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(54) REAGENT TUBE

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(60) Provisional application No. 60/959,437, filed on Jul. 13, 2007.

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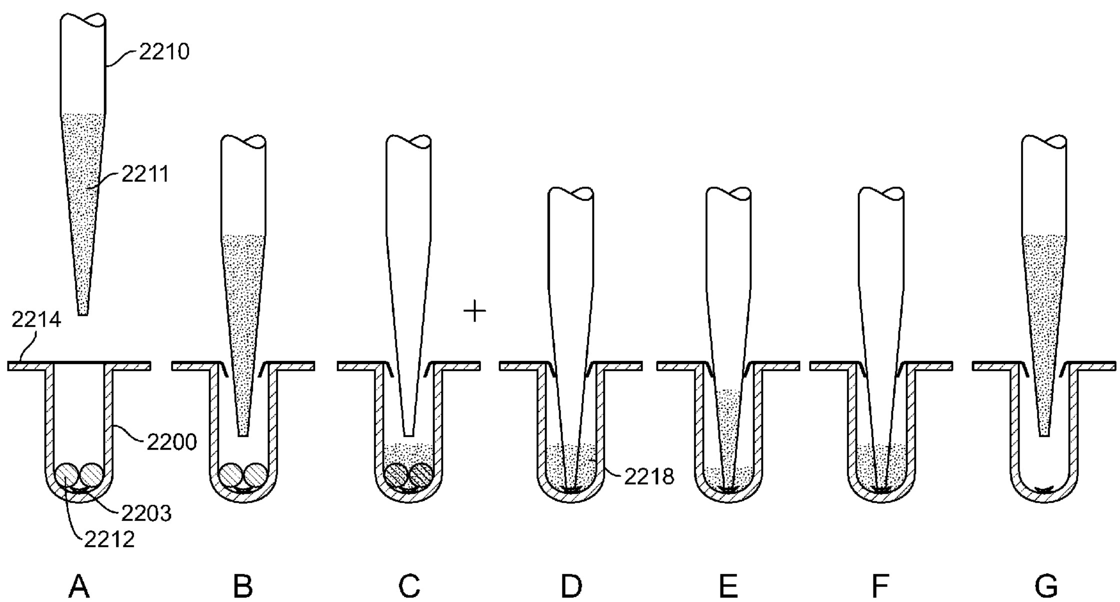
(57) ABSTRACT

A reagent tube configured with a stellated shaped pattern, on its bottom interior surface, configured to facilitate complete or near-complete withdrawal of fluid from the tube, via a pipette tip. The reagent tube may be used for transporting reagents and for carrying out processing operations on biological samples with the reagents, such as preparing polynucleotides extracted from the sample for amplification.



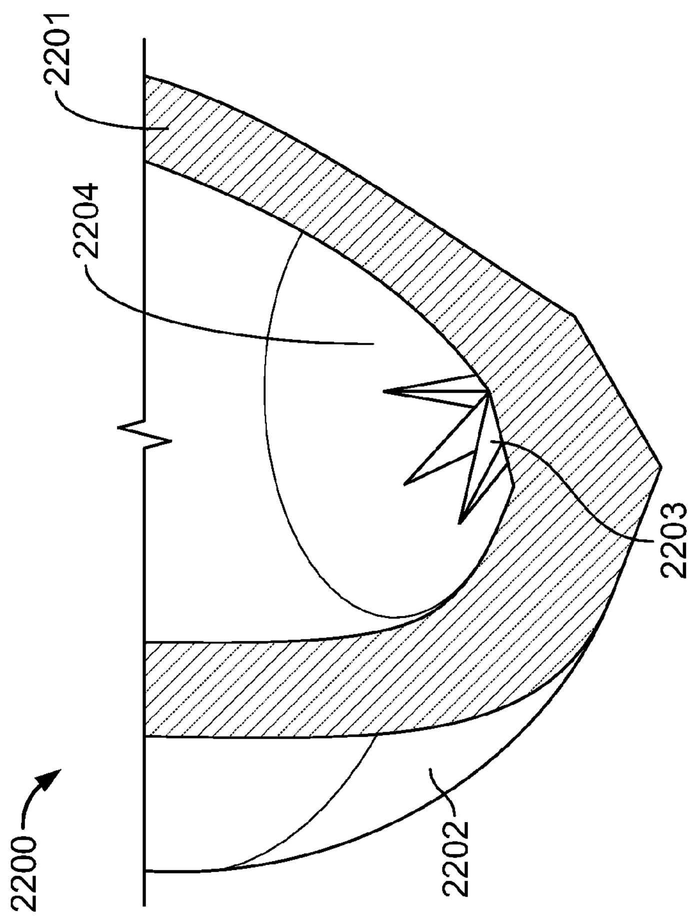

2200
2201
2204
2203
2202

FIG. 1A

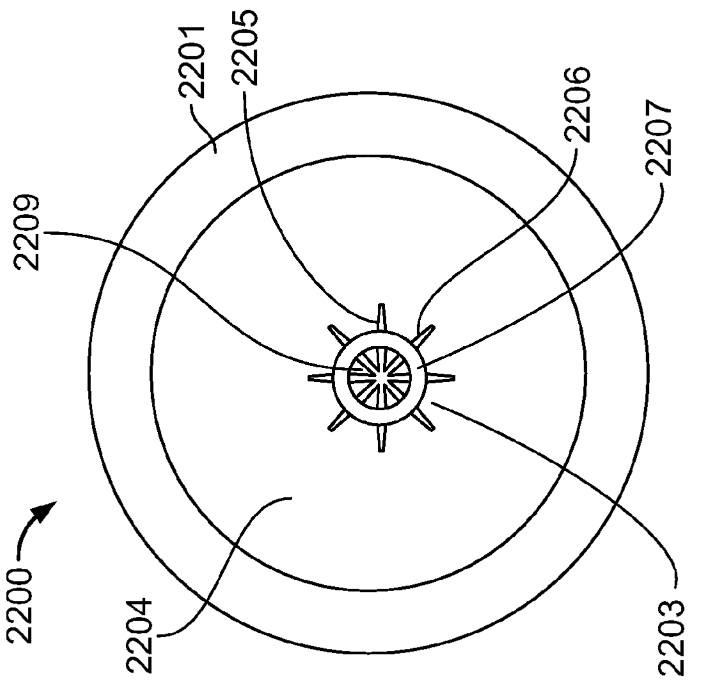

2200
2201
2205
2206
2207
2209
2204
2203

FIG. 1B

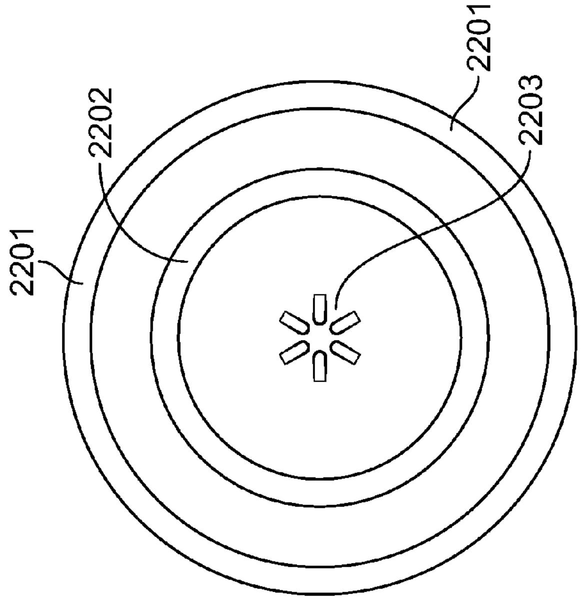


FIG. 2B

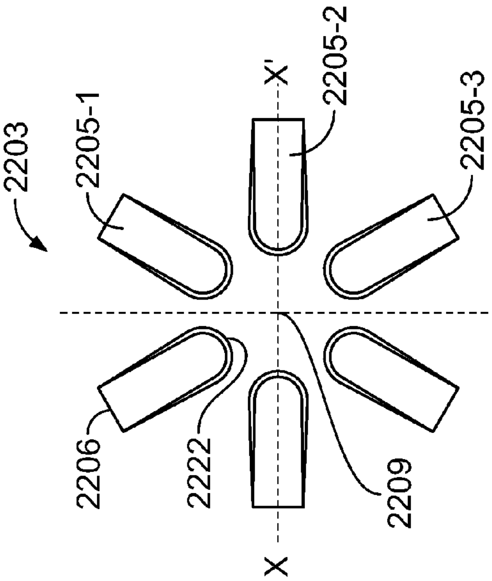


FIG. 2C

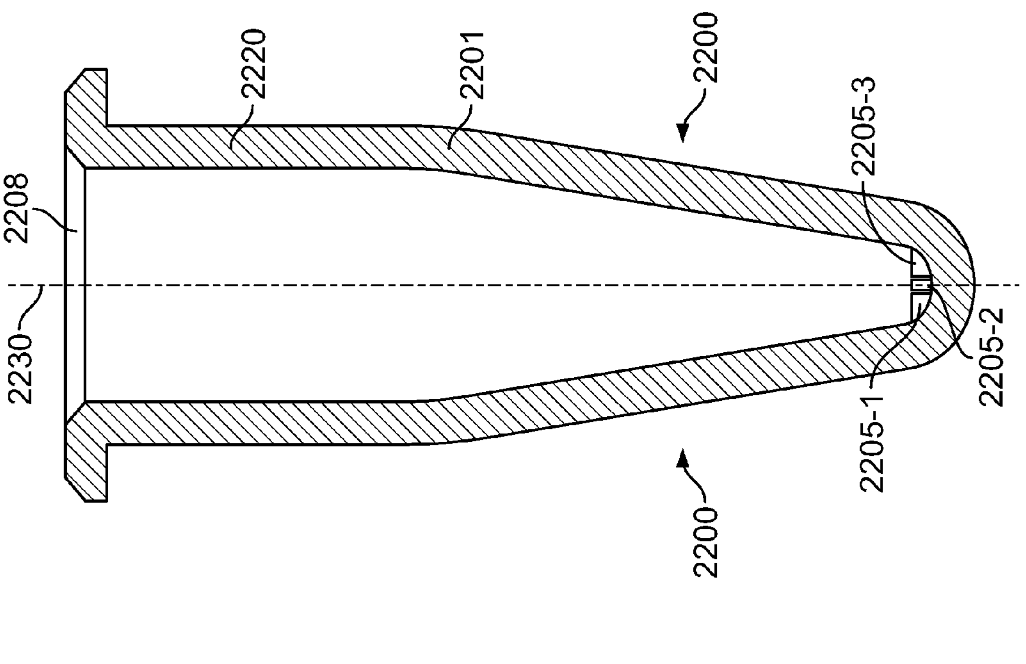


FIG. 2A

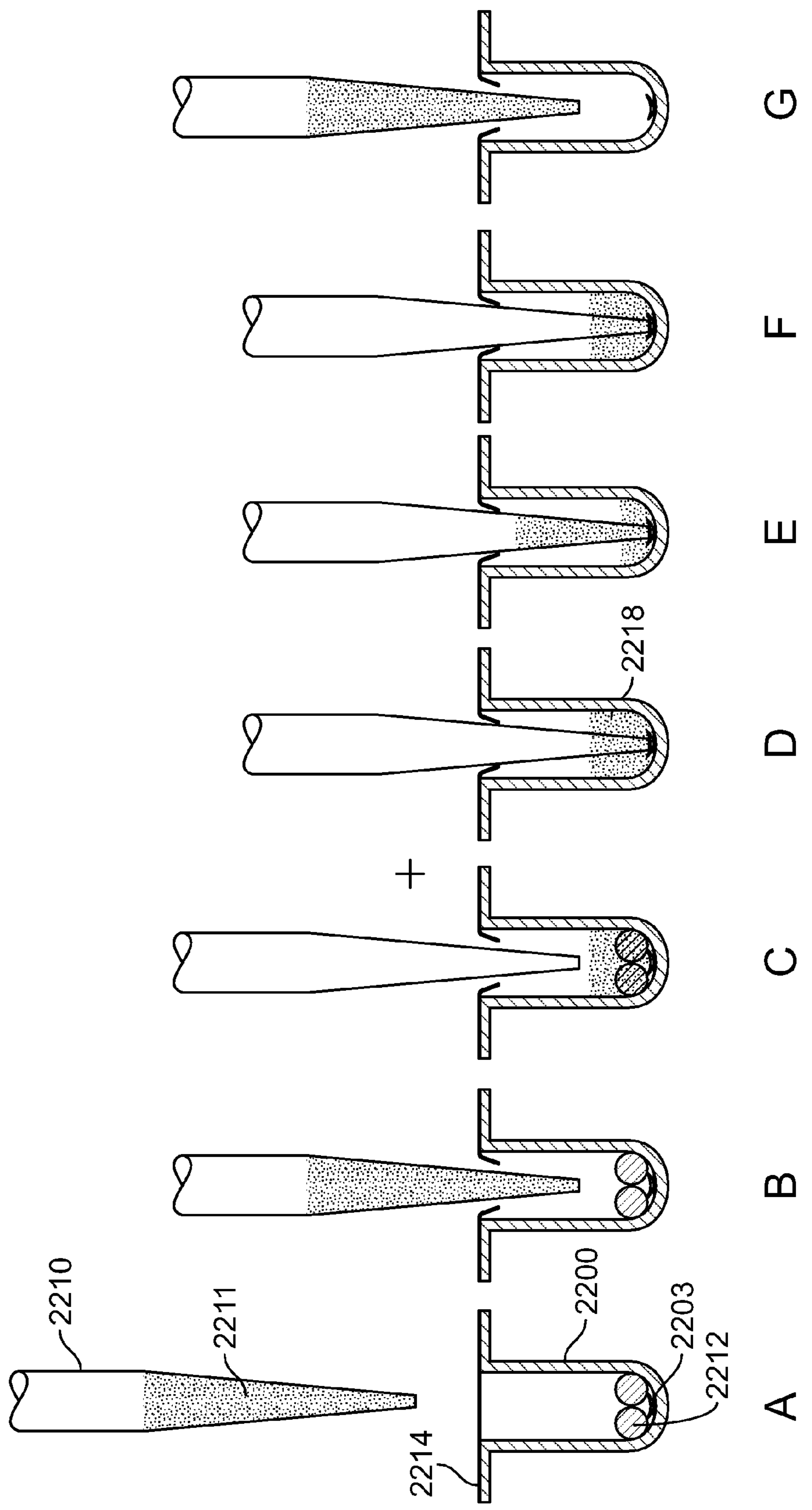


FIG. 3

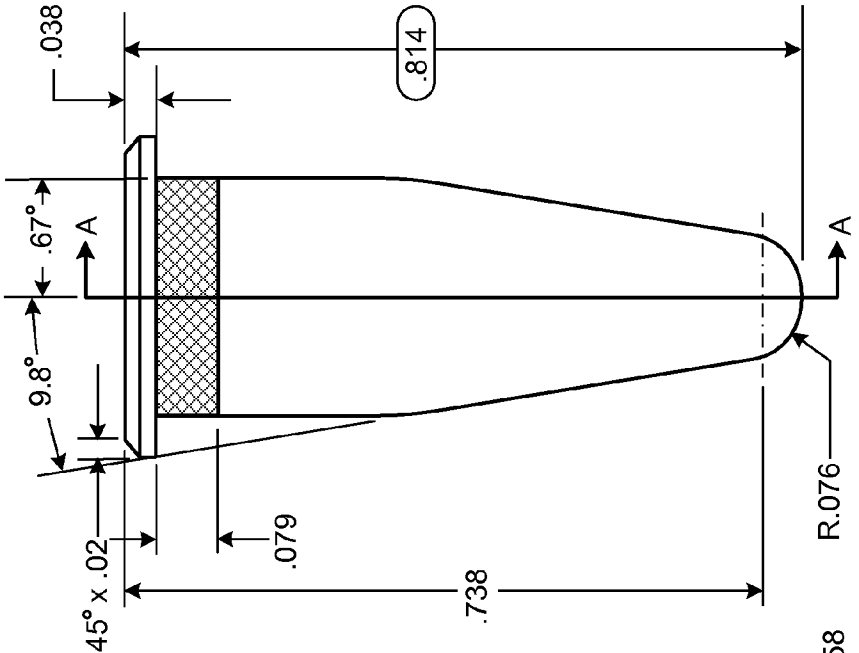


FIG. 4C

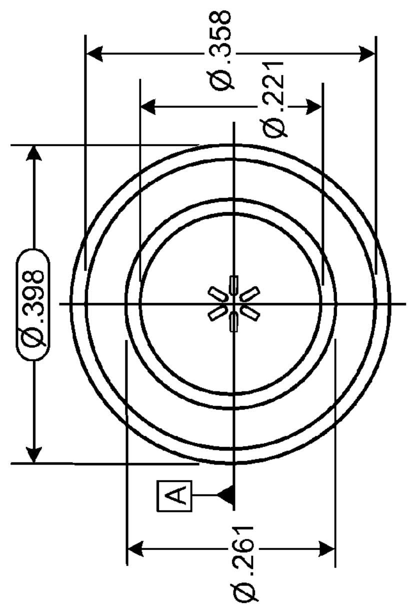


FIG. 4B

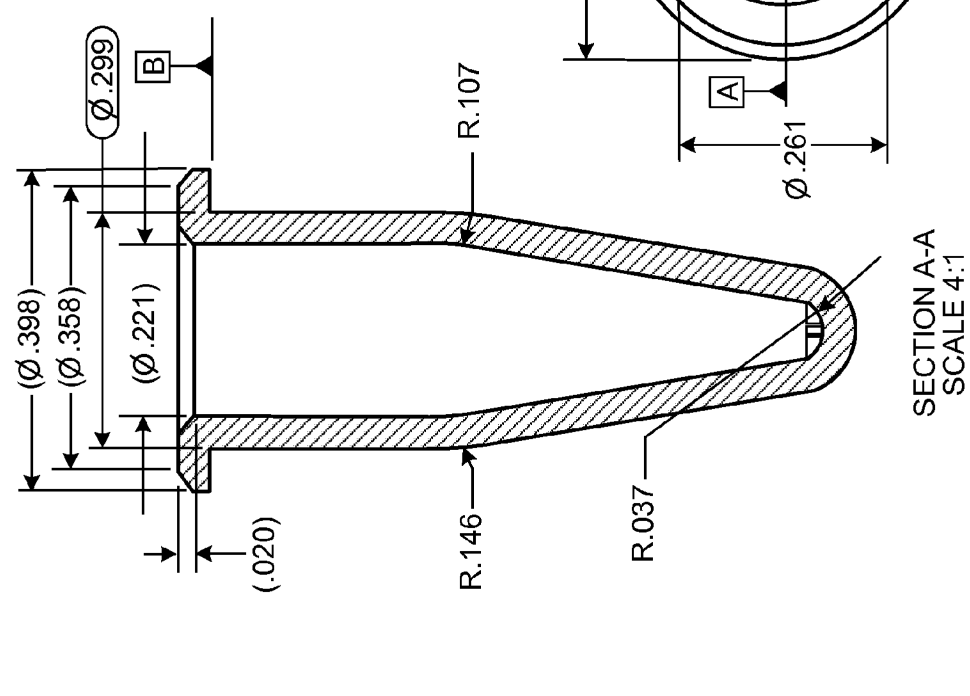


FIG. 4A

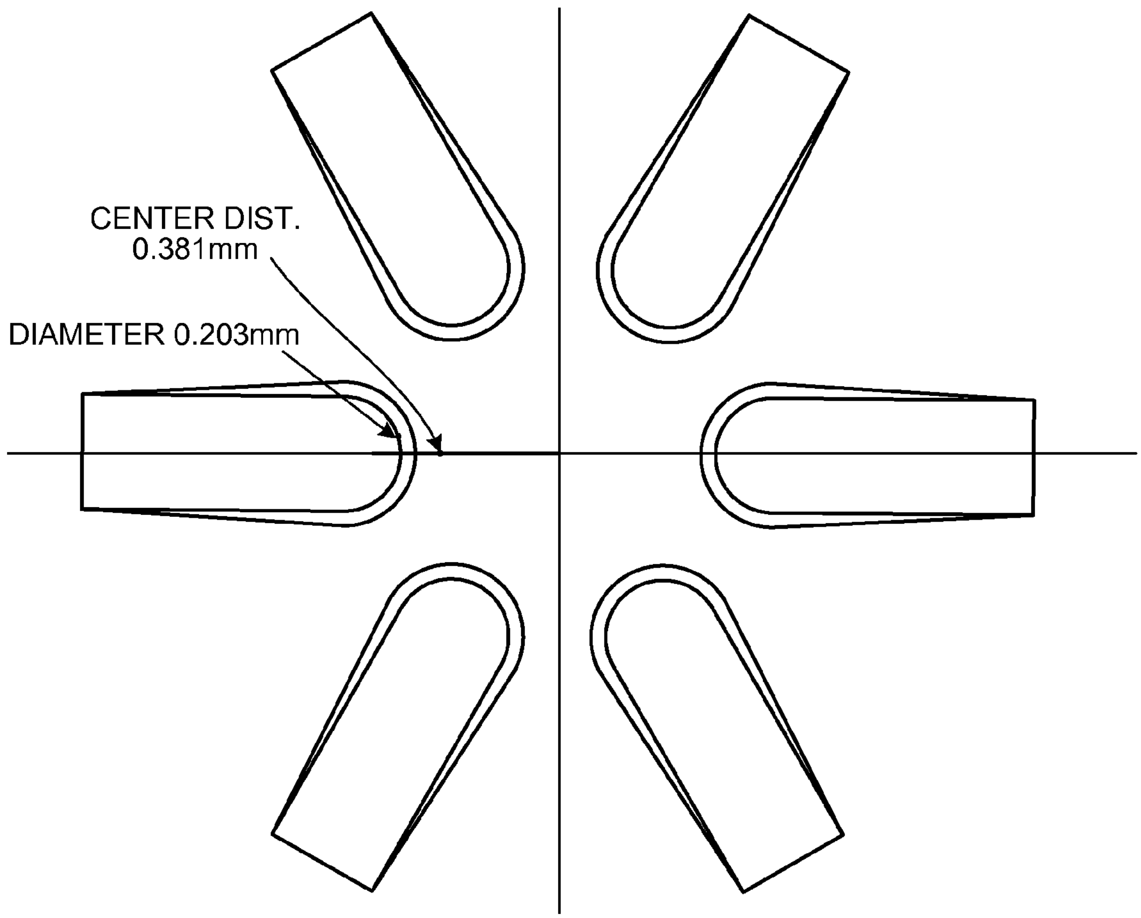


FIG. 4D

REAGENT TUBE

CLAIM OF PRIORITY

[0001] This application is a continuation-in-part of U.S. patent application Ser. No. 12/______, filed by ExpressMail on Jul. 14, 2008 (and entitled "Reagent Tube, Reagent Holder, and Kits Containing Same", in the name of Wilson, et al.), which claims benefit of priority to U.S. provisional Patent Application Ser. No. 60/959,437, filed Jul. 13, 2007, both of which are incorporated herein by reference in their entireties.

TECHNICAL FIELD

[0002] The technology described herein generally relates to reagent tubes designed to facilitate pipetting of small volumes of liquid from within, and more particularly to reagent tubes that are used in extracting microfluidic quantities of polynucleotides in solution following extraction from biological samples.

BACKGROUND

[0003] The medical diagnostics industry is a critical element of today's healthcare infrastructure. At present, however, diagnostic analyses no matter how routine have become a bottleneck in patient care. There are several reasons for this. For example, many diagnostic analyses can only be done with highly specialist equipment that is both expensive and only operable by trained clinicians. Such equipment is found in only a few locations, and often there is just one in any given urban area. This means that most hospitals are required to send out samples for analyses to these locations, thereby incurring shipping costs and transportation delays, and possibly even sample loss or mishandling.

[0004] Understanding that sample flow breaks down into several key steps, it would be desirable to consider ways to automate or make efficient as many of these as possible. In one key step, a biological sample, once extracted from a patient, must be put in a form suitable for a processing and detection regime that typically involves using PCR to amplify a vector of interest. Once amplified, the presence or absence of the vector in the sample needs to be determined unambiguously. Preparing samples for PCR is currently a time-consuming and labor intensive step, though not one requiring specialist skills, and could usefully be automated. By contrast, steps such as PCR and nucleotide detection have customarily only been within the compass of specially trained individuals having access to specialist equipment.

[0005] Sample preparation is labor intensive in part because of the number of reagents required, and the need for multiple liquid transfer (e.g., pipetting) operations. Furthermore, a trend towards portable diagnostic instruments, or those that can be easily installed in almost any healthcare setting (without requiring a dedicated facility), has meant that the instruments are configured to analyze very small (microfluidic or smaller) volumes of polynucleotide-containing solutions. With such volumes, it becomes important to minimize sample loss—such as from liquid transfer operations—during sample preparation. Even a loss of a very small fraction of a processing volume could result in loss of a significant number of copies of target polynucleotide and thereby result in a concomitant loss of amplification and detection sensitivity and—potentially—a false negative diagnosis. A major source of loss of liquid samples and solutions is from incomplete pipetting, where a pipette attempts to suck an entire quantity of fluid from a container, but where some fraction of that quantity is retained in the container, such as on the interior surfaces.

[0006] Various interior surface features in reagent tubes have been described elsewhere. U.S. Pat. No. 4,466,740 describes an array of reaction vessels on a plate, wherein each vessel has a conical interior lower surface that is stepped so that a number of concentric ridges of increasing diameter span between the bottom of the vessel and the vessel at its maximum width. Such a shape of interior surface is likely to present an increased surface area on which solution may remain during pipetting, and are unlikely to effectively channel the solution towards the location of a pipette tip. U.S. Pat. No. 6,143,250 (the '250 patent) describes liquid storage vessels having "ditches" in their lower interior surfaces that follow the interior surface of an inclined edge of the vessel. Although the '250 patent suggests that these grooves can be present in numbers of greater than two, and arranged radially with respect to the center of the vessel, such a configuration has at least the drawback that it would require a complex manufacture of the vessel, and are therefore limited to particular vessels, not necessarily those that are used in routine laboratory processes, such as biological sample preparation.

[0007] There is therefore a need for a method and apparatus of carrying out sample preparation on samples, so that loss of liquid volumes during liquid transfer is reduced. Such methods and apparatus could also find application to liquid transfer operations used in other fields, where mitigation of sample loss during work-up is important.

[0008] The discussion of the background herein is included to explain the context of the inventions described herein. This is not to be taken as an admission that any of the material referred to was published, known, or part of the common general knowledge as at the priority date of any of the claims.

[0009] Throughout the description and claims of the specification the word "comprise" and variations thereof, such as "comprising" and "comprises", is not intended to exclude other additives, components, integers or steps.

SUMMARY

[0010] The technology described herein includes a reagent tube comprising a pattern of ridges extending radially and centered at the bottom of the interior surface of the tube. Also contemplated are radially oriented patterns of grooves on the bottom interior surface of the tube.

[0011] The reagent tube described herein typically comprises a wall having an upper portion, usually cylindrical, and a lower portion, usually conical or tapering towards a bottom, and has an exterior surface and an interior surface. The pattern of ridges is typically star-shaped and is disposed on the interior surface of the tube, at the bottom of the tube.

[0012] The technology described herein further includes methods of using a reagent tube, as described herein, such as a method of removing all, or substantially all, of a liquid from the tube by use of a pipette tip. The pipette tip may be removably attached to a manually, such as hand-operated, pipette, or may be removably attached to an automatic dispensing apparatus.

[0013] The reagent tube herein typically finds use in sample preparation, that sequence of processing steps by which polynucleotide molecules, such as DNA and/or RNA, present in a biological sample (such as blood, sputum, semen, or urine), are extracted from their cellular matrix, and placed in a form

suitable for amplification, such as by PCR, and subsequent detection as part of a diagnostic test.

BRIEF DESCRIPTION OF THE DRAWINGS

[0014] FIGS. **1**A and **1**B show a stellated feature on the interior of a reagent tube, in cross-sectional (FIG. **1**A) and top plan (FIG. **1**B) views.

[0015] FIGS. **2**A, **2**B, and **2**C show a stellated feature on the interior of a reagent tube, in cross-sectional plan (FIG. **2**A), top plan (FIG. **2**B), and close-up (FIG. **2**C) views.

[0016] FIG. **3** shows a sequence of pipetting operations in conjunction with a reagent tube having a stellated feature.

[0017] FIGS. **4**A, **4**B, **4**C, and **4**D show an embodiment of a reagent tube having a stellated feature as further described herein, in cross-sectional (FIG. **4**A), top plan (FIG. **4**B), side plan (FIG. **4**C), and close-up (FIG. **4**D) views.

DETAILED DESCRIPTION

Reagent Tubes

[0018] The reagent tubes described herein are designed to facilitate pipetting of small volumes of liquid from within, such as to transfer the liquid to another container, with very little attendant loss of liquid.

[0019] The reagent tubes can be used in extracting microfluidic quantities of polynucleotides in solution following isolation of such polynucleotides from biological samples, such as in conjunction with a holder of various reagents as described in U.S. patent application Ser. No. 12/______, filed by ExpressMail on Jul. 14, 2008 (and entitled "Reagent Tube, Reagent Holder, and Kits Containing Same", in the name of Wilson, et al.), and an automated pipette head and dispenser as described in U.S. patent application Ser. No. 12/______, filed by ExpressMail on Jul. 14, 2008 (and entitled "Integrated Apparatus for Performing Nucleic Acid Extraction and Diagnostic Testing on Multiple Biological Samples", in the name of Williams, et al.), both of which are incorporated herein by reference. Exemplary procedures for sample preparation from polynucleotide-containing biological samples are found in U.S. patent application Ser. Nos. 12/172,208, and 12/172,214, both filed Jul. 11, 2008, and incorporated herein by reference.

[0020] However, reagent tubes consistent with the embodiments described herein are not exclusively for use with automated pipetting apparatus but also can be used in conjunction with manual processing, such as pipetting by hand.

[0021] Tubes consistent with the embodiments herein may have a variety of volumes, typically in the range 0.1 ml to 0.65 ml, such as 03 ml, 0.6 ml, or in the range 1.5-2.0 ml, or may have intermediate, or greater, volumes than those specifically delimited. They may also have a variety of shapes such as conical, barrel-shaped (wider at a middle portion than at top and bottom portions), or cylindrical with a tapered or conical bottom. Usually, reagent tubes are circular in cross-section, but other cross sections are possible and consistent herewith, and include but are not limited to: rectilinear, such as square or rectangular, like a cuvette; polygonal, such as pentagonal or hexagonal; and oval. Ordinarily, the tubes have a unitary construction, though in certain instances may be constructed from two or more parts fused or otherwise joined together as applicable. Typically, the tubes are configured to accept a pipette tip for deposit and/or retrieval of fluids.

[0022] The features of the reagent tubes as described herein may be found in or on the interior surfaces of many fluid containing vessels, including, but not limited to: vessels configured to carry out reactions, such as PCR tubes; arrays, such as microarray plates, having many vessels arranged in a single substrate; snap-in tubes, such as tubes that contain reagents and are shipped separately or loosely, but when used are snapped into a supporting member such as a rack or a holder; disposable tubes; re-usable tubes; tubes that are sealed to limit contact of their contents with air and/or moisture during storage or transport; tubes that are sealable and re-sealable, such as having a removable, or flip-up cap; tubes that can be labeled for a single use, or labeled for multiple uses; tubes that are made of a clear, or a translucent, or an opaque material, depending upon, e.g., photosensitivity of the contents; tubes that contain liquid reagents such as those that are directly pipetted out of the tubes; and tubes that contain solid, e.g., particulate, or lyophilized, reagents that are constituted into liquid form prior to pipetting, such as by dissolving upon contact with a liquid such as an aqueous buffer solution; and tubes that are made of plastic, or glass, or quartz.

[0023] As described elsewhere herein, the reagent tubes are configured to have a star-shaped—also referred to as stellated—pattern (see FIGS. **1**A and **1**B) on their bottom interior surfaces. Still other tubes for uses referenced herein, as well as for other uses not herein described, can be similarly configured.

[0024] The design of the star shaped pattern is important, especially when present in a reagent tube used for recovery of DNA or RNA present in very small quantities (low copy numbers) in a clinical sample, or an extract therefrom. The star-shaped pattern ensures that when a fluid is withdrawn from the tube, a pipette tip can be bottomed out in the tube and still be able to withdraw the entire, or almost the entire fluid from the tube, as shown in FIG. **3**, further described herein. This is important because, when working with such small volumes, and when target DNA can be present in very few copies, sample loss due to imperfections of pipetting is to be minimized to every extent possible. Additionally, the stellated pattern should be designed to minimize surface area as well as dead-end grooves that tend to have two undesirable effects: to trap liquid, and to increase undesirable retention of molecules such as polynucleotides by adsorption.

[0025] Accordingly, the stellated pattern should enable pipetting of most of the liquid (residual volume <1 microliter) when used with a pipette bottomed out with the bottom of the tube. Although it is not necessary for a pipette tip to bottom out in the reagent tubes described herein, an advantage of it so doing is that a very clear indication of the position of the tip during pipetting is obtained and thereby a consistent positioning can be accomplished across multiple pipetting operations. A requirement that a pipette tip be positioned at some intermediate distance above the bottom of the tube in order to maximize pipetting efficiency, would be harder to verify and to make consistent and reproducible over large numbers of operations even when using an automated pipetting device.

[0026] The design of the stellated or star-shaped pattern can be optimized to maximize the flow rate of liquid through various gaps in the pattern that lie between a bottomed out pipette, such as a p1000 pipette, and the star pattern. It would be understood that, although the description herein pertains to pipettes and pipette tips typically used in sample preparation of biological samples, the principles and detailed aspects of the design are as applicable to other types of pipette and pipette tip, and may be so-adapted.

[0027] FIG. 1A shows a cross sectional perspective view of a reagent tube 2200 having side wall 2201 and bottom portion 2202. Interior surface 2204 of the bottom portion is visible. An exemplary star-shaped feature 2203 is shown in part, as three apical portions, which may be grooves or may be ridges raised above the lower interior surface 2204. Typically, however, the star-shaped pattern is present as a raised portion on the lower interior surface of the tube.

[0028] FIG. 1B shows a plan view of the reagent tube of FIG. 1A, looking down its central axis from the top. Thus wall 2201 in FIG. 1B is shown at its widest diameter, typically corresponding to the top of tube 2200. The exemplary star pattern 2203 shown in FIG. 1B in plan view resembles a "ship's wheel" and comprises a center 2209, a circular ring 2207 centered on center 2209, and eight radial segments 2205 configured as radial ridges or grooves. Each radial segment meets the other radial segment at center 2209, and has a radial end 2206, also referred to as an apex or vertex. Star pattern 2203 in FIG. 1B has eight radial segments, but it would be understood that a star pattern having fewer or a greater number of radial segments, such as 3, 4, 5, 6, 7, 9, 10, or 12, would be consistent with the design herein. The number of radial segments of the star should be a minimum consistent with effective liquid pipetting and ease of manufacture. The radial segments should also be spaced apart enough not to trap the tip of any of the pipette tips to be used in the various liquid handling applications.

[0029] Center 2209 is typically positioned coincidentally with the geometric center of the bottom of reagent tube 2200. Such a tube is typically circular in cross-section, so that identifying its geometric center (e.g., at a crossing point of two diameters) is normally straightforward. Center 2209 may be larger than shown in FIG. 1B, such as may be a circular cutout or raised portion that exceeds in diameter the region formed by the meeting point of radial segments 2205.

[0030] Ring 2207 is an optional feature of star-shaped pattern 2203. Typically ring 2207 is centered on center 2209, and typically it also has a dimension that corresponds to the lower surface or caliber of a pipette tip. Thus, when a pipette tip 'bottoms out' in the bottom of reagent tube 2200, the bottom of the pipette tip rests in contact with ring 2207. Ring 2207 is thus preferably a cut-out or recessed feature that can accommodate the pipette tip and assist in guiding its positioning centrally at the bottom of the tube. Ring 2207 may alternately be a raised or ridge-like feature, according to manufacturing or other preference. In other embodiments more than one, such as 2, 3, or 4, concentric rings 2207 are present, so that pipette tips of varying calibers can be used with the same reagent tube, and each can be suitably positioned, while pipetting, in contact with one of the respective rings.

[0031] In the embodiment shown in FIG. 1B, the segments are narrower (occupy a smaller radial angle) than the gaps between them. In other embodiments, the radial segments may be proportionately wider than the gaps between them. When configured as grooves, radial segments 2205 are separated by ridges (occupying the space in between adjacent grooves). In other embodiments, the grooves and ridges that separate them are of equal widths at each radial distance from the center. It may be more appropriate to describe the stellated features as having ridges or grooves, depending on which occupies the cumulative greater spatial extent.

[0032] FIG. 2A shows in cross-sectional plan view a reagent tube 2200 having another exemplary stellated feature 2203, wall 2201, and sealed top 2208. The tube has a cylindrical upper portion 2220, and a tapering lower portion 2202. Shown as a dashed line 2230 in FIG. 2A is a central axis of symmetry of the tube, about which the tube is rotationally symmetric. FIG. 2B shows a top plan view of the reagent tube in FIG. 2A looking down its central axis towards stellated feature 2203 centered in the bottom of the tube. The ring denoted 2202 in FIG. 2B denotes an intermediate diameter of lower portion 2202. Stellated feature 2203 is shown in further detail in FIG. 2C as having 6 radial segments, three adjacent ones of which are labeled 2205-1, 2205-2, and 2205-3, respectively. The axis labeled X-X' corresponds to the viewpoint looking into the plane of the page in FIG. 2A. Thus, segment 2205-2 is shown as being in the middle of the stellated feature, and segments 2205-1 and 2205-3 are shown in cross-section, in FIG. 2A.

[0033] Characteristic features of the stellated pattern in FIGS. 2A-C include the following: segments 2205 may be configured as grooves or as ridges but are typically ridges, as shown in FIG. 2A; segments 2205 do not meet at center 2209 of the stellated pattern so that, where segments 2205 are ridges, a pipette tip that rests thereupon when pipetting is resting above a space at center 2209; there is no ring corresponding to ring 2207 in FIG. 1B; apices 2206 of segments 2205 are squared off but may be rounded in shape, or may be pointed; segments 2205 have interior apices 2222 that are also rounded, but may be pointed or squared off; and segments 2205 have, in cross-sectional view, rounded or flat bottoms if grooves, or rounded or flat upper surfaces if ridges; segments 2205 may be beveled so that they are narrower in their upper portion than at their lower portion, if ridges, or so that they are narrower in their lower portion than at their upper portion, if grooves.

[0034] A star pattern 2203 as described herein is configured to have dimensions that give an optimal flow-rate of liquid out of the reagent tube into a suitably positioned, such as a bottomed-out, pipette tip. The star pattern in FIGS. 1B and 2B is shown as being significantly smaller in diameter than the diameter of the tube at its widest point. The star pattern may have, in various embodiments, a diameter (measured from center 2209 to apex 2206 of a ridge or groove 2205) that is from 1-10%, or from 5-20%, or from 10-25%, or from 15-30%, or from 20-40%, or from 25-50%, or from 30-50%, or from 40-60%, or from 50-75%, or from 65-90% of the maximum diameter of the reagent tube.

[0035] The radial segments are typically rounded in their lower surfaces, such as semi-circular in cross section, or having a curved surface that is in cross section an arc of a circle, ellipse, parabola, or hyperbola, but may also be V-shaped. The segments may also be trapezoid in cross-section, such as having a wider upper portion than the bottom, which is flat, the upper portion and the bottom being connected by sloping walls.

[0036] In some embodiments, for ease of manufacture, the radial segments end on the same level as one another in the bottom of the tube. Thus the apices 2206 are all disposed on the circumference of a circle whose plane lies perpendicular to the cylindrical axis of the tube. In other embodiments, the segments do not all end on the same level. For example, apices 2206 may alternately be on different levels, and thus the apices are alternately disposed on the respective circumferences of two concentric circles that occupy different, parallel, planes in space from one another.

[0037] Radial segments 2205 are shown in FIGS. 1B and 2C as having equal lengths (as measured from center 2209 to apex **2206**). This need not be so. In alternative embodiments, segments may have different lengths from one another, for example, as alternating lengths on alternating segments, where there are an even number of segments. Furthermore, apices **2206** may be rounded, rather than pointed, or may be squared off. Typically radial segments **2205** each have a length that is longer than the radius of the inlet hole in the largest pipette tip that is used in connection therewith. Typically radial segments **2205** have a width that is narrower than the diameter of the inlet hole in the largest pipette tip that is used in connection therewith, but it need not be the case.

[0038] Typically the radial segments taper uniformly in width and height or depth from center **2209** to each respective apex **2206**. Still other configurations are possible, such as a segment that follows a constant width, or depth, out to a particular radial extent, within 30-60% of its length such as near its midpoint of length, and then narrows and/or becomes shallower towards its apex **2206**. Alternatively, a radial segment may start narrow at center **2209**, widen to a widest region within 30-60% of its length, such as near its midpoint of length, and then narrow towards its apex. Still other possibilities, not described herein, are consistent with the stellated pattern of the reagent tubes herein.

[0039] In a 0.3 ml tube, the radius of the star-pattern formed from the radial segments, measured as the shortest distance from center **2209** to an apex **2206**, is typically around 0.5 mm, but may be from 0.1-1 mm, or from 0.3-0.7 mm, or from 0.5 to 1.5 mm, or from 0.7 to 2 mm.

[0040] In a 0.3 ml tube, the width of each radial segment **2205** at its widest point is typically around 50 microns, and the width typically tapers uniformly from a widest point, closest to or at center **2209**, to a narrower width at the apex **2206**.

[0041] In a 0.3 ml tube, the height (for a ridge) or depth (for a groove) of a segment at the deepest point is typically around 25-50 microns and the height depth typically tapers uniformly from a highest or deepest point respectively, closest to or at center **2209**, to an apex **2206**.

[0042] In another embodiment, in a 0.3 ml tube, the radial segments should be rounded off and less than 100 microns deep (or high), or less than 50 microns deep (or high), or less than 25 microns deep (or high).

[0043] The stellated pattern typically has a rotation axis of symmetry, the axis disposed perpendicular to the bottom of the tube and through center **2209** (concentric with a cylindrical axis of the tube), so that the radial segments are disposed symmetrically about the rotation axis. By this is meant that, for n segments, a rotation by an angle of $2\pi/n$ about the central (rotational) axis can bring each segment into coincidence with the segment adjacent to it.

[0044] The stellated shapes shown in FIGS. **1**B and **2**B, **2**C are not limiting in that they comprise a center, a number of radial segments **2205**, and an optional circular ring **2207**. Other star-shaped geometries may be used, and, depending upon ease of manufacture and efficacy of use, may be preferred. For example, a star-shaped pattern can be created simply be superimposing two or more polygons having a common center, but offset rotationally with respect to one another by a rotation about the central axis. (See, for example "star polygons" described at the Internet site mathworld.wolfram.com/StarPolygon.html.) Such alternative manners of creating star-shaped patterns are utilizable herein.

[0045] Also shown in the side plan view of FIG. **2**A is a top **2208** of tube **2200**. Top **2208** is typically made of aluminum foil, which may be heat-sealed on to the top of the tube. Although other layers, or a combination of layers, such as a laminate layer, as further described in U.S. patent application Ser. No. 12/______, filed Jul. 14, 2008 and entitled "Reagent Tube, Reagent Holder, and Kits Containing Same", can be placed on top of the reagent tube to seal it, typically a layer of aluminum foil is adequate, where the tube contents are solid, e.g., lyophilized, reagents. In some embodiments, the top of the reagent tube has chamfer edges to reduce expansion of the top rim of the tube during heat sealing of a foil on the top of the tube.

[0046] The reagent tube described herein may further comprise an identifiable code, such as a 1-D or a 2-D bar-code on the top **2208**. Such a code is useful for identifying the composition of the reagents stored within, and/or a batch number for the preparation thereof, and/or an expiry date. The code may be printed on with, for example, an inkjet or transfer printer. The code may also be attached, or affixed, or printed on, the side of the tube, such as on an exterior surface of wall **2201**.

Exemplary Manufacture

[0047] A stellated feature such as described herein may be positioned on the interior surface of the bottom of a reagent tube during manufacture of the tube by, for example injection moulding. The stellated feature is typically constructed as a raised feature, proud from the bottom interior surface. Thus, during manufacture of a reagent tube described herein by injection moulding, an outer portion of the mould is a cavity defining the exterior shape of the tube. An interior shape of the tube is formed by an inner portion of the mould positioned concentrically with the outer portion of the mould, and having a star-shaped structure milled out of its tip. Thus, when liquid plastic is injected into the space between the inner and the outer portions of the mould, the star-shape is formed as a raised portion on the bottom interior surface of the tube that is so-formed. Alternately, if the stellated feature is constructed as a recessed feature, the interior portion of the mould will have a complementary stellated feature projecting from its bottom surface.

[0048] Reagent tubes may be manufactured by injection moulding in batches, such as via an array of tube-shaped moulds in a single substrate. Tubes made in batch in this way may be imprinted with a non-functional marking characteristic of the location in the array, for example, for purposes of quality control.

Exemplary Pipetting Operations

[0049] FIG. **3** has a number of panels, A-G, each representing, in sequence, a stage in a pipetting operation carried out in conjunction with a reagent tube **2200** having a stellated pattern **2203**, shown in cross section on the bottom interior surface of the tube **2200** and as further described herein. FIG. **3** is now described, as follows.

[0050] At A, a pipette tip **2210**, containing a liquid **2211** (such as a buffer solution), is positioned directly or approximately above the center of reagent tube **2200**. The tube contains a number of lyophilized pellets **2212**, and is sealed by a layer **2214**, such as of foil, as further described herein.

[0051] At B, the pipette tip is lowered, piercing seal **2214**, and brought into a position above the particles **2212**.

[0052] At C the liquid **2211** is discharged from the pipette tip on to the particles, dissolving the same, as shown at D.

After the particles are fully dissolved, forming a solution **2218**, the pipette tip is lowered to a position where it is in contact with the stellated pattern **2203**.

[0053] At E, the pipette tip is caused to suck up the solution **2218** (typically leaving less than 1 μl of solution **2218** in the tube), and at F, the tip may optionally discharge the solution back into the tube. Steps E and F may be repeated, as desired, to facilitate dissolution and mixing of the lyophilized components into solution.

[0054] At G, after sucking up as much of the solution **2218** as is practicable into the pipette tip, the pipette tip is withdrawn from the tube. Ideally, 100% by volume of the solution **2218** is drawn up into the pipette tip at G. In other embodiments, and depending upon the nature of solution **2218**, at least 99% by volume of the solution is drawn up. In still other embodiments, at least 98%, at least 97%, at least 96%, at least 95%, and at least 90% by volume of the solution is drawn up.

[0055] The following examples illustrate an embodiment of the invention described and claimed herein, and are not intended to be limiting.

EXAMPLES

Example 1

Reagent Tube

[0056] An exemplary reagent tube, showing various dimensions, is shown in FIGS. **4**A-**4**D. Tolerances on the shown dimensions, during manufacture, are as follows: features ≧0.5 inches are machined to within ±0.010 inches; features <0.5 inches are machined to within ±0.005 inches; feature locations, such as theoretical center points and theoretical center lines, are within ±0.010 inches of those shown in the drawings. It is to be understood that dimensions can also be represented in their metric system equivalents without departing from the scope of the technology herein.

[0057] The cross-hatch area shown on the upper portion of the tube in FIG. **4**C is an area on which a marking may be made, such as during manufacture, for the purpose of indicating product origin, identifying the batch, or for quality control.

[0058] The pattern of ridges shown in FIG. **4**D is such that each ridge comprise a rectangular portion capped by a semicircular arc, the semi-circular arc being disposed close to the common center of the pattern of ridges and having a diameter of 0.203 mm. In the embodiment shown in FIG. **4**D, the distance from the center of the circle of which the semicircular arc is formed to the center of the pattern is 0.381 mm.

[0059] The tube is made from polypropylene homopolymer, e.g., available from Carmel Olefins Ltd., and identified as product no. Capilene U77 AV (see, e.g., Internet site www.carmel-olefins.co.il/Media/Uploads/Capilene_nomenclatur.pdf).

[0060] Surfaces are SPI (Society of the Plastics Industry) grade A-2, a known surface quality measurement, or better.

[0061] Any and all flashes and burrs resulting from the manufacture are removed and, in order to be used, the tube should not come into contact with grease, dust, mold release or other foreign substances. The tube should also be free of cracks, crazing, scratches, and internal defects or particulates obvious to the unaided eye.

Example 2

Foil Piercing and Dissolution of Lyophilized Reagents

[0062] The containers of lyophilized reagents provided in conjunction with a holder as described herein are typically sealed by a non-plasticized aluminum foil. Aluminum foil bursts into an irregular polygonal pattern when pierced through a pipette and leaves an air vent even though the pipette is moved to the bottom of the tube. In order to save on reagents, it is desirable to dissolve the reagents and maximize the amount withdrawn from the tube. To accomplish this, a ridged-star (stellated) pattern is placed at the bottom of the container to maximize liquid volume withdrawn, and flow velocity in between the ridges.

[0063] Exemplary steps for dissolving solid particles, and withdrawing fluid are as follows:

[0064] 1. Pierce through the pipette and dispense the fluid away from the lyophilized material. If the pipette goes below the level of the lyophilized material, it will go into the pipette and may cause jamming of the liquid flow out of the pipette.

[0065] 2. Let the lyophilized material dissolve for a few seconds.

[0066] 3. Move pipette down touching the ridged-bottom of the tube

[0067] 4. Perform an adequate number of suck and spit operations (4-10) to thoroughly mix the reagents with the liquid buffer.

[0068] 5. Withdraw all the reagents and move pipette to dispense it into the next processing tube.

[0069] The foregoing description is intended to illustrate various aspects of the present inventions. It is not intended that the examples presented herein limit the scope of the present inventions. The technology now being fully described, it will be apparent to one of ordinary skill in the art that many changes and modifications can be made thereto without departing from the spirit or scope of the appended claims.

What is claimed is:

1. A reagent tube, comprising:

a pattern of ridges extending radially and centered at the bottom of the interior surface of the tube.

2. The tube of claim **2**, wherein the number of ridges is selected from 3, 4, 5, 6, 8, 9, 10, or 12.

3. The tube of claim **1**, wherein the ridges do not meet one another at a center of the pattern.

4. The tube of claim **1**, wherein each of the ridges has a width, wherein the width tapers from a widest point to an apex.

5. The tube of claim **4**, wherein the widest point is closest to a center of the stellated pattern.

6. The tube of claim **4**, wherein the widest point has a width of 50 microns.

7. The tube of claim **1**, wherein each of the ridges has a height, wherein the height tapers from a highest point to an apex.

8. The tube of claim **7**, wherein the highest point is closest to a center of the stellated pattern.

9. The tube of claim **7**, wherein the highest point has a height of 25-50 microns.

10. The tube of claim **1**, wherein each of the ridges has a length, measured as the shortest distance from its widest point to its apex.

11. The tube of claim **10**, wherein the length is 0.5 mm.

12. The tube of claim **1**, wherein the stellated pattern has a rotation axis of symmetry, the axis disposed perpendicular to the bottom of the tube, and wherein the ridges are disposed symmetrically about the rotation axis.

13. The tube of claim **1**, wherein the stellated pattern additionally comprises a circular cutout at the center of the bottom of the tube.

14. The tube of claim **1**, having a volume of 0.3 ml.

15. The tube of claim **1**, having a volume of between 0.1 ml to 0.65 ml

16. The reagent tube of claim **1**, wherein the stellated pattern is designed to enable liquid to be pipetted out of the tube, with less than 1 microliter of residual volume.

17. The reagent tube of claim **1**, where the top of the reagent tube has chamfer edges to reduce expansion of the top rim of the tube during heat sealing of a foil on the top of the tube.

18. The reagent tube of claim **1**, further comprising a reagent contained therein, and wherein the tube is sealed on top by a foil.

19. The reagent tube of claim **18**, further comprising an identifiable code on the top.

20. The reagent tube of claim **18**, wherein the reagent is in liquid or lyophilized form.

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