VII. RESEARCH NEEDS

The recommended standard is based primarily on epidemiologic data and the level of anesthetic gases at which the first adverse effects of any type are seen. Adverse effects to the liver, kidneys, and central nervous system have been reported but are ill-defined. While not considered essential, this type of information should be obtained during the course of other studies.

Inferences and conjectures have been made about the mutagenic potential of anesthetic agents, yet no definitive studies have been reported on the matter. Animal testing of anesthetic agents for mutagenic potential is needed at both acute and chronic exposure concentrations.

Epidemiologic data suggest that there is a higher than normal incidence of congenital abnormalities in children born to exposed women or to wives of exposed personnel. In animals, the teratogenic potential of anesthetic agents has been reported under a variety of conditions but few studies attempted to simulate average occupational conditions. Because the limited data available on congenital abnormalities and spontaneous abortions among children born to wives of exposed dentists, further studies are needed to substantiate the presence or absence of this adverse health effect. This is particularly important because nitrous oxide is the principal inhalation anesthetic used in dentistry. Further animal studies are needed, which more closely simulate occupational exposure to any of the anesthetic agents.

Two epidemiologic studies [12,75] have been cited which raise the issue of whether or not anesthetic agents have contributed to an increased
incidence of cancer in exposed female workers. There is an urgent need for a thorough animal study of the carcinogenic potential of the principal anesthetic agents in use at present. These studies should include chronic exposure to low-level concentrations.

A prospective health survey should be conducted to determine the effects of the improved working environment on the possible adverse effects on reproduction among exposed female workers and wives of male workers. This study should be conducted only after adequate data have been collected on the extent to which waste gas control programs have been implemented.

In April 1976, the Food and Drug Administration (FDA), on the recommendation of the Respiratory and Anesthetic Drugs Advisory Committee, proposed rules amending regulations on new drugs (21 CFR310) under the federal Food, Drug, and Cosmetic Act. This will require animal testing of halogenated inhalation anesthetics and nitrous oxide to determine the carcinogenic potential and reproductive effects, including teratogenicity potential, of such drug products (Federal Register 41:14888-14890, April 8, 1976). The FDA plans to hold meetings with federal research institutes, anesthesiologists, and anesthetic drug producers to establish a common protocol for animal testing so that interpretable data on the comparative potential risk of each drug may be developed.
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IX. APPENDIX I

LEAK TEST PROCEDURES FOR ANESTHETIC EQUIPMENT

Low-Pressure Components: Flowmeters to Y-Piece

This test measures the leak rate of low-pressure components in a carbon dioxide absorption system, beginning at the flowmeters and extending forward to the Y-piece. The test is easily performed with the breathing system connected in the usual manner for clinical anesthesia. The breathing bag and tubing are included and require no special testing. The total contribution of the gas machine to nitrous oxide levels in the room air can be estimated by performing this test in combination with the high-pressure component test.

The low-pressure leak rate should be less than 100 ml/minute; if it is greater than 1 liter/minute the machine should not be used.

(a) Assemble the anesthesia machine as in the usual manner for clinical anesthesia with breathing tubes, Y-piece, breathing bag, and high-pressure hoses or cylinders connected.

(b) Occlude the Y-piece securely with the thumb or palm of hand.

(c) Pressurize the breathing system to 30 cm water, observed on the absorber pressure gauge. This may be accomplished by using the oxygen flush valve.

(d) Add a sufficient flow of oxygen through the low-range flowmeter to maintain a constant pressure of 30 cm water in the breathing system. The oxygen flow required to maintain the pressure is a measure of the leak rate. This test may be abbreviated by using an oxygen flowrate of 100 ml/minute. If pressure in the system increases, the breathing system is below the maximum allowed leak rate.
(e) Determine the presence of check valves downstream from the flowmeters by consulting the manufacturer or a serviceman. These valves must be tested differently. With oxygen flowing as indicated in (d), briefly turn off in turn each flowmeter which is equipped with a check valve until there is a rise in pressure on the absorber gauge. An increase in pressure indicates absence of leakage in the circuit tested.

High-Pressure Components: Hose Connections at Wall to Flowmeters

High-pressure components include wall connectors, supply hoses, connectors at rear of gas machine, and plumbing within the machine up to the flowmeter control valves. Potential leak sites are numerous and leak testing with conventional methods (soap solution) is cumbersome. A convenient method for rapidly testing all rooms in the suite employs the infrared nitrous oxide analyzer. The principle of the test is that at a given fresh air exchange rate, provided by the air-conditioning system and assuming perfect mixing of gases, a given leak rate of nitrous oxide into the room air equilibrates at a predictable concentration. A relatively leak-free high-pressure system will contribute less than 1 ppm nitrous oxide to the room concentration. Room concentrations in excess of 5 ppm nitrous oxide indicate excessive leakage, which should be corrected. High-pressure leak tests should be conducted quarterly.

(a) Do not use the machine for at least 1 hour prior to the test. High pressure hoses must be attached.

(b) Use a nitrous oxide analyzer in each room to determine and record the nitrous oxide concentration.
Scavenging Tubing

Scavenging tubing leading from relief (popoff) valve to interface, if used, to disposal system is leak tested quarterly.

(a) Pressurize the tubing to 10 mmHg.

(b) No pressure drop, except for the initial fall due to stretching of materials, should be noticeable during a 15-second observation period.

Ventilators and Miscellaneous Equipment

No reasonably simple rapid method has been developed to screen ventilators for leakage. Careful assembly following cleaning and quarterly preventive maintenance by qualified servicemen will minimize leakage. When unexpectedly high nitrous oxide concentrations are detected during surgery, the ventilator should be suspected. In cases involving excess leakage, connect the ventilator to the anesthesia machine in conjunction with a test lung, and search for leakage using a gas analyzer, soap solution, etc.

Other equipment such as special bags not associated with the circle system, tubing, and miscellaneous accessories should be inspected at least quarterly.

Accessory Flowmeter: Pressure-Gauge Method

If the anesthetic machine is not equipped with a low-range flowmeter or pressure gauge, they can be applied at the anesthetic gas outlet by attaching a "T" connector in the gas delivery tubing. The low-pressure leak test procedures are then completed, with the precaution that the
tubing be occluded between the absorber and the "T."

**Immersion Method for Localizing Leakage in Absorber**

Employ immersion testing to identify leakage not found by less cumbersome methods. Prepare the machine according to the first three steps in the low pressure test. Precaution must be taken concerning pressurization and the possibility of subsequent damage to the pressure gauge. Caution: the gauge must be kept dry, and screening should be installed if necessary to prevent soda lime from entering the breathing-hose connectors.

**Tests to Determine Leakage in Miscellaneous Equipment**

Equipment such as breathing bags, hoses, and devices with metal-to-metal connections suspected of leakage are tested by standard procedures (standard soap solution, leak detectors, and pressurization-immersion).

Leakage from ventilators exists when trace gas concentrations increase when ventilators are in use. After cleaning, inspect the components and assemble with care, checking that all gaskets are in place and properly fitted.