

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
24 July 2008 (24.07.2008)

PCT

(10) International Publication Number  
WO 2008/088729 A1

- (51) International Patent Classification:  
G01N 21/65 (2006.01) G01N 21/95 (2006.01)
- (21) International Application Number:  
PCT/US2008/000387
- (22) International Filing Date: 11 January 2008 (11.01.2008)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
60/880,247 12 January 2007 (12.01.2007) US
- (71) Applicant (for all designated States except US): PARATA SYSTEMS, LLC [US/US]; 2600 Meridian Parkway, Durham, North Carolina 27713 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): KLEIN, Peter, A. [US/US]; 1817 Woodburn Road, Durham, North Carolina 27705 (US). EBERDT, Jesse, Samuel, III [US/US]; 3711 Bentley Drive, Durham, North Carolina 27707 (US). TOWNSEND, W.L., Douglas, Jr. [US/US]; 3518 Westover Road, Durham, North Carolina 27707 (US). SAPIRSTEIN, Victor [US/US]; 52 High Ridge Road, Pound Ridge, New York 10576 (US). ZHOU, Wang-Long [US/US]; 31 Farrwood Drive, Andover, Massachusetts 01818 (US). YANG, Younwu [US/US]; 364 Brighton Street, Belmont, Massachusetts 02748 (US).
- (74) Agent: CANNON, James, E.; Myers Bigel Sibley & Sajovec, P.A., P.O. Box 37428, Raleigh, North Carolina 27627 (US).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:  
— with international search report

[Continued on next page]

(54) Title: SYSTEM AND METHOD FOR VERIFYING THE CONTENTS OF A FILLED, CAPPED PHARMACEUTICAL PRESCRIPTION

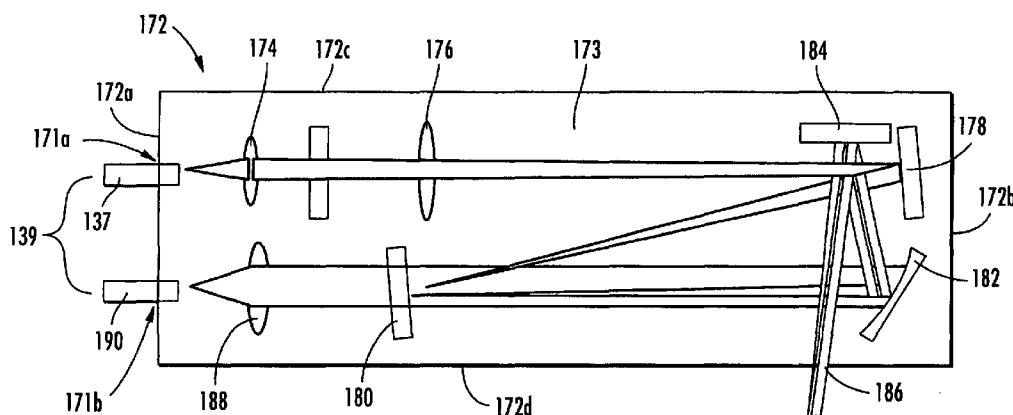


FIG. 3

(57) Abstract: A probe for a system for determining the chemical signature of a pharmaceutical compound. The probe comprises: a housing; an inlet in the housing adapted to be connected to a transmitting optical fiber; a scanning aperture in the housing; a receiving outlet in the housing adapted to be connected to a receiving optical fiber; at least one transmission reflector positioned in the housing to receive laser light from the transmitting optical fiber and reflect the laser light through the detection outlet to a pharmaceutical vial containing a pharmaceutical compound positioned outside the housing, and at least one receiving reflector positioned in the housing to receive light reflected by the pharmaceutical compound and reflect the light to the receiving outlet. This configuration can enable rapid and accurate scanning of a pharmaceutical contained in a vial positioned adjacent the detection outlet.

WO 2008/088729 A1



- 
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

## **SYSTEM AND METHOD FOR VERIFYING THE CONTENTS OF A FILLED, CAPPED PHARMACEUTICAL PRESCRIPTION**

### **Related Application**

This application claims priority from U.S. Provisional Patent Application Serial No. 60/880,247, filed January 12, 2007, the disclosure of which is hereby incorporated herein in its entirety.

5

### **Field of the Invention**

The present invention is directed generally to the identification of pharmaceuticals, and more particularly to the automatic identification of dispensed pharmaceuticals.

10

### **Background of the Invention**

There is an ongoing and predicted long-term shortage of licensed pharmacists. Due to the increasing age of the population and the ever-increasing number of prescription medicines available, the demand for prescription drugs is growing at rate that will far exceed the capacity and numbers of licensed pharmacists. The net impact of this imbalance is that pharmacists are increasingly spending more time doing clerical and administrative tasks such as verifying filled prescriptions and checking data entry done by pharmacy technicians. Since the capacity of any one pharmacist is fixed, the output of a pharmacy has become constrained. Consequently, the labor and total cost per prescription continues to rise. The December 2000 Department of Health and Human Services Report to Congress titled "The Pharmacist Workforce: A Study of the Supply and Demand for Pharmacists", which is hereby incorporated by reference into the present application, provides an overview of the above problem.

20

Due to these increased demands on a pharmacist's time, and the resulting increased reliance on technicians and other non-professional staff to fill prescriptions, there is an increased chance for prescription error. While these errors may take many forms, the likelihood of a dangerous or life threatening "adverse drug event" increases proportionally with the increased chance of prescription fill error. Several studies have shown that prescription error rates are consistently in the 2% to 7% range, with a 4% error rate often cited as a reliable average. The number of deaths due to medication errors is estimated to exceed 7,000 per year in the United States alone. Of course, this number does not include non-fatal conditions from drugs that also result in some form of trauma or injury. The resulting litigation costs associated with these prescription fill errors have also dramatically increased.

Many existing pharmacy filling systems and procedures still require a human operator, whether that operator is a technician or a licensed pharmacist, to validate visually whether the drug that is delivered to the customer is correct. Thus, the human factor can contribute to the majority of prescription fill errors. Existing visual verification techniques rely on comparing an electronic image of the prescribed medication, *i.e.*, a picture of the prescribed medication retrieved from a data library, with the actual medication that is dispensed for the patient. Other systems and procedures rely on comparing the dispensed medication with that in the original manufacturer's supply container, or comparing an electronic image of the filled prescription with an electronic image of the prescribed medication retrieved from a data library.

Each of these verification systems present similar problems. First, these known verification methods assume that all drugs are visually distinct. This assumption causes many problems because many drugs are not, in fact, visually distinct and, in other cases, the visual differences between drugs is very subtle. For instance, manufacturers are rapidly running out of unique shapes, colors and sizes for their solid dosage form products. To further complicate the problem, generic drug manufactures may be using shapes, colors, and sizes that are different than that of the original manufacturer. Second, even though some known systems may utilize a National Drug Code (NDC) bar code to verify that the supply bottle being accessed corresponds correctly to the patient's prescription, a fraction of filled prescriptions that are never picked up are returned to the supply shelves for reuse in later prescriptions. These reused bottles will not,

therefore, have a manufacturer's bar code on them. It is, therefore, difficult, if not impossible, to incorporate such validation schemes for these unused prescriptions. Furthermore, in these circumstances, a supply bottle is not available for a visual comparison with the filled prescription. Finally, each of these known manual verification and validation techniques typically requires that the pharmacist spend a significant portion of his day performing these administrative or clerical tasks and allows less time for patient consultation and other professional pharmacist activities.

Solid dosage pharmaceuticals (e.g. pills, tablets, and capsules) each have a unique chemical composition associated with them. This is often referred to as a chemical signature or fingerprint. Pharmaceuticals with varying dosage levels of the same active ingredient may have unique chemical signatures as well. Even slight variations in the active ingredient typically produce a unique chemical signature. In that regard, most pharmaceuticals can be identified accurately by the use of some form of chemical analysis. This same methodology may be applied to other forms of medication (e.g. liquids, creams, and powders). Particularly with solid dosage pharmaceutical products, while a group or package of products may look identical in the visible portion of the spectrum each product may have a unique chemical signature in the near-infrared wavelength range (800 to 2500 nm). For example, U.S. Patent No. 6,771,369 to Rzasa et al. describes a pharmaceutical discrimination system that relies on NIR for scanning the contents of a pharmaceutical vial. As another example, U.S. Patent No. 7,218,395 to Kaye et al. describes the use of Raman spectroscopy for scanning vial contents.

Each of these systems may have shortcomings related to the time spent scanning and/or the accuracy produced by the scan. As such, other techniques for automatically scanning a dispensed pharmaceutical may be desirable.

### **Summary of the Invention**

As a first aspect, embodiments of the present invention are directed to a probe for a system for determining the chemical signature of a pharmaceutical compound. The probe comprises: a housing; an inlet in the housing adapted to be connected to a transmitting optical fiber; a scanning aperture in the housing; a receiving outlet in the housing adapted to be

connected to a receiving optical fiber; at least one transmission reflector positioned in the housing to receive laser light from the transmitting optical fiber and reflect the laser light through the detection outlet to a pharmaceutical vial containing a pharmaceutical compound positioned outside the housing, and at least one receiving reflector positioned in the housing to receive light  
5 reflected by the pharmaceutical compound and reflect the light to the receiving outlet. This configuration can enable rapid and accurate scanning of a pharmaceutical contained in a vial positioned adjacent the detection outlet.

As a second aspect, embodiments of the present invention are directed to a system for determining the chemical signature of a pharmaceutical compound in a vial, comprising: a stage  
10 configured to receive and hold a pharmaceutical vial; a spectrometer; a fiber optic bundle connected to the spectrometer, the fiber optic bundle including a transmitting optical fiber and a receiving optical fiber; and a probe. The probe comprises: a housing; an inlet in the housing connected to the transmitting optical fiber; a detection outlet in the housing, the detection outlet positioned adjacent the stage; a receiving outlet in the housing connected to the receiving optical  
15 fiber; at least one transmission reflector positioned in the housing to receive laser light from the transmitting optical fiber and reflect the laser light through the detection outlet to a pharmaceutical compound in a pharmaceutical vial positioned on the stage; and at least one receiving reflector positioned in the housing to receive light reflected by the pharmaceutical compound and reflect the light to the receiving optical fiber. The system further comprises a  
20 processor for processing optical signals from the pharmaceutical compound and comparing the processed signals with a database of known pharmaceutical compounds.

As a third aspect, embodiments of the present invention are directed to a method of verifying pharmaceuticals contained in a pharmaceutical vial. The method comprises:  
positioning a pharmaceutical vial containing a pharmaceutical adjacent a verification system;  
25 passing laser light along a transmission path from a laser generator to the pharmaceutical in the vial, the transmission path including at least one redirection of the laser light with a reflector;  
passing light reflected by the pharmaceutical along a receiving path from the pharmaceutical to a detector, the receiving path including at least one redirection of the light with a reflector;  
determining the chemical signature of the pharmaceutical based on the reflected light;

determining the prescribed pharmaceutical for the vial based on a label affixed to the vial; and comparing the determined chemical signature against a database of known chemical signatures to determine whether the pharmaceutical contained in the vial is the pharmaceutical prescribed for the vial.

5

### **Brief Description of the Figures**

**Figure 1** is a schematic flow chart showing the process of verifying the contents of a filled pharmaceutical vial within an automated pharmaceutical vial filling system.

10 **Figure 2** is a schematic perspective view of a system for verifying the contents of a filled pharmaceutical vial.

**Figure 3** is a section view of the probe of the Raman spectrometer of the system of **Figure 2**.

**Figure 4** is an enlarged partial perspective view of the detecting section of the conveying tube of the system of **Figure 2**.

15 **Figure 5** is an enlarged end view of the detecting section of **Figure 2** with the doors shown in an open position.

**Figure 6** is a flow chart representing the sequence of operations controlled by the controller of the system of **Figure 2**.

20

### **Detailed Description of Embodiments of the Invention**

The present invention will now be described more fully hereinafter, in which preferred embodiments of the invention are shown. This invention may, however, be embodied in different forms and should not be construed as limited to the embodiments set forth herein. Rather, these embodiments are provided so that this disclosure will be thorough and complete, and will fully convey the scope of the invention to those skilled in the art. In the drawings, like  
25 numbers refer to like elements throughout. Thicknesses and dimensions of some components may be exaggerated for clarity.

Unless otherwise defined, all terms (including technical and scientific terms) used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this

invention belongs. It will be further understood that terms, such as those defined in commonly used dictionaries, should be interpreted as having a meaning that is consistent with their meaning in the context of the relevant art and will not be interpreted in an idealized or overly formal sense unless expressly so defined herein.

5           The terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting of the invention. As used herein, the singular forms "a", "an" and "the" are intended to include the plural forms as well, unless the context clearly indicates otherwise. It will be further understood that the terms "comprises" and/or "comprising," when used in this specification, specify the presence of stated features, integers, steps, operations,  
10 elements, and/or components, but do not preclude the presence or addition of one or more other features, integers, steps, operations, elements, components, and/or groups thereof. As used herein the expression "and/or" includes any and all combinations of one or more of the associated listed items.

          In addition, spatially relative terms, such as "under", "below", "lower", "over", "upper,"  
15 "front," "rear" and the like, may be used herein for ease of description to describe one element or feature's relationship to another element(s) or feature(s) as illustrated in the figures. It will be understood that the spatially relative terms are intended to encompass different orientations of the device in use or operation in addition to the orientation depicted in the figures. For example, if the device in the figures is turned over, elements described as "under" or "beneath" other  
20 elements or features would then be oriented "over" the other elements or features. Thus, the exemplary term "under" can encompass both an orientation of over and under. The device may be otherwise oriented (rotated 90 degrees or at other orientations) and the spatially relative descriptors used herein interpreted accordingly.

          Well-known functions or constructions may not be described in detail for brevity and/or  
25 clarity.

          Referring now to the figures, a filled vial verification station is illustrated in **Figure 2** and is designated broadly at **100**. The verification station **100** is intended to verify that the contents of the vial are indeed the contents that the prescription calls for. Referring to **Figure 1**, the basic operation of the station **100** begins with the sensing of the contents of the filled, labeled, capped vial through



the vial (**Step 10**). If the contents of the vial match those that the system expects, the vial is accepted and conveyed to an offload station (**Step 30**). If instead the contents of the vial do not match those that the system expects, the vial is rejected and conveyed to a reject area (**Step 20**).

Turning now to **Figure 2**, the verification station **100** includes a box-type housing **102** with  
5 a rear wall **104**, a pair of side walls **106**, a front wall **108** and a ceiling **105** that define a cavity **107**.  
An entry opening **110** is present in the rear wall **104**, from which a conveying tube **111** leads to a  
detection unit **130** (described in detail below). An exit opening **112** is present in one of the side  
walls **106**.

Referring again to **Figure 2**, a reject bin **114** is mounted to one of the side walls **106** and  
10 includes an opening (not shown) for access to the cavity of the housing **102**. The reject bin **114**  
illustratively includes a reject ID detector **116** (such as a biometric identifier) that limits external  
access to the reject bin **114** to authorized personnel.

Referring still to **Figure 2**, the housing **102** may also include other optional components that  
can facilitate operation. A speaker **118** is mounted on the housing **102** to provide an audible signal  
15 regarding operations of the validation station **100**. A display **122** is also mounted on the housing  
**102** to show the status of operations of the validation station **100**, the identity of the prescription  
being processed, or the like. An external bar code reader **120** is also mounted on the housing **102** to  
enable an operator to manually scan the bar code on a filled, labeled pre-packaged or unit of use  
pharmaceutical if desired (for example, pre-packaged tablets in a patient compliance pack or a  
20 packet of birth control pills). Such a scan can facilitate the verification that the NDC on the package  
matches the pharmaceutical on the prescription order. All of these components are optional and  
may be omitted in some embodiments.

Referring again to **Figure 2**, a detection unit **130** is positioned within the cavity **107** of  
the housing **102**. The detection unit **130** includes a Raman spectrometer **134**. The spectrometer  
25 **134** is positioned within the cavity **107** to enable the spectrometer **134** to scan the contents of a  
filled, labeled vial. The spectrometer **134** is connected electrically to a controller **42**, which  
includes a memory module (not illustrated) for storing a spectral signature of a detected  
pharmaceutical compound. The spectrometer **134** also includes a probe **170** that is positioned  
adjacent a detection section **117** at the lower end of the conveying tube **111**. The probe **170** is

connected to the Raman spectrometer **134** via a transmitting fiber **137** of a fiber optic bundle **139**. An exemplary fiber optic bundle is described in PCT Publication No. WO 07/019460, the disclosure of which is hereby incorporated herein in its entirety.

Referring now to **Figure 3**, the probe **170** includes a light-tight rectangular housing **172** that encloses a cavity **173**. Within the cavity are components that focus, redirect, and otherwise manipulate light provided by the transmitting fiber **137** of the fiber bundle **139**. In the illustrated embodiment, the transmitting fiber **137** presents light (in the form of a 0.2 mm laser) to the cavity **173** through an inlet **171a** in one side wall **172a** of the housing **172**; the light then follows a transmission path through a plurality of reflectors (typically mirrors) to a scanning aperture **186** that is adjacent the detecting section **117** of the conveying tube **111**. More specifically, the light (laser beam) passes from the transmitting fiber **137** first through a lens **174** that focuses the light, then through a laser-line filter that filters out noise spectrum of the light source and fiber, then through an adjacent lens **176** that further focuses the light. The light then passes to a reflector **178** mounted on the opposite side wall **172b** of the housing **172**. The reflector **178** is mounted at an oblique angle to the path of the entering light (in this instance, the angle is 6.5 degrees), such that the light is redirected at an angle of 13 degrees back toward the side wall **172a** until it reaches another reflector **180**. In the illustrated embodiment, the reflector **180** is mounted at a similar oblique angle to the reflector **178**, such that the light exiting the reflector **180** travels on a path that is substantially parallel to the segment of the path between the lens **176** and the reflector **178**. Light then passes to a concave reflector **182** that is mounted adjacent the side wall **172b** at an angle of 40 degrees to the light path. The reflector **182** collimates or slightly focuses the laser light and redirects the light toward a reflector **184** that is mounted on a wall **172c** of the housing **172**. Light then reflects from the reflector **184** through the scanning aperture **186** in a wall **172d** (which is opposite the wall **172c**). Once through the scanning aperture **186**, the light can pass into a pharmaceutical vial held in the detecting section **117** of the tube **111** (see **Figure 4**) and be employed to detect the identity of the contents of the vial (the vial typically being held such that the tablet being detected is positioned between about 0.1 and 0.4 inches from the wall **172d**).

When entering the vial, in the illustrated embodiment the light beam has a diameter of between about 2.5 and 3.5 mm, typically about 3 mm, an intensity of between about 200 and 500 milliwatts, and a wavelength of less than about  $140 \text{ cm}^{-1}$ . A beam of this diameter can increase the depth of field of the spectrometer, which can improve the accuracy of the spectrum (because  
5 tablets in a vial are not always at the same depth, increased depth of field can improve the chance of the system finding a table to detect). Also, the light beam enters the flat bottom surface of the vial at an oblique angle to the vial (between about 75 and 85 degrees), which can decrease the degree of undesirable back reflection from the vial surface.

Signal light is reflected from the vial to the Raman spectrometer along a receiving path  
10 that begins at the vial and proceeds through the aperture 186 to the reflector 184 and the reflector 182, then to a lens 188 mounted near the side wall 172a. The reflector 182 transmits Raman signal and rejects source light. For further purifying Raman spectrum, another Raman edge filter may be placed between the reflector 182 and the lens 188. The lens 188 focuses the returning light and directs it to a receiving fiber 190 of the fiber optic bundle 139 via a receiving outlet  
15 171b in the side wall 172a, through which the light passes to the Raman spectrometer for detection and processing. Generation of the spectrum by the spectrometer 134 once light is received in the receiving fiber 190 is well-known and need not be described in detail herein; for further detail, Raman spectrometry and its underlying theory is described generally at, *e.g.*, [http://www.lambdasolutions.com/RamanTechNote\\_English.pdf](http://www.lambdasolutions.com/RamanTechNote_English.pdf), the disclosure of which is  
20 hereby incorporated herein in its entirety. In some embodiments, the generation of the spectrum (*i.e.*, the chemical signal) of the pharmaceutical can involve the combination of the chemical signals of the pharmaceutical and the material of the vial (which is typically amber-colored polypropylene, although polycarbonate and PET may be used for liquids). Also, because scanning is typically relatively rapid (on the order of 0.1 seconds), in some embodiments  
25 multiple scans may be performed and the results averaged to provide a composite spectrum.

Referring once again to **Figure 2**, the detection unit 130 further includes a second bar code scanner 136 that is positioned adjacent the detection section 117 so that it can scan the bar code on the filled, labeled vial. The bar code scanner 136 is also connected electrically to the

controller 42. The bar code on the filled, labeled vial indicates, or is linked to data indicating, *inter alia*, the pharmaceutical that is prescribed and, therefore, should be present in the vial.

Referring now to **Figures 2, 4 and 5**, a diverting unit 142 associated with the detecting section 117 is configured to receive a signal from the controller 42 and divert a filled, labeled vial to either an approved vial conveyer 140 or a rejected vial conveyor 138 based on the signal. The diverting unit 142 includes two plungers 160, 162, each of which is positioned below the detecting section 117 of the conveying tube 111. Two doors 118, 119 that are positioned on the upper portion of the detecting section 117 opposite the plungers 160, 162. Each of the doors 118, 119 is attached to the detecting section via a hinge that enables the door to pivot between a closed position, in which it covers the detecting section 117, and an open position, in which the detecting section 117 is open.

Referring still to **Figure 2**, an approved vial conveyor 140 leads from the detection section 117 to the exit opening 112 in the side wall 106. A rejected vial conveyor 138 leads from the detecting section 117 to the opening in the reject bin 114.

In some embodiments, the verification station 100 also includes a stamping device (not shown). The stamping device is positioned outside the housing 102 at the end of the approved vial conveyor 140 and is electrically connected to the controller 42. In certain embodiments, the stamping device includes a proprietary ink cartridge that participates in the activation of the stamping device (such that the stamping device will not operate without the cartridge being in place).

Referring again to **Figure 2**, the controller 42 includes modules that are associated with the detection unit 130. More specifically, the controller 42 includes a data base 150 that stores the prescription number (hereinafter the "Rx number") associated with each prescription, and a National Drug Code (NDC) number that corresponds to a particular pharmaceutical compound. Also, the controller 42 includes a data base 152 of spectral signatures, each of which corresponds to a particular pharmaceutical compound.

In operation, and with reference to **Figure 6**, a filled, labeled, capped vial V is deposited into the conveying tube 111 (this step can be performed manually by a pharmacist or automatically; for example, a robotic arm associated with an automated pharmaceutical

dispensing machine such as that disclosed in U.S. Patent No. 6,971,541 to Williams et al. may be employed). The conveying tube 111 conveys the vial V to the detecting section 117 (Step 200). When the vial V reaches the detecting section 117, the controller 42 (signaled by a proximity detector or the like that detects the presence of the vial V) signals the bar code scanner 136 to read the bar code on the label L of the vial V (Step 220). This information is passed to the controller 42, which identifies the Rx number and NDC number from the bar code.

Also, after the vial V arrives on the platform 132, the controller 42 signals the spectrometer 134 to scan the contents of the vial V through the vial floor via the probe 141. In some embodiments, the spectrometer 134 may also scan through the side of the vial (assuming favorable positioning and label orientation). In scanning the contents of the vial V, the spectrometer 134 generates a spectral signature of the compound in the vial V (Step 210).

Correlation of the scanned spectrum of the dispensed pharmaceutical and the identity of the prescribed pharmaceutical can be achieved in different ways. For example, as shown in Figure 6, the bar code scanner 136 scans the bar code on the label L and, based on the identity of the prescribed pharmaceutical, retrieves a sublibrary of spectra from the database 150 (Step 230). As discussed above, separately the Raman spectrometer 134 generates a Raman spectrum for the compound in the vial via the probe 170. The controller 42 then compares the scanned spectral signature to the spectral signatures of the sublibrary to determine which spectrum is the best match for the scanned spectrum (Step 240). The identity of the best matched spectrum is then compared the identity of the prescribed pharmaceutical to determine whether they match (Step 250).

In alternative embodiments, the scanned spectrum can be compared directly to the spectrum of the prescribed pharmaceutical to determine whether they match. As another alternative, the scanned spectrum can be compared to all of the spectra in the database, the most closely matching spectrum can be identified, and the identity of that pharmaceutical can be compared to the identity of the prescribed pharmaceutical to determine whether they match.

If the identity of the prescribed pharmaceutical identified on the label of the vial V matches the identity of the pharmaceutical with the best matched spectrum, the vial V is deemed to contain the proper pharmaceutical compound, and the controller 42 actuates the diverting unit

142 to divert the vial V to the approved vial conveyor 140 by extending the plunger 160 and opening the door 118 (Step 270). This action propels the vial V to the approved vial conveyor 140, which then conveys the approved vial V to the stamping device. The stamping device stamps the vial V with a mark (often indelible) that indicates that the contents of the vial V have  
5 been validated. The vial V can then be conveyed, either manually or via another conveyor, to an offloading station.

If the identities of the pharmaceutical determined for the scanned vial V and the pharmaceutical identified by the NDC number on the vial V do not match, the controller 42 signals the diverting unit 142 to divert the vial V to the reject conveyor 138 by extending the  
10 plunger 162 and opening the door 119 (Step 260). This action propels the vial V into the reject conveyor 138, which conveys the vial V to the reject bin 114. The vial V remains in the reject bin 114 until it is removed by approved personnel who can open the reject bin 114 via the reject ID detector 116.

Those skilled in this art will appreciate that the systems and methods described above  
15 may vary. For example, either or both of the approved and rejected vials may be removed from the system manually, based on a visual or auditory signal. The probe may take a different configuration, with different numbers, locations and/or orientations of lenses, reflectors and the inlet and outlets. The configuration of the housing 102 may vary, as may the positions and orientations of the components contained therein. Other variations will be apparent to those of  
20 skill in this art.

The foregoing is illustrative of the present invention and is not to be construed as limiting thereof. Although exemplary embodiments of this invention have been described, those skilled in the art will readily appreciate that many modifications are possible in the exemplary  
25 embodiments without materially departing from the novel teachings and advantages of this invention. Accordingly, all such modifications are intended to be included within the scope of this invention as defined by the claims. The invention is defined by the following claims, with equivalents of the claims to be included therein.

**That Which is Claimed is:**

1. A probe for a system for determining the chemical signature of a pharmaceutical compound, comprising:
- 5 a housing;
- an inlet in the housing adapted to be connected to a transmitting optical fiber;
- a scanning aperture in the housing;
- a receiving outlet in the housing adapted to be connected to a receiving optical fiber;
- at least one transmission reflector positioned in the housing to receive laser light from the transmitting optical fiber and reflect the laser light through the detection outlet to a
- 10 pharmaceutical vial containing a pharmaceutical compound positioned outside the housing, and
- at least one receiving reflector positioned in the housing to receive light reflected by the pharmaceutical compound and reflect the light to the receiving outlet.
2. The probe defined in Claim 1, wherein the housing includes side walls, and
- 15 wherein the inlet is located in a first side wall and the scanning aperture is located in a second side wall.
3. The probe defined in Claim 2, wherein the receiving outlet is located in the first side wall.
- 20
4. The probe defined in Claim 2, wherein the second side wall is generally normal to the first side wall.
5. The probe defined in Claim 1, wherein the at least one transmission reflector is a
- 25 plurality of transmission reflectors.
6. The probe defined in Claim 5, wherein one of the plurality of transmission reflectors is positioned to reflect laser light directly at the pharmaceutical vial at an angle of between about 75 and 85 degrees relative to a bottom surface of the pharmaceutical vial.

7. The probe defined in Claim 5, wherein the plurality of transmission reflectors includes at least three transmission reflectors.

5 8. The probe defined in Claim 5, wherein the plurality of transmission reflectors includes five transmission reflectors.

9. The probe defined in Claim 1, further including a lens positioned to focus laser light transmitted between the inlet and the at least one reflector.

10 10. The probe defined in Claim 1, wherein the at least one receiving reflector is a plurality of receiving reflectors.

11. The probe defined in Claim 10, wherein one of the plurality of receiving reflectors positioned to receive light reflected from the pharmaceutical at an angle of between about 75 and 85 degrees relative to a bottom surface of the pharmaceutical vial.

12. The probe defined in Claim 11, further comprising a lens located between one of the plurality of receiving reflectors and the receiving outlet, the lens configured to focus the reflected light as it passes through the receiving outlet.

13. The probe defined in Claim 1, wherein the at least one transmission reflector is a plurality of transmission reflectors, and wherein the at least one receiving reflector is a plurality of receiving reflectors, and wherein at least one reflector serves as both a transmission reflector and a receiving reflector.

14. A system for determining the chemical signature of a pharmaceutical compound in a vial, comprising:  
a stage configured to receive and hold a pharmaceutical vial;



a spectrometer;

a fiber optic bundle connected to the spectrometer, the fiber optic bundle including a transmitting optical fiber and a receiving optical fiber; and

a probe comprising:

5

a housing;

an inlet in the housing connected to the transmitting optical fiber;

a detection outlet in the housing, the detection outlet positioned adjacent the stage;

a receiving outlet in the housing connected to the receiving optical fiber;

10

at least one transmission reflector positioned in the housing to receive laser light from the transmitting optical fiber and reflect the laser light through the detection outlet to a pharmaceutical compound in a pharmaceutical vial positioned on the stage; and

at least one receiving reflector positioned in the housing to receive light reflected by the pharmaceutical compound and reflect the light to the receiving optical fiber; and

15

a processor for processing optical signals from the pharmaceutical compound and comparing the processed signals with at least one spectrum from a database of known pharmaceutical compounds.

15. The system defined in Claim 14, further comprising a stamping device configured to indicate that a pharmaceutical vial has been approved.

20

16. The system defined in Claim 14, further comprising structure for separating rejected vials from approved vials.

25

17. The system defined in Claim 14, further comprising a bar code scanner positioned to scan a bar code on the pharmaceutical vial as it is positioned on the stage.

18. A method of verifying pharmaceuticals contained in a pharmaceutical vial, comprising:

positioning a pharmaceutical vial containing a pharmaceutical adjacent a verification system;

5 passing laser light along a transmission path from a laser generator to the pharmaceutical in the vial, the transmission path including at least one redirection of the laser light with a reflector;

passing light reflected by the pharmaceutical along a receiving path from the pharmaceutical to a detector, the receiving path including at least one redirection of the light with a reflector;

10 determining the chemical signature of the pharmaceutical based on the reflected light;

determining a prescribed pharmaceutical for the vial based on a label affixed to the vial; and

15 comparing the determined chemical signature against a database of known chemical signatures to determine whether the pharmaceutical contained in the vial is the prescribed pharmaceutical for the vial.

20 19. The method defined in Claim 18, wherein the step of determining the prescribed pharmaceutical for the vial comprises scanning indicia on the label affixed to the vial, the indicia indicating the prescribed pharmaceutical.

20. The method defined in Claim 18, wherein the step of passing laser light comprises passing a beam of laser light that has a diameter of between about 2.5 and 3.5 mm as the light reaches the vial.

25 21. The method defined in Claim 18, further comprising the step of stamping the label affixed to the vial if the pharmaceutical in the vial matches the prescribed pharmaceutical.

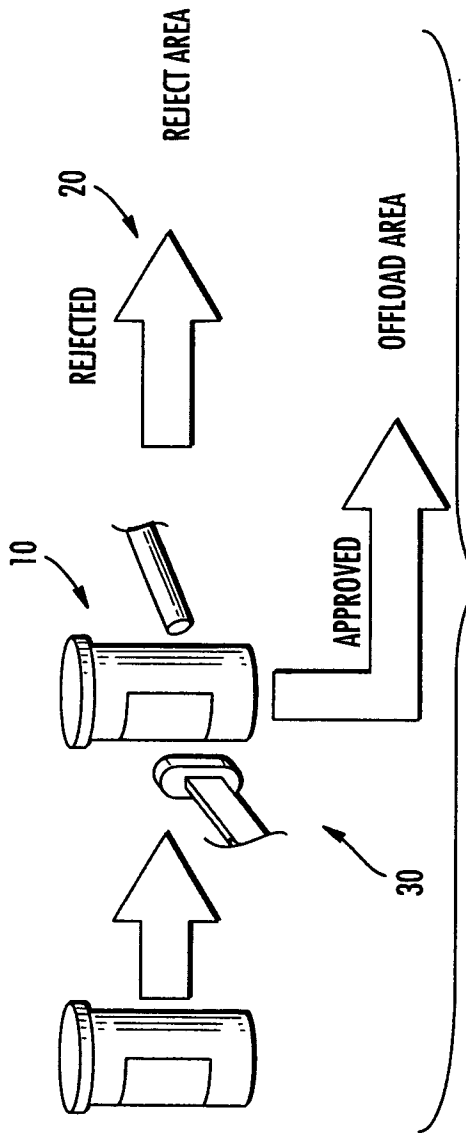
22. The method defined in Claim 18, wherein the vial has a flat bottom surface, and wherein the laser light is directed to the vial at an angle of between about 75 and 85 degrees relative to the vial bottom surface.

5 23. The method defined in Claim 18, wherein the step of determining the chemical signature is performed with Raman spectroscopy.

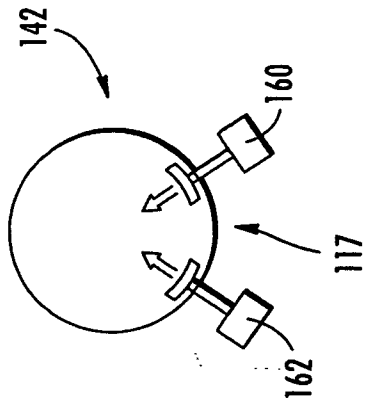
24. The method defined in Claim 18, wherein the wavelength of the laser light is less than about  $140 \text{ cm}^{-1}$ .

10

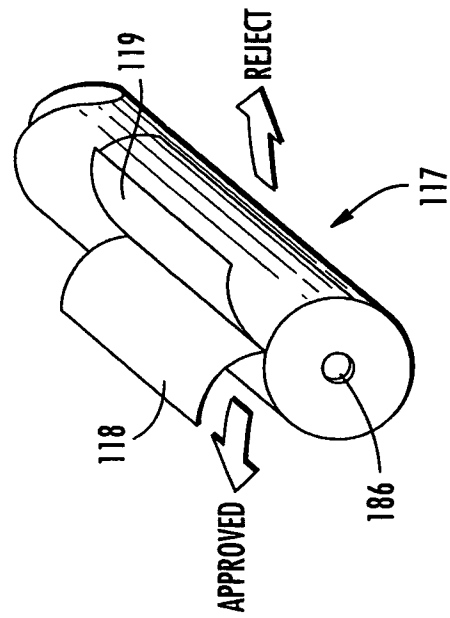
25. The method defined in Claim 18, wherein an initial segment of the transmission path defines a first direction, and wherein an initial segment of the receiving path defines a second direction, and wherein the first and second directions are generally perpendicular.



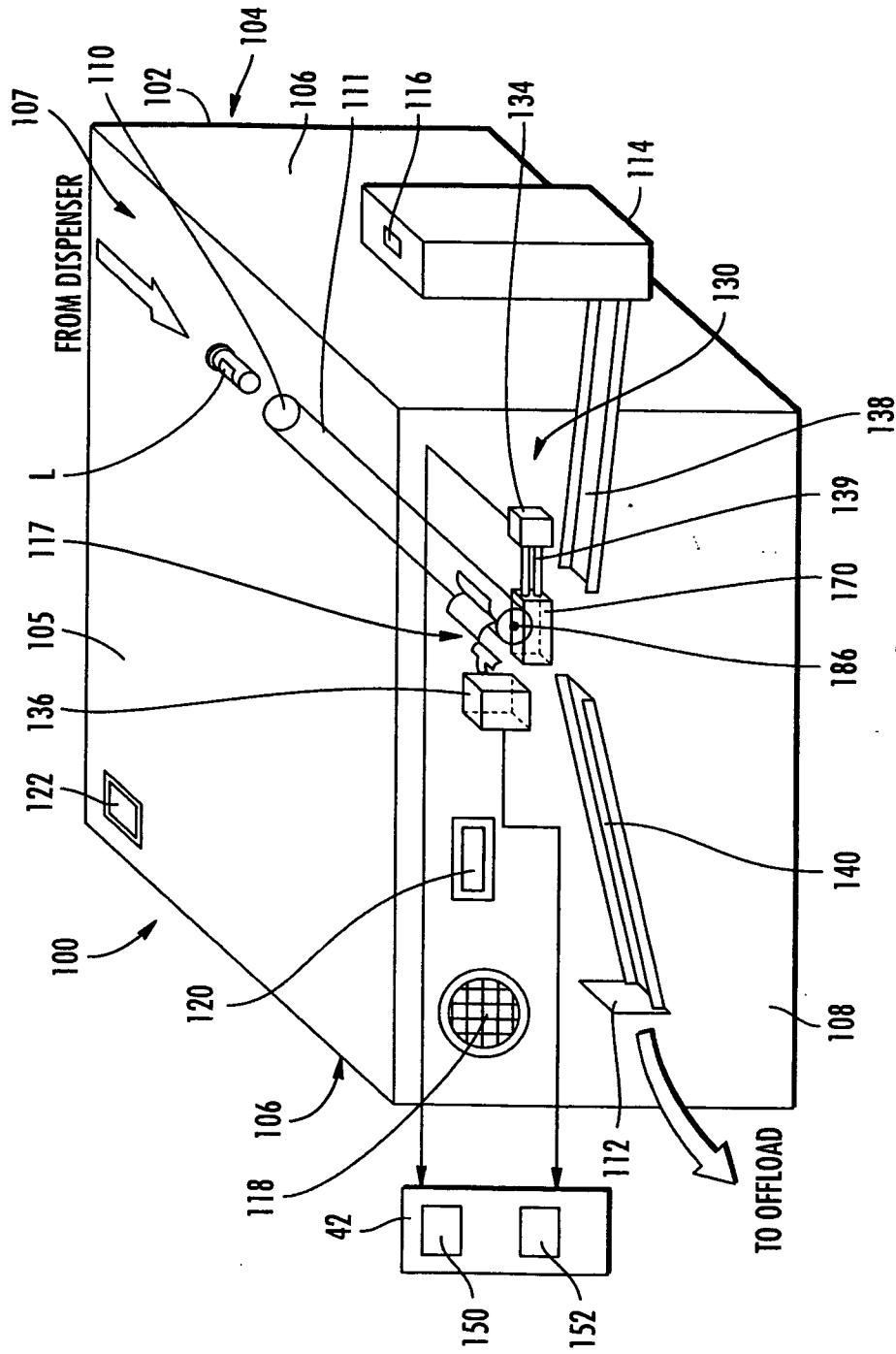
**FIG. 1**



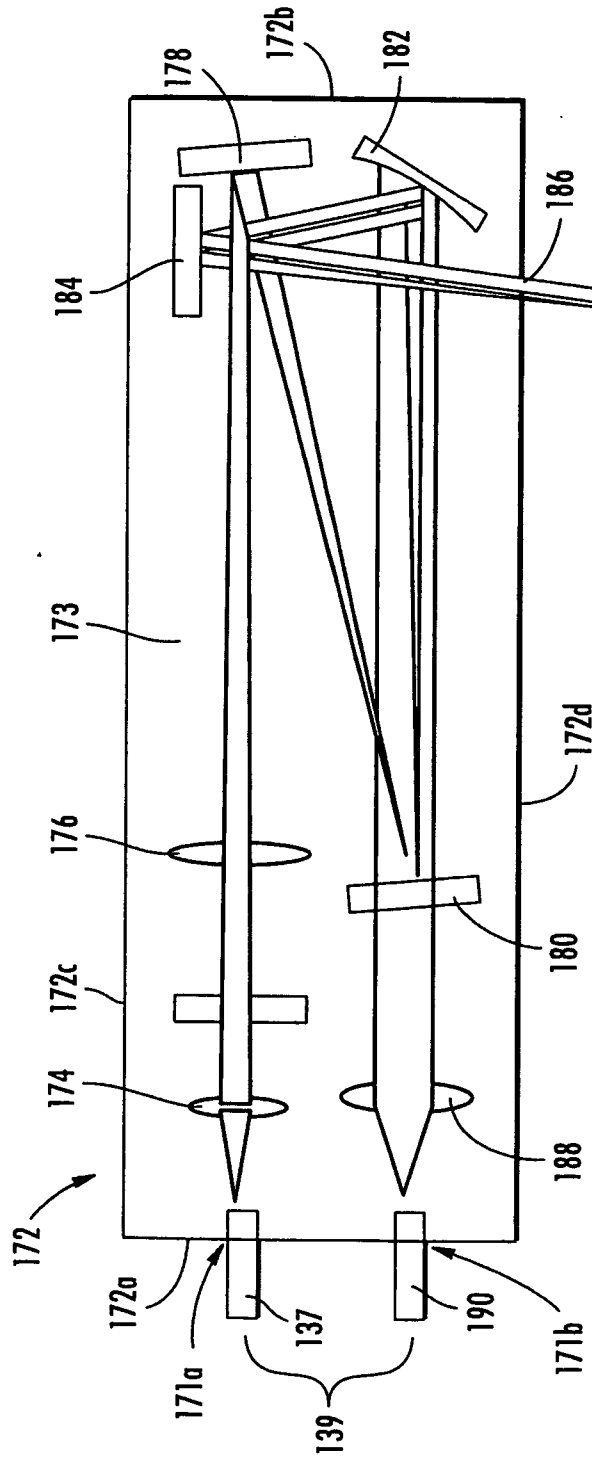
**FIG. 5**

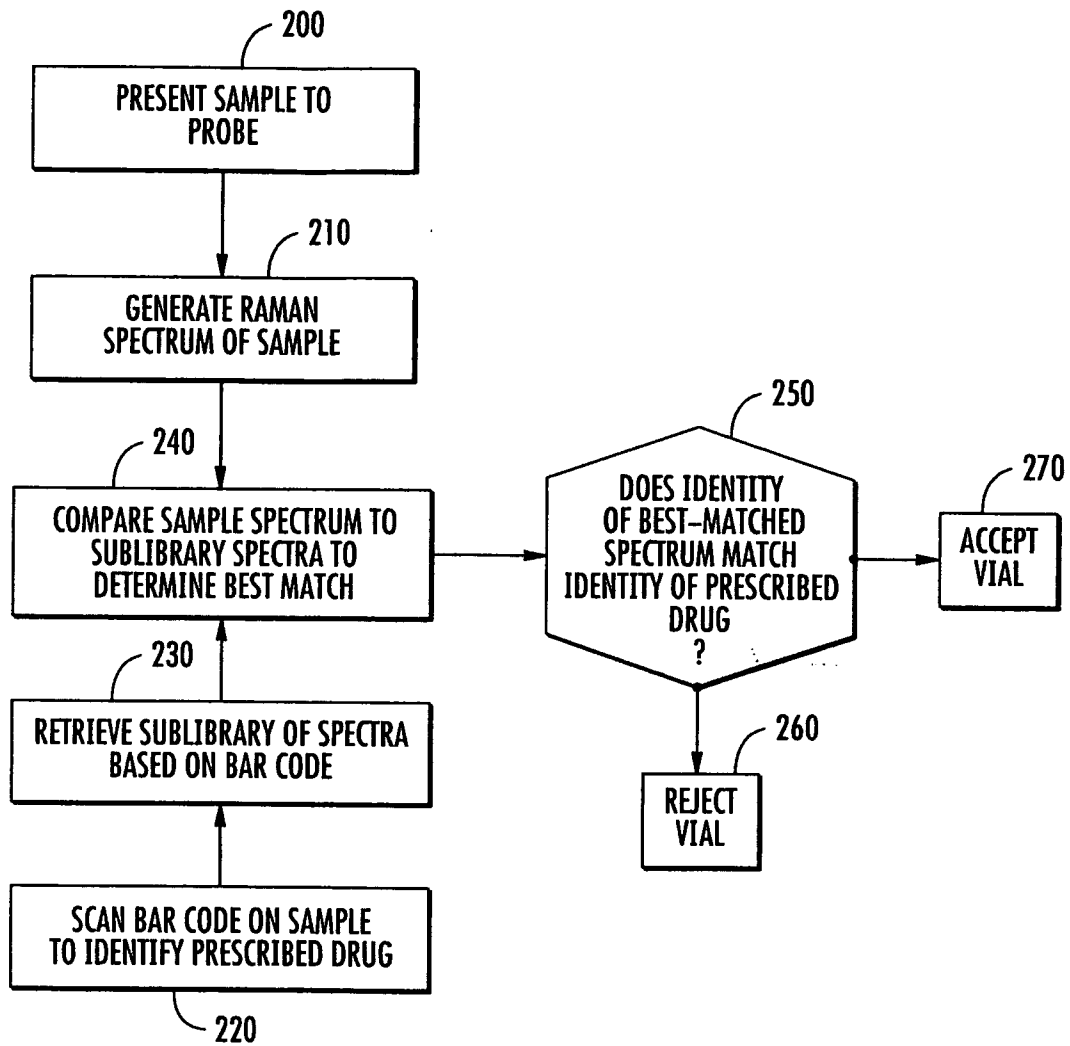


**FIG. 4**



**FIG. 2**





**FIG. 6**

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2008/000387A. CLASSIFICATION OF SUBJECT MATTER  
INV. G01N21/65 G01N21/95

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6 373 567 B1 (WISE KENT LAWSON [US] ET AL) 16 April 2002 (2002-04-16) - figure 1 column 8, line 10 - line 47	1-25
Y	US 2005/248759 A1 (WANG PEIDONG [US] ET AL) 10 November 2005 (2005-11-10) figure 1 paragraph [0006] paragraph [0011] - paragraph [0017] paragraph [0032] - paragraph [0037] paragraph [0065] - paragraph [0006] ----- -/--	1-13

 Further documents are listed in the continuation of Box C. See patent family annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \* & \* document member of the same patent family

Date of the actual completion of the international search

13 June 2008

Date of mailing of the international search report

25/06/2008

Name and mailing address of the ISA/  
European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Verdoodt, Erik



## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2008/000387

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2007/008523 A1 (KAYE STEPHEN T [US] ET AL) 11 January 2007 (2007-01-11) paragraphs [0012] - [0015], [0017] paragraphs [0027], [0028], [0030] - [0034] figures 1,3,6	14-25
A	WO 97/48329 A (UNIV TEXAS [US]; RICHARDS KORTUM REBECCA [US]; MAHADEVAN JANSEN ANITA) 24 December 1997 (1997-12-24) figure 6	1-13
A	US 6 771 369 B2 (RZASA DAVID M [US] ET AL) 3 August 2004 (2004-08-03) the whole document	14-25
A	WO 2006/036434 A (AHURA CORP [US]) 6 April 2006 (2006-04-06) page 17, lines 24-27 page 18, line 6 - line 7	6,11
A	US 6 310 686 B1 (JIANG YANAN [US]) 30 October 2001 (2001-10-30) the whole document	1
A	US 2004/263843 A1 (KNOPP KEVIN J [US] ET AL) 30 December 2004 (2004-12-30) the whole document	1

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/US2008/000387
---

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6373567	B1	16-04-2002	NONE
US 2005248759	A1	10-11-2005	US 2008024777 A1 31-01-2008
US 2007008523	A1	11-01-2007	NONE
WO 9748329	A	24-12-1997	AU 3570197 A 07-01-1998
US 6771369	B2	03-08-2004	AU 2003230624 A1 29-09-2003 CA 2477259 A1 25-09-2003 EP 1502223 A2 02-02-2005 WO 03079267 A2 25-09-2003 US 2003174326 A1 18-09-2003 US 2004207842 A1 21-10-2004
WO 2006036434	A	06-04-2006	EP 1789762 A2 30-05-2007 US 2006170917 A1 03-08-2006
US 6310686	B1	30-10-2001	NONE
US 2004263843	A1	30-12-2004	NONE