listed in table 3. The barometric pressure in Denver is 630 mm. of mercury, so the percentage values are about 76/63 as high as though the values had been calculated for sea level. The high concentrations of fluroxene required were surprising.

The period required for waking is listed in table 4. As might have been expected[5] the waking times were in the same order as the blood/gas and oil/gas solubilities, although they were not closely proportional in this small series. Inasmuch as the concentrations offered the dog were greater than the exhaled concentrations, the animals were still absorbing the anesthetic gas and had not actually reached a *steady state* at the end of the anesthetic period, even though the anesthesia was clinically smooth. Generally speaking, fluroxene and halothane which have lower solubilities permitted reasonably rapid waking, while halopropane and methoxyflurane kept the dogs asleep for a considerable time.

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Impurity in Stored Halothane

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Cohen *et al.*[1] suggested in September, 1963 that the use of copper vaporizers in this country as opposed to nickel-plated or glass vaporizers in many other countries may be significant. They identified one of the impurities in freshly opened and stored halothane as a halogenated butene, 2,3-dichloro-1,1,1,4,4,4-hexafluorobutene-2. These authors reported further that this drug was toxic to dogs when inhaled in anesthetic concentrations, and to rats when exposed to a 0.01 per cent concentration for four hours. They noted that when halothane was refluxed in the presence of copper filings in an oxygen atmosphere the concentration of the halogenated butene increased. These investigators observed that under their conditions of clinical usage the concentration of this contaminant had increased from 0.01 per cent to 0.1 per cent during a five-day period while stored in a Copper Kettle vaporizer. The implication in their presentation was that the chemical reaction produced in their laboratory was duplicated in the copper vaporizers, and that under clinical conditions 2,3-dichloro-1,1,1,4,4,4-hexafluorobutene-2 was formed from halothane. They stated, in addition, that fractional distillation resulted in a *radical* enrichment of the content of the compound in the residual volume.

The above report prompted us to evaluate the practice of storing halothane in our own institution, and to determine the amount of contamination in available samples. The residual halothane in each of eight anesthetic

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machines was drained in the morning before fresh halothane was added to dilute the contents of any reservoir. Vaporizers included the Copper Kettle, the Vernitrol and the Fluotec. The specimens were collected in new, clean, stoppered, glass containers. No fixed policy for emptying and cleaning the vaporizers had been set prior to this time, and unquestionably the residue in most of these had accumulated for many months.

Quantitative analyses by gas-liquid chromatography were carried out on the eight samples obtained from the vaporizers and on one sample of halothane as supplied commercially by the manufacturer, using a calibration sample having a content of the butene derivative specified by the Ayerst Laboratories.† The chromatograms were obtained with a modified Perkin-Elmer Model 154-C Gas Chromatograph. The sampler used for the introduction of gas phase samples employed two detectors in a series: a thermistor thermal conductivity (TC) detector, and a hydrogen flame ionization (HF) detector. The samples were separated on a 20 feet × 1/4 inch copper column packed with 20 per cent Dow-Corning silicone oil No. 550 (SO) on 60–80 mesh Chromosorb P.

The compound, $CF_3CCl = CClCF_3$, may occur as either of two geometric isomers, the *trans* or the *cis* form. In general, the *trans* form is energetically more favorable, and, in fact, this was the preponderant form encountered in all of the specimens, as well as the largest single contaminant. This latter isomer was, therefore, the principal subject of our attention.

TABLE 1. Content of *Trans*-$CF_3CCl = CClCF_3$

Sample	Vaporizer	Per Cent by Weight
Operating Room		
1	Venitrol	0.0352
2	Vernitrol	0.0408
3	Copper Kettle	0.0408
4	Fluotec	0.0362
5	Vernitrol	0.0354
Delivery Room		
106	Vernitrol	0.0537
107	Fluotec	0.0387
112	Fluotec	0.0432
Commercial halothane		0.0285

On table 1 we note that the percentage of trans-$CF_3CCl = CClCF_3$ by weight was 0.0537 in a Vernitrol machine in Delivery Room 106. This was the only vaporizer in which the concentration was higher than the 0.05 per cent maximum standard maintained by the manufacturer. The next highest concentration was 0.0432 per cent, found in the Fluotec vaporizer in Delivery Room 112, and thirdly 0.0408 per cent in Operating Rooms 2 and 3, in Copper Kettle and Vernitrol vaporizers, respectively. There is thus nothing to suggest that a greater disposition to produce trans-$CF_3CCl = CClCF_3$ from halothane exists in the Copper Kettle than in the other types of apparatus.

The higher concentrations of this butene derivative in the stored specimens as compared to the fresh commercial specimen can be reasonably explained by the different boiling points of the two chemicals, namely, 35° C. for halothane and 66° for $CF_3CCl = CClCF_3$. This results in an enrichment of the proportion of this drug due to increased vaporization of halothane. Refilling after partial evaporation will lower the halogenated butene concentration, but it will remain higher than that in the fresh specimen. Repetition of the vaporization and refilling process may bring about further increases, but the limiting concentration for the full container will be that at which the vapor phase has the same partial pressure as the liquid phase used for refill. Whenever evaporation occurs from a liquid with a butene concentration in excess of the limiting concentration, more butene will be lost from the container than will be added in the refill.

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† R. J. Reitz, Chief of the Physical Measurements Laboratory, The Mellon Institute, Pittsburgh, Pennsylvania, performed the quantitative analyses.