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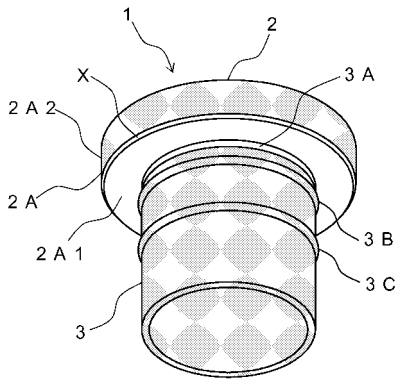
(54) VIAL RUBBER-STOPPER

(57) There is provided a rubber stopper used to seal an opened portion of vials and syringes for keeping medical liquid and, in particular, to a rubber stopper in which stoppering properties can be improved without damaging sealing properties in the absence of silicone coating.

A vial rubber stopper 1 comprises a disc-like top portion 3 and a cylindrical leg portion 2 of smaller diameter compared with that of the disc-like top portion, which is protruded from a bottom surface of the disc-like top portion 3 to shape into a flange 2A upward. An

under-flange ring portion 3A connected to a flange bottom surface 2B is divided on an outer peripheral surface of the cylindrical leg portion 2, and the first ring-like raised portion 3B and the second ring-like raised portion 3C are formed downward of the under-flange ring portion 3A in the circumferential direction. An upper surface of the disc-like top portion 3 including a flange-upper surface, a maximum diametral portion of a flange-peripheral surface, a bottom surface of the disc-like top portion 3 located inside of the cylindrical leg portion 2 and a surface of the cylindrical leg portion 2 other than the under-flange ring portion 3A are laminated with a synthetic resin to leave the flange bottom surface and the surface of the under-flange ring portion 3A as a naked rubber stock.

FIG.1



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Description

Technical Field

[0001] This invention relates to a rubber stopper used to seal an opened portion of vials and syringes as medical vessels which will be hereinafter simply referred to as vial and, in particular, to a rubber stopper in which stoppering properties can be improved without damaging sealing properties in the absence of silicone coating.

Background of the Invention

[0002] It is required for a stopper body used to seal an opened portion of chemical or medical liquid-containing vial to meet various quality requirements such as sealing properties, gas barrier properties, chemical resistance, needling resistance, low reactivity and the like and, in general, a rubber stopper body of high elastic deformation is frequently employed as a product sufficient to satisfy these requirements, which will be hereinafter referred to as rubber stopper.

[0003] A syringe needle is often stuck through the rubber stopper from an upper surface thereof to suck up a chemical or medical liquid in a vial. When the liquid kept in the vial is a medicine, the rubber stopper should meet the quality requirement of the transfusion rubber stopper test according to the Japanese Pharmacopoeia, XV edition and, in speciality, should pass the elution test under a condition of 121°C for one hour using a heat resistant high pressure steam sterilizer.

[0004] There have been conventionally used synthetic rubbers such as butylene rubber and isoprene rubber, thermoplastic styrene elastomers such as SEBS, thermoplastic elastomers mainly comprising polyisobutylene and polybutadiene, and the like as a material for vial rubber stopper which meets the requirement as described above.

[0005] With regard to a general figure of the vial rubber stopper, a cylindrical leg portion is protruded downward from a disc-like top portion to form a flange upward, a diameter of the leg portion being smaller than that of the disc. The cylindrical leg portion of the vial rubber stopper is driven into an opened portion of the vial so that a bottom surface of the flange of the disc-like top portion is stuck firmly to an end surface of the opened portion.

[0006] Further, there has been proposed a vial rubber stopper in which a ring-like protrusion is formed on the periphery of the cylindrical leg portion to be driven into the opened portion of the vial, an outer diameter of the protrusion being a little larger than an inner diameter of the opened portion (see, for example, the patent reference. 1 to 2).

[0007] Conventional vial rubber stoppers tend to stick each other on a conveying line during the production process to cause troubles of the line due to sticky nature of their surface.

[0008] In order to prevent such troubles, a silicone resin oil has been conventionally coated on the surface of the rubber stopper. Coating of silicone oil is now avoided because of a potential harmful effect to human body.

[0009] On the other hand, there has been known another type of vial rubber stopper in which the full surface of the cylindrical leg portion to be in contact with a medical liquid and the bottom surface of the disc-like top portion are laminated by an inactive resin film such as, for example, quite chemically resistant fluorine resin film to prevent change in quality of the medical liquid contained in the vial and, at the same time, to avoid mutual sticking of the rubber stoppers and improve sliding properties thereof (see, the patent references 3 to 5).

[0010] It has been also known to laminate throughout the cylindrical leg portion or partially a portion other than a peripheral root thereof continuing to the flange bottom surface, i.e., a ring portion under the flange for sealing the vial opened portion (see, the patent reference. 6 to 9).

[0011] However, the above mentioned rubber stopper in which all surface of the cylindrical leg portion and the bottom surface of the flange are laminated arouses difficulties in sealing properties of the vial because both of these surfaces in contact with the vial opened portion are all laminated with a laminate film.

[0012] In the case of the rubber stopper in which lamination is applied on the surface other than that of the peripheral root portion of the cylindrical leg (ring portion under the flange), the peripheral root portion is left as a naked rubber stock, thereby improving sealing properties of the vial, while the rubber stopper sometimes comes up to the surface after it is driven into the vial opened portion due to strong friction and repulsion of the naked rubber stock, thereby causing such problems that the stopper might be driven repeatedly plural times or is hardly to drive completely.

[0013] Further, in the case of the rubber stopper in which only the cylindrical leg portion is thoroughly laminated, friction resistance of the rubber stock is decreased but leakage of the naked rubber stock is occurred around the peripheral root portion (ring portion under the flange) to be connected to the bottom surface of the disc-like top portion when the leg is joined monolithically to the disc, thereby causing defective molding frequently.

[0014] The reason why is considered that the cylindrical leg portion set in a mold is caught in a flow of the rubber stock for forming the flange of the disc-like top portion to cause difference in position, so that the rubber stock flows into the thus formed gap between the mold and the cylindrical leg portion.

[0015] On the basis of the reason as described above, a vial rubber stopper GP as shown in Fig. 5 has been conventionally developed and used widely. A wide belt-like ring protrusion R is formed on a cylindrical leg portion L to keep

sealing properties of a vial opened portion, while an inactive film lamination is applied on surfaces of the ring protrusion R and a portion as a periphery of a disc-like top portion T other than a bottom surface T2 of a flange T1 as shown in Fig. 5 by a dark mesh pattern.

[0016] The bottom surface T2 of the flange T1 of the rubber stopper GP is not laminated to leave it as a naked rubber stock, while the upper ring protrusion R of the cylindrical leg portion L is coated with silicone to lower the friction resistance when the cylindrical leg portion L is driven into the vial opened portion as shown in Fig. 5 by a faint mesh pattern.

[0017] However, various harmful effects caused by silicone oil used for silicone coating have been pointed out and are tried to avoid such disadvantages which include, for example, a decrease in strength observed when the silicone oil comes in contact with a medical liquid kept in the vial to absorb the active ingredient or an infection to human body caused by injection of the medical liquid contaminated with a pealed material of silicone oil itself as fine particles. It is now studied to avoid silicone coating to the ring protrusion R of the vial rubber stopper GP as shown in Fig. 5.

Patent Reference 1: Japanese Utility Model No. 1986-2233
Patent Reference 2: Japanese Patent No. 1989-176435
Patent Reference 3: Japanese Patent No. 1990-136139
Patent Reference 4: Japanese Patent No. 2002-209975
Patent Reference 5: Japanese Patent No. 1988-296756
Patent Reference 6: U.S. Patent No. 6,165,402
Patent Reference 7: Japanese Patent No. 1982-53184
Patent Reference 8: Japanese Utility Model No. 1986-31441
Patent Reference 9: Japanese Utility Model No. 1989-17545

Disclosure of the Invention

[0018] This invention has been completed to solve conventional problems as described above and accordingly it is an object of the invention is to provide a vial rubber stopper of high sealing properties, gas barrier properties, chemical resistance and needling resistance as well as low reactivity, having improved productivity in the pharmaceutical manufacturing process and mechanical conveying properties, which is prepared without silicone coating.

[0019] In order to achieve the above mentioned object, a vial rubber stopper comprises a disc-like top portion and a cylindrical leg portion of smaller diameter compared with that of the disc-like top portion, which is protruded from a bottom surface of the disc-like top portion to shape into a flange upward, **characterized in that** an under-flange ring portion connected to a flange bottom surface is divided on an outer peripheral surface of the cylindrical leg portion, and at least one ring-like raised portion is arranged downward of the under-flange ring portion in the circumferential direction, while an upper surface of the disc-like top portion including a flange-upper surface, a maximum diametral portion of a flange-peripheral surface, a bottom surface of the disc-like top portion located inside of the cylindrical leg portion and a surface of the cylindrical leg portion other than the under-flange ring portion are laminated with a synthetic resin to leave the flange bottom surface and the surface of the under-flange ring portion as a naked rubber stock.

[0020] Further, the under-flange ring portion is preferably divided between the flange bottom surface and a top edge portion of a synthetic resin film laminated on the outer peripheral surface of the cylindrical leg portion. A material of the synthetic resin film is preferably a fluororesin or Ultra High Molecular Weight polyethylene.

[0021] It is also preferable for preparing the vial rubber stopper of the invention to conduct press molding of the cylindrical leg portion and lamination of the synthetic resin film thereto simultaneously and to carry out press molding of the disc-like top portion, lamination of the synthetic resin film thereto and integration of the disc-like top portion to the cylindrical leg portion at the same time.

Brief Description of the Drawings

[0022]

Fig. 1 is a perspective view an embodiment of the present vial rubber stopper drawn from a diagonal downward direction, in which a mesh pattern shows laminated portions.
Fig. 2 is a perspective view of a modification of the vial rubber stopper shown in Fig. 1.
Fig. 3 is a side view of the vial rubber stopper shown in Fig. 2, which is monolithically molded.
Fig. 4 is a sectional view of the vial rubber stopper shown in Fig. 2, which is driven into an opened portion.
Fig. 5 is a perspective view of a conventional vial rubber stopper drawn from a diagonal downward direction, in which a dark mesh pattern shows laminated portions and a faint mesh pattern shows a silicone-coated portion.

Effects of the Invention

[0023] According to preferred embodiments of the invention, at least one ring-like raised portion of a slightly larger diameter than that of the vial rubber stopper is formed on the outer peripheral surface of the cylindrical leg portion, which surface is laminated with an inactive synthetic resin film of low friction resistance such as fluororesins. The under-flange ring portion of the cylindrical leg portion is left as a naked rubber stock, which is connected to the bottom surface of the flange arranged around the cylindrical leg portion, distance from the flange bottom surface to the nearest ring-like raised portion is in the range of 1/3 to 5 times of overall height of the ring-like raised portion.

[0024] Because of such structure of the present vial rubber stopper, the ring-like raised portion arranged nearest to the flange bottom surface is pushed against an inner peripheral surface of vial opened portion to cause a shrinkage in diameter when the cylindrical leg portion is driven into the vial opened portion, so that the under-flange ring portion as a naked rubber stock never comes in contact with the inner peripheral surface of the vial opened portion. As a result, improved sealing properties and high stoppering properties can be secured by the present vial rubber stopper without applying conventional silicone coating.

[0025] In addition, as almost all surface of the cylindrical leg portion is laminated with an inactive synthetic resin film, it is possible to avoid contamination of extraneous fine particles such as those eluted from the naked rubber into the medical liquid in the vial.

[0026] As the flange bottom surface and the under-flange ring portion of the cylindrical leg portion are left as a naked rubber stock, the bottom surface in such a naked situation is firmly joined to the surface of the vial opened portion when the present vial rubber stopper is driven into the vial end portion, thereby high sealing properties being secured.

[0027] Further, when force in the upward direction is added to pull out the vial rubber stopper from the open portion, force in the downward direction acts to pull it down in the opposite direction against the under-flange ring portion, thereby the ring-like raised portion being deformed to push the naked rubber stock of the under-flange ring portion against the inner peripheral surface of the vial opened portion. As a result, the under-flange ring portion as the naked rubber stock is allowed to come in contact with the inner peripheral surface of the vial opened portion, thereby more improved sealing properties being obtained.

[0028] With regard to the present vial rubber stopper, the upper and bottom surfaces of the disc-like top portion other than the flange bottom surface, the maximum diametral portion of the flange-peripheral surface and the surface of the cylindrical leg portion other than the under-flange ring portion are laminated with an inactive synthetic resin film such as fluororesins, thereby mutual sticking of rubber stopper being avoided to improve mechanical conveying properties thereof.

Most Preferable Embodiments of the Invention

[0029] As shown in Fig. 1, a vial rubber stopper 1 as an embodiment of the invention comprises a shape in which a cylindrical leg portion 3 is coaxially protruded from a bottom surface of a thick top disk portion 2, a diameter thereof being smaller than that of the than that of the disc-like top portion and a surrounding edge of the disc-like top portion 2 being overhung from upward of the cylindrical leg portion 3 to form a flange 2A.

[0030] An under-flange ring portion 3A is divided in a circular form of predetermined width on an upper end portion of the cylindrical leg portion 3, which is connected to a bottom surface 2A1 of the flange 2A. First and second ring-like raised portions 3B and 3C are formed on a peripheral surface of the cylindrical leg portion 3 below the under-flange ring portion 3A at a predetermined interval in the vertical axial direction and extended in the circumferential direction parallel to the under-flange ring portion 3A.

[0031] With regard to a vial rubber stopper 1 shown in Fig. 2 as a modified example of the embodiment of Fig. 1, there are formed a cutaway portion 3E on the cylindrical leg portion 3 and a separate-type raised portion 3D on the outer peripheral surface thereof.

[0032] The cutaway portion 3E is formed by cutting the cylindrical leg portion 3 upwardly from a tip side opposed to the under-flange ring portion 3A to a line between the first and the second ring-like raised portions 3B and 3C in the axial direction at a predetermined interval. The cutaway portion 3E is shown only one in Fig. 2 but may be formed plurally and, in the case of plurality, each one may be the same size and opposing each other, or may be random size and arranged randomly.

[0033] The separate-type raised portion 3D is formed below the second ring-like raised portion 3C parallel thereto and divided in the circumferentially direction, which cross-sectional shape is, for example, nearly triangle to keep stability.

[0034] Cross-sectional shape of the first ring-like raised portion 3B arranged above the cutaway portion 3E and the second ring-like raised portion 3C cut off by the cutaway portion 3E may be semicircular, semi-oval, triangle, rectangular, trapezoid or any others. Those potions 3B and 3C shown in Fig. 1 may also be shaped similarly.

[0035] With regard to the vial rubber stopper 1 shown in Fig. 2, the first ring-like raised portion 3B arranged above the cutaway portion 3E may be not only one but formed plurally.

[0036] It is preferable that a maximum outer diameter of the first and the second ring-like raised portions 3B and 3C

shown in Fig. 1 and that of similar portions 3B and 3C shown in Fig. 2 are slightly larger, and more definitely about 1 % to 30 % larger, than a caliber of a vial B opened portion shown in Fig. 4, i.e., diameter of an opened inner peripheral portion B1. An increase in maximum outer diameter as described above makes it possible to secure high sealing properties and stoppering properties when the vial rubber stopper is driven into the vial B opened portion.

[0037] Such the increase in diameters of the first and the second ring-like raised portions 3B and 3C varies depending on elasticity of a rubber stock to be used for the rubber stopper 1 and a material of the vial B (glass or synthetic resins) and is not necessarily fixed, although it is desirable to increase diameters thereof in the range of about 1 % to 30 % compared with a caliber of the vial B when elasticity of a synthetic resin used as a material of the vial B is about 2 to 2.5 GPa and Shore A hardness of a rubber stock used as the rubber stopper 1 is about 15 to 45.

[0038] It is especially desirable to increase the maximum outer diameter of the uppermost first ring-like raised portion 3B which greatly influences sealing properties and stoppering properties of the rubber stopper 1 to the vial B opened portion. Excessively smaller diameter causes poor sealing properties and stoppering properties, while in contrast, it is difficult to drive the rubber stopper and seal the vial satisfactorily if the diameter is too large.

[0039] The uppermost first ring-like raised portion 3B is preferably arranged to be fallen in a length range from 1/3 to 5 times of overall height thereof in the downward direction from an upper edge of the under-flange ring portion 3A which coincides in arrangement with the bottom surface 2A1 of the flange 2A. That is to say, the shortest interval of the nearest first ring-like raised portion 3B from the bottom surface 2A1 of the flange 2A is preferably fallen in the range from 1/3 to 5 times of overall height thereof.

[0040] If the uppermost first ring-like raised portion 3B is arranged on an excessively low location, or if the shortest interval from the bottom surface 2A1 of the flange 2A to the first ring-like raised portion 3B is more than 5 times of overall height thereof, the rubber stock of the under-flange ring portion 3A comes in contact with the inner peripheral surface B1 of the vial B opened portion, thereby causing failure in stoppering and loosing sealing properties of the vial B.

[0041] In contrast with this, if the uppermost first ring-like raised portion 3B is arranged on an excessively high location, or if the shortest interval from the bottom surface 2A1 of the flange 2A to the first ring-like raised portion 3B is less than 1/3 time of overall height thereof, it is difficult to mold the rubber stopper 1, which makes the molding yield worse.

[0042] An optimum location of the first ring-like raised portion 3B varies depending on hardness and size of the rubber stopper 1. Hardness (Shore A) of a rubber stock within the optimum designed value is about 15 to 45 and size of the rubber stopper 1 is about 5 to 50 mm in diameter.

[0043] With regard to the present vial rubber stopper 1, the bottom surface 2A1 of the flange 2A is left as a naked rubber stock. Further, the bottom surface 2A1 is molded to adhere to an edge surface B2 of the opened portion of the vial B shown in Fig. 4. When the vial B is made of a synthetic resin, the edge surface B2 of the opened portion is generally shaped into flat and, accordingly, the bottom surface 2A1 of the flange 2A is preferably flat.

[0044] With regard to the present vial rubber stopper 1, the upper surface of the disc-like top portion 2 including the upper surface of the flange 2A, the maximum diametral portion 2A2 of the peripheral surface of the flange 2A, the bottom surface of the disc-like top portion 2 arranged in the cylindrical leg portion 3 and the surface including the outer and inner peripheral surfaces of the cylindrical leg portions 3 other than the under-flange ring portion 3A are laminated with a synthetic resin film as shown in Fig. 1 or Fig. 2 (see, mesh patterns drawn therein). On the other hand, the bottom surface 2A1 of the flange 2A and the surface of the under-flange ring portion 3A of the cylindrical leg portion 3 are left as a naked rubber stock.

[0045] An upper edge of the synthetic resin film laminated on the outer peripheral surface of the cylindrical leg portion 3 is fit upward over the first ring-like raised portion 3B, which the nearest location to the bottom surface 2A1 of the flange 2A, so that the under-flange ring portion 3A is divided between the upper edge and the bottom face 2A1.

[0046] If vertical width of the under-flange ring portion 3A is excessively narrow, it is difficult to mold the vial rubber stopper 1, while too wide width thereof increases frictional resistance of the rubber stock, thereby decreasing stoppering properties of the vial rubber stopper 1. Accordingly, the upper edge of the synthetic resin film is preferably fit downward of the bottom surface 2A1 of the flange 2A at an interval of 0.5 mm or more so as to leave vertical width of 0.5 mm or more for the under-flange ring portion 3A.

[0047] The cutaway portion 3E formed on the cylindrical leg portion 3 of the vial rubber stopper 1 shown in Fig. 2 is effective as will be described in the following. For example, when a solvent or water component in a medical liquid charged in the vial B shown in Fig. 4, should be removed, the vial B with the medical liquid charged therein is placed in an appropriate device such as vacuum dryer while keeping the vial rubber stopper 1 in a half-driven situation. Then, the solvent or water component contained in the vial B is evaporated and suctioned out through the cutaway portion 3E when the vacuum dryer is operated, the medical liquid being thus vacuum dried. Such a half-driven situation of the vial rubber stopper 1 can be kept satisfactorily by means of the separate-type raised portion 3D which is separated in the circumferential direction and has a triangle cross-section.

[0048] Fig. 3 is an illustration of vial rubber stopper 1 shown in Figs. 1 and 2 in which the rubber stopper 1 is placed in a mold in the course of molding. The cylindrical leg portion 3 is subjected to press molding to monolithically mold (laminate) with a synthetic resin film (drawn as mesh patterns in Fig. 3), punched out and set in a bottom force (not shown).

[0049] A material of the disc-like top portion 2 is placed on the cylindrical leg portion 3 in the above mentioned situation, while a synthetic resin film is put on the stock which is then press-molded by means of a force (not shown) . Accordingly, press molding of the disc-like top portion 2, lamination of the disc-like top portion 2 with the synthetic resin film and unification of the disc-like top portion 2 and the cylindrical leg portion 3 are conducted at the same time. The laminated disc-like portion 2 is drawn by mesh patterns in Fig. 3 and implies a continuous surface ranging from the upper surface of the disc-like top portion 2, which includes the upper surface of the flange 2A, and the maximum diametral portion 2A2 of the peripheral surface of the flange 2A.

[0050] The synthetic resin film used to laminate the cylindrical leg portion 3 and that of used to laminate the maximum diametral portion 2A2 of the peripheral surface of the flange 2A may be the same or different. A fluororesin film is preferably used either in the case of same or different, and different fluororesin films are preferably selected in the case of different. An Ultra High Molecular Weight polyethylene resin film is also used preferably as a synthetic resin film other than a fluororesin form standpoints of thermal resistance, chemical resistance, etc.

[0051] As two rubber stocks come in contact with each other when the cylindrical leg portion 3 and the disc-like top portion 2 are unified as shown in Figs. 1 to 3, each rubber stock does not exert any bad influence upon their unification, if the same or different rubber stock useful for unifying these two portions 2 and 3 is used even when the synthetic resin film to be laminated is the same or different.

[0052] The rubber stock for comprising the disc-like top portion 2 and the cylindrical leg portion 3 of the present vial rubber stopper 1 is not restricted to a specific one, if the material is tough and has appropriate hardness, impact resilience and other excellent properties such as thermal resistance, aging resistance, chemical resistance, gas barrier properties, low eluting properties and low reactivity.

[0053] Rubber stocks used in the present invention include, for example, butyl rubber, i.e., isoprene-isobutylene copolymer, halogenated butyl rubber prepared by chlorinating or brominating butyl rubber, acrylonitrile-butadiene copolymer rubber, isoprene terpolymer, isoprene rubber, butadiene rubber, styrene-butadiene rubber, ethylene-propylene rubber, ethylene-propylene-diene rubber, chloro-sulfonated polystyrene, ethylene-vinyl acetate copolymer, styrene-ethylene-butylene-styrene (SEBS) thermoplastic elastomer, thermoplastic elastomer comprising polyisobutylene and polybutadiene as a main component, and a rubber stock in which synthetic rubber such as styrene-isoprene rubber or natural rubber is used as a main component and added with filling agent, cross-linking agent, etc. to secure physical properties and thermal resistance sufficient to a rubber stopper.

[0054] Above all, butyl rubber, halogenated butyl rubber, and thermoplastic elastomer comprising polyisobutylene or polybutadiene as a main component are preferable rubber stocks not only for a reason that they meet the requirements as described above but from a standpoint of their high gas-impermeability, ozone resistance, aging resistance and adhesive properties.

[0055] A fluororesin film is preferably used as a synthetic resin film for laminating the present vial rubber stopper 1, which can be laminated on the rubber stock as an inactive synthetic resin film and has high thermal resistance and chemical resistance as well as lower frictional resistance compared with that of the rubber stock. The fluororesin includes, for example, tetrafluoroethylene resin (PTFE), tetrafluoroethylen-perfluoroethylene copolymer (PFA), tetrafluoroethylene-hexafluoroethylene copolymer (FEP), tetrafluoroethylene-ethylene copolymer (ATFE), polytrichlorotrifluoroethylene (PCTFE), polyfluorinated vinylidene (PVDF), polyfluorinated vinyl (PVF), etc.

[0056] Tetrafluoroethylene resin, which will be hereinafter referred to as PTFE, is especially preferable by the following reasons. PTFE is considerably stable so that it does not solve or swell almost all chemicals, and is one of the most thermally resistant organic materials, simply results in transparent gel but does not exhibit melt-flow characteristics when it is melted at the melting point of 327 °C and has so high continuous working temperature as about 260 °C, while its surface is extremely hydrophobic, oil-repellent and non-adhesive and exhibits low frictional resistance and high sliding properties. Because of intrinsic advantages as described above, PTFE is sufficiently resistant to high temperature sterilizing treatments in the course of pharmaceutical and other processes. Furthermore, when PTFE laminated on the vial rubber stopper 1 comes in contact with chemicals charged in the vial for a long period of time, the laminated material does not absorb the chemicals and nothing is eluted from the lamination, thereby proving chemical stability thereof. PTFE is sufficiently slidable to pressingly drive the rubber stopper into the vial after charging chemicals therein, so that it possesses characteristics to meet physical and chemical properties to be expected as a surface laminating film material, which is used to laminate sealing stoppers for sealing vial containers.

[0057] An Ultra High Molecular Weight polyethylene resin film may also be preferably used as a laminating material other than the fluororesin film from a standpoint of thermal resistance, chemical resistance, etc. The Ultra High Molecular Weight polyethylene refers to those polyethylene polymers of about 100 million to 700 million in molecular weight.

[0058] Thickness of the inactive synthetic resin film such as the above mentioned fluororesin film is preferably about 0.001 to 0.3 mm, more preferably 0.01 to 0.2 mm and most preferably 0.02 to 0.15 mm, and the thickness fallen in this range lowers voids of thin film, thereby reducing the defectiveness level of products with advantage. An excessively thinner film makes it difficult to yield the products and would cause processing failure and inadequate certification of products, while excessively thicker one raises rigidity of the film extremely so that sealing properties and needling

resistance of a completed rubber stopper deteriorate inadequately.

[0059] In order to secure a rigid adhesion surface between an inactive synthetic resin film such as a fluororesin film as described above and a rubber stock surface, a surface of the synthetic resin film is preferably cleaned or treated by means of, primer treatment, corona discharge, plasma discharge, glow discharge, arc discharge, sputtered etching and the like, thereby adhesion between the film and the rubber stock being strengthened.

[0060] The preferred adhesive strength is about 1 to 30 kg/cm. When the adhesive strength is excessively low, exfoliation of the film from the rubber stock possibly occurs not only in the course of pharmaceutical processing but during a storage period after pharmaceutical preparation or under an as-used condition such as needling, and on the contrary, excessively high adhesive strength is no more than saturation of adhesive effect and is not economical.

[0061] As has been described above referring to Fig. 3, the present vial rubber stopper 1 is molded in the following manner. The cylindrical leg portion 3, which has been laminated by press molding in advance, is set in the bottom force (not shown). A molding stock of the disc-like top portion 2 and a laminating synthetic resin film are placed on the upper surface of the leg portion 3, followed by press molding of the synthetic resin film and the molding stock by means of a force (not shown) . Molding of the disc-like top portion 2, lamination of the synthetic resin film on the leg portion 2 and unification of the cylindrical leg portion 3 are conducted simultaneously.

[0062] More in detail, the laminating synthetic resin film is placed on the bottom force (not shown) for molding the cylindrical leg portion 3 first of all, on which an uncured rubber stock to be used to mold the cylindrical leg portion 3 is placed. The cylindrical leg portion 3 is molded and cured by means of press molding and, at the same time, a continuous surface covering over the inner peripheral surface of the cylindrical leg portion 3 and the outer peripheral surface thereof is laminated, the outer peripheral surface including the first ring-like raised portion 3B, the second ring-like raised portion 3C and the separate-type raised portion 3D. Then, the bottom force is opened to take out the cylindrical leg portion 3 which is laminated by the synthetic resin film and cut into a predetermined shape.

[0063] After that, the thus laminated and cut cylindrical leg portion 3 is cleaned and set in a bottom force (not shown), while the uncured rubber stock to be used for molding the disc-like top portion 2 is placed thereon, and then the laminating synthetic resin film is put on the upper surface of the rubber stock, followed by clamping by means of a force (not shown) and press-molding under pressure of about 50 to 150 kg/cm^2 at temperature ob about 150 to 200 °C.

[0064] In this way, curing and molding of the disc-like top portion 2, lamination of a continuous surface covering from the upper surface of the disc-like top portion 2 to the maximum diametral portion 2A2 of the peripheral surface of the flange 2A, and unification of the disc-like top portion 2 and laminated cylindrical leg portion 3 are conducted at the same time. The force (not shown) is opened to take out the product, which is then cut from the middle of the peripheral surface of the flange 2A in the diagonal inside direction as shown in Fig. 3 by a line "x" and washed to yield the present vial rubber stopper 1.

[0065] According to the above mentioned embodiment, molding of the disc-like top portion 2 and lamination thereof are conducted by means of the molding tool for molding the disc-like top portion 2, but there may be used the bottom force for molding the cylindrical leg portion 3 in another embodiment.

[0066] Further, each rubber stock to be used for molding the cylindrical leg portion 3 and the disc-like top portion 2 may either be the same composition or different one as described above, if each rubber stock can be unified.

[0067] An applied example of the present vial rubber stopper 1 is shown in Fig. 4. After a medical liquid M is charged in the vial B, the cylindrical leg portion 3 of the present vial rubber stopper 1 is inserted and driven into the opened portion of the vial B along the inner peripheral surface B1 to adhere the bottom surface 2A1 of flange 2A of the disc-like top portion 2 to the edge surface B2 of the opened portion. The disc-like top portion 2 is covered with an aluminum cap A to caulk around the opened portion of the vial B and seal it. Complete seal of the vial B is thus secured.

Example

[0068] A plate stock of uncured rubber composition shown in Table 1 was used as a rubber stock for molding the cylindrical leg portion 3 and the disc-like top portion 2. There was used "Dai D3" (0.05 mm in thickness), available from Nitto Denka Corporation, as an inactive synthetic resin (PTFE) for laminating the cylindrical leg portion 3 and the disc-like top portion 2.

Table 1

Composition of Rubber Stock	Parts by Weight
butyl rubber	100
wet water-containing silica (1)	30
zinc oxide (2)	1.5

(continued)

Composition of Rubber Stock	Parts by Weight
1,1-bis(t-butylperoxide)-3,3,5-trimethylhexane(3)	2
(1) Nipushiiru ER; available from Nippon Sirika Kogyo (2) Active Chinese White AZO; available from Seido Kagaku Kogyo (3) Perhexane 3M-40; available from NOF Corporation	

[0069] As shown in Fig. 3, using a bottom force (not shown), press molding and lamination of the cylindrical leg portion 3 was conducted at the same time under a condition of molding pressure: 100 kg/cm^2 and molding temperature:

165°C, followed by opening and releasing of the force and washing.

[0070] There used two kinds of bottom forces as detailed in the following:

(1) A bottom force provided with concaves for forming the first and the second ring-like raised portions 3B and 3C having overall height shown in Table 2 and of semicircular in cross section; and
(2) A bottom force provided with, in addition to these concaves for the first and the second ring-like raised portions 3B and 3C, concaves for forming separate-type raised portion 3C having overall height shown in Table 2 and of nearly triangle in cross section.

[0071] With regard to these two kinds of bottom forces, maximum outer diameters (maximum height of the raised portions) of the first and the second ring-like raised portions 3B and 3C as well as the separate-type raised portion 3D are sums of doubled dimensions of their overall height shown in Table 2 and diameter of the cylindrical leg portion 3 as shown in Table 2, respectively.

[0072] Vertical width of the under-flange ring portion 3A divided on the upper end portion of the cylindrical leg portion 3 are also shown in Table 2.

Table 2

dimension of vial rubber stopper 1 (mm)	10 ml-vial	20 ml-vial
diameter of flange 2A	19	13
diameter of cylindrical leg portion 3	14	7.5
Length of cylindrical leg portion 3	10	7
vertical width of under flange ring portion 3A	1	0.6
overall height of first ring like raised portion 3B	0.3	0.3
overall height of second ring-like raised portion 3C	0.3	0.3
overall height of separate type raised portion 3D	0.3	0.3
caliber of opened portion of vial B	13	7

[0073] After the cylindrical leg portion 3 was washed and set in the bottom force (not shown), the plate stock of uncured rubber composition shown in Table 1 and the laminating synthetic resin film were placed thereon and then press molding of the disc-like top portion 2, lamination of the synthetic resin and unification of the disc-like top portion 2 and the cylindrical leg portion 3 were conducted at the same time under the same pressure and temperature condition as described above, followed by opening of the bottom force, cutting as shown in Fig. 3 by the line "x" and washing.

[0074] The thus yielded vial rubber stopper 1 was driven into the opened portion of commercial vials B and it was found that every tested rubber stopper 1 was fitted therein satisfactorily. The vials B were charged with water and kept in a half-stoppered situation with the rubber stopper 1, followed by drying in a vacuum dryer under pressure of 0.5 kg/cm^2 and at temperature of 25 °C for 24 hours. As a result, 90 % of water was removed from all of the vials B sealed with the rubber stopper 1 on which the separate-type raised portion 3D is formed and, on the other hand, a breakdown of such the half-stoppered situation was observed in the course of drying in many cases of the rubber stopper 1 on which the raised portion 3D is not formed and, what is worse, only less than 50 % of water was removed in some cases or complete

stoppering was not sustained after 24 hour drying in other cases.

Comparative Example

[0075] A conventional vial rubber stopper GP shown in Fig. 5 was used to repeat a stoppering test and a vacuum drying test in a similar manner as described above. As a result, it was found that a stoppering process was performed unsatisfactorily in the stoppering test because of considerable frictional resistance caused by rubber stock used as a wide belt ring-like raised portion R, while in the vacuum drying test, vacuum drying itself was performed favorably but the stoppering process after vacuum drying was not proceeded successfully.

Industrial Applicability

[0076] The present vial rubber stopper is conveniently applicable to various vials provided with an opened portion of different calibers. Further, the present stopper can be applied not only to embodiments in which an injection needle pierces the top portion but to those cases in which no needle pierces the top portion.

Claims

1. A vial rubber stopper comprises a disc-like top portion and a cylindrical leg portion of smaller diameter compared with that of the disc-like top portion, which is protruded from a bottom surface of the disc-like top portion to shape into a flange upward, **characterized in that** an under-flange ring portion connected to a flange bottom surface is divided on an outer peripheral surface of the cylindrical leg portion, and at least one ring-like raised portion is arranged downward of the under-flange ring portion in the circumferential direction, while an upper surface of the disc-like top portion including a flange-upper surface, a maximum diametral portion of a flange-peripheral surface, a bottom surface of the disc-like top portion located inside of the cylindrical leg portion and a surface of the cylindrical leg portion other than the under-flange ring portion are laminated with a synthetic resin to leave the flange bottom surface and the surface of the under-flange ring portion as a naked rubber stock.

2. A vial rubber stopper claimed in claim 1 in which shortest interval from a bottom surface of said flange to a ring-like raised portion nearest thereto is fallen in a range from 1/3 to 5 times of the ring-like raised portion.

3. A vial rubber stopper claimed in claim 1 or 2 in which maximum diameter of a ring-like raised portion nearest to a bottom surface of said flange is 1 to 30 % larger than a caliber of an opened portion of a vial to be inserted thereto said cylindrical leg portion.

4. A vial rubber stopper claimed in any claim 1 to 3 in which said under-flange ring portion is divided between a bottom surface of said flange and an upper edge portion of a synthetic resin film to be laminated on an outer peripheral surface of said cylindrical leg portion.

5. A vial rubber stopper claimed in any claim 1 to 4 in which a material of said synthetic resin film is either a fluororesin or Ultra High Molecular Weight polyethylene.

6. A vial rubber stopper claimed in any claim 1 to 5 in which press molding of said cylindrical leg portion and lamination of a synthetic resin film onto said cylindrical leg portion are conducted at the same time, while press molding of said disc-like top portion, lamination of a synthetic resin film onto said disc-like top portion and unification of said disc-like top portion and said cylindrical leg portion are conducted at the same time.

FIG.1

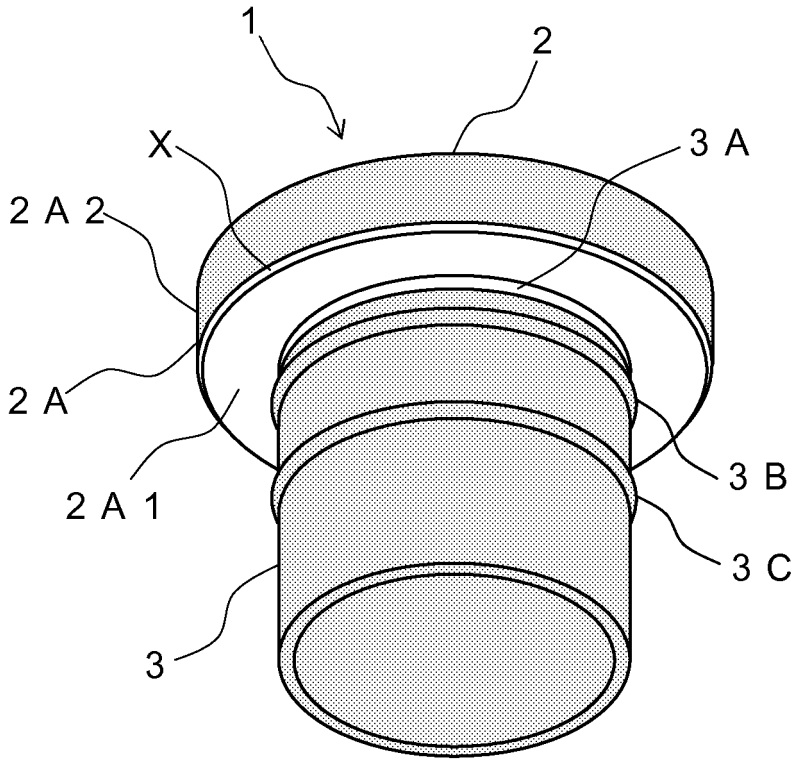


FIG.2

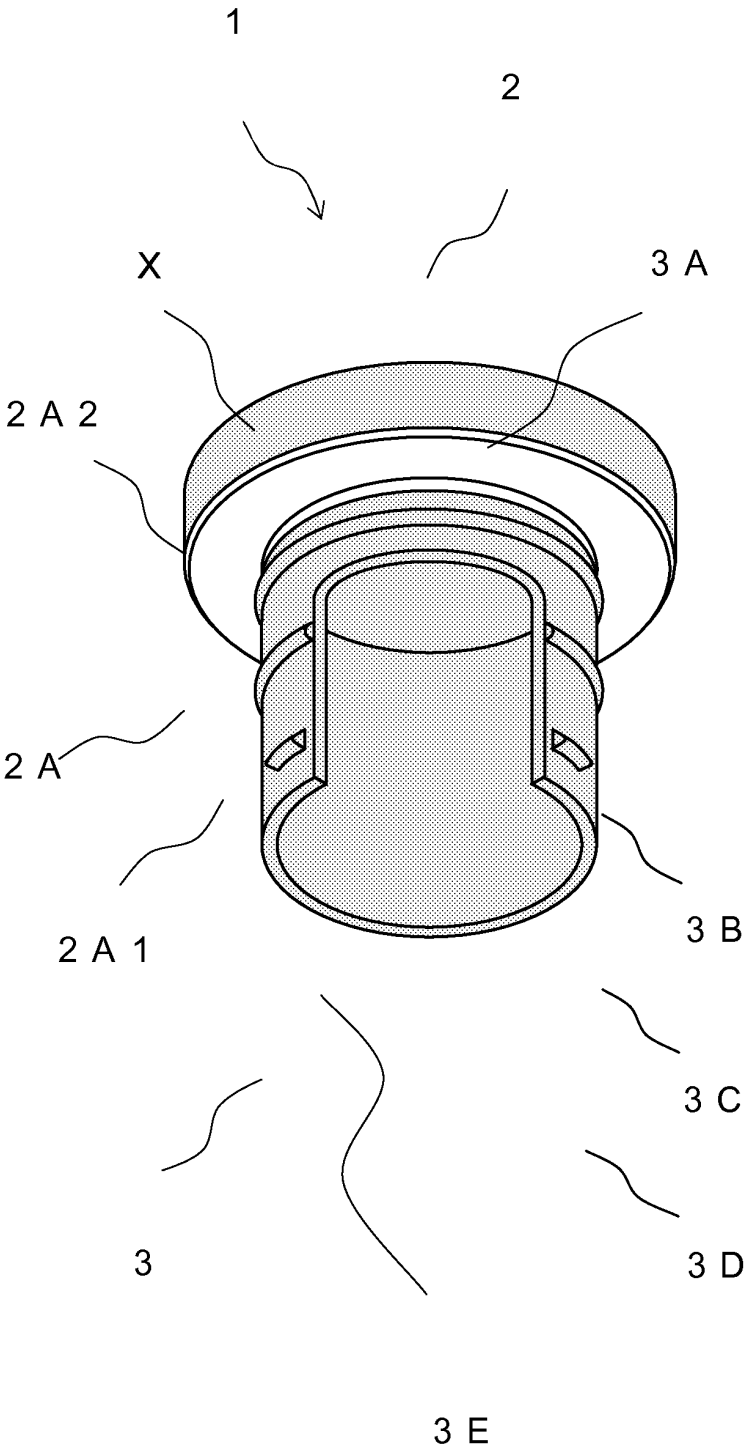


FIG.3

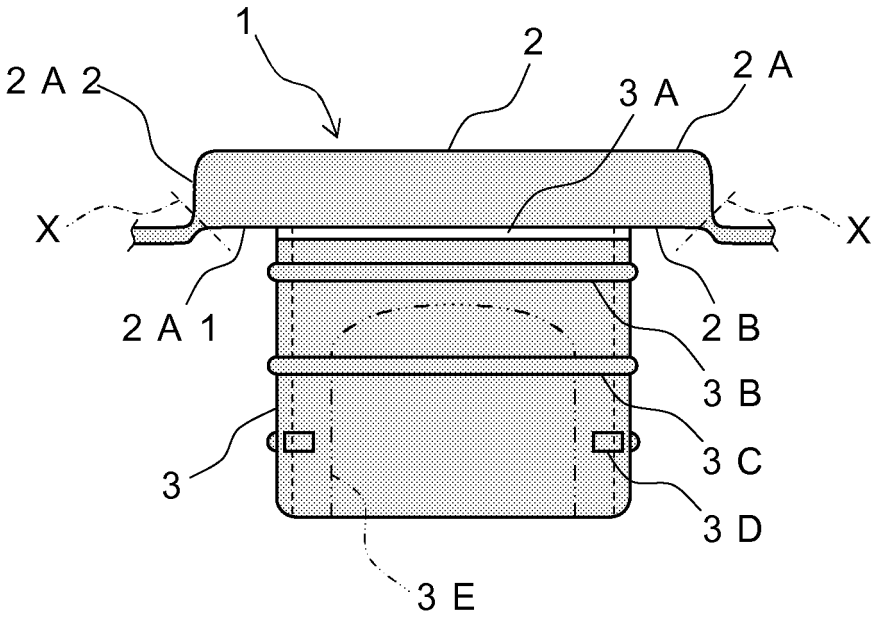


FIG.4

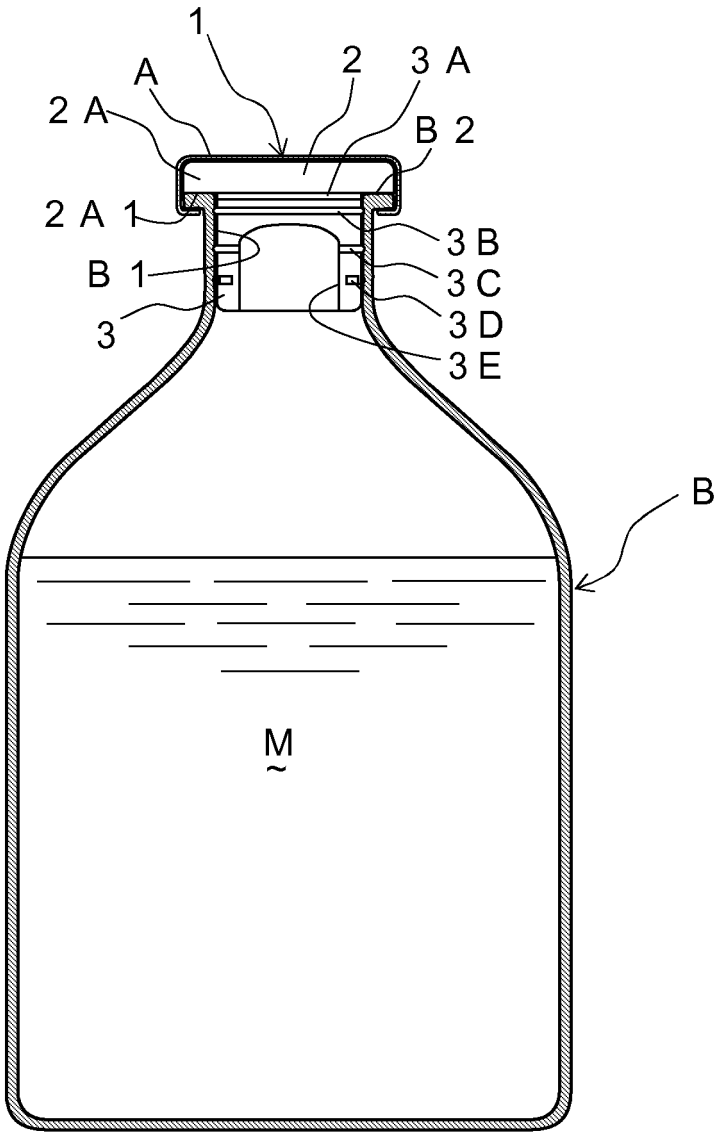
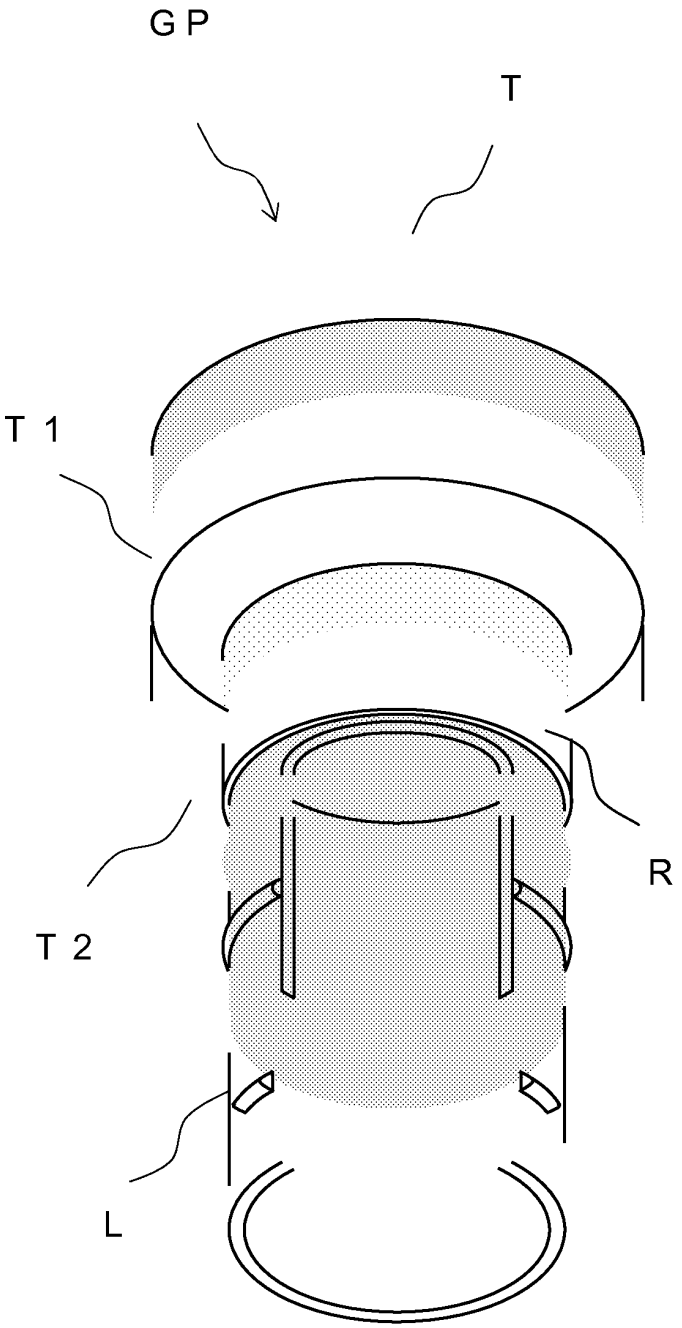


FIG.5



INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2008/069393

A. CLASSIFICATION OF SUBJECT MATTER
B65D39/04(2006.01)i, *A61J1/05*(2006.01)i

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)
B65D39/04, A61J1/05

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Jitsuyo Shinan Koho 1922-1996 Jitsuyo Shinan Toroku Koho 1996-2009
Kokai Jitsuyo Shinan Koho 1971-2009 Toroku Jitsuyo Shinan Koho 1994-2009

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y A	JP 6-98921 A (Daikyo Seiko, Ltd.), 12 April, 1994 (12.04.94), Claim 1; Figs. 4 to 5 (Family: none)	1,4-6 2-3
Y A	JP 2003-128095 A (The Ohtsu Tire & Rubber Co., Ltd.), 08 May, 2003 (08.05.03), Par. No. [0014]; Fig. 2(B) (Family: none)	1,4-6 2-3
Y A	JP 10-203546 A (SRL, Inc.), 04 August, 1998 (04.08.98), Par. No. [0014]; Fig. 2 (Family: none)	1,4-6 2-3

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

* Special categories of cited documents:
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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
23 February, 2009 (23.02.09)	03 March, 2009 (03.03.09)
Name and mailing address of the ISA/ Japanese Patent Office Facsimile No.	Authorized officer Telephone No.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2008/069393

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	JP 63-296756 A (Daikyo Gomu Seiko, Ltd.), 02 December, 1988 (02.12.88), Claim 1; Figs. 3, 8 & EP 0294127 A2 & DE 3852061 C	5
A	JP 8-175554 A (Yugen Kaisha Kazusa Koshitsu Kuromu), 09 July, 1996 (09.07.96), Full text; all drawings (Family: none)	6
A	JP 57-47637 A (Daikyo Gomu Seiko, Ltd.), 18 March, 1982 (18.03.82), Full text; all drawings (Family: none)	6

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REFERENCES CITED IN THE DESCRIPTION

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- JP 57053184 A **[0017]**
- JP 61031441 A **[0017]**
- JP 1017545 A **[0017]**