[0011] It is an object of the present invention to ameliorate at least some of the inconveniences present in the prior art.

[0012] There are provided herein systems and methods for automated processing of biological samples that are executable without handling by a human operator and/or are capable of processing a plurality of batches at the same time without cross-contamination between batches, optionally under conditions that meet GMP guidelines and regulations.

[0012a] In one example, a system for automated processing of a plurality of batches is provided, each batch being derived from one biological sample. The system comprises: an enclosure which can be closed and sterilized for the automated processing of the plurality of batches, the enclosure comprising an enclosure access port; at least two cell processing containers for the automated processing of the plurality of batches, each batch of the plurality of batches comprising one or more cell processing container; a first isolator comprising a first isolator access port, wherein the enclosure is selectively fluidly connected to the first isolator, and objects from outside the system can be received into the enclosure via the first isolator and/or objects from inside the enclosure can be passed out of the system via the first isolator; a plurality of reagent containers for holding reagents within the enclosure; at least one reagent dispenser within the enclosure for dispensing reagents during said automated processing; a particle counter configured to measure a particle count inside the enclosure; an air flow system configured to control an air pressure inside the enclosure to be greater than an air pressure outside the enclosure; at least one of a liquid waste receptacle and a solid waste receptacle, located outside the enclosure that is selectively fluidly connected to the enclosure, wherein the liquid waste receptable comprises an aspirator with a sterile tip configured to establish an air pressure in the liquid waste receptacle that is lower than an air pressure in the enclosure, wherein the solid waste receptacle is configured to establish an air pressure in the solid waste receptacle that is lower than an air pressure in the enclosure;a quality control module within the enclosure for analyzing at least one characteristic of a batch during said automated processing; a harvesting module within the enclosure for harvesting batches; a robotic module within the enclosure, configured for at least one of transporting cell processing containers, decapping or otherwise opening a cell

processing container, pipetting reagents or liquids from a cell processing container, and aspirating liquids from a cell processing container, during said automated processing; a tracking module for electronically tracking the plurality of batches after its introduction to the enclosure; and a control unit (CU) communicatively coupled to the at least one reagent dispenser, the quality control module, the harvesting module, the robotic module, the tracking module, and the particle counter for controlling said automatic processing of said batches. The plurality of batches comprises a first batch and a second batch. The system is configured to receive the second batch into the enclosure before the first batch is transported out of the enclosure. The system is configured to automatically process the first batch and the second batch within the enclosure at the same time, without cross contamination from the other of the first batch and the second batch. The CU is configured to allow receiving of the second batch into the enclosure responsive to the particle count satisfying a predetermined criterion. The CU is configured to keep the cell processing containers closed during said automated processing except during addition or removal of materials to and from the cell processing container, wherein only cell processing containers from one batch at a time are opened to the environment, such that only one batch is exposed to the environment inside the enclosure at any one time. The CU is configured to control said processing of the plurality of batches of cells, responsive to a particle count determined by the particle counter, satisfying a predetermined criteria, to ensure that all components that come into contact with the batches of cells are sterile, such that cross-contamination between the first batch and the second batch is prevented. The enclosure is only accessible from outside of the system through the first isolator, the enclosure and the first isolator being connected by an opening through the enclosure access port and the first isolator access port, wherein a first gate operably opens and closes the opening between the enclosure access port and the first isolator access port.

[0013] In some implementations, systems are designed to maintain sterility to such an extent that they need not be operated in a clean room. For example, the system can be restocked with consumables such as reagents, media, plasticware and the like without disturbing the sterility of the system or exposing the system to the outside environment. In some implementations, systems can perform Quality Control (QC) tests such as verifying cell identity, cell purity, cell potency, and/or batch sterility (i.e., no contamination), during or after processing. In some implementations,

end-to-end processing is provided, i.e., a biological sample is introduced into the system and the desired end product is presented by the system after processing, without requiring handling by a human operator. In some implementations, monitoring, tracking and recording systems keep detailed records of every step of the process, including QC testing. Such records can be used for quality assurance purposes and to verify that all applicable regulations have been met. In some implementations, quality assurance (QA) of the end product and/or end product release is performed without requiring a human operator. In some implementations, the product is stored and/or packaged for transport after completion of QC and QA without requiring a human operator.

[0014] In some implementations, therefore, systems and methods described herein may provide one or more of the following advantages: allowing processing of multiple biological samples or batches in sequence or at the same time without cross-contamination between samples/batches and/or under GMP conditions (conditions that meet Good Manufacturing Practices (GMP) guidelines or regulations); allowing fast, efficient, and/or affordable processing; being executable without human intervention during the processing (except to restock consumables, which can be done without interrupting processing or disrupting sterility / the aseptic environment);

CLAIMS

What is claimed is:

1. A system for automated processing of a plurality of batches, each batch being derived from one biological sample, the system comprising:

an enclosure which can be closed and sterilized for the automated processing of the plurality of batches, the enclosure comprising an enclosure access port;

~~one or more~~at least two cell processing containers for the automated processing of the plurality of batches, each batch of the plurality of batches comprising one or more cell processing container;

a first isolator comprising a first isolator access port, wherein the enclosure is selectively fluidly connected to the first isolator, and objects from outside the system can be received into the enclosure via the first isolator and/or objects from inside the enclosure can be passed out of the system via the first isolator ~~without requiring sterilization between the enclosure and the first isolator~~;

a plurality of reagent containers for holding reagents within the enclosure;

at least one reagent dispenser within the enclosure for dispensing reagents during said automated processing;

a particle counter configured to measure a particle count inside the enclosure;

an air flow system configured to control an air pressure inside the enclosure to be greater than an air pressure outside the enclosure;

at least one of a liquid waste receptacle and a solid waste receptacle, located outside the enclosure that is selectively fluidly connected to the enclosure, wherein the liquid waste receptable comprises an aspirator with a sterile tip configured to establish an air pressure in the liquid waste receptacle that is lower than an air pressure in the enclosure, wherein the solid waste receptacle is configured to establish an air pressure in the solid waste receptacle that is lower than an air pressure in the enclosure;a quality control module within the enclosure for analyzing at least one characteristic of a batch during said automated processing;

a harvesting module within the enclosure for harvesting batches;

a robotic module within the enclosure, configured for at least one of transporting cell processing containers, decapping or otherwise opening a cell processing container, pipetting reagents or liquids from a cell processing container, and aspirating liquids from a cell processing container, during said automated processing;

a tracking module for electronically tracking the plurality of batches after its introduction to the enclosure; and

a control unit (CU) communicatively coupled to the at least one reagent dispenser, the quality control module, the harvesting module, the robotic module, the tracking module, and the particle counter for controlling said automatic processing of said batches,

wherein the plurality of batches comprises a first batch and a second batch, the system being configured to receive the second batch into the enclosure before the first batch is transported out of the enclosure,

the system being configured to automatically process the first batch and the second batch within the enclosure at the same time, without cross contamination from the other of the first batch and the second batch,

wherein:

the CU is configured to allow receiving of the second batch into the enclosure responsive to the particle count satisfying a predetermined criterion;

the CU is configured to keep the cell processing containers closed during said automated processing except during addition or removal of materials to and from the cell processing container, wherein only cell processing containers from one batch at a time are opened to the environment, such that only one batch is exposed to the environment inside the enclosure at any one time,

the CU is configured to control said processing of the plurality of batches of cells, responsive to a particle count determined by the particle counter, satisfying a predetermined criteria, to ensure that all components that come into contact with the batches of cells are sterile, such that cross-contamination between the first batch and the second batch is prevented; and

the enclosure is only accessible from outside of the system through the first isolator, the enclosure and the first isolator being connected by an opening through the enclosure access port and the first isolator access port, wherein a first gate operably opens and closes the opening between the enclosure access port and the first isolator access port.

2. The system of claim 1, wherein the system is configured to automatically process the plurality of batches in compliance with good manufacturing practice (GMP) guidelines.

3. The system of claim 1 or 2, wherein said automatic processing is executable without handling by a human operator.

4. The system of any one of claims 1 to 3, wherein the enclosure is at least a class 100 environment or at least a class 10 environment.

5. The system of any one of claims 1 to 4, wherein:

the enclosure is defined at least in part by a top wall, a first side wall and a second side wall extending opposite the first side wall, and a bottom wall;

the enclosure has an air inlet port defined in one or more of the top wall, the first side wall, the second side wall and the bottom wall;

the enclosure has an air outlet port disposed in one or more of the top wall, the first side wall, the second side wall and the bottom wall,the air flow system being configured to direct air flow into the enclosure via the air inlet port and air flow out of the enclosure via the air outlet port,

an air flow within the enclosure being laminar.

6. The system of any one of claims 1 to 5, wherein the system complies with good manufacturing practice (GMP) guidelines.

7. The system of any one of claims 1 to 6, wherein:

the CU is configured to control automatic processing of batches based on a signal received from the quality control module.

8. The system of any one of claims 1 to 7, wherein each of the at least one reagent dispenser, the quality control module, the harvesting module, and the robotic module is configured to operate on any one of a first batch and a second batch such that:

when the first batch is being operated on by one of the at least one reagent dispenser, the quality control module, the harvesting module, and the robotic module, the second batch is being operated on by an other of the at least one reagent dispenser, the quality control module, the harvesting module, and the robotic module.

9. The system of any one of claims 1 to 8, further comprising:

an automatic sterilizing module communicatively coupled to the CU for automatically sterilizing the enclosure responsive to a particle count, or after introducing thefirst or second batch into the enclosure.

10. The system of any one of claims 1 to 9, further comprising:

an incubator selectively fluidly connected to the enclosure; and

a gate between the enclosure and the incubator being configured to be open for automatic transferring of the batch from the enclosure to the incubator and for automatic transferring of the batch from the incubator to the enclosure,

the enclosure being fluidly connected to the incubator when the gate is open

and the enclosure being sealed from the incubator when the gate is closed.

11. The system of any one of claims 1 to 10, further comprising:

a centrifuge selectively fluidly connected to the enclosure; and

a gate between the enclosure and the centrifuge being configured to be open for automatic transferring of the batch from the enclosure to the centrifuge and for automatic transferring of the batch from the centrifuge to the enclosure,

the enclosure being fluidly connected to the centrifuge when the gate is open and the enclosure being sealed from the centrifuge when the gate is closed.

12. The system of any one of claims 1 to 11, wherein the robotic module comprises a plurality of robotic modules.

13. The system of any one of claims 1 to 12, wherein the liquid is cell culture media.

14. The system of any one of claims 1 to 13, wherein one of the plurality of reagent containers is placed outside of the enclosure and connected to one of the at least one reagent dispensers by a fill line.

15. The system of any one of claims 1 to 14, further comprising a tilt module configured to tilt a container disposed thereon.

16. The system of claim 15, wherein the tilt module is a magnetic tilt module for separating magnetically tagged contents in the container from magnetically untagged contents of the container while tilting the container.

17. The system of any one of claims 1 to 16, wherein the quality control module is one of:

a flow cytometer;

a plate reader;

a microscope; and

a PCR machine.

18. The system of any one of claims 1 to 17, wherein the quality control module comprises a plurality of quality control modules.

19. The system of any one of claims 1 to 18, wherein the harvesting module comprises at least one of:

a container for holding a solution;

a freezer or a cryofreezer; and

a packaging module configured to place the batch in a transport container.

20. The system of any one of claims 1 to 19, wherein:

an air pressure inside the enclosure is greater than an air pressure in the first isolator; and

an air pressure inside the first isolator is greater than an air pressure adjacent to the first isolator in a direction other than the enclosure, or an ambient air pressure outside the system.

21. The system of any one of claims 1 to 20, further comprising a second isolator,
the first isolator being selectively fluidly connected to the second isolator, and
objects from outside the system being received into the first isolator via the second isolator, objects from inside the enclosure being passed out of the system by passing from the enclosure to the first isolator and from the first isolator to the second isolator via the first isolator.

22. The system of any one of claims 1 to 21, further comprising:
a refrigerator and/or a freezer selectively fluidly connected to the enclosure; and
a gate between the enclosure and the one or more refrigerator or freezer being configured to be open for automatic transferring of the batch from the enclosure to the freezer and for automatic transferring of the batch from the one or more refrigerator or freezer to the enclosure,
the enclosure being fluidly connected to the one or more refrigerator or freezer when the gate is open and the enclosure being sealed from the one or more refrigerator or freezer when the gate is closed.

23. The system of any one of claims 1 to 22 comprising a robotic aspirator, the robotic aspirator comprising:

a robotic arm configured to move in at least one direction;

a body connected to the robotic arm;

an aspiration member comprising a fluid flow channel connected to the body, the aspiration member being configured for connection to a pump means;

the body being configured to hold a disposable tip for providing fluid connection between the disposable tip and the fluid flow channel of the aspiration member;

fluid being aspirated through the disposable tip and the fluid flow channel when the disposable tip is fluidly connected to the fluid flow channel and the aspiration member is connected to the pump means;

the robotic aspirator optionally comprising a plurality of prongs connected to the body, the prongs being moveable between a tip holding position and a retracted position, the prongs being configured in the tip holding position to hold the disposable tip for providing fluid connection between the disposable tip and the fluid flow channel of the aspiration member, wherein the plurality of prongs are optionally further configured for gripping objects other than the disposable tip.

24. The system of claim 23, comprising means for engaging and/or disengaging the disposable tip from the robotic aspirator without handling by a human operator.

25. The system of any one of claims 1 to 24, comprising an automated liquid fill station housed inside the enclosure and configured for direct filling of liquid from a supply container disposed inside or outside the enclosure into a cell processing container disposed inside the enclosure, optionally wherein the liquid is media, optionally wherein the liquid fill station is configured to dispense more than 5 mL of liquid at a time.

26. The system of any one of claims 1 to 25, comprising robotic means for capping and decapping screwcap lids of containers.

27. The system of claim 26, wherein the containers are sized to hold volumes of greater than 10 mL or greater than 2 mL.

28. The system of any one of claims 1 to 27, comprising automated means for purifying cell mixtures or obtaining a cell pellet.

29. The system of claim 28, wherein said means comprises a centrifuge.

30. The system of any one of claims 1 to 29, comprising means for incubating cells.

31. The system of any one of claims 1 to 30, comprising automated means for determining cell number or cell confluency in a sample.

32. The system of any one of claims 1 to 31, wherein the system is configured to allow sterilization of the enclosure without removing the batches from the system.

33. The system of any one of claims 1 to 32, comprising robotic means for freezing of batches and/or means for manipulation of samples or reagents at subzero temperatures.

34. The system of any one of claims 1 to 33, the system comprising ~~an enclosure and~~ one or more of the following automated components:

(1) a robotic aspirator housed within the enclosure and configured for use with disposable tips, as described in ~~any one of claims 83 to 84~~claim 23;

(2) a decapper housed within the enclosure and configured to decap a screwcap lid of a container, optionally wherein the container is of 10 mL or greater volume or of 2 mL or greater volume;

(3) a centrifuge, cell sorter, or magnet;

(4) an incubator;

(5) a module for determining confluency of cells and/or cell number;

(6) a liquid fill module housed inside the enclosure and configured for direct filling of liquid from a supply container disposed inside or outside the enclosure into a cell processing container disposed inside the enclosure, optionally wherein the liquid is media, optionally wherein the liquid fill station is configured to dispense more than 5 mL of liquid at a time; and

(7) a tilt module configured for tilting a cell processing container, for removal or collection of cells or media therefrom, optionally wherein the tilt module is magnetic.

35. The system of claim 34 wherein the system comprises two or more, three or more, four or more, five or more, more than 5 or all of the automated components (1) to (7).

36. The system of any one of claims 1 to 35, wherein the system further comprises a module for quality assurance.

37. The system of claim 23 or 24, wherein the disposable tip is sterile prior to fluid being aspirated through the disposable tip to prevent cross-contamination between batches.