(12) STANDARD PATENT (11) Application No. **AU 2015200466 B2**
(19) AUSTRALIAN PATENT OFFICE

(54) Title
Sample preparation and testing system

(51) International Patent Classification(s)
B01L 3/00 (2006.01) ***G01N 1/38*** (2006.01)
G01N 1/08 (2006.01)

(21) Application No: **2015200466** (22) Date of Filing: **2015.01.30**

(30) Priority Data

(31) Number	(32) Date	(33) Country
DE 102014001386.3	**2014.02.01**	**DE**

(43) Publication Date: **2015.08.20**
(43) Publication Journal Date: **2015.08.20**
(44) Accepted Journal Date: **2016.10.27**

(71) Applicant(s)
Dräger Safety AG & Co. KGaA

(72) Inventor(s)
HODER, Matthias;MAHN, Jessika;POLZIUS, Rainer;WUSKE, Thomas

(74) Agent / Attorney
Watermark Patent and Trade Marks Attorneys, Level 1 109 Burwood Road, HAWTHORN, VIC, 3122

(56) Related Art
US 4104025 A

2015200466 30 Jan 2015

ABSTRACT

The invention concerns a sample preparation and testing system (10) with a mixing container (1, 18), where an indicator element (2, 40, 58, 60) is located inside the mixing container (1, 18) that has the function of a shaking indicator.
(Figure 12)

30 Jan 2015
20152004466

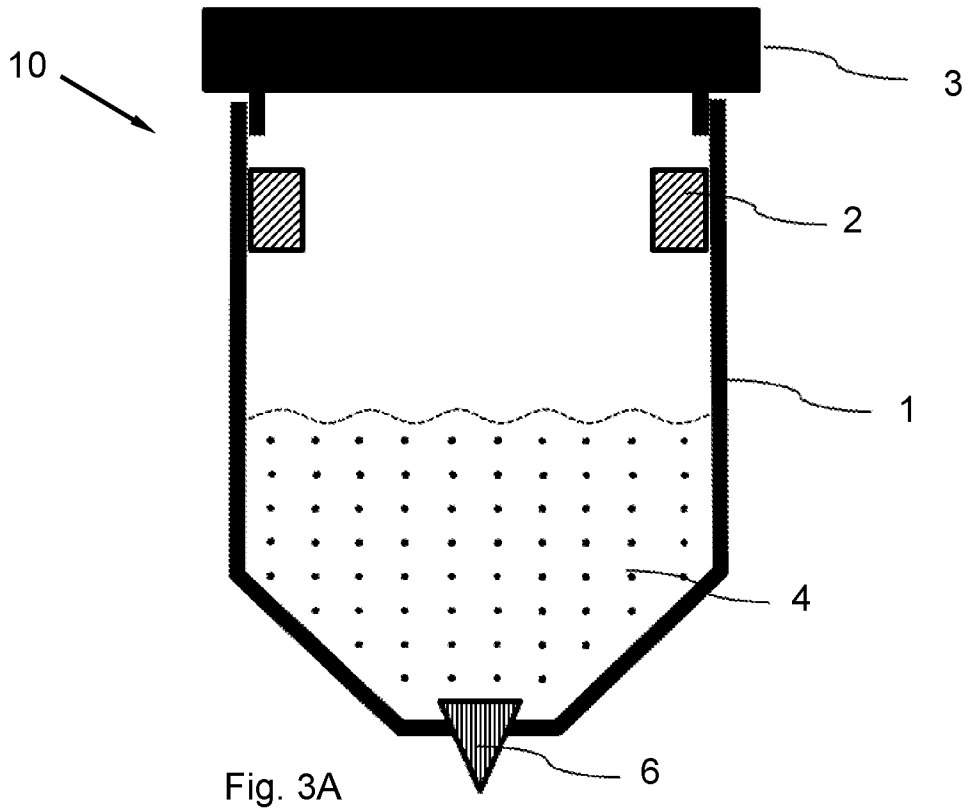

Fig. 3A

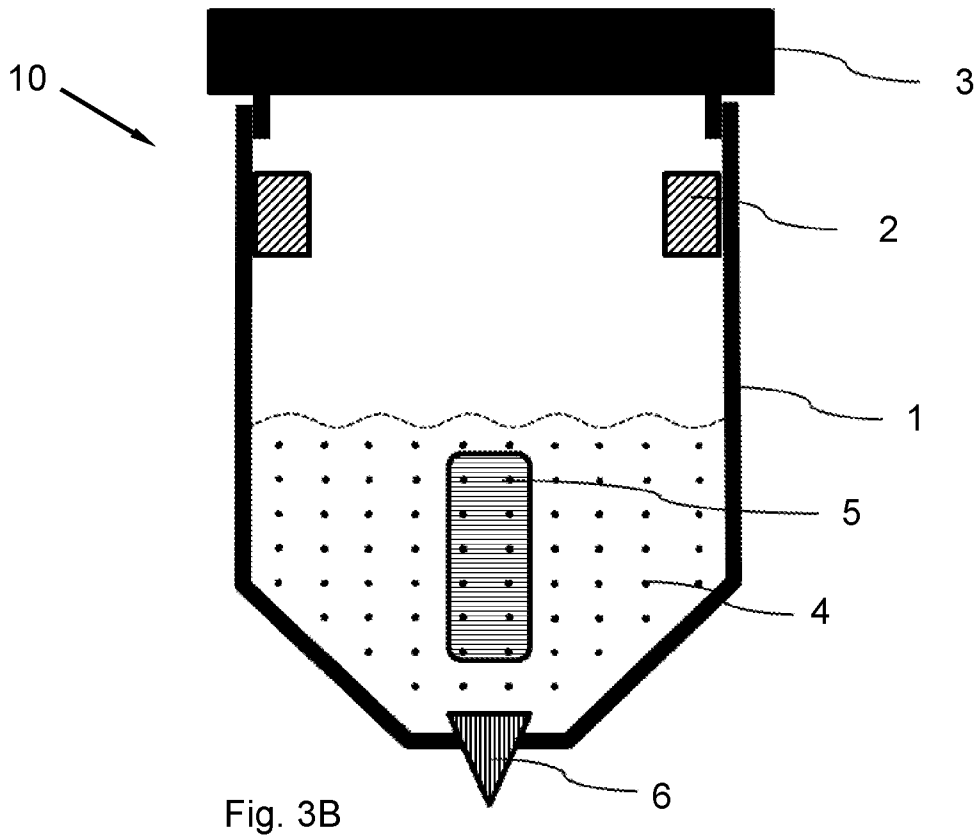

Fig. 3B

2015200466 30 Jan 2015

SAMPLE PREPARATION AND TESTING SYSTEM

FIELD OF THE INVENTION

The invention concerns a sample preparation and testing system, in the following at times simply called a testing device, to quickly receive, store and release samples, in particular liquid samples. The invention concerns, furthermore, a method for the application of the testing device.

BACKGROUND TO THE INVENTION

In the field of diagnostics, the preparation of a sample is an essential first step in the analysis process. This has a significant influence on the precision and correctness of the analysis. Sample preparation often involves the dilution of a liquid sample with a diluting fluid, and mixing the diluted sample with the reagents necessary for the analysis. In the instance of a solid sample, it is extracted using a diluting or extraction fluid. Mechanical agitation is usually employed in promoting the dilution and extraction processes. In a laboratory environment, electromechanical shakers or mixers are typically used (The Immunoassay Handbook, 3rd ed., D. Wild, 2005). In the instance of rapid diagnosis systems, agitation is either an intrinsic function of the test system (for example with immuno-chromatographic test systems) or can be achieved through a manual shaking process.

A diagnostic device is known from patent document DE 199 09 891, which combines an immuno-chromatographic test strip and a sampling system for house dust in a microfluidic system. The house dust sample is collected in a porous sampling tip, extracted though application of a diluting fluid and then applied to the immuno-chromatographic test strip. Extraction and reagent diluting reactions are an intrinsic function of the microfluidic system. One short coming with this system is a perceived low extraction accuracy.

A further diagnostic testing system is known from patent document US 7,713,475, which incorporates various reaction chambers, depots for diluting fluids and reagents, as well as multiple immune-chromatographic test strips. In use of the device, the liquid sample and dry reagents are diluted and mixed with a

2015200466 30 Sep 2016

diluting fluid. The document contains no information concerning the kind of mixing process used.

A diagnostic testing device is known from patent document EP 2 139 601 A, which comprises a mixing chamber with a depot for a dry reagent for fluidic binding to an immune-chromatographic test strip. After adding the liquid sample, the reagent is mixed with the liquid sample through manual agitation. A fluid connection is then opened and the reaction mixture is applied to the immune-chromatographic test strip. The document discloses that the regent may be gold conjugate, which is disposed at the bottom of the mixing chamber and is dissolved through manual shaking of the mixing chamber. The document contains no information concerning time control of the mixing process.

It would be advantageous to provide a testing device with means which enable a user to identify in simple manner a required or sufficient shaking / mixing time in the preparation of the sample. Furthermore, devising a method for using such a testing device in delivering the desired information would be equally useful.

SUMMARY OF THE INVENTION

In accordance with a first aspect of the present invention there is provided a sample preparation and testing device, comprising: a mixing container; an indicator element located inside the mixing container; a sampler; an extractor; and a starter; wherein the indicator element is devised to provide an indication of a time interval during which the mixing container was shaken; and wherein the mixing container is fully or partially transparent, and wherein the indicator element is arranged such that it is visible from outside the mixing container; wherein each of the sampler, extractor and starter having constructional features enabling the sampler to be releasably joined with the extractor and the extractor to be releasably joined with the starter, the sampler and the extractor comprising constructional features whereby the joining of the sampler with the extractor forms said mixing container, the mixing container being sealed temporarily to function as a shaking reactor for a sample received in the mixing container, and wherein the sampler has a sampler body at one end, wherein the extractor has a

2015200466 30 Sep 2016

tubular body into which the sampler body can be inserted in the process of joining the extractor with the sampler to form the shaking reactor, and wherein the sampler and extractor have cooperating constructional features enabling creation and maintenance of a positive pressure inside the shaking reactor when joined together, the cooperating constructional features comprising the extractor being provided with an internal cylindrical surface extending along a length of the tubular body and the sampler having a circumferential external sealing lip which, when the sampler is inserted into the extractor, presses against the cylindrical surface.

In a preferred form, the indicator element comprises material which discolours during a shaking process, preferably continuously as a function of mixing and/or shaking time, so that it is completely discoloured when the dilution and/or extraction of the sample is fully or sufficiently completed, the indicator thus providing visual means for a person handling the sample preparation and testing device that the shaking / mixing process can be stoped. Preferably, a porous indicator element is used in the device.

When using such a testing device, the mixing container and the sample added to the mixing container are shaken until the indicator element is discoloured.

2015200466 30 Jan 2015

One advantage of the invention is that the user is able to easily determine the necessary or sufficiently long duration of the shaking process by way of the discolouration of the indicator element located inside the mixing container. In terms of functionality this ensures that the diluting and extraction processes are happening precisely and completely inside the mixing container, thus ensuring that a high level of analytical accuracy of the subsequent analysis process is achieved.

Advantageous embodiments of the invention are described herein below and in the claims.

In one embodiment, the testing device comprises a sampler, an extractor and a starter, wherein the sampler, extractor and starter comprise joining means arranged to couple the sampler with the extractor and the extractor with the starter, for example through inserting one into the other, and wherein the combination of sampler and extractor define a mixing container in the form of a shaking reactor that seals sufficiently to be suitable for a shaking action. The testing device thus consists of very few, easy to use individual components, and the mixing container is formed by joining two individual components.

The mixing chamber of prior art document EP 2 139 601 A is closed by way of a folding lid. Thus, in contrast to the testing device in accordance with the preferred embodiments of the present invention, the mixing chamber is not formed through the combination of a sampler with another part of the testing device.

The mixing container described in prior art document US 2006/127274 A is a cup-like container which is also closed by way of a lid and not by way of a sampler.

A sampling device is known from prior art document WO 2005/045408 in which a sponge-like sampler with sample fluid is inserted into a first, not hermetically sealed, chamber and squeezed out in the process. A reagent ampoule is destroyed simultaneously during the squeezing process via a moveable pin, thus creating a mixture of sample liquid and reagent, which drips directly through openings disposed at the bottom of the non-sealed chamber into a second chamber, in which further dry reagents are dissolved by the incoming liquid. Insertion of the sampler into the non-sealed first chamber does not

2015200466 30 Jan 2015

establish a sealed mixing container. The chamber is not even designed for shaking since the mixture drips from this chamber into the second chamber, which is also not sufficiently sealed for a shaking process because, firstly, the second chamber is open to the first chamber and, secondly, the second chamber is provided with openings for the insertion of test strips.

In the testing device embodiment with sampler, extractor and starter, there is no need to have a porous indicator element of the above described kind present in the mixing container formed by the combined sampler and extractor. However, an indicator element of this kind can be optionally present in the mixing container, and the following description will be provided with reference to an example of a testing device containing sampler, extractor and starter as well as a porous indicator element, without waiving the universality of having other types of indicators present / used.

In one particular embodiment of the testing device it is provided that a sampling body is disposed at one end of the sampler, that the sampler together with the sampling body are insertable into a tube body of the extractor, such insertion being part of handling the device in use during sampling, and that a positive pressure is generated inside the thereby formed shaking reactor when the sampler is inserted into the extractor. Said positive pressure is helpful when withdrawing the sample mixture from the shaking reactor.

When using such a testing device, a sample is taken with the sampler. The sampler is then joined with the extractor so that sampler and extractor together form the shaking reactor. The shaking reactor is then shaken until the indicator element is discoloured. The resulting sample mixture can easily flow out of the shaking reactor due to the positive pressure generated during joining of sampler and extractor, provided that the shaking reactor is opened according to instructions, for example in that the shaking reactor is joined with the starter and pressed into the starter for analysing the sample mixture.

Further preferred and optional features of the invention will become clearer from the following description of preferred embodiments thereof, which is provided with reference to the accompanying drawings in which functionally or constructionally equivalent components or elements are marked with the same reference numbers.

2015200466 30 Jan 2015

The embodiments are not to be seen as limiting the invention. Rather, alterations and modifications are possible within the scope of the present invention, in particular those variations and combinations that are recognisable to an expert in the field, for example through combination or modification of individual features or elements or processing steps, which are described herein.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 a section through a schematic illustration of a testing device according to the invention with an indicator element for visual monitoring of liquid-liquid mixing reactions or liquid-solid extraction reactions;

Figure 2 a schematic illustration of a testing device as per figure 1 but with a ring-shaped indicator element;

Figure 3A, 3B a schematic illustration of a testing device as per figure 1 with further details;

Figure 4 an isometric, exploded view of a particular embodiment of a testing device embodying the principles of the device as per figure 2, with a sampler, an extractor and a starter;

Figure 5 an isometric view of a shaking reactor formed through the combination of the sampler and the extractor shown in figure 4;

Figure 6 an isometric, exploded view of the sampler of figure 4;

Figure 7 a perspective longitudinal section of the extractor of figure 4;

Figure 8 a further perspective longitudinal section of the extractor of figure 4 illustrating the presence of a liquid reagent depot

Figure 9 an isometric view the extractor of figure 4;

Figure 10 an isometric view of the starter of figure 4;

Figure 11 an isometric shadow section of the starter of figure 4 for illustration of its inside components;

Figure 12 the assembled testing device as per figure 4, in longitudinal section;

Figure 13 an isometric view of a further embodiment of a starter of the testing device;

2015200466 30 Jan 2015

Figure 14 a perspective section through the starter of figure 13;

Figure 15 an exploded isometric view of the device of figure 4 but wherein the starter is replaced with a starter according to figures 13, 14;

Figure 16 an exploded, perspective, longitudinal section of the testing device as per Figure 15, and

Figure 17 an isometric view of further testing device comprising a sampler and extractor as per figure 4 but with a further embodiment of a starter.

DESCRIPTION OF PREFERRED EMBODIMENT

The representation in Figure 1 shows in schematically simplified form a testing device 10 as an example of a device for the visual monitoring of liquid-liquid mixing reactions or liquid-solid extraction reactions in a mixing container 1 with the aid of a porous indicator element 2 which contains a colouring agent in dry form that is visible through a wall or a wall section of mixing container 1. The mixing container 1 is provided with a lid 3 for opening said mixing container 1 as well as for hermetically sealing the mixing container 1.

In the embodiment of the testing device 10 shown in Figure 1, the indicator element 2 is placed into mixing container 1 freely moveable. In the embodiment of the testing device 10 shown in Figure 2, the annular shaped indicator element 2 is attached to the wall of mixing container 1 so that the user is able to see and evaluate it through a wall of mixing container 1 that is transparent in at least this section.

The porous indicator element 2 is impregnated with a colouring agent which, due to mechanical agitation of a liquid in mixing container 1, in particular a liquid provided by a liquid sample or a liquid sample mix, is released from the porous indicator element 2 and dissolves, for example through shaking of the mixing container 1, in the liquid. The discolouration reaction of the porous indicator element 2 is visually recognisable by the user and defines the end of the mixing or extraction reaction (end of shaking process).

The porous indicator element 2 is made from material with preferably defined pore diameters and pore volume. The pore sizes are between 1000 µm

2015200466 30 Jan 2015

and 1 µm. Particularly advantageous from experience are pore sizes between 200 µm and 10 µm. The porous indicator element 2 is impregnated with a water-soluble colouring agent that is located in its pores in dry form.

In a particularly preferred embodiment of the testing device 10, the colouring agent in the porous indicator element 2 is at the same time a reagent which, after dissolving in the liquid and mixing with an analysis sample for diagnostic purposes, is required in a subsequent detection reaction. If immune-chromatographic test strips are used, a particle antibody conjugate can be employed as reagent. Depending on the colour of the particle antibody conjugate itself, it may be possible to forego the application of further colouring agents entirely.

The three-dimensional, porous indicator element 2 may, for example, be made in the shape of a sphere, a cube, a cylinder or a ring. All types of porous materials may be used, for example fibre materials such as polyester or cellulose, foam or sintered materials. Sintered materials such as, for example, metal sinter or plastic sinter, have proven particularly advantageous. The latter permit the manufacture of a precisely defined form of the porous indicator element 2 with a defined pore size. In addition to these characteristics, sintered elements are largely dimensionally stable and may be mounted by way of a press fit, for example, inside mixing container 1, as depicted in the lower part of the drawing in Figure 1. The shape and the pore size of the porous indicator element 2 are crucial for the correct indication of the shaking time, and are thus parameters that can be chosen such as to adjust the indicator's visual indicator function and to tune it to the dilution and extraction processes. The shaking time increases with reducing pore size and an increasing volume of the porous indicator element 2.

When using the testing device 10 according to Figure 1 or Figure 2, a liquid or solid sample is placed inside the mixing container 1 after the user has opened the lid 3. Furthermore, the addition of a diluting fluid into the mixing container 1 is also possible if the liquid sample is to be diluted or a solid sample is to be extracted. After lid 3 is closed, the user shakes the mixing container to initiate the diluting and/or extraction process. At the same time, the colouring agent is flushed out of the indicator element 2 by the shaking process. The user is able to observe the discolouration of the porous indicator element 2 through the

2015200466 30 Jan 2015

transparent wall of mixing container 1. A discoloured, porous indicator element 2 indicates to the user that the shaking process can be stopped. The extracted or diluted sample can now be removed from the mixing container 1 and be delivered to an analysis system, for example an immune-chromatographic test strip.

The two representations in Figure 3A and 3B depict a particular embodiment of the testing device 10 according to Figure 2. The porous indicator element 2 is also in this instance attached to the wall of the mixing container 1. Annular indicator elements 2, which may, for example, be fixed to the wall of the mixing container 1 by a press fit, are suitable for this purpose. The porous indicator element 2 is preferably positioned inside the mixing container 1 in such a way that, after filling-in the liquid sample and/or the diluting fluid 4 (Figure 3A), or after filling-in the diluting fluid 4 and the solid sample 5 (Figure 3B), respectively, no wetting of the porous indicator element 2 takes place at first through the fluid 4 in the preferred position of the mixing container 1. Only once the mixing container 1 is shaken manually does the porous indicator element 2 come in contact with fluid 4 and the colouring agent is flushed out of indicator element 2. In this way, the starting point of the colour reaction process of the porous indicator element 2 and the diluting and extraction reaction are synchronised, thus ensuring correctness of the displayed results.

The user can easily observe the colour change through the wall contact of the porous indicator element 2 within the mixing container 1, which is transparent in at least this section.

Once the colour reaction is complete, the extracted or diluted sample mixture can be removed from mixing container 1 by opening lid 3 and can be fed to an analysis system, for example an immune-chromatographic test strip. In a particular embodiment the mixing container 1 is provided for this purpose with an outlet 6 which is in fluid contact with the analysis system, or which can be brought into fluid contact with such an analysis system.

One particular advantage of the testing device 10, and of a method carried out in its use, is that the diluting and extracting reactions, which are achieved by manual shaking, are conducted in complete and precise manner. The indicator function can be tuned to the dilution or extraction processes, governed by the functionality and adjustability of the porous indicator element 2 as well as its

2015200466 30 Jan 2015

positioning inside mixing container 1. The manufacture and assembly of the porous indicator element 2 can be effected in mass production precisely and economically using immersion and impregnating processes.

One particular embodiment of a testing device 10 will be described in the following. The above described selective discolouration of a porous indicator element 2 is used in this embodiment to increase the operational reliability by making a completed or at least sufficient dilution or extraction reaction readily recognisable.

Figure 4 shows in a schematically simplified representation a special embodiment of an inventive testing device 10 for biological fluids, which in the following will be called test kit 10 simply to distinguish it from the general embodiment of the testing device 10 described with reference to Figures 1 to 3B.

Test kit 10 comprises a sampler 12, an extractor 14 and a starter 16. Through sequential joining of these three geometrically complementary components of test kit 10, one achieves the above described, desired improved functional integration, reduction of the number of operational steps required during the testing process, as well as an improvement in operational reliability.

The representation in Figure 5 shows a new, hermetically sealed reaction space formed by the complimentary interaction between the sampler 12 with the extractor 14, in particular achieved by plugging together these components 12 and 14. The new reaction space will be referred to in the following as a shaking reactor 18, which corresponds functionally to mixing container 1 of testing device 10, and is thus also an example of a mixing container 1. In the joined configuration, the shaking reactor 18 and the starter 16 form the activated test kit 10. The central components 12, 14, 16 of test kit 10 assume not only their own dedicated functions but also multiple communicative (interactive) functions in cooperation with the respectively complementary, adjoining component.

The test kit 10 permits the orientation-independent joining of an original sample on sampler 12 with dry reagents (Figure 7, Figure 8: reagent carrier 58, reagent carrier 60) and initially encapsulated as well as permanently deposited liquid reagents (Figure 8: liquid reagent depot 54) in a chamber formed inside shaking reactor 18. During joining of sampler 12 with extractor 14, a positive pressure builds up in said chamber. The extraction, stripping off or dissolving of

2015200466 30 Jan 2015

the original sample from the sampler 12 and the mixing or diluting of the sample with dry and/or liquid reagents through shaking takes place in a subsequent step in the same chamber. The result of the shaking process will in the following be called a reaction mixture or simply mixture. Completion of the shaking process can hereby be indicated by the colour indication of the type described above.

The individual components 12, 14, 16 of test kit 10 will now be described in more detail:

A. The sampler 12

The depiction in Figure 6 shows the sampler 12 enlarged and in more detail. The sampler 12 is formed at its one end as a handle 20 and at its other end as a receptacle or attachment pin 22 for a sampler body 24. In the embodiment shown, the sampler 12 comprises a circumferential seam 26, a cone-shaped or truncated cone-shaped position locating contour 32 for a sampler body 24 placed onto attachment pin 22, a circumferential sealing lip 28 as well as a circumferential groove or ridge 30 for a positive-locking snap connection with a corresponding contour of the extractor 14. Moreover, the position locating contour 32 is formed as a perforating tip 34, or a separate perforating tip 34 is located subsequent to the position locating contour 32.

The sampler 12 acts as carrier for a sleeve-like (hollow cylindrical) sampler body 24 and optionally an annular indicator ring 36. As shown, the indicator ring 36 may be placed onto attachment pin 22 before the sampler body 24 or placed after the sampler body 24. The indicator ring 36 is in both instances in direct contact with sampler body 24, and sampler body 24 as well as the indicator ring 36 are microporous, thin-walled, dimensionally stable and hydrophilic. Sintering of thermoplastic particles is particularly recommended in the manufacture of such sampler bodies 24 and indicator rings 36. The indicator ring 36 is coloured in its unused state. Its discolouration occurs when the embedded colouring agent is washed out, for example through saliva in the mouth of a sample provider (ie a person).

In a particular embodiment of the sampler 12, the sampler body 24 is freely rotatable on attachment pin 22 by maintaining of a sub-millimetre gap (play). The precision of the contours of attachment pin 22 and sampler body 24 that is required, as well as suitable material forming characteristics for positive-locking

2015200466 30 Jan 2015

and gliding components are known to the person skilled in the art and are achieved, for example, by commonly used injection moulding processes using thermoplastic polymers.

B. The extractor 14

The depictions in Figure 7 and Figure 8 show the extractor enlarged in a longitudinal cross-section with further details. Generally speaking, the extractor 14 is a long, tubular body 40 that acts as the sample preparation unit. The sample preparation unit, in this document simply called extractor 14, has at its top end an opening 42 to accept sampler 12, and at its bottom end an initially closed interface 44 provided for its coupling with starter 16.

When joined, sampler 12 and extractor 14 form the shaking reactor 18 (Figure 5), and inside the shaking reactor 18 they form also a hermetically sealed chamber. A liquid sample is withdrawn from sampler 12 into this chamber, that is, from sampler body 24 of sampler 12, or the stripping off or dissolving of substances in particle form from the sampling body 24 through a shaking process. The shaking reactor 18 can then be opened by way of starter 16 so that the respective reaction mixture can discharge and be provided to a test strip 72 (Figure 12) known per se, but which is not separately shown.

The one-sided open tube body 40 of the extractor 14 is designed at its open end as an insert section 46 for sampler 12. The inner surfaces of tube body 40 have smooth walls as well as snap-in or click-in contours (not shown here) to positively receive and lock-in sampler 12, for example through engaging with its groove 30 (Figure 6). A strictly cylindrical pressure-build-up section 50 is located in approximately the centre of extractor 14. The diameter of the pressure-build-up section 50 corresponds with the diameter of sealing lip 28 (Figure 6) of sampler 12. The sealing lip 28 of sampler 12 slides in this section across the inner surface of pressure-build-up section 50 to provide a seal on the on hand and to generate a defined positive pressure inside shaking reactor 18 on the other hand. The positive pressure is a result of the compressed air volume when sampler 12 and extractor 14 are pushed together. The maximum level of positive pressure is defined by the length of the pressure-build-up section 50.

2015200466 30 Jan 2015

The bottom section of extractor 14 is provided with the already mentioned interface 44, which also acts as a defined breaking point, for joining with the starter 16, which can only be penetrated in conjunction with starter 16. In its unbroken state, the bottom of extractor 14 is hermetically sealed and resistant to positive pressure to a certain degree.

Support ribs 52 are disposed on the tube body wall 40 to elastically clamp an optional liquid reagent depot 54 (Figure 8). The support ribs 52 allow on the one hand the attachment of the liquid reagent depot 54, but on the other hand are not raised high enough above the inner surface of the tube body wall 40 so as to obstruct the insertion of the sampler body 24. The support ribs 52 optionally form, in the direction of the upper opening 42, a support surface 56 for reagent carriers 58 (Figure 8) and/or process indicators. The support surface 56 may also be formed differently, for example in form of a step in the internal contour of the tube body wall 40.

Located at the bottom of extractor 14 may optionally be an additional or an alternative reagent carrier 60 (Figure 12), in particular a microporous reagent carrier that acts as a dry reagent depot, which is preferably made of sintered plastic. The reagent carriers 58, 60 shown in Figure 8 and Figure 12 depict possible positions of such reagent carriers 58, 60. In principle, it is possible that one or more reagent carriers are also disposed in other locations inside shaking reactor 18, for example in form of loose reagent carriers 58, 60, as is depicted in Figure 1 for the loose indicator element 2.

As the shaking reactor 18 is shaken, the one or every reagent carrier 58, 60 is initially wetted during the shaking process and then the respective reagent is slowly dissolved through further shaking. The placement of a reagent carrier 58, 60 above and/or below the sampler body 24 that was inserted into the extractor 14 guarantees that the rinsing and wetting that results from the shaking, affects the sampler body 24 in the same way as the one or every reagent carrier 58, 60, so that a discolouration of the one or every reagent carrier 58, 60 also indicates a sufficient stripping of the sample from the sampler body 24.

A circumferential gap 62 (Figure 12) between sampler body 24 and tube body wall 40 governs the extraction efficiency through shaking when using low volumes of liquid reagents (liquid reagent quantity in liquid reagent depot 54) of

2015200466 30 Jan 2015

between 0.2 and 0.6 ml. The ratio of liquid reagent volume to the volume of the reagent mixture is typically between 1.5:1 and 3:1. Circumferential gaps 62 with a width of 0.5 mm to 3.0 mm have proven to be particularly favourable with respect to a reduced shaking time for a complete mixing of the sample.

In a particular embodiment of test kit 10, the one or every reagent carrier 58, 60 is a sintered body, and the carrier material is microporous. In the instance of a coloured dry reagent, the one or every reagent carrier 58, 60 acts as shaking indicator, and as the pore size of the carrier material is reduced, the process of washing out of coloured dry reagent can be slowed down specifically, if required, to guarantee the complete mixing of the sample with the reagent during the discolouration of the shaking reactor. Thus the one or every reagent carrier 58, 60 of the test kit 10 correspond functionally to indicator element 10 of the testing device 10 and is an example for such an indicator element 2. In a particular embodiment of test kit 10, the indicator colouring agent of the respective reagent carrier 58, 60 is at the same time a colour reagent with reporting function within the scope of an immunoassay on drug substances.

The manual shaking process of shaking reactor 18 ends with the complete discolouration of the indicator component of the shaking indicator of one or each reagent carrier 58, 60. The response characteristic of the indicator, where the reagent carrier 58 is located above the sampler body 24, is proportional to the shaking intensity and shaking frequency in vertical direction, and is thus dependent on the shaking mode of the individual user. The complete discolouration moment indicates and makes certain that the sample in sampler body 24 is equally fully mixed with the liquid reagent and the dry reagent. Making the extractor 14 from a transparent plastic ensures that the discolouration of the shaking indicator is readily recognisable. An extractor 14 with a transparent wall or a partly transparent wall thus corresponds in this respect functionally to the transparent or partly transparent mixing container 1 of testing device 10.

The support ribs 52 surround a virtual cylinder which has a smaller diameter than that of a liquid reagent depot 54 that is to be retained, and which has a larger diameter in comparison to the diameter of the sampler body 24. Ribs 64 extend from the bottom of extractor 14, whose abutting faces 66 are acting as end stop/abutting surface for a liquid reagent depot 54. The ribs 64 accordingly

2015200466 30 Jan 2015

surround a virtual cylinder with a diameter that is smaller in comparison to the virtual cylinder formed by the support ribs 52.

The outside of extractor 14 is optionally provided with a test strip surface 70, which is designed to receive immune-chromatographic test strips 72. The representation in Figure 9 shows the extractor 14 according to Figure 7 and Figure 8 from a different perspective. The test strip surface 70 for attaching immuno-chromatographic test strips 72 is either a component of extractor 14 with vertical orientation that is spatially isolated from the tube body 40, or (see Figure 13, Figure 14) an element with horizontal or vertical orientation associated with starter 16. In both instances, the reaction mixture flows to the test strip surface 70 as soon as the shaking reactor 18 is opened by way of starter 16 after completion of the shaking process and the discharge of the reaction mixture from shaking reactor 18.

C. The starter 16

The representations in Figure 10 and Figure 11 show an embodiment of starter 16 in perspective view and in form of an (enlarged) wireframe model, respectively, which in the following is called a standard configuration simply for differentiation purposes. The standard configuration combines a guiding profile 74, which is open at the top and receives and guides a lower section of the extractor 14, with a base 76 for the vertical positioning of the inserted shaking reactor 18 on a flat surface. The internal contour of starter 16 and the guiding profile 74 are designed such that the extractor 14 is able to perform a downward movement in starter 16 that is guided on one side, whereas an upwards movement is optionally made difficult through barrier contours such as, for example, those similar to the circumferential groove or ridge 30 on sampler 12.

An end stop for the lower end of the extractor 14 is formed in the bottom section of starter 16. From there, a penetration profile 80 rises, which penetrates the defined breaking point 44 of shaking reactor 18 under application of force so that said defined breaking point 44 and the chamber formed inside shaking reactor 18 are opened. The fluid transfer of the reaction mixture from the chamber to the test strip surface 70 is achieved through the positive pressure generated when sampler 12 and extractor 14 are joined. Below the end stop 78 are disposed a drain 82 (see also Figure 12), a base 76 and a front wall 84 of starter

2015200466 30 Jan 2015

16, which together form a sump 86 for the reaction mixture that drains from the shaking reactor 18. The reaction mixture flows reliably into said sump 86 due to the positive pressure in shaking reactor 18 when positioned on a surface in the preferred orientation of test kit 10. At least one immuno-chromatographic test strip 72 dips into sump 86, where said test strip takes up the reaction mixture by capillary action and delivers it to an immuno-chemical reporting reaction.

The representation in Figure 12 shows the test kit 10 with the shaking extractor 18 inserted into the starter 16. As a result of the positive pressure present in shaking reactor 18, the reaction mixture flows from sump 86 to the test strip surface 70 on extractor 14 and to the one or every test strip 72 attached there.

The representations in Figure 13 and Figure 14 show in a perspective view and a longitudinal cross-section, respectively, a further embodiment of starter 16 which include a test strip surface 70 for test strips 72. In this embodiment, the reaction mixture flows, due to the positive pressure in shaking reactor 18, from sump 86 (Figure 14) to the test strip surface 70 of starter 16 and to the one or every test strip 72 attached there horizontally.

The representations in Figure 15 and Figure 16 show a perspective view and a longitudinal cross-section respectively of test kit 10 prior to the joining of sampler 12 and extractor 14 to form the shaking reactor 18, and prior to the insertion of shaking reactor 18 into starter 16, where the joining of sampler 12 and extractor 14 can also take place if the extractor 14 has already been inserted into the starter 16. Some reference numbers have not been repeated to retain the clarity of the drawing. Please refer to previous figures in this respect.

The depiction in Figure 17 shows the test kit 10 with a further embodiment of the starter 16. The depictions in Figures 18 and 19 show the starter 16 from Figure 17 in different elevations and partly in cross-section. It may be provided with a hygienic pouch 90 in form of a pocket hole for storing the sampler 12. The hygienic pouch 90 is fitted such that the sampler 12 that is stored there is fully protected from environmental effects. The sealing lip 28 of sampler 12 isolates the sampler 12 inside the hygienic pouch 90.

In addition to or as an alternative to the hygienic pouch 90, the starter 16 may be fitted with a false start protection 92 in form of a removable strap 94 or

2015200466 30 Jan 2015

similar. In the embodiment shown, said strap 94 is designed as a grippable and moveable protrusion that may, for example, be attached to starter 16 by a thin hinge. Such a false start protection 92, or a similar physical lock, forms an end stop for the extractor 14 when it is joined to starter 16 and the sampler 12 is joined with the extractor 14 under application of force. The false start protection 92 prevents the inadvertent opening of extractor 14 through the starter 16. Only once the strap 94 has been removed manually, for example by folding it back, can the shaking reactor 18 be pressed into starter 16 up to the end stop 78.

When using the sampler 12 to collect a saliva sample, the sample provider inserts sampler 12 into the mouth and moves it to different locations in the oral cavity, for example to the cheek pouch or around the tongue. Due to surface contact with the oral mucosa, the saliva collected with sampler 12 is now located on the surface or in the pores of the capillary-active sampler body 24. The complete or sufficient filling of sampler body 24 is shown by the indicator ring through the complete discolouration or washing out of the embedded, food-grade colouring agent.

When using the sampler 12 to collect very fine solid particles or dust particles, sampling is performed by pressing or rolling the sampler body 24 onto an object or a surface. The surface may be dry or wet. The fact that the sampler body 24 is freely rotatable above the attachment pin 22 of sampler 12 makes the adhesion or absorption of particles during a rotating movement easier. This type of sample collection can be considered, for example, for the forensic detection of drugs in their commercial form. Items of clothing or other objects that may have come into contact with the drugs are investigated in that they are brushed down with the sampling body 24 or the sampling body 24 of sampler 12 is rolled on the object.

D. Sample preparation using a saliva sample as an example

To evaluate a saliva sample, the sampler 12 is inserted by hand into the extractor 14 after the sample had been collected. Joining of the two components 12, 14 is done manually, without regard to their orientation. The extractor 14 may be handled independently from the starter 16, or together with starter 16 when joined together. The open end of the tube body 42 of extractor 14, together with the circumferential seam 26 on sampler 12, act as end stop for sampler 12 when

2015200466 30 Jan 2015

it is inserted. The sampler 12 seals the cylindrical section of extractor 14 via the annular, circumferential sealing lip 28, which functions as a pressure build-up section 50. A snap-in contour of the extractor 14 (not shown here) engages positively with a corresponding click-in contour of sampler 12 in form of, or similar to, the circumferential groove 30, thereby functioning as a sealing lock. The spatially defined shaking reactor 18 is formed during this first step in the sample preparation by the insertion of sampler 12 into extractor 14. During the same step, a liquid reagent depot 54, for example a liquid reagent depot 54 in form of a glass ampoule filled with a liquid reagent, is destructively opened through perforation using the perforating tip 34 of sampler 12.

A subsequent second step includes the shaking of the shaking reactor 18, in particular the shaking of the shaking reactor 18 along its longitudinal axis. The mixing of the saliva sample, which was collected with sampler 12 and which is located on the surface or in the pores of the capillary-active sampler body 24, with dry and/or liquid reagents is only achieved with said agitation. The saliva sample as well as the reagent contained in the one or every reagent carrier 58, 60, for example drug-specific antibody-gold nanoparticle conjugate, come repeatedly into contact with the liquid reagent of the liquid reagent depot 54 during the shaking motion. In the instance where a glass ampoule acts as the liquid reagent depot 54, small glass splinters, that is, glass splinters that are smaller than the gap 62 between the sampler body 24 and the inner surface of the tube body wall 40 located opposite, are accelerated vertically more strongly during the shaking motion than the liquid due to their greater specific weight. The liquid adhering to said splinters makes the vertical transfer inside the shaking reactor 18 easier. Through repeated liquid film formation on sampler body 24 as well as on the one or every reagent carrier 58, 60, followed by drop-breakoff, the sample and the dry reagent are gradually withdrawn (extraction). The shaking process continues until either the coloured reagent carrier 58, 60 is discoloured, or a predetermined shaking time has been reached. Nevertheless, in order to avoid any inaccuracies in the implementation of the shaking process by different individuals, provision is made that the discolouration of the one or every reagent carrier 58, 60 functions as an indicator for a sufficiently long shaking process, which compensates for differences between individuals in the shaking process.

2015200466 30 Jan 2015

The sample preparation ends with the completion of the described shaking process and a subsequent, optional incubation phase during which the shaking reactor 18 remains in a resting position for a certain period before the fluid transfer to the one or more test strips 72 is initiated. If the shaking reactor 18 is not already in the starter 16 during the shaking process, it is inserted into the starter now. In any case, the shaking reactor 18 is pressed into the starter 16 up to the end stop 78 after completion of the shaking process, for which the starter 16 is positioned on a surface. Prior to pressing the shaking reactor 18 into the starter 16, the strap 94 may be bent away, torn off or otherwise removed. Said strap 94 prevents insertion of the penetrating profile 80 into the defined breaking point 44 when the sampler 12 and the extractor 14 are joined inside the starter 16. By pushing the shaking reactor 18 through into the starter 16, the penetrating profile 80 opens the defined breaking point 44 at the bottom of extractor 14, allowing the reaction mixture inside shaking reactor 18 to escape downwards under the sudden loss of pressure. In this third step, the reaction mixture, consisting of a homogeneous mixture of saliva, liquid reagent and antibody-gold nanoparticle conjugate, is transferred to the test strip surface 70. A test strip 72, or multiple test strips 72 on said test strip surface 70 soak up the mixture automatically from the sump 86 due to capillary action.

After the mixture has passed across the test strips 72 within a few minutes, visible coloured test lines have developed, depending on the analyte concentration and a corresponding immunochemical scavenging reaction, which can be evaluated as part of a visual interpretation.

The above description illustrates preferred but non-exhaustive embodiments of the present invention. In the appended claims, dependency statements between claims may serve to identify a further development of a feature or features present in an antecedent claim. However, the claim dependency statements are not to be construed in such manner as waiving the possibility of such features or combination of features being capable of independent protection without the features of intervening claims. Moreover, with reference to an interpretation of the claims by way of which a characteristic or feature is identified for the first time in a sub-claim, the assumption must be that

2015200466 30 Jan 2015

such does not make the presence of such characteristic or feature in the claims to which the sub-claim refers an indispensable requirement.

Finally, the contents of the specification of priority application DE 10 2014 001 386.3 is incorporated herein by way of short hand cross-reference to that specification (description, drawings and claims).

2015200466 30 Jan 2015

Listing of features and reference numbers as appear in the drawings

1	mixing container
2	indicator element
3	lid
4	liquid sample and/or diluting fluid
5	solid sample
6	outlet
10	testing device / test kit
12	sampler
14	extractor
16	starter
18	shaking reactor (mixing container)
20	handle
22	attachment pin
24	sampler body
26	circumferential seam
28	circumferential sealing lip
30	circumferential groove or ridge
32	position locating contour
34	perforating tip
36	indicator ring
40	tube body / tube body wall
42	upper opening of extractor / tube body end
44	an interface functioning as defined breaking point at bottom of extractor
46	insert section (for sampler)
48	--
50	pressure-build-up section
52	support rib
54	liquid reagent depot
56	support surface

2015200466 30 Jan 2015

58	reagent carrier
60	reagent carrier
62	circumferential gap
64	rib
66	abutting face (of rib)
68	--
70	test strip surface
72	test strip
74	guiding profile (in starter; to take up extractor)
76	base (of starter)
78	end stop (on starter)
80	penetrating profile
82	drain
84	front wall (of starter)
86	sump
88	--
90	hygienic pouch
92	false start protection
94	strap (of false start protection)

2015200466 30 Sep 2016

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. Sample preparation and testing device, comprising:

a mixing container;

an indicator element located inside the mixing container;

a sampler;

an extractor;

and a starter;

wherein the indicator element is devised to provide an indication of a time interval during which the mixing container was shaken; and

wherein the mixing container is fully or partially transparent, and wherein the indicator element is arranged such that it is visible from outside the mixing container;

wherein each of the sampler, extractor and starter having constructional features enabling the sampler to be releasably joined with the extractor and the extractor to be releasably joined with the starter, the sampler and the extractor comprising constructional features whereby the joining of the sampler with the extractor forms said mixing container, the mixing container being sealed temporarily to function as a shaking reactor for a sample received in the mixing container, and

wherein the sampler has a sampler body at one end, wherein the extractor has a tubular body into which the sampler body can be inserted in the process of joining the extractor with the sampler to form the shaking reactor, and wherein the sampler and extractor have cooperating constructional features enabling creation and maintenance of a positive pressure inside the shaking reactor when joined together, the cooperating constructional features comprising the extractor being provided with an internal cylindrical surface extending along a length of the tubular body and the sampler having a circumferential external sealing lip which, when the sampler is inserted into the extractor, presses against the cylindrical surface.

2015200466 30 Sep 2016

2. Device according to claim 1, wherein the starter comprises a penetrating profile at a bottom of the starter, wherein the extractor comprises an interface providing a defined breaking point at the bottom of the extractor, and wherein the penetrating profile and interface are shaped to cooperate by opening the bottom of extractor when it is inserted into the starter.

3. Device according to claims 1 or 2, comprising a false start protection on the extractor and on starter.

4. Device according to any one of claims 1 to 3, wherein the extractor has an internal cavity comprising support ribs for retaining a liquid reagent depot inside the extractor.

5. Device according to any one of claims 1 to 4, comprising a hygienic pouch in form of a pocket hole formed in the starter for storing the sampler.

6. Device according to any one of claims 1 to 5, wherein the indicator element comprises a microporous material in which is stored a colouring agent, the microporous material being devised to release the colouring agent into a surrounding sample received in the mixing chamber within a defined period of time during shaking of the mixing chamber, whereby the initially coloured indicator element is discoloured.

DRAEGER SAFETY AG & CO. KGAA

WATERMARK PATENT AND TRADE MARKS ATTORNEYS

P39948AU00

30 Jan 2015
2015200466

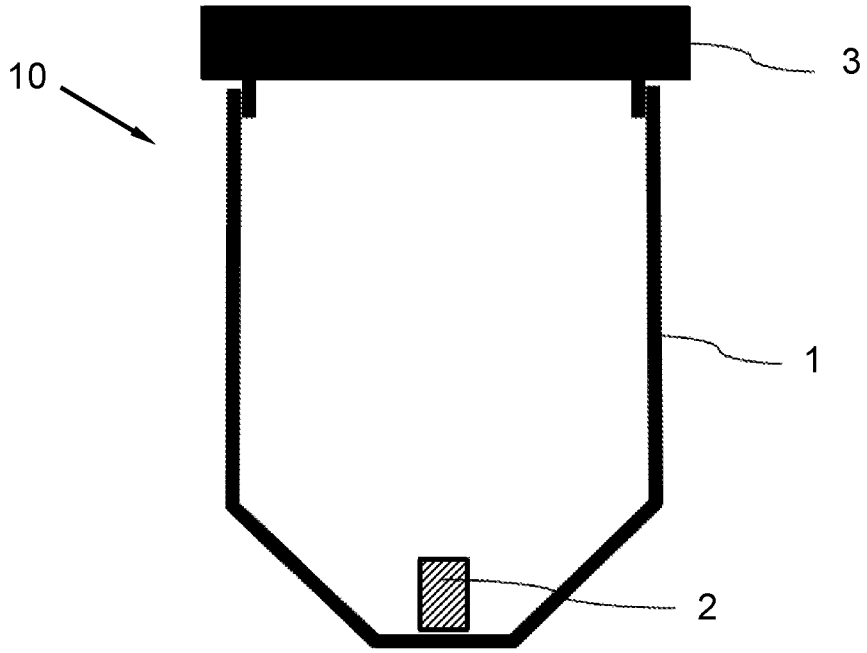

Fig. 1

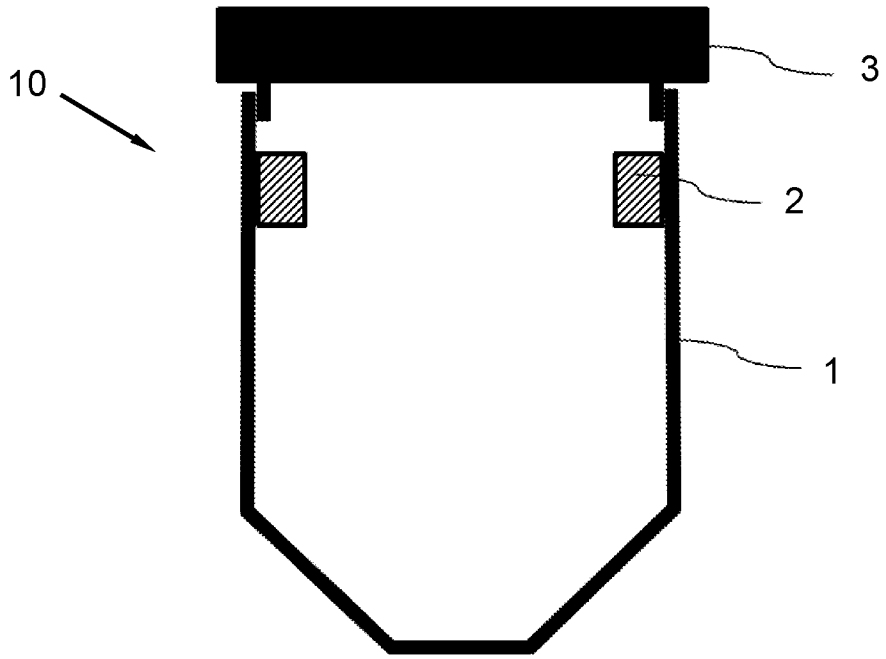

Fig. 2

30 Jan 2015
20152004466

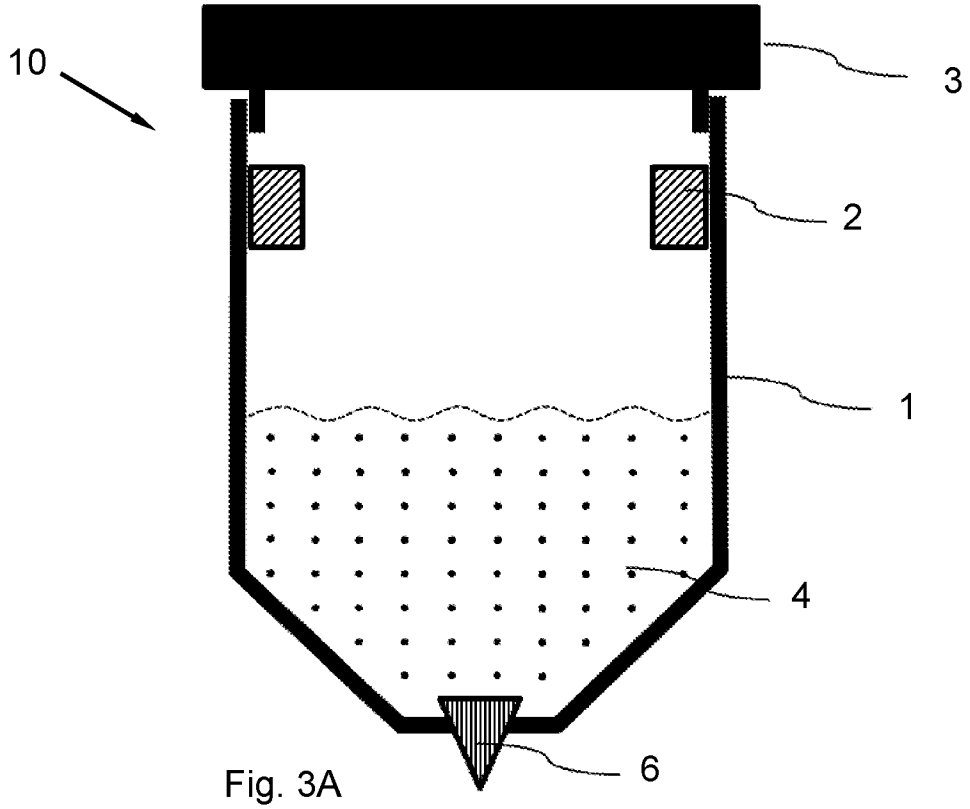

Fig. 3A

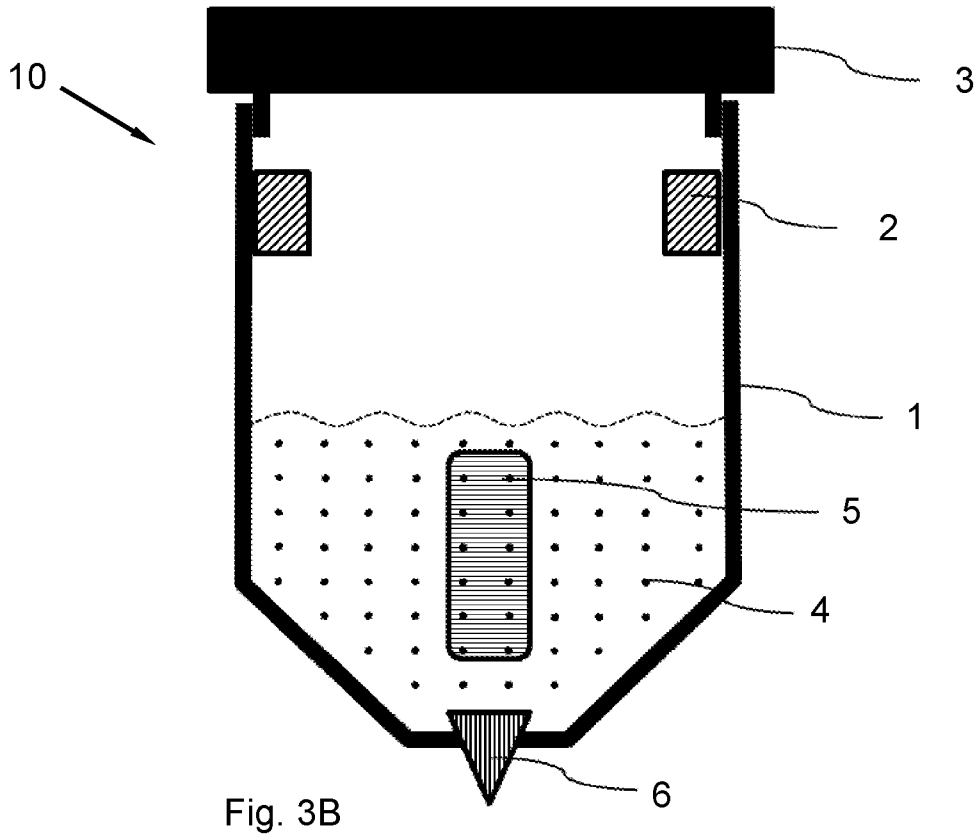

Fig. 3B

30 Jan 2015 2015200466

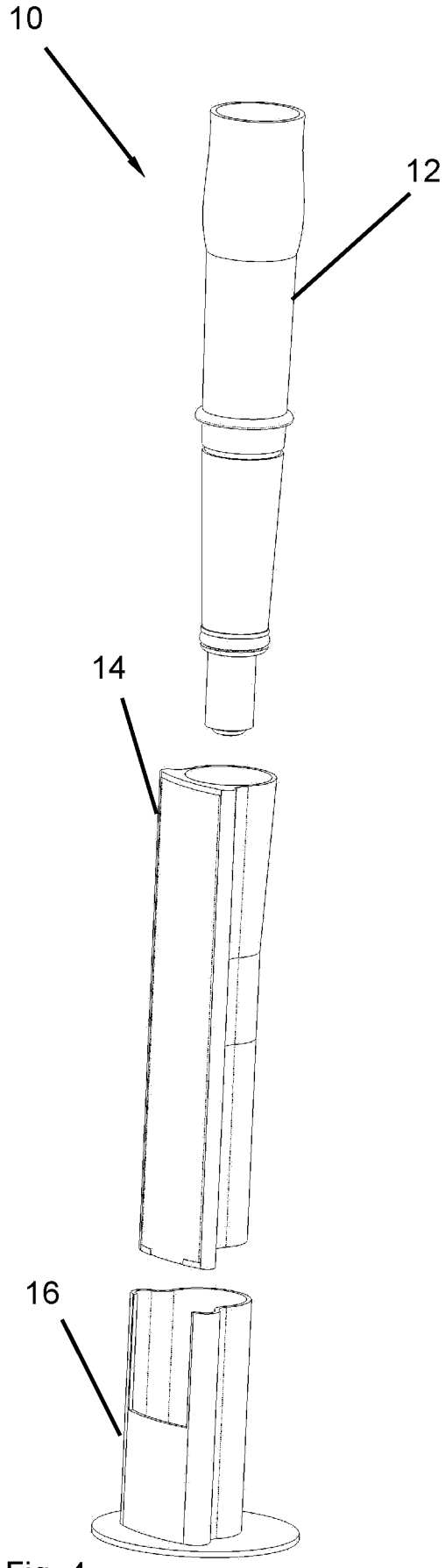

Fig. 4

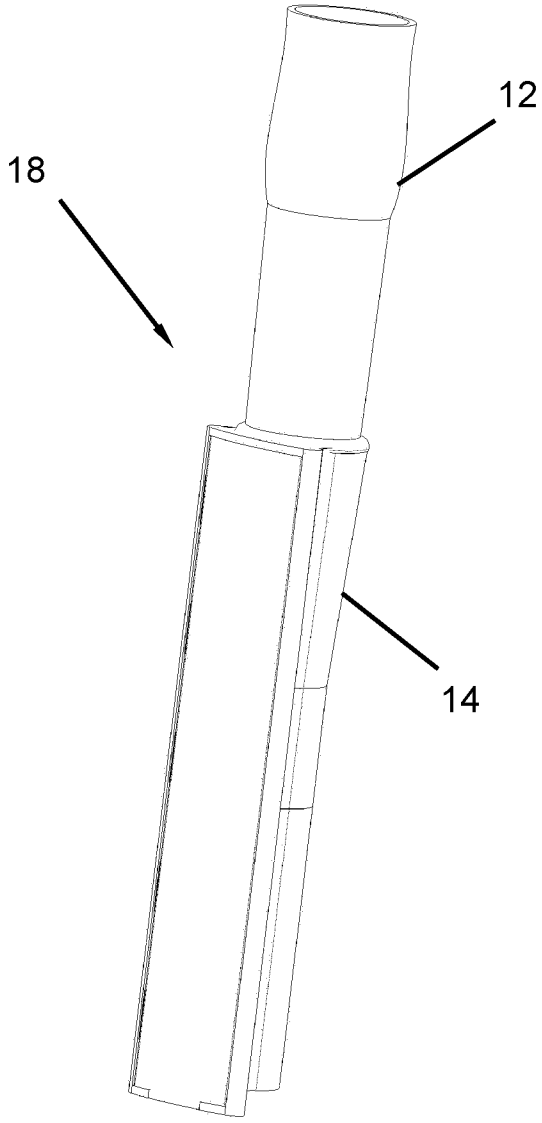

Fig. 5

30 Jan 2015 2015200466

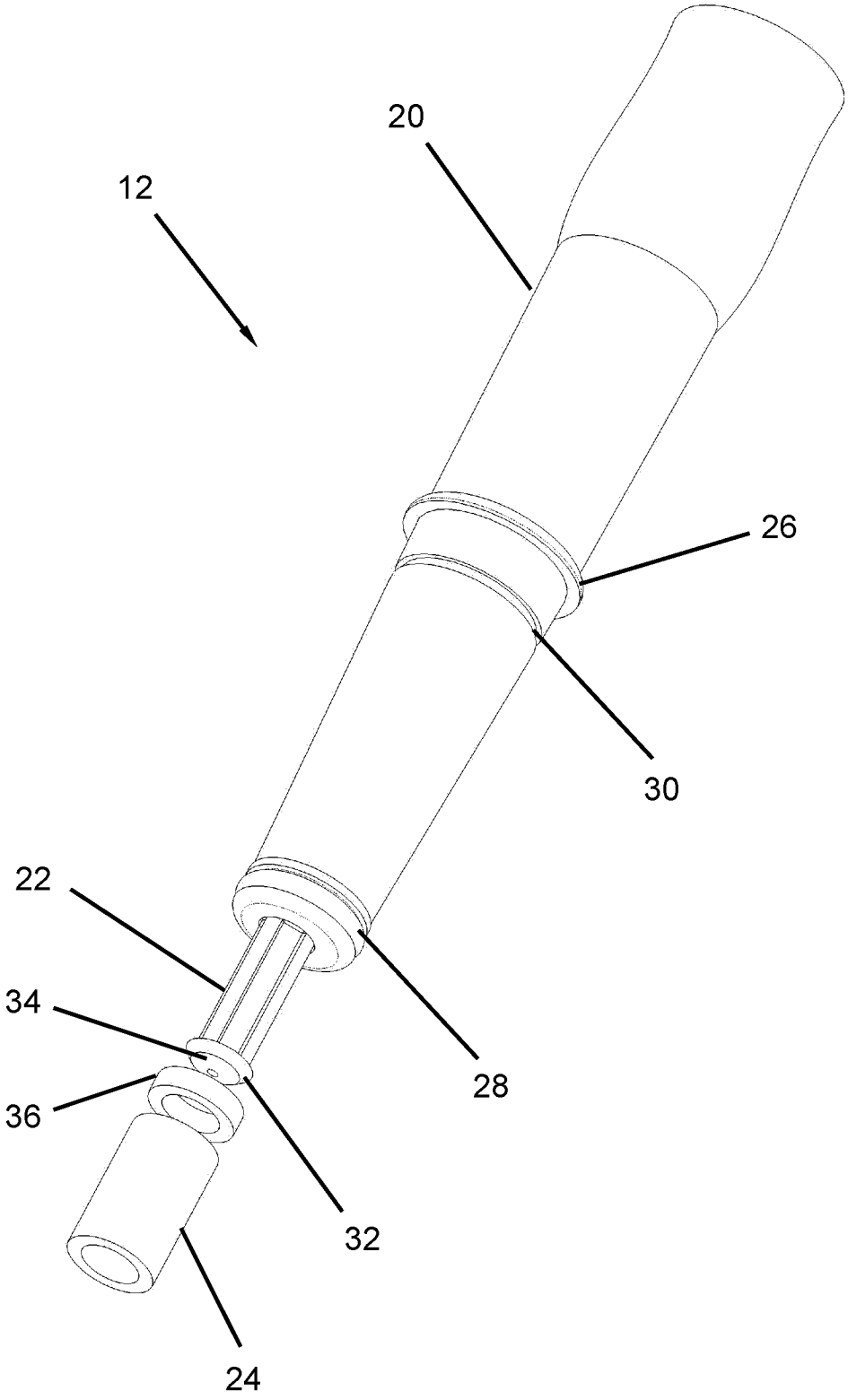

Fig. 6

30 Jan 2015 2015200466

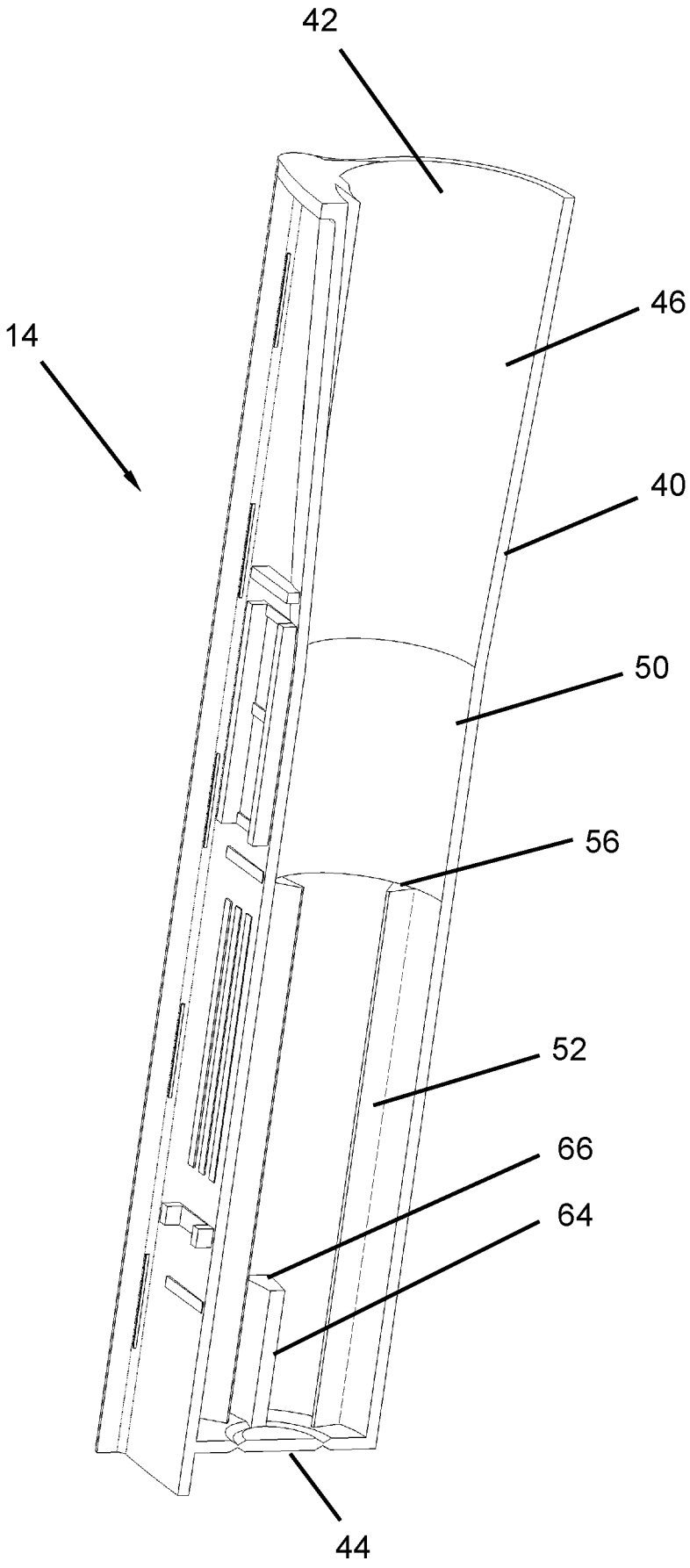

Fig. 7

30 Jan 2015 2015200466

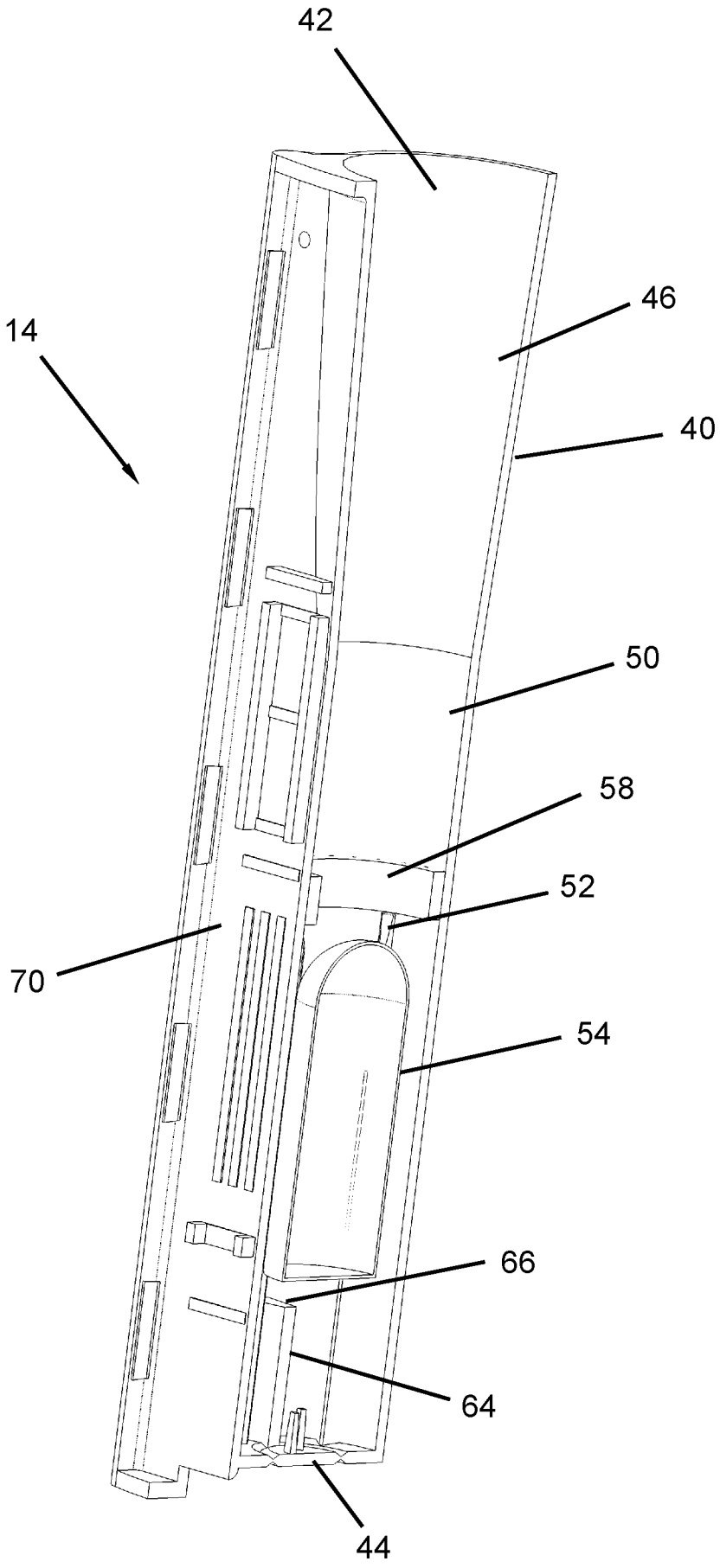

Fig. 8

30 Jan 2015 20152004466

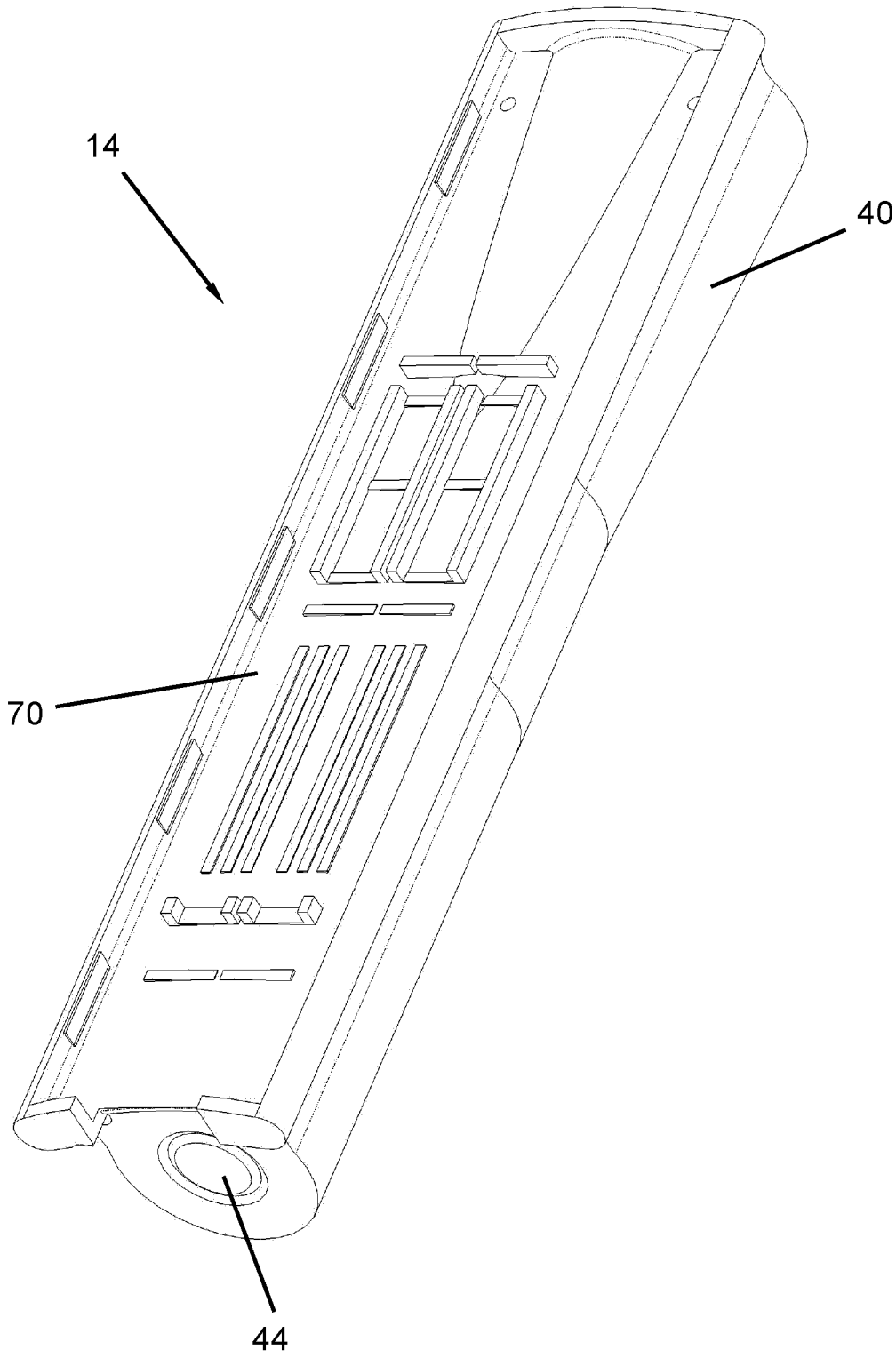

Fig. 9

30 Jan 2015 2015200466

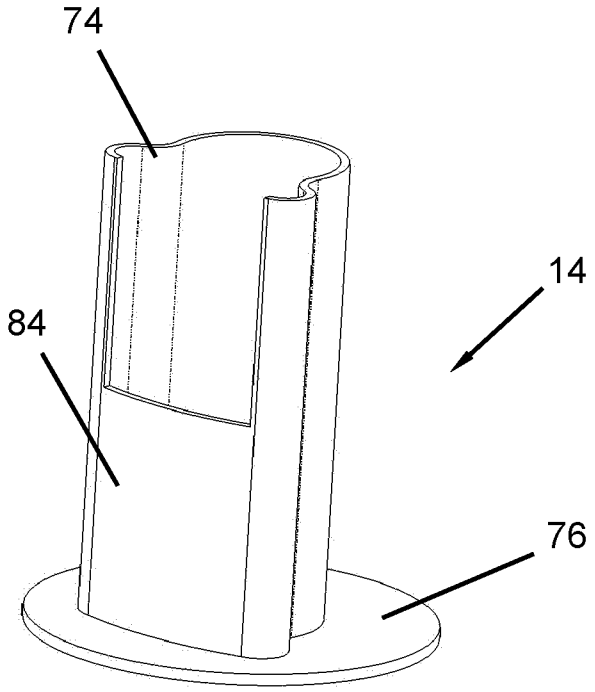

Fig. 10

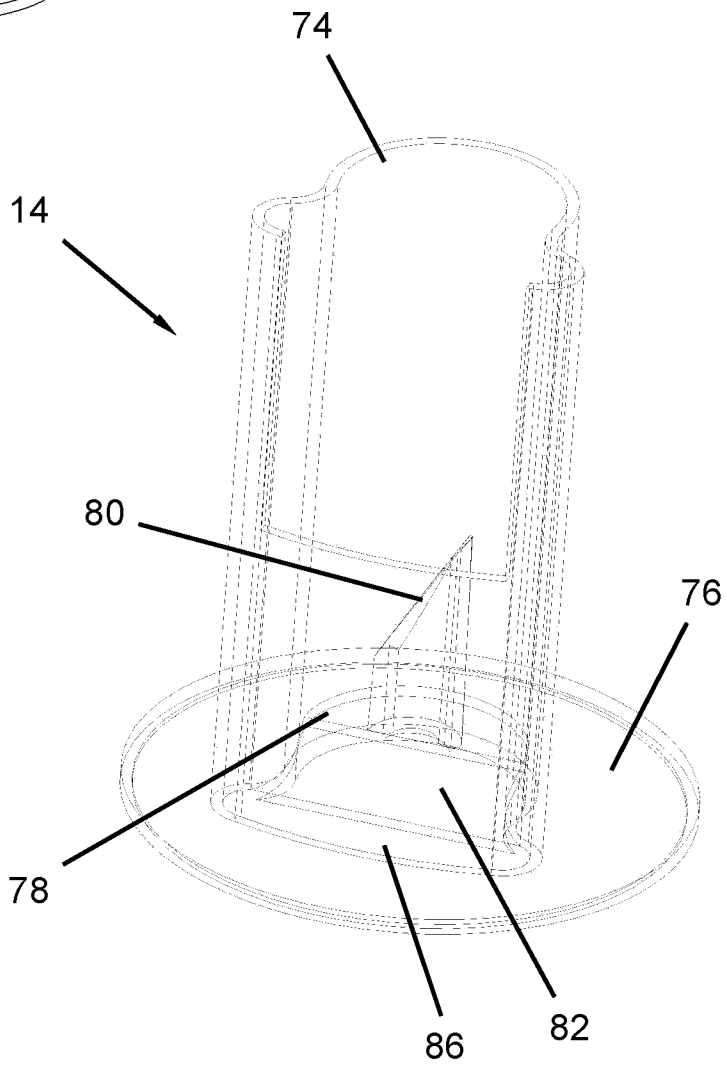

Fig. 11

30 Jan 2015 2015200466

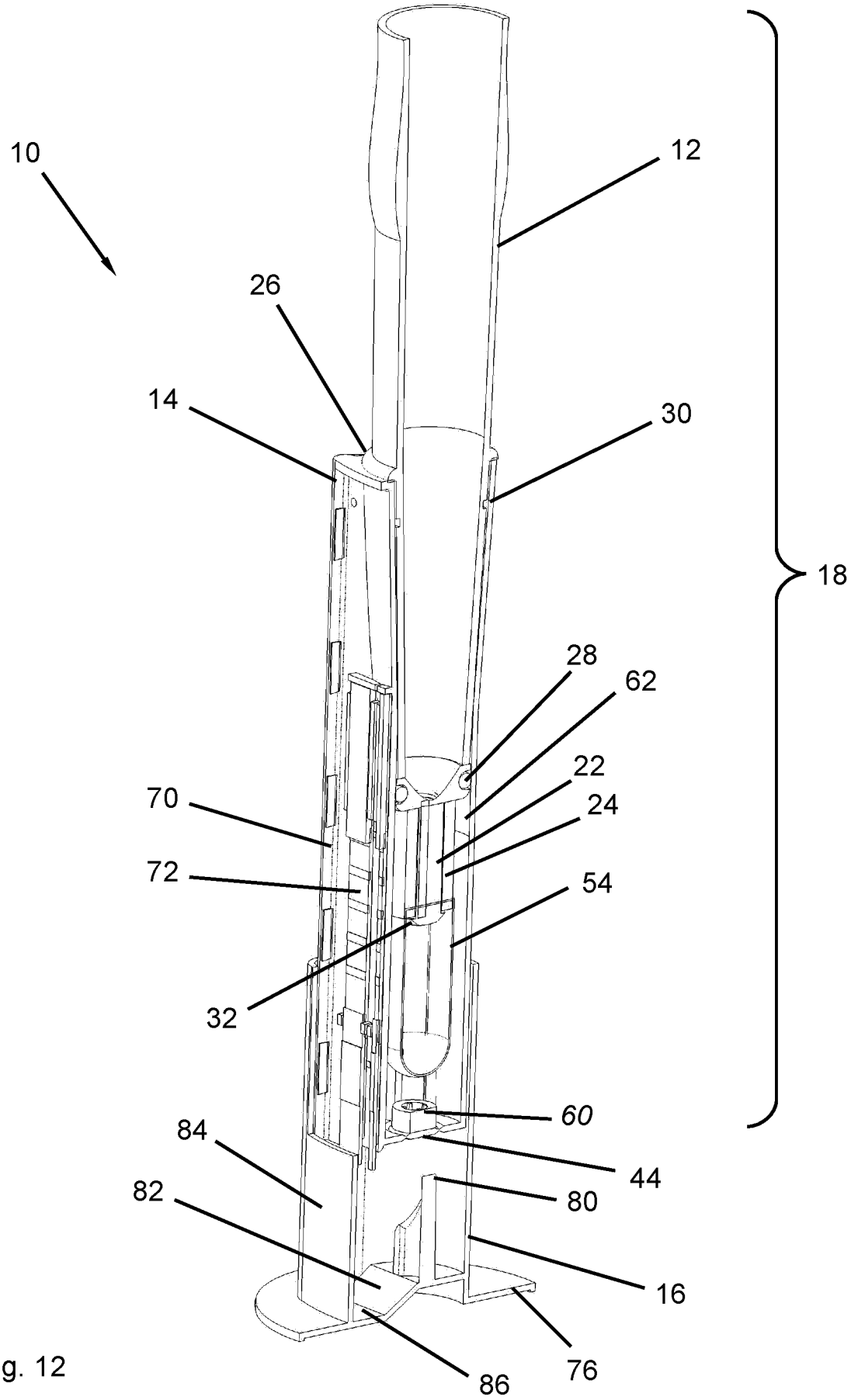

Fig. 12

30 Jan 2015 20152004466

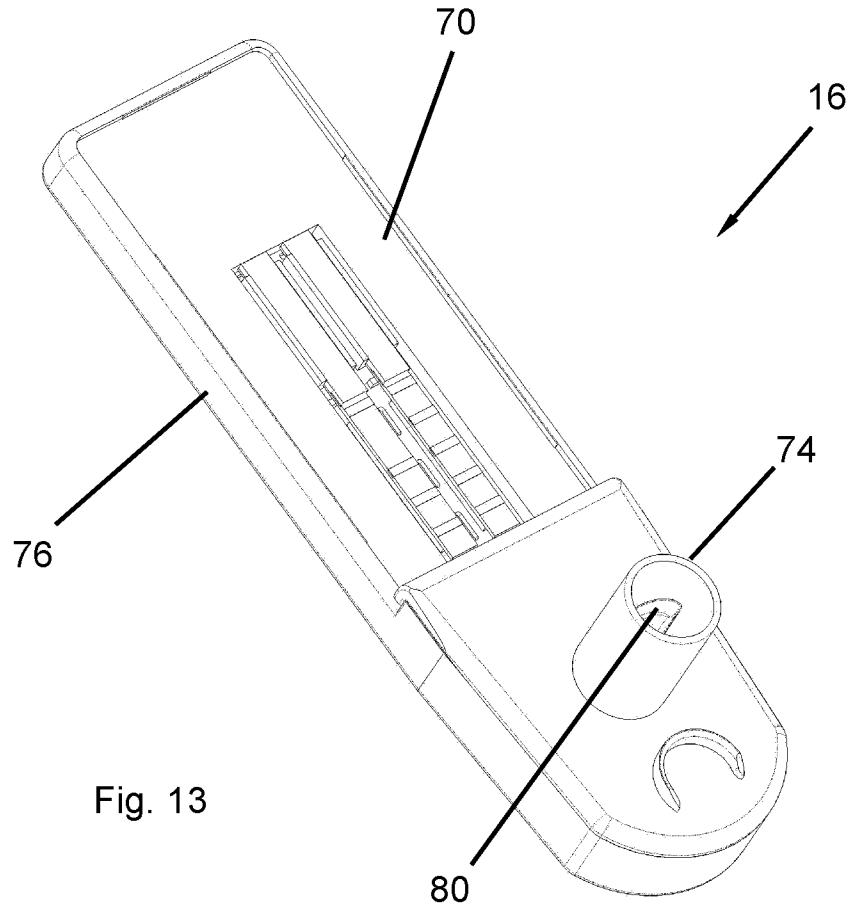

Fig. 13

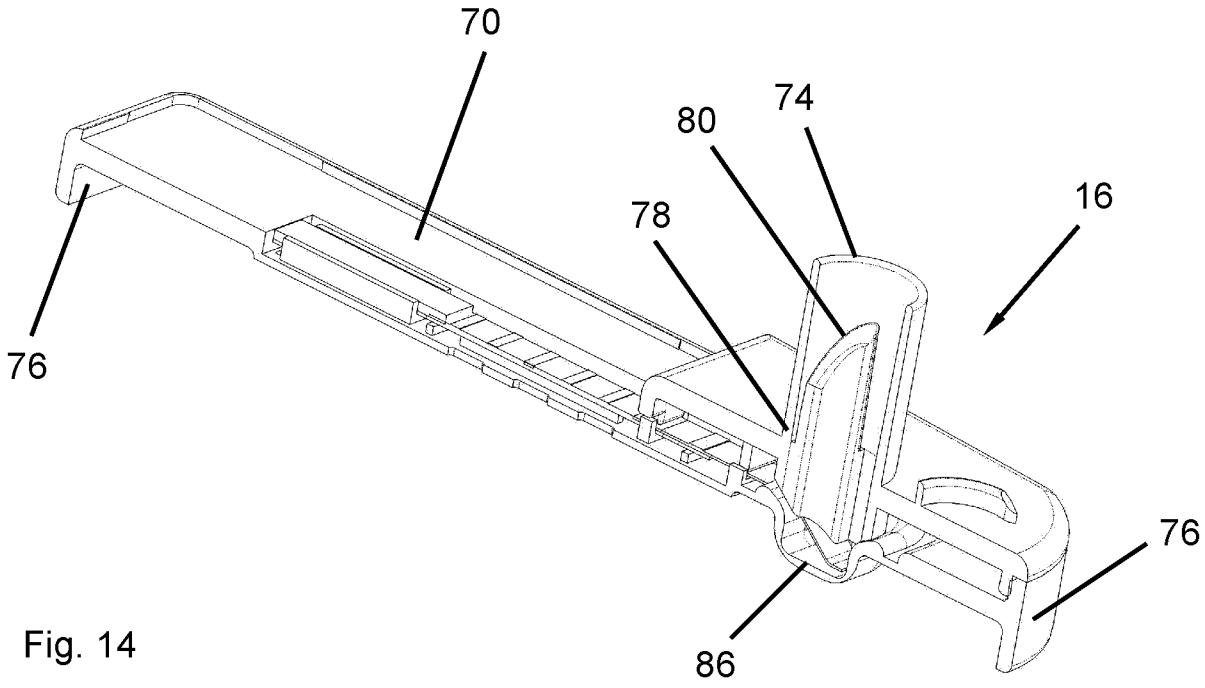

Fig. 14

2015200466 30 Jan 2015

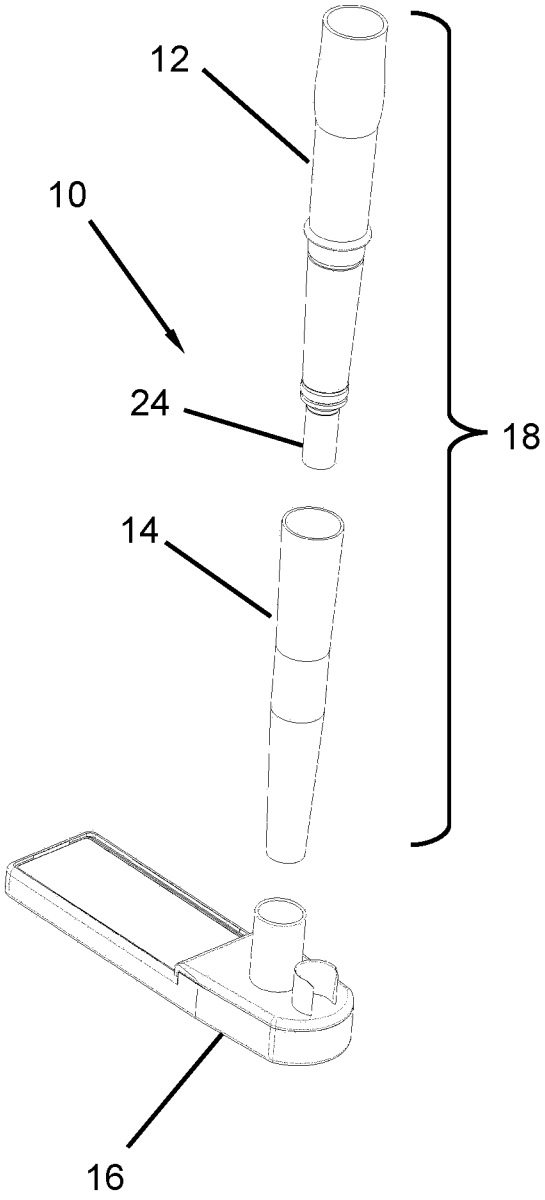

Fig. 15

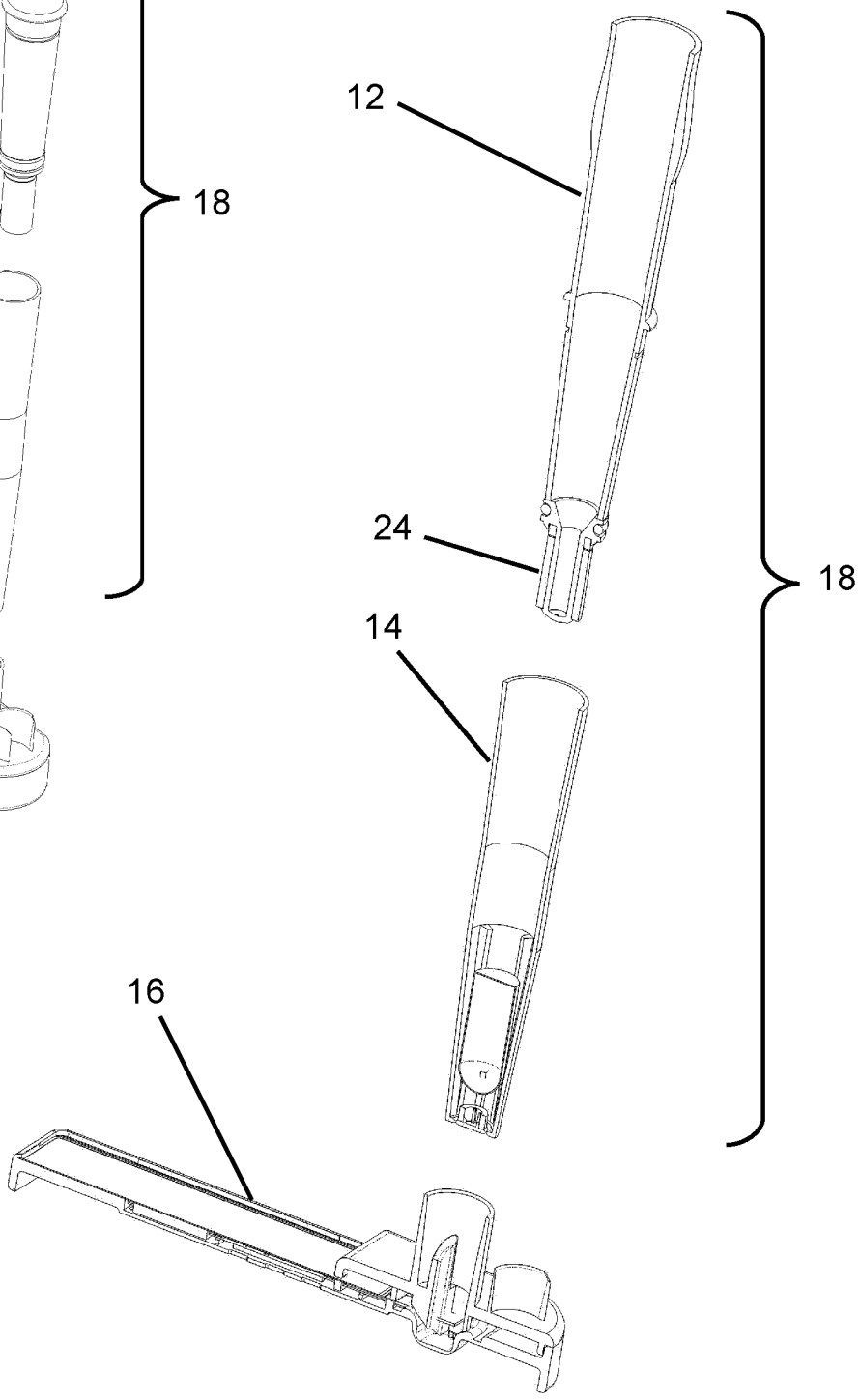

Fig. 16

30 Jan 2015 20152004466

44

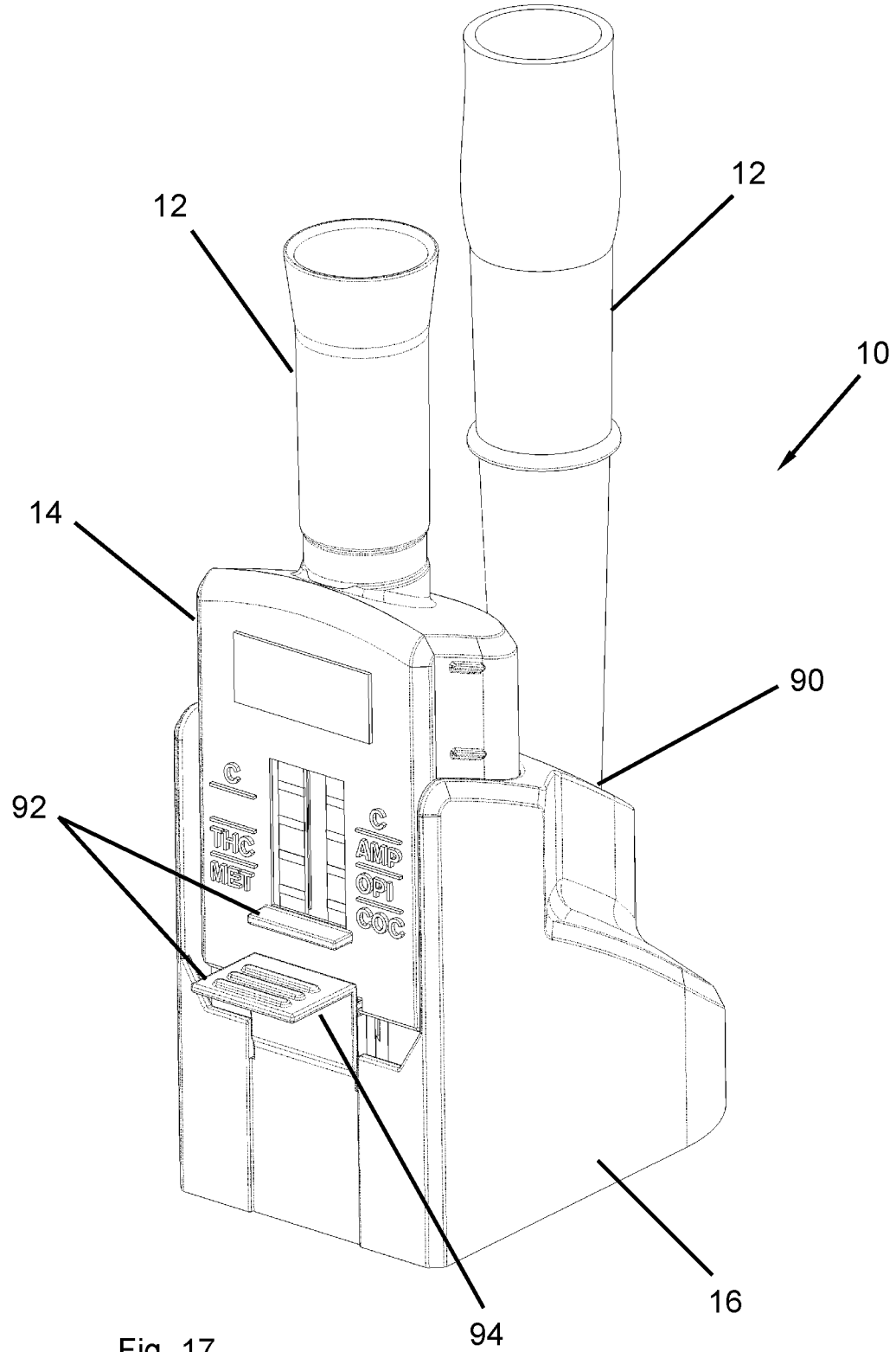

Fig. 17

30 Jan 2015
20152004466

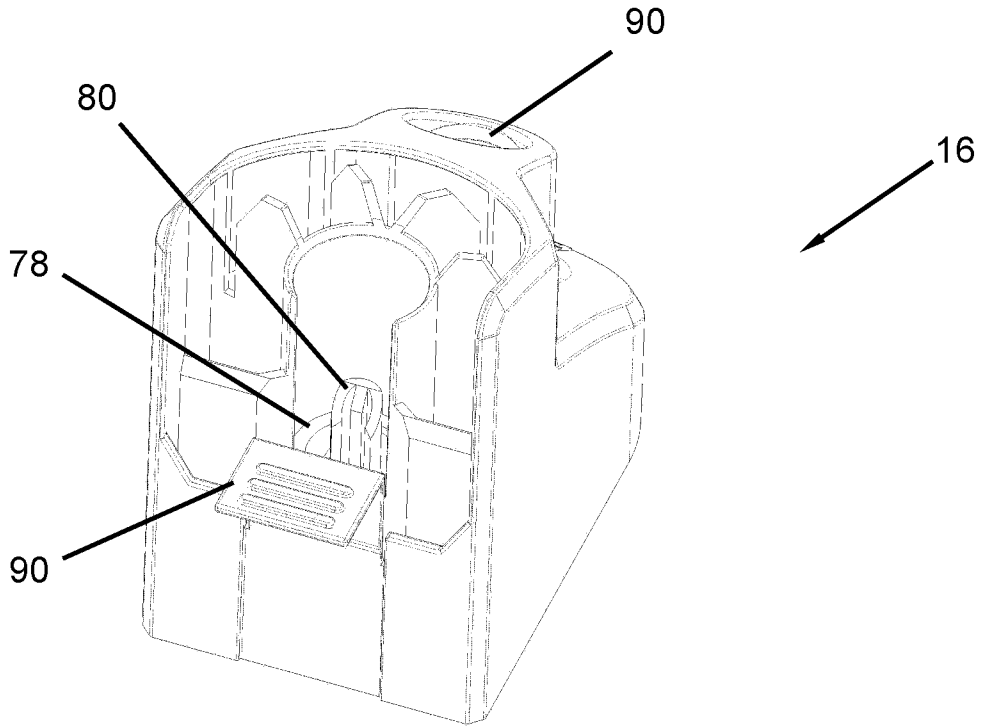

Fig. 18

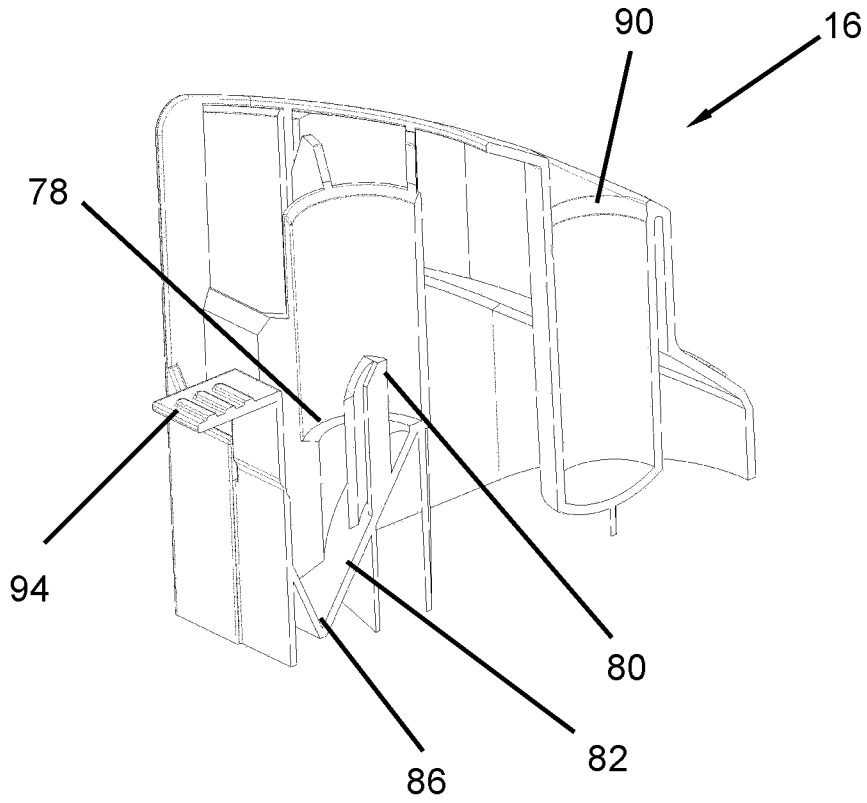

Fig. 19