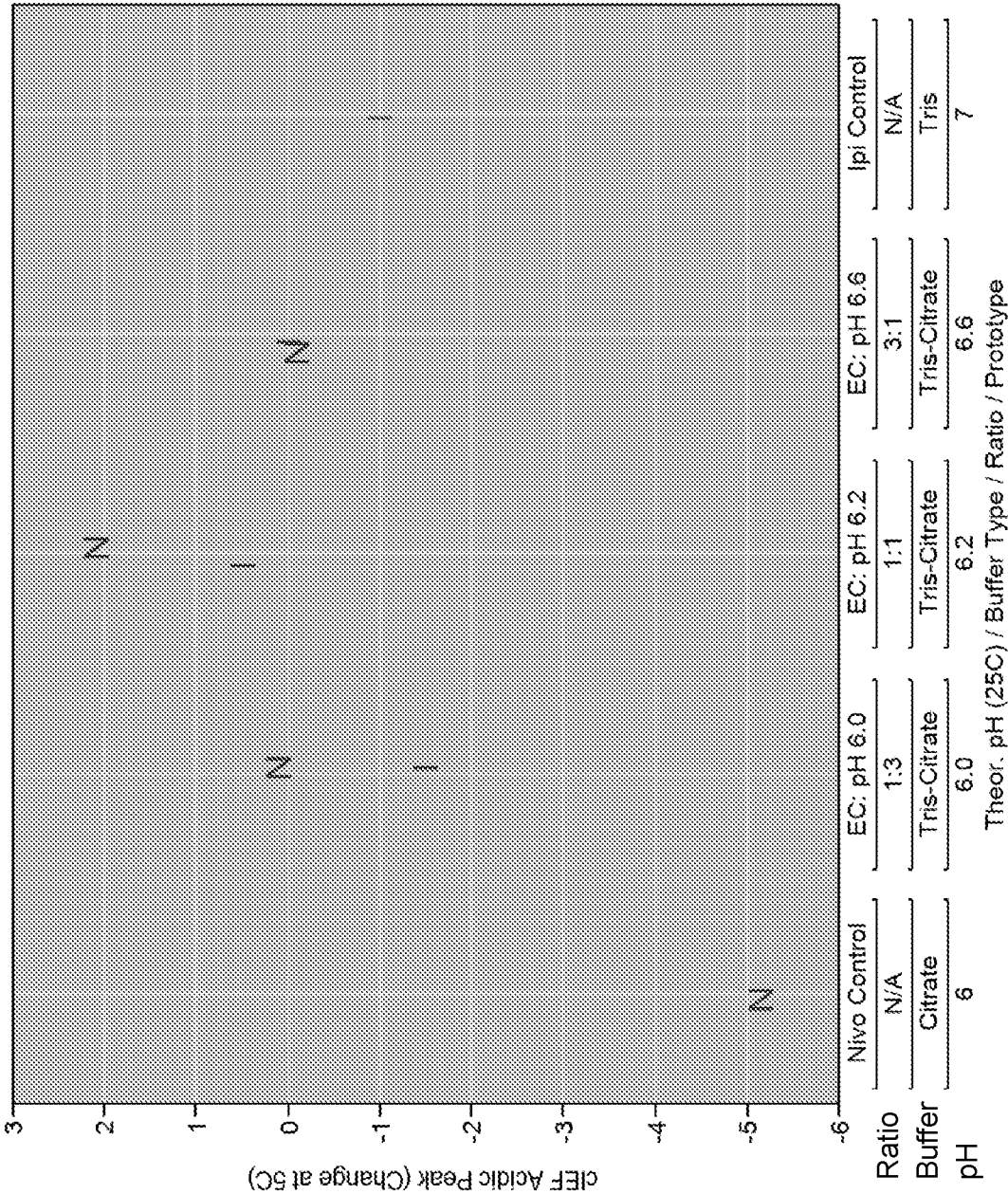
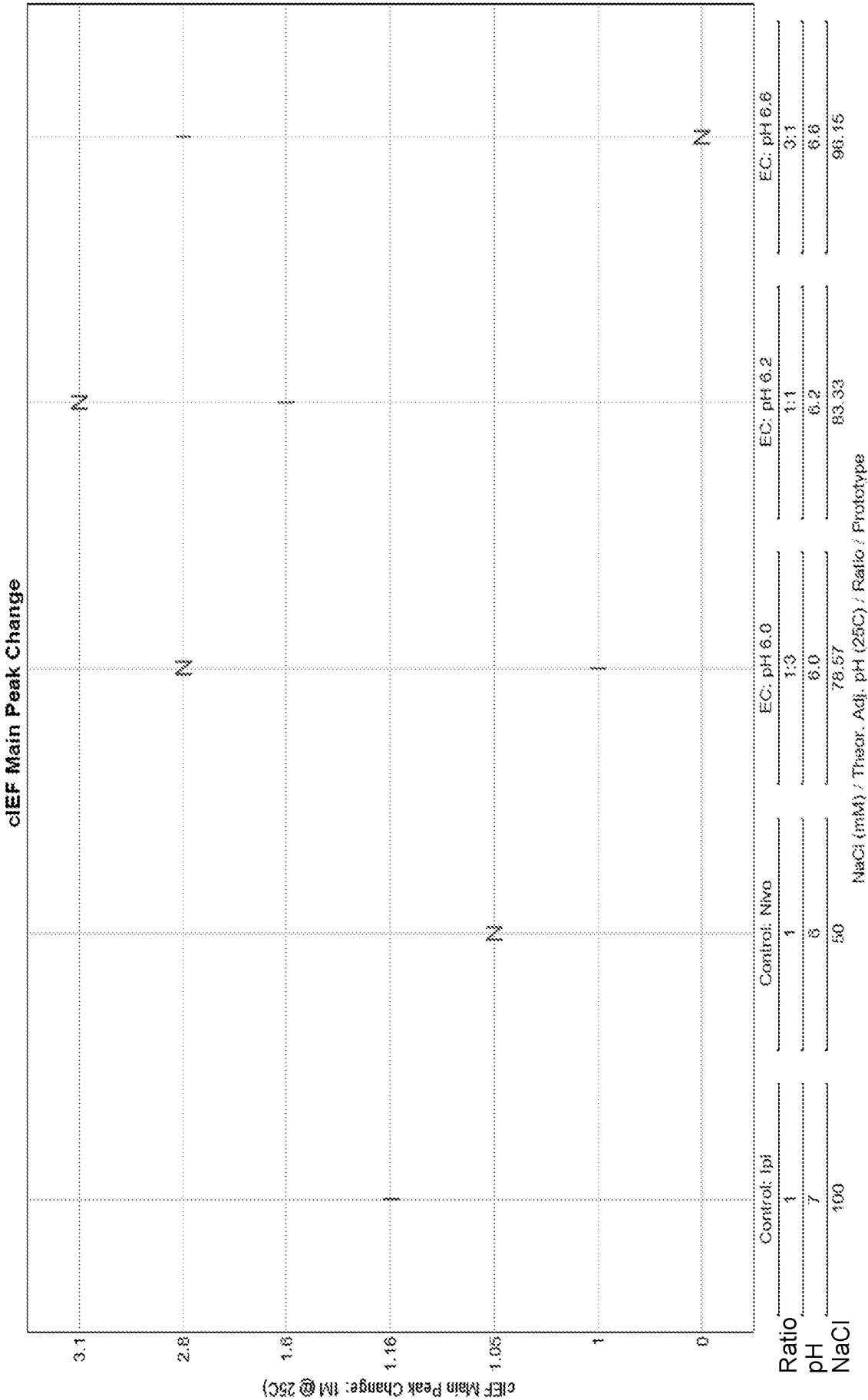


Fig. 4B: 1:3, 1:1, or 3:1 Fixed Dosing Formulations
for Nivolumab and Ipilimumab: cIEF Acidic Peak Change (3M at 5°C)



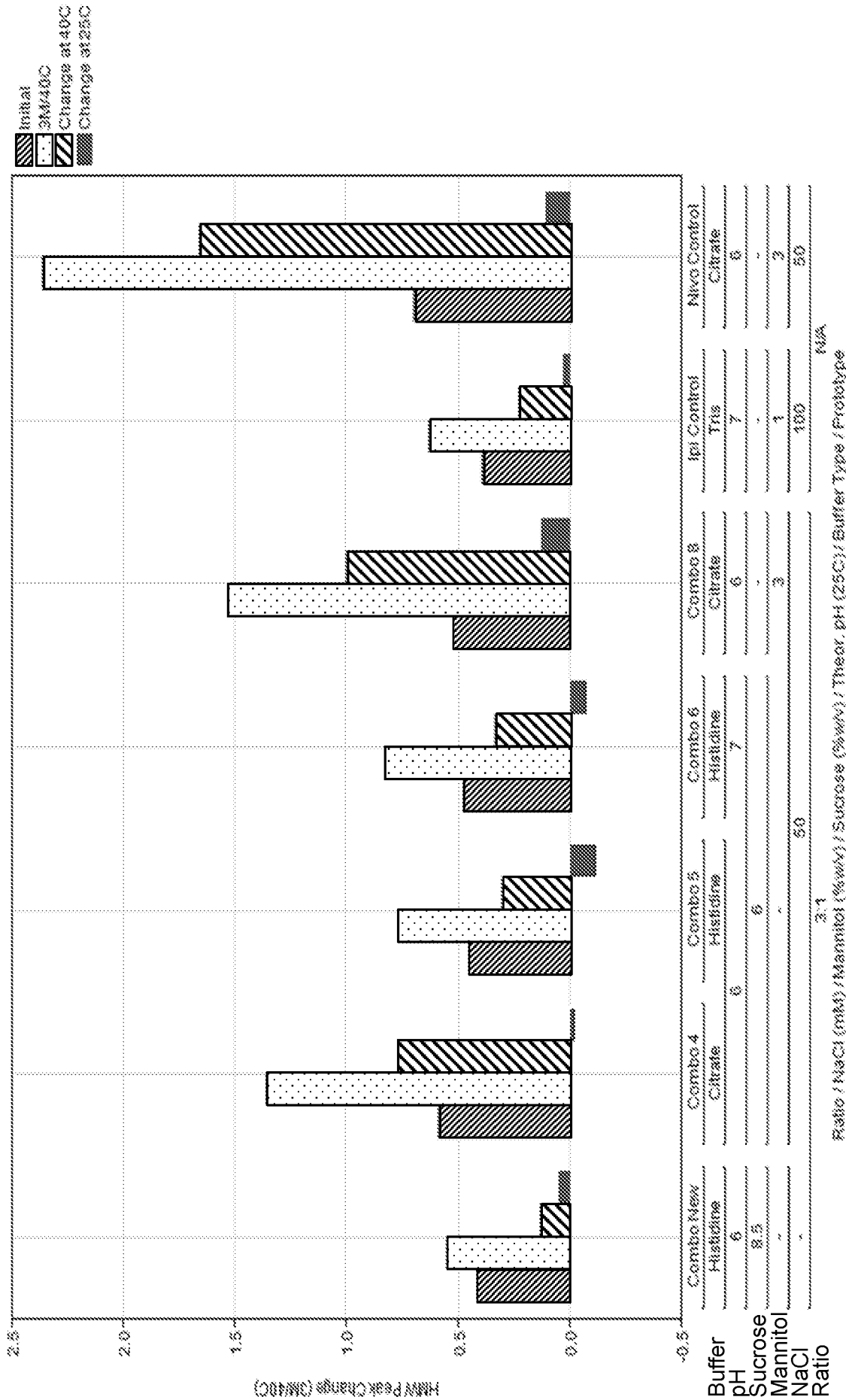
N: Nivolumab Acidic Peak; I: Ipilimumab Acidic Peak

Fig. 4C: 1:3, 1:1, 3:1 Fixed Dosing Formulations
for Nivolumab and Ipilimumab: cIEF Acidic Peak Change (1M at 25°C)



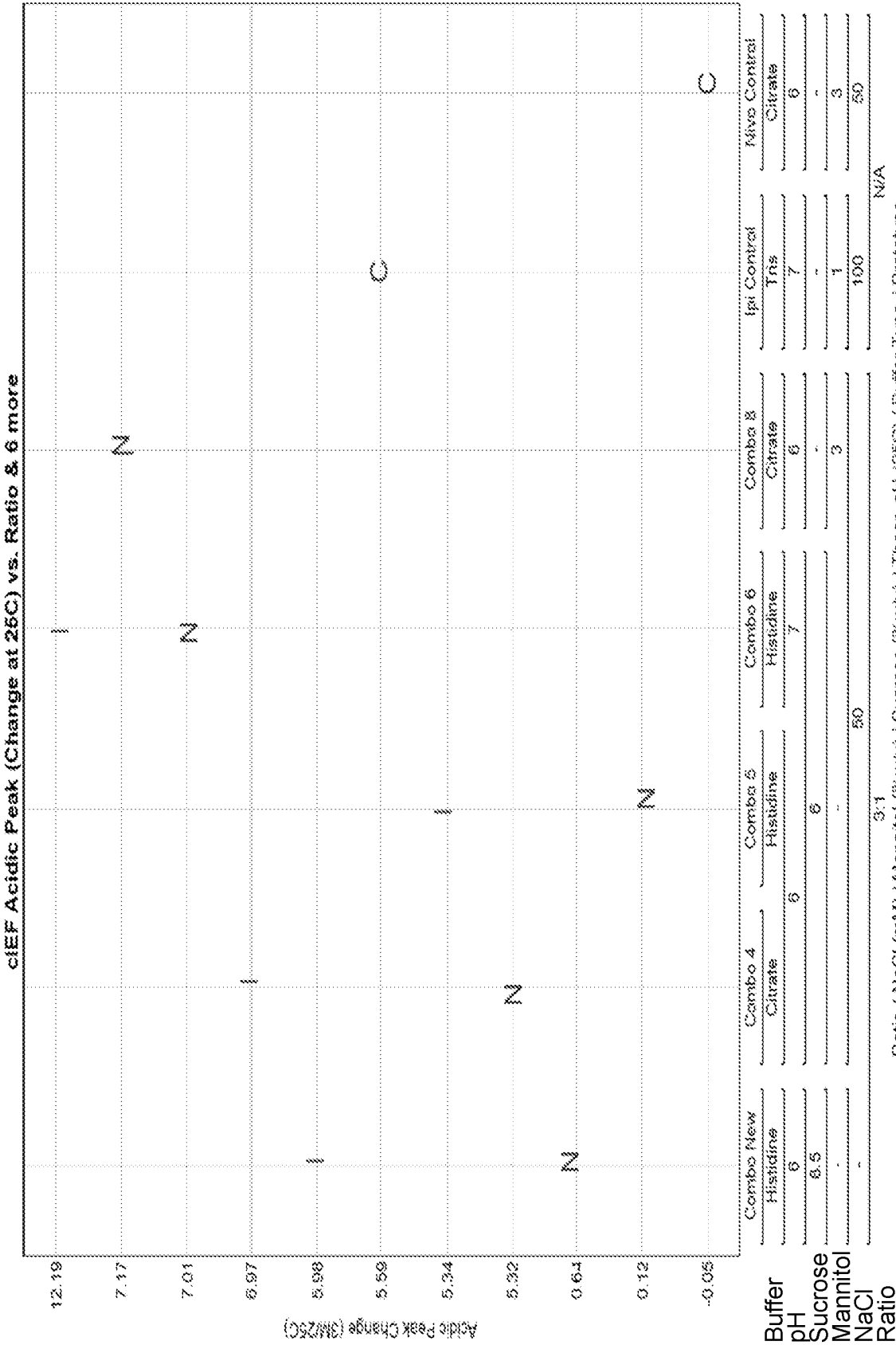
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Fig. 5A: DoE FDRC (3:1) – Novel Formulations
SEC HMW Change (3M at 40°C or 25°C)



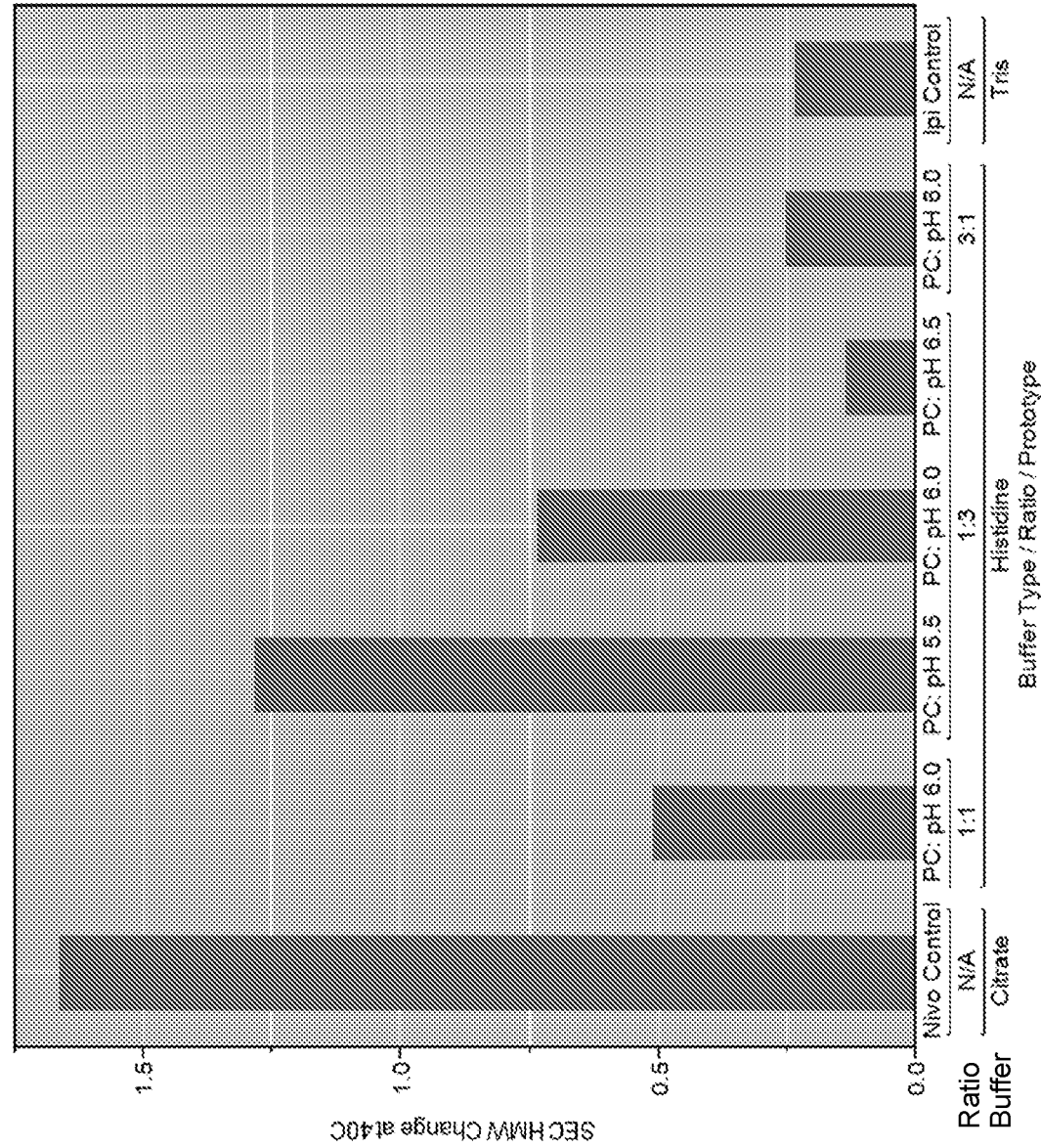
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Fig. 5B: DoE FDRC (3:1) – Novel Formulations
cIEF Acidic Peak (3M at 25°C)



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Fig. 6A: Platform Combined (PC) FDRC
SEC HMW Change (3M at 40°C)



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Fig. 6B: Platform Combined (PC) FDRC
SEC HMW Change (3M at 5°C)

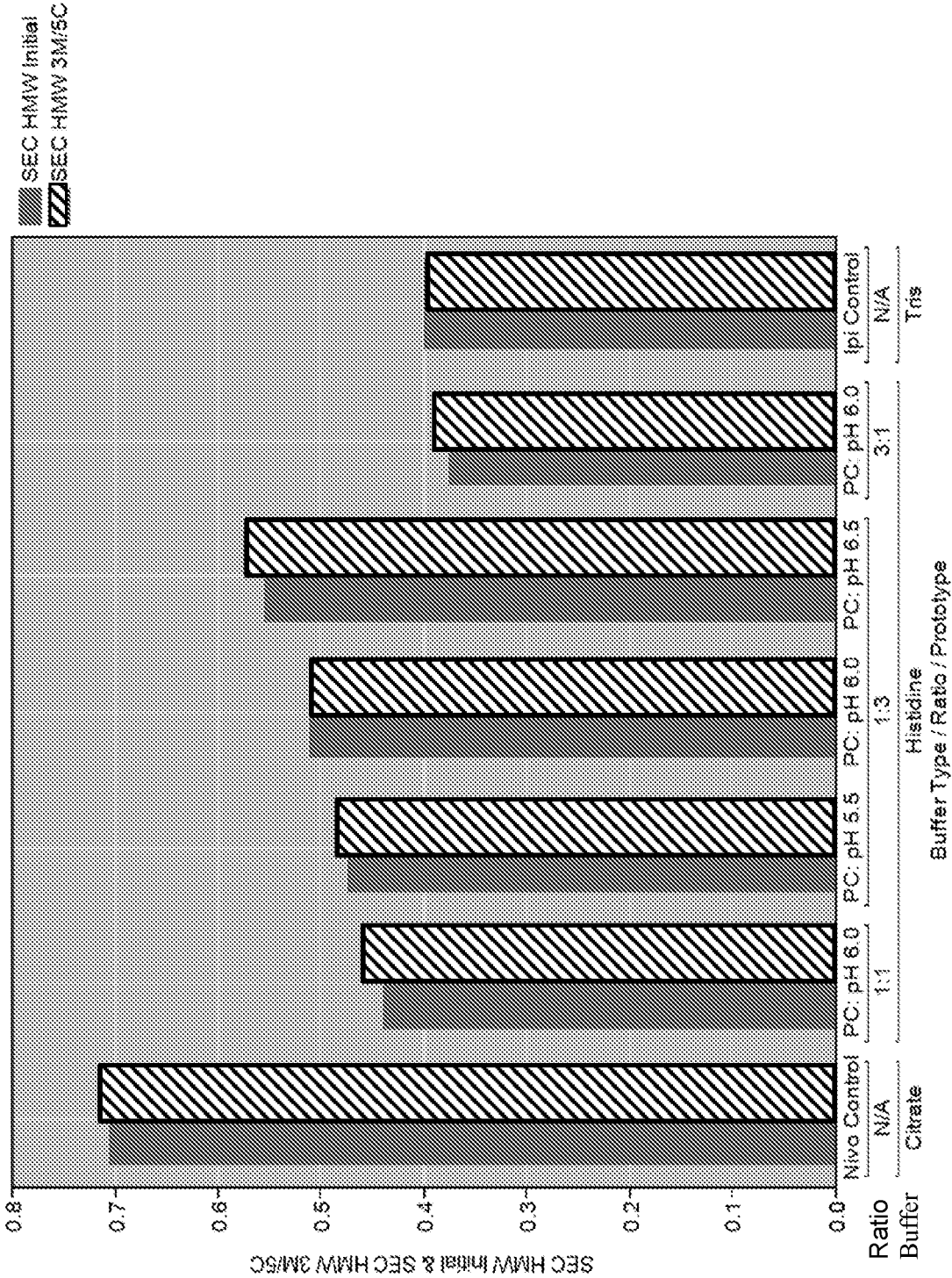


Fig. 7A: Platform Combined (PC) FDRC
cIEF Acidic Peak Change (3M at 25°C)

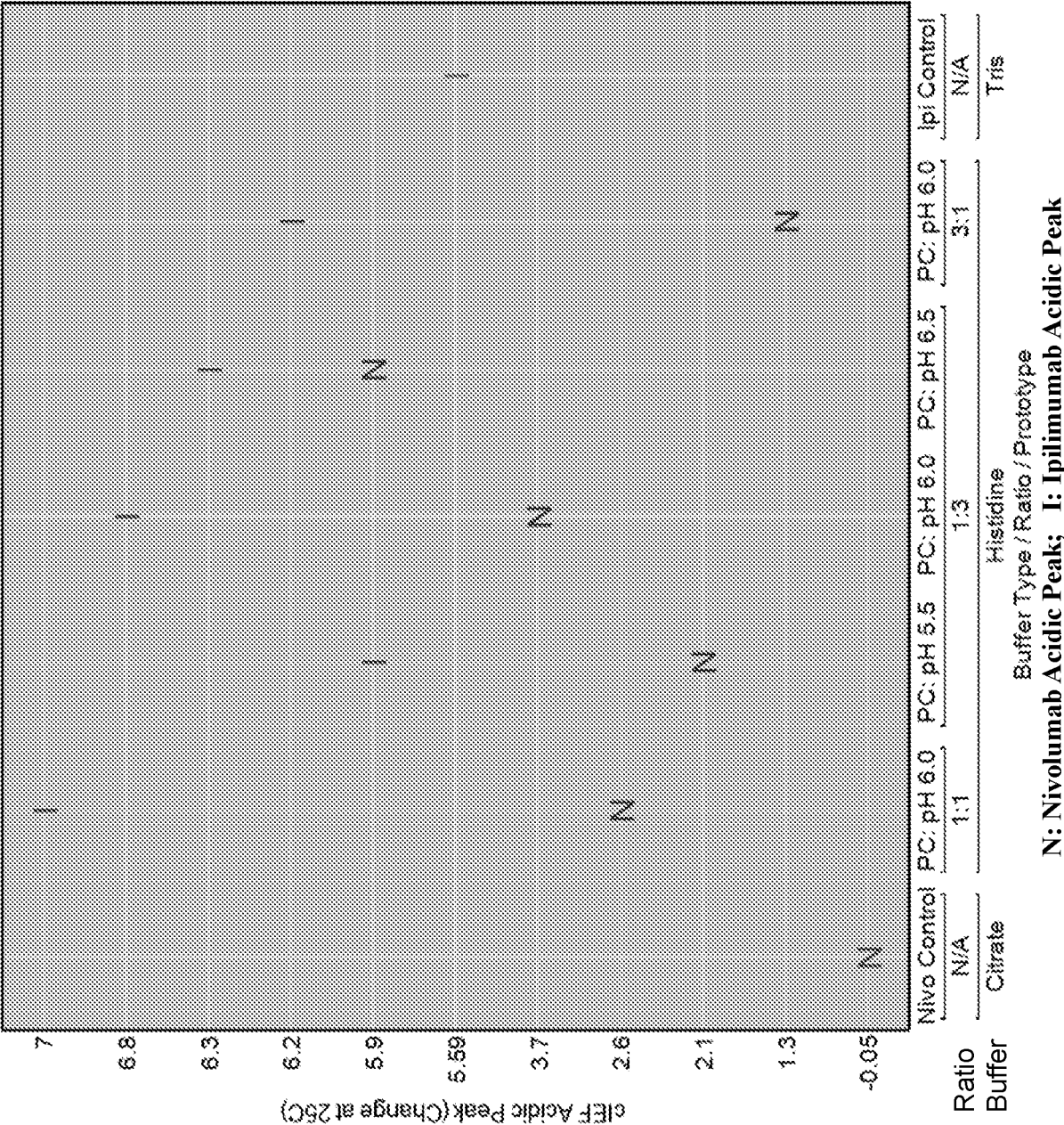
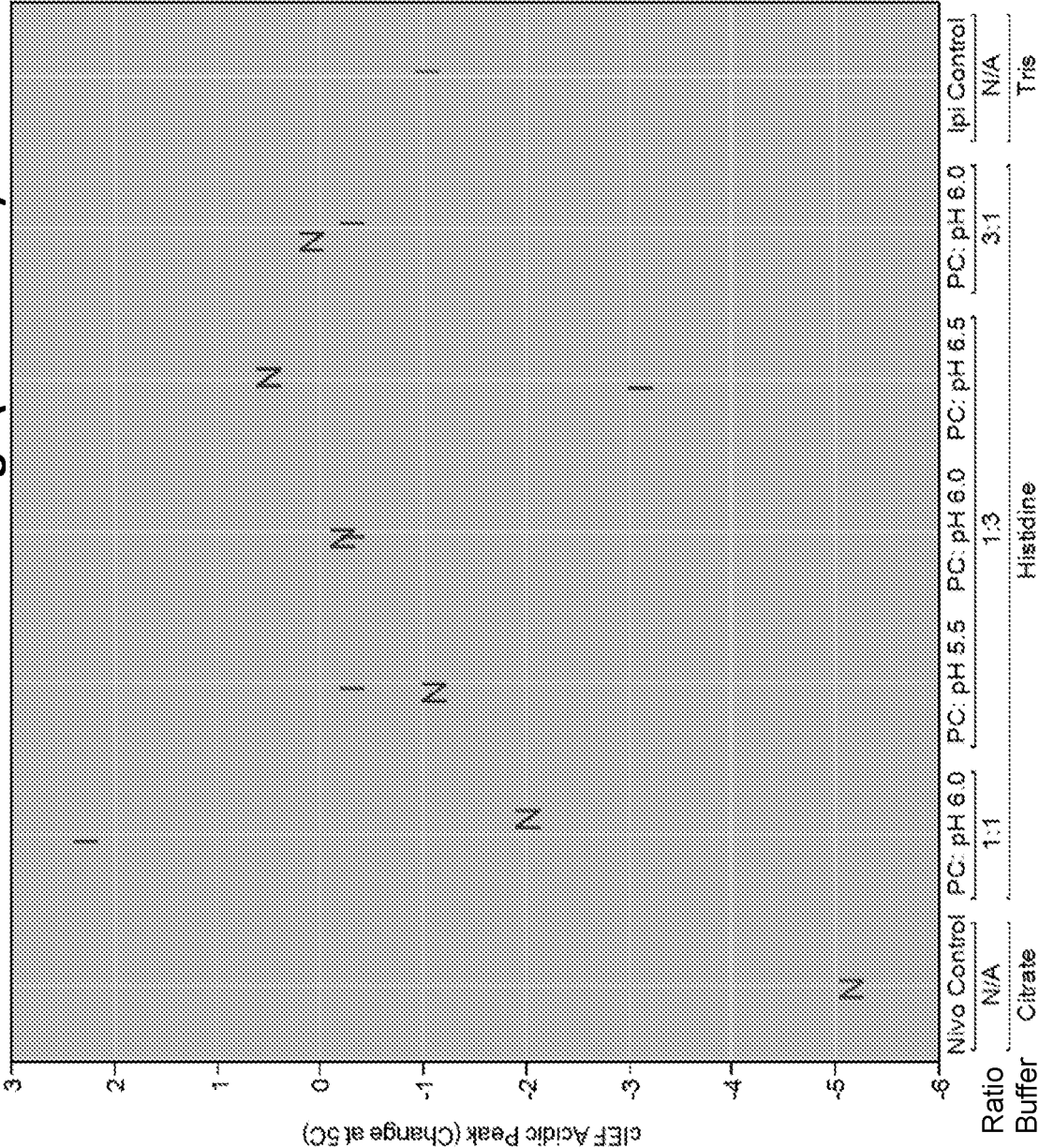


Fig. 7B: Platform Combined (PC) FDRC
cIEF Acidic Peak Change (3M at 5°C)



N: Nivolumab Acidic Peak; I: Ipilimumab Acidic Peak

Fig. 8: Nivolumab-DP-Based FDRC (1:1) Formulations
SEC HMW Change (1M at 40°C)

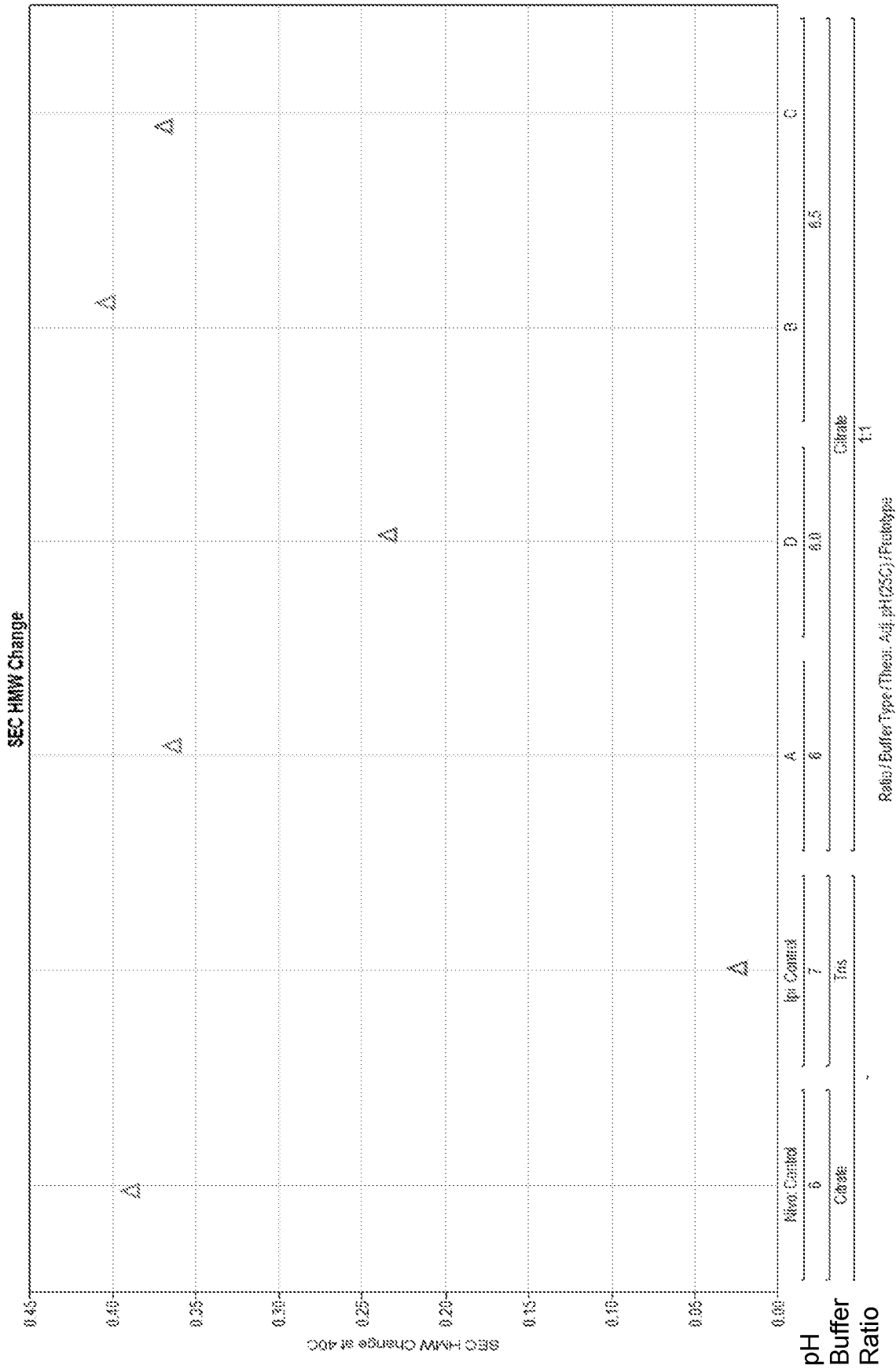
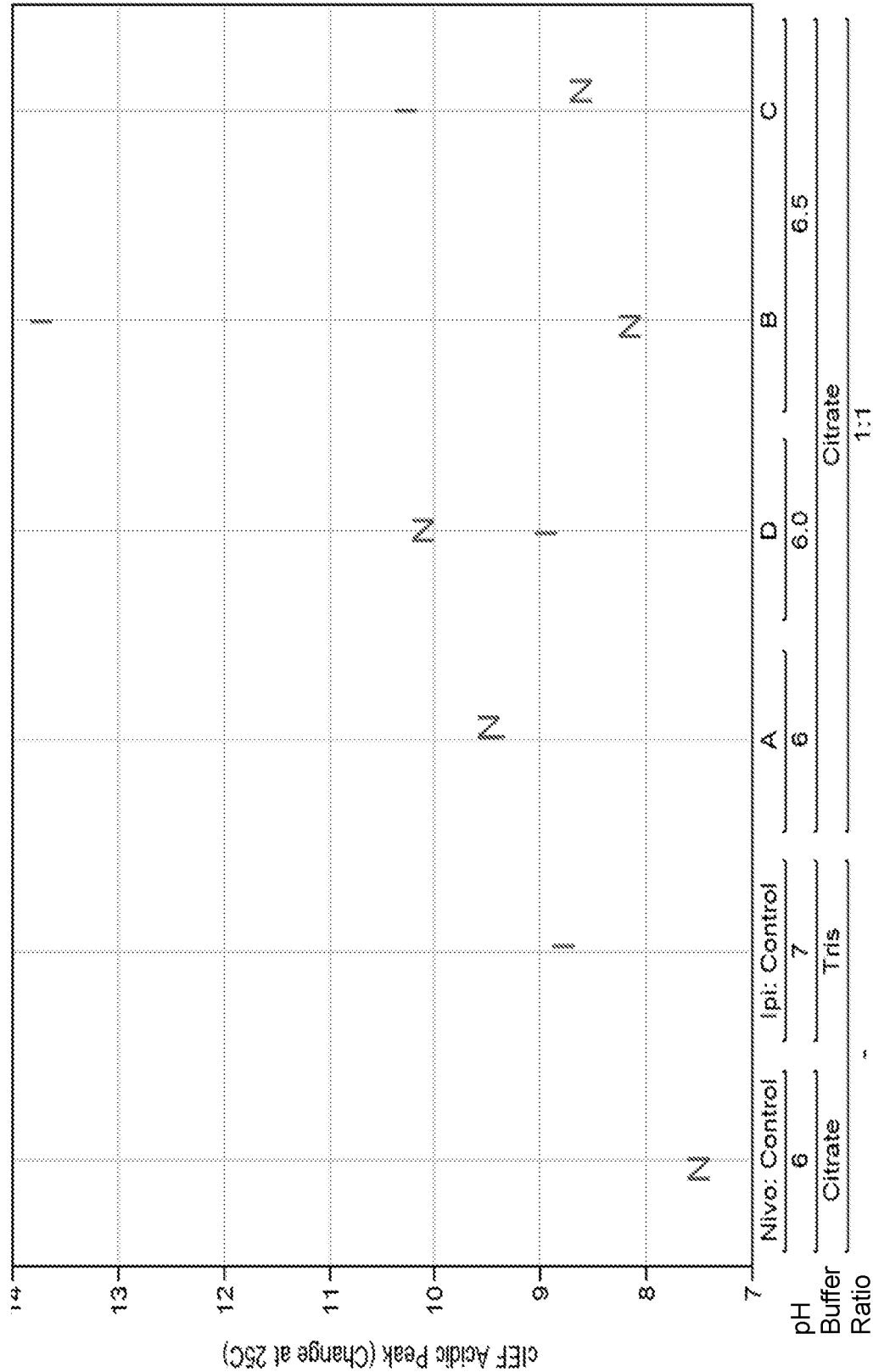


Fig. 9: Nivolumab-DP-Based FDRC (1:1) Formulations
cIEF Acidic Peak Change (3M at 25°C)



N: Nivolumab Acidic Peak; I: Ipilimumab Acidic Peak

Fig. 10: Ipilimumab Acidic Peak Degradation Rate in FDRC and Commercial Composition at 25°C/60%RH

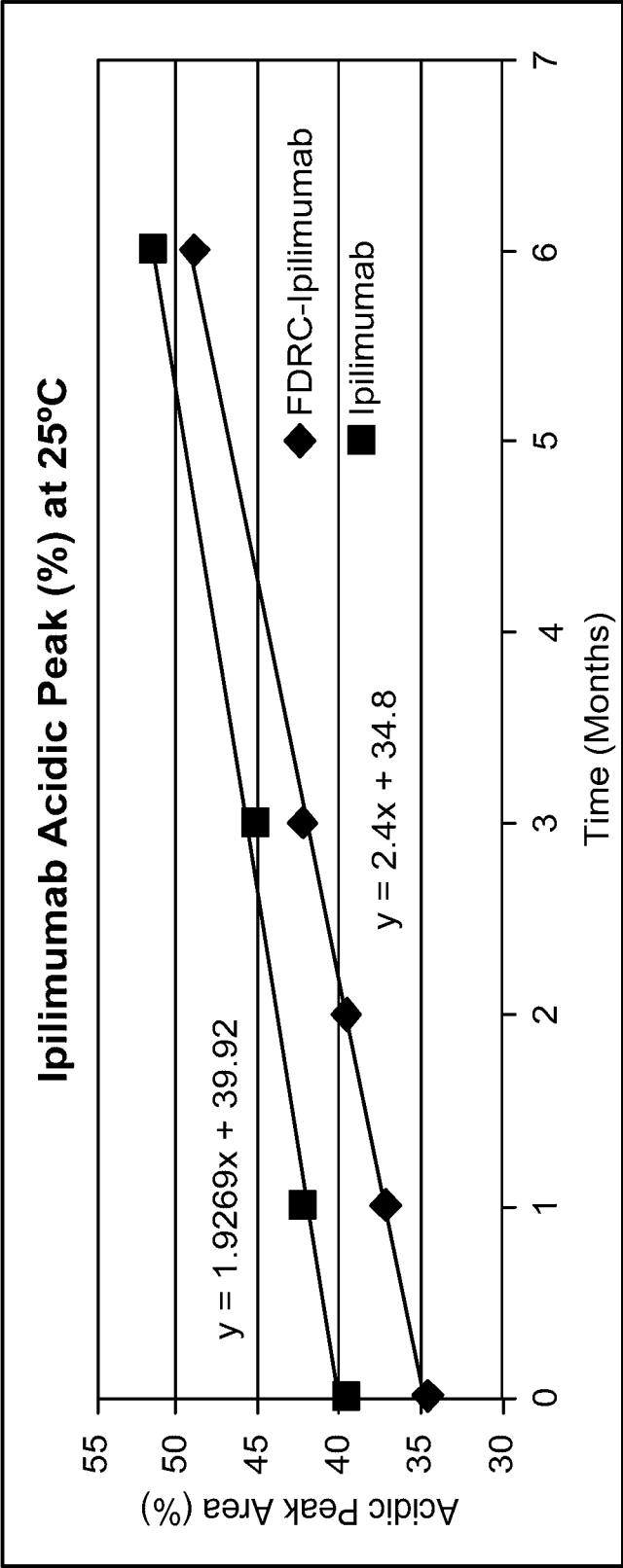


Fig. 11: Nivolumab Acidic Peak (%) in FDRC and Commercial Composition at 25°C/60%RH

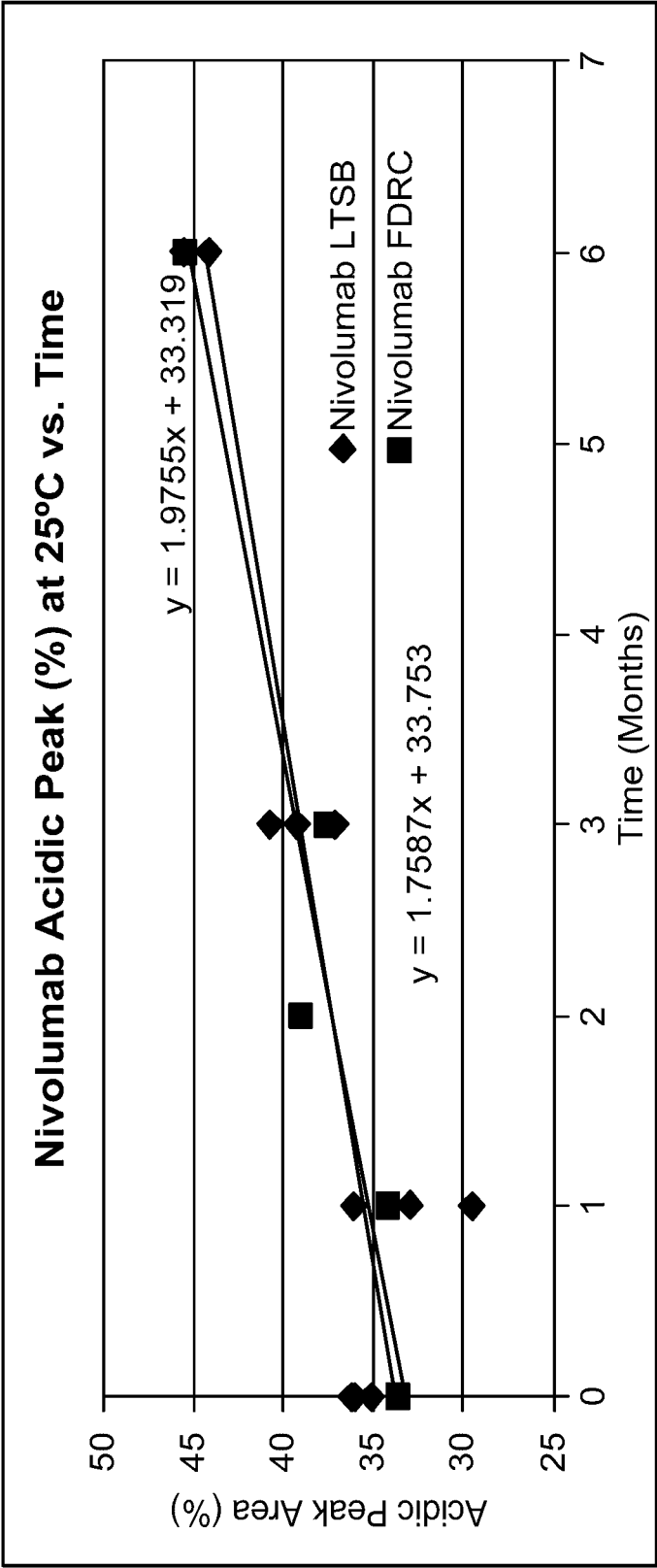


Fig. 12: Acidic Peak Profile at 25°C in pH ranging Study for Ipilimumab and Nivolumab

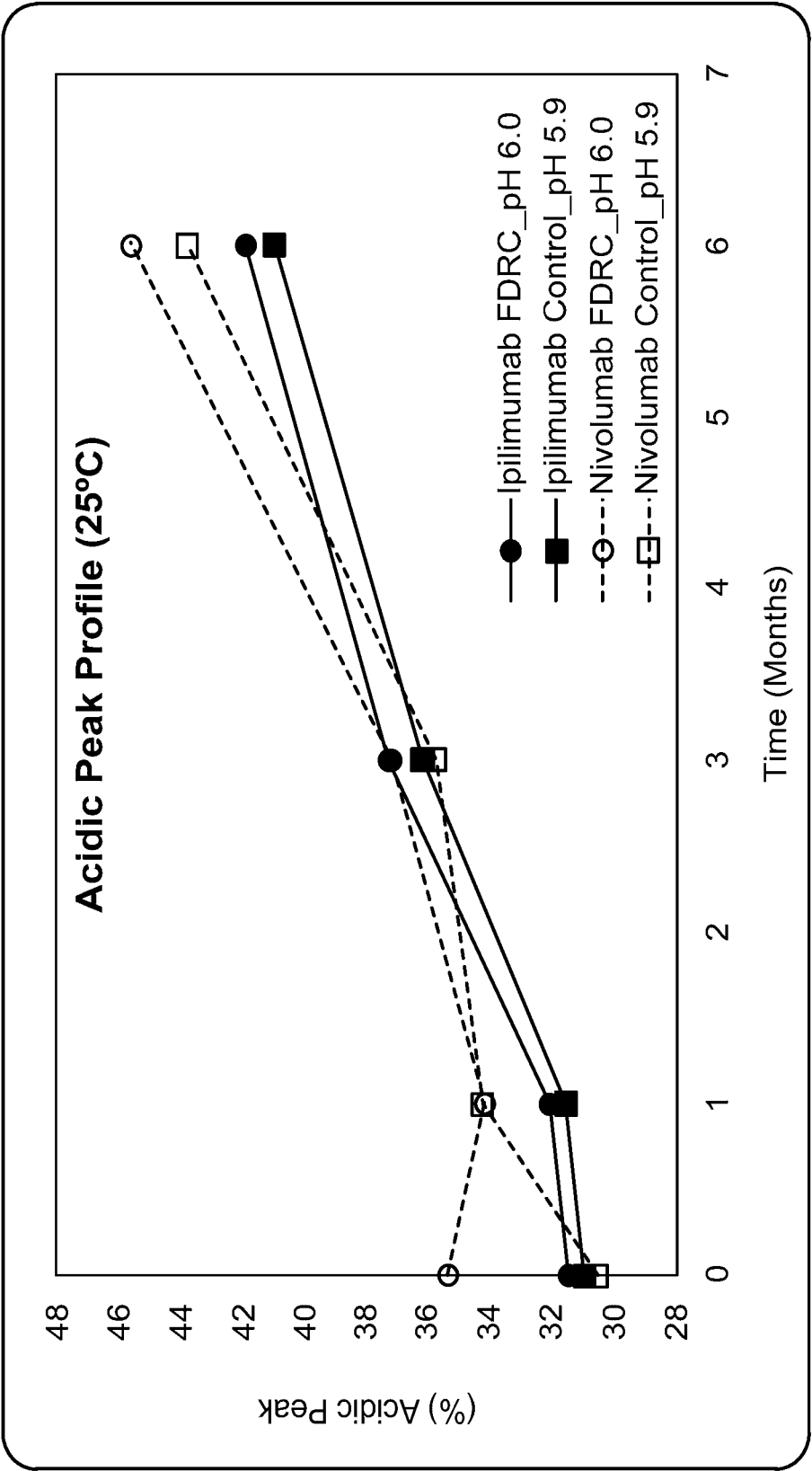


Fig. 13: SEC HMW Profile of DP Prototypes from Ruggedness Study

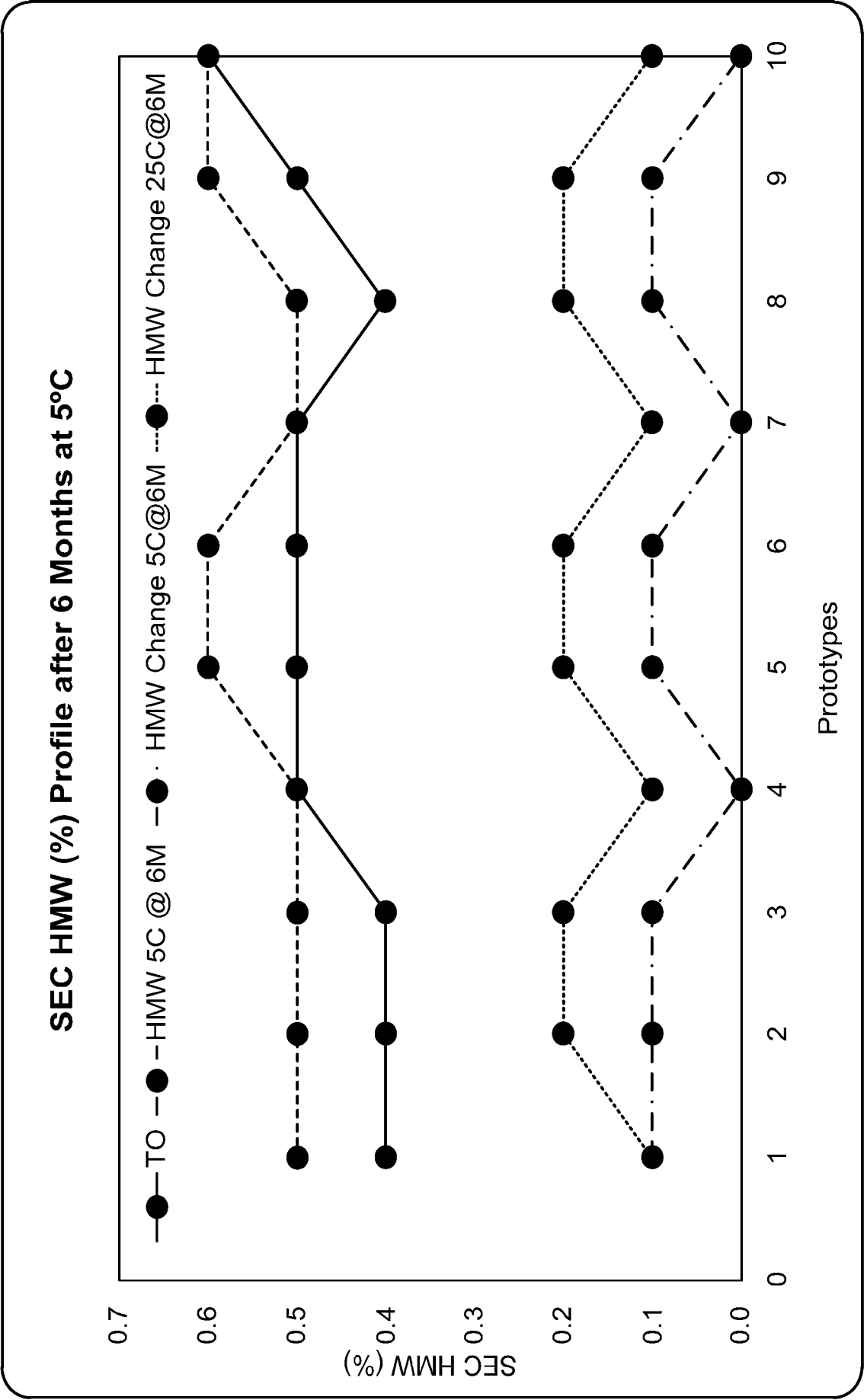


Fig. 14: SEC Monomer Profile

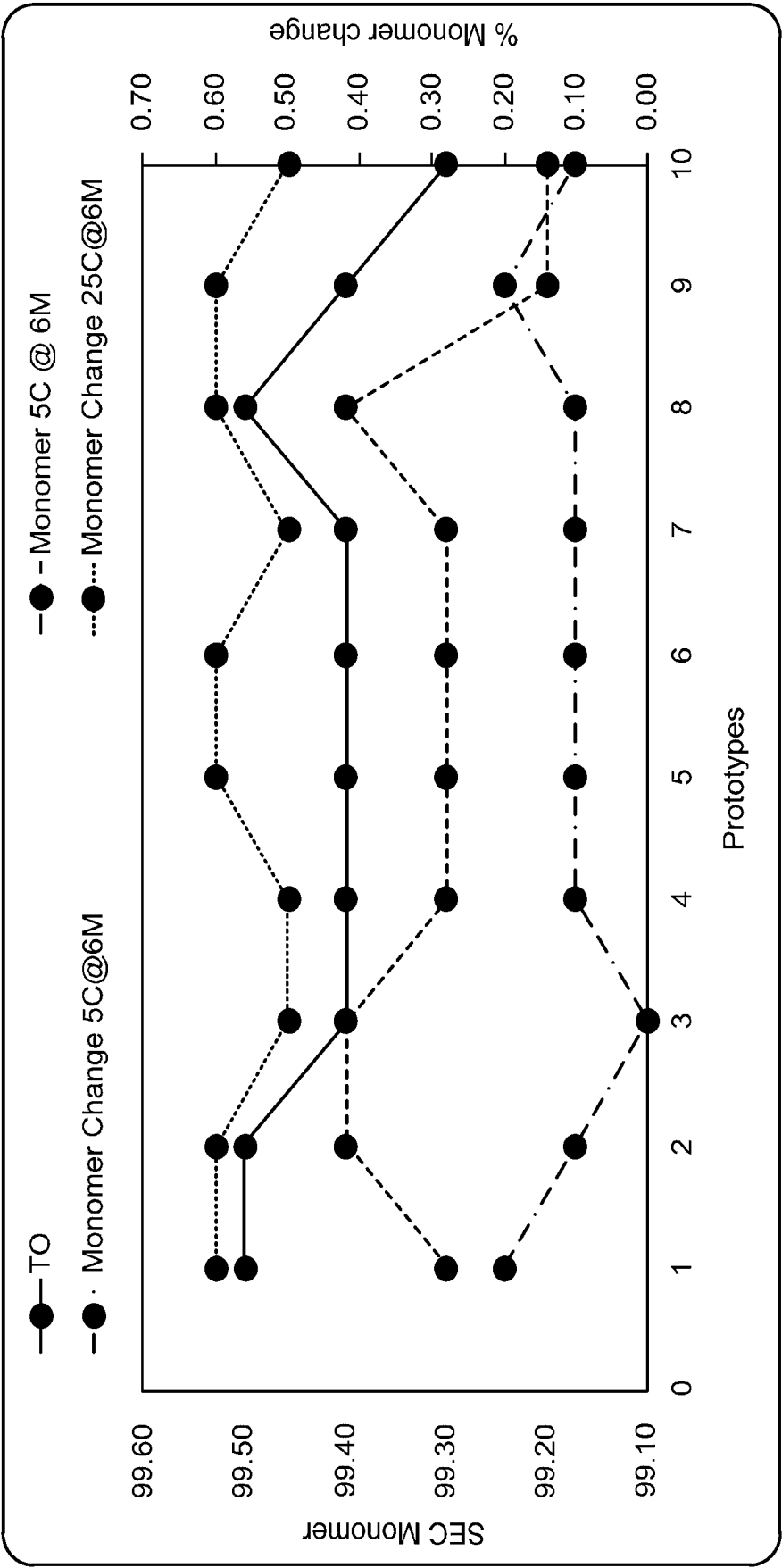


Fig. 15: Ipilimumab Acidic Peak Profile

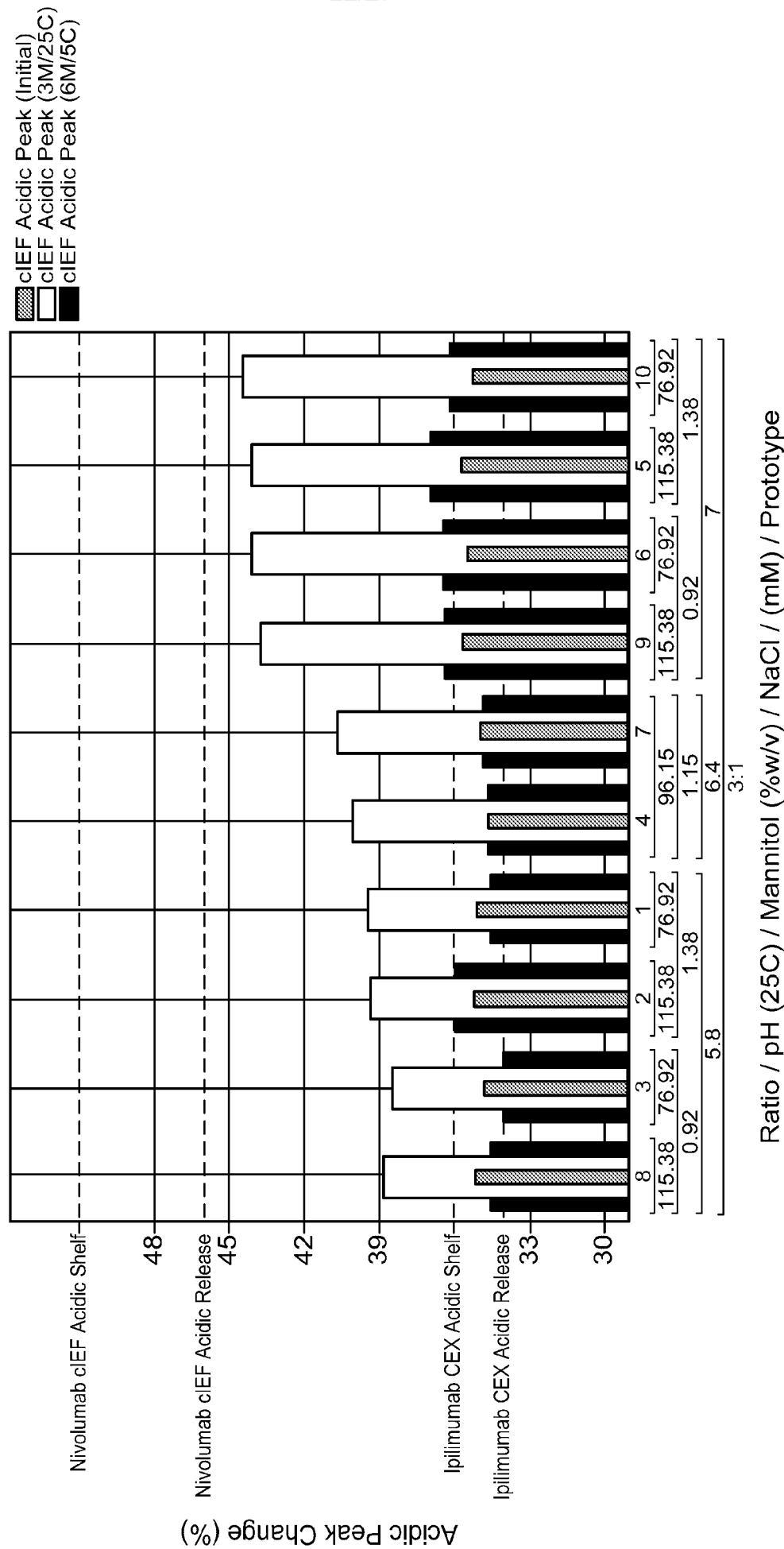


Fig. 16: Nivolumab Acidic Peak Profile

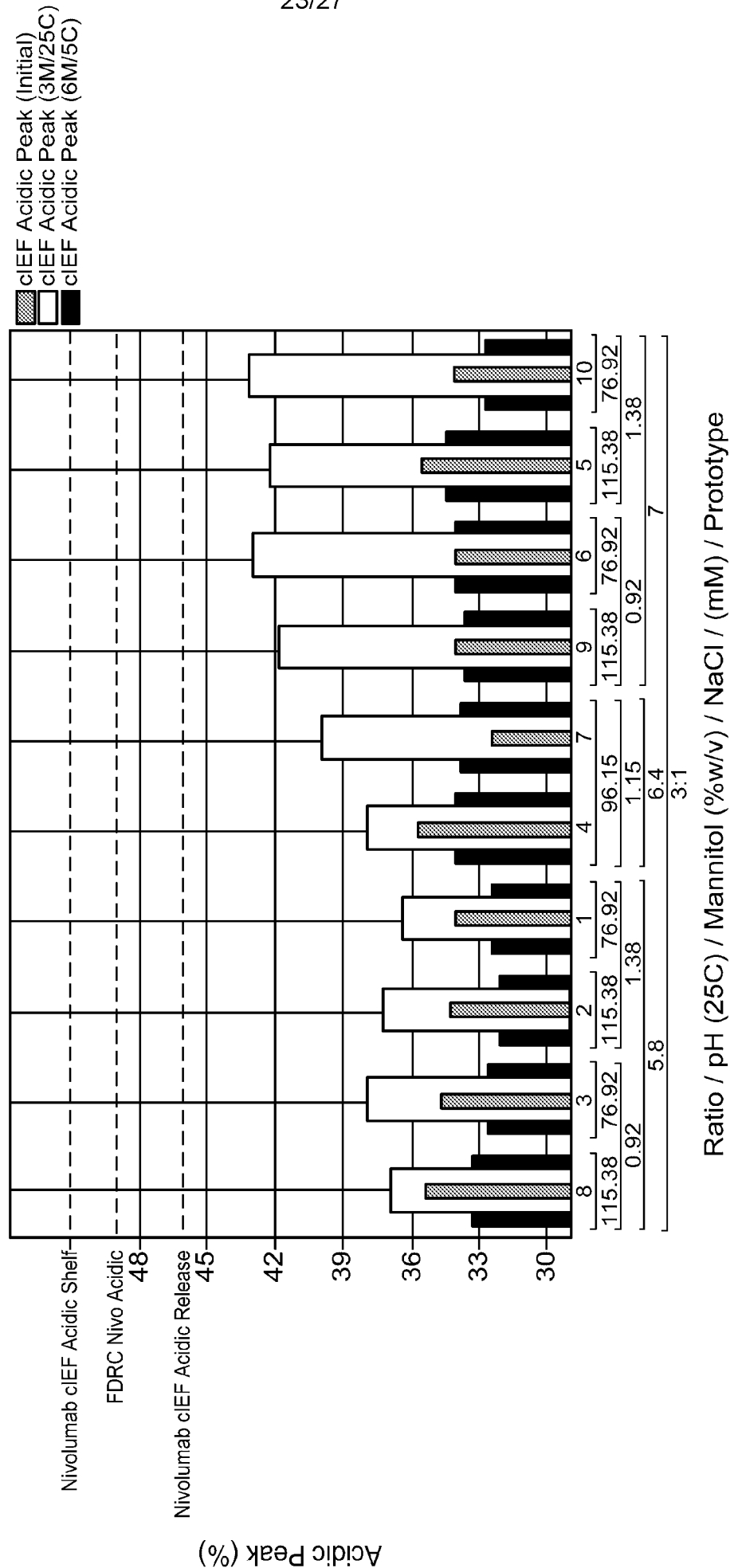


Fig. 17: Ipilimumab Main Peak Profile

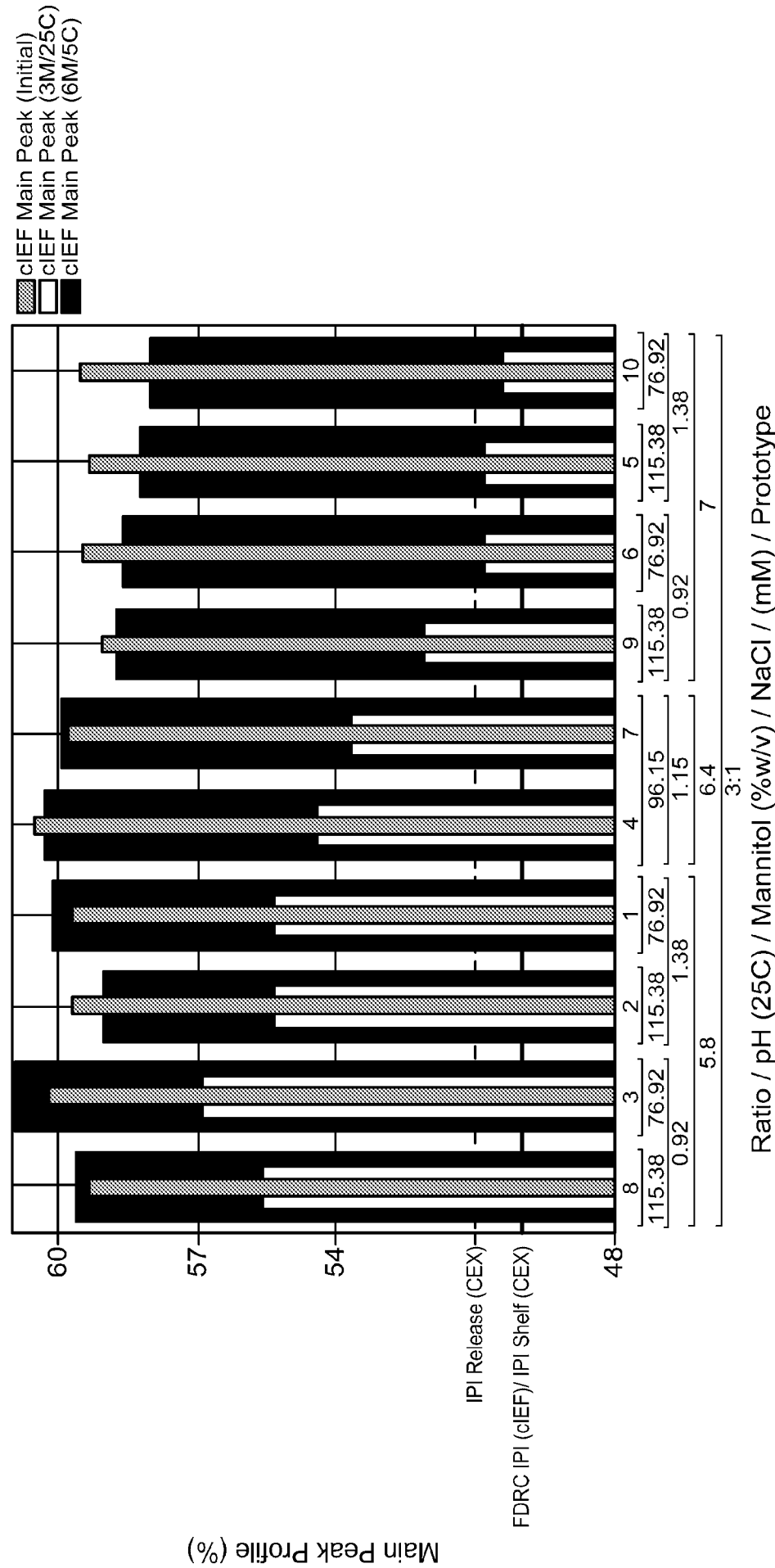


Fig. 18: Nivolumab Main Peak Profile

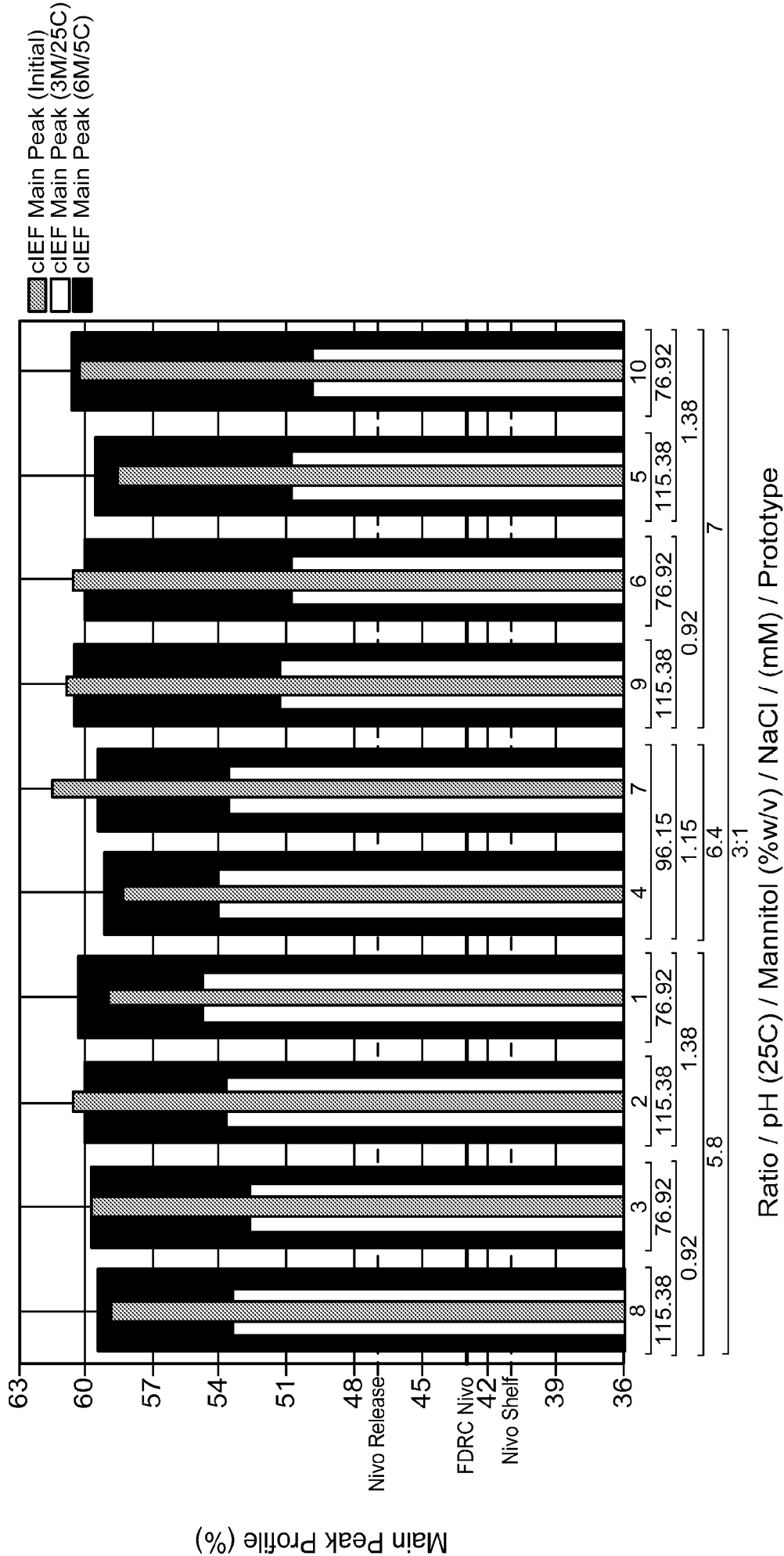
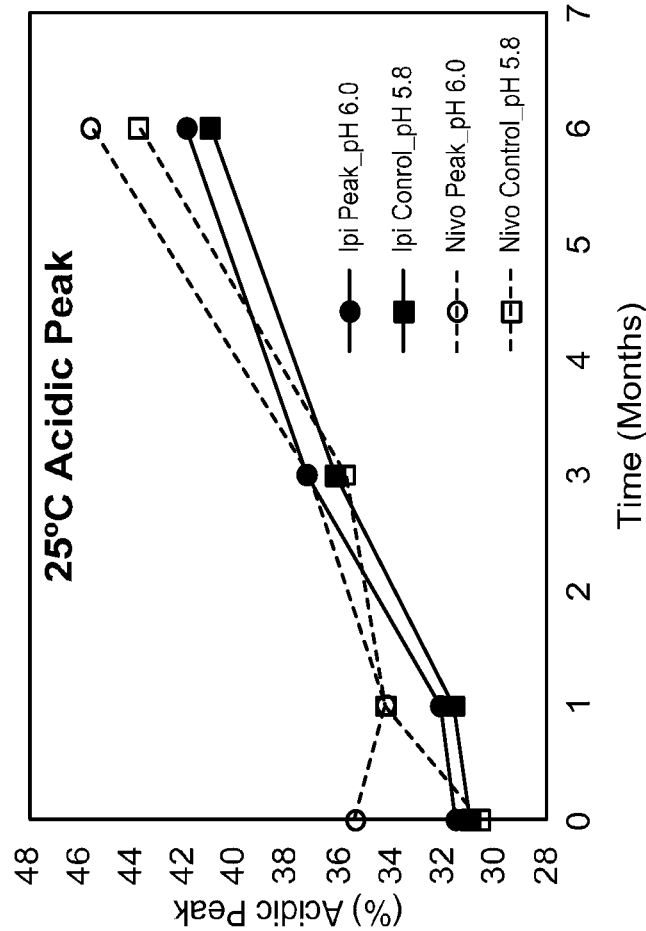
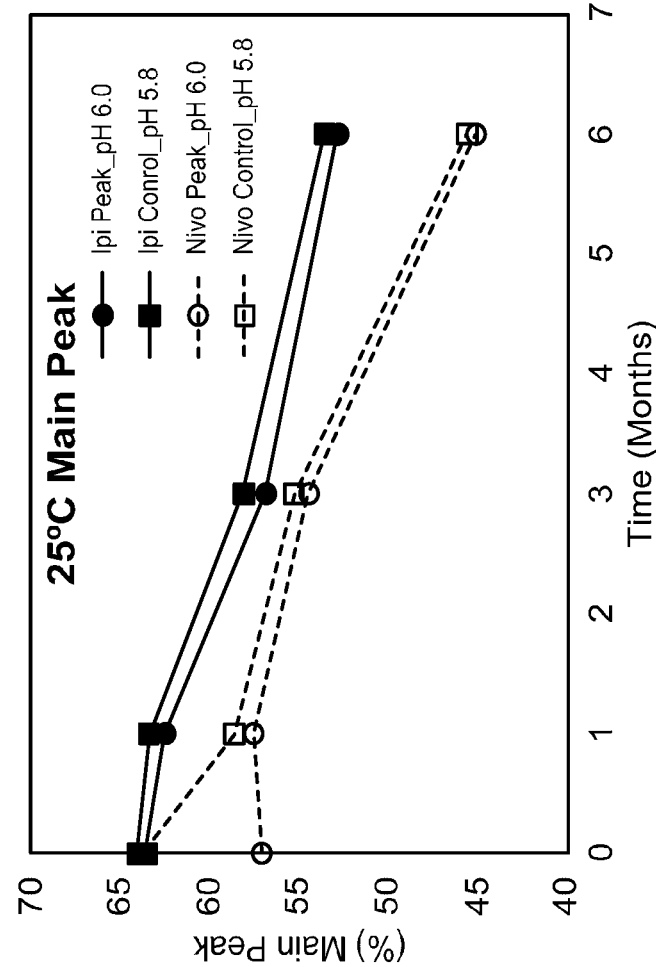


Figure 19. cIEF Peak Profile: Impact of pH



Acidic Peak Change at 5 °C

	pH 5.4	pH 5.7	pH 6.0	pH 6.3	pH 6.6	Controls
Ipi Peak 6M	-1	0.6	0.6	0.9	1.1	1
Nivo Peak 6M	-0.3	-3.7	-1.5	-2.3	-1.9	-0.4

Main Peak Change at 5 °C

	pH 5.4	pH 5.7	pH 6.0	pH 6.3	pH 6.6	Controls
Ipi Peak 6M	-1	1.4	0.8	1.5	1.6	0.6
Nivo Peak 6M	-0.4	-1.8	-1.2	-1.6	-0.7	0.9

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Figure 20. iCIEF Profile: pH range of 5.4 – 6.6

Ipilimumab Rate of Change/month Acidic and Main Peak				
DP	Note: 3 months data for 25°C and 5°C			
	Acidic Peak (%/Month)	Acidic Peak (%/Month)	Main Peak (%/Month)	Main Peak (%/Month)
	25°C	5°C	25°C	5°C
FDRC (5.4)	1.86	0.3	-2.15	-0.4
FDRC (5.7)	2.11	0.27	-2.57	-0.4
FDRC (6.0)	2.03	0.17	-2.32	-0.26
FDRC (6.3)	2.1	0.1	-2.04	-0.23
FDRC (6.6)	2.63	0.47	-2.67	-0.7
Nivolumab Rate of Change/month Acidic and Main Peak				
DP	Note: 3 months data for 25°C and 5°C			
	Acidic Peak (%/Month)	Acidic Peak (%/Month)	Main Peak (%/Month)	Main Peak (%/Month)
	25°C	5°C	25°C	5°C
FDRC (5.4)	1.15	-0.33	-2.15	0.33
FDRC (5.7)	-0.08	-0.6	-0.96	0.36
FDRC (6.0)	0.72	-0.03	-0.96	0.5
FDRC (6.3)	0.8	-0.4	-1.16	0.36
FDRC (6.6)	1.7	-0.07	-1.71	0.1