(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 1 416 297 A1

(12) **EUROPEAN PATENT APPLICATION**

(43) Date of publication:
06.05.2004 Bulletin 2004/19

(51) Int Cl.[7]: **G01T 7/00**, G01T 7/02

(21) Application number: **02024298.8**

(22) Date of filing: **31.10.2002**

(84) Designated Contracting States:
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LU MC NL PT SE SK TR
Designated Extension States:
AL LT LV MK RO SI

(71) Applicant: **AEA Technology QSA GmbH**
38110 Braunschweig (DE)

(72) Inventors:
- **Beinlich, Uwe**
38110 Braunschweig (DE)
- **Thieme, Klaus**
38110 Braunschweig (DE)
- **Fritz, Eberhard, Dr.**
38110 Braunschweig (DE)

(74) Representative: **Teipel, Susanne, Dr.**
Schwabe, Sandmair, Marx
Patentanwälte
Stuntzstrasse 16
81677 München (DE)

(54) **Dose calibrator standard for beta-emitters and method using the same**

(57) The present invention relates to a dose calibrator standard (DCS) for β-emitters comprising beta-decay nuclides, especially for beta-emitting nuclide application kits, and a method for using the same. More in detail the invention relates to a DCS for β-emitters for use in radiation therapy, especially β-emitters in liquid form.

EP 1 416 297 A1

Description

[0001] The present invention relates to a dose calibrator standard (DCS) for β-emitters comprising beta-decay nuclides, especially for beta-emitting nuclide application kits, and a method for using the same. More in detail the invention relates to a DCS for β-emitters for use in radiation therapy, especially β-emitters in liquid form.

Background of the invention

[0002] Beta decay nuclides have shown to be of considerable use and potential in radiation therapy in the past e.g. for cancer treatment. This potential has been increased by the possibility to conjugate or attach these nuclides to specific targeting molecules such as antibodies or DNA, which deliver them specifically to the desired site of treatment, thereby avoiding unnecessary and undesirable exposure of healthy tissue to the emitted radiation. Beta-decay nuclides appear to be especially suitable for radiation therapy due to such advantages as the energy of the emitted radiation, high shielding by tissue, short half lives or ease of activation.

[0003] Beta-decay nuclides have until now mainly been used in form of sealed radiation sources such as tiny sealed cylinders which were implanted at the site of treatment and removed, if considered necessary, afterwards. Little use has, however, so far been made of open radioactive sources and especially liquid injectable sources.

[0004] Use and acceptance of liquid radioactive materials emitting beta-radiation in therapy of human beings, such as solutions of antibodies labeled or loaded with β-decay nuclides (e. g. Y-90, P-32) has been hampered by the fact that these liquids are difficult to dose. More in detail, due to the short half life of a nuclide (such as 64 h for Y-90) constant dosing in radiation therapy appears to be a problem as this requires precise measurements of the amount of radioactive material contained within the liquid within the injection device, typically a syringe, i.e. it requires precise and reliable dosing.

[0005] Determining the amount of beta-decay nuclide in and hence the emitted radiation dose of a certain sample is not a straight forward, simple process, as β-radiation is susceptible to internal shielding effects even by lower Z materials (materials composed of atoms having low atomic order number) such as low Z metals, carbon (tissue materials, plastics), oxygen (air, water), or nitrogen. Furthermore, measurements have been shown to strongly depend on geometrical setup of the measuring device and sample etc.. This is because most or all of the beta particles may be absorbed within the article and mainly Bremsstrahlung photons are observed externally. The spectral energy and the quantity of Bremsstrahlung may be significantly affected by the internal geometry and materials of construction of such an emitter and so it may be difficult or even impossible to make any estimate of the radioactivity content by measuring only the external emissions. Such measurements, if requiring a complicated setup, further increase exposure of medical personal up to an intolerable level by length of the procedure. Despite of their medical potential liquid drugs including β-decay nuclides have therefore until now only rarely been used in radiation therapy.

[0006] One specifically interesting example of a beta-decay nuclide is Y-90. Y-90 is an expensive short lived radioisotope having a half life of 64 hours. So any time delays or sampling losses cannot be afforded by hospitals or radiopharmacies when using this radioisotope.

[0007] Based on the above it is the underlying object of the present invention to provide a DCS for beta-emitters, especially liquid β-emitters, including β-decay nuclides, which allows for simply and effective dosing of these emitters to enable their full exploitation especially in radiation therapy.

[0008] It is another object of the invention to provide a method for dosing β-emitters, especially in liquid form e.g. beta-emitting nuclide application kits, which method overcomes the above problems of the prior art.

Short Description of the Invention

[0009] To achieve these objects and to overcome these and other drawbacks of the prior art the present invention in a first aspect thereof provides a dose calibrator standard (DCS) for a beta-emitter comprising beta-decay nuclides, said DCS comprising:

- beta-radiation emitting means, comprising a beta-decay nuclide;
- conversion means for converting substantially all beta-radiation emitted by the beta radiation emitting means into Bremsstrahlung; and
- optionally a casing;

wherein the shape of the DCS substantially resembles the shape and dimensions of the beta-emitter to be calibrated.

[0010] In a second aspect thereof the present invention provides for a method of calibrating a beta-emitter or beta-emitting nuclide application kit, preferably a liquid beta-emitter, said method comprising the steps of:

(i) measuring the Bremsstrahlung emitted by at least one DCS according to one of the preceding claims, said DCS comprising a known amount of beta-emitting radionuclide,
(ii) measuring the Bremsstrahlung emitted by the beta-emitter to be calibrated, and
(iii) determining the amount of radioactivity of the beta-emitter from the results of i) and ii).

[0011] Preferred embodiments are set out in the appending claims.

Short Description of the Drawing

[0012]

Fig. 1 shows a preferred embodiment of the DCS of the invention in form of a syringe. The conversion means (2) is made up by the syringe cylinder and end plugs (1, 5). The β-radiation emitting means (3) comprises a rod of partly radioactive and partly inactive material, the active material being arranged in the lower bottom part of the syringe and being fixed at the end component (1).

Detailed Description of the Invention

[0013] The present invention concerns a dose calibrator standard for beta-emitters. As used here in a "dose calibrator" is a device for determining the amount of radiation emitted per time (typically seconds) by any radioactive sample. The dose calibrator usually receives the sample in a measuring chamber. Upon the actual measurement the emitted radiation and/or a conversion product thereof (such as Bremsstrahlung) elicits a signal such as an electric current proportional thereto. Dose calibration transfer then occurs by way of comparison of the signal strength as elicited by a sample of known radioactivity (which is then called a "standard") with the signal of the actual sample to be calibrated or dosed. In any given dose calibrator signal strength will amongst other factors depend on device and sample geometry, internal shielding, energy of the emitted radiation and the type of signal itself.

[0014] As discussed above, these factors had previously hampered reliable dosing of beta-emitters, especially those in liquid form. The present invention overcomes these difficulties by providing the above dose calibration standard. This standard not only takes into account geometry of the sample, but also overcomes any error sources connected with e.g. internal shielding effects by not relying on the emitted beta-radiation itself and by measuring the same, but by instead measuring the Bremsstrahlung of the source after conversion of the beta-radiation.

[0015] Therefore, the DCS of the invention comprises a known amount of a beta-decay nuclide and has a shape which substantially resembles the geometry of the later sample to be dosed or, in other words, has equivalent geometry to the sample. At the same time the DCS of the invention converts substantially all, preferably all of the emitted beta-radiation into Bremsstrahlung by the conversion means. By doing so internal shielding is maximized and another type of radiation generated for the actual measurement. This conversion surprisingly allows to overcome measuring errors ascribed to geometrical setup and internal shielding of the sample and the dose calibrator, respectively.

[0016] The conversion further avoids exposure of medical personal handling the DCS of the invention to harmful beta-radiation. This in turn allows for safe and simplified handling of the standard.

[0017] Last, but not least conversion of the emitted beta-radiation into Bremsstrahlung also allows for using a standard comprising one specific beta-decay nuclide for dosing various other nuclides by calculating or experimentally establishing for the given dose calibrator the signal ratio of the respective standard and sample nuclide.

[0018] The DCS of the invention is a DCS for a beta-emitter, said beta-emitter comprising a beta-decay nuclide. As used herein the terms "beta-decay nuclide" or "beta-emitting nuclide" encompasses all nuclides emitting beta-radiation, either exclusively or in combination with other types of radiation. These beta-decay nuclides are well known to the skilled worker. Preferably, beta-decay nuclides with no or low abundance photon emissions are used.

[0019] The term "beta-emitter" as used herein refers to any sample, device or material containing such beta-decay nuclide or a mixture thereof and emitting beta-radiation. The beta-emitter may have gaseous, liquid or solid form and is typically accommodated and preferably sealed within a suitable container. The container may in general be of any suitable material and shape. It provides for the shape of the beta-emitter to be dosed. Preferably the beta-emitter of the invention is in the form of a liquid comprising the beta-decay nuclide, which liquid is contained in a container. In case of samples or beta-emitters for use in radiation therapy these containers used e.g. by hospitals to contain, handle, transport and inject the beta-decay nuclide as the radiopharmaceutical may take numerous forms; commonly glass vials and syringes are used, although there are numerous other forms of containment. The beta-emitter, especially when for medical uses, may also be referred to a beta-emitting nuclide application kit.

[0020] If used for radiation therapy, the beta-decay nuclide in the beta-emitter to be dosed may be conjugated, attached to or loaded on a suitable targeting molecule such as a peptide, protein, antibody, a drug, hormone or nuclide acid.

[0021] The DCS of the invention comprises beta-radiation emitting means, comprising a beta-emitting nuclide or beta-decay nuclide; conversion means for converting substantially all beta-radiation emitted by the beta-radiation emitting means into Bremsstrahlung; and optionally a casing. Critical to the DCS of the invention is that its shape substantially resembles the shape and dimensions of the beta-emitter to be calibrated, i.e. that the DCS has equivalent geometry to the emitter. The term "substantially resembles" as used herein means that the shape and the dimension of the DCS of the invention is very similar to the shape and the dimension of the beta-emitter to be dosed. Practically, this means that, in case the beta-emitter is in the form of a cone, the DCS will have practically the same form of a cone;

if the beta-emitter is in form of a cylinder with flat ends, the DCS will have the form of a cylinder with flat ends; if the emitter has the shape of a liquid filled syringe, the DCS will have the same shape of the syringe. Similarly, the DCS will have comparable or similar dimensions as the emitter to be dosed. Neither with regard to shape nor with regard to dimensions, however, absolute identity is required, although this is preferred. Any deviations should not substantially deteriorate the equivalency of emitted radiation profiles of DCS and beta-emitter. This can be easily determined by the skilled worker.

[0022] The DCS of the invention comprises the conversion means for converting substantially all beta-radiation emitted by the beta-radiation emitting means into Bremsstrahlung. This phenomenon of converting beta-radiation into Bremsstrahlung is well known as such. However, although for conventional sources of Bremsstrahlung typically materials of high Z (high atomic order number) are used, it is well known that materials of lower Z may likewise have the same effect. Use of these materials may require thicker layers/walls to give the desired conversion. As used herein the term "substantially converts" means that more than 95 % and preferably more than 99 %, and most preferably all of the beta-radiation emitted by the beta-decay nuclide of the DCS is converted into Bremsstrahlung. Besides this conversion function the conversion means may also have a partial shielding function so as to direct the Bremsstrahlung emitted by the DCS into certain directions. This may e.g. be achieved by an appropriate selection of the materials or their thickness.

[0023] The DCS of the invention may optionally comprise a casing. The casing may e.g. serve to sealingly enclose the beta-radiation emitting means and the conversion means. It may also serve to mechanically stabilise and/or hold together the DCS. Last, but not least it may provide for any labels characterising the DCS of the invention. In a preferred embodiment the conversion means forms the casing e.g. as a metallic (Al-) cylinder.

[0024] The conversion means may comprise, and preferably substantially consists of a metallic material, preferably a metallic material selected from the group, consisting of metals of low Z, and mixtures, composites and alloys thereof, or may also comprise or consist of glass, ceramic or plastic materials or mixtures or composites of all foregoing materials. The metallic material having a low Z and preferably also low density is preferably selected from the group consisting of Be, Mg, Al, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, oxides, carbides, nitrides and carbonitrides thereof and mixtures, alloys of the same and composites of the foregoing. Conversion means and casing may be provided in a single body consisting of one or more of the above materials. Preferably the conversion means consists of one or more low density materials selected from the above low Z materials, especially Be, Mg, AL, Ti, or glass, ceramics or plastic materials. The conversion means will typically have a wall thickness of between 1 to 10 mm, preferably 4 to 6 mm, the precise thickness of course depending, besides the material, on the beta-energy of the selected beta-decay nuclide, the amount thereof and the desired degree of conversion. Wall thicknesses e.g. for Y-90 with Co are 1,2 mm, with Be = 6 mm, with Mg = 6 mm and with Al = 4 mm.

[0025] Depending on the shape of the emitter to be dosed the DCS according to invention may have a cross-section of rotational symmetry. This does not exclude e.g. handling devices deviating from this symmetry. It may further have an aspect ratio of its longitudinal axis to its diameter of > 1 (preferably ≥ 2, more preferably from 2 to 20, most preferably from 2 to 10). More preferably the DCS according to the invention has the form of a cylinder or a cone, both optionally with modified end components and/or plugs. For example the DCS may have the cylindrical form of a syringe with the modifications of the same in the bottom and top parts.

[0026] Preferably the conversion means forms the casing and substantially provides for the shape of the DCS. In this case more preferably the conversion means is a hollow cylinder with end plugs, which preferably sealingly encloses the means for emitting beta-radiation. The cylinder may comprise and preferably consists of the above materials, most preferably, a low Z metal (e.g. Al), plastics or glass. The end plugs may comprise the same or a differing material as the cylindrical body. In case of a plastic or glass cylinder, the conversion means may e.g. be provided in form of a thin metallic foil or coating on one side of the cylinder body or around the beta-emitting means. In a most preferred embodiment the DCS of the invention has the shape of a syringe (i.e. cylinder with specifically designed end components). The casing of the DCS may even be an ordinary syringe, filled with the beta-emitting means enclosed by the conversion means e.g. a rod of beta-emitting material wrapped in a metallic foil.

[0027] The DCS of the invention may also be provided with a second external conversion means as defmed above. This may be desirable in cases where the beta-emitter to be dosed is equipped with such external conversion means, to mimic exactly the effects of this conversion means of the emitter.

[0028] In the DCS according to the invention the means for emitting beta-radiation is preferably arranged along the longitudinal axis of the conversion means, if such longitudinal axis is compatible with the shape of the DCS. Even more preferably said longitudinal axis is located centrally in the DCS. In case of a cylindrical DCS the means for emitting beta-radiation is thus most preferably arranged along the longitudinal axis of this cylinder.

[0029] In the DCS according to the invention the means for emitting beta-radiation can be in a form selected from a rod, one or more spheres, one or more cylinders, powder, or granulate, possibly itself in a casing. The means for emitting beta-radiation may thus be provided in form of a single body or in form of several bodies up to a fine divided powder. Typically, the means will, however, be of solid nature.

[0030] In a preferred embodiment the means for emitting beta-radiation is fixed within the DCS. If the conversion means is a hollow cylinder with end plugs, the means for emitting beta-radiation may e.g. be fixed to at least one of the end plugs. Preferably, in this case the means for emitting beta-radiation is a rod, which rod is most preferably fixed in both end plugs to stay in the longitudinal axis of the cylinder.

[0031] In the DCS according to the invention the means for emitting beta-radiation comprises a beta-decay nuclide selected from nuclides having a beta-energy of equal or more than 100 keV, preferably 100 keV to 500 MeV. Most preferably, the beta-decay nuclide exclusively emits beta-radiation, i.e. does not emit other types of radiation or is not subject to other decay events. The DCS will typically comprise a known activities of radiation, which will typically be in the same range as is the suspected activity of the beta-emitter to be dosed. For liquid beta-emitters for use in radiation therapy the dosages will typically be in the range of 10 MBq to 10 GBq, preferably 4 MBq to 4 GBq.

[0032] Preferably the beta-decay nuclide for use in the means for emitting beta-radiation selected from the group consisting of Y-90, Tm-170, Sn-123, Re-186, Re-188, P-32, P-33, Sr-89, Pr-144, and Eu-169 and mixtures thereof. Most preferably the beta-decay nuclide is Y-90 or Tm-170.

[0033] However, the DCS of the invention in the means for emitting beta-radiation may alternatively comprises a precursor of the beta-decay nuclide or a radioactive parent nuclide thereof having longer half-live. These are preferably selected from the group consisting of Sr-90, W-188, and Si-32 and mixtures thereof.

[0034] In a second aspect the present invention also relates to a method of calibrating a beta-emitter, preferably a beta-emitting nuclide application kit, by use of a DCS as defined above. Said method in general comprises the steps of:

i) measuring the Bremsstrahlung emitted by at least one DCS according to the invention, said DCS comprising a known amount of beta-decay nuclide,
ii) measuring the Bremsstrahlung emitted by the beta-emitter to be calibrated, and
iii) determining the amount of radioactivity of the beta-emitter from the results of i) and ii).

[0035] For measuring the Bremsstrahlung in steps i) and ii) both the DCS and the beta-emitter (or sample) to be dosed are inserted in the respective measuring chamber of a dose calibrator. The similar shape and dimensions of both the DCS and the beta-emitter to be dosed ensures comparable arrangement in this chamber. Internal shielding of the sample is taken into account by conversion of all beta radiation into Bremsstrahlung, which is again comparable for both the standard of the invention and the emitter to be dosed. Comparing the signals obtained in both steps i) and ii) thus allows for efficient and reliable dosing of the sample beta-emitter. The method is most advantageously applied for calibrating beta-emitters, especially liquid beta-emitters for use in radiation therapy.

[0036] In the method of the invention preferably at least two DCSs, more preferably 2 to 5, most preferably 2 to 3 DCSs, comprising differing amounts of the beta-emitting nuclide are used. Use of more than one DCS in this method results in establishing a calibration curve, by way of which a more precise dosing can be achieved. Such calibration curve can also take into account e.g. varying filling height in case of liquid emitters in a container.

[0037] In the preferred embodiment the method is applied to elongated beta-emitters, especially emitters in form of a solution, comprising a beta-radiation emitting nuclide, within an elongated container. Most preferably the container is a syringe. In this case preferably the above DCSs are used in form of such syringes or cylinders which resemble the shape and dimensions of said syringe. More preferably in this case the means for emitting beta-radiation is a rod, and two DCSs are likewise used comprising rods of varying length of active material. The total rod length may be identical, but only part thereof may comprise the beta-emitting nuclide.

[0038] In one embodiment the method of the invention is preferably carried out such that the at least one DCS and the beta-emitter to be calibrated comprise a beta-emitting nuclide of comparable β-energy. In this case most preferably the at least one DCS and the beta-emitter to be calibrated comprise the same beta-emitting nuclide.

[0039] In another embodiment the DCS may comprise a beta-decay nuclide of differing energy. In this case a factor can be calculated or established for relating signal strength of the DCS to signal strength obtained from the beta-decay nuclide comprised in the beta-emitter to be calibrated or dosed. This embodiment is especially advantageous in cases of beta-decay nuclides of short half lives, as the short half live would require continuous replacement of the DCS, in case of indentical nuclides. Use of a more stable nuclide for the DCS avoids this need for continuous replacement, but allows for long time use of the standard.

[0040] For example, the radioisotope used to simulate Y-90 is Sr-90. Sr-90 is a long-lived radioisotope with a 28 year half life, which decays to produce Y-90 within the source. The DCS is measured and calibrated for its output in terms of its equivalent Y-90 content by comparison with Y-90 reference or standardised solutions. The DCS is then used to compare the outputs of Y-90 samples having equivalent geometry. The Y-90 equivalent activity measured is only valid for the detector type used. Traceability to a national laboratory such as NIST, NPL or PTB is achieved via inter-comparison of measurements using the same type of radiation measurement detector. The DCS of the invention in this case serves as a dose calibrator transfer standard, by way of which local calibration can be correlated with authority standards.

[0041] Direct comparison of the emissions of the sample and the DCS of the invention therefore provides a direct and simple means of determining the Y-90 content of articles. Calibrations can even be carried out using any or all of the common commercially radiation detector systems, such as commercial ion chambers, NaI and CsI detectors and plastic scintillators. This in turn can enable hospitals and radiopharmacies to use any common commercially available detector system to measure the Y-90 content of the samples.

[0042] In case the emitter to be calibrated only partially converts the beta-radiation into Brernsstrahlung by itself, e.g. due to lower wall thicknesses, it can be desirable or appropriate to provide for a respective conversion means as defined above for the emitter as well. This can be in form of a casing or shroud such as a hollow cylinder in which e.g. the syringe or vial is inserted. Such conversion means can either be applied before measurements or can be preinstalled in the measuring chamber of the dose calibrator. In this case beneficially the DCS of the invention is likewise equipped with a comparable second conversion means.

[0043] The invention will be further illustrated by way of the following example, which is not to be construed as to limit the same.

Examples

[0044] The present invention will now be described by way of example, with reference to figures 1 and 2.

Example 1

[0045] A preferred embodiment of the current invention is a sealed Sr-90 source device, which can accurately simulate the volume of Y-90 contained in aqueous solution in a syringe. An example of this is shown in figure 1a. This embodiment comprises a cylindrical aluminium tube (2) as conversion means (wall thickness 4 mm), containing a linear sealed (axially symmetric) welded Sr-90 radiation source as the means for emitting beta-radiation (3) which Sr-90 radiation source is located along the central axis of the tube (2). The source (3) is held in position by its ends using two aluminium end plugs (1) and (5). End component (1) simulates the shape and geometry of a luer lock and end component (5) simulates the syringe plunger handle.

[0046] The sealed strontium source (3) contains the beta-decay nuclide linearly along its axis from end component (1) up to a point designated by the end of the thick line in the diagram. Beyond this point there is an air space up to end component (5). This feature simulates 10 ml of Y-90 solution contained in the simulated syringe. The position of this point in the DCS may vary from customer to customer and product to product as required.

[0047] Aluminum is selected as the preferred material for construction in this embodiment as it withstands radiation damage and totally absorbs all Sr-90 and Y-90 beta particles emitted. The design utilising aluminum ensures that a similar Bremsstrahlung spectrum to that of Y-90 aqueous solution in a plastic syringe is achieved. The precise dimensions of the simulated syringe may be varied according to the type of syringe or precise shape of whatever container the DCS is to simulate. This may vary from user to user and from application to application. The syringe is just one of many possible simulation source designs and applications.

Example 2

[0048] In this embodiment the sealed radiation source (3) is the form of a thin-walled metal tube capable of emitting Y-90 beta particles so they are absorbed within the Aluminium tube (1) to produce Bremsstrahlung. The source is welded at each end. The Sr-90 activity content of the source may be in the form of ceramic or metal wire inserts with spacers and dimensioned to be commensurate with the overall shape and size of the simulated emitter in question.

Example 3

[0049] Another example of a simulation source is shown in figure 2. Here a sealed Sr-90 radiation source (7) of similar design to the source of example 2 is located axially in a tube within an aluminium housing (8), which simulates the shape and size of a typical glass vial, used to hold Y-90 solutions in hospitals and radiopharmacies. An inactive material or gas (9) is provided to simulate the desired quantity of Y-90 solution in the vial and the vial top is simulated by the profile shown in (10).

[0050] The external emissions of the two embodiments described in examples 2 and 3 are compared with Y-90 reference or standardised solutions in real syringes or vials containing the same filling height/volume. This measurement is repeated for all the common types of detector used in hospitals and radiopharmacies. The calibration also covers a range of different Y-90 filling height/volumes for every detector such that calibration factors can be applied.

[0051] Having set out the invention by way of the above description and examples, the scope thereof is exclusively to be defined in the appending claims.

Claims

1. Dose calibrator standard (DCS) for a beta-emitter comprising beta-decay nuclides, said DCS comprising:

- beta-radiation emitting means, comprising a beta-decay nuclide;
- conversion means for converting substantially all beta-radiation emitted by the beta-radiation emitting means into Bremsstrahlung ; and
- optionally a casing;

wherein the shape of the DCS substantially resembles the shape and dimensions of the beta-emitter to be calibrated.

2. DCS according to claim 1, wherein the conversion means forms the casing.

3. DCS according to one of the preceding claims, wherein the conversion means comprises, and preferably substantially consists of a material, selected from the group, consisting of metals of low Z (atomic order number), glass, ceramic or plastic materials and mixtures, alloys and composites of all foregoing materials.

4. DCS according to claim 3, wherein the metal of low Z is selected from the group consisting of Be, Mg, Al, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, carbides, nitrides and carbonitrides thereof and mixtures, alloys of the same and composites of the foregoing, preferably Be, Mg and Al.

5. DCS according to one of the preceding claims having a cross-section of rotational symmetry and an aspect ratio of its longitudinal axis to its diameter of > 1 (preferably ≥ 2, more preferably from 2 to 20, most preferably from 2 to 10).

6. DCS according to claim 5, in form of a cylinder or cone.

7. DCS of claim 5 or 6, wherein the conversion means forms the casing and substantially provides for the shape of the DCS.

8. DCS of claim 7, wherein the conversion means is a hollow cylinder or cone, preferably made of metal or glass, with end plugs, which conversion means encloses the means for emitting beta-radiation.

9. DCS according to one of the preceding claims wherein the means for emitting beta-radiation is arranged along the longitudinal axis of the conversion means.

10. DCS of claim 9, wherein the longitudinal axis is located centrally in the DCS.

11. DCS according to one of the preceding claims, wherein the means for emitting beta-radiation is in a form selected from a rod, one or more spheres, one or more cylinders, powder, or granulate.

12. DCS according to claim 11, wherein the means for emitting beta-radiation is fixed within the DCS.

13. DCS according to claim 12, wherein the conversion means is a metallic hollow cylinder with end plugs, wherein the means for emitting beta-radiation is fixed to at least one of the end plugs.

14. DCS of claim 13, wherein the means for emitting beta-radiation is a rod.

15. DCS according to one of the preceding claims wherein the means for emitting beta-radiation comprises a beta-decay nuclide selected from nuclides having a beta-energy of equal or greater than 100 keV.

16. DCS according to claim 10, wherein the nuclide is selected from the group consisting of Y-90, Tm-170, Sn-123, Re-186, Re-188, P-32, P-33, Sr-89, Pr-144, and Eu-169 and mixtures thereof.

17. DCS of claim 1, wherein the means for emitting beta-radiation comprises a radioactive parent nuclide of the beta-emitting nuclide, said parent nuclide having a longer half live, selected from the group consisting of Sr-90, W-188, and Si-32 and mixtures thereof.

18. DCS of one of the preceding claims in form of a syringe, the conversion means preferably forming the syringe body.

19. Method of calibrating a beta-emitter, preferably a beta-emitting nuclide application kit, said method comprising the step of:

i) measuring the Bremsstrahlung emitted by at least one dose calibrator standard (DCS) according to one of the preceding claims, said DCS comprising a known amount of beta-decay nuclide,
ii) measuring the Bremsstrahlung emitted by the beta-emitter to be calibrated, and
iii) determining the amount of radioactivity of the beta-emitter from the results of i) and ii).

20. Method according to claim 19, wherein at least two DCSs comprising differing amounts of the same beta-decay nuclide are used.

21. Method of claim 19 or 20, wherein at least two DCSs according to claim 13 or 14 are used.

22. Method of claim 21, wherein the means for emitting beta-radiation is a rod, and two DCSs are used comprising rods of varying length.

23. Method of one of claims 19 to 22, wherein the beta-emitting nuclide application kit to be calibrated is a solution, comprising a beta-radiation emitting nuclide, within a container.

24. Method of claim 23, wherein the container is a syringe, a vial or other conventional application device used for medical purposes, and wherein the DCSs used resemble the shape and dimensions of said container.

25. Method of one of claims 19 to 24, wherein the at least one DCS and the beta-emitter to be calibrated comprise a beta-decay nuclide of comparable β-energy.

26. Method of claim 25, wherein the at least one DCS and the beta-emitter to be calibrated comprise the same beta-decay nuclide.

27. Method of claims 19 to 26 for calibrating beta-emitters for use in radiation therapy.

28. Method of claims 19 to 27, wherein the DCS is used as a dose calibrator transfer standard.

Figure 1

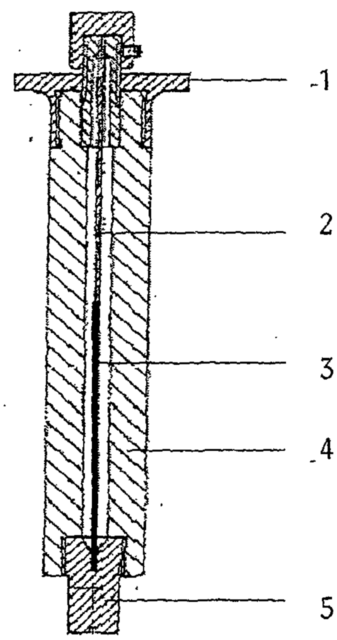
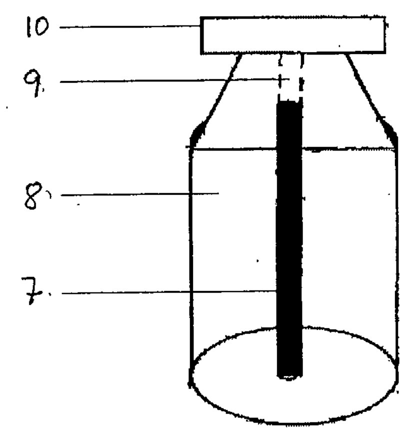


Figure 2



European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 02 02 4298

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X	WO 96 35131 A (CAPINTEC INC) 7 November 1996 (1996-11-07)	1-10,15, 16,18, 19,23, 24,27	G01T7/00 G01T7/02
Y	* the whole document *	11-14, 17, 20-22, 25,26,28	
Y	US 3 204 103 A (LAHR THOMAS N ET AL) 31 August 1965 (1965-08-31) * column 4, line 55 - column 5, line 9 *	11-14,22	
Y	US 3 706 689 A (HASKINS ARLIE W) 19 December 1972 (1972-12-19) * column 2, line 58 - line 66 *	17	
Y	WO 99 62565 A (COULTER PHARM INC ;ZASADNY KENNETH R (US); UNIV MICHIGAN (US); KRO) 9 December 1999 (1999-12-09) * page 6, line 27 - line 31 * * page 18, line 8 - line 15 *	25,26	TECHNICAL FIELDS SEARCHED (Int.Cl.7) G01T
Y	ZIMMERMAN B E ET AL: "Radioassays and experimental evaluation of dose calibrator settings for F" APPLIED RADIATION AND ISOTOPES, PERGAMON PRESS LTD., EXETER, GB, vol. 54, no. 1, 15 January 2001 (2001-01-15), pages 113-122, XP004224061 ISSN: 0969-8043 * page 114 * * figure 1 *	20,21,28	

-/--

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
MUNICH	7 February 2003	Coda, R

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 02 02 4298

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
A	US 6 251 059 B1 (BATES BRIAN L ET AL) 26 June 2001 (2001-06-26) * the whole document * -----	1,19	
			TECHNICAL FIELDS SEARCHED (Int.Cl.7)

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
MUNICH	7 February 2003	Coda, R

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons
& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 02 02 4298

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

07-02-2003

Patent document cited in search report		Publication date	Patent family member(s)			Publication date
WO 9635131	A	07-11-1996	WO	9635131	A1	07-11-1996
US 3204103	A	31-08-1965	DE	1291839	B	03-04-1969
			GB	1025322	A	06-04-1966
US 3706689	A	19-12-1972	NONE			
WO 9962565	A	09-12-1999	AU	4333699	A	20-12-1999
			CA	2331064	A1	09-12-1999
			EP	1083938	A2	21-03-2001
			JP	2002516884	T	11-06-2002
			WO	9962565	A2	09-12-1999
US 6251059	B1	26-06-2001	US	6159141	A	12-12-2000
			AU	738093	B2	06-09-2001
			AU	9479898	A	29-03-1999
			CA	2303193	A1	18-03-1999
			EP	1011813	A1	28-06-2000
			JP	2001515773	T	25-09-2001
			WO	9912609	A1	18-03-1999

EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82