

[0022] The portion of the sampling line 24 between the two filtered lines 32, 34 is fitted to a bi-directional pump 30 (e.g., a peristaltic pump) to help drive the fluid either into one of the sample containers B-1-B-5 or back into the vessel 20, depending on the open/closed position of the valves 1-14 and the rotational direction of the pump head 30.

[0023] Other, alternative arrangements may be used. For example, FIG. 3 shows an alternative to the arrangement shown in FIG. 1 in which the sample containers B-1-B-5 are connected to a common node with a rotary valve 36 disposed at the node for selectively opening one of the sample containers connected to the node while the other sample containers remain closed.

[0024] The aseptic sample withdrawal system described herein includes the dual-filter design that allows the system to be selectively opened to atmosphere without jeopardizing the sterility of the closed system, thereby allowing the culture fluid trapped in the sampling line 24 to be pumped back into the vessel 20 or into one of the sample containers B-1-B-5 by alternating the flow direction within the sampling line 24 after the desired amount has been captured in the selected sample container. This eliminates the wasteful purge step, which can affect the final harvest volume, especially for smaller working volumes, as well as the unsanitary waste reservoir, where cells can die and lyse. The added advantage is that any bi-directional (e.g., peristaltic) pump can be used with this system, since there is no purge step and therefore no limitation in tubing size. The flexibility in tubing size used in the system also enables the user to choose from a wide variety of tube welding or aseptic connection options.

[0025] A sampling procedure for the system as shown in FIGS. 1-3, which can be automated by a computer controller or manipulated manually, is shown by flow chart 50 in FIG. 4 and described below. The procedure is described with respect to the sampling system shown in FIG. 1.

[0026] In step 52, the sampling line 24 is purged to ensure there is no residual fluid in the sampling line 24 by pumping residual fluid from the sampling line 24 back into the vessel 20. In the system of FIG. 1, step 52 is performed by: (a) closing sampling line 24 on the sampling side of the pump by closing valve 4, (b) venting the sample side of the sampling line 24 by opening valve 3 of the sample side vent line 34, (c) opening the sampling line 24 on the vessel side of the pump 30 by opening valve 1, (d) closing the sample side venting line 32 by closing valve 2, and then (e) operating pump 30 in direction B to pump any residual fluid contained in the sampling line 24 into the vessel 20. Steps (a) through (d) do not necessarily need to be performed in the order listed, but step (e), operating the pump, should not be performed until all the valves are opened or closed, as required. Although valve 4 closes off the sampling line to all of the sampling containers B-1 through B-5, valves 5-14, which are downstream of valve 4, may also be closed to redundantly close off the sample containers

[0027] In step 54, a prescribed volume of sample material is withdrawn from the vessel 20 and is deposited in one of the sample containers B-1 through B-5. In the system of FIG. 1, step 54 is performed by: (a) opening the vessel side of the sampling line 24 by opening valve 1, (b) opening the sample side of the sampling line 24 by opening valve 4, (c) closing both vessel side vent line 32 and sample side vent line 34 by closing valves 2 and 3, respectively, (d) opening the first sample container B-1 by opening valve 5, (e) closing the remaining sample containers B-2 through B-5 by closing

valve 6, and then (f) operating the pump 30 in the direction A for a prescribed period of time (or a prescribed number of revolutions) to transfer a prescribed volume of sample material from the vessel 20 into the container B-1. Steps (a) through (e) do not necessarily need to be performed in the order listed, but step (f), operating the pump, should not be performed until all the valves are opened or closed, as required.

[0028] In step 56, any residual sample fluid in the sampling line 24 is pumped back into the vessel 20. In the system of FIG. 1, step 56 is performed by: (a) closing off the sample side of the sampling line 24 by closing valve 4 and/or valve 5, (b) venting the sample side of the sampling line 24 by opening valve 3 of sample side vent line 34, (c) closing valve 2 of the vessel side vent line 32, (d) opening the vessel side of the sampling line 24 by opening valve 1, and (e) operating pump 30 in direction B to move fluid from the sampling line 24 back into the vessel 20 without removing any fluid from container B-1. Again, the order in which the steps are performed, other than operation of the pump, is not necessarily critical.

[0029] In step 58, any remaining residual fluid downstream of valve 4 and/or valve 5 is purged from the sampling line 24. In the system of FIG. 1, step 58 is performed by: (a) closing off the vessel side of the sampling line 24 by closing valve 1, (b) venting the vessel side of the sampling line 24 by opening valve 2 of vessel side vent line 32, (c) closing sample side vent 34 by closing valve 3, (d) opening the container B-1 by opening valves 4 and 5, (e) closing the remaining sample containers B-2 through B-5 by closing valve 6, and then (f) operating pump 30 in direction A to remove any remaining fluid from the sampling line 24 into the sample container B-1 without withdrawing any additional fluid from the vessel 20. Again, the order in which the steps are performed, other than operation of the pump, is not necessarily critical.

[0030] In step 60, the just-filled sample container B-1 is removed from the system. Step 60 is performed by closing the valve 5 and cutting or otherwise removing sample container B-1 from the system.

[0031] Steps 52 to 62 are repeated for each of the other sample containers to be filled. Implementation of the steps differs somewhat in that different valves must be operated to fill different sample containers. For example, to fill sample container B-2, valves 6 and 7 are opened while valves 5 and 8 remain closed. To fill sample vessel B-3, valves 6, 8, and 9 are opened while valves 5, 7, and 10 are closed. To fill sample container B-4, valves 6, 8, 10, and 11 are opened while valves 5, 7, 9, and 12 are closed. And to fill sample container B-5, valves 6, 8, 10, 12, and 13 are opened while valves 5, 7, 9, 11, and 14 are closed.

[0032] In an alternative procedure, the order of steps 56 and 58 can be reversed. That is, after performing step 54, step 58 can be performed with the system of FIG. 1 by: (a) closing off the vessel side of the sampling line 24 by closing valve 1 and (b) venting the vessel side of the sampling line 24 by opening valve 2 of vessel side vent line 32 while (d) continuing to operate pump 30 in direction A to pump remaining fluid from the sampling line 24 into the sample container B-1 without withdrawing any additional fluid from the vessel 20. After step 58, step 56 can be performed with the system of FIG. 1 by: (a) closing off the sample side of the sampling line 24 by closing valve 4 and/or valve 5, (b) venting the sample side of the sampling line 24 by opening valve 3 of sample side vent line 34, (c) closing valve 2 of the vessel side vent line 32, (d) opening the vessel side of the sampling line 24 by opening