Effects of Varying Geometry on Dose Calibrator Response: Cobalt-57 and Technetium-99m

Jacqueline M. Calhoun, Daniel B. Golas, and Susan G. Harris

National Bureau of Standards, Radioactivity Group, Gaithersburg, Maryland; Atomic Industrial Forum, Incorporated, Bethesda, Maryland; and E.I. du Pont de Nemours Company Incorporated, Biomedical Products Department, North Billerica, Massachusetts

A joint project between the National Bureau of Standards (NBS) and Biomedical Products Department, E.I. du Pont de Nemours and Company, Inc. compared the indicated activity of (a) cobalt-57 samples in NBS 5-ml ampoules, plastic syringes, Du Pont 27-ml Vial E epoxy- and solution-filled containers, and (b) technetium-99m solutions in NBS 5-ml ampoules, elution vials, and syringes. The measurements were made in ionization chambers from two manufacturers, Capintec and Radcal.*† The main objective was to examine the use of radionuclides in NBS ampoules and Du Pont Vial E containers as suitable reference sources for ionization chambers used to assay radiopharmaceuticals in elution vials and syringes. The exercise illustrated that regardless of the brand of dose calibrator used, a calibration factor for each geometry should be determined to ensure the highest accuracy. The data show that as much as a 9% difference from the correct activity can be observed for these radionuclides, even when the ampoule reference source gives the appropriate reading.

J Nucl Med 28:1478–1483, 1987

Although most U.S. manufacturers of dose calibrators use radionuclides in NBS-type ampoules to establish instrument settings, laboratory checks are often made with sources in other geometries. Radiopharmaceuticals are often measured in elution vials or injection syringes. The objective of this work was to examine the response of cobalt-57 (^{57}Co) in Du Pont Vial E containers relative to NBS ampoules, and investigate geometry-dependent sources of error in the assay of technetium-99m (^{99m}Tc) in elution vials and syringes in dose calibrators.

Sample position and sample volume may be important factors affecting accuracy in dose calibrator measurements. Container dependence must also be considered for accurate measurements. Containers of various compositions and sizes, that have no uniform specifications, may cause increased systematic error that is geometry dependent. Others who have looked at this problem (*1–5*) indicate that discrepancies of greater than 10% from the true value are not uncommon. Radionuclidic impurities can also cause problems which must be addressed (*6–9*). The U.S. Pharmacopeia requires that radiopharmaceutical doses be within 10% of the labeled amount, and doses of certain iodines and therapeutic administrations are to be within 5% (*10*). NRC misadministration rules require that in certain cases errors in source calibration must be reported (*11*), and NRC Regulatory Guide 10.8, Appendix D states that the extent of geometric variation should be ascertained and correction factors should be computed if variations are significant (> ± 2%) (*12*).

The scope of this work was limited to two radionuclides: ^{57}Co and ^{99m}Tc. It included considerations of various geometries for both as follows.

Cobalt-57

NBS Ampoules	Solution and epoxy
Du Pont Vial 'E's	Solution and epoxy
Syringes	Solution and epoxy at varying volumes

Technetium-99m

NBS Ampoules	Solution
Elution Vials	Solution at varying volumes and varying glass thickness
Syringes	Solution at varying volumes

Received Oct. 20, 1986; revision accepted Feb. 28, 1987.

For reprints contact: Jacqueline M. Calhoun, National Bureau of Standards, Radioactivity Group, Building 245, Room C114, Gaithersburg, MD 20899.

EXPERIMENTAL METHODS

Equipment and Materials

The epoxy used was the same proprietary compound as that used in the preparation of Vial E sources produced and sold by Du Pont. Specifications of the Vial E containers and standard 5-ml ampoules used in the preparation of NBS standard reference materials are given in Figure 1. Dose calibrators used are listed in Table 1, along with the syringes and other containers.

TABLE 1
Chambers

NBS	DuPont
Capintec CRC-7 (S/N 70222)	Capintec CRC-12 (S/N 12070)
Radcal 4045 (S/N 45-0034)	Radcal 4045 (S/N 45-0032)
NBS "4π"γ ionization chamber	

Containers: NBS 5-ml ampoules (specifications given in Figure 1); DuPont vial 'E's (specifications given in Figure 1); Monoject Syringes (3-ml capacity); Becton-Dickinson Syringes [B-D] (3-ml capacity).

Cobalt-57

The ^{57}Co samples were prepared gravimetrically at NBS with corrections applied for air density, mass of balance weights, and density of solution (1.008 ± 0.002 g/ml) or density of epoxy (1.094 ± 0.003 g/ml), as appropriate. Solution samples of ^{57}Co were prepared in the following geometries.

1. Three NBS ampoules −5 ml, ~40 MBq each.
2. Five Du Pont Vial 'E's −20 ml, ~40 MBq each.
3. Six plastic syringes (three Monoject,[‡] 3 B-D[§]) (3-ml capacity)—filled to 1, 2, and 3 ml, ~40 MBq/syringe.

The syringes were prepared by removing the needle and plunger, then flame sealing the plastic end to which the needle was attached, to prevent leakage. The needles were then reattached. After the ^{57}Co was dispensed into each syringe, the plungers were reinserted using a fine wire to allow air to escape while the plungers were pushed down to the top of the liquid level. The plungers were then epoxied in place to prevent any subsequent loss of activity. The wires that were used to allow the air to escape were checked for contamination, and none was found.

One point source was prepared from the ^{57}Co solution for the determination of the amount of ^{56}Co and ^{58}Co impurities with germanium gamma-ray spectrometers. At the time the measurements were performed at NBS and Du Pont, the ratios of the activity of ^{56}Co and ^{58}Co to that of the ^{57}Co was ~0.1% and 0.06%, respectively. Samples of ^{57}Co in epoxy were prepared in the following geometries.

1. One NBS ampoule −5 ml, ~14 MBq.
2. Five Du Pont Vial 'E's −20 ml, ~60 MBq/vial.
3. Five syringes (3 ml capacity, disposable plastic) (Two brands—Monoject and B-D); One each brand −1 ml, ~2.8 MBq/syringe; One each brand −2 ml, ~5.6 MBq/syringe; One Monoject −3 ml, ~8.3 MBq/syringe.

The epoxy samples required curing. Three Vial E's were cured in an oven overnight at ~40°C. All other samples were cured in a hood overnight at room temperature. Approximately 1 g of nonradioactive epoxy was applied on top of the cured radioactive epoxy in all Vial E samples as a sealant. The NBS ampoules were calibrated in the NBS "4π" gamma

NBS Ampoule Specifications

Type I borosilicate glass	
Barium content	less than 2.5 percent
Lead oxide content	less than 0.02 percent
Other heavy elements	trace quantities
Outer diameter (OD)	16.5 ± 0.5 mm
Wall thickness	0.60 ± 0.04 mm
Height (cylinder)	38 mm

5-ml Ampoule

DuPont Vial E Specifications

Vial E

Overall Diameter 30mm
Height 85mm
Volume 20ml epoxy in 27ml plastic vial

Polyethylene bottle with 0.7mm wall thickness

FIGURE 1
Specifications for Vial "E" and standard 5-ml ampoules.

ionization chamber (*13*) and a radioactivity concentration was determined for the original ^{57}Co solution. All other ^{57}Co solution samples were assigned an activity value based on this concentration and the mass of solution dispensed for each sample. The overall uncertainty for each solution sample is estimated to be 1.0%. The epoxy mixture was assigned a concentration based on the total mass of the components and the concentration of the weighed aliquot of the initial ^{57}Co solution. Each ^{57}Co epoxy sample was then assigned an activity value based on the mass of epoxy dispensed and the epoxy concentration. The overall uncertainty for each epoxy sample is estimated to be 1.1%. All the ^{57}Co samples were assayed at Du Pont, in two dose calibrators, a Capintec CRC-12, and a Radcal 4045, using the ^{57}Co setting. The Radcal 4045 ^{57}Co setting was used with and without an applied correction for radionuclidic impurities. Five measurements were taken on each instrument for each sample. The average assay value was corrected for radioactive decay to a common reference time for comparison to the NBS-assigned activity values. For each average data point, the percent difference from the NBS value was calculated. The same sources were also measured at NBS, in Capintec and Radcal dose calibrators. The measurements performed on the Radcal also were done with and without a correction for the radionuclidic impurities. Five measurements were made on each sample. Each syringe was measured hanging from the support disk located in each calibrator's sample holder. Plastic rings were made to center each syringe in the hole of the sample holder. When it was possible to fit the syringe in the bottom of the holder, the syringe was also measured in that configuration to see what sort of maximum effect could be observed by varying the location of the source. The results of this test were not included in the compilation of the measurement results presented in the tables. A difference of up to ~2% was observed when some syringes were measured in the bottom of the sample holder versus hanging from the center ring. The results in the Radcal dose calibrator improved when measurements were made in the bottom of the sample holder, while results in the Capintec dose calibrator showed the opposite effect.

In the Capintec dose calibrator, one measurement on each source was performed, allowing sufficient time to get an average display reading. These data were corrected for radioactive decay to a common reference time for comparison with the Du Pont measurements.

Technetium-99m

An NBS ampoule containing a known quantity of ^{99m}Tc (SRM 4410H-J-4) with an overall uncertainty of 0.88% was assayed at Du Pont, in both a Capintec CRC-12 and a Radcal 4045 dose calibrator using the ^{99m}Tc setting. Five measurements were taken on each instrument. The average assay was corrected for radioactive decay to a common reference time for comparison to the NBS value. The percent difference from the NBS value was calculated for each data point.

Samples of ^{99m}Tc solution were prepared, at Du Pont, gravimetrically in the following geometries.

1. Six B-D plastic syringes (3-ml capacity) ~0.5 and ~1 ml.
2. Seven Du Pont elution vials (~0.5 ml).

The elution vials were later diluted by injecting 10 ml of normal saline to provide samples with a total volume of ~10.5 ml. Each sample was assigned an NBS activity value based on its mass of NBS solution and the activity concentration of this solution at the calibration time. The overall uncertainty was estimated to be 1.1% on each of these sources. An aliquot of the NBS ^{99m}Tc solution was assayed with a germanium gamma-ray spectrometer and no impurities were observed. All of the ^{99m}Tc samples were assayed at Du Pont on both dose calibrators using the ^{99m}Tc setting. Five measurements were taken on each instrument for each sample. The average assay value was corrected for radioactive decay to a common reference time, for comparison to the assigned NBS value. For each averaged data point, the percent difference from the NBS value was calculated.

At NBS, four syringes of ^{99m}Tc were also prepared and counted in the Radcal and Capintec calibrators. B-D syringes were used for this exercise. Three of the syringes were prepared with the tips sealed as described for the ^{57}Co. One syringe was not sealed in order to see if having a small amount of activity in the needle made any difference. At the volumes of solution measured, the amount of extraradioactive material in the needle had at most a 0.4% effect, which was much less than any differences due to other parameters (Table 2). The ^{99m}Tc syringes were prepared gravimetrically from one of the SRM 4410H-J ampoules using the same technique utilized for the preparation of the ^{57}Co syringes. Five measurements were made on each syringe in each calibrator and the results were averaged. The uncertainty on the activity was estimated to be 1.0% for each of these sources. The standard deviation of the

TABLE 2
Technetium-99m—NBS & DuPont Results Response Difference In Percent From NBS Solution Ampoule (Adjusted to 1.00 For NBS Ampoule Response)

Source	Radcal—w/o Imp. corr.		Capintec—w/o Imp. corr.	
	NBS	DuPont	NBS	DuPont
NBS Ampoule (percent difference before adjustment)	1.00 (+1.92)	1.00 (+0.97)	1.00 (+1.75)	1.00 (−1.22)
B-D Syringe, 0.5 ml	−4.46		−2.19	
B-D Syringe, 0.5 ml (average of 2)		−2.95		−4.55
B-D Syringe, ~0.75 ml (average of 2)		−2.45		−2.88
B-D Syringe, 1.0 ml, activity in needle	−4.84		+2.21	
B-D Syringe, 1.0 ml, no activity in needle	−4.48		+2.12	
B-D Syringe, ~1.0 ml (average of 2)		−2.61		−3.08
B-D Syringe, 1.5 ml	−5.04		+1.74	

TABLE 3
Distribution of Elution Vial Glass Thickness

Statistic	Bottom	Walls
Mean of 50 vials	3.617 mm	1.730 mm
Standard deviations (percent of mean)	0.3023 mm (8.36%)	0.2667 mm (15.44%)
Skewness	0.259 (Slight right)	0.078 (Very slight right)

mean for each set of five measurements varied from ~0.02% to 0.10%.

Elution Vials

Fifty elution vials were measured for glass thickness of the bottom and the walls. The distribution of the glass thickness is presented in Table 3. Vials were chosen using the following criteria: average bottom and average wall thickness; thickest bottom and thickest wall thickness; and thinnest bottom and thinnest wall thickness, as well as other combinations listed in Table 4. Seven vials that had dimensions approaching the above criteria were used in this experiment.

RESULTS

The results of the measurements performed at Du Pont and NBS are presented in Tables 2, 4, and 5. Using the NBS assigned activity values on the ampoules and syringes, the deviations in the readings on the dose calibrators consist of at least two components. The first is the deviation in the measured activity of the NBS ampoule. The calibration factors supplied with these dose calibrators were determined using NBS Standard Reference Materials in standard NBS 5-ml ampoules. Ideally, when an NBS ampoule is measured in each of these instruments, it should give a reading identical to the NBS value. In reality this is not the case due to manufacturing tolerances in the construction of the individual chambers and holders. The values listed in parentheses in Tables 2 and 5 for the NBS ampoules show the percent differences between the NBS activity and the reading obtained from each instrument. In addition to this calibration error are other geometry effects due to positioning, volume, container size and construction material, density of the liquid and/or epoxy, etc. In order to show the effect of these other factors, the response of the NBS ampoule was adjusted to a value of 1.00 by adding or subtracting (as appropriate) the deviation of the reading of the NBS ampoule to each value for the syringe or Vial E in that particular column. The uncertainty from one source to the next is estimated to be 0.1%, from determination of the mass of solution or epoxy in each source. Any error in the calibration of the solution would be reflected in all sources and would counterbalance, because the same solution is used for both the ampoules and other geometrics. A total error for geometry and calibration can be obtained by combining the deviation in the ampoule response with the deviations in response due to geometry, and the uncertainty assigned to the activity in each source.

DISCUSSION

Several conclusions can be drawn from the data as follows.

1. All of the dose calibrators gave results within two percent of the NBS activity value for both ^{57}Co and ^{99m}Tc when measurements were made in an NBS ampoule. This geometry should in general give the best results because, as stated above, the NBS ampoule geometry was originally used to determine the calibration factor.

2. The ^{57}Co in epoxy in an NBS ampoule gave a higher response in all calibrators.

3. The Vial 'E' solutions and epoxy also showed a higher response than the NBS ampoule in all dose calibrators. This effect is probably due to the fact that

TABLE 4
Technetium-99m Results—DuPont—Elution Vials Response Difference In Percent From NBS Solution Ampoule (Adjusted to 1.00 For Ampoule Response)

Source	Thickness (mm)		Radcal—w/o Imp. Corr.		Capintec—w/o Imp. Corr.	
	Bottom	Wall	No diluent*	Diluent	No diluent*	Diluent
5 ml NBS Solution Ampoule	—	0.60 ± 0.04	1.00	1.00	1.00	1.00
Elution Vial #10	3.56	1.40	+0.57	−0.88	−7.66	−0.18
Elution Vial #13	3.56	1.91	+0.42	−0.92	−6.80	+0.15
Elution Vial #15	3.56	1.65	+0.65	−0.86	−4.37	+0.66
Elution Vial #16	3.20	1.27	+1.17	−0.19	−3.97	−0.73
Elution Vial #27	3.05	1.78	+1.00	−0.62	−1.81	−0.80
Elution Vial #32	4.32	2.41	−0.24	−1.24	−1.45	−0.11
Elution Vial #40	3.81	1.78	+0.35	−0.92	−1.83	+0.20

*All volumes ~0.45 to ~0.67 ml.

TABLE 5
Cobalt-57—NBS & DuPont Results Response Difference In Percent From NBS Solution Ampoule (Adjusted to 1.00 For Ampoule Response)

	Radcal—w/Imp. corr.		Radcal—w/o Imp. corr.		Capintec—w/o Imp. corr.	
Source	NBS	DuPont	NBS	DuPont	NBS	DuPont
5 ml NBS solution ampoule (average of 3) (percent difference before adjustment)	1.00 (+1.25)	1.00 (+0.52)	1.00 (+1.81)	1.00 (+1.44)	1.00 (−0.45)	1.00 (+0.25)
5 ml NBS epoxy ampoule	+0.88	+0.77	+1.14	+0.63	+0.30	+1.96
20 ml Vial "E" solutions (average of 5)	+0.27	+0.63	+0.37	+0.52	+2.39	+2.14
20 ml Vial "E" epoxy (average of 5)	+1.32	+1.73	+1.48	+1.69	+3.86	+3.15
1 ml Solution—Monoject Syringe	−7.20	−4.78	−7.25	−4.98	+1.47	−0.03
2 ml Solution—Monoject Syringe	−7.63	−5.05	−7.67	−5.46	+0.89	−0.52
3 ml Solution—Monoject Syringe	−8.27	−5.61	−8.29	−5.80	+0.06	−1.37
1 ml Solution—B-D Syringe	−7.03	−4.49	−6.72	−4.79	+1.39	−0.01
2 ml Solution—B-D Syringe	−7.64	−4.98	−7.45	−5.07	+0.89	−0.67
3 ml Solution—B-D Syringe	−8.20	−5.57	−8.10	−5.55	+0.05	−1.36
1 ml Epoxy—Monoject Syringe	−5.09	−4.29	−5.01	−4.31	+2.38	+0.13
2 ml Epoxy—Monoject Syringe	−5.93	−4.28	−5.80	−4.38	+2.50	−0.05
3 ml Epoxy—Monoject Syringe	−6.98	−4.82	−6.82	−5.04	+1.43	−1.14
1 ml Epoxy—B-D Syringe	−4.86	−3.47	−4.72	−4.47	+2.33	−0.33
2 ml Epoxy—B-D Syringe	−5.66	−4.19	−5.65	−3.98	+2.30	+0.18

the vials have plastic walls, which attenuate less than glass ones, and because the vials have a larger diameter which puts more activity closer to the chamber walls.

4. In all cases where the Vial 'E's were measured, the difference observed was never >4% from the NBS value in either solution or epoxy.

5. All syringes showed decreasing response with increasing volume of solution or epoxy, with ^{57}Co.

6. The brand of syringe used had little significance on the results, compared to the difference due to volume or position.

7. For the elution vials, the Capintec calibrator was sensitive to the vial thickness at low volumes, but both calibrators were relatively insensitive to the wall and bottom thickness for vials containing 10 ml of solution.

8. The Radcal calibrator showed the largest deviations from the NBS value for syringes suspended from the sample holder. The Capintec calibrator showed the largest deviations from the NBS value for elution vials at low volumes. This is related to the design of each manufacturer's chamber and sample carrier, and the relationship between the position of the sources being measured and the location of the NBS ampoule used for the original calibration, relative to the sides and bottom of the ionization chamber.

9. The differences between the results for the same syringes measured on different calibrators from the same manufacturer greatly outweigh the random uncertainty in each measurement. This is seen for both the ^{57}Co and the ^{99m}Tc. Because this effect is observed after adjusting the results to the ampoule response to unity, this raises the question of how uniform each manufacturer's chambers are in terms of current collection efficiency from the walls of the chambers (where more of the syringe response is found) relative to the bottom of the chamber (where more of the ampoule or Vial 'E' response would be found).

The measurements made so far illustrate that no matter which calibrator is used, a calibration factor for each geometry should be determined to ensure the greatest accuracy. The data demonstrate that as much as a nine percent difference from the correct activity can be seen in certain situations, even when the ampoule reference source gives the appropriate answer. The results emphasize that recommendations set forth in NRC Regulatory Guide 10.8, Appendix D (*12*), ANSI Standard N42.13-1978 (*14*), and instructions in each dose calibrator manufacturers' instruction manual should be followed to obtain and maintain correct results in a particular dose calibrator.

The ^{57}Co sources prepared for this work have been made available to each of these dose calibrator manufacturers in order to allow them to perform their own measurements.

NOTES

Mention of commercial products does not imply recommendation or endorsement by the National Bureau of Standards, nor does it imply that the products identified are necessarily the best available for the purpose.

* Capintec Instruments, Inc., Pittsburgh, PA.

† Radcal Corporation, Monrovia, CA.

‡ Monoject Syringe, St. Louis, MO.

§ Becton-Dickinson and Company, Rutherford, NJ.

REFERENCES

1. Levine G, Malhi B, Struttman L. Discrepancies in dose calibrator assays for various forms of therapeutic iodine-131. *J Nucl Med Tech* 1984; 25:84–86.
2. Billingshurst MW, Palser RF. Some factors affecting the calibration of Radionuclide Calibrators-I. ^{99m}Tc. *Int J Nucl Med Biol* 1983; 10:117–119.
3. Jain AN, Rehman MA. Quality control of dose calibrators. *Nucl Med* 1981; BandXX/Heft5:247–250.
4. Kowalsky RJ, Johston RE, Chan FH. Dose calibrator performance and quality control. *J Nucl Med Tech* 1977; 5:35–40.
5. Hare D, Hendree WR, Whitney WP, et al. Accuracy of well ionization chamber calibrators. *J Nucl Med* 1974; 15:1138–1141.
6. Harris C. Effects of characteristic x-rays on assay of I-123 by dose calibrator. *J Nucl Med* 1984; 25:1367–1370.
7. Paras P, Hamilton DR, Evans C, et al. Iodine-123 assay using a radionuclide calibrator. *Int J Nucl Med Biol* 1983; 10:111–115.
8. Johnston AS, Colombetti LG, Baker SI, et al. Dose calibrator readings due to radionuclidic impurities found in radiopharmaceuticals. *Nuclearmedizin* 1980; 19:1–6.
9. Suzuki A, Suzuki MN, Weiss AM. Analysis of a radioisotope calibrator. *J Nucl Med Tech* 1976; 4:193–198.
10. United States Pharmacopeia, XXI, Pharmacopeial Convention, Inc. Washington, DC, 1985.
11. Misadministration reporting requirements, US Nuclear Regulatory Commission 10CFR Part 35.43, Washington, DC, May 14, 1980.
12. US Nuclear Regulatory Commission, Guide for the preparation of applications for medical programs, Regulatory guide 10.8, Appendix D, Washington, DC, January 1979.
13. NCRP, A Handbook of Radioactivity Measurement Procedures. NCRP Report No. 58, National Council on Radiation Protection and Measurements, Bethesda, MD, 1985.
14. Institute of Electrical and Electronic Engineers, American National Standard Calibration and Usage of "Dose Calibrator" Ionization Chambers for the Assay of Radionuclides, ANSI N42.13–1978, September 14, 1978.