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# Comparison of Six Respirator Fit-Test Methods with an Actual Measurement of Exposure in a Simulated Health Care Environment: Part I — Protocol Development

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# Comparison of Six Respirator Fit-Test Methods with an Actual Measurement of Exposure in a Simulated Health Care Environment: Part I — Protocol Development

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Quantitative fit tests (QNFT) have been assumed to be predictive of the protection respirators would provide to a wearer in the workplace. Workplace studies have consistently found no correlation between quantitative fit factors and workplace protection factors. This article is the first in a series of three describing a study designed to compare the fit factors from six QNFT methods against the actual dose of 1,1,2 trichloro-1,2,2 trifluoroethane (Freon-113) received under the same laboratory conditions. Five preliminary studies conducted to develop the protocol to assess the respirator wearer's dose through end-exhaled air analysis are described in this article: (1) chamber characterization, (2) end-exhaled air sampling, (3) skin absorption testing, (4) pharmacokinetic modeling, and (5) subject characterization. It was established that the concentration of corn oil aerosol and Freon-113 could be generated simultaneously in the chamber. It was ascertained that the optimum time to sample the exhaled breath was 30 minutes after the subject exited the chamber. It was also found that in a chamber concentration of 500 ppm, without any respiratory exposure, Freon-113 was still present in the end-exhaled air. This was attributed to skin absorption. The end-exhaled air of subjects exposed to 0.5, 3, 5, 25, 50, and 100 ppm (30 minute time-weighted average) of Freon-113 was evaluated at 30 minutes postexposure. This characterization was then used to predict the actual dose of Freon-113 received during the method comparison and validation testing to be described in subsequent articles.

**Keywords: exposure measurement, fit factor, quantitative fit test, respirator, 1,1,2 trichloro-1,2,2 trifluoroethane (Freon-113), workplace protection factor**

Mention of commercial product or trade name does not constitute endorsement by the National Institute for Occupational Safety and Health.

The ability to form a reliable seal (i.e., fit) is an important characteristic of any negative pressure respirator. To evaluate the fit characteristics of facepieces, quantitative fit test (QNFT) methods were developed in the 1960s and the early 1970s.[1–4]

Available QNFT equipment is currently based on either aerosols or pressure. Aerosol methods typically use corn oil, sodium chloride, or ambient aerosols. A series of exercises designed to test the amount of inward leakage through the seal of the respirator's facepiece are performed. The air concentration of challenge aerosol in the facepiece, $C_{in}$, and in the chamber outside the respirator, $C_{out}$, is determined. A fit factor is a quantitative measure of the fit of a particular respirator facepiece to a particular individual. It is defined under the conditions of quantitative fit-testing as the ratio $C_{out}/C_{in}$.[5]

A quantitative fit-test method that does not

use an aerosol as the challenge agent is controlled negative pressure (CNP). The CNP method exhausts air from a temporarily sealed respirator facepiece to generate and then maintain a constant negative pressure inside the facepiece.[6] Measurement of the exhaust stream that is required to hold the pressure constant yields a direct measure of leakage airflow into the respirator.

A fit-test is important for two reasons: (1) it can help ensure each individual has an adequately fitting respirator; and (2) it can be useful for training of proper donning procedures.

Quantitative fit-tests have also been used to establish assigned protection factors (APFs) of respirators.[7] An APF is the minimum expected workplace level of protection that would be provided by a properly functioning respirator or class of respirators, to a stated percentage (typically 95%) of properly fitted and trained wearers.[5] As they are now established by the National Institute for Occupational Safety and Health (NIOSH), APF values take into consideration the poorest performing models of respirators in the class. The majority of APF values adopted by the Occupational Safety and Health Administration (OSHA) and NIOSH were based on QNFT testing.[8] Using laboratory quantitative fit-tests to set APF values is based on the assumption that the fit-test results are good indicators of the protection provided in the workplace. This view was held until workplace protection factor (WPF) testing began.

A WPF is a measure of the actual protection provided in the workplace under conditions of that workplace by a properly functioning respirator when correctly worn and used. It is defined as the ratio of the estimated workplace contaminant concentration that the user would inhale if he or she were not wearing a respirator to the estimated contaminant concentration inside the respirator facepiece.[5] A WPF of 12 means that while correctly using and wearing the respirator a worker's exposure is reduced to one-twelfth of the ambient exposure.

Beginning in the mid 1980s the efficacy of QNFT methods to indicate workplace protection were brought into question after workplace studies failed to find statistically significant correlations between QNFT results and workplace performance as expressed by the WPF.[9–14] For example, quantitative fit factors measured on powered air-purifying respirators were much higher than the WPFs.[9,10,12,13] Therefore, the present laboratory fit tests may not accurately predict the performance of a respirator in the workplace. For the last decade, the inability to identify a correlation between QNFT and WPF values has raised some doubt about the value of quantitative fit testing.

This article is the first in a series of three describing a study designed to compare the fit factors from six QNFT methods under laboratory conditions. The six QNFT methods evaluated were (1) continuous high flow, deep probe; (2) continuous low flow, flush probe; (3) exhalation valve discharge; (4) CNP; (5) Ambient Aerosol 1, using 6 exercises with a duration of 80 seconds each; and (6) Ambient Aerosol 2, using 17 exercises and lasting 30 minutes. Respirator wearers were exposed to a known concentration of Freon-113 vapor and an oil aerosol in a laboratory test chamber. The concentration of Freon-113 in a subject's exhaled breath is reflective of the actual dose received when respirators are worn in a known concentration of Freon-113. Supported by the pharmacokinetic properties of Freon-113, airborne exposure to the vapor could be determined experimentally, by measuring end-exhaled air levels rather than relying on in-facepiece sampling. This eliminates or minimizes the documented biases inherent with current in-facepiece sampling techniques and hardware such as probe location and depth relative to face seal leak location,[15] particle loss,[16] and the relationship of leak sites and facial characteristics.[17,18] The total Freon-113 exposure dose (i.e., actual respirator performance) is calculated from concentration measurements of a subject's end-exhaled air. Therefore, it can be determined whether an increase in fit factor results in better protection (i.e., lower total Freon-113 exposure dose) during a simulated health-care WPF test. It can also be determined, when two respirators are fit-tested with the same method, whether the respirator with the higher fit factor actually provides better protection.

This first article describes the test protocol and a number of ancillary studies conducted as part of this protocol development. The second article will describe the results of the study that evaluates the correlation between each of six quantitative fit-test methods and actual exposure to the challenge agent, Freon-113. The third article will describe the validation testing performed on the selected quantitative fit-test method.

## MATERIALS AND METHODS

The experimental approach using Freon-113 as a biological indicator of exposure was modeled after previously published research.[19] The challenge agent for determining the subject's actual exposure needed to be nontoxic. This allowed the subjects to be exposed to moderate to high concentrations safely so that a wide range of protection factors could be determined. In addition, it needed to have suitable uptake, elimination, and metabolic rates so a constant relationship between the subject's exposure (the amount inhaled) and the amount in the subject's exhaled breath could be determined during the characterization phase of the project. Various agents for the challenge or biomarker gas were reviewed. Freon-113 (Aldrich Chemical Company, catalog number 24,281-0, Milwaukee, Wis.) was chosen for its low toxicity, pharmacokinetic characteristics, and analytical sensitivity. The OSHA permissible exposure limit and the NIOSH recommended exposure limit are 1000 parts per million (ppm) as an 8-hour time-weighted average.[20,21] Five preliminary studies were conducted to develop the protocol.

**(1)** Chamber characterization: determination of the effect of generating corn oil on a given Freon-113 concentration.

**(2)** End-exhaled air sampling: determination of the procedure to be used for analyzing the end-exhaled air and the optimum time between the end of the chamber exposure and the end-exhaled air sample being taken.

**(3)** Skin absorption testing: determining whether the Freon-113 could permeate the skin and be absorbed into the bloodstream.

**(4)** Pharmacokinetic modeling: determining whether the relationship between the Freon-113 concentration in the subject's end-exhaled air and the exposure concentration is linear.

**(5)** Subject characterization: determination of the amount of Freon-113 present in the subject's end-exhaled air for a given known dose.

### Chamber Characterization

This study was conducted using a (4 × 4 × 7 foot) laboratory chamber (Dynatech Frontier Corp., model 222-6, Albuquerque, N.M.) that contained a spatially and temporally uniform concentration of Freon-113 and corn oil aerosol. The detector for the corn oil aerosol was a Dynatech Frontier Corp. model FE250A portable aerosol test system with a Zenith data system Z-386/20 (Zenith Data Systems, Buffalo Grove, Ill.) equipped with LabTech Acquire Software (Laboratory Technologies Corp., Wilmington, Mass.). The portable aerosol test system was able to determine 0.01% leakage (i.e., full scale). Therefore, the maximum fit factor

**TABLE I. Simulated Health Care Motions**

| Motion | Duration (Minutes) | Motion | Duration (Minutes) |
|---|---|---|---|
| Hang IV bag | 1 | reach side to side | 2 |
| Bending | 2 | reaching overhead | 2 |
| Insert syringe into IV bag | 1 | normal breathing while sitting | 2 |
| Carrying weight | 2 | nodding and turning head | 2 |
| Twisting and turning head | 2 | reaching overhead | 2 |
| Open and close door | 1 | stand and normal breath | 1 |
| Normal breathing | 3 | control panel motions | 1 |
| Bending | 3 | walking | 1 |
| Turning head | 2 | | |

that could be determined was 100,000 (a 10% reading on the 0.01% scale). The corn oil aerosol had a measured mass median aerodynamic diameter of approximately 0.6 μm and a mass concentration of 20±5 mg/m³ using an impactor (Anderson Samplers, Inc., model 20-800, Atlanta, Ga.). The Freon-113 generation system consisted of a Sage Instruments (Cambridge, Mass.) model 351 syringe pump for high concentrations or a Cole Parmer (Vernon Hills, Ill.) MasterFlex pump for low concentrations and a glass tube with a heated injection port to vaporize the liquid Freon-113. The concentration of Freon-113 in the chamber was monitored continuously using a Wilks MIRAN-1A infrared analyzer (MIRAN IR) with a separate vacuum pump (Foxboro Co., East Bridgewater, Mass.). The MIRAN IR analyzer was connected to a strip chart recorder (Cole-Parmer Co., model 1101-0000).

The impact of simultaneously generating corn oil aerosol, needed for three of the in-facepiece methods, on the concentration of 500 ppm Freon-113 present in the chamber needed to be ascertained. A concentration of 500 ppm Freon-113 was generated in the chamber with and without corn oil aerosol being generated. The actual Freon-113 concentration in the chamber was determined by the use of the MIRAN IR with the inlet port equipped with a high-efficiency filter to remove the corn oil aerosol. The infrared analyzer was calibrated from 100 to 800 ppm at 100 ppm intervals using the closed loop system provided with the MIRAN IR. A probe from the test chamber was then connected to the inlet of the MIRAN IR. The actual concentrations of Freon-113 in the chamber with and without the corn oil being generated were then compared with the required 500 ppm.

## End-Exhaled Air Sampling

To determine the subject's actual dose, a method and instrument that could measure the Freon-113 in a subject's end-exhaled air accurately and repeatedly needed to be found. According to Ganong, end-exhaled air has more than 250 different chemical components including but not limited to oxygen, nitrogen, carbon dioxide, water vapor, and some ambient chlorofluorocarbons.[22] After reviewing these components, it was determined that the subjects' end-exhaled air could be analyzed using a Nicolet Fourier transform infrared (FT-IR) spectrometer (Madison, Wis.) equipped with a vacuum system consisting of a Welch vacuum pump (Sargent-Welch Co., Skokie, Ill., model 1402), Edwards Datametrics Model 1174 electronic manometer (Wilmington, Mass.), three needle valves, and stainless steel tubing. The FT-IR would produce peaks for the Freon-113 that could easily be distinguished from other peaks caused by all the other chemicals present in the subject's end-exhaled air.

Alveolar (or end-exhaled) air has been demonstrated to produce the most consistent results from exhaled air sampling.[23] Therefore, the subject's end-exhaled air collected using an apparatus consisting of a Vacumed 1197 3-liter balloon (Ventura, Calif.); SensorMedics VMM series ventilation measurement module (Anaheim, Calif.); Hans Rudolph 4285 pneumatic controller with hand switch for remote control (Kansas City, Mo.); Vacumed pneumatic three-way directional valve; Vacumed K270 K-valve, T-version equipped with one-way valves; Vacumed 1026 cardboard mouthpiece; Vacumed 1084 adapter; and Vacumed 1011 Clean Bor tubing.

Another important issue that needed to be addressed was the optimum time for sampling the end-exhaled air. Two factors, the postchamber time at which the desaturation curve stabilized and the comparison of the results from different exposure profiles, were the basis for determining the optimum sampling time. First, testing was done to determine approximately when the end-exhaled air should be sampled after termination of the Freon-113 exposure. For this testing, two subjects were chosen at random. The first subject was given a continuous 3000 ppm-min total Freon-113 exposure dose. The subject remained in the chamber containing 100 ppm Freon-113 and corn oil for 30 minutes without a respirator. The second subject was given an intermittent 3000 ppm-min total Freon-113 exposure dose.

To do the intermittent exposure test, the second subject donned a modified half-mask organic vapor/high-efficiency respirator. The respirator was equipped with a breathing port and cartridge caps. When the breathing port was open and the cartridge caps closed, the subject breathed the chamber atmosphere. With the breathing port sealed and the cartridge caps opened, the subject breathed only purified air. Since multiple sizes of the facepiece were available, the subject selected the most comfortable size based on results of following the manufacturer's fit check guidelines. The sealing area of the facepiece was lined with denture adhesive to prevent face seal leakage. The face seal was then checked before and after the test with a TSI Model 8020 Portacount™ (St. Paul, Minn.) in the count mode. If the Portacount did not detect any particles inside the facepiece, the seal was considered to be intact. The subject then entered the chamber and breathed 500 ppm Freon-113 for 2 minutes at the beginning, middle, and end of the test.

While in the chamber, both test subjects performed the motions listed in Table I. The selection of these motions was based on the professional opinion of several experts highly knowledgeable regarding the health care industry and the health care workers (HCWs) who would most likely be exposed to patients with tuberculosis and a resulting positive skin test. Those HCWs were emergency room clerks, clinicians, nurses, and doctors; nurses doing home health visits; emergency medical service personnel; X-ray technicians; and HCWs in prisons. However, the majority of

these movements are representative of those found in other industries. After exiting the chamber, end-exhaled air samples were taken once every 5 minutes for up to an hour after the exposure was terminated.

In addition, it was necessary to verify that equivalent end-exhaled air concentrations could be obtained with different exposure profiles giving equal doses. Having the exposure occur only at the beginning of the test versus only at the end of the test was considered to be the worst case scenario that would be encountered during the method comparison phase of testing. Three subjects were chosen at random to conduct this phase of testing. Each subject donned a modified half-mask organic vapor/high-efficiency respirator as described previously. The sealing area of the facepiece was lined with denture adhesive to prevent face seal leakage. The face seal was then checked with the Portacount in the count mode (i.e., no particles detected). The subjects then entered the chamber containing 500 ppm Freon-113 and corn oil and remained there for 30 minutes while performing the exercises in Table I. For the first 6 minutes of the test, the breathing port was open and the cartridge caps closed. For the remaining 24 minutes, the breathing port was sealed and the cartridge caps open. After 30 minutes, the subject exited the chamber and the denture adhesive seal was again checked with the TSI Portacount in the count mode. The subject's end-exhaled air was analyzed 30 minutes after exiting the chamber.

The same three subjects again entered the 500 ppm Freon-113 and corn oil atmosphere on a different day. This time, however, the breathing port was sealed and the cartridge caps opened for the first 24 minutes. The breathing port was then opened and the cartridge caps sealed for the last 6 minutes of the test. The denture adhesive seal was checked and the end-exhaled air was analyzed in the same manner as the previous test. Each subject performed both tests in duplicate.

Since the subjects wore respirators that included an organic cartridge, it was necessary to ensure that the Freon-113 did not break through the cartridges (i.e., the sorbent in the cartridge becomes saturated and lets Freon-113 pass through to the wearer's breathing zone) and contribute an unknown amount of Freon-113 to the wearer's exposure. Therefore, a change-out schedule needed to be developed for the organic vapor cartridges to prevent breakthrough of the Freon-113.

The certification test for organic vapor cartridges requires a carbon tetrachloride service life in excess of 50 minutes when tested in the same configuration as used on the respirator at a 1000-ppm challenge and 64 L/min.[24] A study by the NIOSH Pittsburgh Research Center determined that organic vapor cartridges had 70% of the carbon tetrachloride service life when tested against Freon-113 under the same conditions.[25] Therefore, it was expected that the cartridges would last in excess of 70 minutes. To verify this assumption, representative cartridges were tested for service life under chamber conditions. The chamber atmosphere was cycled through the cartridges by a breathing machine at a rate of 24 respirations per minute with a minute volume of 40 liters. The minimum service life seen was in excess of 92 minutes. In addition, the anticipated breathing rate for the simulated work movements would not be as high as the breathing machine's rate. Since each test involving Freon-113 lasted 30 minutes, the cartridges were replaced after every third test in this study. The modified disposable respirator was also tested to ensure that the sorbent removed the Freon-113 for at least 30 minutes. Each modified disposable respirator was used only for one test.

### Skin Absorption

Decker and Crutchfield indicated in their study that Freon-113 may be absorbed through the skin and be eliminated in the end-exhaled air.[19] In addition, it is known that certain commercial solvents can permeate through human skin.[26] Therefore, each subject in this study underwent a skin absorption test for Freon-113. As described previously, each subject wore an organic vapor/high-efficiency half-mask respirator sealed to their face to prevent respiratory exposure to Freon-113. The subjects then entered the chamber containing 500 ppm Freon-113 and corn oil. They remained in the chamber for 30 minutes performing the exercises listed in Table I. After exiting the chamber, the subjects were taken to a nearby room and left their respirators on for 2 additional minutes. This allowed off-gassing of Freon-113 from their clothing to stop before the end-exhaled air sample was collected. Their end-exhaled air was analyzed for Freon-113 and the contribution of dermal absorption was determined.

The subjects also performed skin absorption tests with 10 ppm Freon-113 in the chamber. This was necessary since some of the characterization tests were conducted at the lower concentration. Only one skin absorption test was conducted for both concentrations.

### Pharmacokinetic Modeling

To determine whether the Freon-113 concentration in the end-exhaled air and the exposure concentration were linearly correlated, the literature on pharmacokinetics of inhaled solvents was first reviewed. A physiological model was then developed to obtain end-exhaled air Freon-113 concentration for a given time after the exposure ended, establish the relationship between exposure concentration and end-exhaled air concentration, and evaluate the effects of variables of exposure (continuous exposure, intermittent exposure, and exposure at the beginning or at the end of a fit-test) on end-exhaled air Freon-113 concentration. The physiological model used in this study is based on models describing the pharmacokinetics of volatile chemicals.[27,28] The model simulates the inhalation of Freon-113 into the lung and penetration to the alveoli where Freon-113 is exchanged between the air and the blood. The gas transfer is controlled by ventilation and perfusion rates and the blood:air partition coefficient. A series of mass-balance differential equations are also used to quantify the time course of Freon-113 concentration within four tissue groups: the liver, rapidly perfused tissue, slowly perfused tissue, and fat tissue. Physiological parameters and partition coefficients for the model are obtained from those in the physiologically based mathematical model, described by Auton and Woollen, for the human inhalation pharmacokinetics of Freon-113.[29]

The set of simultaneous differential equations for the model was formulated as a computer program with Statistical Analysis System (SAS) software (SAS Institute, Research Triangle, N.C.).[30] Physiological parameters and partition coefficients are constants in the program. The input variables for the program are the concentration of Freon-113 in inhaled air and exposure schedule. The output includes the concentration in the four tissue groups and in exhaled air. The accuracy of the program was tested using the results reported by Auton and Woollen.[29]

### Subject Characterization

To determine the level of Freon-113 exposure inside the facepiece during the method comparison testing, it was necessary to establish the relationship between total Freon-113 exposure dose and end-exhaled air concentrations. Prior to the start of any

**TABLE II. Characterization Exposures and Time Periods with Probe Cap Removed**

| Chamber Concentration (ppm) | Interval Exposure Time for Each of Three Intervals (minutes) | Dose (ppm-minutes) | 30-Minute Time-Weighted Average (ppm) |
|---|---|---|---|
| 500 | 2 | 3000 | 100 |
| 500 | 1 | 1500 | 50 |
| 500 | 0.5 | 750 | 25 |
| 10 | 5 | 150 | 5 |
| 10 | 3 | 90 | 3 |
| 10 | 0.5 | 15 | 0.5 |

characterization testing, it was necessary to decide whether the Freon-113 exposure was to be constant or intermittent.

No reported evidence exists that supports the theory that face seal leakage occurs at a constant rate during the entire period of use. Evidence from a workplace study[31] and personal observation of fit-tests seem to suggest that the seal breaks due to a certain movement and an exposure occurs, then that movement ends and others occur, the face seal resets and the exposure ends. Therefore, the characterization tests of the 11 subjects were conducted with intermittent exposures of Freon-113 at the beginning, middle, and end of each characterization test. This characterization was the basis for determining the relationship of the Freon-113 in the end-exhaled air to the exposure concentration.

Intermittent exposures corresponding to 30-minute time-weighted exposures of 0.5, 3.0, 5.0, 25, 50, and 100 ppm were used to develop the subject characterization curves. To perform the characterization tests, the subjects donned and sealed the modified respirator described under the optimum sampling time section. The test subjects were characterized in the chamber containing 500 ppm for the 25, 50, and 100 ppm characterization tests and 10 ppm of Freon-113 for the 0.5, 3, and 5 ppm characterization tests. All characterization tests were conducted with approximately 16 mg/m³ of corn oil measured gravimetrically in the chamber along with the Freon-113. While in the chamber, the subjects performed the exercises listed in Table I. To obtain the desired characterization concentration, subjects opened the breathing port and sealed the cartridge caps at the beginning, middle, and end of the 30-minute test period for a specified period of time as noted in Table II.

Each of the six characterization tests were done twice on each subject on different days. Therefore, 12 points were obtained for each subject, which were used to compute their individual end-exhaled air characterization curves.

The subjects used in this study had a wide variety of facial sizes to average out any effect facial size would have on the various methods used in the method comparison phase of the study to be described in a subsequent article. For example, one method may correlate well on subjects with medium size faces but not on small or large faces. If subjects with only medium sizes were included in this study, a method could be chosen that provides quantitative fit factors that correlated total Freon-113 exposure dose only with a few facial sizes. The selection of individuals for participation in the study was random (among those subjects having the appropriate facial size) from the NIOSH Certification and Quality Assurance Branch human test subject pool who agreed to participate.

Six women and five men participated in the study. The panel size of 11 was not chosen based on any statistical analysis. Eleven was the maximum of subjects that could be accommodated in the study. All of the subjects had experience in wearing half-mask respirators and had performed numerous qualitative fit-tests as part of the NIOSH respirator certification program. The subjects were provided instructions on how to don and fit check the respirator.

## RESULTS AND DISCUSSION

### Chamber Characterization

It was determined that corn oil does absorb Freon-113 and thereby reduces the vapor concentration (by ≈4%). However, it was also determined that the corn oil and Freon-113 did reach an equilibrium. Therefore, it was possible to maintain a stable concentration of 500 ppm if Freon-113 was added to the chamber by the syringe pump to compensate for the addition of freshly generated corn oil aerosol and any losses due to the exhaust and opening and closing of the door.

### End-Exhaled Air Sampling

Prior to beginning the study, a required minimum detectable level was determined. For the half-masks being used, 2500 seemed to be a reasonable maximum fit factor that would be attained. This would result in the wearer being exposed to 0.2 ppm. Since it was anticipated that at 30 minutes, only 10% of the exposure concentration would be present in the exhaled breath, it was determined that any instrument used for analyzing the end-exhaled air needed to be able to detect at least 0.02 ppm.

During the preliminary end-exhaled air sampling phase, it was found that FT-IR could be used to characterize only 3 of the 11 subjects participating in the study. The large sample volume

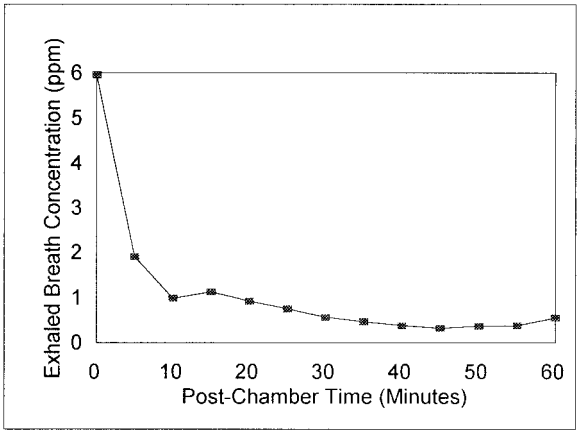


**FIGURE 1. Freon-113 concentration in first subject's end-exhaled air following a constant 100.0 ppm exposure for 30 minutes**

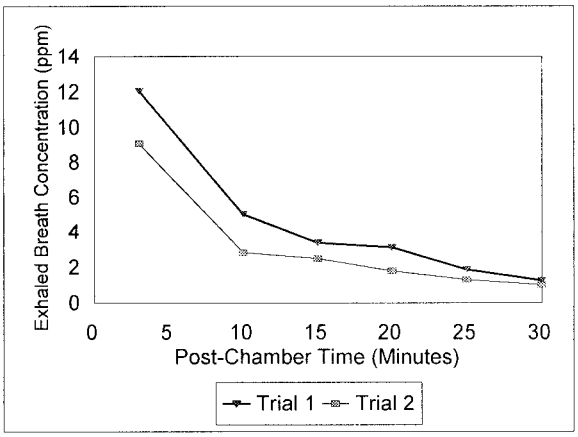


**FIGURE 2. Freon-113 concentration in second subject's end-exhaled air following a 500-ppm intermittent exposure corresponding to 100 ppm 30-minute time-weighted exposure in a single subject**

required for analysis by the FT-IR (approximately 2 liters of end-exhaled air) produced inconsistent results with the remaining eight subjects. A possible explanation for this is that the subjects with consistent results could provide the 2 liters of end-exhaled air with a single breath. The remaining subjects needed more than a single breath to provide the sample. This probably resulted in the samples for these subjects containing varying amounts of relatively Freon-free exhaled air. Therefore, a different method had to be developed to analyze the end-exhaled air of these subjects.

A review of the literature revealed a number of methods had been developed to obtain samples of end-exhaled air for gas chromatographic analysis.[32,33] It was decided to adapt one of these methods to sample the end-exhaled air of the remaining eight subjects who could not be characterized using the FT-IR. However, a suitable gas chromatograph was not immediately available for use. Due to time and other constraints, it was decided to proceed with the study using the three subjects whose exhaled breath could be analyzed using the FT-IR. When the gas chromatograph did become available, the three subjects had already completed all

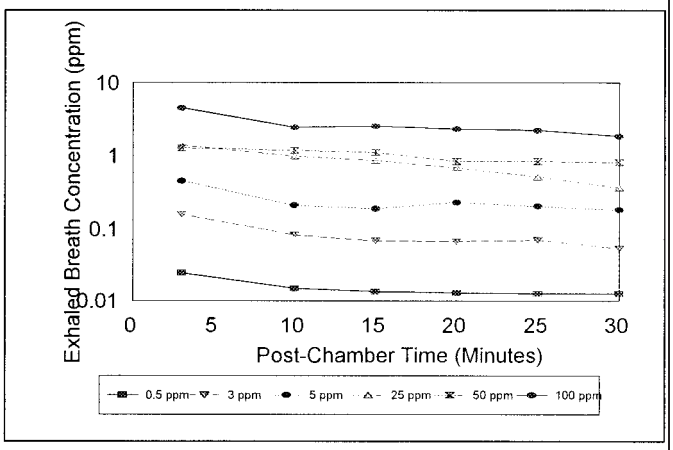


**FIGURE 3. Mean Freon-113 concentration of two trials in end-exhaled air following six different intermittent exposures in a single subject**

**TABLE III. Optimum Sampling Data**

| Subject | Test Type | End-Exhaled Air Concentration (ppm) 3 Min Post | 15 Min Post | 30 Min Post |
|---|---|---|---|---|
| 1 | exposure at beginning | 3.446 | 1.668 | 1.382 |
| 1 | exposure at beginning | 3.738 | 1.821 | 1.336 |
| 1 | exposure at end | 17.580 | 4.039 | 1.951 |
| 1 | exposure at end | 14.305 | 4.053 | 1.701 |
| 2 | exposure at beginning | 1.827 | 1.145 | 0.950 |
| 2 | exposure at beginning | 2.094 | 1.265 | 0.832 |
| 2 | exposure at end | 19.572 | 3.185 | 1.380 |
| 2 | exposure at end | 12.118 | 2.987 | 1.242 |
| 3 | exposure at beginning | 3.643 | 1.680 | 1.270 |
| 3 | exposure at beginning | 3.372 | 1.585 | 1.367 |
| 3 | exposure at end | 17.625 | 3.327 | 1.248 |
| 3 | exposure at end | 13.435 | 3.642 | 1.947 |

testing (characterization, skin absorption, method comparison, and validation) using the FT-IR. The time constraint prevented these tests from being repeated using the gas chromatograph. Not using the same instrument for all of the end-exhaled air analysis is a limitation of the study that will be discussed in further detail in the second article of this series.

For the gas chromatographic method, a 25-mL sample was collected and injected into the gas sampling valve system of a Hewlett-Packard 5890 gas chromatograph with a mass detector (GC/MD; Wilmington, Del.). To collect the end-exhaled air for GC/MD analysis, a subject inhaled deeply and held the breath for approximately 10 seconds. The subject then exhaled as long and as hard as possible through a device consisting of a mouthpiece, two one-way valves, and a sampling port. The device captured the last 25 mL of the end-exhaled air. The sample was then injected into the GC/MD for analysis by way of the gas sampling valve system.

Testing with standards was conducted to ensure that the GC/MD and FT-IR could actually detect 0.02 ppm, and the precision

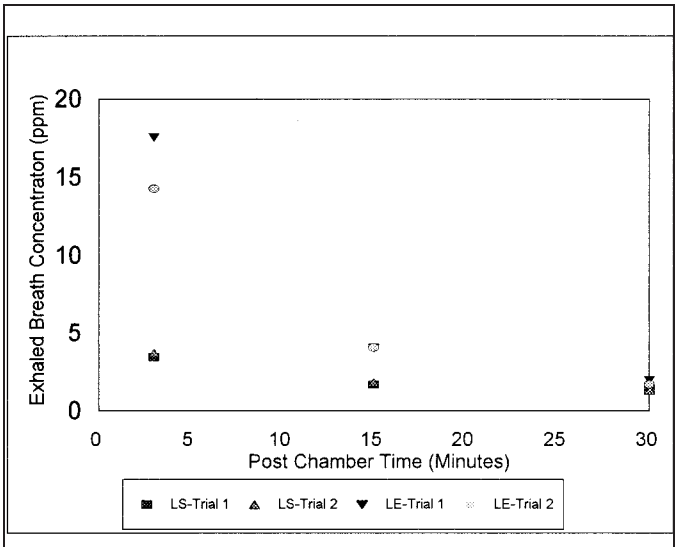


**FIGURE 4. Freon-113 concentration in end-exhaled air following a 6-minute exposure to 500 ppm at the beginning of a 30-minute test (LS) and a 6-minute exposure to 500 ppm at the end of a 30-minute test (LE) for first subject**

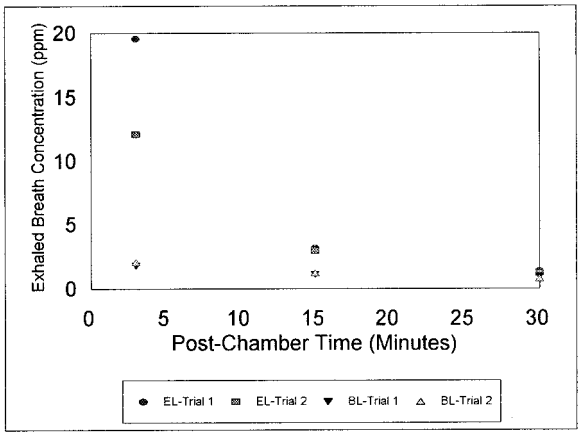


**FIGURE 5. Freon-113 concentration in end-exhaled air following a 6-minute exposure to 500 ppm at the beginning of a 30-minute test (BL) and a 6-minute exposure to 500 ppm at the end of a 30-minute test (EL) for second subject**

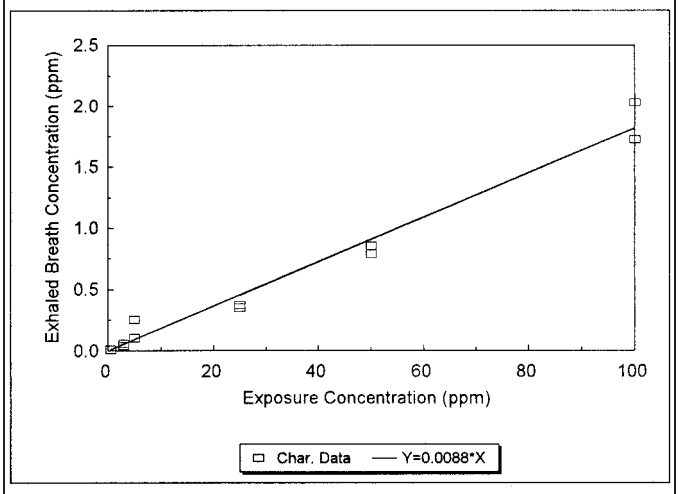


**FIGURE 7. End-exhaled Freon-113 concentrations (30 minute postchamber) resulting from 30-minute intermittent characterization exposures to Freon-113 for a single subject**

and accuracy of the instrumentations were satisfactory for the study. However, the actual minimum level of detection for each instrument may have been less than 0.02 ppm. The actual minimum level of detection was not investigated, since fit factors in excess of 2500 were not expected. In addition, the same instrument was used for each subject throughout the testing. Therefore, using both the GC/MD and FT-IR should not have affected the results of the study.

The off-gassing profiles from two subjects exposed to the 3000 ppm-min dose of Freon-113 are shown in Figures 1 and 2. As can be seen in Figure 1, there is a rapid decline in the Freon-113 concentration in the end-exhaled air within a few minutes of exiting the chamber. To provide consistent results the sampling time delay had to be long enough to avoid this rapid decline. Figure 1 also shows that 30 minutes is sufficient to avoid the rapid decrease of exhaled concentration immediately after the subject left the chamber.

The 30-minute sampling delay was verified by repeating the same test. As shown in Figure 2, 30 minutes postchamber time had the smallest deviation in results between the duplicate trials. In addition, the 30-minute sampling delay was corroborated by having a subject run a series of tests at six different concentrations. For each of the six exposure concentrations, the end-exhaled air concentration started to level off at about 25 to 30 minutes after leaving the chamber (Figure 3). Based on these test results, end-exhaled air sampling could be done at 30 minutes postexposure time. These test results were similar to Decker and Crutchfield who also found that after 25 to 30 minutes the amount of Freon-113 in the end-exhaled air plateaued.[19]

The results of the two exposure scenarios (at the beginning versus at the end of the 30 minutes) are given Table III and are plotted in Figures 4 through 6. These figures show the exhaled breath samples taken at 30 minutes postchamber have the least variation. Therefore, the optimum sampling time was chosen to be 30 minutes postchamber based on the different exposure scenario testing and the off-gassing profiles.

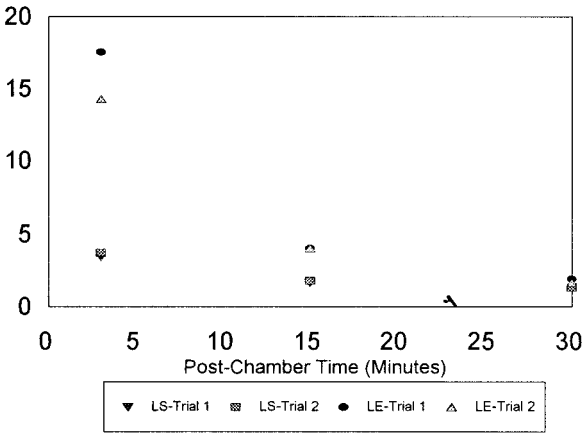


**FIGURE 6. Freon-113 concentration in end-exhaled air following a 6-minute exposure to 500 ppm at the beginning of a 30-minute test (LS) and a 6-minute exposure to 500 ppm at the end of a 30-minute test (LE) for third subject**

### Skin Absorption

The amount of Freon-113 in the end-exhaled air from skin absorption at 500 ppm is summarized in Table IV. It should be noted that all three subjects not exhibiting skin absorption had their breath analyzed by FT-IR. This could be an indication of a difference between the two analytical methods (FT-IR and GC/MD). Further research would be required to make this determination. No skin absorption was detected in any of the subjects at the 10 ppm concentration. Each individual's end-exhaled air was adjusted for the contribution of Freon-113 from skin absorption by subtracting that concentration from the total concentration found in the end-exhaled air before any further analysis was done.

The inhalation equivalent exposure concentration of Freon-113 for skin absorption at 500 ppm is also summarized in Table IV. The average inhalation equivalent exposure concentration of the 11 subjects in this study was found to be 2.81 ppm. Decker and Crutchfield found the inhalation equivalent exposure concentration by skin absorption in their subject to be 1.35 ppm.[19] This

**TABLE IV. Summary of Skin Absorption Data**

| Subject | Freon-113 Concentration in End-Exhaled Air Due to Skin Absorption (ppm)[A] | Inhalation Equivalent Exposure Concentration (ppm)[B] |
|---|---|---|
| 1 | 0.02 | 2.33 |
| 2 | 0.08 | 9.09 |
| 3 | 0.03 | 1.17 |
| 4 | 0.04 | 2.72 |
| 5 | 0.05 | 3.57 |
| 6 | 0.00 | 0.00 |
| 7 | 0.05 | 2.75 |
| 8 | 0.00 | 0.00 |
| 9 | 0.09 | 7.14 |
| 10 | 0.00 | 0.00 |
| 11 | 0.03 | 2.13 |
| Mean | 0.04 | 2.81 |
| Standard deviation | 0.03 | 2.79 |

[A]End-exhaled air was measured at 30 minutes after exposure.
[B]The inhalation equivalent exposure concentration was calculated using the characterization equations in Table VI.

value is slightly smaller than the value found in this study. It may be due to intersubject variability.

### Pharmacokinetic Modeling

End-exhaled air Freon-113 concentrations were obtained for different exposure concentrations put into the SAS computer program. The resulting Freon-113 concentration in the end-exhaled air and the exposure concentration were determined to be linearly correlated with an $R^2$ of 1.0. This was expected because the simultaneous differential equations for the physiological model are first-order and the model does not incorporate saturable metabolism. Auton and Woollen found that the predictions of the physiological model were in good agreement with results of human study.[29] The differences between predictions and measurements were of a similar magnitude to interindividual differences. Auton and Woollen also concluded that the concentrations of Freon-113 in breath or blood after exposure are shown to be insensitive to metabolic clearance.

End-exhaled air Freon-113 concentrations for different scenarios of exposure occurrence at 30 minutes postexposure time were also generated with the computer program and are summarized in Table V. The end-exhaled air Freon-113 concentration at 30 minutes after exposure to 100 ppm (30 minute time-weighted average) of Freon-113 is 1.126 ppm for intermittent exposure. The end-exhaled air Freon-113 concentration for continuous exposure is about the same as that for intermittent exposure. For the worst case scenarios (i.e., exposure at the beginning or end of a fit-test), end-exhaled air Freon-113 concentration was within 9% of the end-exhaled air Freon-113 concentration for intermittent exposure. Thus, the end-exhaled air Freon-113 concentration was only slightly affected by the variables of exposure.

The measured end-exhaled air Freon-113 concentrations for different scenarios of exposure occurrence at 30 minutes postexposure time are also summarized in Table V. The end-exhaled air Freon-113 concentration at 30 minutes after exposure to 100 ppm (30 minute time-weighted average) of Freon-113 was 1.254 ppm for intermittent exposure. The model output is in good agreement with this measurement. The difference is of a magnitude to inter- and intraindividual differences measured in this study. The end-exhaled air Freon-113 concentration for continuous exposure was only 0.570 ppm, which is 55% less than that for intermittent exposure. Making only one measurement could be the reason for the large error. For exposure at the beginning or at the end of a fit-test, end-exhaled air Freon-113 concentrations were 5% less or 26% more than that for intermittent exposure. Thus, the variability in the measured end-exhaled air Freon-113 concentration due to different exposure schedules is larger than that in pharmacokinetic model output. The good agreement in end-exhaled Freon-113 concentration for intermittent exposure between model output and measurement also supported the use of intermittent exposure to characterize subjects.

### Subject Characterization

End-exhaled air concentration (at 30 minutes) was proportional to the Freon-113 exposure concentration and could be expressed by the relationship, $Y=kX$ where Y is the end-exhaled air concentration, X is the exposure concentration, and k is a proportionality constant that differs for each subject. The characterization curve

**TABLE V. Effects of Exposure Schedule on End-Exhaled Freon-113 Concentration**

| Exposure Schedule | End-Exhaled Freon-113 Concentration (ppm) at 30 Min after Exposure to 100 ppm (30-Min Time-Weighted Average) | | | |
|---|---|---|---|---|
| | Experimental Data | | Pharmacokinetic Model Output | |
| | Mean ± SD (n[A]) | % Error[B] | Predicted Mean | % Error[B] |
| Intermittent | 1.254 ± 0.542 (22) | | 1.126 | |
| Continuous | 0.570 (1) | −55% | 1.125 | −0.1% |
| At beginning | 1.201 ± 0.217 (6) | −5% | 1.030 | −8.5% |
| At end | 1.526 ± 0.303 (6) | +26% | 1.224 | +8.7% |

[A]n = number of measurements.
[B]% Error is calculated based on the results for intermittent exposure.

**TABLE VI. Subject Characterization Equations**

| Subject | Characterization Equation[A] | $R^2$ Value |
|---|---|---|
| 1 | Y = 0.0086*X | 0.88 |
| 2 | Y = 0.0088*X | 0.98 |
| 3 | Y = 0.0256*X | 0.84 |
| 4 | Y = 0.0147*X | 0.79 |
| 5 | Y = 0.0140*X | 0.84 |
| 6 | Y = 0.0105*X | 0.95 |
| 7 | Y = 0.0182*X | 0.99 |
| 8 | Y = 0.0092*X | 0.91 |
| 9 | Y = 0.0126*X | 0.92 |
| 10 | Y = 0.0100*X | 0.98 |
| 11 | Y = 0.0141*X | 0.94 |

[A]X = exposure concentration in ppm and Y = end-exhaled air concentration in ppp.

for one subject is shown in Figure 7. This linear function was used to calculate each subject's exposure concentration from his or her end-exhaled air during the method comparison testing that is the topic of a subsequent article. Table VI is a summary of the characterization equations. The proportionality constants ranged from 0.0086 to 0.0256, and $R^2$ values ranged from 0.79 to 0.99. There were significant differences in the proportionality constants among subjects. This indicated that subjects should be characterized on an individual basis.

## SUMMARY AND CONCLUSIONS

The results of this study indicated that end-exhaled air analysis could be used to determine a subject's exposure to Freon-113. The optimum sampling time for sampling the end-exhaled air was determined to be 30 minutes after exposure or fit-test. The end-exhaled air concentrations and exposure concentrations were determined to be linearly correlated. Eleven subjects were characterized at six levels of Freon-113 concentration to establish the linear relationship between end-exhaled air concentrations and exposure concentrations. The data first had to be corrected for skin absorption before being used to develop characterization equations for the method comparison testing. Each level of Freon-113 concentration was the time-weighted average of intermittent exposure. Each subject should be characterized.

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## REFERENCES

1. **Burgess, W.A., L. Silverman, and F. Stein:** A new technique for evaluating respirator performance. *Am. Ind. Hyg. Assoc. J. 22*:422–429 (1961).
2. **Adley, F.E., and D.E. Wisehart:** Methods for performance testing of respiratory protective equipment. *Am. Ind. Hyg. Assoc. J. 23*:251–256 (1962).
3. **Hounam, R.F., D.J. Morgan, D.T. O'Conner, and R. J. Sherwood:** The evaluation of protection provided by respirators. *Ann. Occup. Hyg. 7*:353–363 (1964).
4. **Hyatt, E.C., J.A. Pritchard, and C.P. Richards:** Respirator efficiency measurement using quantitative DOP man tests. *Am. Ind. Hyg. Assoc. J. 33*:635–643 (1972).
5. **American Industrial Hygiene Association Respiratory Protection Committee:** Respirator performance terminology. [Letter to the Editor] *Am. Ind. Hyg. Assoc. J. 46*:B22–B24 (1985).
6. **Crutchfield, C.D., M.P. Eroh, and M.D. Van Ert:** A feasibility study of quantitative fit testing by controlled negative pressure. *Am. Ind. Hyg. Assoc. J. 52*:172–177 (1991).
7. **Los Alamos Scientific Laboratory:** *Respirator Protection Factors* (LA-6084-MS), by E.C. Hyatt. Los Alamos, New Mexico: Los Alamos Scientific Laboratory of the University of California, 1976.
8. **National Institute for Occupational Safety and Health (NIOSH):** *NIOSH Respirator Decision Logic* (DHHS(NIOSH) Publication No. 87-108), by W.R. Myers, N.J. Bollinger, T.K. Hodous, N.A. Leidel, S.H. Rabinovitz, and L.D. Reed. Cincinnati, OH: NIOSH, 1987. pp. 13–18.
9. **Myers, W.R., and M.J. Peach III:** Performance measurements on a powered air-purifying respirator made during actual field use in a silica bagging operation. *Ann. Occup. Hyg. 27*:251–59 (1983).
10. **Myers, W.R., M.J. Peach III, K. Cutright, and W. Iskander:** Field test of powered air-purifying respirators at a battery manufacturing facility. *J. Int. Soc. Respir. Prot. 4*:62–89 (1984).
11. **Myers, W.R., M.J. Peach III and J. Allender:** Workplace protection factor measurements on powered air-purifying respirators at a secondary lead smelter—test protocol. *Am. Ind. Hyg. Assoc. J. 45*:236–241 (1984).
12. **Lenhart, S.W., and D.L. Campbell:** Assigned protection factors for two respirator types based upon workplace performance testing. *Ann. Occup. Hyg. 28*:173–182 (1984).
13. **Myers, W.R., M.J. Peach III, K. Cutright and W. Iskander:** Workplace protection factor measurements on powered air-purifying respirators at a secondary lead smelter—results and discussion. *Am. Ind. Hyg. Assoc. J. 45*:681–688 (1984).
14. **Dixon, S.W., and T.J. Nelson:** Workplace protection factors for negative pressure half-mask respirators. *J. Int. Soc. Respir. Prot. 2*:347–61 (1984).
15. **Oestenstad, R.K., J.L. Perkins, and V.E. Rose:** Identification of faceseal leak sites on a half-mask respirator. *Am. Ind. Hyg. Assoc. J. 51*:280–284 (1990).
16. **Hewett, P., B.G. Pallay, and J.F.Gamble:** A model for correcting workplace protection factors for lung deposition and other effects. *Am. Ind. Hyg. Assoc. J. 54*:142–149 (1993).
17. **Liau, Y., A. Bhattacharya, H. Ayer, and C. Miller:** Determination of critical anthropometric parameters for design of respirators. *Am. Ind. Hyg. Assoc. J. 43*:897–899 (1982).
18. **Myers, W.R., J. Allender, R. Plummer, and T. Stobbe:** Parameters that bias the measurement of airborne concentration within a respirator. *Am. Ind. Hyg. Assoc. J. 47*:106–114 (1986).
19. **Decker, J.A., and C.D. Crutchfield:** Feasibility of a new method to determine respirator performance by biological monitoring of exhaled air. *J. Int. Soc. Resp. Protect. 11*:6–19 (1993).
20. **National Institute for Occupational Safety and Health (NIOSH):** *NIOSH Pocket Guide to Chemical Hazards* (DHHS (NIOSH) pub. no. 94-116). Cincinnati, OH: NIOSH, 1994. pp. 316–317.
21. "Occupational Safety and Health Standards, Toxic and Hazardous Substances, Air Contaminants." *Code of Federal Regulations*, Title 29, Part 1910. 1996. pp. 7–20.
22. **Ganong, W.F.:** *Review of Medical Physiology*. Los Altos, CA: Lange Medical Publications, 1989. pp. 497–498.
23. **American Public Health Association (APHA):** *Methods for Biological Monitoring*. Washington DC: APHA, 1988.
24. "Approval of Respiratory Protective Devices," *Code of Federal Regulations* Title 42, Part 84. 1996. pp. 573–577.
25. **U.S. Bureau of Mines:** *Freon 113 as a Test Material for Chemical Cartridge Respirators* (Report of investigations 7380), by C.F. Swab and B.I. Ferber. Washington, DC: United States Department of the Interior, Bureau of Mines, 1970.

26. **Ursin, C., C.M. Hansen, J.W. Van Dyk, P.O. Jensen, I.J. Christensen, and J. Ebbehoe:** Permeability of commercial solvents through living human skin. *Am. Ind. Hyg. Assoc. J. 56*:651–660 (1995).

27. **Ramsey, J.C., and M.E. Andersen:** A physiologically based description of the inhalation of styrene in rats and humans. *Toxicol. Appl. Pharmacol. 73*:159–175 (1984).

28. **Andersen, M.E., H.J. Clewell III, M.L. Gargas, F.A. Smith, and R.H. Reitz:** Physiologically based pharmacokinetics and the risk assessment process for methylene chloride. *Toxicol. Appl. Pharmacol. 87*: 185–205 (1987).

29. **Auton, T.R., and B.H. Woollen:** A Physiological based mathematical model for the human inhalation pharmacokinetics of 1,1,2-trichloro-1,2,2-trifluoroethane. *Int. Arch. Occup. Environ. Health 63*:133–138 (1991).

30. **SAS Institute Inc.:** *Statistical Analysis System* [Computer Software]. Cary, NC: SAS Institute Inc., 1996.

31. **Myers, W.R., Z. Zhuang, T. Nelson, S. Sides, and D. Wilmes:** Field performance measurements of half-facepiece respirators—study protocol. *Am. Ind. Hyg. Assoc. J. 56*:765–775 (1995).

32. **Ljungkvist, G.M., and R.G. Nordlinder:** A Field method for sampling benzene in end-exhaled air. *Am. Ind. Hyg. Assoc. J. 56*:693–697 (1995).

33. **Wilson, H.K.:** Breath analysis: physiological basis and sampling techniques. *Scand. J. Work Environ. Health 12*:174–192 (1986).