Table 16: % Peak Area of Basic Variants

	40	34.5		32.5	23.4
	-60			34.4	-
	RT/RL		34.8	33.2	-
F5.5N	25			34.0	33.2
	40	34.3		32.5	20.5
	-60			34.4	-
F5.75	25			33.8	32.6
	40	34.2		31.6	21.2
	-60			34.9	-
F6.0	25			34.2	32.1
	40	34.2		30.2	19.4
	-60			35.0	-
F6.25	25			33.3	31.8
	40	34.6		29.0	17.9
	-60			34.5	-

Overall stability profile

[0224] There was not much change in appearance, pH, protein concentration, purity, charge and size variant distribution for the drug product between pH 4.80 to 6.25 during 3-month exposure at -60 °C and 25 °C, indicating that the product is relatively stable under the current specification of pH 5.5±0.5 and at intended storage temperature of 2-8 °C. High temperature exposure at 40 °C did not significantly change appearance, pH, protein concentration, and purity, but provided a strong signal of formation of size and charge-related degradants in the formulations at the stressed condition. The signal of size and charge-related change can be used to establish an overall pH stability profile and to select an optimal formulation pH value. **FIG. 1** shows the percent degradants of these two major groups in the samples with different pH values at 40°C. From the figure, an X-shaped profile is identified with the curves

intersecting at ~pH 5.5. The profile curves clearly show that the size-related degradants (HMWs and LMWs) increased with decreasing pH whereas charge-related degradants (iCIEF acidic species) increased with increasing pH. The pH value of ~5.5 is the cross point and will minimize the possibility for the drug product to be out of specifications established either by iCIEF or SEC.

[0225] At lower temperature of 25°C, the differences were not as strong between pH values for these two types of degradants although there appears a similar trend as that at 40°C (**FIG. 2**). As no or very little degradation occurred over 3 months at 25°C,significantly longer period of exposure at 25°C is likely required to show the similar pH-stability profile observed at 40°C.

[0226] Furthermore, varying the concentration of anti-LAG-3 antibody (4 mg/ml versus 12 mg/ml) did not change the percentage of acidic charge variants during storage at 5°C, 25°C, or 40°C for 1-6 months (**FIGs. 3A and 3B**).

Light impact on drug product stability

[0227] The effect of room temperature/room lighting (RT/RL) is shown in **FIG. 4**. There is essentially no difference between light-exposed and light-protected samples in appearance, pH, protein concentration, purity, HMWs and LMWs for the exposure period (up to 1 month). The particulate count for both samples is also very low and all within the limits established by USP. There is no increase of iCIEF acidic peak area after 2-week exposure to room light, and a very slight increase (~2%) is shown at 1-month time point. This increase could be due to either analytical method variation or a real trend of light-induced reaction. However, there should be no significant impact on the drug product quality as the change in acidic species is relatively minor (<3%). Based on the above comparison between light-exposed and light-protected samples, it is concluded that there will be sufficient stability for the drug product under room light for up to 4 weeks.

Impact of DTPA on drug product stability

[0228] The effect of DTPA on the DP stability is shown in **FIG. 5**. The appearance, pH, protein concentration, and purity of samples containing DTPA were similar to samples without DTPA following storage for up to 3 months at 40 °C. The particulate counts for all samples were also low and within USP limits. However, there was a more significant difference in HMW and LMW species levels between DTPA and non-DTPA samples with

WHAT IS CLAIMED IS:

1. A pharmaceutical composition comprising:

(a) about 80 mg of an anti-LAG-3 antibody or antigen binding fragment thereof comprising CDR1, CDR2, and CDR3 domains of the heavy chain variable region having the sequence set forth in SEQ ID NO:3, and CDR1, CDR2, and CDR3 domains of the light chain variable region having the sequence set forth in SEQ ID NO:5;

(b) about 240 mg of an anti-PD-1 antibody or antigen binding fragment thereof comprising CDR1, CDR2, and CDR3 domains of the heavy chain variable region having the sequence set forth in SEQ ID NO:19, and CDR1, CDR2, and CDR3 domains of the light chain variable region having the sequence set forth in SEQ ID NO:21;

(c) about 20 mM of histidine buffer;

(d) about 250 mM of sucrose;

(e) about 20 μM of DTPA; and

(f) about 0.05% (w/v) of polysorbate 80;

wherein the pharmaceutical composition has a pH of about 5.8.

2. The pharmaceutical composition of claim 1, wherein the anti-LAG-3 antibody or antigen binding fragment thereof comprises heavy chain variable region CDR1, CDR2, and CDR3 domains comprising the sequences set forth in SEQ ID NOs:7, 8, and 9, respectively, and light chain variable region CDR1, CDR2, and CDR3 domains comprising the sequences set forth in SEQ ID NOs:10, 11, and 12, respectively.

3. The pharmaceutical composition of claim 1, wherein the anti-PD-1 antibody or antigen binding fragment thereof comprises heavy chain variable region CDR1, CDR2, and CDR3 domains comprising the sequences set forth in SEQ ID NOs:23, 24, and 25, respectively,

and light chain variable region CDR1, CDR2, and CDR3 domains comprising the sequences set forth in SEQ ID NOs:26, 27, and 28, respectively.

4. The pharmaceutical composition of claim 1, wherein the anti-LAG-3 antibody or antigen binding fragment thereof comprises heavy chain variable region CDR1, CDR2, and CDR3 domains comprising the sequences set forth in SEQ ID NOs:7, 8, and 9, respectively, and light chain variable region CDR1, CDR2, and CDR3 domains comprising the sequences set forth in SEQ ID NOs:10, 11, and 12, respectively, and the anti-PD-1 antibody or antigen binding fragment thereof comprises heavy chain variable region CDR1, CDR2, and CDR3 domains comprising the sequences set forth in SEQ ID NOs:23, 24, and 25, respectively, and light chain variable region CDR1, CDR2, and CDR3 domains comprising the sequences set forth in SEQ ID NOs:26, 27, and 28, respectively.

5. The pharmaceutical composition of claim 1, wherein the anti-LAG-3 antibody or antigen binding fragment thereof comprises heavy and light chain variable regions comprising the sequences set forth in SEQ ID NOs:3 and 5, respectively.

6. The pharmaceutical composition of claim 1, wherein the anti-PD-1 antibody or antigen binding fragment thereof comprises heavy and light chain variable regions comprising the sequences set forth in SEQ ID NOs:19 and 21, respectively.

7. The pharmaceutical composition of claim 1, wherein the anti-LAG-3 antibody or antigen binding fragment thereof comprises heavy and light chain variable regions comprising the sequences set forth in SEQ ID NOs:3 and 5, respectively, and the anti-PD-1 antibody or antigen binding fragment thereof comprises heavy and light chain variable regions comprising the sequences set forth in SEQ ID NOs:19 and 21, respectively.

8. The pharmaceutical composition of claim 1, wherein the anti-LAG-3 antibody comprises heavy and light chains comprising the sequences set forth in SEQ ID NOs:1 and 2, respectively.

9. The pharmaceutical composition of claim 1, wherein the anti-PD-1 antibody comprises heavy and light chains comprising the sequences as set forth in SEQ ID NOs:17 and 18, respectively.

10. The pharmaceutical composition of claim 1, wherein the anti-LAG-3 antibody comprises heavy and light chains comprising the sequences set forth in SEQ ID NOs:1 and 2, respectively, and the anti-PD-1 antibody comprises heavy and light chains comprising the sequences as set forth in SEQ ID NOs:17 and 18, respectively.

11. The pharmaceutical composition of claim 1, wherein the concentrations of the anti-LAG-3 antibody or antigen binding fragment thereof and the anti-PD-1 antibody or antigen binding fragment thereof are 4 mg/mL and 12 mg/mL, respectively.

12. The pharmaceutical composition of claim 1, wherein the composition is for intravenous administration.

13. A vial comprising 20 mL of a pharmaceutical composition comprising:

(a) about 80 mg of an anti-LAG-3 antibody or antigen binding fragment thereof comprising CDR1, CDR2, and CDR3 domains of the heavy chain variable region having the sequence set forth in SEQ ID NO:3, and CDR1, CDR2, and CDR3 domains of the light chain variable region having the sequence set forth in SEQ ID NO:5;

(b) about 240 mg of an anti-PD-1 antibody or antigen binding fragment thereof comprising CDR1, CDR2, and CDR3 domains of the heavy chain variable region having the

sequence set forth in SEQ ID NO:19, and CDR1, CDR2, and CDR3 domains of the light chain variable region having the sequence set forth in SEQ ID NO:21;

(c) about 20 mM of histidine buffer;

(d) about 250 mM of sucrose;

(e) about 20 μM of DTPA; and

(f) about 0.05% (w/v) of polysorbate 80;

wherein the pharmaceutical composition has a pH of about 5.8.

14. The vial of claim 13, wherein the anti-LAG-3 antibody or antigen binding fragment thereof comprises heavy chain variable region CDR1, CDR2, and CDR3 domains comprising the sequences set forth in SEQ ID NOs:7, 8, and 9, respectively, and light chain variable region CDR1, CDR2, and CDR3 domains comprising the sequences set forth in SEQ ID NOs:10, 11, and 12, respectively, and the anti-PD-1 antibody or antigen binding fragment thereof comprises heavy chain variable region CDR1, CDR2, and CDR3 domains comprising the sequences set forth in SEQ ID NOs:23, 24, and 25, respectively, and light chain variable region CDR1, CDR2, and CDR3 domains comprising the sequences set forth in SEQ ID NOs:26, 27, and 28, respectively.

15. The vial of claim 13, wherein the anti-LAG-3 antibody or antigen binding fragment thereof comprises heavy and light chain variable regions comprising the sequences set forth in SEQ ID NOs:3 and 5, respectively, and the anti-PD-1 antibody or antigen binding fragment thereof comprises heavy and light chain variable regions comprising the sequences set forth in SEQ ID NOs:19 and 21, respectively.

16. The vial of claim 13, wherein the anti-LAG-3 antibody comprises heavy and light chains comprising the sequences set forth in SEQ ID NOs:1 and 2, respectively, and the anti-PD-

1 antibody comprises heavy and light chains comprising the sequences as set forth in SEQ ID NOs:17 and 18, respectively.

17. An infusion solution comprising:

(a) about 160 mg of an anti-LAG-3 antibody or antigen binding fragment thereof comprising CDR1, CDR2, and CDR3 domains of the heavy chain variable region having the sequence set forth in SEQ ID NO:3, and CDR1, CDR2, and CDR3 domains of the light chain variable region having the sequence set forth in SEQ ID NO:5;

(b) about 480 mg of an anti-PD-1 antibody or antigen binding fragment thereof comprising CDR1, CDR2, and CDR3 domains of the heavy chain variable region having the sequence set forth in SEQ ID NO:19, and CDR1, CDR2, and CDR3 domains of the light chain variable region having the sequence set forth in SEQ ID NO:21;

(c) about 20 mM of histidine buffer;

(d) about 250 mM of sucrose;

(e) about 20 µM of DTPA; and

(f) about 0.05% (w/v) of polysorbate 80;

wherein the infusion solution has a pH of about 5.8.

18. The infusion solution of claim 17, wherein the anti-LAG-3 antibody or antigen binding fragment thereof comprises heavy chain variable region CDR1, CDR2, and CDR3 domains comprising the sequences set forth in SEQ ID NOs:7, 8, and 9, respectively, and light chain variable region CDR1, CDR2, and CDR3 domains comprising the sequences set forth in SEQ ID NOs:10, 11, and 12, respectively, and the anti-PD-1 antibody or antigen binding fragment thereof comprises heavy chain variable region CDR1, CDR2, and CDR3 domains comprising the sequences set forth in SEQ ID NOs:23, 24, and 25, respectively, and light chain

variable region CDR1, CDR2, and CDR3 domains comprising the sequences set forth in SEQ ID NOs:26, 27, and 28, respectively.

19. The infusion solution of claim 17, wherein the anti-LAG-3 antibody or antigen binding fragment thereof comprises heavy and light chain variable regions comprising the sequences set forth in SEQ ID NOs:3 and 5, respectively, and the anti-PD-1 antibody or antigen binding fragment thereof comprises heavy and light chain variable regions comprising the sequences set forth in SEQ ID NOs:19 and 21, respectively.

20. The infusion solution of claim 17, wherein the anti-LAG-3 antibody comprises heavy and light chains comprising the sequences set forth in SEQ ID NOs:1 and 2, respectively, and the anti-PD-1 antibody comprises heavy and light chains comprising the sequences as set forth in SEQ ID NOs:17 and 18, respectively.

21. An intravenous bag comprising the infusion solution of claim 17.

22. An intravenous bag comprising a dilution of the infusion solution of claim 17.

23. The intravenous bag of claim 22, wherein the diluent is 0.9% Sodium Chloride Injection, USP.

24. The intravenous bag of claim 22, wherein the diluent is 5% Dextrose Injection, USP.