

be, as described, a component of a viral inactivation operation, and the protein in the solution can be of any type, for example a protein such as an antigen binding protein (*e.g.*, 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')<sub>2</sub> 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).

### SUMMARY OF THE INVENTION

In one aspect, the present invention refers to a method of inactivating a virus in a sample comprising an antibody comprising: (a) providing a sample comprising the antibody, 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, and methionine; and (c) exposing the stabilized mixture to a target dose of UV-C light under which the virus is inactivated, wherein the UV-C light is provided by a source operating at a selected power level and selected wavelength for a selected period of time. In another aspect, the present invention refers to 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 antibody; (b) adding a protectant to the sample to form a stabilized mixture, wherein the protectant comprises one or more of tyrosine, tryptophan, and methionine; and (c) exposing the stabilized mixture to a target dose of UV-C light, wherein the UV-C light is provided by a source operating at a selected power level and selected wavelength for a selected period of time. In still another aspect, the present invention refers to a method for inactivating a virus in a therapeutic antibody preparation comprising: (a) providing a sample comprising the therapeutic antibody, wherein the sample is an effluent stream from an antibody purification step and the sample is known or suspected to contain a virus; (b) introducing a protectant into the effluent stream to form a stabilized mixture, wherein the protectant comprises tyrosine, tryptophan, methionine, or combinations thereof, (c) passing the stabilized mixture through a device configured to provide continuous exposure to UV-C light such that a target dose of UV-C light under which the virus is inactivated is delivered to the mixture; and (d) removing the protectant from the mixture following UV-C light exposure.

In one aspect~~example~~ a method of inactivating a virus in a sample comprising a protein component is provided. In one embodiment~~example~~ the method comprises (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.

In one ~~embodiment~~example the sample comprises a chromatography column pool; in specific embodiments the pool can comprise 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. In another ~~embodiment~~example the sample comprises a chromatography column effluent stream; in specific embodiments the effluent stream can comprise 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.

In other ~~embodiments~~examples the protein component can comprise 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')<sub>2</sub> 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.

In still further ~~embodiments~~examples the virus comprises one or more of a dsDNA virus, a ssDNA virus, a dsRNA virus and a ssRNA virus; in specific ~~embodiments~~examples the virus can comprise 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*. In particular ~~embodiments~~examples the virus is the parvovirus MVM, the retrovirus MuLV or the bunya virus CVV.

In yet another ~~embodiment~~example the protectant is added to the sample in a concentration ratio of greater than 1 part protectant to 200 parts protein and in other ~~embodiments~~examples the protectant can comprise one or more of tyrosine, tryptophan, methionine, pyridoxine and riboflavin. In specific ~~embodiments~~examples the protectant comprises one of (i) tyrosine; (ii) tryptophan; and (iii) tyrosine and tryptophan.

In still further ~~embodiments~~examples the UV light has a wavelength in the range of about 200 nm to about 280 nm; in specific ~~embodiments~~ the UV light has a wavelength of about 254 nm. The target dose, in various ~~embodiments~~examples, can be one or more of about 1 mJ/cm<sup>2</sup>, about 10 mJ/cm<sup>2</sup>, about 25 mJ/cm<sup>2</sup>, about 50 mJ/cm<sup>2</sup>, about 75 mJ/cm<sup>2</sup>, about 100 mJ/cm<sup>2</sup>, about 125 mJ/cm<sup>2</sup>, about 200 mJ/cm<sup>2</sup>, about 250 mJ/cm<sup>2</sup>, about 300 mJ/cm<sup>2</sup>, about 350 mJ/cm<sup>2</sup>, about 400 mJ/cm<sup>2</sup>, about 450 mJ/cm<sup>2</sup>, about 500 mJ/cm<sup>2</sup>, about 600 mJ/cm<sup>2</sup>, about 700 mJ/cm<sup>2</sup>, about 800 mJ/cm<sup>2</sup>, about 900 mJ/cm<sup>2</sup>, about 1000 mJ/cm<sup>2</sup> and greater than about 1000 mJ/cm<sup>2</sup>.

In some ~~embodiments~~examples 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.

In another embodimentexample the method is automated and in still another embodimentexample the method is performed as a step in a protein purification operation.

In another aspectexample, a method of reducing protein degradation or modification arising from the presence of a reactive species generated during UV exposure is provided. In one embodimentexample the method comprises (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.

In one embodimentexample the sample comprises a chromatography column pool; in specific embodiments the pool can comprise 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. In another embodimentexample the sample comprises a chromatography column effluent stream; in specific embodiments the effluent stream can comprise 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.

In other embodimentexamples the protein component can comprise 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')<sub>2</sub>

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.

In yet another ~~embodiment~~example the protectant is added to the sample in a concentration ratio of greater than 1 part protectant to 200 parts protein and in other embodiments the protectant can comprise one or more of tyrosine, tryptophan, methionine, pyridoxine and riboflavin. In specific ~~embodiments~~examples the protectant comprises one of (i) tyrosine; (ii) tryptophan; and (iii) tyrosine and tryptophan.

In still further ~~embodiments~~examples the UV light has a wavelength in the range of about 200 nm to about 280 nm; in specific ~~embodiments~~examples the UV light has a wavelength of about 254 nm. The target dose, in various ~~embodiments~~examples can be one or more of about 1 mJ/cm<sup>2</sup>, about 10 mJ/cm<sup>2</sup>, about 25 mJ/cm<sup>2</sup>, about 50 mJ/cm<sup>2</sup>, about 75 mJ/cm<sup>2</sup>, about 100 mJ/cm<sup>2</sup>, about 125 mJ/cm<sup>2</sup>, about 200 mJ/cm<sup>2</sup>, about 250 mJ/cm<sup>2</sup>, about 300 mJ/cm<sup>2</sup>, about 350 mJ/cm<sup>2</sup>, about 400 mJ/cm<sup>2</sup>, about 450 mJ/cm<sup>2</sup>, about 500 mJ/cm<sup>2</sup>, about 600 mJ/cm<sup>2</sup>, about 700 mJ/cm<sup>2</sup>, about 800 mJ/cm<sup>2</sup>, about 900 mJ/cm<sup>2</sup>, about 1000 mJ/cm<sup>2</sup> and greater than about 1000 mJ/cm<sup>2</sup>.

In some ~~embodiments~~examples 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.

In another ~~embodiment~~example the method is automated and in still another ~~embodiment~~example the method is performed as a step in a protein purification operation.

In still another ~~aspect~~example, a method of reducing oxidation of methionine residues, tryptophan residues or both methionine and tryptophan residues in a protein subjected to UV light is provided. In one ~~embodiment~~example the method comprises (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.

In one embodimentexample the sample comprises a chromatography column pool; in specific embodiments the pool can comprise 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. In another embodimentexample the sample comprises a chromatography column effluent stream; in specific embodiments the effluent stream can comprise 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.

In other embodimentexamples the protein component can comprise 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')<sub>2</sub> 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.

In yet another embodimentexample the protectant is added to the sample in a concentration ratio of greater than 1 part protectant to 200 parts protein and in other embodimentexamples the protectant can comprise one or more of tyrosine, tryptophan, methionine, pyridoxine and riboflavin. In specific embodimentexamples the protectant comprises one of (i) tyrosine; (ii) tryptophan; and (iii) tyrosine and tryptophan.

In still further embodimentexamples the UV light has a wavelength in the range of about 200 nm to about 280 nm; in specific embodimentexamples the UV light has a wavelength of about 254 nm. The target dose, in various embodimentexamples can be one or more of about 1 mJ/cm<sup>2</sup>, about 10 mJ/cm<sup>2</sup>, about 25 mJ/cm<sup>2</sup>, about 50 mJ/cm<sup>2</sup>, about 75 mJ/cm<sup>2</sup>, about 100 mJ/cm<sup>2</sup>, about 125 mJ/cm<sup>2</sup>, about 200 mJ/cm<sup>2</sup>, about 250 mJ/cm<sup>2</sup>, about 300 mJ/cm<sup>2</sup>, about 350 mJ/cm<sup>2</sup>, about 400 mJ/cm<sup>2</sup>, about 450 mJ/cm<sup>2</sup>, about 500 mJ/cm<sup>2</sup>, about 600 mJ/cm<sup>2</sup>, about 700 mJ/cm<sup>2</sup>, about 800 mJ/cm<sup>2</sup>, about 900 mJ/cm<sup>2</sup>, about 1000 mJ/cm<sup>2</sup> and greater than about 1000 mJ/cm<sup>2</sup>.

In some embodimentexamples 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.

In another embodimentexample the method is automated and in still another embodimentexample the method is performed as a step in a protein purification operation.

#### BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a plot of percent main peak changes in three different monoclonal antibody samples (Mab X, Mab Y, Mab Z) as a function of UV-C exposure monitored at three different pH levels (ph 4.3, 5.0 and 7.0) by SEC-HPLC assay; the y-axis is plotted as % change in value compared to 0 mJ dose delivered to the solution surface and the x-axis is plotted as calculated dose delivered ( $\text{mJ}/\text{cm}^2$ ) to the solution surface. All samples were filtered viral inactivated pools (FVIP).

Figure 2 is a plot of main peak, acidic peak and basic peak purity of two different monoclonal antibody samples (Mab X, Mab Z) as a function of UV-C exposure monitored at three different pH levels (pH 4.3, 5.0 and 7.0) by CEX-HPLC assay; the y-axis is plotted as % distribution of the measured species, compared to 0  $\text{mJ}/\text{cm}^2$  dose delivered to the solution surface and the x-axis is plotted as calculated dose ( $\text{mJ}/\text{cm}^2$ ) delivered to the solution surface. All samples were filtered viral inactivated pools (FVIP).

Figure 3 is a plot of percent main peak change in three different monoclonal antibody samples (Mab X, Mab Y, Mab Z) as a function of UV-C exposure monitored at three different conductivity levels (Low (30mM HOAc), Standard (100 mM HOAc), and High (300 mM HOAc)) by SEC-HPLC assay; the y-axis is plotted as % change in value compared to 0  $\text{mJ}/\text{cm}^2$  dose delivered to the solution surface and the x-axis is plotted as calculated dose ( $\text{mJ}/\text{cm}^2$ ) delivered to the solution surface.

Figure 4 is a plot of main peak, acidic peak and basic peak purity of two different monoclonal antibody samples (Mab X, Mab Z) as a function of UV-C exposure monitored at three different conductivity levels (Low (30mM HOAc), Standard (100 mM HOAc), and High (300 mM HOAc)) by CEX-HPLC assay; the y-axis is plotted as % distribution of the measured species, compared to 0  $\text{mJ}/\text{cm}^2$  dose delivered to the solution surface and the x-axis is plotted as calculated dose ( $\text{mJ}/\text{cm}^2$ )

respectively. Within light and heavy chains, the variable and constant regions are joined by a “J” region of about 12 or more amino acids, with the heavy chain also including a “D” region of about 10 more amino acids. See generally, Fundamental Immunology 2<sup>nd</sup> ed. Ch. 7 (Paul, W., ed., Raven Press, N.Y. (1989)), ~~incorporated by reference in its entirety for all purposes.~~ The variable regions of each light/heavy chain pair form the antibody binding site such that an intact immunoglobulin has two binding sites.

Naturally occurring immunoglobulin chains exhibit the same general structure of relatively conserved framework regions (FR) joined by three hypervariable regions, also called complementarity determining regions or CDRs. From N-terminus to C-terminus, both light and heavy chains comprise the domains FR1, CDR1, FR2, CDR2, FR3, CDR3 and FR4. The assignment of amino acids to each domain can be done in accordance with the definitions of Kabat et al., (1991) “Sequences of Proteins of Immunological Interest”, 5<sup>th</sup> Ed., US Dept. of Health and Human Services, PHS, NIH, NIH Publication no. 91-3242. Although presented using the Kabat nomenclature system, as desired, the CDRs disclosed herein can also be redefined according an alternative nomenclature scheme, such as that of Chothia (see Chothia & Lesk, (1987) *J. Mol. Biol.* 196:901-917; Chothia *et al.*, (1989) *Nature* 342:878-883 or Honegger & Pluckthun, (2001) *J. Mol. Biol.* 309:657-670).

As used herein, the term “antibody” refers to an intact immunoglobulin or to an antigen binding portion thereof that competes with the intact antibody for specific binding, unless otherwise specified. Antigen binding portions can be produced by recombinant DNA techniques or by enzymatic or chemical cleavage of intact antibodies. Antigen binding portions include, *inter alia*, Fab, Fab’, F(ab’)<sub>2</sub>, Fv, domain antibodies (dAbs), fragments including complementarity determining regions (CDRs), single-chain antibodies (scFv), chimeric antibodies, diabodies, triabodies, tetrabodies, and polypeptides that contain at least a portion of an immunoglobulin that is sufficient to confer specific antigen binding to the polypeptide.

A Fab fragment is a monovalent fragment having the V<sub>L</sub>, V<sub>H</sub>, C<sub>L</sub> and C<sub>H</sub>1 domains; a F(ab’)<sub>2</sub> fragment is a bivalent fragment having two Fab fragments linked by a disulfide bridge at the hinge region; a Fd fragment has the V<sub>H</sub> and C<sub>H</sub>1 domains; an Fv fragment has the V<sub>L</sub> and V<sub>H</sub> domains of a single arm of an antibody; and a dAb fragment has a V<sub>H</sub> domain, a V<sub>L</sub> domain, or an antigen-binding fragment of a V<sub>H</sub> or V<sub>L</sub> domain (US Patent Nos. 6,846,634, and 6,696,245; and US App. Pub. Nos.

## CLAIMS

What is claimed is:

1. A method of inactivating a virus in a sample comprising an antibody comprising:
  - (a) providing a sample comprising the antibody, 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, and methionine; and
  - (c) exposing the stabilized mixture to a target dose of UV-C light under which the virus is inactivated, wherein the UV-C 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-C light has not been delivered to the stabilized mixture.
3. The method of claim 1 or 2, further comprising removing the protectant from the mixture following exposure to UV-C light.
4. The method of claim 1, wherein the sample comprises a chromatography column pool.
5. The method of claim 4, wherein the pool comprises one or more of a Protein A column eluant pool comprising the antibody, a Protein G column eluant pool comprising the antibody, a HIC column pool comprising the antibody, a SEC column pool comprising the antibody, an IEC column pool comprising the antibody, and a hydroxyapatite column pool comprising the antibody.
6. The method of claim 1, wherein the sample comprises a chromatography column effluent stream.

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

8. The method of claim 1, wherein the antibody is a monoclonal antibody, a human antibody, a humanized antibody, a chimeric antibody, a recombinant antibody, a single chain antibody, an IgD antibody, an IgE antibody, an IgM antibody, an IgG1 antibody, an IgG2 antibody, an IgG3 antibody, or an IgG4 antibody.

9. 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.

10. The method of claim 9, 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*.

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

12. 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 antibody.

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

14. The method of claim 1, wherein the UV-C light has a wavelength in the range of 200 nm to 280 nm.
15. The method of claim 14, wherein the UV-C light has a wavelength of 254 nm.
16. The method of claim 1, wherein the target dose is 1 mJ/cm<sup>2</sup>, 10 mJ/cm<sup>2</sup>, 25 mJ/cm<sup>2</sup>, 50 mJ/cm<sup>2</sup>, 75 mJ/cm<sup>2</sup>, 100 mJ/cm<sup>2</sup>, 125 mJ/cm<sup>2</sup>, 200 mJ/cm<sup>2</sup>, 250 mJ/cm<sup>2</sup>, 300 mJ/cm<sup>2</sup>, 350 mJ/cm<sup>2</sup>, 400 mJ/cm<sup>2</sup>, 450 mJ/cm<sup>2</sup>, 500 mJ/cm<sup>2</sup>, 600 mJ/cm<sup>2</sup>, 700 mJ/cm<sup>2</sup>, 800 mJ/cm<sup>2</sup>, 900 mJ/cm<sup>2</sup>, 1000 mJ/cm<sup>2</sup> or greater than 1000 mJ/cm<sup>2</sup>.
17. 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.
18. The method of claim 1, wherein the method is automated.
19. The method of claim 1, wherein the method is performed as a step in an antibody purification operation.
20. 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 antibody;
  - (b) adding a protectant to the sample to form a stabilized mixture, wherein the protectant comprises one or more of tyrosine, tryptophan, and methionine; and
  - (c) exposing the stabilized mixture to a target dose of UV-C light, wherein the UV-C light is provided by a source operating at a selected power level and selected wavelength for a selected period of time.
21. The method of claim 20, 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-C light has not been delivered to the stabilized mixture.

22. The method of claim 20 or 21, further comprising removing the protectant from the mixture following exposure to UV-C light.

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

24. The method of claim 23, wherein the pool comprises one or more of a Protein A column eluant pool comprising the antibody, a Protein G column eluant pool comprising the antibody, a HIC column pool comprising the antibody, a SEC column pool comprising the antibody, an IEC column pool comprising the antibody, and a hydroxyapatite column pool comprising the antibody.

25. The method of claim 20, wherein the sample comprises a chromatography column effluent stream.

26. The method of claim 25, wherein the effluent stream comprises one or more of a Protein A column effluent stream comprising the antibody, a Protein G column effluent stream comprising the antibody, a HIC column effluent stream comprising the antibody, a SEC column effluent stream comprising the antibody, an IEC column effluent stream comprising the antibody, and a hydroxyapatite column effluent stream comprising the antibody.

27. The method of claim 20, wherein the antibody is a monoclonal antibody, a human antibody, a humanized antibody, a chimeric antibody, a recombinant antibody, a single chain antibody, an IgD antibody, an IgE antibody, an IgM antibody, an IgG1 antibody, an IgG2 antibody, an IgG3 antibody, or an IgG4 antibody.

28. The method of claim 20, wherein the protectant is added to the sample in a concentration ratio of greater than 1 part protectant to 200 parts antibody.

29. The method of claim 20, wherein the protectant comprises (i) tyrosine; (ii) tryptophan; or (iii) tyrosine and tryptophan.

30. The method of claim 20, wherein the UV-C light has a wavelength in the range of 200 nm to 280 nm.

31. The method of claim 30, wherein the UV-C light has a wavelength of 254 nm.

32. The method of claim 20, wherein the target dose is 1 mJ/cm<sup>2</sup>, 10 mJ/cm<sup>2</sup>, 25 mJ/cm<sup>2</sup>, 50 mJ/cm<sup>2</sup>, 75 mJ/cm<sup>2</sup>, 100 mJ/cm<sup>2</sup>, 125 mJ/cm<sup>2</sup>, 200 mJ/cm<sup>2</sup>, 250 mJ/cm<sup>2</sup>, 300 mJ/cm<sup>2</sup>, 350 mJ/cm<sup>2</sup>, 400 mJ/cm<sup>2</sup>, 450 mJ/cm<sup>2</sup>, 500 mJ/cm<sup>2</sup>, 600 mJ/cm<sup>2</sup>, 700 mJ/cm<sup>2</sup>, 800 mJ/cm<sup>2</sup>, 900 mJ/cm<sup>2</sup>, 1000 mJ/cm<sup>2</sup> or greater than 1000 mJ/cm<sup>2</sup>.

33. The method of claim 20, wherein the method is automated.

34. The method of claim 20, wherein the method is performed as a step in an antibody purification operation.

35. A method for inactivating a virus in a therapeutic antibody preparation comprising:

(a) providing a sample comprising the therapeutic antibody, wherein the sample is an effluent stream from an antibody purification step and the sample is known or suspected to contain a virus;

(b) introducing a protectant into the effluent stream to form a stabilized mixture, wherein the protectant comprises tyrosine, tryptophan, methionine, or combinations thereof,

(c) passing the stabilized mixture through a device configured to provide continuous exposure to UV-C light such that a target dose of UV-C light under which the virus is inactivated is delivered to the mixture; and

(d) removing the protectant from the mixture following UV-C light exposure.

36. The method of claim 35, further comprising measuring the absorbance of the stabilized mixture at 254 nm by in-line absorption spectroscopy prior to UV-C light exposure; and adjusting the flow rate of the stabilized mixture through the device based on the absorbance measurement such that the target dose of UV-C light is continually delivered to the stabilized mixture passing through the device.

37. The method of claim 35, wherein the sample is an effluent stream from a Protein A column.

38. The method of claim 35, wherein the sample is an effluent stream from a depth filtration step.

39. The method of claim 35, wherein the therapeutic antibody is a monoclonal antibody, a human antibody, a humanized antibody, a chimeric antibody, a recombinant antibody, a single chain antibody, an IgD antibody, an IgE antibody, an IgM antibody, an IgG1 antibody, an IgG2 antibody, an IgG3 antibody, or an IgG4 antibody.

40. The method of claim 35, wherein the target dose is 1 mJ/cm<sup>2</sup>, 10 mJ/cm<sup>2</sup>, 25 mJ/cm<sup>2</sup>, 50 mJ/cm<sup>2</sup>, 75 mJ/cm<sup>2</sup>, 100 mJ/cm<sup>2</sup>, 125 mJ/cm<sup>2</sup>, 200 mJ/cm<sup>2</sup>, 250 mJ/cm<sup>2</sup>, 300 mJ/cm<sup>2</sup>, 350 mJ/cm<sup>2</sup>, 400 mJ/cm<sup>2</sup>, 450 mJ/cm<sup>2</sup>, 500 mJ/cm<sup>2</sup>, 600 mJ/cm<sup>2</sup>, 700 mJ/cm<sup>2</sup>, 800 mJ/cm<sup>2</sup>, 900 mJ/cm<sup>2</sup>, 1000 mJ/cm<sup>2</sup> or greater than 1000 mJ/cm<sup>2</sup>.

41. The method of claim 35, wherein the method provides a viral LRV of greater than or equal to 3.0, 3.5, 4.0, 4.5, 5.0, 5.5, 6.0, 6.5 or greater than 6.5.

42. The method of claim 35, wherein the UV-C light has a wavelength in the range of 200 nm to 280 nm.

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

44. The method of claim 35, wherein the virus comprises one or more of a dsDNA virus, a ssDNA virus, a dsRNA virus and a ssRNA virus.

45. The method of claim 44, 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*.

46. The method of claim 45, wherein the virus is the parvovirus MVM, the retrovirus MuLV or the bunya virus CVV.

## 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')<sub>2</sub> 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/cm<sup>2</sup>, 10 mJ/cm<sup>2</sup>, 25 mJ/cm<sup>2</sup>, 50 mJ/cm<sup>2</sup>, 75 mJ/cm<sup>2</sup>, 100 mJ/cm<sup>2</sup>, 125 mJ/cm<sup>2</sup>, 200 mJ/cm<sup>2</sup>, 250 mJ/cm<sup>2</sup>, 300 mJ/cm<sup>2</sup>, 350 mJ/cm<sup>2</sup>, 400 mJ/cm<sup>2</sup>, 450 mJ/cm<sup>2</sup>, 500 mJ/cm<sup>2</sup>, 600 mJ/cm<sup>2</sup>, 700 mJ/cm<sup>2</sup>, 800 mJ/cm<sup>2</sup>, 900 mJ/cm<sup>2</sup>, 1000 mJ/cm<sup>2</sup> and greater than 1000 mJ/cm<sup>2</sup>.
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')<sub>2</sub> 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/cm<sup>2</sup>, 10 mJ/cm<sup>2</sup>, 25 mJ/cm<sup>2</sup>, 50 mJ/cm<sup>2</sup>, 75 mJ/cm<sup>2</sup>, 100 mJ/cm<sup>2</sup>, 125 mJ/cm<sup>2</sup>, 200 mJ/cm<sup>2</sup>, 250 mJ/cm<sup>2</sup>, 300 mJ/cm<sup>2</sup>, 350 mJ/cm<sup>2</sup>, 400 mJ/cm<sup>2</sup>, 450 mJ/cm<sup>2</sup>, 500 mJ/cm<sup>2</sup>, 600 mJ/cm<sup>2</sup>, 700 mJ/cm<sup>2</sup>, 800 mJ/cm<sup>2</sup>, 900 mJ/cm<sup>2</sup>, 1000 mJ/cm<sup>2</sup> and greater than 1000 mJ/cm<sup>2</sup>.

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')<sub>2</sub> 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/cm<sup>2</sup>, 10 mJ/cm<sup>2</sup>, 25 mJ/cm<sup>2</sup>, 50 mJ/cm<sup>2</sup>, 75 mJ/cm<sup>2</sup>, 100 mJ/cm<sup>2</sup>, 125 mJ/cm<sup>2</sup>, 200 mJ/cm<sup>2</sup>, 250 mJ/cm<sup>2</sup>, 300 mJ/cm<sup>2</sup>, 350 mJ/cm<sup>2</sup>, 400 mJ/cm<sup>2</sup>, 450 mJ/cm<sup>2</sup>, 500 mJ/cm<sup>2</sup>, 600 mJ/cm<sup>2</sup>, 700 mJ/cm<sup>2</sup>, 800 mJ/cm<sup>2</sup>, 900 mJ/cm<sup>2</sup>, 1000 mJ/cm<sup>2</sup> and greater than 1000 mJ/cm<sup>2</sup>.

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.