

CLAIMS

We claim:

1. An integrated diagnostic cartridge, comprising:

a loading module having a fill chamber within the cartridge having a volume sufficient to hold a sample, a fluid inlet in fluid communication with the fill chamber, a fluid outlet in fluid communication with fill chamber;

a lysis module;

a purification module; and

a reaction module;

wherein the loading module is in fluidic communication with the lysis module and the purification module is in fluidic communication with the reaction module;

further wherein the loading module, the lysis module, the purification module and the reaction module are arranged for use while the cartridge is in a vertical orientation; and

~~1. A method of testing a sample suspected of containing one or more target pathogens, comprising:~~

~~accepting a further wherein when the cartridge having is in a horizontal sample port assembly containing the sample suspected of containing the one or more target pathogens;~~

~~advancing the sample suspected of containing the one or more target pathogens to a lysis chamber having at least one lysis reagent therein;~~

~~mixing the sample with the at least one lysis agent to generate a lysed sample;~~

~~passing the lysed sample through a first porous solid support to capture a nucleic acid on the porous solid support;~~

~~releasing the captured nucleic acid from the first porous solid support to generate an enriched nucleic acid;~~

~~distributing the enriched nucleic acid to two or more assay chambers;~~

~~combining the enriched nucleic acid with one or more amplification reagents;~~

~~isolating each one of loading orientation the two or more assay chambers from each one of a fluid inlet accesses the other two or more assay chambers; and~~

~~performing an isothermal amplification reaction within each one of the two or more assay chambers while simultaneously detecting amplification product, wherein presence of an amplification product is an indication of a presence, an absence or a quantity of the target pathogen in the sample suspected of containing the target pathogen.~~

5 ~~2. — A method of testing a sample according to claim 1, wherein the sample is a biological sample obtained from a mammal.~~

~~3. — A method of testing a sample according to claim 2 wherein the mammal is a person providing a biological sample.~~

10 ~~4. — The method of testing a sample according to claim 1, wherein the sample is obtained from a food product, a natural non-growth hormone crop sample, a crop sample, a water sample, a non-biological fluid sample or a soil sample.~~

~~5. — The method of testing a sample according to claim 2, wherein the step of accepting a cartridge step further comprises reading a bar code on the cartridge and determining to proceed with the method of testing.~~

15 ~~6. — The method of testing a sample according to claim 1, the accepting a cartridge step further comprising: obtaining and analyzing an image of a sample window of the sample port assembly and determining to proceed with the method of testing.~~

~~7. — The method of testing a sample according to claim 6, wherein the sample in the sample port assembly is in fluid communication with a fill chamber, a metering chamber, and an overflow chamber.~~

20 ~~8. — The method of testing a sample according to claim 6, wherein the sample window is transparent and formed in at least a portion of a wall of a metering chamber wherein obtaining an image further comprises obtaining an image of the transparent viewing window.~~

25 ~~9. — The method of testing a sample according to claim on 8, wherein analyzing an image further comprises assessing a height of a sample liquid in the meteringfill chamber via an upper surface of the transparent viewing window.~~

~~10. — The method of testing a sample according to claim 8, wherein the step of obtaining and analyzing an image further comprises obtaining an image of the metering chamber comprising a buoyant ball and analyzing the image comprises identifying a location of the ball within the metering chamber and determining to proceed with the method based on the location of the ball.~~

11. — The method of testing a sample according to claim 1, the accepting a cartridge step further comprising: obtaining and analyzing an image of a patient ID label and determining to proceed with the method of testing.

12. — The method of testing a sample according to claim 1, the accepting a and when the cartridge step further comprising: confirming a rotary valve on the cartridge is in a shipping configuration before proceeding to the advancing the sample step.

13. — The method of testing a sample according to claim 1, the accepting a cartridge step further comprising: obtaining a reading from an interference sensor on a valve drive assembly and confirming based on the reading that a rotary valve on the cartridge is not in an operational configuration prematurely.

14. — The method of testing a sample according to claim 1, the accepting a cartridge step further comprising: engaging a rotary valve on the cartridge with a valve drive assembly and rotating the rotary valve into an operational configuration.

15. — The method of testing a sample according to claim 14, wherein rotating the rotary valve in an operational configuration places a rotary valve gasket into contact with a stator on the cartridge.

16. — The method of testing a sample according to claim 1, the step of accepting a cartridge further comprising moving a clamping block for engaging the cartridge with a door support assembly, a pneumatic interface assembly, and a thermal clamp assembly.

17. — The method of testing a sample according to claim 16, wherein the moving step is a single continuous movement.

18. — The method of testing a sample according to claim 1, the step of accepting a cartridge further comprising moving a frangible seal block having a plurality of frangible seal pins into position to engage one or more frangible seals on the cartridge.

19. — The method of testing a sample according to claim 18, wherein moving the frangible seal block simultaneously engages the plurality of frangible seal pins with the one or more frangible seals on the cartridge.

20. — The method of testing a sample according to claim 18, wherein moving the frangible seal block sequentially engages the plurality of frangible seal pins with the one or more frangible seals on the cartridge.

21. — The method of testing a sample according to claim 18, wherein the step of moving a frangible seal block is performed after performing the step of moving a clamp block

22. — The method of testing a sample according to claim 18, wherein the step of moving a frangible seal block is performed initially with the clamp block and ends in a position separate from the clamp block.

5 23. — The method of testing a sample according to claim 1, the step of accepting a cartridge further comprising moving a clamp block and a frangible seal block together for engaging the cartridge.

24. — The method of testing a sample according to claim 23, further comprising moving the clamp block together with the frangible seal block until the cartridge is engaged with a door support assembly, a pneumatic interface assembly, and a thermal clamp assembly.

10 25. — The method of testing a sample according to claim 24, further comprising: only driving the frangible seal block assembly to engage one of more frangible seals on the cartridge simultaneously or sequentially.

26. — The method of testing a sample according to claim 1, wherein in mixing the sample with the at least one lysis agent, the lysis agent is a mechanical agent.

15 27. — The method of testing a sample according to claim 26, wherein the mechanical agent is ceramic beads, glass beads or steel beads, and the mixing the sample step comprises rotating the stir bar at at least 1000 rpm.

20 28. — The method of testing a sample according to any one of claim 26 or claim 27 further wherein mixing the sample comprises rotating the stir bar or the ceramic, glass or steel beads along with a chemical lysis agent.

29. — The method of testing a sample according to any one of claim 26, claim 27 or claim 28, wherein the suspected pathogen is a gram-positive bacterium, a fungus or a plant cell.

30. — The method of testing according to claim 1, wherein in the mixing the sample with the at least one lysis agent step, the at least one lysis agent is a chemical lysis agent.

25 31. — The method of testing a sample according to claim 30 wherein the one or more target pathogens is a virus or a gram-negative bacterium and the lysis reagent is a chaotropic agent.

32. — The method of testing a sample according to claim 1, wherein prior to passing the lysed sample through the porous solid support, the method further comprises passing the lysed sample through a size-exclusion filter, wherein nucleic acid passes through the filter.

33. — ~~The method of testing a sample according to claim 1, wherein the enriched nucleic acid is combined with one or more amplification reagents before the distributing step.~~

34. — ~~The method of testing a sample according to claim 33, wherein the one or more amplification reagents are selected from the group consisting of a DNA polymerase, a reverse transcriptase, a helicase, nucleotide triphosphates (NTPs), a magnesium salt, a potassium salt, an ammonium salt, and a buffer.~~

35. — ~~The method of testing a sample according to claim 34, wherein the one or more amplification reagents further comprise a primer.~~

36. — ~~The method of testing a sample according to claim 35, wherein isothermal amplification is initiated prior to distributing the enriched nucleic acid to the two or more assay chambers.~~

37. — ~~The method of testing a sample according to claim 34, wherein after the distributing step, but prior to perform the isothermal amplification reaction, the method further comprises combining the enriched nucleic acid with a primer set specific to one of the one or more target pathogens.~~

38. — ~~The method of testing a sample according to claim 1, wherein a first assay chamber contains a primer set specific to a first nucleic acid sequence.~~

39. — ~~The method of testing a sample according to claim 38, wherein the first nucleic acid sequence is present in one of the one or more target pathogens.~~

40. — ~~The method of testing a sample according to claim 38, wherein prior to mixing the sample with at least one lysis agent, a process control is added to the sample and the first nucleic acid sequence is present in the process control.~~

41. — ~~The method of testing a sample according to claim 38, wherein prior to passing lysed sample through the porous solid support, a process control is added to the lysed sample and the first nucleic acid sequence is present in the process control.~~

42. — ~~The method of testing a sample according to claim 38, wherein a second assay chamber contains a primer set specific to a second nucleic acid sequent, wherein the second nucleic acid sequence is present in one of the one or more target pathogens.~~

43. — ~~The method of testing a sample according to claim 1, wherein the performing an isothermal amplification reaction step is completed in less than 20 minutes.~~

44. — ~~The method of testing a sample according to claim 43, wherein the performing an isothermal amplification reaction step is completed in less than 15 minutes.~~

45. — ~~The method of testing a sample according to claim 43, wherein the performing an isothermal amplification reaction step is completed in less than 10 minutes.~~
- 5 46. — ~~The method of testing a sample according to claim 1, further comprising: providing a result containing a determination made during the performing step relating to the presence, the absence or the quantity of the target pathogen in the sample suspected of containing the target pathogen.~~
47. — ~~The method of testing a sample according to claim 1, wherein the method further comprises, prior to advancing the sample to a lysis chamber, pretreating the sample with a chemical reaction.~~
48. — ~~The method of testing a sample according to claim 47, wherein the sample is sputum and the chemical reaction is incubation with a mucolytic agent.~~
- 10 49. — ~~The method of testing a sample according to claim 48, wherein the mucolytic agent is dithiothreitol or n-acetylcysteine.~~
50. — ~~The method of testing a sample according to claim 1, wherein the method further comprises, prior to advancing the sample to a lysis chamber, pretreating the sample with an enzymatic reaction.~~
- 15 51. — ~~The method of testing a sample according to claim 50, wherein the enzymatic reaction is incubation of the sample with a nuclease, a protease, an amylase, a glycosylase, or a lipase.~~
52. — ~~The method of testing a sample according to claim 50, wherein pretreating comprising incubating the sample with a DNase.~~
53. — ~~The method of testing a sample according to claim 50, wherein pretreating comprises incubating the sample with a protease.~~
- 20 54. — ~~The method of testing a sample according to claim 53, wherein the protease is selected from pronase, chymotrypsin, trypsin and pepsin.~~
55. — ~~The method of testing a sample according to claim 1, wherein the method further comprises, prior to advancing the sample to a lysis chamber, pretreating the sample with a physical treatment.~~
- 25 56. — ~~The method of testing a sample according to claim 55, wherein the physical treatment comprises passing the sample through a size-exclusion filter in a first direction.~~
57. — ~~The method of testing a sample according to claim 56, wherein the target pathogen passes through the filter.~~

58. — The method of testing a sample according to claim 56, wherein the target pathogen does not pass through the filter and is thereby captured on a fill port side of the size-exclusion filter.

59. — The method of testing a sample according to claim 58, further comprising passing a volume of suspension buffer through the size-exclusion filter in a second direction, wherein second direction is opposite the first direction, thereby releasing the target pathogen from the fill port side of the filter.

60. — The method of testing a sample according to claim 59, wherein the volume of suspension buffer is less than the volume of the sample, and the target pathogen is more concentrated than in the loaded sample.

61. — The method of testing a sample according to claim 58, wherein the physical treatment comprises exposing the sample to a capture agent immobilized on a solid substrate.

62. — The method of testing a sample according to claim 61, further comprising, after exposure, separating the solid substrate from the sample.

63. — The method of testing a sample according to claim 61, wherein the capture agent is a capture antibody.

64. — The method of testing a sample according to claim 61, wherein the capture agent is an antibody with affinity for red blood cells.

65. — The method of testing a sample according to claim 61, wherein the solid substrate is a magnetic bead, the capture agents has affinity for a class of cells comprising the one or more target pathogens and the method further comprises (1) incubating the magnetic beads with the sample, (2) engaging a magnet to draw the magnetic beads to a location within the sample loading structure, (3) washing away unbound sample, (4) releasing the magnet, and (5) resuspending the magnetic beads and passing the suspension, including target pathogen bound to the magnetic beads, to the lysis chamber.

66. — The method of testing a sample according to claim 1, wherein the sample is sputum and the method further comprises, prior to mixing the sample with the at least one lysis reagent, bead beating the sputum to liquify the sample.

67. — The method of testing a sample according to claim 66, wherein the bead beating comprises mixing the sputum with ceramic, glass, or steel beads.

68. — The method of testing a sample according to claim 66, wherein the bead beating comprises mixing the sputum with ceramic, glass, or steel beads and dithiothreitol.

69. — The method of testing a sample according to claim 1, wherein prior to distributing the enriched nucleic acid to the assay wells, the method further comprises passing the enriched nucleic acid through a second porous solid support.

70. — The method of testing a sample according to claim 69, wherein the second porous solid support is the same as the first porous solid support.

71. — The method of testing a sample according to claim 70, wherein the enriched nucleic acid is mixed with a matrix binding agent prior to passing through the second solid support.

72. — The method of testing a sample according to claim 71, wherein matrix binding agent is an alcohol or a salt solution.

73. — The method of testing a sample according to claim 69, wherein the second porous solid support is different than the first porous solid support, and the second solid support has an affinity for nucleic acid and the method further comprises releasing the captured nucleic acid from the second solid support to generate a twice enriched nucleic acid.

74. — The method of testing a sample according to claim 69, wherein the second porous solid support is different than the first porous solid support.

75. — The method of testing a sample according to claim 1, wherein prior to passing the lysed sample through a first porous solid support, the method further comprises passing the lysed sample through a second porous solid support, wherein the second solid support does not bind nucleic acid and has affinity for one or more contaminants, thereby removing contaminant from the lysed sample.

76. — The method of testing a sample according to claim 1, further comprising releasing the cartridge from engagement with a clamp block and a frangible seal block after completing the performing an isothermal amplification reaction step.

77. — The method of testing a sample according to claim 1, further comprising displaying a result produced after the step of performing an isothermal amplification reaction step.

78. — The method of testing a sample according to claim 1, further comprising storing in a computer memory a result produced after the step of performing an isothermal amplification reaction step.

79. — The method of testing a sample according to claim 1, further comprising maintaining the cartridge in a vertical orientation while performing the steps of testing a sample.

80. — The method of testing a sample according to claim 79, wherein the cartridge is inclined no more than 30 degrees while in the is in a vertical orientation.

81. — The method of testing a sample according to claim 79, wherein the cartridge is inclined no more than 15 degrees while in the vertical sample processing orientation.

5 82. — The method of testing a sample according to claim 1 wherein during the combining the enriched nucleic acid step in each of the two or more assay chambers the enriched nucleic acid combines with a dried reagent contained in each one of the two or more assay chambers.

83. — The method of testing a sample according to claim 82 wherein the dried reagent is on a surface of a plug in each one of the two or more assay chambers.

10 84. — The method of testing a sample according to claim 83 wherein the dried reagent is on a surface of the plug formed from a material transmissive to excitation wavelengths and emission wavelengths in at least one of a red spectrum, a blue spectrum and a green spectrum used during the performing step.

85. — The method of testing a sample according to claim 83 wherein the plug is as in any one of claims 202 to 213 and 214.

15 86. The method of testing a sample according to claim 1, the distributing step further comprising distributing the enriched nucleic acid to two or more assay chambers using a rotary valve on the cartridge and a pneumatic signal introduced into the rotary valve further wherein the pneumatic signal continues to be introduced while the performing step is performed.

20 87. The method of testing a sample according to claim 1 wherein performing the isolation step temporarily isolates each one of the two or more assay chambers are from each one of all the other two or more assay chambers.

88. The method testing a sample according to claim 87 wherein the isolation step is performed using a pneumatic signal, a mechanical system to occlude one or more fluid channels to occlude one or more passages or channels of a cartridge.

25 89. — The method of testing a sample according to claim 88 wherein the mechanical system is one of a single pinch valve, a plurality of pinch valves, and a non-heated staker bar.

90. The method of testing a sample according to claim 1 wherein performing the isolation step permanently isolates each one of the two or more assay chambers from each one of all the other two or more assay chambers.

91. ~~The method of testing a sample according to claim 90 wherein after performing the isolation step, a~~ the fluid inlet is positioned adjacent to an upper portion of the fill chamber and the fluid outlet is arranged for the sample to flow out of a lower portion of the cartridge is melted or is plastically deformed. fill chamber.

5 92. ~~—The method of testing a sample according to claim 1 wherein after completing the performing step, each one of the two or more assay chambers are isolated from each one of all the other two or more assay chambers.~~

10 93. ~~—The method of testing a sample according to claim 1, the distributing step further comprising distributing the enriched nucleic acid to two or more assay chambers using a rotary valve on the cartridge and a pneumatic signal introduced into the rotary valve further wherein the pneumatic signal continues to be introduced while performing the isolating step by moving a heat staker into contact with the cartridge to isolate each one of the two or more assay chambers from each one of all the other two or more assay chambers.~~

15 94. ~~—The method of testing a sample according to claim 93 wherein after performing the isolating step, a single heat stake isolates each one of the two or more assay chambers from each one of all the other two or more assay chambers.~~

95. ~~—The method of testing a sample according to claim 94 further wherein the single heat stake isolates a waste chamber on the cartridge.~~

20 96. ~~—The method of testing a sample according to claim 1, the isolating step further comprising moving a heat staker into contact with the cartridge to seal each one of the two or more assay chambers from each one of all the other two or more assay chambers.~~

97. ~~—The method of testing a sample according to claim 96, further comprising providing a pneumatic pressure in the cartridge while moving the heat staker into contact with the cartridge.~~

25 98. ~~—The method of testing a sample according to claim 1, the isolating step further comprising forming a heat stake region in the cartridge to isolate each one of the two or more assay chambers from each one of all the other two or more assay chambers.~~

99. ~~—The method of testing a sample according to any one of claim 96, claim 97 and claim 98 further comprising: obtaining a first image of a level of fluid in each of the one or more assay chambers after the step of distributing the enriched nucleic acid to each one of the two or more assay chambers.~~

~~100. The method of claim 85 further comprising obtaining a second image of a level of fluid in each of the one or more assay chambers after the isolating step.~~

~~101. The method of testing a sample according to claim 100, further comprising determining the quality of the heat stake by comparing the level of fluid in the first image to the level of fluid in the second image.~~

~~102. The method of testing a sample according to claim 1, further comprising rotating a rotary valve on the cartridge prior to performing the advancing the sample step.~~

~~103. The method of testing a sample according to claim 102, further comprising advancing the sample to the lysis chamber using a pneumatic signal introduced into a cartridge pneumatic interface.~~

~~104. The method of testing a sample according to claim 1, further comprising rotating a rotary valve on the cartridge prior to performing the step of passing the lysed sample through a first porous solid support to capture a nucleic acid on the porous solid support.~~

~~105. The method of testing a sample according to claim 104, further comprising passing the lysed sample through the first porous solid support using a pneumatic signal introduced into the rotary valve.~~

~~106. The method of testing a sample according to claim 1, further comprising distributing the enriched nucleic acid to two or more assay chambers using a rotary valve on the cartridge and a pneumatic signal introduced into the rotary valve.~~

~~107. An apparatus, comprising:~~

~~an enclosure;~~

~~a fixed support bracket within the enclosure;~~

~~a first imaging system mounted on the fixed support bracket within the enclosure adjacent to an opening, the first imaging system configured to collect images from a first imaging area within the enclosure;~~

~~a second imaging system mounted on the fixed support bracket within the enclosure configured to collect images from a second imaging area within the enclosure wherein the second imaging area is in non-overlapping relation to the first imaging area;~~

~~a moving support bracket within the enclosure and moveable relative to the fixed support bracket, the first imaging system and the second imaging system;~~

~~a drive system on the fixed support bracket configured to position the moving support bracket relative to the fixed support bracket; and~~

~~an opening positioned in the enclosure to provide access to an interior portion of the enclosure between the fixed support bracket and the moving support bracket.~~

5 ~~108.—The apparatus of claim 107 wherein the moving support bracket is positioned between the first imaging system and the second imaging system.~~

~~109.—The apparatus of claim 107 wherein a rotary connector, a pneumatic connector and a multiple pin block are connected to and move with the moving support bracket.~~

10 ~~110.—The apparatus of claim 109 wherein the multiple pin block is directly connected to the drive system.~~

~~111.—The apparatus of claim 109 wherein the multiple pin block is configured to move together with the rotary connector and the pneumatic connector and independent of the rotary connector and the pneumatic connector.~~

15 ~~112.—The apparatus of claim 107 wherein the opening is a slot, wherein the slot is aligned to access an upper rail within the enclosure aligned to an upper portion of the slot and a lower rail within the enclosure aligned to a lower portion of the slot.~~

~~113.—The apparatus of claim 112 further comprising a loading and ejection mechanism within the enclosure in sliding relation to the lower rail.~~

20 ~~114.—The apparatus of claim 113 wherein the loading and ejection mechanism moves between a loading position and a loaded position wherein when in the loading position the loading and ejection mechanism is positioned in a forward most position towards the slot and when in the loaded position the loading and ejection mechanism is engaged with a load position sensor.~~

~~115.—The apparatus of claim 114 wherein the load position sensor provides an electronic indication when the loading and ejection mechanism has translated into the loaded position.~~

25 ~~116.—The apparatus of claim 107 further comprising a first heater and a second heater mounted on the fixed support bracket.~~

~~117.—The apparatus of claim 116 wherein the first heater is positioned to heat a portion of the fixed support bracket between the first imaging area and the second imaging area.~~

~~118.—The apparatus of claim 116 wherein the second heater is positioned to heat a portion of the fixed support bracket only within the second imaging area.~~

~~119.—The apparatus of claim 107 further comprising a channel in the fixed support bracket and a heat stake assembly positioned to move a heating element through the channel.~~

~~120.—The apparatus of claim 119 wherein the channel is positioned on the fixed support bracket to allow the heating element to interact within the enclosure between the first imaging area and the second imaging area.~~

~~121.—The apparatus of claim 119 wherein the channel is positioned within the fixed support bracket such that the heating element may perform a heat staking operation directly adjacent to but outside of the second imaging area.~~

~~122.—The apparatus of claim 107 wherein the moving support bracket partially blocks the channel when the moving support bracket is positioned at a closest position to the fixed support bracket.~~

~~123.—An apparatus, comprising:~~

~~an enclosure;~~

~~a fixed support bracket within the enclosure;~~

~~a moving support bracket within the enclosure and moveable relative to the fixed support bracket;~~

~~a drive system configured to position the moving support bracket relative to the fixed support bracket;~~

~~an opening positioned in the enclosure to provide access to an interior portion of the enclosure between the fixed support bracket and the moving support bracket; and~~

~~an upper rail and a lower rail in the enclosure positioned adjacent to the opening wherein a cartridge positioned between the upper rail and the lower rail remains in a vertical position between the fixed support bracket and the moving support bracket.~~

~~124.—The apparatus of claim 123 further comprising a feature within the upper rail or the lower rail positioned to interfere with the movement of a cartridge improperly aligned with respect to the upper rail and the lower rail.~~

~~125.—The apparatus of claim 123 further comprising a loading and ejection assembly within the enclosure positioned to engage with a cartridge moving along the upper rail and the lower rail.~~

~~126.—The apparatus of claim 123 further comprising a latch and pin assembly positioned adjacent to the upper rail adapted to engage a pin with a cartridge moving along the upper rail.~~

~~127.—The apparatus of claim 123 further comprising a touch screen display on an exterior of the enclosure.~~

5 ~~128.—The apparatus of claim 123 further comprising a cellular communications module within the enclosure.~~

~~129.—The apparatus of claim 123 wherein the cellular communication module is adjacent to the opening.~~

10 ~~130.—The apparatus of claim 123 further comprising: a cartridge heater, a driving magnet system, a chemistry heater, a rehydration motor, a reaction camera and a heat stake assembly coupled to the fixed support bracket and positioned to interact with a corresponding portion of a cartridge positioned between the upper rail and the lower rail.~~

15 ~~131.—The apparatus of claim 123 further comprising a first imaging system mounted on the fixed support bracket within the enclosure adjacent to the opening, the first imaging system configured to collect images from a first imaging area within the enclosure and a second imaging system mounted on the fixed support bracket within the enclosure configured to collect images from a second imaging area within the enclosure wherein the second imaging area is in non-overlapping relation to the first imaging area.~~

20 ~~132.—The apparatus of claim 131 wherein the first imaging area includes a label of a cartridge positioned within the enclosure between the upper rail and the lower rail.~~

~~133.—The apparatus of claim 131 wherein the second imaging area includes one or more assay chambers of a cartridge positioned within the enclosure between the upper rail and the lower rail.~~

25 ~~134.—The apparatus of claim 123 further comprising a clamp block, a frangible seal block, a valve driver, a pneumatic interface, a thermal clamp, and a driven magnet system coupled to move along with the moving support bracket during operation of the drive system.~~

~~135.—The apparatus of claim 130 further comprising a plenum adjacent to the chemistry heater and a fan in fluid communication with the plenum.~~

30 ~~136.—The apparatus of claim 130 the heat stake assembly further comprising a staker blade positioned to move relative to a depth stop frame, the staker blade coupled to a linear actuator motor and a spring with pivot washer.~~

~~137. —An integrated diagnostic cartridge, comprising:~~

~~a loading module;~~

~~a lysis module;~~

~~a purification module; and~~

~~a reaction module;~~

~~wherein the loading module is in fluidic communication with the lysis module and the~~

~~purification module is in fluidic communication with the reaction module; and~~

~~further wherein the loading module, the lysis module, the purification module and the reaction module are arranged for use while the cartridge is in a vertical orientation.~~

10 ~~1382.~~ The integrated diagnostic cartridge of claim ~~1371~~ further comprising one or more fluid filling conduits arranged to flow into an upper portion of a vertically oriented chamber within a fluidic card of the integrated diagnostics cartridge and one or more fluid outlet conduits arranged to flow out of a lower portion of the vertically oriented chamber within the fluidic card of the integrated diagnostics cartridge.

15 ~~1393.~~ The integrated diagnostic cartridge of claim ~~1382~~, wherein the ~~chamber is one or more of a lysis chamber, a metering chamber, a wash buffer chamber or an elution buffer chambers.~~

~~140. —The integrated diagnostic cartridge of claim 139, wherein the~~vertically oriented ~~chamber further comprises a filter assembly in fluid communication with a fluid outlet conduit of the~~vertically oriented ~~chamber.~~

20 ~~141.4.~~ The integrated diagnostic cartridge of claim ~~1371~~, wherein the lysis module comprises a mixing assembly having a vertically oriented lysis chamber containing a lysis agent and a non-magnetized stir bar.

~~1425.~~ The integrated diagnostic cartridge of claim ~~1414~~, wherein the non-magnetized stir bar is made from a metal having a magnetic permeability to be responsive to a rotating magnetic field
25 induced between a drive magnetic element and a driven magnetic element of a magnetic drive system.

~~1436.~~ The integrated diagnostic cartridge according to claim ~~1414~~, wherein the non-magnetized stir bar is coated with an impermeable material to prevent corrosion by a chemical lysis buffer in the vertically oriented lysis chamber.

1447. The integrated diagnostic cartridge of claim 1414 wherein, when in use within a diagnostic instrument, the non-magnetized stir bar is disposed between a driving magnet system and a driven magnet system of a magnetic mixing assembly in the diagnostic instrument, wherein the driving magnet system is configured to rotate the non-magnetized stir bar within the vertically oriented lysis chamber at least 1000 rpm.

1458. The integrated diagnostic cartridge of claim 1414, further comprising a fluid inlet to the vertically oriented lysis chamber and a fluid outlet to lysis chamber wherein the vertically oriented lysis chamber is isolated from the other modules on the cartridge by a first frangible seal in fluid communication with the fluid inlet to the vertically oriented lysis chamber and a second frangible seal in fluid communication with the fluid outlet to the vertically oriented lysis chamber.

1469. The integrated diagnostic cartridge according to claim 1371 further comprising a fluidic card and a cover.

14710. The integrated diagnostic cartridge of claim 1469, wherein the fluidic card further comprises a first film adhered to a surface of at least a portion of the fluidic card, wherein the first film forms one surface of one or more chambers, compartments, or fluid conduits of the loading module, the lysis module, the purification module and the reaction module.

14811. The integrated diagnostic cartridge of claim 1469 further comprising an interference feature on the cover, wherein the interference feature is sized and positioned to interact with one of an upper rail or a lower rail of a loading apparatus of a diagnostic instrument.

14912. The integrated diagnostic cartridge according to claim 14811, wherein a thickness of the fluidic card is selected for sliding arrangement within an upper rail and a lower rail of a loading apparatus of the diagnostic instrument.

~~150. —The integrated diagnostic cartridge of claim 14613.~~ The integrated diagnostic cartridge of claim 11 further comprising a cartridge front face and a cartridge rear face forming an upper spacing and a lower spacing wherein each of the upper spacing and the lower spacing is sized and positioned to engage with the upper rail and lower rail of the diagnostic instrument.

14. The integrated diagnostic cartridge of claim 15 further comprising an interference feature within the upper spacing or the lower spacing positioned to ensure the cartridge engages with the upper rail and the lower rail in a desired orientation.

15. The integrated diagnostic cartridge of claim 9 wherein a total sample process volume of the integrated diagnostic cartridge is related to a thickness of the cartridge corresponding to a spacing between the one or more chambers, compartments, or fluid conduits of the loading module, the lysis module, the purification module and the reaction module formed in the fluidic card and the first film.

~~154~~16. The integrated diagnostic cartridge of claim ~~150~~15, wherein a diagnostic instrument is adapted and configured to accommodate a variation of the thickness of the cartridge by increasing a width of ~~an opening~~a loading slot of the diagnostic instrument to accommodate the increased thickness of the cartridge or a displacement range of a cartridge clamping system of the diagnostic instrument is adapted to accommodate the increased thickness of the cartridge.

~~152.—The integrated diagnostic cartridge of claim 148 further comprising a cartridge front face and a cartridge rear face forming an upper spacing and a lower spacing wherein each of the upper spacing and the lower spacing is sized and positioned to engage with the upper rail and lower rail of the diagnostic instrument.~~

~~153.—The integrated diagnostic cartridge of claim 152 further comprising an interference feature within the upper spacing or the lower spacing positioned to ensure the cartridge engages with the upper rail and the lower rail in a desired orientation.~~

~~154.—The integrated diagnostic cartridge of claim 137~~17. The integrated diagnostic cartridge of claim 1 further comprising a plurality of frangible seal chambers in fluid communication with at least one or more of the loading module, the lysis module, the purification module or the reaction module.

~~155~~18. The integrated diagnostic cartridge of claim ~~137~~1, the integrated diagnostic cartridge further comprising a machine-readable code adapted and configured to identify the cartridge to a diagnostic instrument or an image of a patient identification marking.

~~156.—An integrated diagnostic cartridge, comprising:~~

~~a loading module comprising a sample port assembly having a fill chamber, a metering chamber, and an overflow chamber arranged in fluid communication;~~

~~a lysis module;~~

~~a purification module; and~~

~~a reaction module;~~

wherein the loading module is in fluidic communication with the lysis module and the purification module is in fluidic communication with the reaction module.

157. — The integrated diagnostic cartridge of claim 156, wherein the metering chamber comprises a transparent viewing window for observing the height of a sample within the metering chamber.

5 158. — The integrated diagnostic cartridge of claim 157 further comprising a ball float in the metering chamber adapted for use with the transparent viewing window.

159. — The integrated diagnostic cartridge of claim 156, wherein the fill chamber comprises a cap operable to provide access to the fill chamber.

10 160. — The integrated diagnostic cartridge of claim 159, wherein the cap is positioned for interaction with a closing apparatus of a diagnostic instrument.

161. — The integrated diagnostic cartridge of claim 156, wherein, the cartridge is in a vertical orientation when in use within a diagnostic instrument and a fluid channel connects an outlet at a lower portion of the fill chamber with an inlet to the metering chamber located in an upper portion of the metering chamber.

15 162. — The integrated diagnostic cartridge of claim 156, wherein the metering chamber comprises a transparent viewing window.

163. — The integrated diagnostic cartridge of claim 162 further comprising a buoyant ball within the metering chamber, said buoyant ball adapted to appear adjacent to the transparent viewing window permitting an assessment of the height of the sample liquid in the metering chamber.

20 164. — The integrated diagnostic cartridge of claim 156, wherein the metering chamber comprises a buoyant ball for assessing a height of a sample liquid in the metering chamber.

165. — An integrated diagnostic cartridge, comprising:

a loading module;

a lysis module comprising a mixing assembly having a lysis chamber containing a lysis agent and
25 a non-magnetized stir bar;

a purification module; and

a reaction module;

wherein the loading module is in fluidic communication with the lysis module and the purification module is in fluidic communication with the reaction module.

166. ~~The integrated diagnostic cartridge of claim 165, wherein the non-magnetized stir bar is made from a metal having a magnetic permeability to be responsive to a rotating magnetic field induced between a drive magnetic element and a driven magnetic element of a magnetic drive system.~~

167. ~~The integrated diagnostic cartridge of claim 166 wherein the metal comprises a ferritic stainless steel or a duplex stainless steel.~~

168. ~~The integrated diagnostic cartridge of claim 166 wherein the non-magnetized stir bar is made from a metal selected from the group consisting of a carbon steel, a mild carbon steel, a low alloy steel, a tool steel, a metal alloy contain nickel, a metal alloy containing cobalt, a non-austenitic stainless steel, a ferritic grade of stainless steel including 430 steel, Atlas CR12 steel, 444 steel, F20S steel, a duplex grade of steel including 2205 steel, 2304 steel, 2101 steel, 2507 steel and a martensitic grade of steel such as 431 steel, 416 steel, 420 steel and 440C steel wherein the metal has a magnetic permeability to be responsive to a rotating magnetic field produced within the mixing chamber.~~

169. ~~The integrated diagnostic cartridge of claim 168 wherein the metal has a magnetic permeability between 500-1,000,000.~~

17019. The integrated diagnostic cartridge according to ~~any one of claims 165-169~~, wherein the non-magnetized stir bar is coated with an impermeable material to prevent corrosion by a chemical lysis buffer in lysis chamber.

171. ~~The integrated diagnostic cartridge of claim 170, wherein the impermeable material is PTFE, parylene C, parylene D, a functionalized perfluoropolyether (PFPE), Xylan Fluoropolymer, epoxy, or urethane.~~

172. ~~The integrated diagnostic cartridge of claim 165 wherein, when in use within a diagnostic instrument, the non-magnetized stir bar is disposed between a driving magnet system and a driven magnet system of a magnetic mixing assembly in the diagnostic instrument, wherein the driving magnet system is configured to rotate the non-magnetized stir bar within the lysis chamber at at least 1000 rpm.~~

173. ~~The integrated diagnostic cartridge of claim 165, wherein the lysis agent is a mechanical agent.~~

174. ~~The integrated diagnostic cartridge of claim 173, wherein the mechanical agent is ceramic beads, glass beads or steel beads.~~

175. ~~The integrated diagnostic cartridge of claim 165, wherein the lysis agent is a chemical agent.~~

~~176.—The integrated diagnostic cartridge of claim 175, wherein the chemical agent is an anionic detergent, a cationic detergent, a non-ionic detergent or a chaotropic agent.~~

~~177.—The integrated diagnostic cartridge of claim 176, wherein the cartridge is configured for testing of one or more target pathogens that is a virus or a gram-negative bacterium.~~

5 ~~178.—The integrated diagnostic cartridge of claim 165, further comprising a fluid inlet in fluid communication with the lysis chamber and a fluid outlet in fluid communication with the lysis chamber and a filter assembly in fluid communication with the fluid outlet of the lysis chamber.~~

10 ~~179.—The integrated diagnostic cartridge of claim 165, further comprising a fluid inlet to the lysis chamber and a fluid outlet to lysis chamber wherein the lysis chamber is isolated from the other modules on the cartridge by a first frangible seal in fluid communication with the fluid inlet to the lysis chamber and a second frangible seal in fluid communication with the fluid outlet of the lysis chamber.~~

~~180.—The integrated diagnostic cartridge of claim 178 or claim 179 further comprising: a process control chamber having an inlet, an outlet and a plug comprising a process control wherein the process control chamber is in fluid communication with the lysis chamber inlet.~~

15 ~~181.—An integrated diagnostic cartridge, comprising:~~

~~a loading module;~~

~~a lysis module;~~

~~a purification module comprising~~claim 1, the purification module further comprising: a rotary valve comprising:

20 a. a stator comprising a stator face and a plurality of passages, each passage comprising a port at the stator face;

b. a rotor operably connected to the stator and comprising a rotational axis, a rotor valving face, and a flow channel having an inlet and an outlet at the rotor valving face, wherein the flow channel comprises a porous solid support; and

25 c.- _____ a retention element biasing the stator and the rotor together at a rotor-stator interface to form a fluid tight seal;~~and.~~

~~a reaction module;~~

~~wherein the loading module is in fluidic communication with the lysis module and the purification module is in fluidic communication with the reaction module.~~

~~182~~ 20. The integrated diagnostic cartridge of claim ~~181~~19, wherein the rotary valve further comprises a gasket between the stator face and the rotor valving face, and wherein the stator comprises a displaceable spacer for preventing the gasket from sealing against at least one of the rotor and stator, and wherein, when the spacer is displaced the gasket seals the rotor and stator together in a fluid-tight manner.

~~183~~21. The integrated diagnostic cartridge of claim ~~182~~20, wherein, when the cartridge is positioned within a diagnostic instrument, engagement with a ~~rotor driver~~valve drive assembly of the diagnostic instrument displaces the spacer and seals the rotor and stator together in a fluid-tight manner.

~~184~~22. The integrated diagnostic cartridge of claim ~~183~~, wherein a rotation movement performed by the rotor driver of the diagnostic instrument displaces the spacer and seals the rotor and the stator together in a fluid-tight manner.

~~185.—The integrated diagnostic cartridge of claim 181 further comprising at least one pair of ridges and spaces on a retention ring and at least one pair of ridges and spaces on the rotor wherein while the at least one pair of ridges and spaces of the retention ring is engaged with the at least one pair of ridges and spaces of the rotor sealing of the rotor and stator is prevented wherein, relative movement between the at least one pair of ridges and spaces on the retention ring and the at least one pair of ridges and spaces on the rotor seals the rotor and stator together in a fluid-tight manner.~~

~~186.—The integrated diagnostic cartridge of claim 185, wherein, when the cartridge is positioned within a diagnostic instrument, engagement with a rotor driver of the diagnostic instrument produces the relative movement between the at least two pairs of ridges and spaces on the retention ring and the rotor that seals the rotor and stator together in a fluid-tight manner.~~

~~187.—The integrated diagnostic cartridge of claim 186, wherein a rotation movement of less than one full rotation of the rotor performed by the rotor driver of the diagnostic instrument seals the rotor and stator together in a fluid-tight manner.~~

~~188.—The integrated diagnostic cartridge of any one of claims 185, 186 and 187 further comprising a gasket interposed at the rotor-stator interface.~~

~~189.—The integrated diagnostic cartridge of claim 181, wherein the rotary valve is maintained in a storage condition while a threaded portion of a retention ring is engaged with a threaded portion of the rotor wherein relative motion between the threaded portion of the retention ring and the threaded portion of the rotor seals the rotor and stator together in a fluid-tight manner.~~

~~190.—The integrated diagnostic cartridge of claim 189 wherein, when the cartridge is positioned within a diagnostic instrument, engagement with a rotor driver of the diagnostic instrument produces the relative movement between the threaded portion of the retention ring and the threaded portion of the rotor.~~

5 ~~191.—The integrated diagnostic cartridge of claim 190, wherein a rotation movement of less than one full rotation of the rotor performed by the rotor driver of the diagnostic instrument seals the rotor and stator together in a fluid-tight manner.~~

~~192.—The integrated diagnostic cartridge of any one of claim 189, claim 190 and claim 191 further comprising: a gasket interposed at the rotor-stator interface.~~

10 ~~193.—The integrated diagnostic cartridge of claim 181~~19, the purification module further comprising: a waste collection element, a wash buffer reservoir and an elution buffer reservoir.

~~194~~23. The integrated diagnostic cartridge of claim ~~181~~19 further comprising a pneumatic interface in fluidic communication with at least the purification module.

~~195.—The integrated diagnostic cartridge of claim 181 wherein the porous solid support is polymeric.~~

15 ~~196.—The integrated diagnostic cartridge of claim 181 wherein the porous solid support is selected from the group consisting of alumina, silica, celite, ceramics, metal oxides, porous glass, controlled pore glass, carbohydrate polymers, polysaccharides, agarose, Sepharose™, Sephadex™, dextran, cellulose, starch, chitin, zeolites, synthetic polymers, polyvinyl ether, polyethylene, polypropylene, polystyrene, nylons, polyacrylates, polymethacrylates, polyacrylamides, polymaleic anhydride, membranes, hollow~~
20 ~~fibers and fibers, and any combination thereof.~~

~~197.—The integrated diagnostic cartridge of claim 181 wherein the rotor valving face comprises a gasket interposed at the rotor-stator interface.~~

~~198.—The integrated diagnostic cartridge of claim 197 the gasket further comprising a fluid connector or a fluid selector comprising a volume dimensioned to provide an aliquot of liquid when filled.~~

25 ~~199.—The integrated diagnostic cartridge of claim 181 wherein the rotor comprises a plurality of flow channels, each flow channel comprising an inlet, an outlet, and a porous solid support.~~

~~200.—The integrated diagnostic cartridge of claim 181 the rotor valving face further comprising a fluid connector or a fluid selector comprising a volume dimensioned to provide an aliquot of liquid when filled.~~

201.—The integrated diagnostic cartridge of any one of claim 181 to claim 200, the purification module further comprising: a waste collection element, a wash buffer reservoir and an elution buffer reservoir.

202.—An integrated diagnostic cartridge, comprising:

a loading module;

a lysis module;

a purification module; and

a reaction module comprising a plurality of individual assay chambers, wherein at least one wall in each one of the plurality of individual assay chambers is provided by a plug comprising:

a body with a bottom surface;

a central opening in the body; and

a dried reagent on the bottom surface, wherein the body is formed from a material transmissive to excitation wavelengths and emission wavelengths in at least one of a red spectrum, a blue spectrum and a green spectrum;

wherein the loading module is in fluidic communication with the lysis module and the purification module is in fluidic communication with the reaction module.

203.—The integrated diagnostic cartridge of claim 202, wherein the bottom surface of the plug body comprises a cavity in the bottom surface with the dried reagent within the cavity, and wherein the plug has a plug thickness between a central opening bottom and the plug body bottom, and further wherein a depth of the cavity is less than 90% of the plug thickness, is less than 70% of the plug thickness or is less than 50% of the plug thickness.

204.—The integrated diagnostic cartridge of claim 202, wherein the plug has a polished or smooth finish facilitating the transmissivity of the excitation wavelengths and the emission wavelengths.

205.—The integrated diagnostic cartridge according to any one of claim 202, claim 203 and claim 204, wherein the dried reagent is selected from the group consisting of nucleic acid synthesis reagents, nucleic acids, nucleotides, nucleobases, nucleosides, monomers, detection reagents, catalysts or combinations thereof.

206.—The integrated diagnostic cartridge of claim 202 further comprising: a cartridge perimeter, wherein each one of the plurality of individual assay chambers is in communication with an air chamber and each air chamber is closer to the cartridge perimeter than the plug in each one of the plurality of individual assay chambers.

207.—The integrated diagnostic cartridge of claim 202 further comprising: a reaction area perimeter, wherein each one of the plurality of individual assay chambers is in communication with an air chamber and further wherein each plug in each one of the plurality of individual assay chambers is within the reaction area perimeter and each air chamber is outside of the reaction area perimeter.

208.—The integrated diagnostic cartridge of claim 202 further comprising: a cartridge perimeter and a reaction area perimeter wherein each one of the plurality of individual assay chambers is in communication with an air chamber and each air chamber is closer to the cartridge perimeter than the plug in each one of the plurality of individual assay chambers and is located outside of the reaction area perimeter and each one of the plurality of individual assay chambers is within the reaction area perimeter.

209.—The integrated diagnostic cartridge according to claim 202, wherein the body of the plug protrudes into the monolithic substrate of the assay chamber at a depth such that the assay chamber volume can be readily changed by altering the depth at which the body of the plug protrudes into the monolithic substrate of the assay chamber.

210.—The integrated diagnostic cartridge according to claim 202 further comprising at least one fluid inlet conduit to each one of the plurality of individual assay chambers of the reaction module wherein each one of the at least one fluid inlet conduits further comprises a heat staked region.

211.—The integrated diagnostic cartridge according to claim 210 wherein a heat stake in the heat staked region fluidically isolates the reaction module from the loading module, the lysis module, and the purification module.

212.—The integrated diagnostic cartridge according to any one of claim 202 to claim 211, wherein the dried reagent is a continuous film adhered to the plug bottom surface.

213.—The integrated diagnostic cartridge according to any one of claim 202 to claim 212, wherein the dried reagent is a lyophilized reagent.

214.—An integrated diagnostic cartridge, comprising:

a loading module;

a lysis module;

a purification module; and

a reaction module comprising one or more assay chambers, wherein each assay chamber comprises:

~~a. a tapered inlet;~~

~~a. a tapered outlet;~~

~~a. a plug comprising a bottom surface and a central opening in the body, wherein the body is formed from a material transmissive to excitation wavelengths and emission wavelengths in at least one of an ultraviolet spectrum, a blue spectrum, a green spectrum and a red spectrum;~~

~~a. two curved boundaries, wherein each curved boundary extends from the tapered inlet to the tapered outlet such that together, the two curved boundaries and the plug enclose a volume of the assay chamber; and~~

~~a. a shoulder extending from each curved boundary wherein the plug contacts each shoulder such that a boundary of the assay chamber is provided by the two curved boundaries, the shoulders extending from each of the curved boundaries and the plug.~~

~~215. The integrated diagnostic cartridge of claim 214, the plug as in any one of claim 203 to claim 213.~~

~~216. An integrated diagnostic cartridge, comprising:~~

~~a loading module;~~

~~a lysis module;~~

~~a purification module; and~~

~~a reaction module comprising:~~

~~a. a common fluid pathway, and~~

~~a. a plurality of independent, continuous fluidic pathways connected to the common fluid pathway, wherein each independent, continuous fluidic pathway comprising:~~

~~i. an assay chamber, and~~

~~i. a pneumatic compartment;~~

~~1. wherein the assay chamber is connected to the common fluid pathway, the assay chamber having a fluid volume defined in part by a plug having a dried reagent thereon; and~~

~~1. the pneumatic compartment, having a pneumatic volume, is connected to the common fluid pathway via the assay chamber;~~

~~wherein, each fluidic pathway of the plurality of independent, continuous fluidic pathways is a closed system excluding the connection between the assay chamber and common fluid source, wherein each assay chamber further comprises:~~

a. ~~a double tapered chamber, the double tapered chamber comprising:~~

ii. ~~a tapered inlet in fluidic communication with a terminus of the entry conduit of the fluidic pathway;~~

i. ~~a tapered outlet in fluidic communication with a terminus of the pneumatic compartment, and~~

i. ~~two curved boundaries, wherein each curved boundary extends from the tapered inlet to the tapered outlet such that together, the two curved boundaries enclose the volume of the assay chamber;~~

a. ~~a shoulder extending from each curved boundary wherein the plug contacts each~~

~~shoulder such that a boundary of the assay chamber is provided by the two curved~~

~~boundaries, the shoulders extending from each of the curved boundaries and the plug,~~

~~wherein the loading module is in fluidic communication with the lysis module and the purification module is in fluidic communication with the reaction module.~~

217. ~~The integrated diagnostic cartridge of claim 216, wherein the two curved boundaries are formed in a monolithic substrate or a fluidic card of the cartridge.~~

218. ~~The integrated diagnostic cartridge according to any one of claim 202 to claim 217, wherein the body of the plug protrudes into the monolithic substrate of the assay chamber at a depth such that the assay chamber volume can be readily changed by altering the depth at which the body of the plug protrudes into the monolithic substrate of the assay chamber.~~

219. ~~An integrated diagnostic cartridge, comprising:~~

~~a loading module;~~

~~a lysis module;~~

~~a purification module; and~~

~~a reaction module comprising a reagent storage component comprising a capsule capable of~~

~~holding a liquid or solid sample, said capsule comprising an opening, a closed end and a wall extending from the closed end to the opening, wherein the capsule is oval shaped and the wall is rounded, and wherein the closed end and wall define an interior volume having a substantially smooth surface;~~

~~wherein the loading module is in fluidic communication with the lysis module and the purification module is in fluidic communication with the reaction module.~~

220. ~~An integrated diagnostic cartridge, comprising:~~

a loading module;

a lysis module;

a purification module; and

a reaction module comprising a capsule capable of holding a liquid or a solid sample, said capsule comprising

an inner surface extending from the bottom of said capsule to an oval-shaped opening at the top of the capsule, wherein said inner surface is substantially smooth and comprises a concave shape extending from the bottom of the capsule; and

a planar layer affixed around the oval-shaped opening of said capsule and oriented in the same plane as the oval-shaped opening of said capsule, wherein said planar layer comprises a top surface and a bottom surface, said top surface aligned with the inner surface of said capsule at said oval-shaped opening to provide a continuous surface;

wherein the loading module is in fluidic communication with the lysis module and the purification module is in fluidic communication with the reaction module.

221.—An integrated diagnostic cartridge of claim 219 or claim 220 wherein said capsule is capable of holding a volume from approximately 50 μ L to approximately 200 μ L or wherein said oval-shaped opening is contained within an area of 9 mm x 9 mm.

222.—An integrated diagnostic cartridge of claim 219 or claim 220 wherein said capsule comprises a dried reagent according to any one of claim 205, claim 212 or claim 213.

223.—The integrated diagnostic cartridge according to any one of claim 137 to claim 222 further comprising a fluidic card and a cover.

224.—The integrated diagnostic cartridge of claim 223, wherein at least two of the loading module, the lysis module, the purification module and the reaction module are formed in or supported by the fluidic card.

225.—The integrated diagnostic cartridge of claim 223, wherein at least two of the loading module, the lysis module, the purification module and the reaction module are formed in or supported by the cover.

226.—The integrated diagnostic cartridge of claim 223, the fluidic card further comprising a slot positioned to engage with a latch and pin assembly of a diagnostic instrument to secure the integrated diagnostic cartridge in a testing position within the diagnostic instrument.

~~227.—The integrated diagnostic cartridge of claim 223 further comprising an interference feature on the cover, wherein the interference feature is sized and positioned to interact with one of an upper rail or a lower rail of a loading apparatus of a diagnostic instrument.~~

~~228.—The integrated diagnostic cartridge according to any one of claim 223 to claim 227, wherein a thickness of the fluidic card is selected for sliding arrangement within an upper rail and a lower rail of a loading apparatus of the diagnostic instrument.~~

~~229.—The integrated diagnostic cartridge of any one of claim 137 to claim 228 wherein a total sample process volume of the integrated diagnostic cartridge is provided by increasing the thickness of the cartridge.~~

~~230.—The integrated diagnostic cartridge of claim 229, wherein a diagnostic instrument is adapted and configured to accommodate the increased thickness of the cartridge by increasing a width of an opening of the diagnostic instrument to accommodate the increased thickness of the cartridge or a displacement range of a cartridge clamping system of the diagnostic instrument is adapted to accommodate the increased thickness of the cartridge.~~

~~231.—The integrated diagnostic cartridge of any one of claim 137 to claim 230 further comprising a cartridge front face and a cartridge rear face forming an upper spacing and a lower spacing wherein each of the upper spacing and the lower spacing is sized and positioned to engage with an upper rail and a lower rail of the instrument.~~

~~232.—The integrated diagnostic cartridge of claim 231 further comprising an interference feature within the upper spacing or the lower spacing positioned to ensure the cartridge engages with the upper rail and the lower rail in a desired orientation.~~

~~233.—The integrated diagnostic cartridge of any one of claim 137 to claim 232 further comprising a plurality of frangible seal chambers in fluid communication with at least one or more of the loading module, the lysis module, the purification module or the reaction module.~~

~~234.—The integrated diagnostic cartridge of any one of claim 137 to claim 233 further comprising a label section.~~

~~235.—The integrated diagnostic cartridge of any one of claim 137 to claim 234 further comprising one or more machine readable marking indicating the sample type to be used in the cartridge or target pathogen to be detected.~~

236.—The integrated diagnostic cartridge of any one of claim 137 to claim 235 further comprising a pneumatic interface.

237.—The integrated diagnostic cartridge of any one of claim 137 to claim 236 wherein prior to loading the cartridge into a diagnostic instrument a lysis chamber in the cartridge contains a lysis buffer.

5 238.—The integrated diagnostic cartridge of any one of claim 137 to claim 237, the integrated diagnostic cartridge further comprising a machine-readable code adapted and configured to identify the cartridge to a diagnostic instrument or a patient identification marking.

239.—The integrated diagnostic cartridge of claim 217 or claim 218 further comprising a film adhered to a surface of the monolithic substrate, wherein the film forms one wall of the assay chamber.

10 240.—The integrated diagnostic cartridge of any one of claim 137 to claim 239, further comprising a first film adhered to a surface of at least a portion of the cartridge, wherein the first film forms one wall of one or more chambers, compartments, or fluid conduits of the loading module, the lysis module, the purification module and the reaction module.

15 241.—The integrated diagnostic cartridge of claim 240, further comprising a second film adhered to the first film, wherein the second film has a higher melting temperature than the first film.

242.—The integrated diagnostic cartridge of claim 241 further comprising a heat staked region formed in each of the fluidic pathways using the first film or the second film wherein the heat staked region seals off the common fluid pathway from the assay chamber and the pneumatic chamber.

20 243.—The integrated diagnostic cartridge of claim 242 further comprising a raised platform within each of the plurality of independent, continuous fluidic pathways the raised platform positioned between an inlet to the assay chamber and the common fluid pathway wherein the heat staked region is formed using a portion of the raised platform.

244.—An integrated diagnostic cartridge, comprising:

25 a loading module having a fill chamber within the cartridge having a volume sufficient to hold a sample, a fluid inlet in fluid communication with the fill chamber, a fluid outlet in fluid communication with fill chamber;

a lysis module;

a purification module; and

a reaction module;

~~wherein the loading module is in fluidic communication with the lysis module and the purification module is in fluidic communication with the reaction module;~~

~~further wherein the loading module, the lysis module, the purification module and the reaction module are arranged for use while the cartridge is in a vertical orientation; and~~

~~further wherein when the cartridge is in a horizontal sample loading orientation the fluid inlet accesses the fill chamber via an upper surface of the cartridge and when the cartridge is in a vertical sample processing orientation the fluid inlet is positioned adjacent to an upper portion of the fill chamber and the fluid outlet is arranged for the sample to flow out of a lower portion of the fill chamber.~~

245.—The integrated diagnostic cartridge of claim 244 further comprising one or more fluid filling conduits arranged to flow into an upper portion of a vertically oriented chamber within a fluidic card of the integrated diagnostics cartridge and one or more fluid outlet conduits arranged to flow out of a lower portion of the vertically oriented chamber within the fluidic card of the integrated diagnostics cartridge.

246.—The integrated diagnostic cartridge of claim 245, wherein the vertically oriented chamber further comprises a filter assembly in fluid communication with a fluid outlet conduit of the vertically oriented chamber.

247.—The integrated diagnostic cartridge of claim 244, wherein the lysis module comprises a mixing assembly having a vertically oriented lysis chamber containing a lysis agent and a non-magnetized stir bar.

248.—The integrated diagnostic cartridge of claim 247, wherein the non-magnetized stir bar is made from a metal having a magnetic permeability to be responsive to a rotating magnetic field induced between a drive magnetic element and a driven magnetic element of a magnetic drive system.

249.—The integrated diagnostic cartridge according to claim 247, wherein the non-magnetized stir bar is coated with an impermeable material to prevent corrosion by a chemical lysis buffer in the vertically oriented lysis chamber.

250.—The integrated diagnostic cartridge of claim 247 wherein, when in use within a diagnostic instrument, the non-magnetized stir bar is disposed between a driving magnet system and a driven magnet system of a magnetic mixing assembly in the diagnostic instrument, wherein the driving magnet

system is configured to rotate the non-magnetized stir bar within the vertically oriented lysis chamber at least 1000 rpm.

251. — The integrated diagnostic cartridge of claim 247, further comprising a fluid inlet to the vertically oriented lysis chamber and a fluid outlet to lysis chamber wherein the vertically oriented lysis chamber is isolated from the other modules on the cartridge by a first frangible seal in fluid communication with the fluid inlet to the vertically oriented lysis chamber and a second frangible seal in fluid communication with the fluid outlet to the vertically oriented lysis chamber.

252. — The integrated diagnostic cartridge according to claim 244 further comprising a fluidic card and a cover.

253. — The integrated diagnostic cartridge of claim 252, wherein the fluidic card further comprises a first film adhered to a surface of at least a portion of the fluidic card, wherein the first film forms one surface of one or more chambers, compartments, or fluid conduits of the loading module, the lysis module, the purification module and the reaction module.

254. — The integrated diagnostic cartridge of claim 252 further comprising an interference feature on the cover, wherein the interference feature is sized and positioned to interact with one of an upper rail or a lower rail of a loading apparatus of a diagnostic instrument.

255. — The integrated diagnostic cartridge according to claim 254, wherein a thickness of the fluidic card is selected for sliding arrangement within an upper rail and a lower rail of a loading apparatus of the diagnostic instrument.

256. — The integrated diagnostic cartridge of claim 252 wherein a total sample process volume of the integrated diagnostic cartridge is related to a thickness of the cartridge corresponding to a spacing between the one or more chambers, compartments, or fluid conduits of the loading module, the lysis module, the purification module and the reaction module formed in the fluidic card and the first film.

257. — The integrated diagnostic cartridge of claim 256, wherein a diagnostic instrument is adapted and configured to accommodate a variation of the thickness of the cartridge by increasing a width of a loading slot of the diagnostic instrument to accommodate the increased thickness of the cartridge or a displacement range of a cartridge clamping system of the diagnostic instrument is adapted to accommodate the increased thickness of the cartridge.

258. — The integrated diagnostic cartridge of claim 254 further comprising a cartridge front face and a cartridge rear face forming an upper spacing and a lower spacing wherein each of the upper spacing and

the lower spacing is sized and positioned to engage with the upper rail and lower rail of the diagnostic instrument.

~~259.—The integrated diagnostic cartridge of claim 258 further comprising an interference feature within the upper spacing or the lower spacing positioned to ensure the cartridge engages with the upper rail and the lower rail in a desired orientation.~~

~~260.—The integrated diagnostic cartridge of claim 244 further comprising a plurality of frangible seal chambers in fluid communication with at least one or more of the loading module, the lysis module, the purification module or the reaction module.~~

~~261.—The integrated diagnostic cartridge of claim 244, the integrated diagnostic cartridge further comprising a machine-readable code adapted and configured to identify the cartridge to a diagnostic instrument or an image of a patient identification marking.~~

~~262~~24. An integrated diagnostic cartridge, comprising:

a loading module;

a lysis module;

a purification module comprising a rotary valve comprising:

a. a stator comprising a stator face and a plurality of passages, each passage comprising a port at the stator face;

b. a rotor operably connected to the stator and comprising a rotational axis, a rotor valving face, and a flow channel having an inlet and an outlet at the rotor valving face, wherein the flow channel comprises a porous solid support; and

c. a retention element biasing the stator and the rotor together at a rotor-stator interface to form a fluid tight seal; and

a reaction module comprising a plurality of individual assay chambers, wherein at least one surface in each one of the plurality of individual assay chambers is provided by a plug comprising:

a body with a bottom surface;

a central opening in the body; and

a dried reagent on the bottom surface, wherein the body is formed from a material transmissive to excitation wavelengths and emission wavelengths in at least one of a red spectrum, a blue spectrum and a green spectrum,

further wherein the loading module is in fluidic communication with the lysis module and the purification module is in fluidic communication with the reaction module; and wherein the loading module, the lysis module, the purification module and the reaction module are arranged for use while the cartridge is in a vertical orientation.

26325. The integrated diagnostic cartridge of claim **26224**, wherein the bottom surface of the plug body comprises a cavity in the bottom surface with the dried reagent within the cavity, and wherein the plug has a plug thickness between a central opening bottom and the plug body bottom, and further wherein a depth of the cavity is less than 90% of the plug thickness, is less than 70% of the plug thickness or is less than 50% of the plug thickness.

26426. The integrated diagnostic cartridge of claim **26224**, wherein the plug has a polished or smooth finish facilitating the transmissivity of the excitation wavelengths and the emission wavelengths.

26527. The integrated diagnostic cartridge according to claim **26224**, wherein the dried reagent is selected from the group consisting of nucleic acid synthesis reagents, nucleic acids, nucleotides, nucleobases, nucleosides, monomers, detection reagents, catalysts or combinations thereof.

26628. The integrated diagnostic cartridge according to claim **26224**, wherein the body of the plug protrudes into the monolithic substrate of the assay chamber at a depth such that the assay chamber volume can be readily changed by altering the depth at which the body of the plug protrudes into the monolithic substrate of the assay chamber.

26729. The integrated diagnostic cartridge according to claim **26224** further comprising at least one fluid inlet conduit to each one of the plurality of individual assay chambers of the reaction module wherein each one of the at least one fluid inlet conduits further comprises a heat staked region.

26830. The integrated diagnostic cartridge according to claim **26729** wherein a heat stake in the heat staked region fluidically isolates the reaction module from the loading module, the lysis module, and the purification module.

269.—The integrated diagnostic cartridge according to claim 244, the purification module further comprising: a rotary valve comprising:

a.—a stator comprising a stator face and a plurality of passages, each passage comprising a port at the stator face;

b.—a rotor operably connected to the stator and comprising a rotational axis, a rotor valving face, and a flow channel having an inlet and an outlet at the rotor valving face, wherein the flow channel comprises a porous solid support; and

c.—a retention element biasing the stator and the rotor together at a rotor-stator interface to form a fluid-tight seal.

270.—The integrated diagnostic cartridge of claim 269, wherein the rotary valve further comprises a gasket between the stator face and the rotor valving face, and wherein the stator comprises a displaceable spacer for preventing the gasket from sealing against at least one of the rotor and stator, and wherein, when the spacer is displaced the gasket seals the rotor and stator together in a fluid-tight manner.

271.—The integrated diagnostic cartridge of claim 270, wherein, when the cartridge is positioned within a diagnostic instrument, engagement with a valve-drive assembly of the diagnostic instrument displaces the spacer and seals the rotor and stator together in a fluid-tight manner.

272.—The integrated diagnostic cartridge of claim 269, the purification module further comprising: a waste-collection element, a wash-buffer reservoir and an elution-buffer reservoir.

273.—The integrated diagnostic cartridge of claim 269 further comprising a pneumatic interface in fluidic communication with at least the purification module.

274.—A method of testing a sample suspected of containing one or more target pathogens, comprising:

accepting a cartridge having a sample port assembly containing the sample suspected of containing the one or more target pathogens;

advancing the sample suspected of containing the one or more target pathogens to a lysis chamber within the cartridge having at least one lysis reagent therein;

mixing the sample with the at least one lysis agent to generate a lysed sample;

passing the lysed sample through a porous solid support within the cartridge to capture a nucleic acid on the porous solid support;

releasing the captured nucleic acid from the first porous solid support to generate an enriched nucleic acid;

introducing the enriched nucleic into a rehydration chamber within the cartridge containing one or more dried reagents;

5 after introducing the analyte/reagent solution into a metering channel, mixing the contents of the rehydration chamber to produce an analyte/reagent solution;

distributing the analyte/reagent solution to two or more assay chambers within the cartridge after performing the mixing step;

10 combining the analyte/reagent solution with one or more amplification reagents after performing the distributing step;

sealing each one of the two or more assay chambers within the cartridge containing analyte/reagent solution from each one of all the other two or more assay chambers within the cartridge containing analyte/reagent solution and a waste chamber; and

15 performing an isothermal amplification reaction within each one of the two or more assay chambers in the cartridge while simultaneously detecting amplification product, wherein presence of an amplification product is an indication of a presence, an absence or a quantity of the target pathogen in the sample suspected of containing the target pathogen.

275.—The method of testing a sample according to claim 274, wherein in mixing the sample with the at least one lysis agent, the lysis agent is a mechanical agent.

20 276.—The method of testing a sample according to claim 275, wherein the mechanical agent is ceramic beads, glass beads or steel beads, and the mixing the sample step comprises rotating a stir bar within the lysis chamber at at least 1000 rpm.

277.—The method of testing a sample according to claim 276, wherein mixing the sample comprises rotating the stir bar or the ceramic, glass or steel beads along with a chemical lysis agent.

25 278.—The method of testing according to claim 274, wherein the at least one lysis agent is a chemical lysis agent.

279.—The method of testing a sample according to claim 278, wherein the one or more target pathogens is a virus or a gram negative bacterium and the lysis reagent is a chaotropic agent.

280.—The method of testing a sample according to claim 274, wherein prior to passing the lysed sample through the porous solid support, the method further comprises passing the lysed sample through a size exclusion filter, wherein nucleic acid passes through the filter.

281.—The method of testing a sample according to claim 274, wherein the enriched nucleic acid is combined with one or more amplification reagents before the distributing step and further wherein the one or more amplification reagents comprise a primer.

282.—The method of testing a sample according to claim 281, wherein the performing of the isothermal amplification reaction step is initiated prior to the distributing the enriched nucleic acid to the two or more assay chambers step.

283.—The method of testing a sample according to claim 274, wherein after the distributing step, but prior to performing the isothermal amplification reaction step, the method further comprises combining the enriched nucleic acid with a primer set specific to one of the one or more target pathogens.

284.—The method of testing a sample according to claim 274, wherein a first assay chamber contains a primer set specific to a first nucleic acid sequence.

285.—The method of testing a sample according to claim 284, wherein the first nucleic acid sequence is present in one of the one or more target pathogens.

286.—The method of testing a sample according to claim 284, wherein prior to mixing the sample with at least one lysis agent, a process control is added to the sample and the first nucleic acid sequence is present in the process control.

287.—The method of testing a sample according to claim 284, wherein prior to passing lysed sample through the porous solid support, a process control is added to the lysed sample and the first nucleic acid sequence is present in the process control.

288.—The method of testing a sample according to claim 284, wherein a second assay chamber contains a primer set specific to a second nucleic acid sequence, wherein the second nucleic acid sequence is present in one of the one or more target pathogens.

289.—The method of testing a sample according to claim 274, wherein the performing an isothermal amplification reaction step is completed in less than 15 minutes.

290.—The method of testing a sample according to claim 274, further comprising: providing a result containing a determination made during the performing step relating to the presence, the absence or the quantity of the target pathogen in the sample suspected of containing the target pathogen.

291.—The method of testing a sample according to claim 274, wherein the method further comprises, prior to advancing the sample to a lysis chamber, pretreating the sample with a chemical reaction.

292.—The method of testing a sample according to claim 291, wherein the sample is sputum and the chemical reaction is incubation with a mucolytic agent.

5 293.—The method of testing a sample according to claim 274, wherein the method further comprises, prior to advancing the sample to a lysis chamber, pretreating the sample with an enzymatic reaction.

294.—The method of testing a sample according to claim 293, wherein the enzymatic reaction is incubation of the sample with a nuclease, a protease, an amylase, a glycosylase, or a lipase.

10 295.—The method of testing a sample according to claim 274, wherein the method further comprises, prior to advancing the sample to a lysis chamber, pretreating the sample with a physical treatment.

296.—The method of testing a sample according to claim 295, wherein the physical treatment comprises passing the sample through a size-exclusion filter in a first direction.

297.—The method of testing a sample according to claim 295, wherein the physical treatment comprises exposing the sample to a capture agent immobilized on a solid substrate.

15 298.—The method of testing a sample according to claim 297, further comprising, after exposure, separating the solid substrate from the sample.

299.—The method of testing a sample according to claim 297, wherein the capture agent is an antibody with affinity for red blood cells.

20 300.—The method of testing a sample according to claim 274, wherein the sample is sputum and the method further comprises, prior to mixing the sample with the at least one lysis reagent, bead beating the sputum to liquify the sample.

301.—The method of testing a sample according to claim 300, wherein the bead beating comprises mixing the sputum with ceramic, glass, or steel beads.

25 302.—The method of testing a sample according to claim 274, wherein prior to distributing the enriched nucleic acid to the assay chambers, the method further comprises passing the enriched nucleic acid through a second porous solid support.

303.—A method of testing a sample suspected of containing one or more target pathogens, comprising:

accepting a cartridge having a sample port assembly containing the sample suspected of containing the one or more target pathogens;

advancing the sample suspected of containing the one or more target pathogens to a lysis chamber within the cartridge having at least one lysis reagent therein;

mixing the sample with the at least one lysis agent to generate a lysed sample;

passing the lysed sample through a porous solid support within the cartridge to capture a nucleic acid on the porous solid support;

releasing the captured nucleic acid from the first porous solid support to generate an enriched nucleic acid;

introducing the enriched nucleic into a rehydration chamber within the cartridge containing one or more dried reagents to generate an analyte/reagent solution;

after introducing the analyte/reagent solution into a metering channel, mixing the contents of the rehydration chamber to homogenize an analyte/reagent solution;

distributing the analyte/reagent solution to two or more assay chambers within the cartridge after performing the mixing step;

combining the analyte/reagent solution with one or more amplification reagents after performing the distributing step to generate an amplification solution;

sealing each one of the two or more assay chambers within the cartridge containing amplification solution from each one of all the other two or more assay chambers within the cartridge containing amplification solution and a waste chamber; and

performing an isothermal amplification reaction within each one of the two or more assay chambers in the cartridge while simultaneously detecting amplification product, wherein presence of an amplification product is an indication of a presence, an absence or a quantity of the target pathogen in the sample suspected of containing the target pathogen.

304.—The method of testing a sample according to claim 303, wherein in mixing the sample with the at least one lysis agent, the lysis agent is a mechanical agent.

305.—The method of testing a sample according to claim 304, wherein the mechanical agent is ceramic beads, glass beads or steel beads, and the mixing the sample step comprises rotating a stir bar within the lysis chamber at at least 1000 rpm.

306.—The method of testing a sample according to claim 305, wherein mixing the sample comprises rotating the stir bar or the ceramic, glass or steel beads along with a chemical lysis agent.

307.—The method of testing according to claim 303, wherein the at least one lysis agent is a chemical lysis agent.

5 308.—The method of testing a sample according to claim 307, wherein the one or more target pathogens is a virus or a gram-negative bacterium and the lysis reagent is a chaotropic agent.

309.—The method of testing a sample according to claim 303, wherein prior to passing the lysed sample through the porous solid support, the method further comprises passing the lysed sample through a size exclusion filter, wherein nucleic acid passes through the filter.

10 310.—The method of testing a sample according to claim 303, wherein a first assay chamber contains a primer set specific to a first nucleic acid sequence.

311.—The method of testing a sample according to claim 310, wherein the first nucleic acid sequence is present in one of the one or more target pathogens.

15 312.—The method of testing a sample according to claim 310, wherein prior to mixing the sample with at least one lysis agent, a process control is added to the sample and the first nucleic acid sequence is present in the process control.

313.—The method of testing a sample according to claim 310, wherein prior to passing lysed sample through the porous solid support, a process control is added to the lysed sample and the first nucleic acid sequence is present in the process control.

20 314.—The method of testing a sample according to claim 310, wherein a second assay chamber contains a primer set specific to a second nucleic acid sequence, wherein the second nucleic acid sequence is present in one of the one or more target pathogens.

315.—The method of testing a sample according to claim 303, wherein the performing an isothermal amplification reaction step is completed in less than 15 minutes.

25 316.—The method of testing a sample according to claim 303, further comprising: providing a result containing a determination made during the performing step relating to the presence, the absence or the quantity of the target pathogen in the sample suspected of containing the target pathogen.

317.—The method of testing a sample according to claim 303, wherein the method further comprises, prior to advancing the sample to a lysis chamber, pretreating the sample with a chemical reaction.

318.—The method of testing a sample according to claim 317, wherein the sample is sputum and the chemical reaction is incubation with a mucolytic agent.

319.—The method of testing a sample according to claim 303, wherein the method further comprises, prior to advancing the sample to a lysis chamber, pretreating the sample with an enzymatic reaction.

5 320.—The method of testing a sample according to claim 319, wherein the enzymatic reaction is incubation of the sample with a nuclease, a protease, an amylase, a glycosylase, or a lipase.

321.—The method of testing a sample according to claim 303, wherein the method further comprises, prior to advancing the sample to a lysis chamber, pretreating the sample with a physical treatment.

10 322.—The method of testing a sample according to claim 321, wherein the physical treatment comprises passing the sample through a size-exclusion filter in a first direction.

323.—The method of testing a sample according to claim 321, wherein the physical treatment comprises exposing the sample to a capture agent immobilized on a solid substrate.

324.—The method of testing a sample according to claim 323, further comprising, after exposure, separating the solid substrate from the sample.

15 325.—The method of testing a sample according to claim 323, wherein the capture agent is an antibody with affinity for red blood cells.

326.—The method of testing a sample according to claim 303, wherein the sample is sputum and the method further comprises, prior to mixing the sample with the at least one lysis reagent, bead beating the sputum to liquify the sample.

20 327.—The method of testing a sample according to claim 326, wherein the bead beating comprises mixing the sputum with ceramic, glass, or steel beads.

328.—The method of testing a sample according to claim 303, wherein prior to distributing the analyte/reagent solution to the two or more assay chambers, the method further comprises passing the analyte/reagent solution through a second porous solid support.

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