Proposed Claim Amendments:

1. A settling device operable for use in the production of cell therapy products, biological proteins, polypeptides or hormones, vaccines, viral vectors or gene therapy products, comprising:

a lower conical portion with a port;

a cylindrical portion with a lower end contacting and extending upwardly from the lower conical portion, an upper end, and an interior wall;

a plurality of cones provided within the settling device, each cone of the plurality of cones including a body with a first opening oriented toward the lower conical portion, a second opening that is larger than the first opening, and an exterior edge proximate to the second opening that is spaced from the interior wall, the plurality of cones approximately centered around a longitudinal axis of the settling device;

an upper portion connected to the upper end of the cylindrical portion, wherein the upper portion has a shape that is conical with a first end that has a first diameter and a second end with a second diameter that is larger than the first diameter, the first end being oriented toward the lower conical portion; and

an outer conduit extending from the upper portion and downwardly in an ~~annual~~ annular space between the interior wall of the cylindrical portion and the exterior edges of the cones.

2. The settling device of claim 1, wherein the outer conduit is oriented approximately parallel to the longitudinal axis.

3. The settling device of claim 1, wherein the outer conduit comprises a lumen and an orifice to withdraw fluid from the settling device, the orifice positioned between the upper and lower ends of the cylindrical portion to ~~withdrawn~~ withdraw fluid from a predetermined level within the settling device.

4. The settling device of claim 1, further comprising a sensor associated with the outer conduit to measure a condition within the settling device.

5. The settling device of claim 4, wherein the sensor is operable to measure at least one of pH, dissolved oxygen (DO), dissolved CO_2, glucose, lactate, glutamine, ammonia, and temperature.

6. The settling device of any one of claims 1-5, wherein the sensor is positioned between the upper and lower ends of the cylindrical portion.

~~7. The settling device of claim 1, wherein the upper portion has a shape that is conical with a first end that has a first diameter and a second end with a second diameter that is larger than the first diameter, the first end being oriented toward the lower conical portion.~~

~~8~~7. The settling device of ~~claim 7~~ claim 1, wherein the first end of the upper portion is positioned between ~~a~~ the first opening and ~~a~~ the second opening of an uppermost cone of the plurality of cones.

~~9~~8. The settling device of ~~claim 7~~ claim 1, further comprising a second conduit extending from the first end of the upper portion, the second conduit extending downwardly through ~~a~~ the first opening of an uppermost cone of the plurality of cones and into a central column defined by the first openings of the plurality of cones.

~~10~~9. The settling device of ~~claim 9~~ claim 8, wherein the second conduit includes a sensor to measure a condition of fluid in the central column.

~~11~~10. The settling device of any one of claims 1-5 or ~~7-10~~ 7-9, wherein the second conduit has a lumen and an orifice to withdraw fluid from the central column.

~~12~~11. The settling device of claim 1, further comprising a first distributor element positioned within the settling device below ~~a~~ the second opening of a lowest cone of the plurality of cones, the first distributor element configured to introduce fluid into or withdraw fluid from the settling device.

~~13~~12. The settling device of ~~claim 12~~ claim 11, wherein the first distributor element comprises a first ring extending around an exterior surface of the lowest cone, the first ring connected to a first tube extending upwardly in the ~~annual~~ annular space and to the upper portion.

~~14~~13. The settling device of any one of claims 1-5, ~~7-10~~ 7-9, or ~~12-13~~ 11-12, further comprising a second distributor element positioned within the settling device, the second distributor element being separate from the first distributor element and comprising:

a second ring extending around the exterior surface of the lowest cone and positioned between the first ring and ~~a~~ the first opening of the lowest cone of the plurality of cones; and

a second tube extending upwardly in the ~~annual~~ annular space and to the upper portion.

~~15~~14. The settling device of any one of claims 1-5, ~~7-10~~ 7-9, or ~~12-13~~ 11-12, wherein the first distributor element comprises a body with:

a lower surface;

a lower protrusion extending from the lower surface to define a channel between the lower surface of the body and an interior surface of the lower conical portion;

an upper surface;

an upper protrusion extending from the upper surface to define a space between the upper surface of the body and the lowest cone of the plurality of cones; and

a plurality of holes extending through the body proximate to a large end of the body.

~~16~~15. The settling device of any one of claims 1-5, ~~7-10~~ 7-9, or ~~12-13~~ 11-12, wherein an interior surface of each cone of the plurality of cones is convex and oriented at an angle of between approximately 5 degrees to about 85 degrees relative to the longitudinal axis, and wherein a longitudinal cross-section of a body of a cone of the plurality of cones forms a line with an arcuate shape, the line having a first radius of curvature proximate to the first opening and a second radius of curvature proximate to the second opening, the second radius of curvature being different than the first radius of curvature.

~~17~~16. A method of settling particles in a suspension, comprising:

introducing a liquid suspension of particles into a settling device ~~which includes~~, the settling device comprising:

a lower conical portion with a port;

a cylindrical portion with a lower end contacting and extending upwardly from the lower conical portion, an upper end, and an interior wall;

a plurality of cones provided within the settling device, each cone of the plurality of cones including a body with a first opening oriented toward the lower conical portion, a second opening that is larger than the first opening, and an exterior edge proximate to the second opening that is spaced from the interior wall;

an upper portion connected to the upper end of the cylindrical portion;

a first conduit extending from the upper portion and including an orifice positioned within a central column defined by the first openings of the plurality of cones;

an outer conduit extending from the upper portion and downwardly in an ~~annual~~ annular space between the interior wall of the cylindrical portion and the exterior edges of the cones; and

a sensor associated with the outer conduit;

measuring one or more of pH, dissolved oxygen (DO), dissolved CO_2, glucose, lactate, glutamine, ammonia and temperature in the ~~annual~~ annular space with the sensor associated with the outer conduit;

collecting a clarified liquid through the orifice of the first conduit; and

collecting a concentrated liquid suspension from the port of the lower conical portion.

~~18~~17. The method of ~~claim 17~~ claim 16, wherein the liquid suspension comprises at least one of:

(a) a recombinant cell suspension, an alcoholic fermentation, a suspension of solid catalyst particles, a municipal waste-water, industrial waste-water, mammalian cells, bacterial cells, yeast cells, plant cells, algae cells, plant cells, mammalian cells, murine hybridoma cells, stem cells, CAR-T cells, red blood precursor and mature cells, cardiomyocytes, yeast in beer, and eukaryotic cells;

(b) recombinant microbial cells selected from at least one of Pichia pastoris, Saccharomyces cerevisiae, Kluyveromyces lactis, Aspergillus niger, Escherichia coli, and Bacillus subtilis; and

(c) one or more of microcarrier beads, affinity ligands, and surface activated microspherical beads; and

wherein the clarified liquid collected comprises at least one of biological molecules, organic or inorganic compounds, chemical reactants, chemical reaction products, hydrocarbons (e.g., terpenes, isoprenoids, polyprenoids), polypeptides, proteins (e.g., brazzein, colony stimulating factors), alcohols, fatty acids, hormones (e.g., insulin, growth factors), carbohydrates, glycoproteins (e.g., erythropoietin, monoclonal antibodies), beer, and biodiesel.

~~19~~18. The method of ~~claim 17~~ claim 16, further comprising controlling at least one of pH, dissolved oxygen, dissolved CO_2, glucose, lactate, glutamine and ammonia within the settling device by manipulating the flow rates of at least one of air, O_2, CO_2 and N_2 introduced into the settling device through a first distributor element or manipulating the flow rates of different liquid media components pumped in through a second distributor element.

~~20~~19. The method of ~~claim 17~~ claim 16, wherein introducing a liquid suspension of particles into the settling device comprises pumping the liquid suspension through a distributor element positioned within the settling device below ~~a~~ the second opening of a lowest cone of the plurality of cones.

~~21~~20. The method of ~~claim 17~~ claim 16, wherein the settling device includes:

a first distributor element positioned within the settling device and which includes:

a first ring extending around an exterior surface of a lowest cone of the plurality of cones, the first ring being positioned between ~~a~~ the first opening and ~~a~~ the second opening of the lowest cone; and

a first tube extending upwardly from the first ring into the ~~annual~~ annular space and to the upper portion; and

a second distributor element positioned within the settling device and which includes:

a second ring extending around the exterior surface of the lowest cone, the second ring being positioned between the first ring and the first opening of the lowest cone; and

a second tube extending upwardly from the second ring into the ~~annual~~ annular space and to the upper portion.

~~22~~21. The method of ~~claim 17~~ claim 16, further comprising measuring one or more of pH, dissolved oxygen (DO), dissolved CO2, glucose, lactate, glutamine, ammonia and temperature in the central column with a sensor associated with a second conduit extending from the upper portion.

~~23~~22. The method of ~~claim 17~~ claim 16, wherein the upper portion has a shape that is conical with a first end that has a first diameter and a second end with a second diameter that is larger than the first diameter, the first end being oriented toward the lower conical portion.

~~24~~23. The method of one of ~~claims 17-23~~ claims 16-22, wherein the first end of the upper portion is positioned between ~~a~~ the first opening and ~~a~~ the second opening of an uppermost cone of the plurality of cones.

~~25~~24. A settling device operable for use in the production of cell therapy products, biological proteins, polypeptides or hormones, vaccines, viral vectors or gene therapy products, comprising:

a lower portion with a middle port and at least one outer port;

a cylindrical portion;

an upper portion with a central port and at least one peripheral port, wherein the upper portion has a shape that is conical with a first end that has a first diameter and a second end with a second diameter that is larger than the first diameter, the first end being oriented toward the lower portion;

~~a cylindrical portion;~~

~~a lower portion with a middle port and at least one outer port;~~

a stack of cones located within the settling device, each cone of the stack of cones including a first opening, a second opening that is larger than the first opening, and an aperture proximate to the second opening, each of the first openings oriented towards one of the upper portion and the lower portion, the stack of cones approximately centered around a longitudinal axis of the settling device;

an alignment element oriented approximately parallel to the longitudinal axis and extending through the apertures of the cones; and

a distributor element positioned below a lowest cone of the stack of cones.

~~26~~25. A method of settling particles in a suspension, comprising:

introducing a liquid suspension of particles into a settling device which includes:

a lower portion with a middle port and at least one outer port;

a cylindrical portion;

an upper portion with a central port and at least one peripheral port, wherein the upper portion has a shape that is conical with a first end that has a first diameter and a second end with a second diameter that is larger than the first diameter, the first end being oriented toward the lower portion;

~~a cylindrical portion;~~

~~a lower portion with a middle port and at least one outer port;~~

a stack of cones located within the settling device, each cone of the stack of cones including a first opening, a second opening that is larger than the first opening, and an aperture proximate to the second opening, each of the first openings oriented towards one of the upper portion and the lower portion, the stack of cones approximately centered around a longitudinal axis of the settling device;

an alignment element oriented approximately parallel to the longitudinal axis and extending through the apertures of the cones; and

a distributor element positioned below a lowest cone of the stack of cones;

collecting a clarified liquid from the central port of the upper portion; and

collecting a concentrated liquid suspension from the middle port of the lower portion.