A SYSTEM AND METHOD TO DETERMINE CRITICAL PROCESS PARAMETERS FOR A CONTINUOUS VIRAL INACTIVATION REACTOR TO DESIGN AND MANUFACTURE SAME

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This application claims the benefit of U.S. Provisional Application No. 62/742,506, filed on October 8, 2018, the content of which is expressly incorporated herein by reference thereto.

FIELD OF THE INVENTION

[0002] The present disclosure generally relates to a system and a method to determine critical process parameters for a continuous viral inactivation reactor and to design and manufacture the same.

BACKGROUND OF THE INVENTION

[0003] Presently, defining the residence time of the viral particles in a plug-flow-reactor (PFR) is difficult to quantify due to fluid dynamics phenomena that occur during flow of a process stream in circular piping where the flow of a process stream in the center of the pipe can be twice as fast as the average flow of the process stream and almost stagnant near the wall of the pipe. Thus, presently the only way to determine the correct PFR parameters for viral inactivation is by experimentation. This trial-and-error approach is inefficient and time-consuming.

SUMMARY

[0004] In the disclosure, a method for designing, selecting, making, and/or manufacturing of an actual plug-flow reactor is described. The method includes introducing a process stream including detectable particles/tracer into an experimental reactor having a known radius of curvature and a known internal diameter, wherein the experimental reactor is in communication

with at least one of a first detector and a second detector; detecting a flow rate of the process stream in the experimental reactor by at least one of the first detector and the second detector; detecting fluid-phase parameters of the process stream by at least one of the first detector and the second detector; detecting the detectable particles/tracer exiting the experimental reactor by the second detector; determining, based on the introduced process stream including the detectable particles/tracer, empirical values relating to at least one of experimental reactor parameters and fluid-phase parameters; determining non-empirical values relating to at least one of the experimental reactor parameters and the fluid-phase parameters; and designing, selecting, making, and/or manufacturing the actual reactor based on the determined empirical values and the determined non-empirical values. In an aspect, the present disclosure provides a method for designing an actual reactor for viral inactivation comprising: introducing a process stream, including detectable particles/tracer, into an experimental reactor having a known radius of curvature and a known internal diameter, wherein the experimental reactor is in communication with at least one of a first detector and a second detector; detecting a flow rate of the process stream in the experimental reactor by at least one of the first detector and the second detector; detecting fluid-phase parameters of the process stream by at least one of the first detector and the second detector; detecting the detectable particles exiting the experimental reactor by the second detector; determining, based on the introduced process stream including the detectable particles, empirical values relating to at least one of experimental reactor parameters and fluid-phase parameters; determining non-empirical values relating to at least one of the experimental reactor parameters and the fluid-phase parameters; and designing the actual reactor based on the determined empirical values and the determined non-empirical values.

[0005] In the disclosure, a system to determine, select, make, and/or manufacture an actual reactor size is described. The system comprises a processor; and a non-transitory machine-readable storage medium storing machine-readable instructions that are executable by the processor to receive parameters of an experimental reactor that is in communication with at least one of a first detector and a second detector; detect flow rate of a process stream including detectable particles/tracer in the experimental reactor by at least one of the first detector and the second detector; detect fluid-phase parameters of the process stream in the experimental reactor by at least one of the first detector and the second detector; detect the detectable particles/tracer exiting the experimental reactor by the second detector; determine empirical values of at least one of reactor parameters of the experimental reactor and fluid parameters of the process stream; determine non-empirical values of at least one of the reactor parameters of the experimental reactor and the fluid parameters of the process stream; design, select, make, and/or manufacture an actual reactor for an actual process stream having a predetermined volume of fluid, wherein the

fluid includes substantially similar parameters as the fluid parameters in the experimental reactor. In an aspect, the present disclosure provides a system to determine an actual viral inactivation reactor size comprising: a processor **(1001)**; and a non-transitory machine-readable storage medium **(1002)** storing machine-readable instructions that are executable by the processor **(1001)** to: receive parameters of an experimental reactor **(100)** that is in communication with at least one of a first detector **(30)** and a second detector **(40)**; detect a flow rate of a process stream including detectable particles in the experimental reactor **(100)** by at least one of the first detector **(30)** and the second detector **(40)**; detect fluid-phase parameters of the process stream in the experimental reactor **(100)** by at least one of the first detector **(30)** and the second detector **(40)**; detect, by the second detector **(40)**, the detectable particles by detecting a first detectable particle exiting the experimental reactor **(100)** and a last detectable particle exiting the experimental reactor **(100)**; determine empirical values **(200)** of at least one of reactor parameters of the experimental reactor **(100)** and fluid parameters of the process stream; determine non-empirical values **(300)** of at least one of the reactor parameters of the experimental reactor **(100)** and the fluid parameters of the process stream; and design an actual reactor **(400)** for an actual process stream having a predetermined volume of fluid, wherein the fluid includes substantially similar parameters as the fluid parameters in the experimental reactor **(100)**.

[0006] In the disclosure, a system for designing, selecting, making, and/or manufacturing an actual reactor for continuously inactivating virus during manufacturing of a biological product is described. The system comprises an experimental reactor having a known

radius of curvature and a known diameter and designed to receive a process stream; at least one of a first detector and a second detector in communication with the experimental reactor, wherein the at least one of the first detector and the second detector detects fluid-phase parameters of the process stream and wherein the second detector detects detectable particles/tracer exiting the experimental reactor; a processor; and a non-transitory machine-readable storage medium storing machine-readable instructions that are executable by the processor to: determine empirical values corresponding to parameters of at least one of the experimental reactor and fluid of the process stream; determine non-empirical values corresponding to parameters of at least one of the experimental reactor and fluid of the process stream; and based on the determined empirical values and the determined non-empirical values, design, select, make, and/or manufacture the actual reactor for an actual process stream having a predetermined volume of fluid. In another aspect, the present disclosure provides a system for designing an actual reactor for continuously inactivating virus during manufacturing of a biological product, the system comprising: an experimental reactor **(100)** having a known radius of curvature and a known diameter and designed to receive a process stream; at least one of a first detector **(30)** and a second detector **(40)** in communication with the experimental reactor **(100)**, wherein the at least one of the first detector **(30)** and the second detector **(40)** detects fluid-phase parameters of the process stream and wherein the second detector **(40)** detects detectable particles exiting the experimental reactor **(100)**; a processor **(1001)**; and a non-transitory machine-readable storage medium storing machine-readable instructions **(1002)** that are executable by the processor **(1001)** to: determine empirical values **(200)** corresponding to parameters of at least one of the experimental reactor **(100)** and fluid of the process stream; determine non-empirical values **(300)** corresponding to parameters of at least one of the experimental reactor **(100)** and fluid of the process stream; and

based on the determined empirical values and the determined non-empirical values, design the actual reactor for an actual process stream having a predetermined volume of fluid.

[0007] In the disclosure, a system for designing, selecting, making, and/or manufacturing an actual reactor for continuously inactivating virus during manufacturing of a biological product is provided. The system comprises an experimental reactor having an inlet, an outlet, and a tubular flow path comprising a set of alternating turns that form a serpentine pattern between the inlet and the outlet, wherein the serpentine pattern includes a predetermined radius of curvature and a predetermined diameter and wherein the experimental reactor is designed to receive a process stream; at least one of a first detector and a second detector in communication with the experimental reactor, wherein the at least one of the first detector and the second detector

detects fluid-phase parameters of the process stream and wherein the second detector detects detectable particles/tracer exiting the experimental reactor; a processor; and a non-transitory machine-readable storage medium storing machine-readable instructions that are executable by the processor to: determine empirical values of at least one of the experimental reactor parameters and the fluid parameters of the process stream; determine non-empirical values of at least one of the reactor parameters of the experimental reactor and the fluid parameters of the process stream; and design, select, make, and/or manufacture the actual reactor based on the determined empirical values and the determined non-empirical values, wherein the actual reactor includes a serpentine pattern substantially similar to the serpentine pattern of the experimental reactor, but configured to accommodate an actual process stream having a predetermined volume of fluid. In a further aspect, the present disclosure provides a system for designing an actual reactor for continuously inactivating virus during manufacturing of a biological product, the system comprising: an experimental reactor **(100)** having an inlet, an outlet, and a tubular flow path comprising a set of alternating turns that form a serpentine pattern between the inlet and the outlet, wherein the serpentine pattern includes a predetermined radius of curvature and a predetermined diameter and wherein the experimental reactor **(100)** is designed to receive a process stream; at least one of a first detector **(30)** and a second detector **(40)** in communication with the experimental reactor **(100)**, wherein the at least one of the first detector **(30)** and the second detector **(40)** detects fluid-phase parameters of the process stream and wherein the second detector **(40)** detects detectable particles exiting the experimental reactor **(100)**; a processor **(1001)**; and a non-transitory machine-readable storage medium storing machine-readable instructions that are executable by the

processor **(1001)** to: determine empirical values **(200)** of at least one of experimental reactor **(100)** parameters and the fluid parameters of the process stream; determine non-empirical values **(300)** of at least one of the reactor parameters of the experimental reactor **(100)** and the fluid parameters of the process stream; and design the actual reactor based on the determined empirical values and the determined non-empirical values, wherein the actual reactor includes a serpentine pattern substantially similar to the serpentine pattern of the experimental reactor **(100)**, but designed and configured to accommodate an actual process stream having a predetermined volume of fluid.

[0008] In the disclosure, a system for designing, selecting, making, and/or manufacturing an actual reactor for continuously inactivating virus during manufacturing of a biological product is provided. The system comprises an experimental reactor having an inlet, an outlet, and at least one interwoven tubular flow path comprising a plurality of turns that are in different, non-parallel planes; at least one of a first detector and a second detector in communication with the experimental reactor, wherein the at least one of the first detector and the second detector detects fluid-phase parameters of the process stream and wherein the second detector detects detectable particles/tracer exiting the experimental reactor; a processor; and a non-transitory machine-readable storage medium storing machine-readable instructions that are executable by the processor to: determine empirical values of at least one of the experimental reactor parameters and the fluid parameters of the process stream; determine non-empirical values of at least one of the reactor parameters of the experimental reactor and the fluid parameters of the process stream; and design, select, make, and/or manufacture the actual reactor based on the

determined empirical values and the determined non-empirical values, wherein the actual reactor includes an interwoven tubular flow path substantially similar to the interwoven tubular flow path of the experimental reactor, but designed and configured to accommodate an actual process stream having a predetermined volume of fluid. In yet another aspect, the present disclosure provides a system for designing an actual reactor for continuously inactivating virus during manufacturing of a biological product, the system comprising: an experimental reactor **(100)** having an inlet, an outlet, and at least one interwoven tubular flow path **(10Z)** comprising a plurality of turns that are in different, non-parallel planes; at least one of a first detector **(30)** and a second detector **(40)** in communication with the experimental reactor **(100)**, wherein the at least one of the first detector **(30)** and the second detector **(40)** detects fluid-phase parameters of a process stream and wherein the second detector detects detectable particles exiting the experimental reactor **(100)**; a processor **(1001)**; and a non-transitory machine-readable storage medium storing machine-readable instructions that are executable by the processor **(1001)** to: determine empirical values **(200)** of at least one of experimental reactor parameters and the fluid parameters of the process stream; determine non-empirical values **(300)** of at least one of the reactor parameters of the experimental reactor **(100)** and the fluid parameters of the process stream; and design the actual reactor based on the determined empirical values and the determined non-empirical values, wherein the actual reactor includes an interwoven tubular flow path **(10Z)** substantially similar to the interwoven tubular flow path of the experimental reactor **(100)**, but designed and configured to accommodate an actual process stream having a predetermined volume of fluid.

[0009] Additional features and advantages of various examples will be set forth, in part, in the description that follows, and will, in part, be apparent from the description, or may be learned by the practice of various examples. The objectives and other advantages of various examples will be realized and attained by means of the elements and combinations particularly pointed out in the description herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] The present disclosure in its several aspects and embodiments can be more fully understood from the detailed description and the accompanying drawings, wherein:

[0011] Fig. 1A is a top view of a tubular flow path of a continuous tubular reactor, according to an example of the present disclosure;

[0012] Fig. 1B is a partial perspective view of a continuous tubular reactor, according to an example of the present disclosure;

[0013] Fig. 1C is a side view and an isometric view of the continuous tubular reactor, according to an example of the present disclosure;

[0014] Fig. 1D illustrates a plurality of continuous tubular reactors connected to one another, according to an example of the present disclosure;

[0015] Fig. 1E is an isometric view of an exemplary continuous flow reactor tube having a single run, according to an example of the present disclosure;

[0016] Fig. 1F illustrates the continuous flow reactor tube of Fig. 1E having turns on a

CLAIMS

1. A method for designing an actual reactor for viral inactivation comprising:

introducing a process stream, including detectable particles/tracer, into an experimental reactor having a known radius of curvature and a known internal diameter, wherein the experimental reactor is in communication with at least one of a first detector and a second detector;

detecting a flow rate of the process stream in the experimental reactor by at least one of the first detector and the second detector;

detecting fluid-phase parameters of the process stream by at least one of the first detector and the second detector;

detecting the detectable particles exiting the experimental reactor by the second detector;

determining, based on the introduced process stream including the detectable particles, empirical values relating to at least one of experimental reactor parameters and fluid-phase parameters;

determining non-empirical values relating to at least one of the experimental reactor parameters and the fluid-phase parameters; and

designing the actual reactor based on the determined empirical values and the determined non-empirical values.

2. The method of claim 1, wherein the detectable particles are at least one of a viral particle and a surrogate tracer and/or

wherein the empirical values and non-empirical values are task-dependent and/or

wherein the experimental reactor parameters and the fluid-phase parameters corresponding to the empirical values and the non-empirical values are theoretical or

estimated minimum residence time, theoretical or estimated maximum residence time, internal diameter, volumetric flow rate, path length of a flow path, radius of curvature, density of the process stream, dynamic viscosity, and variance.

3. The method of claim 1 or 2, wherein the empirical values are values corresponding to least one of the experimental reactor parameters and the fluid-phase parameters that are linear to an experimental set of data and wherein the non-empirical values correspond to at least one of theoretical or estimated minimum residence time, theoretical or estimated maximum residence time, internal diameter, volumetric flow rate, path length of a flow path, and radius of curvature

wherein detecting the detectable particles exiting the experimental reactor further comprises determining a minimum residence time experienced by one of the detectable particles that is equivalent to an incubation time for batch viral inactivation and a maximum residence time experienced by a last significant amount of the detectable particles to exit the experimental reactor and/or

wherein the experimental reactor parameters comprise determining at least one of a minimum residence time experienced by one of the detectable particles that is equivalent to an incubation time for batch viral inactivation, a maximum residence time experienced by a last significant amount of the detectable particles to exit the experimental reactor, internal diameter of a reaction tube, volumetric flow rate, length of the reaction tube, radius of curvature, and a volume of the experimental reactor and/or

wherein the fluid-phase parameters comprise at least one of a density and a dynamic viscosity.

4. The method of one or more of claims 1 to 3, wherein designing the actual reactor comprises at least one of scaling dimensions of the experimental reactor to the actual

reactor having a same aspect ratio as the experimental reactor, but a different internal diameter; scaling the dimensions of the experimental reactor to the actual reactor having a same aspect ratio and a same internal diameter as the experimental reactor; scaling the dimensions of the experimental reactor to the actual reactor having a different aspect ratio than the experimental reactor and a different diameter than the experimental reactor; scaling the dimensions of the experimental reactor to the actual reactor having a different aspect ratio as the experimental reactor, but a same diameter as the experimental reactor.

5. The method of claim 4, wherein when the actual reactor comprises the scaling dimensions of the experimental reactor to the actual reactor having the same aspect ratio as the experimental reactor, the method requires derivation of HETP, reactor volume, and internal diameter, based on average flow velocity, utilizing equations (a)-(g) below:

(a) $HETP = \frac{\sigma^2_{time} * L}{T_{Ave}{}^2}$

(b) $HETP = f(v) = (av^3 + bv^2 + cv + d)$, wherein a, b, c, and d are based on empirical data fits for all Dean numbers

(c) $L = \frac{1}{2} * \left(25f(v)^2 \pm 5 * \sqrt{25f(v)^4 + 4f(v)^2\, Tmin * v} + 2 * Tmin * v\right)$

(d) $A = \Pi r^2 = \Pi \left(\frac{i.d.}{2}\right)^2 T_{Ave\ Defined} = \frac{L}{v} = \frac{CA*L}{Q}$

(e) $T_{Ave\ Defined} = \frac{CA*L}{Q}$

(f) $\frac{Q*T_{Ave\ Defined}}{L*\Pi} = r^2$

(g) $i.d. = 2\sqrt{\frac{Q*T_{Ave\ Defined}}{L*\Pi}}$.

6. The method of claim 4, wherein when the actual reactor comprises the scaling dimensions of the experimental reactor to the actual reactor having the same aspect ratio as the experimental reactor, the method requires derivation of HETP, reactor volume, and internal diameter based on reduced HETP and Dean Number utilizing equations (a)-(e)

below:

(a) $HETP = \frac{\sigma^2_{time} * L}{T_{Ave}{}^2}$

(b) $\frac{HETP}{i.d.} = h = (aDe^3 + bDe^2 + cDe + d) = f(De)$

(c) T_{Ave}=T_{min}+(n*σ_{max})

(d) T_{Ave}=T_{max} – (m*(σ_{max}))

(e) $T_{Ave} = \frac{RV}{Q} = \frac{CA * L_{T_{Ave}}}{Q}$.

7. The method of claim 4, wherein when the actual reactor comprises scaling the dimensions of the experimental reactor to the actual reactor having a same aspect ratio and a same internal diameter as the experimental reactor, the method requires derivation of at least HETP and path length utilizing equations below:

(a) $HETP = \frac{\sigma^2_{time} * L_{T_{Ave}}}{T_{Ave}{}^2}$;

(b) $\sqrt{HETP} = f(De) = \frac{\sigma_{time} * \sqrt{L_{T_{Ave}}}}{T_{Ave}} = (aDe^3 + bDe^2 + cDe + d)$;

Wherein a, b, c, and d are based on empirical data fits only valid for Dean numbers ≥100

(c) $T_{Ave} = Tmin + (\mathrm{n} * \sigma_{\mathrm{time}})$;

(d) $T_{Ave} = Tmax - (\mathrm{m} * \sigma_{\mathrm{time}})$;

(e) $T_{Ave} = \frac{RV}{Q} = \frac{CA * L_{T_{Ave}}}{Q}$; and

(f) $L_{T_{Ave}} = \frac{25 * CA^2 * f(De)^2 \pm 5 * \sqrt{25 * CA^4 * f(De)^4 + 4 * CA^3 * f(De)^2 * Q * T_{min}} + 2 * CA * Q * T_{min}}{2CA^2}$.

8. The method of one or more of claims 1 to 7, wherein the experimental reactor includes a reaction tube that comprises at least one of (i) a set of alternating turns that form a serpentine pattern between an inlet and an outlet and (ii) an interwoven path.

9. A system to determine an actual viral inactivation reactor size comprising:

a processor **(1001)**; and

a non-transitory machine-readable storage medium **(1002)** storing machine-readable instructions that are executable by the processor **(1001)** to:

receive parameters of an experimental reactor **(100)** that is in communication with at least one of a first detector **(30)** and a second detector **(40)**;

detect a flow rate of a process stream including detectable particles in the experimental reactor **(100)** by at least one of the first detector **(30)** and the second detector **(40)**;

detect fluid-phase parameters of the process stream in the experimental reactor **(100)** by at least one of the first detector **(30)** and the second detector **(40)**;

detect, by the second detector **(40)**, the detectable particles by detecting a first detectable particle exiting the experimental reactor **(100)** and a last detectable particle exiting the experimental reactor **(100)**;

determine empirical values **(200)** of at least one of reactor parameters of the experimental reactor **(100)** and fluid parameters of the process stream;

determine non-empirical values **(300)** of at least one of the reactor parameters of the experimental reactor **(100)** and the fluid parameters of the process stream; and

design an actual reactor **(400)** for an actual process stream having a predetermined volume of fluid, wherein the fluid includes substantially similar parameters as the fluid parameters in the experimental reactor **(100)**.

10. The system of claim 9, wherein the experimental reactor **(100)** is a hypothetical reactor and/or

wherein the empirical values and the non-empirical values are derived from detectable particles in a process stream introduced into the experimental reactor (**100**) and/or

wherein the empirical values and the non-empirical values are task-dependent and/or

wherein the empirical values of at least one of reactor parameters of the experimental reactor (**100**) and the fluid parameters and the non-empirical values of at least

one of reactor parameters of the experimental reactor (**100**) and the fluid parameters correspond to are theoretical or estimated minimum residence time, theoretical or estimated maximum residence time, internal diameter, volumetric flow rate, path length of a flow path, radius of curvature, density of the process stream, dynamic viscosity, and variance and/or

wherein the empirical values are values corresponding to least one of experimental reactor (**100**) parameters and fluid-phase parameters that are linear to an experimental set of data and wherein the non-empirical values correspond to at least one of theoretical or estimated minimum residence time, theoretical or estimated maximum residence time, internal diameter, volumetric flow rate, path length of a flow path, and radius of curvature and/or

wherein the reactor parameters comprises at least one of a minimum residence time experienced by detectable particles or tracer in a process stream equivalent to an incubation time for batch viral inactivation, a maximum residence time experienced by a last significant detectable particles/tracer to exit the experimental reactor (**100**), internal diameter of a reaction tube, volumetric flow rate, length of the reaction tube, radius of curvature, and a volume of the experimental reactor (**100**) and/or

wherein the fluid parameters comprise at least one of density and dynamic viscosity.

11. The system of claim 9 or 10, wherein the designed actual reactor comprises at least one of a scaled-size of the experimental reactor **(100)** having a same aspect ratio as the experimental reactor **(100)**, but a different internal diameter than the experimental reactor **(100)**, a scaled-sized size of the experimental reactor **(100)** having a same aspect ratio and a same internal diameter as the experimental reactor **(100)**; a scaled-size of the experimental reactor **(100)** having a different aspect ratio than the experimental reactor **(100)** and a different internal diameter than the experimental reactor **(100)**, a scaled-size of the

experimental reactor **(100)** having a different aspect ratio than the experimental reactor **(100)**, but a same internal diameter as the experimental reactor **(100)**,

preferably wherein the aspect ratio is from 0.01 to 10.

12. The system of one or more of claims 9 to 11, wherein the designed reactor includes a reaction tube that comprises at least one of (i) a set of alternating turns that form a serpentine pattern **(1-9)** between an inlet **(10)** and an outlet **(20)** and (ii) an interwoven path **(10Z)**.

13. A system for designing an actual reactor for continuously inactivating virus during manufacturing of a biological product, the system comprising:

an experimental reactor **(100)** having a known radius of curvature and a known diameter and designed to receive a process stream;

at least one of a first detector **(30)** and a second detector **(40)** in communication with the experimental reactor **(100)**, wherein the at least one of the first detector **(30)** and the second detector **(40)** detects fluid-phase parameters of the process stream and wherein the second detector **(40)** detects detectable particles exiting the experimental reactor **(100)**;

a processor **(1001)**; and

a non-transitory machine-readable storage medium storing machine-readable instructions **(1002)** that are executable by the processor **(1001)** to:

determine empirical values **(200)** corresponding to parameters of at least one of the experimental reactor **(100)** and fluid of the process stream;

determine non-empirical values **(300)** corresponding to parameters of at least one of the experimental reactor **(100)** and fluid of the process stream; and

based on the determined empirical values and the determined non-empirical values, design the actual reactor for an actual process stream having a predetermined volume of fluid.

14. A system for designing an actual reactor for continuously inactivating virus during manufacturing of a biological product, the system comprising:

an experimental reactor **(100)** having an inlet, an outlet, and a tubular flow path comprising a set of alternating turns that form a serpentine pattern between the inlet and the outlet, wherein the serpentine pattern includes a predetermined radius of curvature and a predetermined diameter and wherein the experimental reactor **(100)** is designed to receive a process stream;

at least one of a first detector **(30)** and a second detector **(40)** in communication with the experimental reactor **(100)**, wherein the at least one of the first detector **(30)** and the second detector **(40)** detects fluid-phase parameters of the process stream and wherein the second detector **(40)** detects detectable particles exiting the experimental reactor **(100)**;

a processor **(1001)**; and

a non-transitory machine-readable storage medium storing machine-readable instructions that are executable by the processor **(1001)** to:

determine empirical values **(200)** of at least one of experimental reactor **(100)** parameters and the fluid parameters of the process stream;

determine non-empirical values **(300)** of at least one of the reactor parameters of the experimental reactor **(100)** and the fluid parameters of the process stream; and

design the actual reactor based on the determined empirical values and the determined non-empirical values, wherein the actual reactor includes a serpentine pattern substantially similar to the serpentine pattern of the experimental reactor **(100)**, but designed and configured to accommodate an actual process stream having a predetermined volume of

fluid.

15. The system of claim 14, wherein the set of alternating turns in the experimental reactor **(100)** comprises at least two alternating turns **(1-9)** having an angle of from about 270° to about 280° and/or

wherein the set of alternating turns in the experimental reactor **(100)** comprises from 2 to 325 or more alternating turns **(1-9)** having an angle of from 270° to 280° and/or

wherein the tubular flow path in the experimental reactor **(100)** includes a diameter of from 0.6 cm to 0.7 cm **(12)**.

16. The system of claim 14 or 15, wherein the set of alternating turns are segmented vertically into at least two stacked layers **(16)**, preferred

(i) wherein each of the at least two stacked layers comprises 12.5 alternating turns in a single plane **(16)**, wherein each of the alternating turns **(1-9)** includes an angle of from 270° to 280° or

(ii) wherein each of the at least two stacked layers **(16)** include a thickness of from 0.7 cm to 1.2 cm or

(iii) wherein each of the at least two stacked layers **(16)** is connected to one another via a 180° turn of the tubular flow path, more preferred in this system **(10)**, wherein the at least two stacked layers are 26 layers connected to one another via 25 180° turns of the tubular flow path.

17. The system of one or more of claims 14 to 16, wherein the actual reactor comprises at least two reactors substantially similar to the experimental reactor **(100)** connected in series and/or

wherein the set of alternating turns is arranged to generate a vortex to induce mixing the process stream having a laminar flow with a Reynolds Number of from 187.7 to 375.5 and/or

wherein the actual reactor includes a tubular flow path having dimensions such that the process stream is in the actual reactor for at least 30 minutes.

18. The system of one or more of claims 14 to 17, wherein the experimental reactor **(100)** and the designed actual reactor include substantially similar aspect ratios, preferably

wherein the aspect ratio is a radius of a reaction tube of the experimental reactor **(100)** over the radius of the curvature of the experimental reactor **(100)**.

19. A system for designing an actual reactor for continuously inactivating virus during manufacturing of a biological product, the system comprising:

an experimental reactor **(100)** having an inlet, an outlet, and at least one interwoven tubular flow path **(10Z)** comprising a plurality of turns that are in different, non-parallel planes;

at least one of a first detector **(30)** and a second detector **(40)** in communication with the experimental reactor **(100)**, wherein the at least one of the first detector **(30)** and the second detector **(40)** detects fluid-phase parameters of a process stream and wherein the second detector detects detectable particles exiting the experimental reactor **(100)**;

a processor **(1001)**; and

a non-transitory machine-readable storage medium storing machine-readable instructions that are executable by the processor **(1001)** to:

determine empirical values **(200)** of at least one of experimental reactor parameters and the fluid parameters of the process stream;

determine non-empirical values **(300)** of at least one of the reactor parameters of the experimental reactor **(100)** and the fluid parameters of the process stream; and

design the actual reactor based on the determined empirical values and the determined non-empirical values, wherein the actual reactor includes an interwoven tubular flow path **(10Z)** substantially similar to the interwoven tubular flow path of the experimental reactor **(100)**, but designed and configured to accommodate an actual process stream having a predetermined volume of fluid.

20. The system of claim 19, wherein the experimental reactor **(100)** and the actual reactor comprise a predetermined radius of curvature and a predetermined diameter, and wherein the experimental reactor **(100)** is designed to receive a process stream and/or

wherein the plurality of turns includes at least a first pattern and a second pattern different from the first pattern , wherein the first pattern includes a predetermined number of turns, and the second pattern includes a predetermined number of turns, and wherein the predetermined number of turns in the first pattern is same or different from the predetermined number of turns in the second pattern and/or

wherein the plurality of turns includes a repeated pattern of turns after a predetermined number of turns and/or

wherein each of the plurality of turns includes an angle of from 125° to 180° **(50Z)** and/or

wherein the plurality of turns follows a three-dimensional path that includes flow direction changes at approximately 45°, at a turn center **(14Z)** and/or

wherein the interwoven tubular flow path **(10Z)** includes from 6.5 to 93.2 turns per 1 m^3. and/or

wherein the interwoven tubular flow path **(10Z)** comprises a plurality of bends, each bend being rotated with respect to one another, at an angle around a longitudinal

axis of the interwoven tubular flow path, prefered in this system wherein the angle around the longitudinal axis of the interwoven tubular flow path is from 25° to 60° **(60Z)**.