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Czaplinski et al.

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[54] **DISPOSABLE PHARMACEUTICAL STERILE CLOSURES**

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[52] **U.S. Cl.** **210/233**, 210/446, 210/451, 210/455, 128/272

[51] **Int. Cl.** **B01d 35/00**

[58] **Field of Search**.....210/233, 446, 450, 451, 453, 210/455; 128/272, 214 R; 222/189, 541

[56] **References Cited**

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[57] **ABSTRACT**

Disclosed herein is a disposable sealed sterile closure for use primarily in radiopharmaceutical preparations. The stopper is of the type that can be pierced by a hypodermic needle to aseptically remove sterile, pyrogen-free material from a vial or generator.

4 Claims, 2 Drawing Figures

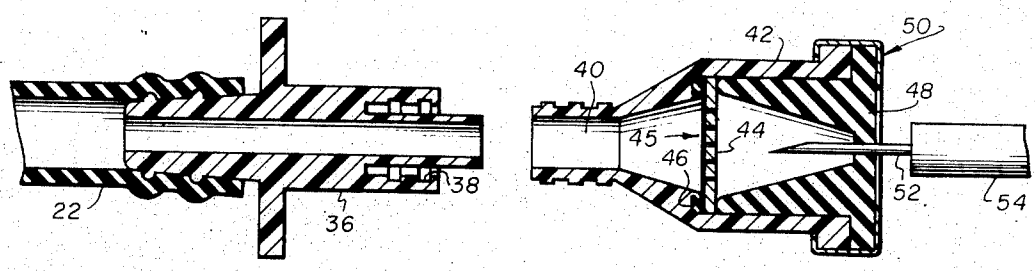
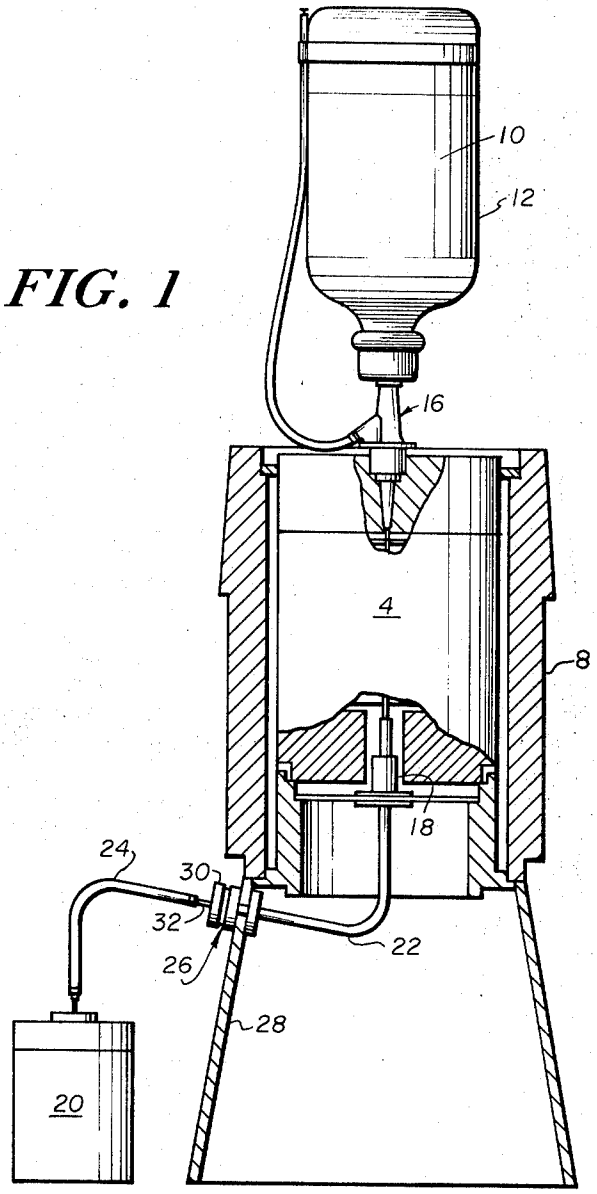


FIG. 1



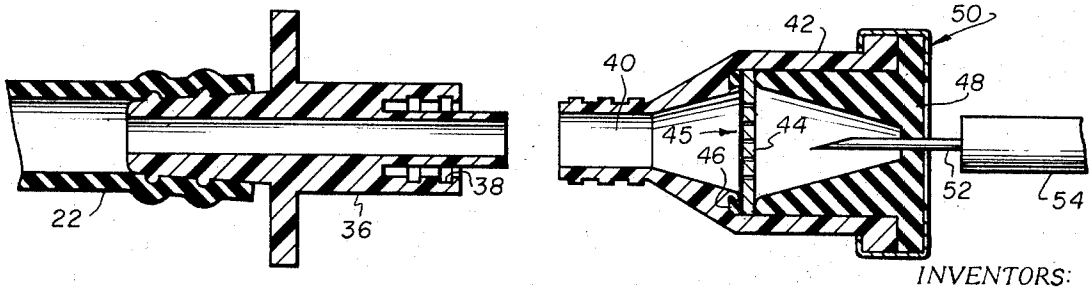


FIG. 2

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DISPOSABLE PHARMACEUTICAL STERILE CLOSURES

PRIOR ART

Within the past two decades the use of radiopharmaceuticals have gained wide acceptance by radiologists as aids in diagnosing various anatomical conditions. Various radioneuclides have become valuable diagnostic tools to the practicing physician to locate tumors and check the functioning body organs, such as the liver, kidneys, pancreatic tissue, and so forth. One of the primary sources of radioisotopes is delivered by a system commonly referred to as a radioisotope generator. In its operation a parent radioisotope is placed on a support and allowed to decay. The decayed product (daughter isotope) is then milked to yield the desired radioisotope. The daughter radioisotope is then utilized as a tracer and depending on the isotope utilized or the composition tagged with the daughter isotope, it will localize in various areas of the body. The body is then scanned with a suitable apparatus for detecting radiation, such as a scintillation spectrometer, to detect any abnormal localization of the daughter isotope.

Among the generators presently in use routinely or being investigated are tellurium-iodine; molybdenum-technetium; strontium-yttrium; tin-indium, and so forth.

With the development of a sterile, pyrogen-free generator as set forth in U.S. Pat. No. 3,369,121, many of the systems previously utilized only experimentally have been accepted for routine use by the radiologists and the Atomic Energy Commission. One system at the present stage still in experimental use is the tin-indium generator. This generator is extremely useful since the half-life of Sn-113m is approximately 118 days, whereas the half-life of its daughter indium In-113m is merely 1.73 hours. Thus the system can be set up to provide the practicing physician with available indium-113m for scanning organisms for a period of from about 6 to 9 months. However, as it will be repeatedly utilized over this period of time, it is necessary to maintain sterility and non-pyrogenicity within the unit. One of the most vulnerable areas of possible contamination is the site of delivery. The discovery of a sterile, sealed disposable closure substantially reduces the likelihood of contamination to the system and allows the unit to be operational for long periods of time. Prior to this it was considered that the entire system was to be kept constantly sealed at all points.

DESCRIPTION OF INVENTION

In order to reasonably assure the sterility and non-pyrogenicity of a tin-indium 113m generator, it has been discovered a disposable, sealed, sterile closure comprising a housing having a configuration wherein one end is closed by a pierceable membrane and the opposite end remains open, a membrane filter placed between said membrane and said open end, and a seal around said closed end of the housing to retain said membrane in position will limit the hazards of contamination over the long period of time such a system is in operation.

The invention can be more fully understood by referring to the drawings, wherein:

FIG. 1 is a schematic view of a generator system having a sterile, sealed disposable closure therein; and

FIG. 2 is a sectional view of the parts of a disposable sealed, sterile closure;

Referring to FIG. 1 eluting solution 10 is within elution bottle 12 or any other container, e.g., plastic bag. The elution bottle 12 is contacted in tandem with generator system 4 by hypodermic needle 16. This allows for eluting solution 10 to flow into generator system 4. Lead shielding 8 to prevent radioactive emission from the system encloses generator system 4. The details of generator system 4 are more fully set out in U.S. Pat. No. 3,369,121. The eluate of this system having the daughter isotope therein is removed via hypodermic needle 18 from the bottom of the generator system 4 and allowed to pass into an evacuated vial 20 through conduits 22 and 24. At point 26 on stand 28 which supports generator system 4 and shielding 8, there is a disposable sealed, sterile closure 30 of this invention which can be penetrated by hypodermic needle 32. It is to be understood that the generator system described herein can be modified in various ways. For example, a continuous system where in lieu of hypodermic needles 16 and 18, the eluting solution and generator may be directly connected to stopper 30 by plastic conduits or fittings at 16 and 18.

The construction of closure 30 is more clearly seen in FIG. 2, wherein delivery conduit 22 is connected to retainer 36; retainer 36 being capable of fitting into outlet 26 of stand 28 and having grooves 38 or other coupling means to receive open end 40 of housing 42.

Within housing 42 which may be of teardrop configuration is membrane filter 45 which is cushioned on gasket 46 and supported by perforated filter support 44.

Pierceable membrane 48 closes housing 42 at one end and is retained in position by seal 50. Seal 50 is an aluminum seal generally utilized in autoclaving pharmaceutical preparations by placing the seal around the pierceable membrane 48 and crimping said seal. This type of seal allows for stopper 48 to be satisfactorily autoclaved and maintained in sterile condition. When the generator is ready for use, milking needle 52 is inserted into pierceable membrane 48 and eluate from elution bottle 12 passes through generator system 14. This can be accomplished by gravity flow methods or preferably by utilizing evacuated collecting vial 20 shown in FIG. 1.

Housing material 42 as well as the other materials of this invention may be made of plastic or metal material which withstands autoclaving, e.g., about 115°–125° C. for from 20–30 minutes at 15 lb./sq. in. gauge. Therefore, a plastic, such as polypropylene, can be utilized. In addition, other methods of sterilizing may be utilized, such as by gas sterilization with ethylene oxide. The membrane filter 45 may be between about 0.22 and 0.45 micron when utilized for sterilizing an eluate if further assurance of sterility is desired. However, if a clear eluate solution is the only requirement, then a membrane filter having a pore size greater than about 0.50 micron can be utilized, but not to exceed 20 microns.

Pierceable membrane 48 can be made of rubber or any other pharmaceutically acceptable grade latex material which can be pierced.

In operation the disposable stopper of the invention is contained within a sterile pyrogen-free wrapper. The

technician desiring to utilize it merely opens the wrapper and passes it into connecting outlet **26**. This procedure is generally carried on at least once a week or can be repeated as often as the technician deems to do so.

We claim:

1. In combination with a stand having an aperture, a disposable closure comprising a male portion and a female portion, the female portion comprising a housing, having one end closed by a pierceable membrane and the other end open and provided with coupling means adapted to be joined to the male portion, a perforated filter support disposed in the interior of said housing, between the pierceable membrane and open end, but spaced from said open end, a filter on the support in operable relation with said membrane, said filter and support being retained in a recess in said housing, and a seal around said closed end of the housing to retain said membrane in position; and the male portion comprising a housing, said male housing comprising coupling means on opposite ends of said male housing, one end of said coupling means being adapted to be joined to a delivery conduit and the other end being constructed and arranged to be joined to the coupling means of said female portion, said other end of said male coupling means being constructed to fit through said aperture, thereby retaining said closure on said stand.

2. The closure of claim **1** wherein the filter is a membrane filter having a pore size of from about 0.22 to about 0.45 micron.

3. The closure of claim **2** having a teardrop configuration.

4. The closure of claim **1** wherein the filter is a membrane filter having a pore size of from about 0.50 to 20 microns.

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