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A method to determine respirator protection factors using biological monitoring of exhaled air

Decker, John Alan, M.S.
The University of Arizona, 1990
A METHOD TO DETERMINE RESPIRATOR PROTECTION FACTORS
USING BIOLOGICAL MONITORING OF EXHALED AIR

by

John Alan Decker

A Thesis Submitted to the Faculty of the
DEPARTMENT OF PHARMACOLOGY AND TOXICOLOGY
In Partial Fulfillment of the Requirements
for the Degree of
MASTER OF SCIENCE
WITH A MAJOR IN TOXICOLOGY
In the Graduate College
THE UNIVERSITY OF ARIZONA

1990
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[Date] July 18, 1990
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The purpose of this study was to develop methodology involving the use of biological monitoring of exhaled air to determine respirator protection factors. The concentration of fluorocarbon 113 in breath was correlated to the original exposure concentration while wearing a full facepiece negative pressure respirator. Protection factors calculated from breath sampling were compared to fit factors derived from a negative pressure test device.

Although biological monitoring indicated a nearly three fold increase in fluorocarbon 113 penetration rates compared to the negative pressure fit test results, a correlation of 0.86 suggests that this methodology may be used in the design of a workplace protection study. No correlation was found between the biological and quantitative mask sampling methods.
INTRODUCTION

Respirators are widely used as a control strategy to protect workers from harmful atmospheres in many industries. It is estimated that over two million American workers rely on respirators to protect themselves from the inhalation of toxic substances in the work environment (Rosenthal and Paull, 1982).

The degree of protection provided by a respirator is related to the extent that the respirator is actually used in harmful atmospheres, the ability of the respirator cartridge to remove the contaminants, and the effectiveness of the seal between the respirator and the face of the subject. The American National Standards Institute, Inc. (ANSI) has published a national consensus standard addressing the use of respiratory protective equipment (ANSI Z88.2, 1980). According to the ANSI standard, an integral part of a respiratory protection program must include respirator fit testing. Furthermore, when respirators are used as part of a company's respiratory protection program, fit testing is mandated under federal law. OSHA section 1910.134(e)(5) in the Code of Federal Regulations outlines a general industry standard for respiratory protection. It requires that an employer must provide respirator fit testing to insure that the respirators issued to its employees will provide an adequate level of protection.
Many of the guidelines published in ANSI Standard Z88.2 have been incorporated by reference into OSHA laws.

Sources of Leak into a Respirator

Leakage into respirators may occur at the sealing periphery between the facepiece and face, through the respirator cartridges, and at the exhalation valve. Contaminant penetration through the faceseal pathway is the most critical cause of leakage affecting the protection provided by a respirator. The causes of faceseal leakage include:

1. Design and size of the respirator
2. Facial characteristics
3. Training of the wearer

Leakage through the cartridges and exhalation valve are more easily characterized and controlled than faceseal leakage.

Respirator Fit Testing

Qualitative Fit Tests. Currently, respirator fit testing can be performed by one of two methods, quantitative or qualitative fit testing. Qualitative fit tests rely on a respirator wearer's subjective ability to detect by odor or taste a designated test chemical. Commonly used test chemicals include isoamyl acetate, saccharin, and irritant smoke (Prichard, 1976). For example, if isoamyl acetate is used as the challenge agent, the respirator does not fit properly when the individual can detect the banana-like odor of isoamyl acetate.
Other qualitative fit tests are based on negative and positive pressure that is induced in the respirator mask by the individual's lungs. This type of fit test provides gross estimates of fit and are usually performed immediately after an individual puts on a respirator.

Unfortunately, qualitative fit tests are subjective, and accuracy and reproducibility are variable. A major disadvantage of qualitative fit testing is that different individuals have varying odor thresholds. Furthermore, olfactory fatigue may occur during the test, impairing the subject's ability to detect leakage. Qualitative fit testing provides limited information about respirator fit since the method lacks numerical documentation. Nonetheless, qualitative fit testing methods predominate in industry because they are inexpensive and simple to administer.

Quantitative Fit Testing. Quantitative fit tests involve exposure of a respirator wearer to a test atmosphere containing a detectable aerosol, vapor or gas which has a low order of toxicity. Instrumentation is utilized to sample both the test atmosphere and air within the respirator to assess the effectiveness of fit. With this information, a quantitative fit factor can be determined. The fit factor is an index that rates the effectiveness of respirator fit. It is calculated by dividing the
concentration of challenge agent within the exposure chamber by the concentration within the respirator mask.

Another type of quantitative fit test utilizes negative pressure instead of a chemical tracer. An exhaust pump removes air from the sealed respirator at a rate that generates a designated negative pressure inside the respirator. The designated negative pressure is set to approximate the negative pressure generated during an inhalation. The rate of air exhausted from the mask is used as a direct measure of the leakage rate into the mask. (Eroh, 1986). The leakage flow rate is divided into the theoretical mean inspiratory flow rate to calculate a fit factor.

Problems with Quantitative Fit Testing The data generated by quantitative fit testing is subject to various parameters that bias the measurement of airborne contaminant concentrations within a respirator. A study by Myers, et al. (1986) utilized acetone as a challenge agent to document in mask sampling bias. Aerosol sampling bias ranged from -99% to +98%, with a mean bias of -17%. Parameters that biased measurement of airborne contaminants within a respirator included:

1. Probe location on respirator midline.
2. Depth of probe within the respirator.
3. Leak site.
4. Breathing distribution pattern.
5. Sample rate from the respirator.
Myers' research demonstrated that faceseal leakage does not mix immediately or uniformly within the respirator. It is thought that during inhalation, streamlining of faceseal leakage occurs within the mask. The location of the streamlines with respect to the location of the sampling probe may contribute to the sampling bias. For this reason, NIOSH has recommended revising the sampling probe type and probe location within the respirator mask.

Aerosol leakage rates into respirators are also particle size dependent. Holton and Willeke (1987) reported maximum leakage into a respirator using aerosol sizes of 0.2 - 1.0 micrometer count median diameter. Holton (1987) questioned the accuracy of using quantitative aerosol fit tests since the true protection factor is dependent on the size of aerosols in the workplace. Standard aerosol quantitative fit tests utilize polydispersed aerosols between 0.1 and 1.0 micrometer count median diameter, which differs from conditions typically found in many industrial environments.

Other sources of error in quantitative fit test systems include lung deposition, measurement method, inaccurate collection time, imprecise sample flow rate from the mask, different head and facial movements, and breathing rates during work activities. Many of these sources of error have not been studied extensively.

**Respirator Protection Factors** Respirator fit factors
are intended to be used as measures of the anticipated protection from harmful atmospheres in the workplace. For example, NIOSH assigns a minimum protection factor of 10 for a half-mask negative pressure air purifying respirator with carbon cartridge filters. In the case where an industrial environment is contaminated with 500 ppm of an organic vapor, it is assumed that the maximum exposure of a worker wearing such as respirator will not exceed 50 ppm. It is generally expected that a respirator should provide a level of protection, if properly worn and maintained, that is equal to or greater than the assigned fit factor of 10. The relationship between measured respirator fit factors and actual worker protection factors has not, however, been demonstrated. Instead, the relationship is based on results extrapolated from laboratory fit factor tests in which a group of respirator wearers perform a specific regimen of head and body movement while in a test chamber containing a challenge agent. The question of whether workplace protection factors do indeed equal or exceed the assigned fit factor values has not been demonstrated. Complicating the question of workplace protection factors is the debate over the validity of data generated by quantitative fit test systems.

**Workplace Protection Factors** Workplace protection factors are determined by calculating the ratio of the time-
weighted average (TWA) concentration within the facepiece cavity to the TWA concentration of contaminant outside the respirator as it is worn in the actual work environment. Workplace protection studies have been performed in environments where workers were exposed to lead, copper, and cadmium (Myers et al., 1984; Lenhart et al., 1984; Grauvogei, 1986; Moore et al., 1976; Smith et al., 1980). The studies utilized conventional methods of determining workplace protection factors, which are confounded by sampling biases previously explained. Furthermore, there were no efforts to compare the actual workplace protection factors to results of respirator fit factor tests.

A few workplace protection studies have involved workers in lead smelters. A notable study was performed by Grauvogei (1986). He compared fit factors utilizing conventional quantitative methods with blood lead levels. Biological monitoring of blood lead levels was feasible because:

1. Atomic absorption, a highly sensitive analytical technique, allows the detection of low blood lead levels.

2. Since blood lead levels do not immediately change as the result of abrupt changes in lead exposure, routine blood sampling is simplified.

3. Methodology and Biological Exposure Indices (BEI's) for blood lead levels in the work environment have been established by the American Conference of Governmental Industrial Hygienists (ACGIH, 1989).

Specifically, Grauvogel studied the effectiveness of a
positive pressure respirator for controlling lead exposure in acid storage battery manufacturing. The results indicated that the lead exposure levels inside the air helmets generally corresponded to the blood levels, which were taken at two month intervals. Quantitative fit factors ranged from 2 to 74. Inhaled lead exposures (while wearing respirators) below the action limit for lead were consistent with low lead blood levels for most workers. Deviations were attributed to the employees' personal hygiene since oral ingestion can be a significant route of uptake. The study, however, did not attempt to calculate protection factors based on lead blood levels, but only indicated general trends which were compared to the calculated quantitative fit factors.

Respiration Processes and Breathing

Respiration Processes. Respiration is divided into two related processes: internal respiration and external respiration. Internal respiration is the exchange of oxygen and carbon dioxide between the internal cells of the body and interstitial fluid. External respiration is the exchange of gases between the alveoli in the lungs and the blood within the capillaries that surround the alveoli. Ventilation is the process in which air moves in and out of the lungs during breathing (Ganong, 1979).

Lung Volumes. The amount of air that enters the lungs
during quiet breathing is known as the tidal volume. The tidal volume is about 0.5 liter. Of this volume, only 350 milliliters actually ventilate the alveoli. The difference (approximately 150 milliliters) that does not ventilate the alveoli is known as the anatomical dead space. The anatomical dead space includes the volumes between the nose or mouth and the bronchioles. The volume exhaled by an active expiratory effort after passive expiration is the expiratory reserve volume. The expiratory reserve volume is typically 1.0 liters in males and 0.7 liters in females (Ganong, 1979).

The vital capacity is the greatest amount of air that can be expired after a maximal inspiratory effort. The ventilation rate is generally about 6 liters/minute (500 ml/breath X 12 breaths/minute) at rest, equating to an alveolar ventilation of about 4.2 liters/minute. The maximum voluntary ventilation is the maximum amount of gas that can enter and exit the lungs in one minute. Normally, it is about 125 to 170 liters per minute (Ganong, 1979).

Uptake and Elimination of Gases and Vapors.

Gas exchange in the lungs is dependent on the volume of air and capillary blood in contact. The lung surface area between the blood and air is about 100 square meters. Gases and vapors are transferred across the alveolar membrane by passive diffusion. The rate of diffusion may be described
by Fick's Law of diffusion and the associated coefficient of
diffusion. The coefficient of diffusion is high enough for
oxygen, carbon dioxide, and carbon monoxide to assume
complete equilibrium between capillary blood and alveolar
air. Much less information is available about industrial
chemical vapors, but most are sufficiently lipid soluble to
also assume complete equilibrium.

Uptake and Elimination of Vapors as Reverse Processes.
Vapors may be absorbed through the mucous membranes and the
alveolar membrane of the lung. Absorption is rapid because
of the large surface area of the alveoli. Arterial blood
transfers an inhaled vapor from the lungs to the tissues.
Since some of the vapor is retained by the tissues, the
concentration of vapor in arterial blood is greater than the
concentration of venous blood exiting the tissue.
Eventually, the concentration of vapor in the tissues
increases until a steady state situation occurs. This
process is known as saturation. When a subject leaves the
contaminated atmosphere, or when the exposure concentration
is reduced, the reverse process occurs. The concentration
of vapor in arterial blood entering tissues is less than the
concentration of vapor in the exiting venous blood, until
all of the vapor is eliminated or a new steady state
equilibrium is achieved. This process is known as
desaturation. Saturation and desaturation are reverse
processes that are controlled by the same principles. The kinetics are complicated in the case of a chemical that is metabolized.

**Partition Coefficients** Although the rate of transfer across membranes is governed by Fick's Law of diffusion, the final equilibrium between the blood and alveolar air is described by partition coefficients of the inhaled gas or vapor (Fiserova-Bergerova, 1980). The solubilities of vapors and gases play a decisive role in their uptake, distribution, and elimination from the body. Partition coefficients are an indication of the solubility of substances. Originally established for gases, they are based on Henry's law of gas solubility in liquids which states that, at a given temperature, the mass of a gas dissolved in a given liquid is directly proportional to the pressure of the gas in equilibrium with the liquid. The application of partition coefficients for gases extends to vapors as well. A partition coefficient indicates how many times the concentration in blood or tissue can exceed the exposure concentration. The rate of absorption and excretion of vapors through the lungs is variable and shows a high correlation with the blood:gas partition coefficient, that is, the vapor's solubility in blood. The blood:gas partition coefficient is dependent on both lipid and water solubility (Fiserova-Bergerova, 1980).
Intrasubject and intersubject variability of partition coefficients can result from variations in hematocrit, lipid content of the blood, body build, cardiac output, ventilation, and metabolic clearance (Fiserova-Bergerova, 1980). The effect of hematocrit on partition coefficients is variable. Coefficients for agents such as ethyl ether and acetone decline with increasing hematocrit. Vapors such as chloroform and ethane show increasing coefficients with increasing hematocrit. Still other vapors, such as trichloroethylene and fluroxene, appear to be independent of hematocrit. (Lowe, et al., 1969; Steward, et al., 1975; Ellis, et al., 1975; Young, et al., 1979)

Since the blood:gas partition coefficient is partially dependent on lipid content of blood, and the lipid content is partially dependent on dietary intake, it is rational to expect that the coefficient would be affected by the ingestion of food. Fiserova-Bergerova and Holiday (1980) investigated seven lipid soluble vapors to determine the effect of meals in exposed subjects on blood:gas partition coefficients. In a study involving five subjects, it was found that the partition coefficients increased after meals. Partition coefficients increased the most for the highly lipid soluble vapors. Generally, vapors with blood:gas partition coefficients greater than 5 were most significantly affected by meals. According to this study,
the effect of a meal on a blood:gas partition coefficient can be estimated by the following equation derived from experimental data:

\[ y = 0.61x + 0.246 \]  

[Equation 1]

where, \( y \) = partition coefficient after fasting  
\( x \) = partition coefficient after eating

Equation 1 indicates that blood:gas partition coefficients increase after eating.

Body build, mainly fatty tissue, is an important variable that affects the kinetics of a vapor in the body. Body build affects the clearance of lipid soluble vapors more than less soluble vapors. In experimentation performed by Fiserova-Bergerova (1980), lipid soluble vapor concentrations in obese individual's tissues were lower than in thin individuals. However, slim people were observed to have faster pulmonary clearance than obese people when exposed to the same vapor concentrations. Droz and Guillemin (1986) found small differences between different body builds in breath concentrations taken 0.5 hour after termination of exposure, but large differences in concentrations when taken 15 hours after termination of exposure. This was attributed to redistribution of vapor into tissues having a high adipose content. Alveolar ventilation and cardiac output for different body builds can be adjusted in proportion to body surface area using

Values of Partition Coefficients. The values of partition coefficients range widely depending on their solubilities. Among the chlorofluorocarbons, there are significant differences in partition coefficients. Table I lists partition coefficients for selected chlorofluorocarbons. Fluorocarbon-113 is considered to be a low solubility vapor, with a partition coefficient of 0.8 (Morgan, et al, 1972). Since the water solubility of fluorocarbon-113 is 0.017 g/100 ml water (Weist, 1975), the value of the blood:gas partition coefficient must depend heavily on its lipid solubility. The olive oil:gas partition coefficient for fluorocarbon 113 is 32.0 (Morgan, et al, 1972). Substances with greatly differing solubilities have much different partition coefficients. For example, acetone has a blood:gas partition coefficient of 245 in man (Sato, et al, 1979), while sulfur hexafluoride has a value of 0.0064 (Wagner, et al, 1974).

As previously discussed, the blood:gas partition coefficient strongly influences the rate of absorption and excretion of vapors through the lungs. If a vapor has a very low solubility in blood, the rate of transfer is most dependent on cardiac output. That is, the vapor requires a large volume of exposed blood to dissolve a given amount of vapor. Increasing respiratory rate would increase the
### Table I

<table>
<thead>
<tr>
<th>Chemical Vapor</th>
<th>Partition Coefficient</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dichlorodifluoromethane (Fluorocarbon-12)</td>
<td>0.15</td>
<td>Niazi, 1974</td>
</tr>
<tr>
<td>Chlorodifluoromethane (Fluorocarbon-22)</td>
<td>0.9</td>
<td>Fiserova, 1983</td>
</tr>
<tr>
<td>Dichlorotetrafluoroethane (Fluorocarbon-114)</td>
<td>0.15</td>
<td>Niazi, 1974</td>
</tr>
<tr>
<td>Trichlorotrifluoroethane (Fluorocarbon-113)</td>
<td>0.80</td>
<td>Morgan, 1972</td>
</tr>
<tr>
<td>Chlorotrifluoromethane (Fluorocarbon-13)</td>
<td>1.4</td>
<td>Fiserova, 1983</td>
</tr>
<tr>
<td>Trichlorofluoromethane (Fluorocarbon-11)</td>
<td>0.9</td>
<td>Morgan, 1972</td>
</tr>
<tr>
<td>Bromochlorotrifluoroethane (Halothane)</td>
<td>2.6</td>
<td>Saraiva, 1977</td>
</tr>
<tr>
<td>2-chloro-1,1,2-trifluoro-ethyl-difluoromethyl ether</td>
<td>1.9</td>
<td>Steward, 1973</td>
</tr>
</tbody>
</table>

exposure of the vapor to blood, but if the blood is already saturated to an extent, the rate of dissolution of vapor in blood will be slow. For example, sulfur hexafluoride is considered to be a low solubility gas. Cardiac output would be the rate limiting factor for saturation and desaturation of sulfur hexafluoride in the body. On the other hand, if a vapor has a high solubility in blood, the rate of transfer is dependent on the rate and depth of respiration. In this
instance, the blood can absorb any given amount of exposed vapor, even if the cardiac output is low. Acetone, having a very high blood:gas partition coefficient, is rate limited by alveolar ventilation. The transition between these two types of behavior centers around a blood:gas partition coefficient of 1.2 (Cassaret and Doull, 1986). In the more moderate example of fluorocarbon-113, both cardiac output and ventilation rate and depth has an effect in the rate of transfer between the body and the environment. However, it would be expected that cardiac output will have a greater effect than alveolar ventilation.

**Distribution of Gases and Vapors.** The distribution of gases and vapors in the various tissues of the body is dependent on the blood:tissue partition coefficients of gases or vapors in the individual tissues. Many lipid soluble gases and vapors are stored by physical dissolution in neutral fat and tissues which contain a substantial amount of fat. Table II lists the water and fat content of some tissues of adults (Fiserova-Bergerova, 1980). It has been suggested that tissue:gas partition coefficients could be calculated from tissue fat content. Neutral fat is a rather stable reservoir since it has a relatively low blood flow. Because of the low blood flow, the uptake and elimination rate of vapors and gases in fat is slower than that of other structures in the body.
Table II

Fat and Water Content of Tissues in Adults
Normal Values (% of weight of wet tissue)

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Water</th>
<th>Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>79</td>
<td>0.6</td>
</tr>
<tr>
<td>Brain, gray matter</td>
<td>82</td>
<td></td>
</tr>
<tr>
<td>white matter</td>
<td>72</td>
<td>16</td>
</tr>
<tr>
<td>Heart</td>
<td>77</td>
<td>8.3</td>
</tr>
<tr>
<td>Intestine</td>
<td>85</td>
<td>6.5</td>
</tr>
<tr>
<td>Kidney</td>
<td>80</td>
<td>2.4 - 8.4</td>
</tr>
<tr>
<td>Lung</td>
<td>78</td>
<td>1.7</td>
</tr>
<tr>
<td>Muscle</td>
<td>79</td>
<td>7.5</td>
</tr>
<tr>
<td>Skeleton</td>
<td>44</td>
<td>10</td>
</tr>
<tr>
<td>Skin</td>
<td>73</td>
<td>15</td>
</tr>
</tbody>
</table>

Compartmental Theory Associated with the Uptake. Distribution, and Elimination of Vapors in the Body. The different tissues and organs in the body are all compartments which a vapor may or may not enter or leave with different rate constants. The rates of distribution among the various tissues and organs are not greatly dispersed, so the kinetics behave as if the chemical were distributed among one, two, or at the most, a few compartments. A compartment is described mainly by its pharmacokinetic parameters since it may be difficult to define in precise anatomical terms. In a one-compartment model, it is assumed that there are no barriers to movement of vapor within the total body space. Figure #1 illustrates
a typical elimination curve for data that fits a one compartment model. A semilog plot (Figure 2) of the data from Figure 1 yields a straight line (Remington, 1980).

Figure 1: A typical elimination curve for a substance exhibiting ideal one compartment characteristics (Olso, 1980).
Theoretical blood concentration if distribution had been instantaneous upon injection

Half-time, 3.2 hours

Figure 2: An elimination curve for a substance exhibiting ideal one compartment characteristics, plotted as the log of concentration (Olso, 1980).

In a two-compartment model, the body is considered to consist of two compartments in dynamic equilibrium as depicted in Figure #3. The compartment into which vapor is directly absorbed is called compartment 1 or the central compartment. Certain fractions of the blood are part of the central compartment. However, erythrocytes and plasma proteins may behave kinetically as if they were part of compartment 2, otherwise referred to as the peripheral compartment. The peripheral compartment is sometimes referred to as the "tissue compartment," which is misleading.
Figure 3: An illustration of the two compartment kinetic model (Olso, 1980).

since some tissues may be kinetically in compartment 1. The peripheral compartment is closed and communicates with the environment only through the central compartment. Figure 4
(page 34) illustrates diffusion kinetics of a vapor equilibrating between two compartments. A semilog plot of the elimination of vapor over time, displaying two-compartment kinetics, yields a curved line (as opposed to a straight line in a one compartment model). This is illustrated in Figure 5. The decline in concentration is manifested by two monoexponential components which are discernible in the semilog plot of concentration verses time. The method by which these monoexponential components are isolated will be described in the Results section (method of residuals or Feathering) (Olso, 1980).

Effect of Exercise on Uptake, Distribution, and Elimination of Vapors. It is evident that physical workload will have an effect on the uptake, distribution, and elimination of vapors, since cardiac output and ventilation increase. Physical work increases the uptake of vapors and increases the elimination of vapors. When measuring vapor concentrations in breath following cessation of exposure and physical activity, higher concentrations of vapor will be detected in breath. It is reported that the effect is more pronounced for chemicals that have high blood:gas partition coefficients (Droz and Guillemin, 1986).

In a series of experiments by Fiserova-Bergerova (1983), the uptake and effect of exercise of two groups of vapors was studied in man. In group 1, highly soluble vapors were
Figure 4: A display of diffusion kinetics of a vapor equilibrating between two compartments (Olso, 1980).

Figure 5: A semilog plot of concentration verses time for a substance exhibiting two compartment characteristics (Olso, 1980).
studied (xylene, styrene, acetone, and butyl alcohol). The vapors studied in group 2 (methylene chloride, trichloroethylene, and toluene) had lower solubilities than group 1 vapors. It was found that the pulmonary uptake for all vapors increased at work loads of 50, 100, and 150 watts compared to resting conditions. The pulmonary uptake of vapors in group 1 correlated with alveolar ventilation, and the percentage uptake increased with increasing workload. The situation was different for group 2 vapors. The uptake was largely increased by the first work load (50 watts), but further work load increases had little or no effect on pulmonary uptake. The difference between the two groups of vapors was attributed to different equilibration rates in tissues. Because of the high solubility of the vapors in the first group, no tissue approached equilibration during the exposures at different work rates. Therefore, when cardiac output and ventilation rate increased, the rate limiting effect of blood flow to the tissues was reduced, and uptake was enhanced.

The ability for retaining vapors in the second group was smaller. While resting, the well perfused tissues quickly equilibrated, but the concentration in muscle and adipose was low as the result of the rate limiting effect on perfusion to these tissues. Therefore, the increased pulmonary uptake during exercise in the second group (low
solubility) vapors was caused by increased uptake by tissues that have increased perfusion during exercise. At the 50 watt level of work, the exercising muscles probably reached equilibration. Further increases in work rate enhanced uptake into adipose, but since only a small percentage of cardiac output is delivered to adipose tissue, pulmonary uptake increased very little.

Pulmonary ventilation and cardiac output can be artificially modified for physiological reasons that may not be readily apparent. For instance, anxiety during breath sampling could cause hyperventilation. Both hyperventilation and hypoventilation can influence the behavior of a toxicant absorbed into the blood or released from the blood.

**Percutaneous Absorption of Gases and Vapors**

Most of the data in the literature refers to liquid penetration of chemicals through the skin. The diffusion rate for nonpolar chemicals is related to lipid solubility and inversely related to molecular weight (Marzulli, et al., 1965). Jacobs, et. al., (1990) found that percutaneous absorption of vapor was less than absorption through liquid contact for benzene, toluene, and butanol. Information on the penetration of gases and vapors through the human skin is limited because of ethical problems associated with human exposures. Nerve gases, such as sarin, are easily absorbed
through intact skin (Casarett and Doull, 1986). McDougal, et. al. (1990) studied the penetration of styrene, xylene, toluene, perchloroethylene, benzene, halothane, hexane, and isoflurane through the skin of rats. It was found that permeability constants ranged from 1.75 cm/hr for styrene to 0.03 cm/hr for isoflurane. The permeability constants for rats were estimated to be 2 to 4 times greater than in humans.

Breath Sampling.

Uses of Breath Sampling. Breath sampling is generally restricted to volatile substances, either gases or vapors. It is possible, however, that workers exposed to certain nonvolatile substances might metabolize the substance into a volatile one, which would allow breath sampling. Breath sampling may be used for different purposes:

1. Identification of worker's exposure to chemicals. Breath sampling is used to determine if the worker has, indeed, been exposed to a chemical.

2. Evaluation of extent of exposure. This data may be used to complement traditional environmental sampling methods by taking into account factors that influence the amount of chemical received, such as ventilation rate, workload, skin absorption, and oral ingestion.

3. Assessment of body burden of a chemical. The actual dose received by the worker can be determined, which should correlate more closely to toxic effects.

Generally, breath sampling is not appropriate for reactive gases such as hydrogen chloride or nitrogen oxides (American Public Health Association, 1989).

**Characteristics of Breath Samples.** Breath is not a homogeneous mixture of gases and vapors. The portion of breath sampled is important since there is a changing concentration gradient from the alveolar air in the lung to the air in the mouth. The concentration of a vapor in breath will vary according to the portion of breath sampled during a breathing cycle and the history of the air parcel within the lung. The concentration of vapor exiting different regions of the lung can vary as a result of varying ventilation/perfusion ratios, diffusion capacities, accessibilities, etc. (Droz, et al., 1986).

**Composition of Alveolar Air.** The composition of dry atmospheric air compared to alveolar air is presented in Table III (Ganong, 1979). The composition of alveolar air is remarkably constant, at rest and under a variety of other conditions as well. Traces of other gases such as methane from the intestines are also found in breath. Ethanol and acetone are present in expired air when present in the body. In fact, over 250 different volatile substances have been detected in human breath (Ganong, 1979).

**Alveolar Breath Samples.** The air that is in intimate contact with the bronchioles and alveoli within the lung is
Table III
Comparison of Dry Atmospheric Air and Alveolar Air

<table>
<thead>
<tr>
<th></th>
<th>Dry Atmosphere</th>
<th>Alveolar Air</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen</td>
<td>21%</td>
<td>13.1%</td>
</tr>
<tr>
<td>Nitrogen</td>
<td>78%</td>
<td>74.4%</td>
</tr>
<tr>
<td>Other</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Carbon Dioxide</td>
<td>0.04%</td>
<td>5.3%</td>
</tr>
<tr>
<td>Water Vapor</td>
<td>-</td>
<td>6.2%</td>
</tr>
</tbody>
</table>

termed "alveolar air." It is best to limit breath sampling to alveolar air, the air at the end of a forced exhalation maneuver. Alveolar air provides the highest consistency in breath sampling, since the anatomical dead space is not contributing variable portions of the sample. The air within the anatomical dead space is a mixture of atmospheric and alveolar air. Air in the alveolar region is in intimate contact with blood, and is therefore most representative of blood concentrations of vapor. The desaturation curves for gases and vapors in alveolar air parallel blood concentrations for benzene and toluene (Sato, 1977).

Sampling Time. The degree to which breath samples represent exposure depends to a large extent on the sampling time chosen with respect to exposure. Breath sampling is usually performed after a given amount of time following the exposure. In the case of a substance that exhibits two
compartment kinetics, the rate of change in concentration after the initial rapid elimination from the central compartment is substantially reduced. When the change in breath concentration is small, a reduced variability and increased reproducibility of the sampling is possible. A disadvantage of taking breath samples during or immediately after exposure is that the breath is essentially a reflection of instantaneous uptake and does not correlate with average exposure in variable environments.

**Sampling Techniques.** Industrial hygienists have long used sampling bags made of various materials in order to sample gases or vapors in the workplace. Advantages of sampling bags are their relatively low cost, ease of use, and the ability to sample large volumes. The type of material used to construct a sample bag will affect wall losses and other reactions. Materials that have been used in sampling bags are Mylar, Teflon, and Tedlar (American Public Health Association, 1989). The porosity of a bag material with respect to the type of analyte being sampled must be taken into account. Sampling bags can be reused, but several flushings with clean air may be required. Bleed out of analyte from the previous sample may occur, invalidating a new sample. Since breath is nearly saturated with water vapor, water condensation within the bag may limit its reuse.
**Glass Tubes.** Breath sampling tubes made of glass suffer less from problems of diffusion and adsorption on the wall surface, and are easily washed, thermally desorbed, disinfected, and reused. The subject simply breaths through the tube and the tube is appropriately capped. The samples, however, are limited in size and the glass tubes are breakable. It has been found that warming a glass sampling tube to body temperature (37 °C) reduces wall losses for certain chemicals (Pasquini, 1975). Warming the tubes is thought to reduce wall losses that result from analyte adsorption or other interactions on the glass and condensation losses resulting from dissolution of the vapor in breath condensate in the tubes. Additional heating of glass tubes can result in increased leakage due to pressure build-up in the tubes and glass breakage (Pasquini, 1975).

**Selection of a Tracer Chemical.**

Considerations involved in the selection of a tracer chemical include:

1. The toxicity of the chemical.
2. The ability of the chemical to adsorb onto respirator cartridges.
3. The biological kinetic characteristics involved in the uptake, distribution, and elimination of the gas or vapor from the body.
4. The ability to analytically detect and quantify the chemical substance in breath.
5. The need for the chemical to be chemically inert and non-metabolized in humans.
The tracer chemical used in this project was fluorocarbon 113. The following discussion will explain the rational behind the selection of this particular chlorofluorocarbon.

**Toxicity Criteria.** To reduce risks to human subjects involved in this project, it was decided that the chosen chemical should have an occupational exposure limit of at least 1000 ppm for an eight hour time weighted average. The toxicological characteristics of several chlorofluorocarbons allow this level of exposure. Other classes of chemicals had lower exposure limits or were excluded for other reasons.

**Occupational Limits.** The legal Permissible Exposure Limit (PEL) set by OSHA for fluorocarbon 113 is 1000 ppm for an eight hour time weighted average (Code of Federal Regulations, 1989). An identical limit has been set by the American Conference of Governmental Industrial Hygienists (ACGIH, 1989). There are several other chlorofluorocarbons that have occupational limits of 1000 ppm, but were excluded for other reasons which will be discussed in the next few paragraphs.

**Toxicology of Fluorocarbon 113.** Fluorocarbon 113 is classified as a central nervous system depressant and a mild mucous membrane irritant. It can also act as a simple asphyxiant. Although fluorocarbon 113 is not directly implicated, sniffing high concentrations of
chlorofluorocarbons has resulted in deaths from cardiac arrest, possibly due to cardiac sensitization to epinephrine (Proctor and Hughes, 1988). Exposure of human volunteers indicates that exposure to 4500 ppm for 30 to 100 minutes resulted in impairment of psychomotor performance. Subjects reported decreased manual dexterity, loss of concentration and drowsiness. The effects disappeared 15 minutes following termination of the exposure (Proctor and Hughes, 1988). In dogs, cardiac sensitization to intravenous epinephrine occurred at concentrations ranging from 5000 to 10,000 ppm (Proctor and Hughes, 1988). Mild, transient throat irritation is reported in a few cases where humans were exposed to 500 to 1000 ppm fluorocarbon 113 (Documentation of the TLV, 1985). Fluorocarbon 113 has poor warning properties since it is nearly odorless and its irritant effects are slight and transient at concentrations near the TLV (U.S. Department of Labor, 1978).

Adsorption to Carbon. Carbon cartridge filters on respirators will adsorb chlorofluorocarbons, which is necessary for their use in this study. However, negative pressure respirators with carbon cartridge filters would not normally be used in an occupational environment containing chlorofluorocarbons because of their poor warning characteristics. For instance, OSHA requires the use of supplied air respirators or self contained breathing
apparatus in occupational environments above 1000 ppm fluorocarbon 113 (U.S. Department of Labor, 1978).

Partition Coefficient. Among the fluorocarbons listed in Table I, fluorocarbon 113 has a blood:gas partition coefficient of 0.80 which is high enough to expect sufficient retention in the body so that breath decay curves can be accurately determined. Fluorocarbons 11 and 13 and the anesthetics have a higher partition coefficient, but were eliminated from consideration because of higher toxicity. Fluorocarbons 12 and 114 were judged to have partition coefficients that were too low to achieve sufficient retention in the body. These kinetic characteristics were confirmed by Morgan (1972) in actual experiments involving exposure of humans to fluorocarbons. Fluorocarbons that did not have published blood:gas partition coefficients were not considered.

There were two possible fluorocarbons which could be considered for this project: fluorocarbons 22 and 113. Fortunately, both had a relatively low water solubility (0.011 and 0.017 g/100ml respectively) which would limit dissolution (and loss) problems associated with water condensation in the sample tubes. Furthermore, low water solubility is desirable since dissolution in the mucous membranes of the respiratory tract would be limited. Initially, it was thought that fluorocarbon 22 would be the
preferred fluorocarbon for two reasons. The first reason was that fluorocarbon 22 had a slightly higher partition coefficient, which would result in slightly higher concentrations in breath. Secondly, fluorocarbon 22 is a gas, while fluorocarbon 113 is a vapor. It is simpler to make low concentration standards from a pure gas rather than a vapor, which is liquid at room temperature.

Analytical Sensitivity. The problem with fluorocarbon-22 was analytical. Using the gas chromatography column that was available (J & W Scientific DB-624 megabore 30 M capillary), it was impossible to fully separate the fluorocarbon 22 peak from the oxygen peak. The separation problem resulted from the extremely low boiling point (-28 °C) of fluorocarbon 22 (Weist, 1975). Although an electron capture detector was employed, the sensitivity for fluorocarbon 22 was not as great as expected. The sensitivity is related to the height to width ratio of the peak (number of plates on the column), the number of halogens on the molecule, and the type of halogens (sensitivity decreases with decreasing atomic weight of the halogens) on the molecule. Because of the sensitivity and separation problems, fluorocarbon 113 was substituted for fluorocarbon 22. Fluorocarbon 113 has a much higher boiling point, which allowed excellent resolution from the oxygen peak. Also, fluorocarbon 113 has three more halogens than
fluorocarbon 22, making it approximately 10 to 100 times more sensitive to the electron capture detector (Hewlett Packard Company, 1988).

**Interferences.** As discussed previously, over 250 different volatile substances have been detected in human breath. This leads to the question of interferences in the analysis of fluorocarbon 113. Fortunately, the ECD is most sensitive to halogenated substances, which are generally not naturally present in breath. Fluorocarbon 113 was once used as a fluorocarbon propellant additive to reduce the boiling point of the propellant in aerosol containers. Generally, fluorocarbons have been removed from aerosol containers, but are still used in metered dose inhalers used to administer medications into the lungs. Contamination from this route is unlikely since individuals with respiratory disease are disqualified from this study. Although the ECD will detect other naturally occurring chemicals that contain aldehyde groups, alcohols, and other electronegative atoms, the sensitivity for these substances is much less than for halogenated chemicals. Consequently, the chromatograms of ambient air and breath are nearly identical.

**Physical and Chemical Characteristics.** Fluorocarbon 113, also known as Freon 113 (Dupont), halocarbon 113, or 1,1,2-trichloro-1,2,2-trifluoroethane (CAS # 76-13-1) is a colorless noncombustible liquid.
The following is a list of selected physical data for fluorocarbon 113: (U.S. Department of Labor, 1978)

1. Molecular weight: 187.4
2. Boiling point: 47.6 °C
3. Density: 1.565 g/ml
4. Vapor Density (air = 1): 6.5
5. Vapor Pressure: 284 mm Hg (20 °C)
6. Solubility in water: 0.017 g/100ml

Reactivity: (U.S. Department of Labor, 1978)

1. Reacts with chemically active metals such as calcium, zinc, and magnesium.
2. Hydrogen chloride, hydrogen fluoride, phosgene, and carbon monoxide may be released upon thermal decomposition of fluorocarbon 113.
3. Fluorocarbon 113 will attack some forms of plastics and rubbers.

Metabolism. There is no information in the literature as to whether fluorocarbon 113 is metabolized. Theoretically, it may undergo reductive dechlorination (Casarett and Doull, 1986). Halothane, which is structurally similar to fluorocarbon 113, is metabolized by cytochrome P-450 catalyzed reductive metabolism (Goodman and Gilman, 1980). Approximately 60 to 80 percent of absorbed halothane is eliminated in exhaled air. Of the fraction that remains in the body, about 15 percent is metabolized. The remainder is excreted unchanged by other routes, such as skin (Goodman and Gilman, 1980).
**Research Objective**

The specific research problem addressed is that of developing a methodology involving the use of biological monitoring of expired air to determine respirator protection factors. The project involved evaluating the concentration of 1,1,2-trichloro-1,2,2-trifluoroethane (fluorocarbon 113) in end-exhaled air from subjects wearing respirators in a test atmosphere of the vapor. The amount of vapor in the exhaled air was correlated to known exposure concentrations. The data generated was then directly compared to quantitative fit test data generated by the negative pressure fit test system and the probe sampling fit test method. Measurement of unbiased workplace protection factors would result in accurate risk assessments related to the use of respirators in the workplace. The methodology could be used to objectively examine the correlation between respirator fit factors and workplace protection factors. A relationship between fit factors and workplace protection factors has not been demonstrated. A correlation analysis by Myers (1984) between fit factors and workplace protection factors suggested that no association between them has been demonstrated.
Materials and Methods

Summary of Method

The elimination kinetics of fluorocarbon 113 from the body were characterized for three representative exposure levels (1.25, 6, and 12 ppm for 30 minutes). Biological breath decay curves between 1 and 60 minutes post-exposure were developed at these three exposure levels. The data was used to determine the optimal time post-exposure to sample breath, which would be correlated to original exposure.

Additional exposure concentrations (0.5, 1.2, 6, 12, 30, 50, 60 ppm for 30 minutes) were also performed. End exhaled breath concentrations were measured at 25, 30, and 35 minutes post-exposure. The amounts of fluorocarbon 113 found in breath were correlated to the original exposure concentration.

The next phase involved the use of a subject exposed to a test atmosphere of 500 ppm while wearing respirators. Breath concentrations obtained post-exposure were utilized to calculate original in-mask exposure while wearing the respirator. The protection factors generated from breath monitoring were compared to the negative pressure fit test system and mask sampling data.

Experimental Parameters

Human Subjects. The University of Arizona Human Subjects Committee approved human inhalation exposure to
fluorocarbon 113 under certain restrictions. The exposure was limited to a maximum of 500 ppm for two hours or less while wearing a respirator. The actual experiments were limited to 30 minutes or less. Since NIOSH assigns a minimum protection factor of 10-fold for negative pressure respirators, the net exposure generally did not exceed 50 ppm. Approval was granted for a maximum of seven subjects. The chance of serious adverse effects occurring was judged to be remote because the low exposure concentrations of fluorocarbon 113 relative to a Permissible Exposure limit of 1000 ppm established by OSHA.

One subject was utilized in this study. A screening health history form (Appendix J) was completed for this person. Had there been additional subjects, volunteers who had a stated history of cardiac or respiratory disease would have been excluded.

Exposure Chamber. A Dynatech Frontier Corporation (Albuquerque, NM) Model 222 man test chamber (Figure 6) with airlock bulkhead was used to expose subjects to fluorocarbon 113. The respirator test chamber is an air tight fiberglass chamber in which concentrations of test agents can be maintained during human exposures. Two fan assemblies are present within the main chamber to ensure adequate mixing of vapor. The chamber is nominally 52 inches wide, 76 inches long, and 93 inches tall. The volume is about 3000 liters.
Maintenance of Exposure Chamber Concentrations

Fluorocarbon 113 vapor was produced by bubbling air through a Midget Impinger (#24/40, Pyrex, 30ml) containing liquid fluorocarbon 113. A portable air pump (MSA Model S, part #466118) was used to push air through the impinger. Polypropylene tubing delivered fluorocarbon 113 from the exit port of the impinger to the chamber. A rotameter (100ml/min) and a needle valve were connected between the pump and the impinger to control the flow of air into the impinger and subsequently the vapor into the chamber.
Monitoring of Chamber. The concentration of fluorocarbon 113 was monitored with a Miran 1A infrared analyzer (Wilks Miran 1A-CVF 20 meter cell, variable length), and recorded with a computer (Hewlett Packard Model 85B) and data acquisition control unit (Hewlett Packard Model 3421A). There were three calibration ranges developed on the infrared analyzer. A low concentration range of 1 to 20 ppm was needed to simulate exposures to vapor that would be expected for subjects wearing respirators in an atmosphere containing 500 ppm vapor. An intermediate calibration range of 20 to 70 ppm at a lower pathlength was developed to accommodate low fit factors. A high concentration range was needed for chamber concentrations in the 500 ppm range, which would be used to expose subjects wearing respirators. The procedure for the low concentration calibration range is outlined in Appendix A. The procedure for the intermediate and high concentration ranges can be found in Appendix B.

Respirator. The respirator used in this experiment was a medium sized full facepiece MSA (Mine Safety Appliances) model M3C1 negative pressure respirator. For each exposure the respirator was equipped with new MSA organic vapor cartridges (Type: GMA type fill, part number: 464031).

Characterization of Adsorption Efficiency of Cartridges

The adsorption efficiency of cartridges was determined as
follows:

1. A respirator cartridge in an airtight holder was placed in the chamber.

2. The respirator cartridge was connected by tubing to a high volume pump (Gilian Aircon 520AC, #2543).

3. The chamber was maintained at 500 ppm fluorocarbon 113.

4. The pump drew 15.0 liters per minute through the cartridge for 30 minutes.

5. Air samples were collected from the pump exhaust into a gas sampling bulb (Alltech Associates, 265 ml). The samples were taken for two minutes to ensure that the gas sampling bulb was adequately flushed. Samples were taken at 1-3 minutes, 15-17 minutes, and 28-30 minutes.

6. The samples were analyzed for fluorocarbon 113 by gas chromatography using halothane for an internal standard. The calibration curve used is shown in Figure 22d.

Production of Artificial Leaks in the Respirator

To test a wide variety of leak rates, it was necessary to modify the respirator as follows:

1. Leak produced by a 20 gauge needle placed in the septa covering the mask sampling nozzle.

2. Leak produced by an 18 gauge needle placed in the septa covering the mask sampling nozzle.

3. Leak produced by placing two rubber bands between the mask and forehead.

4. No artificial leak in mask (no modifications).

Calibration Curve for Fluorocarbon 113 in Breath

Loss from Filter flasks

Prior to beginning the calibration procedure, a series of preliminary experiments
were performed. First, it was necessary to determine if there was significant loss of fluorocarbon 113 from the filter flasks (500 ml Kimax No. 27060) which were used to contain the final fluorocarbon 113 breath standards. The loss was evaluated at 13 ppb, 28 ppb, 60 ppb, and 1.0 ppm concentrations over a period of 30 minutes. The concentrations were prepared in the same manner as the breath standards, which are described in Appendix C.

**Analytical Variability** It was also necessary to determine the analytical variability of the gas chromatography method of quantitating fluorocarbon 113. This was determined at 13 ppb, 28 ppb, and 60 ppb. These concentrations are most representative of the amounts expected in breath.

**Calibration Curve** The method utilizes gas chromatography with electron capture detection. The calibration curves were produced by direct injections of fluorocarbon 113 onto the chromatograph. The specific procedures for producing the calibration curve for breath can be found in Appendix C.

**Breath Sampling Tubes** Custom made glass tubes (see Appendix H for specifications and source) with plastic screw caps were utilized to collect breath samples. A teflon lined septa was placed within each cap to seal the tube. A pre-drilled hole in the cap allowed entry of a syringe which
allowed samples to be taken from the tube for analysis.

**Loss from Sampling Tubes** An experiment analyzing the amount of fluorocarbon 113 lost over three hours from breath sample tubes was performed at 25 ppb, 90 ppb, and 420 ppb. This was performed by preparing concentrations using the low concentration breath standard method described in Appendix C, and evaluating the concentration of fluorocarbon 113 at 30 or 60 minute intervals. The only difference here (opposed to Appendix C) is that the final dilution occurred in a breath sampling tube, having an internal volume of 46 milliliters.

**Characterization of Elimination Kinetics**

At three concentrations (1.25, 6, and 12 ppm), breath samples were taken at the following post-exposure times: 1, 3, 6, 10, 15, 20, 25, 30, 35, 45, and 60 minutes. Each exposure concentration was repeated in triplicate and each sample was analyzed in triplicate. The data were used to characterize the elimination curve of fluorocarbon 113 in breath. From this data, the optimal time points were selected for breath sampling could be determined, which would be correlated to original exposure.

**Correlation of Fluorocarbon 113 in Breath to Exposure.**

The concentration of fluorocarbon 113 in breath 30 minutes post-exposure was correlated to actual exposures in the exposure chamber. This was done by exposing the subject
(without a respirator) to fluorocarbon 113 concentrations that are expected while wearing a respirator in an atmosphere containing 500 ppm fluorocarbon 113. The exposure concentrations were 0.5, 1.5, 6.0, 12.0, 30, 50, and 60 ppm (for 30 minutes). Each exposure concentration was repeated in triplicate and each sample was analyzed in triplicate.

The Effect of "Dead Space" on Dose. Increased carbon dioxide content in the dead space of the respirator results in increased ventilation rate. Therefore, when an individual wears a respirator, the total volume of air breathed is increased to overcome the dead space effect of the respirator. To characterize the possible effect of increased ventilation rate on dose, an individual was exposed to 5.0 ppm fluorocarbon 113 while wearing a respirator equipped with particulate filters. The particulate filters allowed full passage of fluorocarbon 113 into the respirator. Breath concentrations were measured and compared to exposures while not wearing respirators.

Characterization of Skin or Clothing Effects.

Absorption of fluorocarbon 113 vapor through the skin was characterized since this effect could confound the results of the project. Residual fluorocarbon 113 vapor in the clothing or hair could also be a source of exposure during the immediate post-exposure period. To reduce the
clothing/hair effect, the respirator continued to be worn for five minutes post-exposure.

To measure the absorption of fluorocarbon 113 through the skin, an individual entered the exposure chamber containing 500 ppm fluorocarbon 113 wearing a Self Contained Breathing Apparatus (SCBA). It was assumed that the SCBA completely eliminated inhalation exposure, since it maintains a continuous positive pressure within the mask. The experiments were run for 15 and 30 minute exposures. It seems reasonable that saturation of the clothing by fluorocarbon 113 would be the same whether the individual was exposed for 15 or 30 minutes. Therefore, if the amount of fluorocarbon 113 detected in breath was the same for the 15 and 30 minute exposures, it could be assumed that clothing desorption after leaving the chamber was causing the exposure. On the other hand, if the concentration in breath was half as much for the 15 minute exposure compared to the 30 minute exposure, it could be assumed that skin absorption of vapor was contributing to the exposure. In this case, the amount of fluorocarbon 113 absorbed through the skin is directly related to the exposure time.

Quantitative Fit Testing by Mask Sampling

During the tests that did not involve artificial leaks produced by needles, tubing was connected between the mask sampling nozzle and a pump outside the exposure chamber. An
MSA Model C-210 #468200 low flow pump was used to fill a six liter gas sampling bag (Calibrated Instruments Co., Teflon lined bag). The pump was set to run at 0.2 liters per minute from the mask, which produced a six liter sample over 30 minutes. The six liter sample was then pumped through a 265 ml Alltech gas sampling bulb. Since the gas sampling bulb had a known volume, the correct amount of halothane internal standard could be injected in the sample. The sample was then analyzed by direct injection on the gas chromatograph, using 5.0 ul injections to avoid overwhelming the detector with high concentrations of fluorocarbon 113.

Quantitative Fit Testing by Negative Pressure.

The negative pressure system used in this research was the same prototype model used by Booth (1989) and Murphy (1989). While maintaining a pre-selected negative pressure within the respirator, the system measures mask leakage flow rate. Negative pressure fit tests were performed prior to entry into the exposure chamber. Some fit tests were also performed following the 30 minute exposure to determine if there was a change in basic fit. At least five negative pressure tests are performed for each experiment; the mean value was used for comparison purposes.

The negative pressure fit test instrument includes the following equipment: a vacuum pump, a mass flow controller, a pressure transducer, a digital volt meter, and a
computerized data aquisition system. The cartridges are replaced by two air-tight manifolds, one of which is connected to the system's pressure transducer and the other to the mass flow controller. The system maintained a negative pressure within the respirator of -0.40 w.g. during testing. Leakage flow rate was measured at a rate of 20 times per second. The average inspiratory flow rate, which is divided by the leakage flow rate to calculate the fit factor, was set at 30 liters per minute. Only leakage flow rates within a 5% pressure tolerance level were measured.

Basic Experimental Procedure

1. **Preliminary Procedures** Prior to experimentation, standard curves were verified to detect contamination or instrumental problems. The glassware was prepared as explained in the Appendix C and alveolar breath samples were taken prior to exposure to ensure that no fluorocarbon 113 or halothane was present in breath or glassware.

2. **Exposure While Wearing a Respirator** Initially, the subject donned a full face piece negative pressure respirator (MSA Model M3Cl) connected to the negative pressure system manifolds (in place of the carbon cartridges). He was then fit tested at least five times using the negative pressure fit test method. The respirator remained in place throughout the experiment.
After completion of the negative pressure fit tests, the manifolds were exchanged for carbon cartridges (Type: GMA fill, part #464031). The subject then entered the chamber containing 500 ppm fluorocarbon 113. For tests not involving artificial leaks produced by needles in the mask, direct mask sampling was performed concurrently, as explained previously. The chamber level was maintained at 500 ppm (± 1 ppm). After exactly 30 minutes of exposure, the subject left the chamber and moved to an uncontaminated environment (outdoors). The respirator was worn for five minutes post-exposure.

3. **Sample Time** Three breath samples were taken at 25, 30, and 35 minutes following termination of exposure.

4. **Breath Sampling Method** Subject breathing was normal post-exposure. At a designated time point, the expiratory reserve volume was exhaled through the tube. One end of the glass tube was sealed with the lips and the other end was left open. While the subject exhaled the expiratory reserve volume through the tube, the distal end of the tube was capped. After the distal cap was secure, the proximal end was removed from the mouth and immediately secured with a cap. This procedure provided an alveolar breath sample.
5. **Addition of Internal Standard** Immediately after the breath samples were collected, 0.3 ml halothane internal standard was added to each of the tubes. The procedure for making the halothane vapor standard can be found in Appendix C.

6. **Storage of Breath Samples** Breath samples were analyzed as soon as possible after collection, usually within 15 minutes following sample collection. Fluorocarbon 113 has been demonstrated to be stable for up to three hours after collection of the breath sample. Details may be found in Appendix H.

7. **Analysis of Breath Sample** Breath samples were analyzed by gas chromatography as explained in Appendix C. Analysis was performed by direct injection of 20 ul of breath. Each sample was analyzed in triplicate, and a mean value was calculated.

8. **Data Analysis** The mean concentration of the three breath samples (25, 30, and 35 minute time points) were plotted as a function of exposure concentration. The mean concentration from the three time points was referred to as the "30 minute post-exposure time." The breath concentration post-exposure was correlated to original exposure.
RESULTS

Calibration Curve for Chamber Exposures

The four calibration curves created with the Miran 1A analyzer can be found in Appendix D. The ranges covered were 0-7 ppm, 0-21 ppm, 20-70 ppm, and 200-750 ppm.

Calibration Curve for Fluorocarbon 113 in Breath

The four calibration curves created by direct injection gas chromatography can be found in Appendix E. The ranges covered were 0.005-0.100 ppm, 0.005-0.300 ppm, 0.100-3.2 ppm, and 0.4-7 ppm.

Analytical Variability Appendix G illustrates the analytical variability of the method for three representative concentrations (13.4, 28.1, and 62.0 ppb). The standard deviation, as a percent of the mean concentration tested, decreased as the concentration increased.

Loss from Kimax Filter Flasks Appendix F contains the results of experiment to determine the loss of fluorocarbon 113 from filter flasks, which contained the individual breath standards used to develop standard curves. No loss was demonstrated over a period of 40 minutes.

Loss of Fluorocarbon 113 from Sample Tubes

Appendix H contains the results of experiments to determine loss of fluorocarbon 113 from breath sampling
tubes. No significant loss was demonstrated when the tubes were stored at 37 °C over a period of three hours. Tubes stored at 25 °C showed some loss.

**Efficiency of Cartridges**

Results of experiments to evaluate the adsorption efficiency of carbon cartridges for fluorocarbon 113 indicated that only 6 to 18 ppb penetrated a cartridge at 15 liters per minute for 30 minutes.

**Breath Decay Curves**

Complete breath decay curves at 1.25, 6, and 12 ppm exposure concentrations were characterized for one subject. Breath samples were collected at 1, 3, 6, 10, 15, 20, 25, 30, 35, 45, and 60 minutes post-exposure. Each curve was repeated in triplicate. Figure 7 illustrates the three breath decay plots. Although the 1.25 and 6 ppm exposure plots appear flatter than the 12 ppm exposure, individual plots of each exposure level using appropriate scaling show that the contour is approximately the same. Figure 8 is a comparison of breath concentrations between 25 and 60 minutes post exposure. Figures 9a, 9b, and 9c illustrate the individual breath decay curves for 30 minute exposures of 1.25, 6, and 12 ppm. After approximately 20 minutes, the rate of change in breath concentrations of fluorocarbon 113 was small and the results are more reproducible. For these reasons, it was decided that breath samples at 25, 30 and 35
minutes would be utilized to predict original exposure concentrations. Since the slope of the curve is essentially flat for time points greater than 20 minutes, the mean concentration of the 25, 30, and 35 minute time points was used for correlation to original exposure.

Figure 7: Concentrations of fluorocarbon 113 in breath following 1.25, 6.0, and 12.0 ppm 30 minute exposures. The error bars indicate ± 1 standard deviation unit resulting from three trials. Each data point from a particular trial is the mean resulting from the analysis of the sample in triplicate.
Figure 8: Concentrations of fluorocarbon 113 in breath following a 1.25, 6.0, and 12.0 ppm 30 minute exposure in a single subject. The error bars indicate ± 1 standard deviation unit over three trials.

Figure 9a: Concentrations of fluorocarbon 113 in breath following a 1.25 ppm 30 minute exposure in a single subject. The error bars indicate ± 1 standard deviation unit for three trials.
Figure 9b: Concentrations of fluorocarbon 113 in breath following a 6.0 ppm 30 minute exposure in a single subject. The error bars indicate ± 1 standard deviation unit resulting from three trials.

Figure 9c: Concentrations of fluorocarbon 113 in breath following a 12.0 ppm 30 minute exposure in a single subject. The error bars indicate ± 1 standard deviation units resulting from three trials.
Modeling of Fluorocarbon 113 Desaturation. Since alveolar breath concentrations of chemicals in expired air parallel blood concentrations, standard pharmacokinetic methods of modeling can be applied to exhaled air desaturation data (Fiserova-Bergerova, 1983). The logarithm of concentration against post-exposure time is plotted, which yields a curved line, indicating a multiexponential expression of desaturation (Figure 10). If the chemical were equally distributed throughout the body and equally eliminated from all tissues, a straight line would fit the experimental data and a one compartment model could be applied. The data for fluorocarbon 113 fits a two-compartment model. The general desaturation equation for a two-compartment model is:

\[ C = Ae^{-a(t)} + Be^{-b(t)} \]  

[Equation 2]

\( C \) = concentration

\( A \) = concentration at time 0 for the central compartment

\( a \) = first order elimination rate constant for the central compartment

\( B \) = concentration at time 0 for the peripheral compartment

\( b \) = first order elimination rate constant for the peripheral compartment

Each rate constant is affected by all compartments and cannot be wholly allocated to any single compartment.
Figure 10: The logarithm of fluorocarbon 113 1.25 ppm 30 minute exposure in an individual subject.

The individual exponential components are isolated using the method of residuals (also called "feathering," after Feathering, who introduced the method). Feathering is illustrated in Figure 11 (Olso, 1980). The peeling of the curve begins from the right hand side of the curve. A straight line is fitted to the tail of the curve (line 1) and extended to the left (dotted line). The antilog of the y-intercept (dotted line 1) is the "B" coefficient in the above equation for a two-compartment model. The half-life is determined as the x-coordinate for the antilog of the y-intercept divided by 2. The elimination rate constant for
line 1 (peripheral compartment) and is calculated by dividing 0.693 by the half life.

The experimental data points obtained during the first 25 minutes deviate from line 1. The differences in concentrations between the dotted line 1 and the experimental values are plotted as the value of the y-coordinate. Since the y-axis is plotted as the log of concentration, the log of the differences in concentration (antilogs of values from graph) between the dotted line 1 and the actual data points must be plotted as the y-

\[ C = 0.1349e^{-0.1754(t)} + 0.032e^{-0.0126(t)} \]

Figure 11: Logarithm of fluorocarbon 113 concentration (ppm) is plotted against post-exposure time (minutes) illustrating the method of residuals for isolating individual exponential components using a two-compartment model. Data is from a 1.25 ppm 30 minute exposure.
coordinates for the respective x-coordinate time points. A straight line is then fitted to the reduced values (dotted line 2). The y-intercept is the "A" coefficient and the "alpha" exponent is calculated from the half life in the same manner as described for the "beta" exponent above (Olso, 1980).

Desaturation equations for 1.25, 6, and 12 ppm exposures were derived using the above method of residuals. At these concentrations, "alpha" and "beta" values were similar (Figures 11, 12a, and 12b). The "A" and "B" coefficients corresponded to exposure concentration (Figures 13a and 13b). The mean half-lives of the central and peripheral compartments were calculated to be 4.2 and 52 minutes respectively.

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![Figure 12a](image)

**Figure 12a:** Diagram of data derived from a 6.0 ppm 30 minute exposure to fluorocarbon 113.
Figure 12b: Diagram of data derived from a 12.0 ppm 30 minute exposure to fluorocarbon 113.

Figure 13a: The "A" coefficient plotted against 30 minute exposure concentrations.
Figure 13b: The "B" coefficient plotted against 30 minute exposure concentrations.

Correlation of 30 Minute Exposure Concentrations to Breath Concentrations 30 Minutes Post-Exposure.

Figure 14 illustrates relationship between breath concentration and original in-mask exposure. The "30 minute post-exposure time" is actually the mean of samples taken at 25, 30, and 35 minutes. At higher concentrations (above 30 ppm), an unexpected non-linearity of the relationship became apparent.

The optimal time to take breath samples was at least 25 minutes post exposure since only the peripheral compartment
(half life of 60 minutes) would be affecting the amount of fluorocarbon 113 in breath. Excretion from the central compartment would not be indicative of a half hour exposure.

Figure 14: Resultant breath concentrations (ppm) 30 minutes post-exposure following a 30 minute exposure to fluorocarbon 113.

The Determination of the Effect of Respirator "Dead Space" on Dose. The individual was exposed to 5.0 ppm while wearing a respirator with particulate filters to assess the effect of increased ventilation on dose. It was found that there was no difference in breath concentrations 30 minutes
post-exposure as compared to trials without the respirator. The mean breath concentration (with respirator dead space) over three trials was 0.081 ppm as compared to the predicted 0.079 ppm from the calibration equation in Figure 14.

Experiments to Assess the Effect of Clothing and Skin Absorption of Fluorocarbon 113 Vapor. The experiment involving the use of an SCBA, which eliminated inhalation exposure to fluorocarbon 113, suggests that skin absorption of fluorocarbon 113 vapor may represent a small but significant route of entry into the body. Table IV lists the data generated from the SCBA experiment. Since the amount of fluorocarbon 113 in breath decreased by approximately 50% when the exposure time was decreased by 50%, the implication is that skin absorption occurred. If release by clothing was a significant source of exposure, it would seem reasonable that the breath exposure occurring post-exposure would be the same regardless of the original exposure chamber time, as previously discussed in the "Methods" section.

Comparison of Fit Factors Derived from the Negative Pressure Method and Biological Monitoring.

The data in Figure 15 (page 76) indicates that the protection factors derived from biological monitoring are about 2.85 times smaller than the fit factors derived from the negative pressure test. That is, the biological
monitoring method indicates that the percent penetration is about 2.85 times greater than with the negative pressure method. A plot of penetration rates comparing the two methods may be found in Figures 16a (page 76) and 16b (page 77). Note that the regression line in Figure 16b goes through the origin when the data in Figure 16a is corrected for skin absorption. The numerical data may be found in Appendix I.

Table IV
Percutaneous Absorption of Fluorocarbon 113

<table>
<thead>
<tr>
<th>Trial No.</th>
<th>Exposure Time (minutes)</th>
<th>Calculated Equivalent Breath Exposure (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30</td>
<td>1.29</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>1.49</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>1.26</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td>1.35</td>
</tr>
<tr>
<td>S.D.</td>
<td></td>
<td>0.10</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>0.61</td>
</tr>
</tbody>
</table>
Figure 15: A comparison of results from the negative pressure method and biological monitoring method (data corrected for skin absorption). Each data point represents a single test.

Figure 16a: A comparison of percent penetration derived from the negative pressure system and the biological method. The biological test data were not corrected for skin absorption.
Figure 16b: A comparison of percent penetration derived from the negative pressure system and the biological method. The breath data were corrected for skin absorption.

Comparison of Fit Factors Derived from Mask Sampling and Biological Monitoring.

A poor correlation was observed between fit factors derived from mask sampling and biological monitoring, as indicated in Figure 17.

Comparison of Fit Factors Derived from Mask Sampling and the Negative Pressure Method.

No correlation existed between fit factors derived from mask sampling and the negative pressure, as indicated in Figure 18.
\[ y = 88.773 + 0.52122 \times (x) \]
\[ r = 0.55 \]

**Figure 17:** A comparison of fit factors derived from mask (probe) sampling and the biological monitoring method.

\[ r = 0.02 \]

**Figure 18:** A comparison of fit factors derived from mask (probe) sampling and the negative pressure method.
DISCUSSION

Maintenance of Exposure Concentrations.

The exposure chamber maintained very stable concentrations of fluorocarbon 113. Generally, the concentration was controlled to ± 1 ppm during the tests. The Hewlett Packard data logger, which recorded data in parts per million each minute, assisted the maintenance of constant chamber concentrations. The greatest disruption in concentration occurred when the individual entered the chamber, which was already set at 2 or 3% over the desired level. This disruption, generally in the order 5 to 10 ppm, could usually be rectified within one or two minutes.

Analytical Technique for Breath.

The gas chromatograph, equipped with electron capture detection, proved to be a reliable, albeit time consuming, analytical method for fluorocarbon 113 in breath. The system is very sensitive to fluorocarbon 113. The limitation of the system for low concentrations of fluorocarbon 113 is not the sensitivity, but the ability to reliably make standards at very low levels (less than 5 ppb). The calibration curves were readily reproducible.

Breath Sampling Tubes, Contamination, and Storage

The glass tubes selected for breath analysis experiments performed as expected. Since very low concentrations of
fluorocarbon 113 were collected in these tubes, it was very important that the tubes be washed and baked in the oven after each use. Tubes which were simply opened to the air for several hours were found to be contaminated with low levels of residual fluorocarbon 113.

Since fluorocarbon 113 exhibits a relatively long biological half-life (nearly an hour) from the peripheral compartment, a space of several hours between experiments on an individual subject was necessary. This observation was a disadvantage when repeating experiments.

Warming breath analysis tubes to 37 °C after taking samples reduced losses to a negligible amount. Increased loss was observed for samples that were not warmed, which is consistent with information in the literature (Pasquini, 1975). Specific information on breath analysis tubes may be found in Appendix H.

**Non-linear Relationship of Breath Concentration to Exposure.**

The reason for the non-linear relationship between breath levels and 30 minute exposures from 30 and 60 ppm is unknown (see Figure 14). One possible explanation might be related to metabolism of fluorocarbon 113 through a rate limited reductive dechlorination by cytochrome P-450. At lower exposures a greater percentage of fluorocarbon 113 might be metabolized than at higher exposures. However, chromatographs of breath did not show additional peaks that
could have accounted for metabolites, although metabolites might be present as organic fluorine compounds in urine.

If fluorocarbon 113 causes a hemodynamic or other physiological change in the body, a change in distribution of fluorocarbon 113 among the tissues in the body might affect the compartmentalization and uptake into the body. There is no information in the literature to support these speculations.

**Comparison of Biological and Negative Pressure Methods.**

The graphs comparing percent penetration calculated by the negative pressure system and the biological exposure method indicated a Pearson's correlation coefficient of 0.86. The spread in the data was greatest for the fit tests that involved extremely small leaks. There were seven tests performed, utilizing a respirator with just face seal leaks (no artificial leaks); there were three tests performed for each of the artificial leak rates. The correlation coefficient would have been greater if more fit tests had been run involving higher leak rates. As previously discussed, the biological method indicated leakage that was nearly three times greater than that measured with the negative pressure method.

**Leakage Resulting from Head Movement.** The nearly three fold difference in penetration rates observed between the negative pressure and biological method cannot be fully
explained at this time. One suggested explanation is related to the fact that the negative pressure test gives an instantaneous fit, while the individual holds his breath and remains perfectly still. The negative pressure tests were performed while the individual's head was straight ahead. However, during the course of the biological method test, the subject was able to move his head freely during the 30 minute exposure.

A study by Boothe (1989), using the negative pressure system, found the position of the head did not significantly affect the amount of leakage into the facepiece. He also found that the basic fit of the mask does not change during the performance of exercise protocols. The results presented here are consistent with Boothe's conclusions. Negative pressure fit tests performed prior to the 30 minute exposure and immediately post-exposure indicated virtually no difference in fit. Therefore, it does not appear likely that the apparent increased leakage into the mask can be attributed to changes in basic fit during the 30 minute exposure to fluorocarbon 113.

Although the basic fit of a mask generally does not change, it seems reasonable that instantaneous changes in fit may occur as a person moves facial muscles or his head during inhalation and exhalation. These effects cannot be characterized using the negative pressure method, since the
person must hold his breath and remain perfectly still during the test. Because of biases associated with the use of quantitative aerosol systems, it does not appear that reliable data exists in the literature to estimate the magnitude of this type of leakage.

**Leakage through the Exhalation Valve.** The passage of fluorocarbon 113 through the exhalation valve would not explain the difference in apparent penetration rates since this type of leak would also be detected by the negative pressure system.

**Efficacy of the Inhalation Valve.** Campbell, et al (1990) found that inhalation valves which allow backflow during the exhalation cycle significantly decreased the protection provided against an acetone vapor challenge. A schematic representation of the hypothesized mechanism is shown in Figure 19. Specifically, it is thought that during exhalation, contaminated air flows past the inhalation valve, is trapped temporarily upstream of the inhalation valve, and reenters the respirator during the next inhalation. The temporary trapping was found to result from two mechanisms: "volume trapping" and "sorbent trapping." Volume trapping is the simple physical trapping of vapor between the sorbent and the inhalation valve. Sorbent trapping involves a temporary trapping on the cartridge sorbent.
Campbell found that the backflow effect caused by the inhalation valve can result in an 80 to 90 percent increase in pulmonary (inhaled) concentration of acetone vapor, using a full facepiece negative pressure respirator.

Since the backflow effect might have been occurring during the fluorocarbon 113 exposures, some of the discrepancy between the biological method and the negative pressure method might be explained by this hypothesis.

Figure 19: The hypothesized mechanism by which an inhalation valve that allows backflow during exhalation can affect the protection afforded by a respirator. In step (a), the components of a respirator are shown. In step (b), clean air is shown flowing through the inhalation valve. In step (c), an inhalation valve that does not result in backflow is illustrated. In step (d), and inhalation valve causing backflow is shown.
Increased Ventilation Caused by Respirator Deadspace.

An increase in apparent penetration rates of fluorocarbon 113 might be related to the increased ventilation resulting from the additional dead-space contributed by the respirator. Increased ventilation increases exposure which might increase dose. As discussed previously, test results indicate that this is not a significant factor, at least in the case of fluorocarbon 113. The concentration in breath was the same, whether the individual wore no respirator or a respirator equipped with particulate filters when exposed to 5.0 ppm fluorocarbon 113 for 30 minutes. This result was expected since fluorocarbon 113 is classified as a low solubility vapor (blood:gas partition coefficient less than 1.2). Its extent and rate of uptake is, therefore, more dependent on cardiac output than ventilation. This observation is generally expected for low solubility gases. Although not addressed in this study, it is possible that some difference in dose resulting from dead space might be amplified and observed under conditions of work or other high metabolic states.

Increased Dose Caused by Rebreathing. At the end of an exhalation the dead space in the respirator contains exhaled air that is rebreathed during the next inhalation. When fluorocarbon 113 is inhaled, only a very small fraction is absorbed into the body through the lungs (Morgan, 1972).
More than 95% of the fluorocarbon 113 that reaches the alveoli in a single breath is exhaled, some of which remains within the respirator. During the next inhalation, the exhaled fluorocarbon 113 plus the additional contribution of leakage during inhalation reaches the lungs. This process continues, resulting in a higher plateau of exposure. The increase in dose resulting from this phenomenon is dependent on the fraction of vapor retained by the body after exhalation. In a worst case situation, as much as a two fold increase in mask concentration can occur (Hinds, 1990). An example calculation is as follows:

Assumptions:
1. less than 5% lung absorption of fluorocarbon 113.
2. 180 ml anatomical dead space.
3. 500 ml tidal volume
4. 500 ml mask dead space
5. 320 ml alveolar ventilation per breath
6. 680 ml total dead space
7. 900 ml total dead space + anatomical space.

Assume that the mask initially contains 0 ppm fluorocarbon 113. The concentration in 500 ml of inhaled air to produce a theoretical 5.0 ppm concentration in 900 ml of total space is 9 ppm. Since in each breath, 500 ml of 9 ppm fluorocarbon 113 is inhaled, and only a very small fraction is retained in the body, the mask concentration will approach 9 ppm after a few minutes.

Efficiency of Cartridges. Experiments to evaluate the efficiency of carbon cartridges for fluorocarbon 113 indicate only small amounts of leakage through the cartridges. The results indicate that only 6 to 18 ppb penetrated a cartridge under conditions of 15 liters per
minute for 30 minutes. A contribution of dose by this route is therefore negligible.

Absorption through Skin. The SCBA experiments indicated that skin absorption is a small, albeit discernable, route of exposure. The equivalent inhalation exposure by skin was about 1.35 ppm (S.D. = 0.10 ppm) when exposed to 500 ppm. This amount of exposure significantly affects fit factors and percent penetration for the experiments involving low leak rates. The leaks produced by artificial means (needles, rubber bands) were so large that the skin effect contributed only a small fraction of the exposure. It is interesting to note that when the percent penetration (biological method) is corrected for skin absorption, the plot comparing negative pressure and biological methods runs through the origin (compare Figures 18 and 19) rather than a "y" intercept.

Further investigation of the effect of skin absorption is necessary. Variations in skin characteristics between individuals may result in changes in skin absorption of fluorocarbon 113. The effect of work and heat stress might affect the absorption of vapor. Increased blood flow to the skin under these physical stresses might increase absorption. Sweat and changes in skin porosity may also affect uptake through skin.

Since skin from different areas of the body absorbs
substances at different rates, future studies should involve whole body exposures, which are representative of workplace conditions.

**Contamination from Clothing, Excretion from Skin.** The experiments indicate that the emission of fluorocarbon 113 from clothing following an exposure is not a significant source of inhalation exposure. In the experiments involving the SCBA, a halving of exposure time resulted in an approximate 50 percent decrease in breath concentrations. If the amount of fluorocarbon 113 in breath was the result of exposures from clothing or hair after removal of the respirator or by direct contamination during breath sample collection, it seems reasonable to expect that the length of exposure would make little difference. Contamination of the breath from the excretion of fluorocarbon 113 from skin has not been investigated. This would not appear to be a significant problem since most fluorocarbon 113 is excreted through the lungs.

**Comparison of the Biological and Mask Sampling Methods.**

No correlation was found between penetration rates derived from biological monitoring and sampling from the mask. As discussed previously, sidestreaming within the mask is a major factor that biases sampling within the mask. Sidestreams can change depending on the location of point source leaks in the faceseal. The results of this study
indicate that mask sampling is an invalid method of
determining the degree of protection afforded by a
respirator.

**Comparison of the Negative Pressure and Mask Sampling Methods.**

A very weak correlation was found between fit factors
derived from the negative pressure method and mask sampling
methods. Again, this is the result of biases associated
with mask sampling which were described above.

**Areas Requiring Further Study.**

*Intrasubject Variability*  When characterizing the
elimination characteristics of fluorocarbon 113, small
shifts in the breath decay curves were observed when
repeating the experiments in triplicate. This might have
been due to the effect of meals (and blood lipids) on the
blood:gas partition coefficient. As mentioned in the
Introduction, mathematical adjustments can be made to
account for the effect of food (Equation 1). Slight
differences in metabolic rate (i.e. amount of walking,
temperature) might also have affected excretion from the
body. Future studys will need to further characterize and
control for intrasubject variability.

*Intersubject Variability*  The question of intersubject
variability was not addressed in this project, since there
was only one experimental subject. Morgan (1972)
investigated the percent retention of $^{38}$Cl-labeled fluorocarbon 113 (7mg/150ml) into the body for three subjects. The average unadjusted retention into the body over 30 minutes was 19.8 percent with a standard deviation of 0.9 percent (three trials).

Equations introduced by Fiscerova-Bergerova (1980) can be applied to adjust for different body builds. A detailed discussion of the Fiscerova-Bergerova equations, however, is beyond the scope of this paper. The question of intersubject variability on the uptake and excretion of fluorocarbon 113 requires further study before a workplace protection study can be designed based on this methodology.

**Influence of Workrate on Uptake of Fluorocarbon 113**

Increased uptake of fluorocarbon 113 through the lungs result from exercise or other increased metabolic states. This effect was not evaluated in this project. Of course, increased uptake through the skin may also occur. At higher work rates, increased blood perfusion through the muscle and skin, along with changes in permeability due to sweating, may significantly increase the skin effect. These effects must be addressed in future studies.

**Conclusion**

The results of this study indicate that a biological monitoring methodology may be used successfully to determine workplace respirator protection factors. The data indicate
that there is a reasonable correlation between the negative pressure and biological method involving breath analysis with fluorocarbon 113. As a result, the methodology described here may be used to design a workplace respirator protection study, which could examine in a comprehensive fashion the relationship between negative pressure fit factors and protection factors derived from biological monitoring of exhaled breath.
APPENDIX A

Low Concentration Chamber Calibration

The procedure utilized the following materials and instrumentation:

1. 50 ul Hamilton syringe
2. Mariotti bottle, volume measured at 19.25 liters
3. Miran 1A infrared analyzer closed loop circuit, which has a known internal volume of 5.65 liters.
4. Fluorocarbon 113, VanWaters and Rogers lot #129926.
5. Rubber septa, rubber stopper (No. 7 1/2), 30 mm X 8 mm ID glass tube, and teflon coated aluminum adhesive paper (Bytac, by Chemplast, Inc.).

The procedure is as follows:

1. Cover rubber stopper with teflon coated aluminumized adhesive paper. Cut an appropriately sized hole in the stopper, and insert the 30 mm X 8 mm ID glass tube. Place the rubber septa on the end of the glass tube.

2. Inject 168 ul of fluorocarbon 113 into the Mariotti bottle (19.25 liters), which contains mixing sticks.

3. Calculation of the vapor concentration in the Mariotti bottle:

Density of fluorocarbon 113: 1.5635 g/ml
Molecular weight: 187.38 g/mole
Barometric pressure in Tucson: about 703 mm Hg
Temperature: 25 °C
\[
\begin{align*}
1.5635 \text{ g/ml} & \times 2.24 \times 10^7 \text{ ul/mole} \times 1 \text{ ml/1000 ul} \times 760 \text{ mm Hg} \times \\
187.38 \text{ g/mole} & \times 703 \text{ mm Hg} \\
= 220.56 \text{ ul vapor/ul liquid}. \\

e^\frac{298}{273} = 187.38 \text{ g/mole} \times 703 \text{ mm Hg} \\
168 \text{ ul}_1 \times 220.56 \text{ ul}_v/\text{ul}_1 = 37054.1 \text{ ul vapor injected into Mariotti bottle.} \\
37054.1 \text{ ul} \times 10^6 = 1924.88 \text{ ppm in Mariotti bottle} \\
19.25 \times 10^6 \text{ ul} = \text{internal volume of Miran}
\end{align*}
\]

4. The vapor from the Mariotti bottle is then injected into the Miran 1A calibration loop. Table V lists the concentrations of vapors used in the standards. An example calculation for 0.5 ppm is as follows:

\[
\begin{align*}
\text{Concentration}_1 \times \text{Volume}_1 & = \text{Concentration}_2 \times \text{Volume}_2 \\
1924.88 \text{ ppm} \times \text{Volume}_1 & = 0.5 \text{ ppm} \times 5650 \text{ ml} \\
\text{Volume}_1 & = 1.59 \text{ ml}
\end{align*}
\]

<table>
<thead>
<tr>
<th>Amount of Vapor (milliliters)</th>
<th>Resultant Concentration (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.59</td>
<td>0.5</td>
</tr>
<tr>
<td>3.17</td>
<td>1.1</td>
</tr>
<tr>
<td>9.51</td>
<td>3.2</td>
</tr>
<tr>
<td>19.02</td>
<td>6.5</td>
</tr>
<tr>
<td>38.05</td>
<td>10.8</td>
</tr>
<tr>
<td>76.09</td>
<td>21.6</td>
</tr>
</tbody>
</table>

5. The absorbance is read at each of the resultant concentrations and plotted. The wavelength used is
8.4 microns and the pathlength is 15.75 meters.

6. A second calibration curve ranging from 20 to 70 ppm uses a wavelength of 8.4 microns and a pathlength of 8.25 meters. The procedure is identical to the high concentration calibration procedure outlined in Appendix B.
APPENDIX B

High Concentration Chamber Calibration

The procedure is performed by direct injections of liquid fluorocarbon 113 into the Miran 1A closed loop circuit. The procedure requires the following items:

1. 25 ul Hamilton syringe (#702)
2. Fluorocarbon 113
3. Miran 1A infrared analyzer

The concentrations used in the standards are listed in Table VI. The concentrations are calculated as follows for a 5.0 microliter injection:

\[
\frac{5.0 \text{ ul}_l \times 220.56 \text{ ul}_v/\text{ul}_l \times 10^6}{5.65 \times 10^6 \text{ ul}} = 196 \text{ ppm}
\]

\( v = \text{vapor} \)
\( l = \text{liquid} \)

220.56 is the number of microliters vapor from one microliter of liquid fluorocarbon 113.

5.65 * 10^6 is the number of microliters internal volume in the Miran.

Table VI

Amounts of Liquid Fluorocarbon 113 Needed to Produce the Following Resultant Concentrations in the Miran 1A Infrared Analyzer

<table>
<thead>
<tr>
<th>Amount of Fluorocarbon 113 (milliliters liquid)</th>
<th>Resultant Concentration (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.0</td>
<td>196</td>
</tr>
<tr>
<td>7.5</td>
<td>294</td>
</tr>
<tr>
<td>10.0</td>
<td>390</td>
</tr>
<tr>
<td>12.5</td>
<td>486</td>
</tr>
<tr>
<td>15.0</td>
<td>585</td>
</tr>
<tr>
<td>20.0</td>
<td>780</td>
</tr>
</tbody>
</table>

The absorbance is then read at a wavelength of 8.4 microns and a pathlength of 2.25 meters.
APPENDIX C

Procedure for Breath Standards

The following is a list of materials used in the procedure:

1. 500 ml filter flasks
2. Rubber Septa
3. Rubber Stoppers
4. Aluminumized Teflon Adhesive paper (Bytac, made by Chemplast, Inc.)
5. Glass beads
6. Fluorocarbon 113 (VanWaters & Rogers, Lot #129926)
7. 2-bromo-2-chloro-1,1,1-trifluoroethane (halothane) (Halocarbon Labs, Lot #27813)
8. UHP Nitrogen

The following is a list of equipment used in the procedure:

1. (2) 25 ul syringes (Hamilton, #702)
2. (2) 10 ul syringes (Hamilton, gas tight)
3. (2) 1.0 ml syringes (Precision, Pressure Lok)
4. (1) 5.0 ml syringe (Precision, Pressure Lok)
5. (1) 10.0 ml syringe (Precision, Pressure Lok)
6. Oven (Fisher Isotemp, Model 496)
7. Miran 1A infrared analyzer with closed loop calibration circuit (Wilks Miran 1A-CVF, #A154062).
8. A Hewlett Packard Model 5890 gas chromatograph with an electron capture detector (Serial #L6433).
9. A J & W Scientific 30 M X 0.53 ID, film 3.0 u, Durabond DB-624 phase Megabore capillary column. UHP nitrogen was used as a carrier gas and make-up gas.

The following is a description of the procedure used for making standards:

Preparation of the Glassware:

1. Filter flasks and rubber stoppers are rinsed with hot water and placed in an oven at 60 °C for 30 minutes.
2. Rubber stoppers are covered with aluminum/Teflon paper.
3. Glass beads are added to the filter flasks, and a rubber septa is placed on the side arm.
4. Five exhalations of breath are placed into the flasks, which are sealed with the aluminum/Teflon coated rubber stoppers.
5. An injection of 20 ul on the gas chromatographic is performed to ensure that there is no contamination of fluorocarbon 113 or other chemicals. Table VII lists the chromatograph settings.

Table VII
Chromatography Conditions

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Oven temperature:</td>
<td>30 °C</td>
</tr>
<tr>
<td>Injector temperature:</td>
<td>40 °C</td>
</tr>
<tr>
<td>Detector Temperature:</td>
<td>275 °C</td>
</tr>
<tr>
<td>Nitrogen Carrier Flow:</td>
<td>12 ml/minute, 100 kPa</td>
</tr>
<tr>
<td>Nitrogen Make-up:</td>
<td>60 ml/minute</td>
</tr>
<tr>
<td>Range &amp; Attenuation on GC:</td>
<td>0</td>
</tr>
<tr>
<td>Attenuation on integrator:</td>
<td>3</td>
</tr>
<tr>
<td>Area reject on integrator:</td>
<td>5000</td>
</tr>
<tr>
<td>Threshold on integrator:</td>
<td>1</td>
</tr>
</tbody>
</table>
Preparation of Standards

1. 10.0 ul of liquid fluorocarbon 113 is injected into the Miran which has an internal volume of 5.65 liters.

\[ \frac{220.56 \text{ ul} / \text{ul}}{5.65 \times 10^6 \text{ ul}} \times 10.0 \text{ ul} \times 10^6 = 390 \text{ ppm} \]

A concentration of 390 ppm yields an absorbance of 0.520 @ 8.4 u wavelength and 2.25 M pathlength

2. The final standards were made in 500 ml filter flasks. Table VII indicates the amounts of 390 ppm vapor injected into filter flasks and the resultant concentrations. The following is an example calculation:

(A typical 500 ml filter flask has a total volume of 590 ml.)

\[ \text{Concentration}_1 \times \text{Volume}_1 = \text{Concentration}_2 \times \text{Volume}_2 \]

\[ 390 \text{ ppm} \times \text{Volume}_1 = 0.5 \text{ ppm} \times 590 \text{ ml} \]

\[ \text{Volume}_1 = 0.75 \text{ ml} \]

Therefore, inject a 0.75 ml of a 390 ppm vapor into a 590 ml flask to make a final concentration of 0.5 ppm. This procedure is used for making standards that are 0.1 ppm or above.

3. To make standards of 5 ppb, 25 ppb, and 50 ppb, a slight deviation from the procedure in step #2 is employed. 5.62 ml of a 390 ppm vapor from the Miran is injected into a 562 ml filter flask. This results in a concentration of 3.90 ppm. Using
calculations similar to those in step #2,
Table IX indicates the amounts of 3.90 ppm vapor
added to filter flasks to yield the low
concentration standards.

4. 5.0 ul of halothane is injected into a 575 ml
filter flask. 5.75 ml of this vapor is injected
into another 575 ml filter flask. Inject 5.0 ml
vapor of this final halothane vapor (volume
adjusted to flask volume) into each standard. This
is the internal standard, which yields a mean
response of 816264 integrator units.

---

**Table VIII**

<table>
<thead>
<tr>
<th>Flask No.</th>
<th>#3</th>
<th>#4</th>
<th>#5</th>
<th>Vapor Conc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flask Volume (ml)</td>
<td>570</td>
<td>565</td>
<td>580</td>
<td></td>
</tr>
<tr>
<td>Vapor Added (ml)</td>
<td>0.15</td>
<td>0.15</td>
<td>0.16</td>
<td>0.11 ppm</td>
</tr>
<tr>
<td></td>
<td>0.39</td>
<td>0.38</td>
<td>0.40</td>
<td>0.27 ppm</td>
</tr>
<tr>
<td></td>
<td>0.63</td>
<td>0.62</td>
<td>0.65</td>
<td>0.43 ppm</td>
</tr>
<tr>
<td></td>
<td>1.58</td>
<td>1.56</td>
<td>1.61</td>
<td>1.08 ppm</td>
</tr>
<tr>
<td></td>
<td>4.73</td>
<td>4.71</td>
<td>4.81</td>
<td>3.24 ppm</td>
</tr>
<tr>
<td></td>
<td>11.06</td>
<td>10.97</td>
<td>11.25</td>
<td>7.57 ppm</td>
</tr>
</tbody>
</table>
3. Two calibration curves were produced. A calibration curve based on 20 ul injections is utilized for concentrations under 3 ppm. Another calibration curve based on 5 ul injections ranges up to 7.57 ppm. Smaller injections are necessary for higher concentrations to avoid overwhelming the EC detector or producing marked non-linearity.

Table IX

Amounts of 39 ppm Vapor Injected into Filter Flasks and the Resultant Concentrations

<table>
<thead>
<tr>
<th>Flask No.</th>
<th>Flask Volume (ml)</th>
<th>5 ppb (ml)</th>
<th>25 ppb (ml)</th>
<th>50 ppb (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>570</td>
<td>0.73</td>
<td>3.65</td>
<td>7.30</td>
</tr>
<tr>
<td>4</td>
<td>565</td>
<td>0.72</td>
<td>3.62</td>
<td>7.24</td>
</tr>
<tr>
<td>5</td>
<td>580</td>
<td>0.74</td>
<td>3.71</td>
<td>7.41</td>
</tr>
</tbody>
</table>
APPENDIX D

Calibration Curves for the Miran Infrared Analyzer.

Figures 20a, 20b, 20c, and 20d are calibration curves that were used to measure chamber concentrations of fluorocarbon 113. All calibrations were created at 8.4 microns wavelength; the pathlengths varied according to the concentration range being measured.

Figure 20a: Relationship of fluorocarbon 113 concentration (0 to 6 ppm) and absorbance units at a pathlength of 15.75 meters. Error bars indicate the standard deviation over three trials.
Figure 20b: Relationship of fluorocarbon 113 concentration (0 to 20 ppm) and absorbance units at a pathlength of 15.75 meters. Error bars indicate the standard deviation over three trials.

\[ y = 1.0640E^{-3} + 9.5687E^{-3} \times x \]
\[ r = 0.998 \]

Figure 20c: Relationship of fluorocarbon 113 concentration (20 to 70 ppm) and absorbance units at a pathlength of 8.25 meters. Error bars indicate the standard deviation over three trials.

\[ y = 1.9615E^{-2} + 5.0641E^{-3} \times x \]
\[ r = 0.9969 \]
Figure 20d: Relationship of fluorocarbon 113 concentration (200 to 700 ppm) and absorbance units at a pathlength of 2.25 meters. Error bars indicate the standard deviation over three trials.
Calibration Curves for Fluorocarbon 113 in Breath.

A calibration ranging from 0.005 ppm to 3.2 ppm was completed for fluorocarbon 113 in breath. Halothane was used as an internal standard to normalize the injections. The peak area (integrator units) was standardized to the mean peak area of the internal standard, which was 816264 integrator area units. The conditions and equipment used are described in the "Methods" section. The calibration was nearly linear over the entire range and did not change over the course of the project. Figure 21a illustrates the calibration curve covering the entire concentration range between 0.005 ppm and 3.2 ppm. Figures 21b and 21c illustrate the same data for lower concentration ranges. The regression equations were very slightly different for the low ranges than for the entire range. Figures 21a, 21b, and 21c used 20 ul injections. In all cases, the error bars represent ± 1 standard deviation from three trials.

Figure 21d is a calibration curve for fluorocarbon 113 developed from 5.0 ul injections. This standard curve was used to measure samples taken directly from the mask during the 30 minute exposures. This calibration curve is normalized to 204066 halothane integrator units, and was used to avoid overwhelming the detector with high concentrations of fluorocarbon 113.
Figure 21a: Calibration curve for fluorocarbon 113 in breath between 0.005 and 3.2 ppm. As mentioned in the text, the peak area (integrator units) for fluorocarbon 113 was standardized to the mean internal standard (halothane) peak area of 816264 integrator units.

Figure 21b: Calibration curve for fluorocarbon 113 in breath between 0.005 and 0.27 ppm.
Figure 21c: Calibration curve for fluorocarbon 113 in breath between 0.005 and 0.1 ppm.

Figure 21d: Calibration curve for fluorocarbon 113 in breath between 0 and 7 ppm. Error bars represent standard deviations resulting from three trials. 5.0 ul direct injections were used for this curve.
APPENDIX F

Loss of fluorocarbon 113 from filter flasks over time.
Figures 22a, 22b, 22c, and 22d indicate that loss of fluorocarbon 113 from filter flasks was not a problem. Figure 22a was done at 13 ppb, Figure 22b at 28 ppb, Figure 22c at 62 ppb, and Figure 22d at 1 ppm. Error bars indicate ± 1 standard deviation resulting from three trials.

Figure 22a: Loss from a 500 ml Kimax filter flask at 13 ppb.
Figure 22b: Loss from a 500 ml Kimax filter flask at 28 ppb.

Figure 22c: Loss from a 500 ml Kimax filter flask at 62 ppb.
Figure 22d: Loss from a 500 ml Kimax filter flask at 1 ppm.
APPENDIX G

Analytical Variability in Quantitating

Fluorocarbon 113 Utilizing Gas Chromatography

Figures 23a, 23b, and 23c illustrate the analytical variability at concentrations of 13 ppb, 28 ppb, and 62 ppb, respectively. The standard deviation as a percent of the mean value increased as the concentration decreased.

Figure 23a: The analytical variability associated with repeatedly injecting 13 ppb of fluorocarbon 113 using gas chromatography. Each bar represents a single injection.
Figure 23b: The analytical variability associated with repeatedly injecting 28 ppb fluorocarbon 113 using gas chromatography. Each bar represents a single injection.

Figure 23c: The analytical variability associated with repeatedly injecting 62 ppb fluorocarbon 113 using gas chromatography. Each bar represents a single injection.
APPENDIX H

Specifications of glass sampling tubes:

- 15 mm inside diameter
- 100 mm length
- 46 ml internal volume

Source:

Contes of California
1470 Zephyr Avenue
Hayward, California 94544
(800) 255-1672

---

Loss of fluorocarbon 113 from sample tubes.

Figure 24 illustrates the loss of fluorocarbon 113 at three different concentrations, when maintained at 37 °C. Figure 25 indicates the loss of fluorocarbon 113 in a sampling tube that was maintained at 25 °C.

The particular dimensions of the sampling tube were selected to minimize the surface area to volume ratio, assuming that concentration decay is related to wall losses. Additionally, the volume of the tube needed to be at least seven times smaller than the expiratory reserve volume. This is necessary to purge 99.9% of the original atmospheric air from the sampling tube.
Figure 24: The stability of three concentrations of fluorocarbon 113 in glass breath sampling tubes stored at 37 °C for three hours. Each concentration was repeated in triplicate. The data points represent the mean of three separate trials.

\[y = 4.8850 \times 10^{-1} - 1.3857 \times 10^{-3} (x) + 5.2002 \times 10^{-6} (x^2)\]

\[r = 0.9337\]

Figure 25: Storage of fluorocarbon 113 over three hours in a glass breath sampling tube that was maintained at 25 °C. The error bars indicate the standard deviation over three trials.
APPENDIX I

Numerical Data

Table X

Numerical Fit Testing Data

<table>
<thead>
<tr>
<th>Test</th>
<th>Fit Factor Biological</th>
<th>Fit Factor Skin Corrected</th>
<th>Fit Factor Negative Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base 1</td>
<td>243 (2.06)*</td>
<td>707</td>
<td>723</td>
</tr>
<tr>
<td>Base 2</td>
<td>489 (1.02)</td>
<td></td>
<td>881</td>
</tr>
<tr>
<td>Base Bag 1</td>
<td>178 (2.81)</td>
<td>343</td>
<td>881</td>
</tr>
<tr>
<td>Base Bag 2</td>
<td>136 (3.68)</td>
<td>215</td>
<td>822</td>
</tr>
<tr>
<td>Base Bag 3</td>
<td>326 (1.53)</td>
<td>2721</td>
<td>566</td>
</tr>
<tr>
<td>Base Bag 4</td>
<td>86 (5.81)</td>
<td>112</td>
<td>416</td>
</tr>
<tr>
<td>Base Bag 5</td>
<td>83 (6.02)</td>
<td>107</td>
<td>441</td>
</tr>
<tr>
<td>Needle 20-1</td>
<td>65 (7.69)</td>
<td>79</td>
<td>291</td>
</tr>
<tr>
<td>Needle 20-2</td>
<td>70 (7.14)</td>
<td>86</td>
<td>302</td>
</tr>
<tr>
<td>Needle 20-3</td>
<td>71 (7.04)</td>
<td>88</td>
<td>300</td>
</tr>
<tr>
<td>Needle 18-1</td>
<td>106 (4.72)</td>
<td>149</td>
<td>173</td>
</tr>
<tr>
<td>Needle 18-2</td>
<td>77 (6.49)</td>
<td>97</td>
<td>198</td>
</tr>
<tr>
<td>Needle 18-3</td>
<td>83 (6.02)</td>
<td>107</td>
<td>181</td>
</tr>
<tr>
<td>Loose Bag 1</td>
<td>54 (9.26)</td>
<td>63</td>
<td>177</td>
</tr>
<tr>
<td>Loose Bag 3</td>
<td>34 (14.71)</td>
<td>37</td>
<td>123</td>
</tr>
<tr>
<td>Loose Bag 5</td>
<td>37 (13.51)</td>
<td>41</td>
<td>94</td>
</tr>
</tbody>
</table>

Base...........No artificial leaks, no mask sampling.
Base Bag....No artificial leaks, mask sampling into bag.
Needle 20...Leak produced by 20 gauge needle, no mask sampling.
Needle 18...Leak produced by 18 gauge needle, no mask sampling.
Loose Bag...Leak produced by two rubber bands in the forehead area, mask sampling into bag. (trials 2 and 4 were excluded because of experimental errors)

* The values in parentheses are the calculated exposures in parts per million while wearing the respirator.
### Table XI

**Fit Factors from Mask Sampling**

<table>
<thead>
<tr>
<th>Test</th>
<th>Mask Concentration (ppm)</th>
<th>Fit Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base Bag 1</td>
<td>2.53</td>
<td>198</td>
</tr>
<tr>
<td>Base Bag 2</td>
<td>7.58</td>
<td>66</td>
</tr>
<tr>
<td>Base Bag 3</td>
<td>1.74</td>
<td>287</td>
</tr>
<tr>
<td>Base Bag 4</td>
<td>3.82</td>
<td>131</td>
</tr>
<tr>
<td>Base Bag 5</td>
<td>9.80</td>
<td>51</td>
</tr>
<tr>
<td>Loose Bag 1</td>
<td>1.90</td>
<td>263</td>
</tr>
<tr>
<td>Loose Bag 3</td>
<td>8.47</td>
<td>59</td>
</tr>
<tr>
<td>Loose Bag 5</td>
<td>3.52</td>
<td>142</td>
</tr>
</tbody>
</table>

### Table XII

**Percent Penetration Comparisons**

<table>
<thead>
<tr>
<th>Test</th>
<th>Biological</th>
<th>Biological Skin Corrected</th>
<th>Negative Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base 1</td>
<td>0.412</td>
<td>0.142</td>
<td>0.138</td>
</tr>
<tr>
<td>Base 2</td>
<td>0.204</td>
<td></td>
<td>0.114</td>
</tr>
<tr>
<td>Base Bag 1</td>
<td>0.562</td>
<td>0.292</td>
<td>0.128</td>
</tr>
<tr>
<td>Base Bag 2</td>
<td>0.735</td>
<td>0.465</td>
<td>0.122</td>
</tr>
<tr>
<td>Base Bag 3</td>
<td>0.307</td>
<td>0.037</td>
<td>0.177</td>
</tr>
<tr>
<td>Base Bag 4</td>
<td>1.163</td>
<td>0.893</td>
<td>0.240</td>
</tr>
<tr>
<td>Base Bag 5</td>
<td>1.205</td>
<td>0.935</td>
<td>0.227</td>
</tr>
<tr>
<td>Needle 20-1</td>
<td>1.538</td>
<td>1.268</td>
<td>0.344</td>
</tr>
<tr>
<td>Needle 20-2</td>
<td>1.429</td>
<td>1.159</td>
<td>0.331</td>
</tr>
<tr>
<td>Needle 20-3</td>
<td>1.408</td>
<td>1.138</td>
<td>0.333</td>
</tr>
<tr>
<td>Needle 18-1</td>
<td>0.943</td>
<td>0.673</td>
<td>0.578</td>
</tr>
<tr>
<td>Needle 18-2</td>
<td>1.299</td>
<td>1.029</td>
<td>0.505</td>
</tr>
<tr>
<td>Needle 18-3</td>
<td>1.205</td>
<td>0.935</td>
<td>0.552</td>
</tr>
<tr>
<td>Loose Bag 1</td>
<td>1.852</td>
<td>1.582</td>
<td>0.565</td>
</tr>
<tr>
<td>Loose Bag 3</td>
<td>2.941</td>
<td>2.671</td>
<td>0.813</td>
</tr>
<tr>
<td>Loose Bag 5</td>
<td>2.703</td>
<td>2.433</td>
<td>1.064</td>
</tr>
</tbody>
</table>
APPENDIX J

Screening Health History

Name________________________ Age______ Sex______

Height______ Weight______

1) HISTORY OF HEART DISEASE: Yes______ No______
2) HISTORY OF HYPERTENSION: Yes______ No______
3) HISTORY OF LUNG PROBLEMS: Yes______ No______
4) HISTORY OF NERVOUS SYSTEM PROBLEMS: Yes______ No______ (epilepsy, seizures)

5) PLEASE LIST ANY MEDICATIONS THAT YOU ARE TAKING: _______

6) ARE YOU WORKING IN A LABORATORY WHERE YOU ARE EXPOSED TO VOLATILE CHEMICALS? Yes______ No______ If yes, please specify__________________________
SELECTED BIBLIOGRAPHY


Code of Federal Regulations, Title 29, part 1910.134, section (e) (5).


