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**ORNL/NTRC-026
Rev. 0**

**INTERNAL PRESSURE
STANDARDS ACCEPTANCE
TESTING FOR RADIOISOTOPE
SAMPLE VIALS TRANSPORTED
BY AIR**

Revision 0
December 2007



National Transportation
Research Center



ORNL-27 (4-00)

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ORNL/NTRC-026
Rev. 0

Nuclear Science and Technology Division

**Internal Pressure Standards Acceptance Testing for
Radioisotope Sample Vials Transported by Air**

Scott B. Ludwig

Date Published: December 2007

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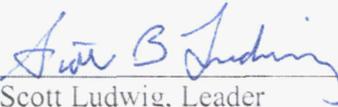
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APPROVALS

Radioisotope sample vial internal pressure standards acceptance test

This certifies that the sample vial configurations described in Section 4 can withstand the pressure differential of 95 kPa as required by the U.S. Department of Transportation [49 CFR Part 173.410 (i)(3)] and the International Air Transport Association regulations [Paragraph 5.0.2.9], when prepared as described in Section 5.

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ABBREVIATIONS AND ACRONYMS

DOE	U.S. Department of Energy
DOT	U.S. Department of Transportation
IATA	International Air Transport Association
ORNL	Oak Ridge National Laboratory
NSTD	Nuclear Science and Technology Division
NTRC	National Transportation Research Center
PRF	Packaging Research Facility
TTG	Transportation Technologies Group

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1. INTRODUCTION

Use of short half-life radioisotopes demands rapid delivery to end-user medical facilities for subsequent diagnostic and radiotherapy applications. As such, radioisotopes are typically produced continuously and packaged in glass vials ready for immediate application upon delivery. Examples of such isotopes include Iodine-131 (I-131), Yttrium-90 (Y-90) and Lutetium-177 (Lu-177). In order to ensure that radioisotopes used for radiopharmaceutical preparation reach the end users rapidly, manufacturers rely on transport by air and rapid delivery services (e.g., overnight delivery services such as FedEx).

1.1 Test Apparatus

The test apparatus employed to provide near vacuum external pressure conditions was a stainless steel vacuum chamber (containment vessel) connected to the Packaging Research Facility's (PRF's) Varian Model 959 Helium Leak Detection system that has previously been utilized to conduct low-pressure gradient leak detection of special nuclear material interim storage containers. The test apparatus provided an ideal means to evaluate leakage from sealed glass vials based on the presence of internal pressure, as might occur when vials sealed at sea level were subjected to the absence of pressure at higher altitude.

1.2 Acknowledgment

The testing of sealed glass sample vials for radioisotope transport was conducted at the National Transportation Research Center (NTRC) by Transportation Technologies Group (TTG) staff member Rick Michelhaugh on August 24, 2007. Mr. Michelhaugh also developed the test procedure listed in Appendix A.

2. PURPOSE

The purpose of this report is to document that tests conducted at Oak Ridge National Laboratory (ORNL) by the NSTD/TTG at the PRF located at the NTRC to demonstrate that sealed glass vials used for shipments of radioisotopes by air can withstand, without leakage, an internal pressure which produces a pressure differential of not less than 95 kPa (0.95 bar or 13.8 lb/in²), as required by both the U.S. Department of Transportation (DOT) regulations (Ref. 1) and the International Air Transport Association (IATA) regulations (Ref. 2). The tests were conducted in accordance with the TTG's quality assurance program (as documented in Ref. 3) as supplemented by the test procedure provided in Appendix A.

The specific applicable text from the U.S. DOT and IATA regulations has been included in the following paragraphs. The pertinent section of the U.S. DOT regulation is found in 49 CFR 173.410 (General Design Requirements), and the pertinent IATA regulation is found in Paragraph 5.0.2.9 (Internal Pressure Standards). Please be aware that there is no attempt to qualify any other requirement or performance characteristic of the package.

U.S. Department of Transportation regulations (Ref. 1)

TITLE 49--TRANSPORTATION

PART 173_SHIPPERS_GENERAL REQUIREMENTS FOR SHIPMENTS AND PACKAGINGS--

Sec. 173.410 General design requirements.

"(i)(3) Packages containing liquid contents will be capable of withstanding, without leakage, an internal pressure that produces a pressure differential of not less than 95 kPa (13.8 lb/in²)."

International Air Transport Association, Dangerous Goods Regulations (Ref. 2)

5.0.2.9 Internal Pressure Standards

"Packagings, for which retention of liquid is a basic function, must be capable of withstanding, without leakage, an internal pressure which produces a pressure differential of not less than 95 kPa (0.95 bar or 13.8 lb/in²), not less than 75 kPa (0.75 bar or 10.9 lb/in²) for liquids in Packing Group III of Class 3 or Division 6.1, or a pressure related to the vapour pressure of the liquid to be conveyed, whichever is the greater. The pressure related to the vapour pressure must be determined by one of the methods described in 5.0.2.9.1 to 5.0.2.9.3."

3. PACKAGE DESCRIPTION

Radioisotopes are typically shipped in liquid solutions to facilitate immediate use, and a common configuration to contain the radioactive liquid is a glass vial and stopper, sealed by a metal crimp seal ring.

Two different vial system configurations were tested by TTG. Each system used a 3 mL graduated glass V-vial. Vial system 1, shown in Figure 1, utilized a 20 mm white T/S (Teflon coated silicone) seal, while vial system 2, shown in Figure 2, utilized a 20 mm gray Teflon faced stopper. Each system used a 20 mm aluminum seal cap, closed by a special sealing tool. Table 1 provides specific manufacturer information of the components tested.



Figure 1. Vial system 1 components.



Figure 2. Vial system 2 components.

Table 1. Vial system component manufacturer information

Vial System 1:

Vial - 3 mL graduated glass V-vial	Kimble Glass, Inc. Art. No., 60720-3
Closure - 20 mm seal T/S w/retaining ring	Sun SRI, # 500-272
Crimp Seal - 20 mm Al seal cap	VWR # 16171-851

Vial System 2:

Vial - 3 mL graduated glass V-vial	Kimble Glass, Inc., Art. No. 60720-3
Closure - Gray, Teflon faced stopper seal	West Pharmaceutical Services, # 4432/50
Crimp Seal - 20 mm Al seal cap	VWR # 16171-851

Figure 3 shows the vial system 2 components and crimping tool. Figure 4 shows the same vial system 2 assembled but prior to crimping, and Figure 5 shows the same configuration after crimping.



Figure 3. Vial system 2 components with crimper.

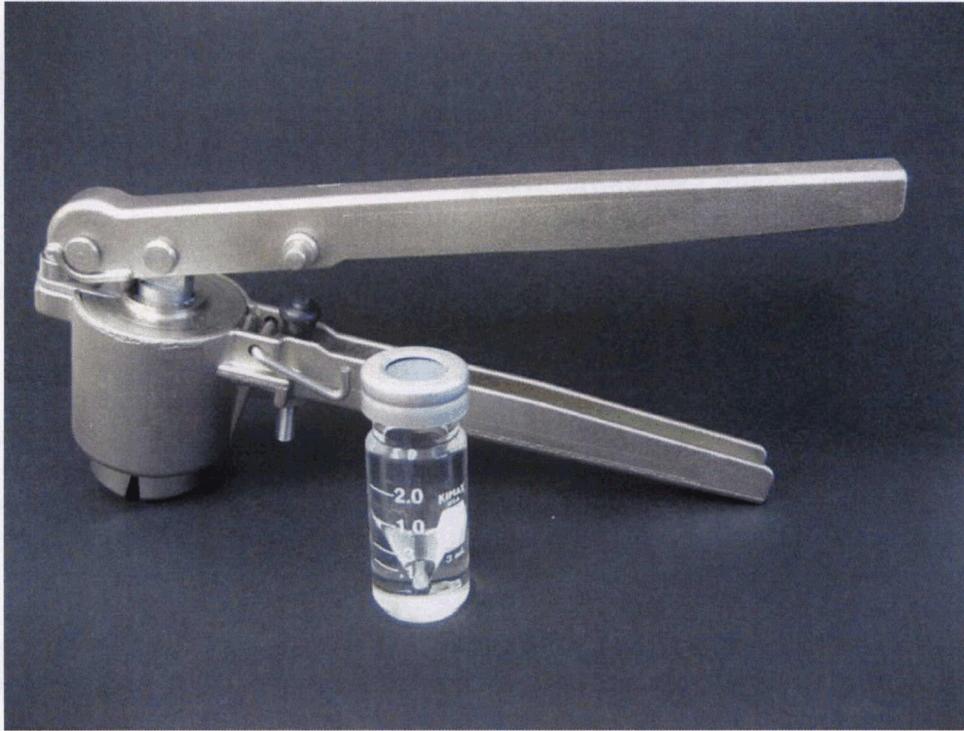


Figure 4. Vial system 2 vial before crimping.



Figure 5. Vial system 2 vial after crimping.

4. PACKAGE PREPARATION

The two vial system configurations described in Section 3 were each prepared according to the procedure listed in Appendix A. A total of two vials for each vial system configuration were prepared and tested. Figure 6 shows vial system 1 filled and sealed with approximately 2.5 mL of fluroscein solution. Figure 7 shows vial system 2 filled and sealed with approximately 2.5 mL of fluroscein solution. Fluroscein powder was dissolved in water to provide a convenient determination of leakage, as leaked fluroscein is easy to detect visually using a blacklight. The concentration of fluroscein in water was not recorded (nor is it a relevant parameter in these tests), as even the smallest trace of leaked, iridescent green, fluroscein solution is very observable when inspected for using a blacklight.

Prior to filling, each sample vial was inspected to ensure that each vial was clean (i.e., not contaminated by fluroscein) (Appendix A, step 1). Each sample vial was labeled with a unique identifier (see Figures 6 and 7) (Appendix A, step 2). The vacuum chamber was also inspected with a black light to ensure that no prior contamination with fluroscein had occurred (Appendix A, step 3).

The fluroscein was mixed with water and each sample vial was carefully filled with at least 2 mL of fluroscein solution, checked to ensure that no fluroscein contamination to either the outside or sealing surface of the vial had occurred, sealed, and then rechecked to ensure that neither the outside nor the seal region contained any contamination (Appendix A, steps 4–9). Each sealed vial was then placed sealed end down in a small receptacle (i.e., paper cup) on the vacuum chamber base flange (Appendix A, step 10).



Figure 6. Vial system 1 with fluroscein solution.



Figure 7. Vial system 2 with fluorescein solution.

5. PACKAGE TESTING

Following preparation of the packages (i.e., sealed vials containing fluorescein solution) and placement on the vacuum chamber base flange, two photos were taken to show the orientation of the vials (Appendix A, step 11 - see Figures 8 and 9 below) relative to the vacuum chamber. The vacuum chamber was closed and sealed (Appendix A, step 12), and the closure bolts were each secured to a torque value of 19 ft-lbs. The torque wrench used was a Craftsman model with a maximum torque range up to 250 in-lbs, serial number 4020727674, ORNL Metrology tag M212114, calibrated 9/7/2006 (due for recalibration 9/7/2007).

The vacuum chamber leak detector fixture (located on the upper portion of the vacuum chamber) was then attached to the He leak detector (Appendix A, step 13) and a photo of the test setup was taken (Appendix A, step 14 – see Figure 10 below). The He leak detector is typically calibrated prior to each use, using a calibrated helium “leak” that provides a constant leak rate against which the leak detector’s measurement is compared to and then adjusted to match that of the calibrated leak. For this particular test, however, the helium leak detector serves only as a vacuum pump in order to evacuate and maintain the vacuum chamber at a pressure of less than 100 mTorr (0.0133 kPa) for the duration of the test. It should be noted that the He leak detector had been used frequently for other helium leak tests in the days just prior to this particular test, was calibrated against a Varian calibrated helium leak (Serial number LLD1005, calibrated 9/12/2006, due for recalibration 9/12/2007), and operated flawlessly during this test.

Just prior to the start of the test, the current barometric pressure and room temperature readings were taken and recorded (Appendix A, step 15). The barometric pressure was measured using TTG’s CALT 8 Leak Tester, Serial Number 29, calibrated by the ORNL Metrology Lab on 9/12/2006 (due for recalibration 9/12/2007). The CALT 8 “gauge” function also lists the current room temperature (in Celsius), which was then converted to Fahrenheit and recorded. The temperature was 75.6°F and the barometric pressure was 982 mBar ($=14.242 \text{ lb/in}^2 = 98.2 \text{ kPa}$)¹.

5.1 Units of Measurement (Pressure Units)

A sometimes confusing multitude of pressure measurement units were used (e.g., lb/in^2 , Bar, mBar, Torr, mTorr or milliTorr, kPa). The reason for presenting the results in multiple units is a combination of the fact that there was no single common pressure units presented in the regulations, reported from the various instruments used in the test, or even noted on the test procedure. For example, the U.S. DOT regulations listed the pressure units in kPa (and lb/in^2) units, the IATA regulations listed the requirements in kPa (and Bar or lb/in^2) units, while the Varian leak detector reported its vacuum condition in mTorr, the CALT 8 reported barometric pressure in mBar, and the test procedure data sheet lists both mBar and milliTorr. Thus, these multiple units have been maintained within this report, first utilizing the native units that each measurement was actually reported in, and then converting those units into one single unit of measure consistent with the primary unit of measurement listed in the regulations (kPa).

¹ Pressure unit conversions were performed using the Pressure Conversion Calculator found at <http://www.ilpi.com/msds/ref/pressureunits.html>

5.2 Pressure Differential Test

In order to conduct the pressure differential test, the helium leak detector vacuum pump was used to evacuate the atmosphere from the vacuum chamber that contains sealed glass vials, which had an internal pressure equal to barometric pressure present when the vials were filled and sealed, 982 mBar (or 98.2 kPa).

The He leak detector vacuum pump was activated, which resulted in the atmosphere in the vacuum chamber being removed, achieving a pressure of less than or equal to 100 mTorr (= 0.00193 lb/in² = 0.0133 kPa), as indicated on a display panel on the detector. The actual vacuum pressure measurement is not relevant as long as the pressure differential between the inside and outside of the glass vials exceeds 95 kPa. For comparison, the normal atmospheric pressure at sea level is 760 Torr (= 14.7 lb/in² = 101.3250 kPa).

The He leak detector was activated to begin the pump-down process, which required roughly 25 minutes for the vacuum chamber's internal pressure to reach 100 mTorr (Appendix A, step 16). The test vials were maintained within the vacuum chamber at 100 mTorr pressure for 2 hours (an arbitrary time period, more than sufficient to permit leakage from each sealed vial due to its internal pressure of 98.2 kPa) (Appendix A, step 17). The pressure differential (95 kPa minimum required) was determined to be **98.187 kPa** (98.2 kPa – 0.013 kPa) and was sufficient to demonstrate that the regulatory test conditions (**95 kPa minimum pressure differential**) had been achieved (Appendix A, step 18).



Figure 8. Sealed vials placed in cups on vacuum chamber base flange.



Figure 9. Top view of sealed vials positioned on vacuum chamber base flange.

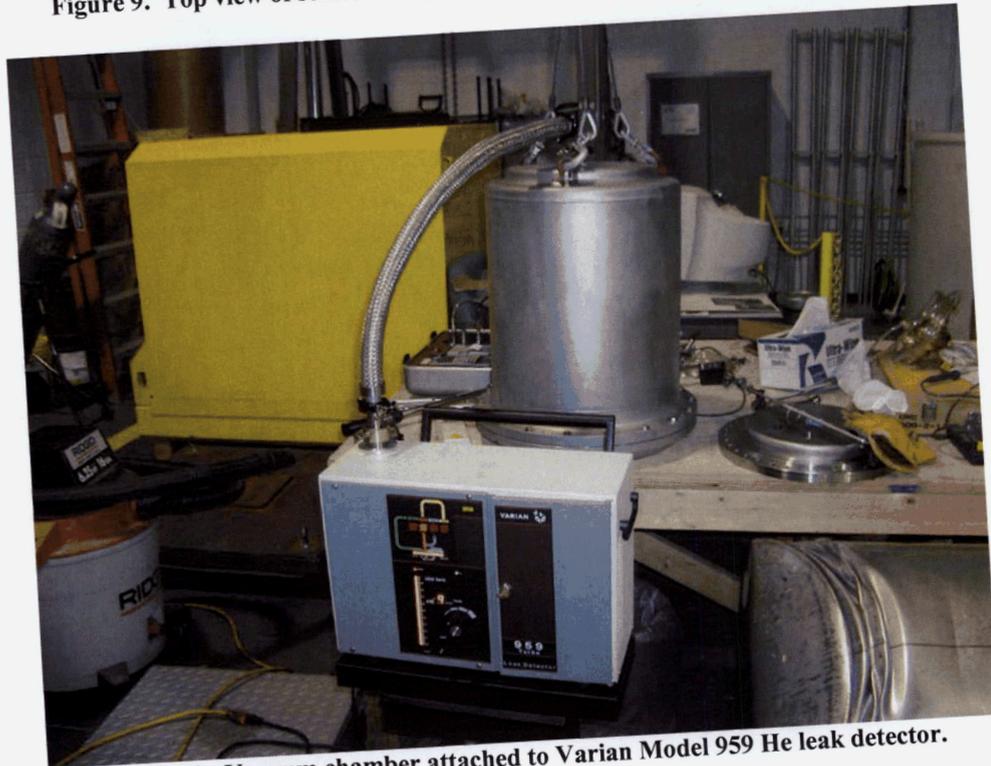


Figure 10. Vacuum chamber attached to Varian Model 959 He leak detector.

6. PACKAGE TEST RESULTS

At the completion of the 2-hour test period, the He leak detector vacuum pump was deactivated, and the vacuum chamber was vented to return the interior to atmospheric pressure (Appendix A, step 19). The vacuum chamber was then opened, and each vial and receptacle was examined with black light for presence of leaked fluorscein (Appendix A, steps 20 and 21). No fluorscein leakage was observed, indicating that the vials had passed the test as stated in the DOT and IATA regulations. Table 2 shows the completed data sheet from this procedure.

Table 2. Data sheet from test procedure

15. Barometric pressure: 982 mBar Temperature: 75.6 F

16. Pump start time: 14:35

17. Test start time: 15:00

18. Pressure differential achieved (barometric pressure minus 100 milliTorr)
982 mBar - .13 mBar = 981.87 mBar (98.2 kPa - 0.013 kPa = 98.187 kPa)

19. Test end time: 17:00

21. Observations: No Leakage Detected

Signed: Rick Michelhaugh Date: 8-24-2007

(Note: 100 mTorr = 0.1333 mBar = 0.01333 kPa)

7. CONCLUSIONS

Two different sealed glass vial system configurations used for the transport of small quantities (~2 mL liquid solutions) of radioisotopes were tested by the NSTD Transportation Technologies Group. Each system used a 3 mL graduated glass V-vial. Vial system 1 utilized a 20 mm white T/S seal, while vial system 2 utilized a 20 mm gray Teflon faced stopper. Each system used a 20 mm aluminum seal cap, closed through the use of a special sealing tool.

The sealed vial systems were subjected to a reduced external pressure environment to demonstrate that the internal pressure in each vial would not result in leakage, as required by both the U.S. DOT and IATA regulations. Based on the results of the test described herein, the sample vial configurations described in Section 4 can withstand the internal pressure differential of 95 kPa as required by the U.S. Department of Transportation [49 CFR Part 173.410 (i)(3)] and the International Air Transport Association regulations [Paragraph 5.0.2.9], when prepared as described in Section 5.

8. REFERENCES

1. U.S. Code of Federal Regulations, Title 49, Part 173, "Shippers-General Requirements for Shipments and Packagings."
2. International Air Transport Association, Dangerous Goods Regulations, 48th Edition, Effective 1 January – 31 December 2007.
3. Quality Assurance Plan for the Package Testing Program at the National Transportation Research Center Packaging Research Facility, NTRC-PRF-QAP-001, Rev. 0, February 13, 2004.

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Appendix A: Test Procedure

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The following is the procedure prepared by Rick Michehaugh of the TTG for pressure testing sample vials in order to subject each vial to a 95 kPa reduced-pressure differential to confirm that the vials do not leak under such pressure conditions. The Data Sheet (following the procedure listed below) is used to record the test data.

Procedure for Pressure Testing of Sample Vials To Meet Pressure Test Requirements for Transport by Aircraft

1. Check all sample vials with black light to ensure they are clean and not contaminated.
2. Label each sample vial with a unique identifier.
3. Check and clean (as necessary) the vacuum chamber for fluorescein contamination.
4. Mix fluorescein in water.
5. Carefully add 2 mL to each sample vial.
6. Check vial for contamination of fluorescein on the outside and the sealing surfaces with black light.
7. Cap the vials: two with rubber septums and two with Teflon septums.
8. Check vial for contamination of fluorescein on the outside and on the sealing surfaces with black light.
9. Clean vials (as needed) to remove any external contamination.
10. Place each vial, cap end down, into a small receptacle (e.g., paper cup) and place the group of receptacles within the vacuum chamber.
11. Take a photo of the receptacles within the vacuum chamber prior to closure.
12. Close vacuum chamber. Torque each bolt to 19 ft-lb.
13. Attach the He leak detector to vacuum chamber.
14. Take a photo of the test setup.
15. Record the value of barometric pressure and temperature.
16. Activate the He leak detector vacuum pump-down process.
17. When the vacuum reaches 100 mTorr, start timing of 2 hour test period.
18. Calculate the maximum pressure differential attained.
19. After 2 hours, vent the vacuum chamber.
20. Open vacuum chamber.
21. Check for leakage from vials with black light. Record any observations of leakage.

Data Sheet

(Note: the item numbers below coincide with the steps noted in the above procedure)

11. Photo

14. Photo

15. Barometric pressure: _____ Temperature: _____

16. Pump start time: _____

17. Test start time: _____

18. Pressure differential achieved (barometric pressure minus 100 milliTorr)

19. Test end time: _____

21. Observations: _____

Signed: _____ Date: _____

(Note: 100 mTorr = 0.1333 mBar = 0.01333 kPa)

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