

CLAIMS

What is claimed is:

1. A method of inactivating a virus in a sample comprising an antigen binding protein comprising:
 - (a) providing a sample comprising an antigen binding protein, wherein the sample is known or suspected to contain a virus;
 - (b) adding a protectant to the sample to form a stabilized mixture, wherein the protectant comprises one or more of tyrosine, tryptophan, methionine, pyridoxine and riboflavin; and
 - (c) exposing the stabilized mixture to a target dose of UV light under which the virus is inactivated, wherein the UV light is provided by a source operating at a selected power level and selected wavelength for a selected period of time.
2. The method of claim 1, further comprising:
 - (d) assessing the UV-C exposure level of the stabilized mixture; and
 - (e) modulating one or more of the wavelength, the UV light source power and the UV light exposure time if the assessment indicates the target dose of UV light has not been delivered to the stabilized mixture.
3. The method of claim 1, wherein the sample comprises a chromatography column pool.
4. The method of claim 3, wherein the pool comprises one or more of a Protein A column eluant pool comprising the antigen binding protein, a Protein G column eluant pool comprising the antigen binding protein, a HIC column pool comprising the antigen binding protein, a SEC column pool comprising the antigen binding protein, an IEC column pool comprising the antigen binding protein, and a hydroxyapatite column pool comprising the antigen binding protein.
5. The method of claim 1, wherein the sample comprises a chromatography column effluent stream.

6. The method of claim 5, wherein the effluent stream comprises one or more of a Protein A column effluent stream comprising the antigen binding protein, a Protein G column effluent stream comprising the antigen binding protein, a HIC column effluent stream comprising the antigen binding protein, a SEC column effluent stream comprising the antigen binding protein, an IEC column effluent stream comprising the antigen binding protein, and a hydroxyapatite column effluent stream comprising the antigen binding protein.

7. The method of claim 1, wherein the antigen binding protein is a monoclonal antibody, a human antibody, a humanized antibody, a chimeric antibody, a recombinant antibody, a single chain antibody, a diabody, a triabody, a tetrabody, a Fab fragment, a F(ab')₂ fragment, an IgD antibody, an IgE antibody, an IgM antibody, an IgG1 antibody, an IgG2 antibody, an IgG3 antibody, an IgG4 antibody, or fragments thereof.

8. The method of claim 1, wherein the virus comprises one or more of a dsDNA virus, a ssDNA virus, a dsRNA virus and a ssRNA virus.

9. The method of claim 8, wherein the virus comprises a virus of one or more of the virus families *adenoviridae*, *asfarviridae*, *herpesviridae*, *iridoviridae*, *papillomaviridae*, *polyomaviridae*, *poxviridae*, *circoviridae*, *hepadnaviridae*, *parvoviridae*, *birnaviridae*, *reoviridae*, *arenaviridae*, *vornaviridae*, *bunyaviridae*, *deltaviridae*, *filoviridae*, *orthomyxoviridae*, *paramyxoviridae*, *rhabdoviridae*, *arterioviridae*, *astroviridae*, *caliciviridae*, *coronaviridae*, *flaviviridae*, HEV-like viruses, *nodaviridae*, *picornaviridae*, *togaviridae*, and *retroviridae*.

10. The method of claim 9, wherein the virus is the parvovirus MVM, the retrovirus MuLV or the bunya virus CVV.

11. The method of claim 1, wherein the protectant is added to the sample in a concentration ratio of greater than 1 part protectant to 200 parts protein.

12. The method of claim 1, wherein the protectant comprises (i) tyrosine; (ii) tryptophan; or (iii) tyrosine and tryptophan.

13. The method of claim 1, wherein the UV light has a wavelength in the range of 200 nm to 280 nm.

14. The method of claim 13, wherein the UV light has a wavelength of 254 nm.

15. The method of claim 1, wherein the target dose is one or more of 1 mJ/cm², 10 mJ/cm², 25 mJ/cm², 50 mJ/cm², 75 mJ/cm², 100 mJ/cm², 125 mJ/cm², 200 mJ/cm², 250 mJ/cm², 300 mJ/cm², 350 mJ/cm², 400 mJ/cm², 450 mJ/cm², 500 mJ/cm², 600 mJ/cm², 700 mJ/cm², 800 mJ/cm², 900 mJ/cm², 1000 mJ/cm² and greater than 1000 mJ/cm².

16. The method of claim 1, wherein the method provides a viral log reduction value (LRV) of greater than or equal to 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, 5.0, 5.5, 6.0, 6.5 or greater than 6.5.

17. The method of claim 1, wherein the method is automated.

18. The method of claim 1, wherein the method is performed as a step in a protein purification operation.

19. A method of reducing protein degradation or modification arising from the presence of a reactive species generated during UV exposure comprising:

- (a) providing a sample comprising an antigen binding protein known or suspected to be degraded or modified in the presence of a reactive species;
- (b) adding a protectant to the sample to form a stabilized mixture, wherein the protectant comprises one or more of tyrosine, tryptophan, methionine, pyridoxine and riboflavin; and
- (c) exposing the stabilized mixture to a target dose of UV light, wherein the UV light is provided by a source operating at a selected power level and selected wavelength for a selected period of time.

20. The method of claim 19, further comprising:

- (d) assessing the UV-C exposure level of the stabilized mixture; and

- (e) modulating one or more of the wavelength, the UV light source power and the UV light exposure time if the assessment indicates the target dose of UV light has not been delivered to the stabilized mixture.

21. The method of claim 19, wherein the sample comprises a chromatography column pool.

22. The method of claim 21, wherein the pool comprises one or more of a Protein A column eluant pool comprising the antigen binding protein, a Protein G column eluant pool comprising the antigen binding protein, a HIC column pool comprising the antigen binding protein, a SEC column pool comprising the antigen binding protein, an IEC column pool comprising the antigen binding protein, and a hydroxyapatite column pool comprising the antigen binding protein.

23. The method of claim 19, wherein the sample comprises a chromatography column effluent stream.

24. The method of claim 23, wherein the effluent stream comprises one or more of a Protein A column effluent stream comprising the antigen binding protein, a Protein G column effluent stream comprising the antigen binding protein, a HIC column effluent stream comprising the antigen binding protein, a SEC column effluent stream comprising the antigen binding protein, an IEC column effluent stream comprising the antigen binding protein, and a hydroxyapatite column effluent stream comprising the antigen binding protein.

25. The method of claim 19, wherein the antigen binding protein is a monoclonal antibody, a human antibody, a humanized antibody, a chimeric antibody, a recombinant antibody, a single chain antibody, a diabody, a triabody, a tetrabody, a Fab fragment, a F(ab')₂ fragment, an IgD antibody, an IgE antibody, an IgM antibody, an IgG1 antibody, an IgG2 antibody, an IgG3 antibody, an IgG4 antibody, or fragments thereof.

26. The method of claim 19, wherein the protectant is added to the sample in a concentration ratio of greater than 1 part protectant to 200 parts protein.

27. The method of claim 19, wherein the protectant comprises (i) tyrosine; (ii) tryptophan; or (iii) tyrosine and tryptophan.

28. The method of claim 19, wherein the UV light has a wavelength in the range of 200 nm to 280 nm.

29. The method of claim 28, wherein the UV light has a wavelength of 254 nm.

30. The method of claim 19, wherein the target dose is one or more of 1 mJ/cm², 10 mJ/cm², 25 mJ/cm², 50 mJ/cm², 75 mJ/cm², 100 mJ/cm², 125 mJ/cm², 200 mJ/cm², 250 mJ/cm², 300 mJ/cm², 350 mJ/cm², 400 mJ/cm², 450 mJ/cm², 500 mJ/cm², 600 mJ/cm², 700 mJ/cm², 800 mJ/cm², 900 mJ/cm², 1000 mJ/cm² and greater than 1000 mJ/cm².

31. The method of claim 19, wherein the method is automated.

32. The method of claim 19, wherein the method is performed as a step in a protein purification operation.

33. A method of reducing oxidation of methionine residues, tryptophan residues or both methionine and tryptophan residues in an antigen binding protein subjected to UV light comprising:

- (a) providing a sample comprising an antigen binding protein comprising a methionine residue/methionine residues, a tryptophan residue/tryptophan residues or both a methionine and a tryptophan residue/methionine and tryptophan residues;
- (b) adding a protectant to the sample to form a stabilized mixture, wherein the protectant comprises one or more of tyrosine, tryptophan, methionine, pyridoxine and riboflavin; and
- (c) exposing the stabilized mixture to a target dose of UV light, wherein the UV light is provided by a source operating at a selected power level and selected wavelength for a selected period of time.

34. The method of claim 33, further comprising:

- (d) assessing the UV-C exposure level of the stabilized mixture; and

- (e) modulating one or more of the wavelength, the UV light source power and the UV light exposure time if the assessment indicates the target dose of UV light has not been delivered to the stabilized mixture.

35. The method of claim 33, wherein the sample comprises a chromatography column pool.

36. The method of claim 34, wherein the pool comprises one or more of a Protein A column eluant pool comprising the antigen binding protein, a Protein G column eluant pool comprising the antigen binding protein, a HIC column pool comprising the antigen binding protein, a SEC column pool comprising the antigen binding protein, an IEC column pool comprising the antigen binding protein, and a hydroxyapatite column pool comprising the antigen binding protein.

37. The method of claim 33, wherein the sample comprises a chromatography column effluent stream.

38. The method of claim 37, wherein the effluent stream comprises one or more of a Protein A column effluent stream comprising the antigen binding protein, a Protein G column effluent stream comprising the antigen binding protein, a HIC column effluent stream comprising the antigen binding protein, a SEC column effluent stream comprising the antigen binding protein, an IEC column effluent stream comprising the antigen binding protein, and a hydroxyapatite column effluent stream comprising the antigen binding protein.

39. The method of claim 33, wherein the antigen binding protein is a monoclonal antibody, a human antibody, a humanized antibody, a chimeric antibody, a recombinant antibody, a single chain antibody, a diabody, a triabody, a tetrabody, a Fab fragment, a F(ab')₂ fragment, an IgD antibody, an IgE antibody, an IgM antibody, an IgG1 antibody, an IgG2 antibody, an IgG3 antibody, an IgG4 antibody, or fragments thereof.

40. The method of claim 33, wherein the protectant is added to the sample in a concentration ratio of greater than 1 part protectant to 200 parts protein.

41. The method of claim 33, wherein the protectant comprises (i) tyrosine; (ii) tryptophan; or (iii) tyrosine and tryptophan.

42. The method of claim 33, wherein the UV light has a wavelength in the range of 200 nm to 280 nm.

43. The method of claim 42, wherein the UV light has a wavelength of 254 nm.

44. The method of claim 33, wherein the target dose is one or more of 1 mJ/cm², 10 mJ/cm², 25 mJ/cm², 50 mJ/cm², 75 mJ/cm², 100 mJ/cm², 125 mJ/cm², 200 mJ/cm², 250 mJ/cm², 300 mJ/cm², 350 mJ/cm², 400 mJ/cm², 450 mJ/cm², 500 mJ/cm², 600 mJ/cm², 700 mJ/cm², 800 mJ/cm², 900 mJ/cm², 1000 mJ/cm² and greater than 1000 mJ/cm².

45. The method of claim 33, wherein the method is automated.

46. The method of claim 33, wherein the method is performed as a step in a protein purification operation.

CLAIMS

What is claimed is:

1. A method of inactivating a virus in a sample comprising a protein component comprising:
 - (a) providing a sample comprising a protein component, wherein the sample is known or suspected to contain a virus;
 - (b) identifying a target dose of UV light under which the virus is inactivated;
 - (c) adding a protectant to the sample to form a stabilized mixture;
 - (d) exposing the stabilized mixture to UV light provided by a source operating at a selected power level and selected wavelength for a selected period of time;
 - (e) assessing the UV-C exposure level of the stabilized mixture; and
 - (f) modulating one or more of the wavelength, the UV light source power and the UV light exposure time if the assessment indicates the target dose of UV light has not been delivered to the stabilized mixture.
2. The method of claim 1, wherein the sample comprises a chromatography column pool.
3. The method of claim 5, wherein the pool comprises one or more of a Protein A column eluant pool comprising the protein component, a Protein G column eluant pool comprising the protein component, a HIC column pool comprising the protein component, a SEC column pool comprising the protein component, an IEC column pool comprising the protein component, and a hydroxyapatite column pool comprising the protein component.
4. The method of claim 1, wherein the sample comprises a chromatography column effluent stream.
5. The method of claim 4, wherein the effluent stream comprises one or more of a Protein A column effluent stream comprising the protein component, a

Protein G column effluent stream comprising the protein component, a HIC column effluent stream comprising the protein component, a SEC column effluent stream comprising the protein component, an IEC column effluent stream comprising the protein component, and a hydroxyapatite column effluent stream comprising the protein component.

6. The method of claim 1, wherein the protein component comprises one or more of (i) an antigen binding protein comprising one or more of a monoclonal antibody, a human antibody, a humanized antibody, a chimeric antibody, a recombinant antibody, a single chain antibody, a diabody, a triabody, a tetrabody, a Fab fragment, a F(ab')₂ fragment, an IgD antibody, an IgE antibody, an IgM antibody, an IgG1 antibody, an IgG2 antibody, an IgG3 antibody, or an IgG4 antibody, and fragments thereof, (ii) an Fc domain; (iii) a peptide; (iv) an Fc fusion protein; and (v) a therapeutic protein.

7. The method of claim 1, wherein the virus comprises one or more of a dsDNA virus, a ssDNA virus, a dsRNA virus and a ssRNA virus.

8. The method of claim 7, wherein the virus comprises a virus of one or more of the virus families *adenoviridae*, *asfarviridae*, *herpesviridae*, *iridoviridae*, *papillomaviridae*, *polyomaviridae*, *poxviridae*, *circoviridae*, *hepadnaviridae*, *parvoviridae*, *birnaviridae*, *reoviridae*, *arenaviridae*, *vornaviridae*, *bunyaviridae*, *deltaviridae*, *filoviridae*, *orthomyxoviridae*, *paramyxoviridae*, *rhabdoviridae*, *arterioviridae*, *astroviridae*, *caliciviridae*, *coronaviridae*, *flaviviridae*, HEV-like viruses, *nodaviridae*, *picornaviridae*, *togaviridae*, and *tertroviridae*.

9. The method of claim 8, wherein the virus is the parvovirus MVM, the retrovirus MuLV or the bunya virus CVV.

10. The method of claim 1, wherein the protectant is added to the sample in a concentration ratio of greater than 1 part protectant to 200 parts protein.

11. The method of claim 1, wherein the protectant comprises one or more of tyrosine, tryptophan, methionine, pyridoxine and riboflavin.

12. The method of claim 11, wherein the protectant comprises one of (i) tyrosine; (ii) tryptophan; and (iii) tyrosine and tryptophan.
13. The method of claim 1, wherein the UV light has a wavelength in the range of about 200 nm to about 280 nm.
14. The method of claim 13, wherein the UV light has a wavelength of about 254 nm.
15. The method of claim 1, wherein the target dose is one or more of about 1 mJ/cm², about 10 mJ/cm², about 25 mJ/cm², about 50 mJ/cm², about 75 mJ/cm², about 100 mJ/cm², about 125 mJ/cm², about 200 mJ/cm², about 250 mJ/cm², about 300 mJ/cm², about 350 mJ/cm², about 400 mJ/cm², about 450 mJ/cm², about 500 mJ/cm², about 600 mJ/cm², about 700 mJ/cm², about 800 mJ/cm², about 900 mJ/cm², about 1000 mJ/cm² and greater than about 1000 mJ/cm².
16. The method of claim 1, wherein the method provides a viral log reduction value (LRV) of greater than or equal to about 0.5, about 1.0, about 1.5, about 2.0, about 2.5, about 3.0, about 3.5, about 4.0, about 4.5, about 5.0, about 5.5, about 6.0, about 6.5 or greater than about 6.5.
17. The method of claim 1, wherein the method is automated.
18. The method of claim 1, wherein the method is performed as a step in a protein purification operation.
19. A method of reducing protein degradation or modification arising from the presence of a reactive species generated during UV exposure comprising:
 - (a) providing a sample comprising a protein component known or suspected to be degraded or modified in the presence of a reactive species;
 - (b) identifying a target dose of UV light;
 - (c) adding a protectant to the sample to form a stabilized mixture;

- (d) exposing the stabilized mixture to UV light provided by a source operating at a selected power level and selected wavelength for a selected period of time;
- (e) assessing the UV-C exposure level of the stabilized mixture; and
- (f) modulating one or more of the wavelength, the UV light source power and the UV light exposure time if the assessment indicates the target dose of UV light has not been delivered to the stabilized mixture.

20. The method of claim 19, wherein the sample comprises a chromatography column pool.

21. The method of claim 20, wherein the pool comprises one or more of a Protein A column eluant pool comprising the protein component, a Protein G column eluant pool comprising the protein component, a HIC column pool comprising the protein component, a SEC column pool comprising the protein component, an IEC column pool comprising the protein component, and a hydroxyapatite column pool comprising the protein component.

22. The method of claim 19, wherein the sample comprises a chromatography column effluent stream.

23. The method of claim 22, wherein the effluent stream comprises one or more of a Protein A column effluent stream comprising the protein component, a Protein G column effluent stream comprising the protein component, a HIC column effluent stream comprising the protein component, a SEC column effluent stream comprising the protein component, an IEC column effluent stream comprising the protein component, and a hydroxyapatite column effluent stream comprising the protein component.

24. The method of claim 19, wherein the protein component comprises one or more of (i) an antigen binding protein comprising one or more of a monoclonal antibody, a human antibody, a humanized antibody, a chimeric antibody, a recombinant antibody, a single chain antibody, a diabody, a triabody, a tetrabody, a Fab fragment, a F(ab')₂ fragment, an IgD antibody, an IgE antibody, an IgM antibody,

an IgG1 antibody, an IgG2 antibody, an IgG3 antibody, or an IgG4 antibody, and fragments thereof, (ii) an Fc domain; (iii) a peptide; (iv) an Fc fusion protein; and (v) a therapeutic protein.

25. The method of claim 19, wherein the protectant is added to the sample in a concentration ratio of greater than 1 part protectant to 200 parts protein.

26. The method of claim 19, wherein the protectant comprises one or more of tyrosine, tryptophan, methionine, pyridoxine and riboflavin.

27. The method of claim 26, wherein the protectant comprises one of (i) tyrosine; (ii) tryptophan; or (iii) tyrosine and tryptophan.

28. The method of claim 19, wherein the UV light has a wavelength in the range of about 200 nm to about 280 nm.

29. The method of claim 28, wherein the UV light has a wavelength of about 254 nm.

30. The method of claim 19, wherein the target dose is one or more of about 1 mJ/cm², about 10 mJ/cm², about 25 mJ/cm², about 50 mJ/cm², about 75 mJ/cm², about 100 mJ/cm², about 125 mJ/cm², about 200 mJ/cm², about 250 mJ/cm², about 300 mJ/cm², about 350 mJ/cm², about 400 mJ/cm², about 450 mJ/cm², about 500 mJ/cm², about 600 mJ/cm², about 700 mJ/cm², about 800 mJ/cm², about 900 mJ/cm², about 1000 mJ/cm² and greater than about 1000 mJ/cm².

31. The method of claim 19, wherein the method is automated.

32. The method of claim 19, wherein the method is performed as a step in a protein purification operation.

33. A method of reducing oxidation of methionine residues, tryptophan residues or both methionine and tryptophan residues in a protein subjected to UV light comprising:

- (a) providing a sample comprising a protein component comprising a methionine residue, a tryptophan residue or both a methionine and a tryptophan residue;
- (b) identifying a target dose of UV light;
- (c) adding a protectant to the sample to form a stabilized mixture;
- (d) exposing the stabilized mixture to UV light provided by a source operating at a selected power level and selected wavelength for a selected period of time;
- (e) assessing the UV-C exposure level of the stabilized mixture; and
- (f) modulating one or more of the wavelength, the UV light source power and the UV light exposure time if the assessment indicates the target dose of UV light has not been delivered to the stabilized mixture.

34. The method of claim 33, wherein the sample comprises a chromatography column pool.

35. The method of claim 33, wherein the pool comprises one or more of a Protein A column eluant pool comprising the protein component, a Protein G column eluant pool comprising the protein component, a HIC column pool comprising the protein component, a SEC column pool comprising the protein component, an IEC column pool comprising the protein component, and a hydroxyapatite column pool comprising the protein component.

36. The method of claim 33, wherein the sample comprises a chromatography column effluent stream.

37. The method of claim 36, wherein the effluent stream comprises one or more of a Protein A column effluent stream comprising the protein component, a Protein G column effluent stream comprising the protein component, a HIC column effluent stream comprising the protein component, a SEC column effluent stream comprising the protein component, an IEC column effluent stream comprising the protein component, and a hydroxyapatite column effluent stream comprising the protein component.

38. The method of claim 33, wherein the protein component comprises one or more of (i) an antigen binding protein comprising one or more of a monoclonal antibody, a human antibody, a humanized antibody, a chimeric antibody, a recombinant antibody, a single chain antibody, a diabody, a triabody, a tetrabody, a Fab fragment, a F(ab')₂ fragment, an IgD antibody, an IgE antibody, an IgM antibody, an IgG1 antibody, an IgG2 antibody, an IgG3 antibody, or an IgG4 antibody, and fragments thereof, (ii) an Fc domain; (iii) a peptide; (iv) an Fc fusion protein; and (v) a therapeutic protein.

39. The method of claim 33, wherein the protectant is added to the sample in a concentration ratio of greater than 1 part protectant to 200 parts protein.

40. The method of claim 33, wherein the protectant comprises one or more of tyrosine, tryptophan, methionine, pyridoxine and riboflavin.

41. The method of claim 33, wherein the protectant comprises one of (i) tyrosine; (ii) tryptophan; and (iii) tyrosine and tryptophan.

42. The method of claim 33, wherein the UV light has a wavelength in the range of about 200 nm to about 280 nm.

43. The method of claim 42, wherein the UV light has a wavelength of about 254 nm.

44. The method of claim 33, wherein the target dose is one or more of about 1 mJ/cm², about 10 mJ/cm², about 25 mJ/cm², about 50 mJ/cm², about 75 mJ/cm², about 100 mJ/cm², about 125 mJ/cm², about 200 mJ/cm², about 250 mJ/cm², about 300 mJ/cm², about 350 mJ/cm², about 400 mJ/cm², about 450 mJ/cm², about 500 mJ/cm², about 600 mJ/cm², about 700 mJ/cm², about 800 mJ/cm², about 900 mJ/cm², about 1000 mJ/cm² and greater than about 1000 mJ/cm².

45. The method of claim 33, wherein the method is automated.

46. The method of claim 33, wherein the method is performed as a step in a protein purification operation.