

April 22, 1969

G. A. BRUNO ET AL

3,440,423

PROCESS FOR PREPARING STERILE RADIOACTIVE MATERIAL
OF THE PARENT-DAUGHTER TYPE

Filed April 10, 1967

Sheet 1 of 3

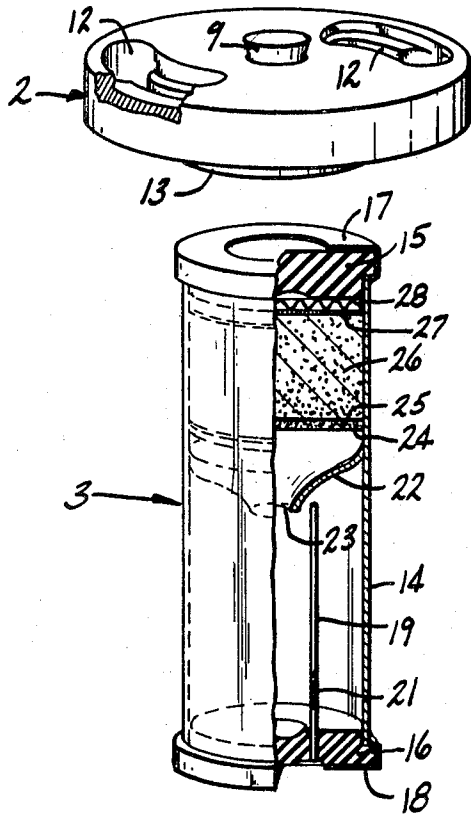
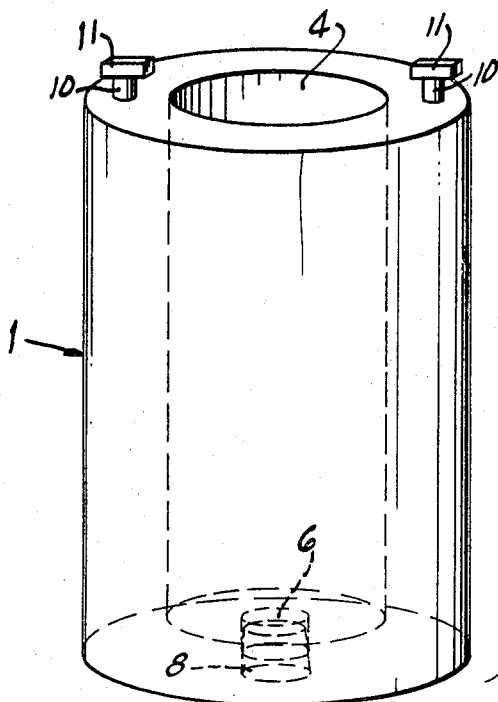
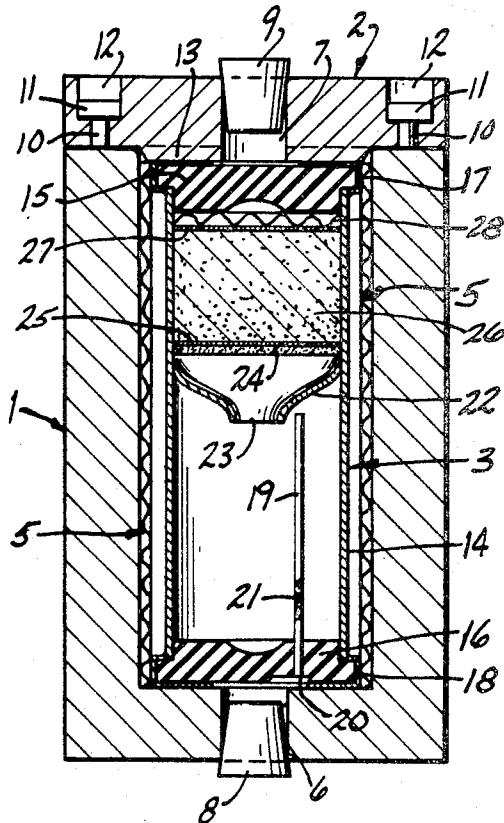


FIG-2

FIG-1

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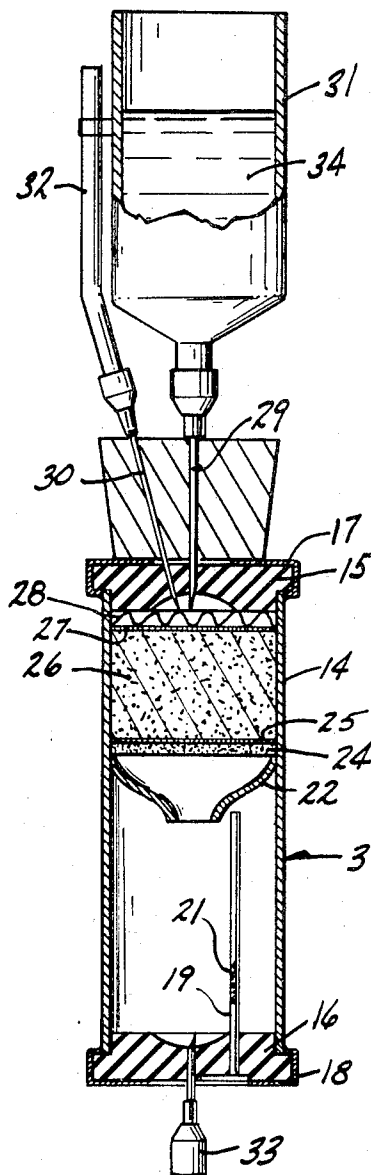


FIG - 3

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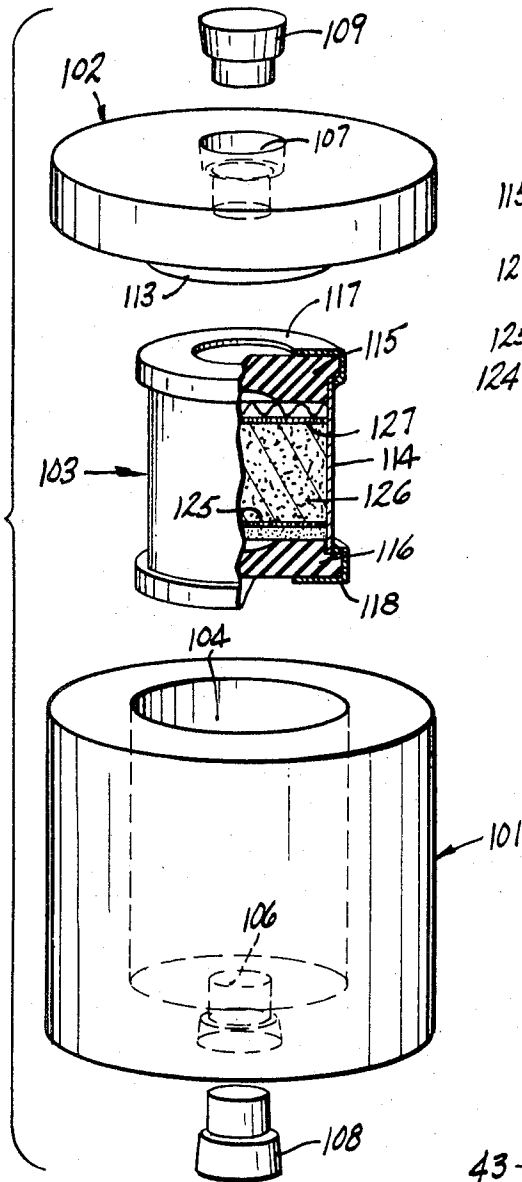


FIG-4

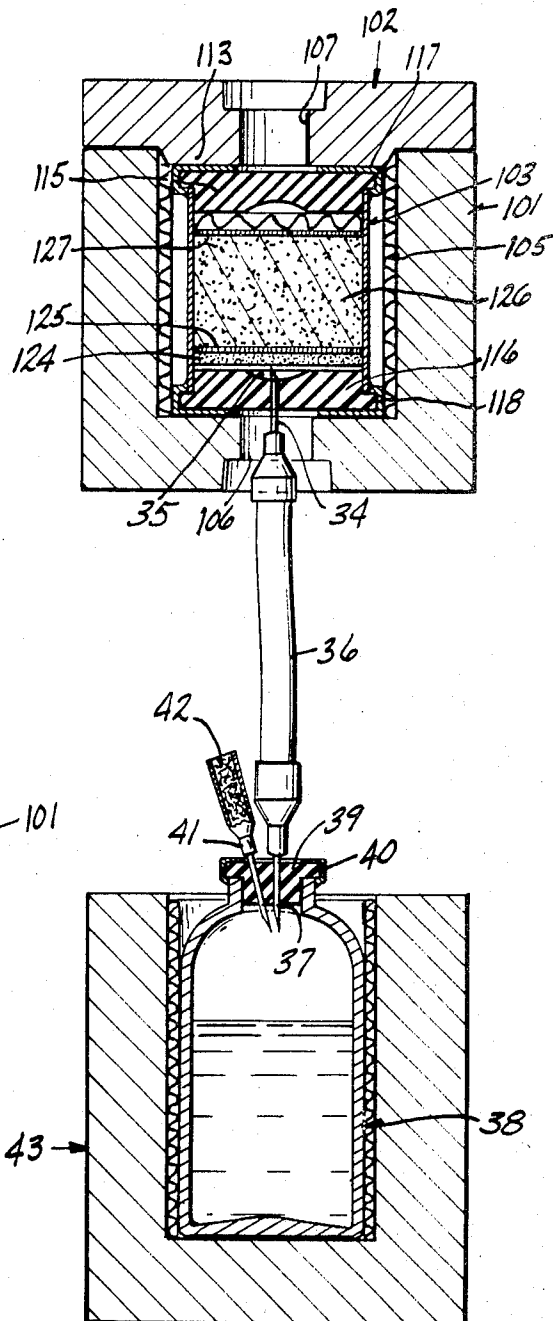


FIG-5

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3,440,423

PROCESS FOR PREPARING STERILE RADIOACTIVE MATERIAL OF THE PARENT-DAUGHTER TYPE

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Continuation-in-part of application Ser. No. 540,689, Apr. 6, 1966. This application Apr. 10, 1967, Ser. No. 629,782

The portion of the term of the patent subsequent to Feb. 13, 1985, has been disclaimed and dedicated to the Public

Int. Cl. G21h 5/00; C09k 1/28; C01g 1/00

U.S. Cl. 250—106

10 Claims

ABSTRACT OF THE DISCLOSURE

This invention relates to a new process for preparing sterile radioactive material and essentially entails using a closed sterile system for the preparation of radioactive material and its recovery. To achieve this a column of elutable radioactive material, closed at both ends by pierceable closures, preferably made from resilient material is maintained in a sterile condition. By use of a closed system such as one consisting of the column, a hypodermic syringe containing a sterile eluting solution, a hypodermic needle therefor, that is used to pass through the aperture in the closure and pierce the top of the column so that the solution can be introduced into the top of the column, a tube containing hypodermic needles at both ends, one needle of which is inserted into the bottom of the column and the other needle through the closure of an empty sealed vial which is also pierced by another hypodermic needle open to the atmosphere through a sterile plug of cotton, a sterile system for eluting the column and recovering the eluate containing the desired radioactive material is achieved. The preferred radioactive material contains the element Mo⁹⁹, yielding radioactive technetium as the eluted radioactive material.

This application is a continuation-in-part of our application, Ser. No. 540,689, filed Apr. 6, 1966, now U.S. Patent No. 3,369,121.

This invention relates to a new process for preparing sterile radioactive material and essentially entails using a closed sterile system for the preparation of radioactive material and its recovery.

The use of radioactive isotopes for the diagnosis and treatment of various medical conditions is well known. Unfortunately, however, certain radioactive isotopes have so short a half-life that they cannot be economically shipped from the manufacturer to the attending physician. This has made it necessary for the physician to prepare such isotopes as and where they are to be used. One such isotope is the 99m isotope of technetium which is used for the localization of brain tumors, for example. For a more detailed discussion of the subject, reference is made to an article by Smith in the Journal of Nuclear Medicine, volume 5, pages 871-882 (1964). This isotope has a half-life of six hours and is obtained as the daughter product of molybdenum Mo⁹⁹. It is separated in the form of the pertechnetate ion from Mo⁹⁹, absorbed on an alumina column, by elution with dilute hydrochloric acid or saline. Since maximum growth of radioactivity of the Tc^{99m} occurs in about 23 hours, a column containing Mo⁹⁹ may be eluted daily to yield Tc^{99m}. Because of its high radioactivity, such column must be shielded at all times to prevent unnecessary exposure to its radioactivity.

Prior to this invention, such columns were in the form of open ended cylinders and were shipped in shielding con-

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tainers, made of lead or a lead salt or other material used as a gamma ray shielding agent. In use, such columns were removed from the containers. The eluate was collected in a collecting container, such as a beaker or vial, and had to be sterilized prior to use, either in situ by use of a sterile filter, which did not insure non-pyrogenicity, or as a separate step, thereby increasing both the hazard and difficulty in using such a generator system.

It is an object of this invention, therefore, to provide a novel process for preparing and recovering radioactive material, whereby a column of radioactive material can be eluted to yield a sterile, non-pyrogenic radioactive eluate, thereby obviating the need for a subsequent sterilization step.

It is another object of this invention to provide a novel process for preparing and recovering radioactive material, whereby a column of radioactive material enclosed in a radioactive shielding container can be eluted without necessitating removal of the column from the container.

These objects are achieved by the processes of this invention using novel columns and containers, preferred embodiments of which are illustrated in the accompanying drawing wherein:

FIGURE 1 is a perspective view of the separated components that comprise one embodiment of the package of this invention;

FIGURE 2 is an axial section view of the package shown in FIGURE 1, with the components assembled and the package closed;

FIGURE 3 is an elevational view showing the equipment used to load and wash the column of the package of FIGURE 1 of this invention;

FIGURE 4 is a perspective view of the separated components that comprise a second embodiment of the package of this invention; and

FIGURE 5 is an axial section view of the package shown in FIGURE 4, showing the package in use.

Considering the embodiment shown in FIGURES 1, 2 and 3 of the drawings, the package of this invention comprises generally a container having a body 1, a removable top closure 2, and a radioactive column 3 positioned inside the body 1. Since the principal purpose of the container is to store radioactive material, the container is fabricated of lead or other material used as a gamma ray shielding material, such as a lead-antimony alloy iron, or a lead salt, such as lead carbonate or lead sulfide, embedded in plastic. The body 1 is of generally cylindrical shape having a hollow center 4 preferably of circular cross-section and of greater diameter than that of column 3. When the column is placed inside the container, the space between the column and the inner wall of body 1 is preferably filled with a shock absorbant packing material 5, such as corrugated paper, foam plastic or a plastic sleeve.

To permit access through the bottom of the container and limited access through the top of container, without removing top closure 2, both the bottom wall and the top closure have centrally positioned apertures 6 and 7, sealed by removable plugs 8 and 9, which are also fabricated of gamma shielding materials.

After column 3 has been placed in the body of the container, the container is closed at its top by means of removable closure 2. In the embodiment shown in the drawing, the closure is retained on the body by means of a pair of lugs 10, 10, having enlarged heads 11, 11. The closure 2 is equipped with a pair of arcuate keyhole shaped slots 12, 12, the enlarged openings of which are of greater diameter than are the heads 11. These slots are countersunk so that the outer portions thereof are of sufficient width to accommodate the heads, whereas the inner portions thereof are of width smaller than the heads 11, but of sufficient width to accommodate the shank portions of lugs

10. The closure is also fabricated of lead or other material relatively impervious to radioactivity and, to insure a tight fit with body 1, the closure is equipped on its inner surface with a circular projection 13 having a circumference slightly less than the circumference of the hollow center.

Although in the preferred embodiment, the closure 2 is retained on the body by means of lugs and keyhole shaped slots, other means may be used to removably connect the closure to the body. Thus, the closure may be simply taped or stapled to the body, or threading may be used.

The column 3 is preferably made principally of glass or a transparent plastic material and is composed of a cylindrical tube 14 closed at its top and bottom by means of stoppers 15 and 16. These stoppers are preferably fabricated of resilient material, such as rubber, that can be pierced by a hypodermic needle, and are held permanently in place by means of a pair of annular aluminum discs 17 and 18 that pass over the outer edges of the stoppers, the sides of the stoppers and are then crimped to the adjacent walls of tube 14, as shown in FIGURE 2. To permit easy access by air to the inside of tube 14, the bottom stopper 16 is equipped with a breather tube 19 that passes through stopper 16 to about half the height of tube 14. So that the outside end of the breather tube 19 is in communication with the atmosphere (after removal of plug 8) even when the column 3 is seated in body 1, the bottom stopper 16 is equipped on its outer surface with a groove 20 extending at least from the outer end of breather tube 19 to aperture 6. To assure sterility, the breather tube 19 is equipped with a plug 21 of cotton or similar material.

The tube 14 is equipped with a partition 22 which divides the tube 14 into an upper and lower portion. This partition is preferably integral with the tube 14 along its outer end and tapers downward toward the bottom of tube 14 so as to provide a restricted opening 23 at its lower end. The partition can be and preferably is fabricated of the same material as tube 14. Although the exact position of the partition in tube 14 is not critical, it is preferably positioned in the upper half of tube 14 in such a way that the restricted opening 23 is slightly below the upper end of breather tube 19.

Seated on the upper end of partition 22 is a perforated disc 24 (preferably a glass fritted disc) on which preferably rests a filter pad 25. Resting on top of disc 24, or the filter pad 25, if one is used, is a granulation 26 of a radioactive containing alumina, and optionally also a cation exchange resin, such as Dowex-50-X-8, to prevent passage of the alumina through the tube during elution.

The granulation 26 can be retained in place either by use of a perforated disc (preferably a cloth disc 27 retained in place by a retaining ring 28), as shown in the drawing, or merely by means of stopper 15.

To prepare the column 3 for use, the granulation 26 is packed into the top portion of the column, the stoppers 15 and 16 are inserted and crimped into place by means of aluminum discs 17 and 18. As shown in FIGURE 3, the top stopper 15 is then pierced by two hollow needles 29 and 30, one of which is connected to a reservoir 31 and the other to a tube 32 open at its other end to the atmosphere. A third hollow needle 33 is inserted through bottom stopper 16 to allow for drainage.

To load the column, the reservoir 31 is filled with a source of radioactivity, such as an aqueous solution of radioactive (Mo^{99}) ammonium molybdate, and the solution is permitted to drip through needle 29 onto and through granulation 26. Most of the radioactive molybdenum is adsorbed in the granulation. The excess molybdenum and water pass through the column and are removed through drainage needle 33. The column is then washed with acid and saline to remove any non-adsorbed molybdenum, the needles 29, 30 and 33 are removed, and the column is sterilized, as by autoclaving.

The column 3 is inserted into body 1. The closure 2 is then so positioned over the top of body 1 that the lugs

pass through the enlarged portions of slots 9, and rotated to firmly connect the closures to said body. The package is then ready for shipment.

When the package is to be used, the plugs 8 and 9 are removed and the column 3 is then eluted, by injecting a sterile, non-pyrogenic eluting solution, such as sterile, non-pyrogenic isotonic saline, through the top stopper 15 into the upper portion of tube 14. The injection is accomplished by passing the needle of a hypodermic syringe containing the eluting solution through aperture 7 and through stopper 15. The eluate, containing the radioactive material, is collected and maintained in the bottom of tube 14. When the eluate is to be used, it is removed from tube 14 by piercing the stopper 16 with a sterile hypodermic needle (connected to a syringe) by passing the needle through aperture 6 and stopper 16.

Considering now the embodiment shown in FIGURES 4 and 5 of the drawings, the package of this embodiment of the invention differs from the first embodiment primarily in the omission of the lower chamber in the column. It comprises generally a container having a body 101, a removable top closure 102, and a radioactive column 103 positioned inside the body 101. The body 101 and closure 102 are fabricated from gamma ray shielding material as described hereinbefore. The body 101 is of generally cylindrical shape having a hollow center 104 preferably of circular cross-section and of greater diameter than that of column 103. When the column is placed inside the container, the space between the column and the inner wall of body 101 is preferably filled with a shock absorbant packing material 105, such as corrugated paper, foam plastic or a plastic sleeve.

To permit access through the bottom of the container and limited access through the top of the container, without removing top closure 102, both the bottom wall and the top closure have centrally positioned apertures 106 and 107, sealed by removable plugs 108 and 109, which are also fabricated of gamma shielding materials.

After column 103 has been placed in the body of the container 101, the container is closed at its top by means of removable closure 102. This may be done by positioning the closure 102 on the container 101 and affixing it by means of a strip of adhesive tape (not shown) or other means. To assure a tight fit, the closure 102 is equipped on its inner surface with a circular projection 113 having a circumference slightly less than the circumference of the hollow center.

The column 103 is preferably made principally of glass or a plastic material and is composed of a cylindrical tube 114 closed at its top and bottom by means of stoppers 115 and 116. These stoppers are preferably fabricated of resilient material, such as rubber, that can be pierced by a hypodermic needle and are held permanently in place by means of a pair of annular aluminum discs 117 and 118 that pass over the outer edges of the stoppers, the sides of the stoppers and are then crimped to the adjacent walls of tube 114, as shown in FIGURE 5.

Positioned in the tube 114, preferably spaced from but near the bottom thereof, is a perforated disc 124 (preferably a glass fritted disc) on which preferably rests a filter pad 125. Resting on top of disc 124, or the filter pad 125 if one is used, is a granulation 126 of the same material used in the first embodiment. The granulation 126 can be retained in place either by use of a perforated disc 127, as shown in FIGURES 4 and 5 of the drawing, or merely by means of stopper 115.

The column is prepared for use by the same method used in the first embodiment of this invention, as shown by FIGURE 3. The loaded column 103 is then inserted into body 101 and the closure 102 is positioned over the opening in body 101 and retained thereon by means of an adhesive strip or other means. The package is then ready for shipment.

When the package is to be used, the plugs 108 and 109 are removed and the column 103 is eluted, by injecting

a sterile, non-pyrogenic eluting solution, such as sterile, non-pyrogenic isotonic saline, through the top stopper 115 into the upper portion of tube 114. The injection is accomplished by passing the needle of a hypodermic syringe (not shown) containing the eluting solution through aperture 107 and through stopper 115. The elute, containing the radioactive material, is withdrawn from the bottom of tube 114 by means of a hypodermic needle 34. This needle 34 passes through aperture 106 and bottom stopper 116 into the space between perforated disc 124 and stopper 116. To increase this space, stopper 116 is preferably fabricated to have a concave center portion 35.

The under end of needle 34 is connected through tubing 36 to a second hypodermic needle 37 that passes into a sterile empty vial or other container 38 through a rubber stopper 39 closing the vial and retained thereon by means of a crimped annular aluminum disc 40. To permit the air in the vial to escape as the eluate flows into the vial, the stopper 39 is also pierced by a third hypodermic needle 41, exposed to the atmosphere. To assure sterility of the system, needle 41 is equipped with a plug 42 of cotton or similar material. To minimize the exposure to radiation, vial 38 is retained in a shield 43 of gamma ray shielding material.

In use, the eluate passes from column 103 through needle 34, tubing 36, and needle 37 into vial 38. When the eluate is to be used, it is removed from vial 38 by piercing the stopper 39 with a sterile hypodermic needle (connected to a syringe).

Although in both embodiments of this invention, the closures 2 and 102 are designated as top closures, the columns 3 and 103, respectively, can of course be introduced upside down into the bodies 1 and 101, in which case the top closure becomes a bottom closure.

By use of the packages of this invention it is possible to carry out the entire elution operation under sterile conditions without ever removing the column 3 or 103 from the protective shield, thereby minimizing the possibility of exposure to the relatively high radioactivity of the column. Furthermore, since the whole eluting operation is carried out under sterile conditions, the need to sterilize the radioactive eluate prior to use is obviated.

What is claimed is:

1. A process for preparing sterile non-pyrogenic radioactive material, which comprises preparing a closed system containing a source of sterile non-pyrogenic eluting solution and a column of sterile elutable radioactive material and a sterile collecting container, and eluting said column into said container.

2. The process of claim 1, wherein the source of the radioactive material contains the element Mo⁹⁹.

3. The process for preparing sterile non-pyrogenic radioactive material, which comprises preparing a column of elutable radioactive material, closed at its top and bottom by closures and having positioned therein and spaced from the bottom thereof a source of sterile non-pyrogenic elutable radioactive material, passing through said top closure a sterile eluting solution contained in a closed system, and passing the eluate containing the radioactive material through said bottom closure into a closed collecting system.

4. The process of claim 3, wherein the source of radioactive material contains the element Mo⁹⁹.

5. The process of claim 4, wherein the closures are fabricated of resilient material and the sterile eluting solution is introduced into the column by piercing the top closure with a hypodermic needle connected to a hypodermic syringe containing the sterile eluting solution.

6. The process of claim 5, wherein the eluate is removed from the column by piercing the bottom closure with a hypodermic needle connected to a closed collecting system.

7. The process of claim 6, wherein the collecting system comprises a sterile tube having hypodermic needles at both ends, one needle of which pierces the bottom closure and the other needle of which pierces a resilient closure of a sterile collecting vial.

8. The process of claim 7, wherein the resilient closure of the collecting vial is also pierced by a second hypodermic needle sterily connected to the atmosphere.

9. The process of claim 3, wherein the column is retained in a shielding container having side and bottom walls, said bottom wall containing a restricted aperture therein through which the eluate is passed.

10. The process of claim 9, wherein the container has a removable closure for the top, said closure having a restricted aperture therein through which the eluting solution is passed.

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ARCHIE R. BORCHELT, *Primary Examiner*.

U.S. Cl. X.R.

23—337; 252—301.5