[0006] Some manufacturers of automated inspection equipment for pharmaceutical products have proposed, and implemented, techniques that attempt to address these problems. For example, U.S. Patent No. 8,036,444 (Nielsen), entitled "Method and System for Irradiating and Inspecting Liquid-Carrying Containers," describes an imaging system in which two line scan cameras generate flattened images of a spinning container. One camera is aligned with the central axis of the container, while the other camera is offset from the central axis. The technique leverages the basic principle that, when the container is rotated, particles on the outside of a container will move a longer distance horizontally (i.e., in a direction orthogonal to the container central axis) than particles inside the container. Images from the two line scan cameras are compared after multiple images have been acquired at different rotations, and the distances between particles are computed. This distance can in some cases be used to distinguish particles on the inside and outside of the container.

[0007] As another example, European Patent No. 3,062,292 (Kwoka), entitled "Inspection Method and Inspection Device for Monitoring Production Processes," describes an imaging system that uses a single area scan camera. When a particle is detected at a position along the central axis of the container, the position is digitally shifted to a point where it would be if it were on the outside of the container and the container were precisely rotated about its central axis a preset angle (~45^{o}). The container is then rotated and a new image is taken. If the particle is in fact on the outside of the container, it should overlap with the digitally shifted image. If the particle is instead inside the container, it will be offset from the digitally shifted particle by some amount.

[0008] While the techniques of U.S. Patent No. 8,036,444 (Nielsen) and European Patent No. 3,062,292 (Kwoka) may improve upon the conventional image subtraction method described above in some respects, both approaches have significant drawbacks of their own. One difficulty is that, with both approaches, any slight vibration of the container between images can cause significant errors. Moreover, if a particle on the inside of the container "slips" while the container is rotated, it may not be in the expected position to be properly detected. Furthermore, limitations on the spatial resolution of imagers may make the techniques insufficient to distinguish small blemishes inside the glass, which can be a large source of false rejects.

[0009] Further, while promising 3D imaging techniques are being developed and offer the ability to determine particle size and morphology from images, they are very computationally expensive, and may not work at typical manufacturing line rates (e.g., 300 to 600 containers per minute). Accordingly, there remains a need for improved methods to detect particles inside liquid-filled drug product containers, particularly (but not only) for containers holding highly viscous samples/products.

SUMMARY

[0009a] According to a first aspect of the present invention, there is provided a method for imaging a container holding a sample, the method comprising: illuminating the container with a laser sheet that impinges upon the container in a first direction corresponding to a first axis, wherein a plane of the laser sheet is defined by the first axis and a second axis orthogonal to the first axis; moving the container through a plurality of rotations, about a central axis of the container, while illuminating the container with the laser sheet; capturing, by an imager having an imaging axis that is substantially orthogonal to at least the first axis, ~~an~~ a plurality of images of the container, with each image corresponding to a respective one of the plurality of rotations; and analyzing, by one or more processors, the plurality of images of the container to detect particles within, and/or on an exterior surface of, the container, wherein analyzing the plurality of images includes: identifying an object appearing between walls of the container, in a first image corresponding to a first rotation of the container, as a candidate particle, and determining whether the candidate particle is an actual particle based on whether the object appears in additional images corresponding to other rotations of the container, wherein the determining includes determining that the candidate particle is not an actual particle when the object appears in the additional images, and determining that the candidate particle is an actual particle when the object does not appear in the additional images.

[0009b] According to a second aspect of the present invention, there is provided an imaging system comprising: ~~positioning means for positioning a container;~~ illumination means for generating a laser sheet that impinges upon ~~the~~ a container in a first direction corresponding to a first axis, wherein a plane of the laser sheet is defined by the first axis and a second axis orthogonal to the first axis; ~~and~~ positioning means for positioning the container, wherein the positioning means moves the container through a plurality of rotations, about a central axis of the container, while the illumination means illuminates the container with the laser sheet; imaging means for capturing ~~one or more~~ a plurality of images of the container, with each image corresponding to a respective one of the plurality of rotations, the means for capturing ~~one or more~~ the plurality of images of the container having an imaging axis that is substantially orthogonal to at least the first axis.; and processing means for analyzing the plurality of images of the container to detect particles within, and/or on an exterior surface of, the container, wherein analyzing the plurality of images includes identifying an object appearing between walls of the container, in a first image corresponding to a first rotation of the container, as a candidate particle, and determining whether the candidate particle is an actual particle based on whether the object appears in additional images corresponding to other rotations of the container, wherein the determining includes determining that the candidate particle is not an actual particle when the object appears in the additional images, and determining that the candidate particle is an actual particle when the object does not appear in the additional images.

[0010] Embodiments described herein relate to systems and methods that improve upon conventional automated visual inspection techniques. In particular, an imaging system illuminates a container with a relatively thin sheet of laser light, with the laser sheet impinging upon the container from a direction substantially orthogonal to the imaging axis of the camera. The laser sheet may pass through the central axis of the container, for example. With this lighting configuration, particles can only be seen in the resulting image (or can only be seen with a certain intensity level, etc.) if those particles are within the thickness of the laser sheet. Thus, by using the laser sheet and the orthogonal orientation of the camera, it can easily be determined whether a particle seen in an image is inside or outside of the container: any imaged particles that are outside the container will be outside the container walls in the image, and any imaged particles that are inside the container will be between the container walls in the image.

[0011] In some embodiments, the container is rotated a number of times about its central axis, and imaged at each rotation while the laser sheet is still applied, in order to inspect the entire volume of the drug product (or other sample) within the container. While numerous rotations may be required, the image processing and computational load can be very light, and the probability of false rejects can be very low. Moreover, the technique has the unexpected benefit that some of the laser light scatters within the sample, or refracts at the container/sample (e.g., glass/liquid) interface, and travels around the inside

What is claimed is:

1. A method for imaging a container holding a sample, the method comprising:

illuminating the container with a laser sheet that impinges upon the container in a first direction corresponding to a first axis, wherein a plane of the laser sheet is defined by the first axis and a second axis orthogonal to the first axis;

moving the container through a plurality of rotations, about a central axis of the container, while illuminating the container with the laser sheet;

capturing, by an imager having an imaging axis that is substantially orthogonal to at least the first axis, ~~an~~ a plurality of image~~s~~ of the container, with each image corresponding to a respective one of the plurality of rotations; and

analyzing, by one or more processors, the plurality of image~~s~~ of the container to detect particles within, and/or on an exterior surface of, the container, wherein analyzing the plurality of images includes:

identifying an object appearing between walls of the container, in a first image corresponding to a first rotation of the container, as a candidate particle, and

determining whether the candidate particle is an actual particle based on whether the object appears in additional images corresponding to other rotations of the container, wherein the determining includes

determining that the candidate particle is not an actual particle when the object appears in the additional images, and

determining that the candidate particle is an actual particle when the object does not appear in the additional images.

2. The method of claim 1, wherein illuminating the container with the laser sheet includes illuminating the container with a laser sheet that passes through a central axis of the container.

3. The method of claim 1 or 2, wherein a thickness of the laser sheet, at a position where the laser sheet enters the container and along a third axis orthogonal to the first and second axes, is less than 3 millimeters.

4. The method of any one of claims 1-3, wherein a thickness of the laser sheet covers between 1/360th and 1/30th of a perimeter of the container.

~~5. The method of any one of claims 1-4, further comprising:~~

~~moving the container through a plurality of rotations, about a central axis of the container, while illuminating the container with the laser sheet;~~

~~capturing, by the imager, a plurality of images of the container, with each image corresponding to a respective one of the plurality of rotations; and~~

~~analyzing, by the one or more processors, the plurality of images of the container to detect particles within, and/or on the exterior surface of, the container.~~

~~6~~5. The method of any one of claims 1-~~4~~5, wherein:

the laser sheet is a first laser sheet of a first color;

the imager is a first imager configured to filter out colors other than the first color;

the method further comprises

simultaneously with illuminating the container with the first laser sheet, illuminating the container with a second laser sheet of a second color different than the first color, wherein the second laser sheet impinges upon the container in a second direction that is not parallel to the first axis, and wherein a plane of the second laser sheet is defined by the second direction and a third direction substantially parallel to the second axis, and

capturing, by an additional imager configured to filter out colors other than the second color and having an imaging axis that is substantially orthogonal to at least the second direction, an additional image of the container; and

analyzing the image of the container includes analyzing both the image of the container and the additional image of the container to detect particles within, and/or on an exterior surface of, the container.

~~7~~6. The method of any one of claims 1-~~4~~5, wherein:

the laser sheet is a laser sheet of a first color;

the imager is a first imager configured to filter out colors other than the first color;

the method further comprises

simultaneously with illuminating the container with the laser sheet, illuminating the container with light of a second color different than the first color, wherein the light of the second color illuminates at least a majority of an entire volume of the container, and

capturing, by an additional imager configured to filter out colors other than the second color, ~~an~~ additional image~~s~~ of the container; and

analyzing the plurality of image~~s~~ of the container includes analyzing both the plurality of image~~s~~ of the container and the additional image~~s~~ of the container to detect particles within, and/or on an exterior surface of, the container.

~~8~~7. The method of any one of claims 1-~~6~~7, wherein the first direction is substantially orthogonal to a central axis of the container.

~~9~~8. The method of any one of claims 1-~~6~~7, wherein the first direction is substantially parallel to a central axis of the container.

~~10~~9. The method of any one of claims 1-~~8~~9, wherein the imaging axis is substantially orthogonal to the first axis and the second axis.

~~11~~10. An imaging system comprising:

~~positioning means for positioning a container;~~

illumination means for generating a laser sheet that impinges upon ~~the~~ a container in a first direction corresponding to a first axis, wherein a plane of the laser sheet is defined by the first axis and a second axis orthogonal to the first axis; ~~and~~

positioning means for positioning the container, wherein the positioning means moves the container through a plurality of rotations, about a central axis of the container, while the illumination means illuminates the container with the laser sheet;

imaging means for capturing ~~one or more~~ a plurality of images of the container, with each image corresponding to a respective one of the plurality of rotations, the means for capturing ~~one or more~~ the plurality of images of the container having an imaging axis that is substantially orthogonal to at least the first axis; and

processing means for analyzing the plurality of images of the container to detect particles within, and/or on an exterior surface of, the container, wherein analyzing the plurality of images includes

identifying an object appearing between walls of the container, in a first image corresponding to a first rotation of the container, as a candidate particle, and

determining whether the candidate particle is an actual particle based on whether the object appears in additional images corresponding to other rotations of the container, wherein the determining includes

determining that the candidate particle is not an actual particle when the object appears in the additional images, and

determining that the candidate particle is an actual particle when the object does not appear in the additional images.

~~12~~11. The imaging system of claim ~~11~~10, wherein the illumination means is for generating a laser sheet that passes through a central axis of the container.

~~13~~12. The imaging system of claim ~~11~~10 or ~~12~~11, wherein the illumination means is for generating a laser sheet having a thickness, at a position where the laser sheet enters the container and along a third axis orthogonal to the first and second axes, of less than 3 millimeters.

~~14~~13. The imaging system of any one of claims ~~11~~10-~~13~~12, wherein the illumination means is for generating a laser sheet having a thickness that covers between 1/360th and 1/30th of a perimeter of the container.

~~15. The imaging system of any one of claims 11-14, wherein the positioning means is also for rotating the container a plurality of times while the container is illuminated with the laser sheet.~~

~~16~~14. The imaging system of any one of claims ~~11~~10-~~15~~13, wherein:
the illumination means is a first illumination means for generating a first laser sheet of a first color;
the imaging means is a first imaging means for filtering out colors other than the first color; and
the imaging system further comprises

a second illumination means for generating a second laser sheet, of a second color different than the first color, that impinges upon the container in a second direction that is not parallel to the first axis, wherein a plane of the second laser sheet is defined by the second direction and a third direction substantially parallel to the second axis, and

a second imaging means for filtering out colors other than the second color, is positioned to capture images of the container, and has an imaging axis aligned with a fifth direction orthogonal to at least the second direction.

~~17~~15. The imaging system of any one of claims ~~11~~10-~~15~~13, wherein:
the illumination means is a first illumination means for generating a first laser sheet of a first color;
the imaging means is a first imaging means for filtering out colors other than the first color; and
the imaging system further comprises

a second illumination means for illuminating the container with light of a second color different than the first color, wherein the light of the second color illuminates at least a majority of an entire volume of the container, and

a second imaging means for filtering out colors other than the second color, and is positioned to capture images of the container.

~~18~~16. The imaging system of any one of claims ~~11~~10-~~17~~15, wherein the first direction is substantially orthogonal to a central axis of the container.

~~19~~17. The imaging system of any one of claims ~~11~~10-~~17~~15, wherein the first direction is substantially parallel to a central axis of the container.

~~20. The imaging system of any one of claims 11-19, further comprising:~~

~~processing means for analyzing the image of the container to detect particles within, and/or on an exterior surface of, the container.~~