

The results for 1 ppm and 500 ppm hydrogen peroxide obtained by peptide mapping (LC-MS) and HIC-HPLC are qualitatively consistent (Table 3-5 and Figure 10).

The H4H12166P samples incubated with hydrogen peroxide were also analyzed for charge variants (CEX-UPLC) and molecular size variants (SE-UPLC). A minimal (~1%) decrease in acidic charge variants and a comparable increase in basic charge variants was observed only at 100 and 500 ppm hydrogen peroxide (Figure 11 and Figure 12).

There was no meaningful increase in formation of HMW species even at the highest tested concentration of hydrogen peroxide (Figure 13) indicating that even high levels of H4H12166P methionine oxidation do not generate conformational species that are prone to self-association or aggregation.

Example 4: Comparison of Viscosities of H4H12166P and Comparator Molecules at High Concentrations

Viscosity was measured using a Rheosense m-VROC viscometer. Prior to analysis, standards and formulations were filtered through a 0.22 µm PVDF spin filter. Two standards of known viscosities were measured before the unknown sample viscosity analysis: 2 cP and glycerol standards. Viscosity measurements were performed at 20°C.

Table 4-1. Viscosity of H4H12166P and various anti-C5 antibodies #

Antibody	Arginine HCl Concentration	Viscosity at 20°C (cps)					
		150 mg/mL	175 mg/mL	200 mg/mL	211 mg/mL	220 mg/mL	242 mg/mL
Pozelimab (H4H12166P)	0	9.4	12.4	24.6	27.4	34.7	63.5
	50	-	8.3	14.3	19.2	24.1	42.3
Tesidolumab (SEQ ID NOs: 362 and 363)	0	124	too high	too high			
	50	24	48	91			
Eculizumab (SEQ ID NOs: 366 and 367)	0	17.8	N/A	N/A			
	50	9.8	22.4	38.6			

Ravulizumab	0	67.8	too high	too high*	
(SEQ ID NOs: 364 and 365)	50	22.3	50.5	117.8	

#All molecules were analyzed in 10 mM histidine, pH 5.5.

* Sample stored at 5°C turned into a cloudy gel (probably due to low solubility).

` C-terminal lysine included

Example 5: Long-term and Accelerated Stability Testing of 200 mg/ml H4H12166P.

Stability studies evaluated the stability of a liquid, aqueous H4H12166P 200 mg/mL formulation under long term storage and stress conditions. Two stability studies were initiated:

- (1) 0.5 mL fill in a 2 mL type 1 borosilicate glass vial stored in the upright orientation, and
- (2) 2.5 mL fill in a 5 mL type 1 borosilicate glass vial stored in the inverted orientation

Table 5-1. Study Design

		2 mL Glass Vial, Stored Upright	5 mL Glass Vial, Stored Inverted
Storage	Condition	5°C	5°C
	Duration	0, 1, 3, 6, 9, 12, 18, 24, and 36 months	0, 1, 3, 6, 9, 12, 18, 24, and 36 months
Accelerated	Condition	25°C/60% RH	25°C/60% RH
	Duration	0, 0.5, 1, 3, 6 months	0, 1, 3, 6 months
Thermal Stress	Condition	40°C/75%RH	40°C/75% RH
	Duration	0, 0.25, 0.5, 1, 2 and 3 months	0, 0.5, 1 and 3 months

Results

The attributes of an aqueous formulation comprising 200 mg/mL H4H12166P, 20 mM histidine, pH 5.8, 100 mM L-arginine hydrochloride, 2% (w/v) sucrose, 0.15% (w/v) polysorbate 80, following 6 months of long term (5°C) storage in 2 mL Schott Type 1 borosilicate glass vials (stored upright), are set forth in Table 5-2. Table 5-3 and Table 5-4 summarizes the attributes of liquid, aqueous H4H12166P 200 mg/mL formulation after storage at accelerated condition of 25°C, 60%RH and at stressed conditions of 40°C, 75%RH, respectively.