



March 18, 1980

Material Licensing Branch Division of Fuel Cycle and Material Safety U. S. Nuclear Regulatory Commission Washington, D. C. 20555

Gentlemen:

Enclosed is the information required to amend Nuclear Medicine License #21-12916-01 to provide for Xenon Gas Studies at this Medical Center.

Sincerely yours,

A. M. HOLMAN, M. D.

Acting Medical Center Director

Enclosures

RECEIVED

1980

ACCLEAR FULDIOINE SERVICE

CONFISSION O S'HOO'S NAME O'

JAMES J. SMITH. M. D. (115)

Washington, D.C. 20420

Director, Mic oar Medicine Servic FEE EXEMPT

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In Reply Refer To:

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INSPECTION AND ENFORCEMENT

REQUEST FOR AMENDMENT OF NUCLEAR MEDICINE LICENSE TO PROVIDE FOR XENON GAS VENTILATION STUDIES

1. Name & Address of Institution:

VA Medical Center West "H" Street Iron Mountain, Michigan 49801

2. Current Radioactive Materials:

License # 21-12916-01

3. Radioactive Material:

Xenon Xel33 Gas

4. Type of Study:

Pulmonary Ventilation Study

5. Possession Limit: 300mC

Estimate: 100mC/week maximum, adjusted for 4 days precalibration would equal approximately 170mC (100mC x 1.7 precalibration factor). A maximum of 100mC trapped and decaying. Total estimated inventory 170 + 100 = 270mC.

6. Dose Employed: Average dose per patient - 10mC. Higher doses will be used only when professional medical judgement indicates it to be necessary.

7. Patient Load:

Estimate: A maximum of 10 patients per week, 520 patients per year.

8. Source of Radiopharmaceutical:

New England Nuclear Corporation Atomic Light Place North Billerica, Massachusettes 01862

Catalog Number NRP-127-Xenon Xel33 Gas in unit dose vials. (See Attachment A for NDA approved package insert).

9. Imaging Equipment:

Searle PHO GAMMA V

10. Special Equipment:

Instruction for Xenon Delivery System (See Attachment B).

- a. Atomic Products Delivery System 130-330 Atomic Products Corporation Center Moriches, New York, 11934, product literature obtained.
- b. Atomic Products Gas Trap System Model #127-313 Atomic Products Corporation Center Moriches, New York, 11934, product literature obtained.

11. Dose Calibration:

Capintec Dose Calibrator Model CRC-22NB Nuclear Chicago (Searle) Mediac Calibrator

All doses for patient use will be checked immediately prior to administration using the above equipment.

12. Personnel Safety:

All personnel working in the dpeartment will use both whole body film badges and TLD finger badges.

13. Scale Drawing of Nuclear Medicine Service (See Attachment C).

14. Description of Storage Area (Hot Lab):

The Xenon 133 Gas will be stored in its 1/8 inch thick lead shipping container within the storage cave until used. A description of this storage area, the work area, radiation monitoring equipment and radiological safety procedures are the same as described in the original license submission. The ventilation in this storage area is by two exhaust ducts having a total airflow of 500 cfm. This may be increased to 3587 cfm by repositioning a selector switch on the wall. The selector switch is equipped with indicator lights which identify operating status. An audio alarm will sound if the system fails. The total volume of this room is 370 cu. ft. Air can enter the room through a vent in the door. All air leaving the room is through the vents which also keep the room at a slight negative air flow. The maximum concentration of Xenon 133 over forty hours in seven consecutive days for this Restricted Area has been calculated on the following basis:

- a. Maximum amount of Xenon 133 activity lost per week is 300mC (Xenon Trap will be stored in this area when not in use).
- b. Estimated escape fraction (maximum Xenon 133 activity lost due to leakage and inadvertent release) is 0.25.
- c. Air flow volume will be 500 cfm.

Therefore, using the above data and appropriate conversion factors, C can be calculated:

 $\frac{A}{C=VX} = \frac{300mC (1x10^3)}{ft^3/min(6.797x10^7)} \times 0.25 = .022x10^{-5}uC/m1/40 \text{ hr. week}$

This verifies that the MPC of 1 x 10⁻⁵uC/ml as stated in Section 20.103 CFR Part 20 and Schedule B table 1 of Part 20 will be exceeded.

In the event of an accidental release of the Xenon 133 in this area, the following procedure will be implemented: The selector switch will be positioned to the high speed flow velocity. The door has a louver installed. The room will remain unoccupied for five minutes. Upon re-entry, the room will be surveyed with a low level survey meter to insure the radiation levels have returned to normal for the area. Upon verification of the above, the selector switch will be returned to slow speed position. The five minutes will insure 48 changes of the room air based on the following calculations: TOTAL AIR VOLUME=3587 ft³/min. Volume of Room = 370 ft.

Therefore: Room Volume Air Volume/Min. = Turnover Time = $\frac{270}{3587}$ = .103 min.

Twenty air exchanges of room air would require five minutes. The air which is exhausted from this room is released directly into an Unrestricted Area located on the roof of the hospital. This release point is isolated from all air intakes and adjacent buildings by distances exceeding 50 feet. All Restricted Areas are in common with this release point, and the calculations for the Unrestricted Area are presented at the end of the Utilization Phase discussion.

15. Description of Procedure:

The Xenon 133 gas will be used in the following manner: The dose will be measured in the dose calibrator. The patient will be instructed on the details of the procedure with special emphasis on the areas where his cooperation is needed. Just prior to the study, one or more practice runs will be done before the Xenon 133 gas is used. The unit dose vial will be loaded into the shielded Calidose Dispenser furnished by New England Nuclear. It will then be taken to the Imaging Area where the lung ventilation procedure will be done. The dispenser will be connected to the Atomic Products Delivery System. The Xenon 133 gas will be administered to the patient via this unit. Nose clamps will be used to prevent the patient from exhaling the Xenon 133 into the room.

The lung ventilation procedure will be composed of the three standard phases of breath hold, equilibrium, and washout. These phases are automatically accomplished as the technician operates the remove control handles on the unit. Upon completion of the study, the used Xenon 133 will be drawn directly into the Atomic Products Xenon Gas Trap System.

16. Description of Utilization Phase (Imaging Room): All Xenon lung ventilation procedures will be performed in Imaging Room 226 as shown in Attachment B and described in the original license submission. Air will enter this room through the vented door. The air will leave the room via exhaust ducts, which have a measured air flow of 600cfm. This vent is connected to the exhaust duct in the hot room. This

room has a slight negative pressure at all times. The maximum concentration of Xenon 133 for this restricted area is calculated below:

- a. Maximum amount of Xenon 133/week is 100mC. Estimate based on 100mC/week resulting from patient use.
- b. Estimated Escape Fraction (Maximum Xenon 133 activity lost due to leakage and inadvertent release) is 0.25.
- c. Air flow volume will be 600 ft3/min.

Therefore, using the preceding values and appropriate conversion factors, C can be calculated:

 $\frac{\text{C=A X F} = \frac{100\text{mC} (1\text{x}10^3) \times 0.25}{600\text{ft}^3/\text{min}(6.797 \times 10^7)} = .0613 \times 10^{-5} \text{uc/ml/40 hr. week}$

This verifies that the MPC of 1 x $10^{-5}uC/ml$ as stated in Section 20.103 CFR Part 20 and Schedule B table 1 of Part 20 will not be exceeded.

The maximum concentration of Xenon 133 for the Unrestricted Area, the roof exhaust, is calculated below:

a. Maximum amount of Xenon 133 released per year is based upon 300 mC/week times the Escape Fraction of 0.25:

300 mC/week x 0.25 Escape Fraction x 52 weeks/year = 3900mC

b. Total air flow volume from all areas equals 500 ft³/min. from hot lab and 600 ft³/min in imaging room. These are added together because they are dumping into the same exhaust duct which leads to the roof. (NOTE: If the exhaust ducts were not connected, then each situation would be a separate one. Individual concentration calculations would have to be made for each independent exhaust duct leading to Unrestricted Areas.) Therefore, using the preceding values and appropriate conversion factors, C can be calculated:

 $C = \frac{A}{V} = \frac{3900 \text{ mC}(1 \times 10^3)}{1100 \text{ ft}^3/\text{min} (1,484 \times 10^{10} \text{ ml/year})} = 2.46 \times 10^{-7}$

This verifies that the MPC of 3 x 10^{-7} uC/ml as stated in Section 20.106 10 CFR Part 20 and Schedule B table 2 of Part 20 will not be exceeded, and that Section 20.1 (c) of 10 CFR Part 20 is being complied with.

c. In the event that there is an accidental release of Xenon 133 in Imaging Room, the following emergency procedure will be implemented: The patient will be removed from the room. The door will be closed. The fan selector will be set to high speed. The door to the hot lab will be opened and all personnel will leave both the imaging room and hot lab for 10 minutes. Upon re-entry, both rooms will be surveyed to insure that radiation levels have returned to normal for these areas. Upon verification of the above, the selector switch for the fan will be returned to slow speed. The 10 minutes will insure 18.5 changes of the air in both rooms based on the following calculations:

Total air flow volume = 6300 ft³/min. Volume for both rooms 3430 ft³. Therefore: Volume 3430 Air Flow/min = turnover time 6300 = .54 min.

17. Description of the Disposal Phase: The disposal phase of the Xenon 133 gas will be done by trapping the Xenon 133 gas in an Atomic Products Cas Trap System Model 127-32. The potential leakage of Xenon 133 from this unit, as well as other sources of leakage, are included in the Escape Fraction figure. To insure that the trap is working efficiently, the exhausted air will be monitored from the trap using the following procedure:

Immediately after the last Xenon 133 lung ventilation procedure each week, a 5 liter polyethylene bag will be placed over the exhaust port of the Xenon Trap, and the unit will be operated until the bag is full. The bag will be sealed end placed in front of the Gamma Camera and counted for one minute on the appropriate settings. The Counts Per Minute (CPM) will be recorded in a record book and compared with previous readings. A replacement cartridge will be installed whenever there is a significant increase in the weekly CPM. The saturated cartridge will be placed in the hot lab in a radiation waste barrel with other radioactive waste, and disposed of as ordinary trash when reading reaches background levels.

18. Equipment Operation and Monitoring for Leskage:

- a. The Atomic Products Delivery System, model 130-330, will be checked prior to use to insure proper operation. The manufacturer's operating instructions will be followed.
- b. The Atomic Products Gas Trap will be checked prior to each ventilation procedure to insure that it is securely connected to the Delivery System. Xenon leakage from the exhaust port will be monitored as previously described. The manufacturer's operating instructions will be followed and the desiccant in the water trap will be checked daily and replenished as needed.
- c. All exhaust vents will be checked twice a year to confirm their continued efficiency. In addition, they will be checked whenever structural changes are made which could affect their efficiency. Records verifying these procedures will be maintained.

RADIATION DOSIMETRY

The estimated absorbed radiation doses (2) to an average patient (70 kg) for pulmonary perfusion and cerebral blood flow studies from a maximum dose of 30 millicuries of Xenon Xe 133 in 3 liters of air are shown in Table III.

Table III Radiation Doses

	Effective Half-time	Lungs*	Brain	Whole Body
	rads/30mCi			
Pulmonary Perfusion Cerebral Blood Flow	2 min. 5 min.	0.25		0.0027

*99% of activity is in lungs

(2) Method of Calculation: A Scheina for Absorbed-Dose Calculation for Biologically Distributed Radionuclides, Supplement No. 1, MIRD pamphlet No. 1, J. Nucl. Med., p. 7, 1968.

HOW SUPPLIED

The Xenon Xe 133 gas is supplied as part of the Calidose® system, consisting of 2 ml unit dose vials and the Calidose dispenser* for shielded dispensing.

Normally vials containing other 10 or 20 mCi/vial, packed up to 5 vials per shield tube, ire supplied. Vial sets containing up to 100 mCi/vial are available.

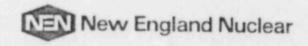
*Patent Pending



Atomlight Place North Billerica, Mass. 01862 Attachment A
Item #8
VAMC, Iron Mt., Michigan

XENON Xe 133 GAS

Catalog Number NRP-127



10 127 7-73 Rev 1

Printed in U.S.A.

5-7349

 Xenon Xe 133 for diagnostic use is hable as 5% gas in carbon dioxide diluent 95%.

ACTIONS

Xenon Xe 133 is a readily diffusible gas which is neither utilized nor produced by the body. It passes through cell membranes and freely exchanges between blood and tissue, It tends to concentrate more in body fat than in blood, plasma, water or protein solutions. In the concentrations used for diagnostic purposes it is physiologically inactive. Inhaled Xenon Xe 133 gas will enter the alveolar wall and enter the pulmonary venous circulation via the capillaries. Most of the Xenon Xe 133 that enters the circulation from a single breath is returned to the lungs and exhaled after a single pass through the peripheral circulation.

INDICATIONS

Inhalation of Xenon Xe 133 gas has proved valuable for the evaluation of pulmonary function and for imaging the lungs. It may also be applied to assessment of cerebral flow.

CONTRAINDICATIONS

To date, no known contraindications to the use of Xenon Xe 133 gas have been reported.

WARNINGS

This radiopharmaceutical should not be administered to pregnant or lactating women unless the benefits to be gained outweigh the potential hazards.

Ideally, examinations using radiopharmaceuticals, especially those elective in nature, of a woman of childbearing capability should be performed during the first few (approximately 10) days following the onset of the menses.

Radiopharmaceuticals should be used only by physicians who are qualified by specific training in the safe use and handling of radionuclides produced by nuclear reactor or particle accelerator, and whose experience and training have been approved by the appropriate governmental agency authorized to license the use of radionuclides.

PRECAUTIONS

As in the use of any other radioactive material care should be taken to insure minimum radiation exposure to the patient, consistent with proper patient management, and to insure minimum radiation exposure to occupational workers. Expired Xenon Xe 133 gas should be controlled in a manner that is in compliance with the appropriate governmental agency regulations.

Xenos: Xe 133 adheres to some plastics and rubber and should not be allowed to stand in tubing or respirator containers. Such unrecognized loss of radioactivity from the dose for administration may render the study non-diagnostic. Xenon Xe 133 gas delivery systems, i.e., respirators or spirometers, and associated tubing assemblies must be leakproof to avoid loss of radioactivity into the laboratory environs not specifically protected by exhaust systems.

ADVERSE REACTIONS

To date, no adverse reactions based on the use of Xenon Xe 133 gas have been reported.

DOSAGE AND ADMINISTRATION

Xenon Xe 133 gas is administered by inhalation from

closed respirator systems or spirometers.

the suggest activity range employed for inhalation by the average adult patient (70 kg) is:

Pulmonary function including imaging: 2-30 mCi in 3 liters of air.

Cerebral blood flow: 10-30 mCi in 3 liters of air.

The patient dose should be measured by a suitable radioactivity calibration system immediately prior to administration.

PHYSICAL CHARACTERISTICS

Xenon Xe 133 decays by beta and gamma emissions with a physical half-life of 5.27 days (1). Photons that are useful for imaging studies are listed in Table I.

Table I Principal Radiation Emission Data Xenon Xe 133

Radiation	Mean % per Disintegration	Mean Energy (keV)
Beta-2	99.3	100.6
Gamma-2	34.99	81.0
K int. con. electrons, -2	47.24	45.0
L int. con. electrons, -2	7.87	75.7
M int. con.		
electrons, -2	9.84	80.0
K x-rays	34.70	30.8
K x-rays	7.67	35.2

(1) Dillman, L.T., Radionuclide Decay Schemes and Nuclear Parameters for Use in Radiation-Dose Estimation, Part 2, Supplement No. 4, MIRD pamphlet No. 6, J. Nucl. Med., p. 28, 1970.

The specific gamma ray constant for Xenon Xe 133 is 0.44 R/mCi-hr. at 1 cm. The half value layer is 1 mm of Pb. To correct for physical decay of this radionuclide, the fractions that remain at selected time intervals before and after the date of calibration are shown in Table II.

Table II Xenon Xe 133 Physical Decay Chart (Half-life 5.27 days)

Day	Fraction Remaining	Day	Fraction Remaining
-5	1.930	- 8	.349
-4	1.693	9	.302
-3	1.483	10	.268
-2	1.300	11	.235
-1	1.140	1.2	.206
0*	1.063	13	.181
1	.877	14	.159
2	.769	1.5	.139
3	.674	16	.122
3 4	.591	17	.107
5	.518	18	.094
- 6	.454	19	.082
7	.398	20	.072

^{*}Calibration Day

Atomlab

Attachment B Instruction Manual for Xenon Delivery System VAMC, Iron Mountain, Michigan

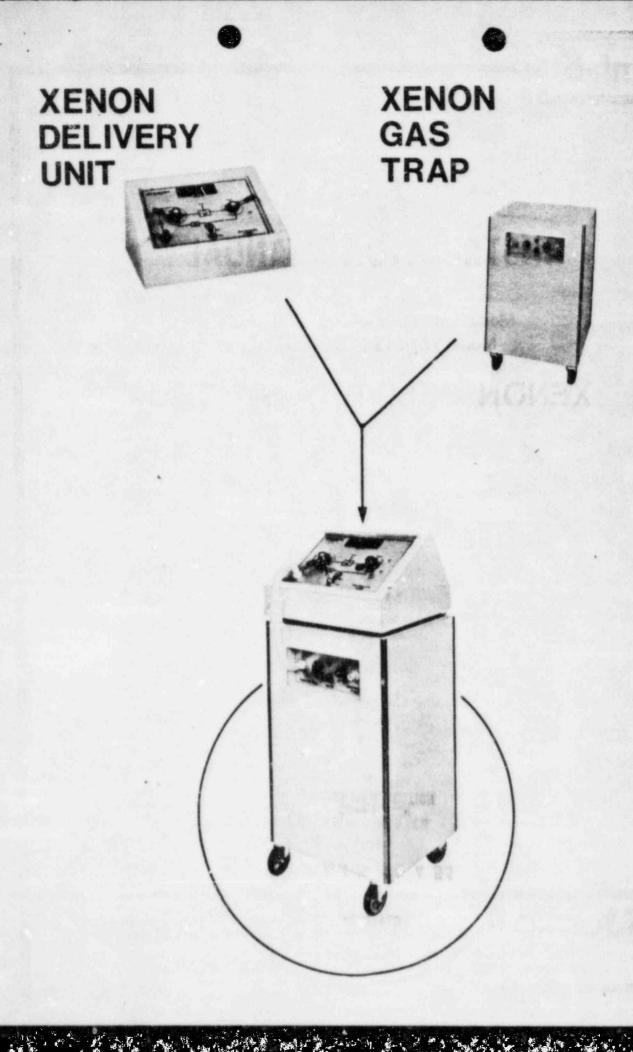
INSTRUCTION MANUAL

Model 130-330 Xenon Delivery Unit Model 127-313 Xenon Gas Trap

XENON DELIVERY SYSTEM

Atomic Products Corporation3316

Center Moriches, New York 11934, U.S.A. (516) 878-1074



XENON SYSTEM INSTRUCTION MANUAL

Setting up the system

- Carefully unpack the Model 130-330 delivery unit and the Model 127-313 trap.
- Place the delivery unit on top of the gas trap so that both instrument panels are facing the same direction.
- From the plastic bag that accompanied the delivery system, remove the cartridge that contains the blue crierite granules, and 8" connecting tubes.
- 4. Connect one tubing end to the delivery system port marked "trap" - and the other end to the trap port marked "gas inlet". This serves as a moisture trap. Change the granules when the color changes from blue to pink.
- Open the rear of the delivery system by pulling on the round handle attached to the door.
- Reach into the delivery unit and remove the empty plastic cartridge (similar to moisture trap cartridge).
- 7. Fill the cartridge with soda lime (available in your hospital pharmacy) and return it to the interior of the delivery system. Close the delivery system door. This is the CO₂ trap. Only fill the cartridge about half way. Change the soda lime between patients.
- At the rear of the delivery system, just below the access door, is the patient port.
- Connect one end of either the 8" or 40" tubing to the patient port. Connect the other end of the tubing to the mouthpiece/bacteria trap/T-adapter combination. Whenever possible, use the shortest length of tubing.
- Unwrap the electric cord on the trap and plug into a nearby electrical outlet.

The Xenun System is now ready for use.

- 11. Set the scintillation camera for TC-99m.
- Position the patient for a posterior view and, using a flood source (Atomic Products Model No. 045-150).
 Position the lungs so that they are included in the camera's field of view.
- 13. Place an oxygen tank next to the Xenon System. Take a piece of ¼" plastic tubing and attach one end to the oxygen tank and the other end to the chrome fitting marked "oxygen" which is located in the lower middle of the delivery unit front panel. If necessary, clamp the oxygen hose onto the oxygen fitting.
- 14. Reset the camera for Xenon-133.
- Turn the oxygen *ank valve to 5 lbs. PSI. Leave the valve on during the entire study.
- Place the delivery system valve handles so that the black handles are facing outward and the black dots are facing inward. (See illustration #1).

- Press the button just above the oxygen fitting on the delivery system (marked "push to add oxygen").
- Hold the button down until the breathing bag is half filled. The bag can be observed through the window on the delivery system front panel.
- The bag is filled half way when the pleats start to come apart.
- 20. Clip the patient's nose and place the patient on the mouth-piece. (No nose clip is necessary if you use a face mask instead of a mouthpiece) Quickly turn the handles so that both black dots are facing straight down and the black handles are straight up. This is the closed circuit or rebreathing position. (See illustration #2)
- 21. Have the patient take a couple of breaths and observe the breathing bag. More oxygen can be added at any time during the study if the breathing bag indicates or the patient signals.
- Start the gamma camera and all data obtained recorded on tape.
- 23. Using a gun or syringe, puncture the mouthpiece and add the Xenon as the patient takes a deep inspiration. If you desire a single breath study, have the patient hold his or her breath as long as possible, then continue to breathe for the equilibrium study.
- 24. Allow the patient to breathe normally on the closed circuit position until equilibrium is reached, approximately two to three minutes. Add oxygen if necessary.
- The patient will be at equilibrium with the Xenon air mixture in the system when the counting rate on the camera stabilizes.
- 26. About one minute before equilibration, start the trap by turning the timer switch to the desired washout time. Six minutes is average. Turn the air speed control to the desired flow rate; seventy-five is about average.
- After equilibration switch the valve handles so that the black plastic is down and the black dot is up.
 This is the open circuit or washout circut. (See illustration #3)
- Take washout data on the camera (typical framing: first picture, 15 seconds; second, 30 seconds; third, 60 seconds).
- 29. Allow the patient to breathe normally. Breathing during the washout can be eased by removing the plug from the mouthpiece adapter. This lowers dead space and is especially helpful for patients with extreme breathing difficulty.
- If the patient indicates that he is feeling breathing resistance, increase the trap flow speed gradually.
- Continue washout until patient is free of Xenon.
 Additional time can be added by turning the timer switch further clockwise.
- When the washout is completed, remove the patient from the mouthpiece and turn the handles back to the original position (black plastic outward, black dots inward).

- 33. Restart the trap and set the time at half the time it took the patient to washout. Example: Six minute washout, set timer at three minute. The trap will now remove any excess air within the trap's overflow reservoir.
- 34. Check the operation of the trap by filling a plastic bag or balloon from the port on the trap marked "vent". Hold the bag in front of the gamma camera. If the count is considerably above background:
 - a. Trap is running too fast.
 - Drierite cartridge (moisture trap) is exhausted or not present
 - Charcoal cartridge is exhausted.
 (This check should be performed at regular intervals)
- 35. Flush the system by once more filling the breathing bag with oxygen. Start the trap and place the handle at your left hand, black dot up, handle down; and the

handle at your right hand, black dot down, black handle up. The trap will remove the oxygen from the breathing bag and flush the system in about one minute.

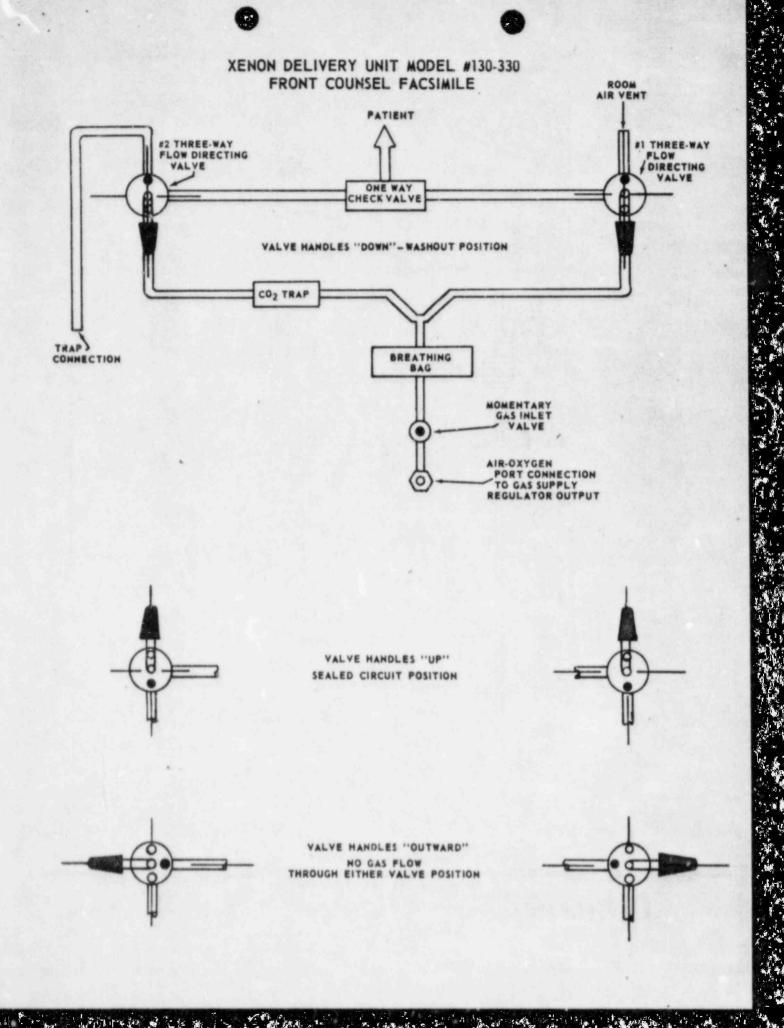
The Study is now complete

- 36. To prepare for the next study:
 - Reset the handles in the original oxygen fill position (black handles outward, black dots inward).
 - In the delivery system, refill the CO₂ trap with new soda lime.
 - Replace the drierite in the moisture trap if the color has changed to pink.
 - d. Change the mouthpiece or mask and the becteria trao.

NOTES:

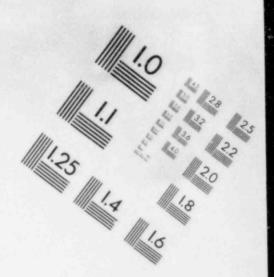
- Before you perform patient studies, practice on yourself with the Xenon.
- Before placing the patient on the system, have him or her practice breathing with the mouthpiece and nose clip.
- Remember, the front panel of the delivery system is a picture of the internal circuits. Include the handles in the front panel diagram and you can visualize the air flow at any moment.
- These instructions are meant as a general broad outline. Feel free to change sequence at your own or patient's perference.
- 5. An example of a different sequence is as follows:
 - a. Fill the system with O2 as usual.
 - b. Place the handles down, dots up (washout).

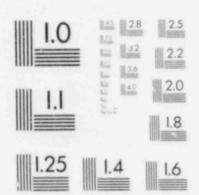
- Remove the 8" tube that connects to the port on the delivery system marked "Trap".
- Place the patient on the mouthpiece and let him breathe on the open circuit to become adjusted.
- Instruct the patient to take a deep breath and add the xenon at the mouthpiece.
- While the patient is holding his breath after the deep inspiration, turn the handle up, dots down, for equilibrium.
- g. Re-connect the 8" tube.
- h. Start the trap Just to let it build momentum.
- When the patient reaches equilibrium, turn the handles back to washout (handles down, dots up).
- j. Open the one way port at the mouthpiece.
- k. Continue the washout and system flushing as you have done previously.

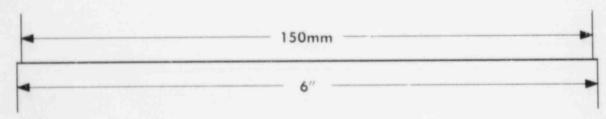


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IMAGE EVALUATION TEST TARGET (MT-3)

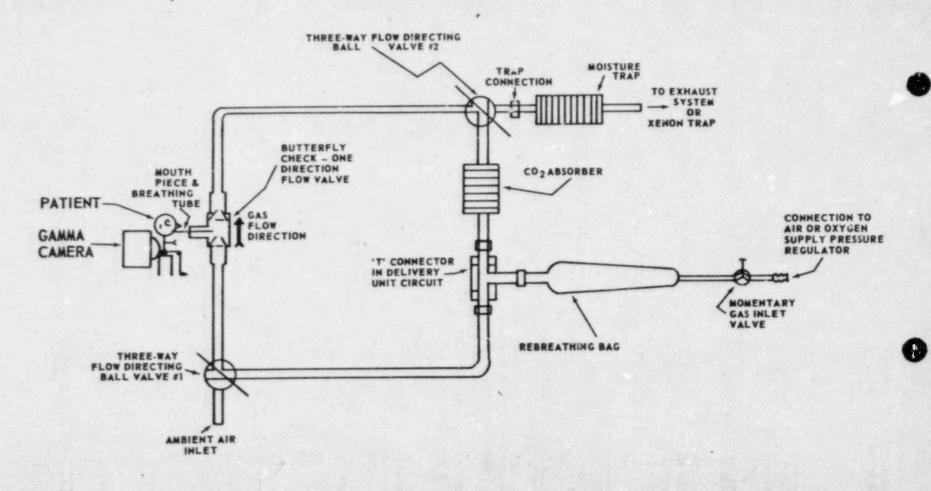






97 M SEIM SEIM OT MINE OT MINE

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SCHEMATIC DIAGRAM OF

XENON GAS TRAP

TEST PROCEDURE FOR MONITORING TRAP EXHAUST

Trap exhaust is monitored by using the gamma camera without a collimator. The following simple technique is used:

- 1. Remove the collimator from the camera.
- 2. With a 5 percent window, calibrate for Xe-133.
- 3. Fill a large plastic bag with a know volume of air (typically, 50 liters).
- Inject a known quantity of Xe-133 (such as 100uCi) into the bag. The concentration will be 2 x 10-3 uCi cm³).
- Place the bag in front of the crystal and count for a known period of time.The c/m obtained is a measure of the efficiency.
- Collect the exhaust of a typical study in another bag of the same volume (50 liters) and count as defined in Step #5.
- Ratio the count rates to the standard taken to determine exhaust concentration.

For example:

If 2×10^{-3} uCi/cm³ yielded 600,000 c/m above background, and collected effluent from the patient study was 150 c/m above background, then:

Ratio =
$$\frac{1.5 \times 10^2 \text{ c/m}}{-6 \times 10^5}$$
 = 2.5 x 10-4

Exhaust Concentration

= R (2 x 10-3 uCi/cm3)

 $= (2.5 \times 10^{-4}) (2 \times 10^{-3})$

= 5 x 10-7 uCi/cm3*

*MPC Xe-133 controlled area should not exceed 1 x 10-5 uCi/cm³

Atomic Products Corporation

Center Moriches, New York 11934, U.S.A. (516) 878-1074

