CORE
Metadata, citation and similar papers at core.ac.uk
Provided by D-Scholarship@Pitt

AUTOMATED BREATHING AND METABOLIC SIMULATOR (ABMS)

EVALUATION OF N95 RESPIRATOR USE WITH SURGICAL MASKS

by

Edward James Sinkule

B.S., West Virginia University, 1978

M.S., West Virginia University, 1980

Submitted to the Graduate Faculty of

the School of Education in partial fulfillment

of the requirements for the degree of

Doctor of Philosophy

University of Pittsburgh

2013

UNIVERSITY OF PITTSBURGH

SCHOOL OF EDUCATION

This dissertation was presented by

Edward J. Sinkule

It was defended on February 7, 2013 and approved by

David Hostler, PhD, Associate Professor, Department of Emergency Medicine

Elizabeth Nagle, PhD, Assistant Professor, Department of Health and Physical Activity

Nina L. Turner, PhD, Team Lead, Human Performance Team, NIOSH/NPPTL/TRB

Dissertation Advisor: Fredric Goss, PhD, Associate Professor, Department of Health and Physical Activity

Copyright © by Edward J. Sinkule

2013

AUTOMATED BREATHING AND METABOLIC SIMULATOR (ABMS) EVALUATION OF N95 RESPIRATOR USE WITH SURGICAL MASKS

Edward James Sinkule, Ph.D.

Objective: To reduce the threat of exhausting N95 filtering face piece respirator (FFR) supplies during pandemic influenza outbreaks, the Institute of Medicine has recommended using surgical mask covers (SM) over FFR among healthcare workers as one strategy to avoid surface contamination of the FFR. The objective of this investigation was to measure and evaluate breathing air quality (average inhaled CO_2 and O_2 concentrations), peak inhalation (InPr) and exhalation (ExPr) breathing pressures, and average inhaled dry-bulb (Tdb) and wet-bulb (Twb) temperatures when using FFR with FDA-cleared SM and without SM.

Methods: Thirty NIOSH-approved FFR models with and without SM were evaluated using the NIOSH Automated Breathing and Metabolic Simulator (ABMS). The ABMS protocol consisted of the following levels of O_2 consumption, CO_2 production, and minute ventilation performed consecutively for minimum of five min each (units in STPD): 0.5, 0.4, and 9.8 $L \cdot min^{-1}$; 1.0, 0.8, and 25.3 $L \cdot min^{-1}$; 1.5, 1.3, and 38 $L \cdot min^{-1}$; 2.0, 1.9, and 62 $L \cdot min^{-1}$; 2.5, 2.5, and 70 $L \cdot min^{-1}$; and 3.0, 3.15, and 80 $L \cdot min^{-1}$, respectively.

Results: The mean across all FFR without SM (FFR-alone) for average inhaled CO_2 and O_2 ranged from 2.7% and 17.1%, respectively, for the lowest metabolic rate to 1.7% and 19.2%, respectively, for the greatest metabolic rate. The mean across all FFR with SM (FFR+SM) for average inhaled CO_2 and O_2 ranged from 3.0% and 16.7%, respectively, for

the lowest metabolic rate to 1.9% and 18.9%, respectively, for the greatest metabolic rate. The mean across all FFR-alone for InPr and ExPr ranged from -5 and 7 mmH_2O, respectively, for the lowest metabolic rate to -41 and 24 mmH_2O, respectively, for the greatest metabolic rate. The mean across all FFR+SM for InPr and ExPr ranged from -7 and 8 mmH_2O, respectively, for the lowest metabolic rate to -51 and 30 mmH_2O, respectively, for the greatest metabolic rate. The mean across all FFR-alone for Tdb and Twb ranged from 29 to 27°C, respectively, for the lowest metabolic rate to 32 and 28°C for the greatest metabolic rate. The mean across all FFR+SM for Tdb and Twb ranged from 29 to 27°C, respectively, for the lowest metabolic rate to 33 and 30°C for the greatest metabolic rate.

When grouped by respirator type and compared to FFR-alone, average inhaled CO_2 concentration was significantly higher for cup FFR+SM and significantly lower for horizontal flat-fold FFR+SM. Reciprocal significant changes were observed for average inhaled O_2 concentrations. ExPr was significantly higher for cup FFR+SM at $\dot{V}O_2$ >1.0 $L \cdot min^{-1}$. InPr was significantly higher for cup FFR+SM at all levels of energy expenditure, and higher for other flat-fold FFR+SM at $\dot{V}O_2$ >1.5 $L \cdot min^{-1}$. Tdb and Twb was significantly higher for cup FFR+SM at $\dot{V}O_2$ >0.5 $L \cdot min^{-1}$.

Conclusions: The orientation of the SM on the FFR may have a significant effect on the inhaled breathing quality at lower levels of energy expenditure and breathing pressures at higher levels of energy expenditure. The measureable InPr and ExPr caused by SM on FFR for healthcare users likely will be imperceptible at lower activity levels. While statistically significant, the changes in Tdb and Twb for FFR+SM compared to FFR-alone were small.

FOREWARD

This project was successful because of many individuals, but several colleagues deserve special recognition. The dissertation committee members are appreciated for their patience and guidance (Drs. Fredric Goss, David Hostler, Elizabeth Nagle, and Nina Turner), with special emphasis to Dr. Goss and Dr. Turner for their mentorship and support over many years. Several colleagues provided me with opportunities that made the final stretch of this journey possible and know how much they are appreciated: Dean Kenneth Metz (a former advisor and former Dean of the School of Education, whose friendly demeanor taught me many aspects of teaching and interacting with students); Dean Louis Pingel (as Associate Dean of the School of Education saw my potential as a scientist and granted me the opportunity to finish this terminal degree with his generous support); Dean Abbott Brayton (my first dean of faculty at Davis & Elkins College, whose patience with me taught me how to be patient with others); Dr. Pervis Major (everyone should have the privilege of a friend that says what needs to be heard instead of saying what a friend wants to hear, and tactfully); Leslie Boord (former Division Director of CDC/NIOSH/NPPTL, never questioned or refused any request for assistance on behalf of my education); and, Drs. Andrea Kriska, Kristi Storti, and Robert Robertson for their patience and support.

The dissertation project could not be possible without the support of my family: Melinda (my lovely wife); patient children (Emily, Olivia, and Elianna); my mother (Margie Sinkule, R.I.P.) and father (David Sinkule, R.I.P.), and a very supportive grandmother and matriarch (Pauline Goudy, R.I.P.).

TABLE OF CONTENTS

LIST OF TABLES

Page

LIST OF FIGURES

1.0 INTRODUCTION

1.1 Rationale

At the request of the Department of Health and Human Services, the Institute of Medicine (IOM) convened a Committee on the Development of Reusable Facemasks for Use During an Influenza Pandemic in order to report on the solutions, limitations, threats, and possible opportunities of reusing respirators for infection control during an influenza pandemic (National Academy of Sciences, 2006). The Committee offered recommendations for extending the life of disposable N95 filtering face piece respirators (FFR) for individual users. One recommendation involved limiting contamination by placing a surgical mask over the respirator in order to prevent surface contamination and extending the usefulness of the FFR during a shift. Previous research reported elevated concentrations of inhaled carbon dioxide (CO_2) and decreased concentrations of inhaled oxygen (O_2) associated with wearing FFRs (Sinkule, Turner, and Hota, 2003). Others have proposed that the adverse effects of wearing FFR (e.g., headache and increased sick days) are the result of elevated inhaled CO_2 concentrations (Lim et al. 2006). The increased inhaled CO_2 concentrations and decreased inhaled O_2 concentrations within the breathing zone of negative-pressure (air-purifying) respirators, including FFR, are directly related to dead space(Sinkule, Turner, and Hota, 2003; Sinkule and Turner, 2004). No study examined the effects of the increased resistance from the application of a surgical mask (SM) on the characteristics of FFR and FFR dead

space. It is unknown, therefore, how the Committee's recommendation will affect the breathing gas concentrations and breathing resistance of FFR users.

The computer-controlled Automated Breathing and Metabolic Simulator (ABMS) is an ideal laboratory device for evaluating inhaled CO_2 and O_2 concentrations and resistance pressures in respirators due to its high degree of accuracy and repeatability in duplicating human CO_2 production and O_2 consumption. The ABMS produces CO_2 and simulates O_2 consumption at fixed breathing frequencies and tidal volumes to simulate human metabolic processes. The goal of this study was to characterize the inhaled CO_2 concentrations, inhaled O_2 concentrations, and inhalation and exhalation pressures of NIOSH-certified FFR with and without a FDA-cleared SM using an ABMS-based test.

The selection of NIOSH-certified FFR was determined by several criteria including the market share of three types of FFR, each with and without exhalation valves. The three types were cup, horizontal flat-fold, and other flat-fold. Market share was acquired through interview with trade organizations and respirator distributors. Preference was assigned to those FFR and surgical mask cover (SM) contained within the U.S. Strategic National Stockpile (SNS). The SM used was Medline NON27382 which was also in the SNS. This SM was a random selection between two SM available from the SNS that did not have ear loops for attachments thus compatible with a head form without ears.

The information from this investigation will be used to generate a report from NIOSH that could be used to influence recommendations on extending the lifetime of FFRs using a SM as a protective covering. The ABMS test method developed to investigate the use of N95 with SMs will be shared with the group from the International Organisation of Standards responsible for ABMS test standards (ISO / TC94 / Standards Committee 15 / Working

Group 1 / Project Group 4 – Respiratory Protective Device Test Methods) and the American National Standards Institute (ANSI). The information collected from this project may be used in the development of a NIOSH test method. Depending on the results, the information may be used to launch another investigation using human volunteers. For a human research study, this simulator study will provide the direction and magnitude of expected changes, identify any unexpected changes that may subject human volunteers to unhealthy or hazardous conditions, and provide the information needed to configure the sample size.

1.2 Purpose

The major purpose of this study was to evaluate the inhaled CO_2 and O_2 concentrations and breathing resistance of NIOSH-certified FFRs with and without a FDA-cleared SM using an ABMS-based test. An ABMS test protocol, which is valid and relevant for the FFR class, was used to characterize performance in terms of average inhaled CO_2 concentrations, average inhaled O_2 concentrations, and inhalation and exhalation pressures. The evaluations were repeated with the same FFRs worn while using a FDA-cleared SM as a protective covering. The investigation for measuring inhaled CO_2 and O_2 concentrations for FFRs with SMs will benefit: 1) policymakers when they make recommendations for extending the life of disposable FFRs, 2) those involved in testing and certifying these respirators by providing them with a valid, consistent method for evaluating inhaled CO_2 and O_2 concentrations, 3) workers required to wear these types of respirators by ensuring that inhaled breathing gas concentrations and resistances will be within acceptable limits, and 4) industrial hygienists that make respirator selections by providing an objective, repeatable test method for inhaled CO_2 concentrations for these types of respirators.

1.3 Research Hypotheses

1. A SM on FFRs will cause higher inhaled CO_2 concentrations compared to FFRs alone.
2. A SM on FFRs will cause lower inhaled O_2 concentrations compared to FFRs alone.
3. A SM on FFRs will cause higher peak inhalation and exhalation pressures compared to FFRs alone.
4. A SM on FFRs without exhalation valves will cause higher peak inhalation and exhalation pressures compared to a SM on FFRs with exhalation valves.

1.4 Significance

At the request of the Department of Health and Human Services, the Institute of Medicine convened a Committee on the Development of Reusable Facemasks for Use During an Influenza Pandemic in order to report on their solutions, limitations, threats, and possible opportunities of reusing respirators as a control for healthcare and public health applications during a pandemic (National Academy of Sciences, 2006). The Committee offered recommendations for extending the life of disposable FFRs for individual users. One recommendation involved limiting contamination by placing a SM over the respirator in order to prevent surface contamination. It is unknown if the Committee considered whether the addition of the SM would increase the physiological burden of wearing a FFR. Changes caused by the addition of a SM could include increased levels of CO_2, breathing resistance, and temperature, and decreased levels of O_2. There is no NIOSH certification test that

measures minimum and average inhaled carbon dioxide (CO_2) concentrations, or maximum and average inhaled oxygen (O_2) concentrations for FFRs.

The effects of wearing FFR and other types of respiratory protection have been widely studied using a variety of measurement methods (Li et al., 2005). Some of these investigations have been quantitative (e.g., levels of inhaled CO_2), qualitative (e.g., levels of fatigue), or can reflect characteristics that range from inconvenient (e.g., decreased levels of comfort) to hazardous (e.g., decreased inhaled levels of O_2). FFR use has been associated with an increased frequency of headaches and sick days (Lim et al. 2006). The physiological effects of breathing ~3 - 4% inhaled CO_2 include impaired visual performance (Yang et al. 1997), decreased exercise endurance (Raven et al. 1979), and severe dyspnea, headache, dizziness, and perspiration occurs if inhaled CO_2 is ~7% (Compressed Gas Association, 1999). Psychological effects include decreased reasoning and alertness, and increased irritability when inhaled CO_2 concentration was 6.5%; and short-term memory loss at 7.5% (Sayers et al. 1987). Subjects performing physical activity while breathing decreased O_2 concentrations (17%) experienced higher levels of lactic acid accumulation at lower levels of energy expenditure compared to normal O_2 concentrations, in addition to achieving lower levels of peak exercise performance (Hogan et al. 1983). Increased breathing resistance from respirators has been identified as the cause of respiratory fatigue and impaired physical work capacity, a shift to anaerobic metabolism from an increased rate of oxygen debt; early exhaustion at lighter workloads; and headache and dyspnea with inhaled CO_2 concentrations of 3% (Raven et al. 1979). Increased subjective fatigue and mental errors have been associated with wearing SMs (Raven et al. 1979). In a study that compared physiologic effects and subjective perceptions of comfort between using FFRs and SMs, significantly

higher levels of heart rate, mask temperature and humidity occurred during FFR wear compared to the SMs (Li et al. 2005). While wearing SMs, subjects felt drier, cooler, breathed easier and were more comfortable compared to wearing FFRs. Since some studies did not measure inhaled concentrations of CO_2 or O_2, or end-tidal PCO_2, the relationship of objective and subjective responses to gas concentrations could not be made. To date, no laboratory or field studies have been published to provide data on the effect from protective (e.g., SMs) on the concentrations of respiratory gases in the breathing zone of FFRs.

Subjective effects are associated with user comfort. Comfort, or discomfort, may be extensive enough to cause the wearer to remove the respiratory protection or prevent the wearer from donning respirators. One example is inhalation temperature. Normally, exhalation temperature is several degrees (Celsius) lower than body temperature. The next inhaled breath will include the dead air space mixed with the temperature of ambient air. The upper respiratory tract will warm and humidify the inhaled air to physiologic levels prior to entry in the lower respiratory area. This arrangement is different for wearers of negative pressure non-powered air purifying respirators, such as FFRs. The inhaled air within the breathing zone of the respirator is warmed from the preceding breath. A greater relative portion of the breath is pre-warmed from the respirator for smaller individuals compared to larger ones with a relative smaller tidal volume. With increased physical activity or ambient temperature conditions, increased body temperature will cause higher exhaled air temperatures. The burden of additional breathing resistance from respirators will increase the basal metabolic requirements from additional aerobic work by the respiratory accessory muscles. While wearing negative pressure respiratory protection, the inhaled temperature (and humidity) may affect the wearer's subjective level of comfort and capacity to wear the

respirator for extended periods of time. For this investigation, no human subjects will be used to report subjective comfort measurements. Inhalation temperature (dry-bulb) and wet-bulb temperature will be measured and reported. The inhaled and exhaled dry-bulb and wet-bulb temperatures will be used to determine the humidity of the inhaled and exhaled air while wearing the respirators with and without SMs.

2.0 LITERATURE REVIEW

2.1 Introduction

Primary respiratory responses to breathing through a negative pressure respiratory protective device include increased inhaled concentrations of CO_2 which would cause hypercapnia and decreased inhaled concentrations of O_2 which would cause hypoxia. Secondary responses include reduced inspiratory and expiratory ventilation times and smaller tidal volumes from increased inhalation and exhalation resistance (pressure).

The following chapter provides an overview of the respiratory consequences from breathing while wearing respiratory protection.

2.2 Respiratory Response Mechanisms with Respiratory Protection

Within the last 10 years, there has been increased awareness of elevated concentrations of inhaled CO_2 and decreased levels of inhaled oxygen (O_2) concentration associated with wearing respiratory protection. Field data suggest that CO_2 concentrations in several nonNIOSH-certified surgical helmets ranged from 0.55 to 1.17% during a 15-minute sampling period (Echt et al. 1996). A recent study found CO_2 levels exceeding the NIOSH STEL[1] of 3% in a prototype powered air-purifying respirator (PAPR) operating with the blower turned off (Beeckman, Turner, and Campbell, 1998). Average inhaled CO_2 concentrations were shown to exceed 2.0% in a wildland fire fighter's particulate filtering

[1] Short-term exposure limits (STEL's) are based on a 15-minute time-weighted average exposure that should not be exceeded at any time during a workday. Exposures at the STEL should not be longer than 15 min and should not be repeated more than four times per day.

device during testing over a range of work rates. NIOSH reported extremely high inhaled CO_2 concentrations and low inhaled O_2 concentrations in three nonNIOSH-certified air-purifying escape hood respirators evaluated with the automated breathing and metabolic simulator (average inhaled CO_2 concentrations range: 0.5 – 6.5% at the lowest level of energy expenditure; average inhaled O_2 concentrations range: 13.4 – 8.8%); in men during treadmill exercise (minimum inhaled CO_2 concentrations range: 0.4 – 2.3% at the lowest level of energy expenditure; maximum inhaled O_2 concentrations range: 19.9 – 19.0%); and in women during treadmill exercise (minimum inhaled CO_2 concentrations range: 0.9 – 4.0% at the lowest level of energy expenditure; maximum inhaled O_2 concentrations range: 19.6 – 17.0%) (Sinkule and Turner, 2004). The NIOSH IDLH[2] value for CO_2 is 40,000 ppm, or 4%. As a result of this research, NIOSH developed a standard test procedure (STP 0454) to measure inhaled CO_2 and O_2 concentrations for air-purifying escape-only respirators during physical activity (NIOSH, 2006).

Recently, NIOSH reported increased levels of CO_2 concentrations using an automated breathing and metabolic simulator at the lowest levels of energy expenditure among negative pressure respirators; with FFRs having the highest average inhaled CO_2 and O_2 concentrations of 3.5% and 16.8%, respectively (Sinkule, Turner, and Hota, 2003). Twenty-six different models from 17 manufacturers representing each type of FFR (cup, cup with fit enhancements, cone/duck-bill, and flat-folding) were examined. Results indicated the highest inhaled CO_2 values among the cup type with fit enhancements (a foam shell molded into the facial contact area used to improve the respirator's fit characteristics), especially at

[2] Immediately dangerous to life or health; a concentration from which a worker could escape without injury or without irreversible health effects in the event of respiratory protection equipment failure (e.g., contaminant breakthrough in a cartridge respirator or stoppage of air flow in a supplied-air respirator) and a concentration above which only "highly reliable" respirators would be required.

the lower levels of energy expenditure. The other respirators included approximately 390 models of various powered air-purifying respirators, elastomeric air-purifying respirators, air-supplied respirators with an airline (positive pressure devices), and gas masks.

2.3 The Automated Breathing and Metabolic Simulator

The computer-controlled Automated Breathing and Metabolic Simulator (ABMS) produces CO_2 and simulates O_2 consumption at fixed breathing frequencies and tidal volumes to simulate human metabolic processes (Deno, 1984 and Kyriazi, 1986). The ABMS is an ideal device for evaluating inhaled CO_2 and O_2 concentrations in respirators due to its high degree of accuracy and repeatability in duplicating human CO_2 production and O_2 consumption.

Several metabolic simulators have been developed, including machines used for evaluating military aircraft, evaluating crew conditions aboard vessels for space flight, and "calibrators" for metabolic measurement systems. Breathing machines have been used for testing and certifying respirators in the United States since 1970 (Kyriazi, 1986). These machines have several advantages, which are as follows: breathing machines relieve the need of using human test subjects; respirators which have been developed with a novel design or respirators which have been used can be characterized without causing a threat to human test subjects; and the mechanical and electrical engineering used in the operation of the breathing machines provide very accurate reproducibility between test periods and between the respirators that are to be evaluated. The disadvantages to breathing machines include the unpredictable frequency to mechanical and electronic malfunctions and wear, and current breathing machines cannot physiologically respond to changes caused by a respirator.

Two types of breathing machines have been used for the evaluation of respirators, breathing simulators (or, breathing machines) and a combination of breathing and metabolic

simulators. Breathing simulators are designed to simulate the characteristics of the human breathing pattern during respiratory ventilation, i.e. inhalation and exhalation. Typically, these machines include a motor-driven rotating cam that is connected to piston. The piston moves inside a fixed volume cylinder. The motor speed is determined by the respiration rate needed to maintain minute ventilation. Breathing and metabolic simulators are designed to simulate the characteristics of both human breathing and metabolic functions. By design, a metabolic simulator replicates breathing ventilation (respiratory frequency, tidal volume, flow, temperature and humidity), O_2 consumption, and CO_2 production. Where the breathing simulator uses air at ambient conditions, a metabolic simulator produces human respiratory air qualities at approximately 33ºC and saturated with water vapor.[3] Due to their complexity, metabolic simulators usually are managed by a computer program. The computer uses a routine of energy expenditures (protocol) to make adjustments and provide measurements of respiratory gas concentrations, pressures and temperatures. A protocol can be a single level of exercise, described by a constant $\dot{V}_E$, $\dot{V}O_2$, $\dot{V}CO_2$ and breathing waveform, for any desired duration. A protocol also can be a series of different levels of energy expenditures with correspondingly different $\dot{V}_E$, $\dot{V}O_2$, $\dot{V}CO_2$ and breathing waveforms, which may contain periods of similar or different durations. The computer programming performs adjustments to the lung motor and to the metabolic valves for breath-by-breath exhaust, CO_2 and nitrogen concentrations in order to maintain the criteria set forth in the protocol. During these adjustments, the computer displays the metabolic measurements (all output volumetric values in STPD unless stated otherwise) on a video display terminal and printer, and logs the information in a temporary data file.

[3] While 37ºC represents the resting human temperature, this parameter can be modified to a similar exercising human temperature of 38-39ºC.

There has been one benchmark research report where the responses from the ABMS with air-purifying escape hoods for use in a chemical, biological, or radioactive, or nuclear contaminated environment (CBRN) were similar as responses from human subject volunteers using the same respiratory protection (Sinkule and Turner, 2004). A statistical comparison between the ABMS and human subject data was not conducted.

3.0 METHODS

3.1 Respirator and SM Selection

This study was a laboratory-based evaluation using the ABMS to assess inhaled CO_2 and O_2 concentrations and breathing resistance (inhalation and exhalation pressures) caused by NIOSH-certified non-powered air-purifying respirators (disposable N95 particulate filtering face piece respirators, or FFR) with and without FDA-cleared SMs. The N-series respirator is restricted for use in workplaces free of oil aerosols, and 95 means the filter device is 95% efficient for filtering a mean particle size up to 0.075 ±0.020 micrometer (Figure 1). Bacteria may be as small as 0.2 micrometer contained within a fluid medium. FFR are a preferred respiratory protection device for healthcare because it is disposable, inexpensive, and meets filtration standards by NIOSH. In addition to filtration, NIOSH performs the following evaluations for FFR certification: breathing resistance ($\leq$35mmH_2O for inhalation and $\leq$25mmH_2O for exhalation at 85 ±2 liters·min^{-1} constant flow) and exhalation valve leak ($\leq$30 ml·min^{-1} at 25mmH_2O inhalation pressure). A sample of four respirators of a consistent common size (medium, medium/large, or universal) of each the following types initially were included in the research design:

N95 cup
N95 cup with fit enhancement (foam face, or fit, shell)
N95 duck-bill
N95 flat-fold

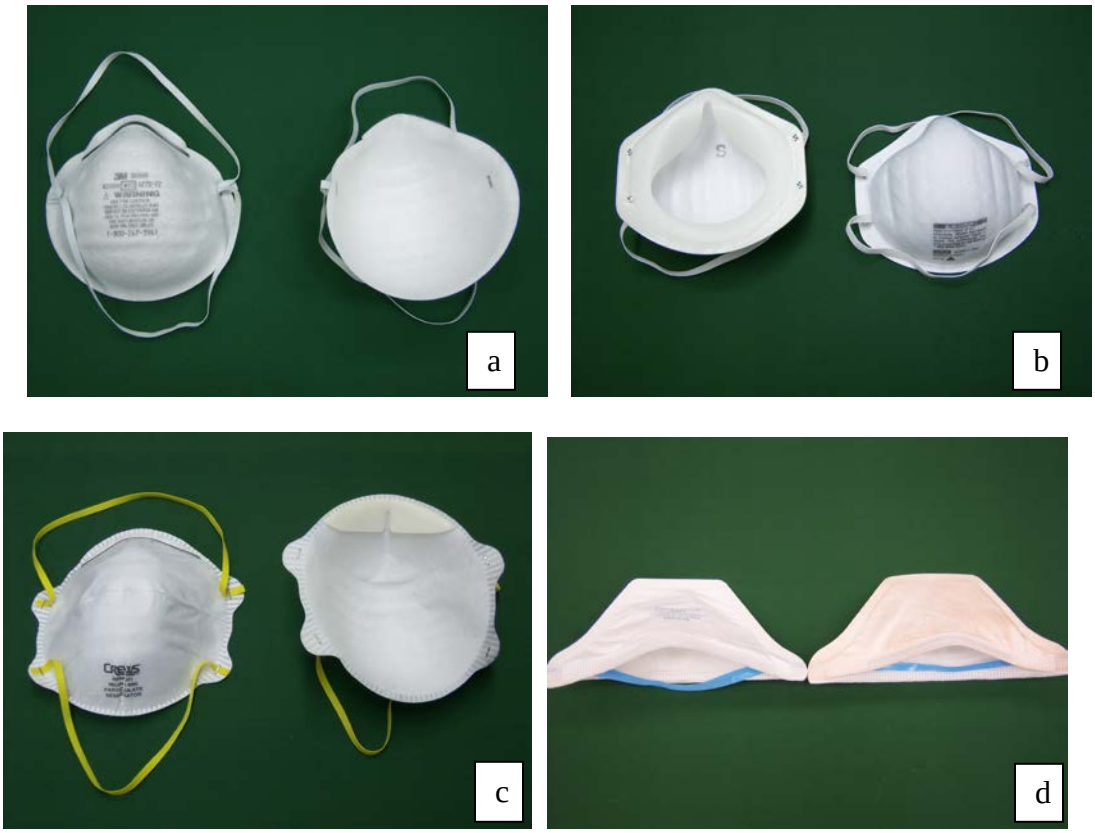

Figure 1. Example of NIOSH-approved N95 particulate filtering facepiece respirators. *a*, N95 cup. *b*, N95 cup with fit shell. *c*, N95 cone/duck bill. *d*, N95 horizontal flat-fold

In the sample of FFR used in this investigation, including those from the SNS, "medium" sized FFR were selected when various sizes were available. Size specifications of several FFR, however, included intermediate sizes, such as "one-size-fits-all" (also known as, "universal size") and "medium-large" size. Intermediate sizes and manufacturer-specific FFR were unbalanced in the sample between FFR with and without exhalation valves (Table 1). In addition, the sizes between models of FFR for the same manufacturer may not be equal. Furthermore, since there are no federal, industry, or standards body regulations for sizing FFR, dissimilar sizes between manufacturers occurred and would affect respirator dead-space.

At the beginning of the study, market changes were discovered and additional FFR in the U.S. Strategic National Stockpile required several changes in the selection of NIOSH-approved FFR. Market analyses were acquired through trade organizations and respirator distributors. First, an insufficient number of N95 cup FFR with fit shell were available in the N95 configuration. The "cup" type of FFR for analysis included cup FFR with and without fit shells, and with and without exhalation valves. Second, NPPTL management requested investigating additional FFR selected from the U.S. Strategic National Stockpile (SNS) (U.S. Department of Health and Human Services, 2009). The SNS is a large quantity of medicines and medical supplies maintained by the Centers for Disease Control and Prevention and the U.S. Department of Health and Human Services, mandated by Congress in 1999. The supplies within the SNS are to be used during national disasters or outbreaks when the local necessary supplies critically would be strained or exhausted. Preference was assigned to those respirators contained within the SNS. Third, in order to maintain a balanced design of FFR types after FFR from the SNS were selected, two additional FFR configurations were included – vertical flat-fold and tri-fold FFRs (Figure 2), and with and without exhalation valves. The vertical flat-fold FFR and the tri-fold FFR were combined into the "other flat-fold" type of FFR. Two duck-bill FFR were included in the sub-set of horizontal flat-fold FFR because they appeared similar with a horizontal fold that separated the top half and bottom half. The duck-bill FFR and horizontal flat-fold FFR, both with and without exhalation valves, were combined into the sub-set of "horizontal flat-fold" FFR. The type of FFR respirator is determined by the market and is not recognized classification in a NIOSH standard. The final groupings used in the research design were as follows: cup, horizontal flat-fold, and other flat-fold (Table 1).

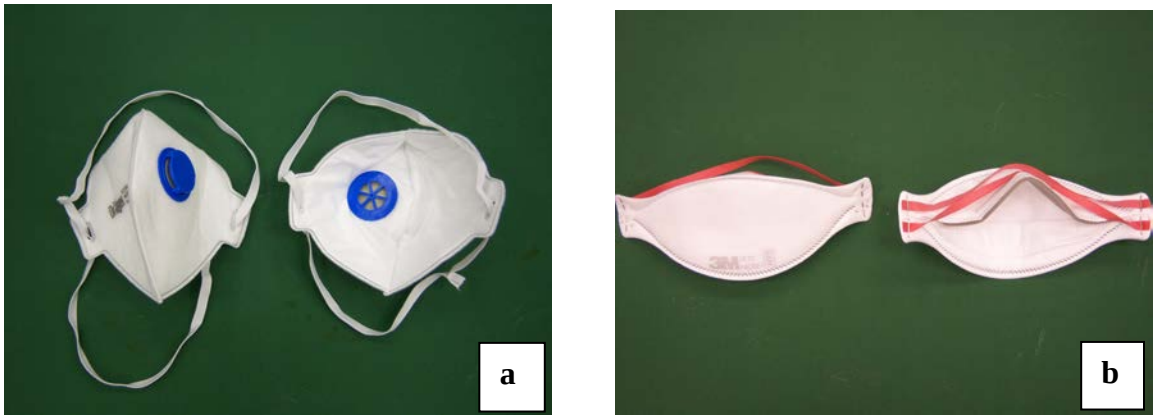

Figure 2. Added FFR to the research design.
a, vertical flat-fold FFR; and *b*, tri-fold FFR

According to the NIOSH Certified Equipment List, there are approximately 350+ models of NIOSH-approved FFR manufactured for use in the United States (NIOSH, 2011). The NIOSH Certified Equipment List (CEL) is a web-based repository of current and past NIOSH-certified respirators. The number of available nonNIOSH-approved N95 FFR models is unknown. After this investigation was launched, the NIOSH-approved FFR was expanded with more FFR available in the SNS. None of the FFR from the SNS contained exhalation valves. The final FFRs selected, therefore, included additional FFR types from the SNS and a balance of FFR types with exhalation valves. The number of FDA-cleared SM models and NIOSH-approved FFR models was limited due to the urgency of available data needed for policy guidance and a restriction of project funding.

SMs are evaluated under the guidance of the FDA, a.k.a. FDA-cleared, for fluid resistance, filtration efficiency, breathing resistance, and flammability. The tests may be conducted by an independent laboratory or a manufacturer's laboratory, and then reported to

the FDA by the SM manufacturer. The FDA does not conduct laboratory evaluations for clearing SMs. A SM may be of several types, e.g. pleated, flat-fold, cup, etc. A SM also may be a NIOSH-certified FFR. A combination NIOSH-certified FFR and FDA-cleared SM need only supply the NIOSH certification number (for filter efficiency and breathing resistance) with results for fluid resistance and flammability. The selection of the FDA-cleared SM was based on the models available within the SNS (Figure 3). The SM was a random selection between two SM available from the SNS that did not have ear loops for attachments thus compatible with a head form without ears.

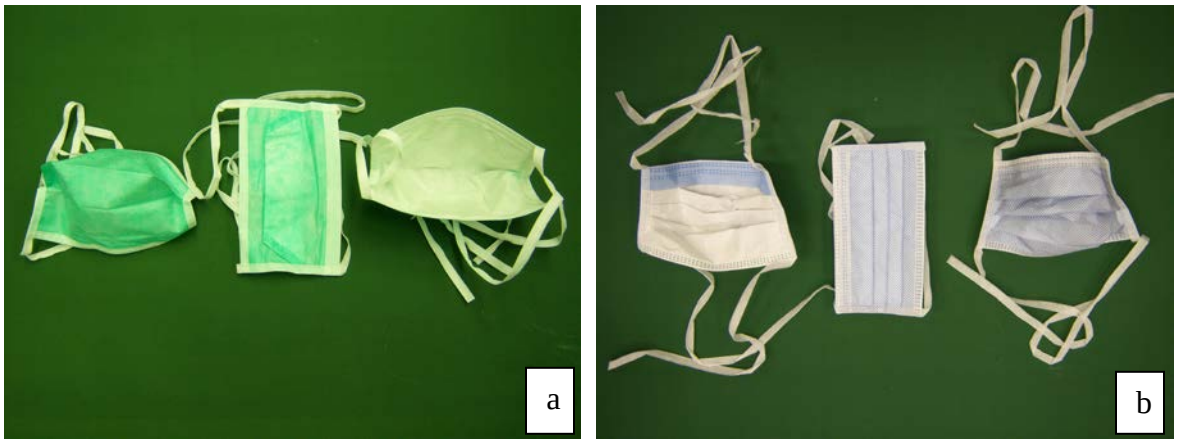

Figure 3. Examples of surgical mask covers.
a, FDA-cleared surgical mask from U.S. Strategic National Stockpile (Medline NON27382).
b, non-FDA-cleared surgical mask.

3.2 Automated Breathing and Metabolic Simulator (Figures 4 and 5)

The automated breathing and metabolic simulator (ABMS) with the abilities to simulate O_2 consumption, CO_2 production, and ventilation with heated and humidified air is ideal for quantitative and repeatable testing and evaluation of FFR (Figures 4 and 5). The ABMS (Ocenco, Inc., Pleasant Prairie, WI) has the capability to simulate the following metabolic parameters: O_2 consumption rate, CO_2 production rate, respiratory frequency, tidal volume,

breathing waveform shape, and heated and humidified breathing gas. In addition, any number of work rates may be combined in any order to simulate various activities. The capacity ranges for the parameters are as follows: minute ventilation, 0-160 $L \cdot min^{-1}$; O_2 consumption, 0-7 $L \cdot min^{-1}$; CO_2 production, 0-7 $L \cdot min^{-1}$; respiratory frequency, 0-100 $breaths \cdot min^{-1}$; tidal volume, 0-5 liters; and human-like breathing gas temperatures, 30-45 ºC. All gas volume parameters are at STPD (standard temperature (0 ºC) and pressure (760 mmHg), dry, unless stated otherwise. A sinusoid waveform was used for ventilation rates below 50 $L \cdot min^{-1}$. A trapezoid or human-like waveform was used for ventilation rates above 50 $L \cdot min^{-1}$.

The ABMS monitored the following parameters: flow-weighted average inhaled concentrations of O_2 and CO_2 concentrations, peak inhalation and exhalation breathing pressures, and inhaled dry-bulb and wet-bulb gas temperatures. The capacity ranges for these parameters are as follows: O_2 concentration, 0-100%; CO_2 concentration, 0-15%; breathing pressure, ±700 millimeters of water (H_2O); and inhaled dry-bulb and wet-bulb temperatures, 0-100ºC. The cyclic changes seen at the mouth of the ABMS reflect inhaled air concentrations from the environment and respirator dead space, adjusted by subtracting the gas transport time and analyzer response time, and weighing the instantaneous CO_2 and O_2 concentrations by the air flow rate in order to account for the relative contribution of the gases at each point under the flow curve. The average inhaled gas concentrations were determined by electronically measuring the instantaneous gas concentrations at the mouth (see placement of the "O_2 and CO_2 sample line", Figure 5) at a high sampling rate (200 Hz), weighing each value by multiplying it by the instantaneous flow rate, multiplying each product by the sampling interval, summing the volumes over inhalation, and dividing the

Figure 4. Automated breathing and metabolic simulator (ABMS).

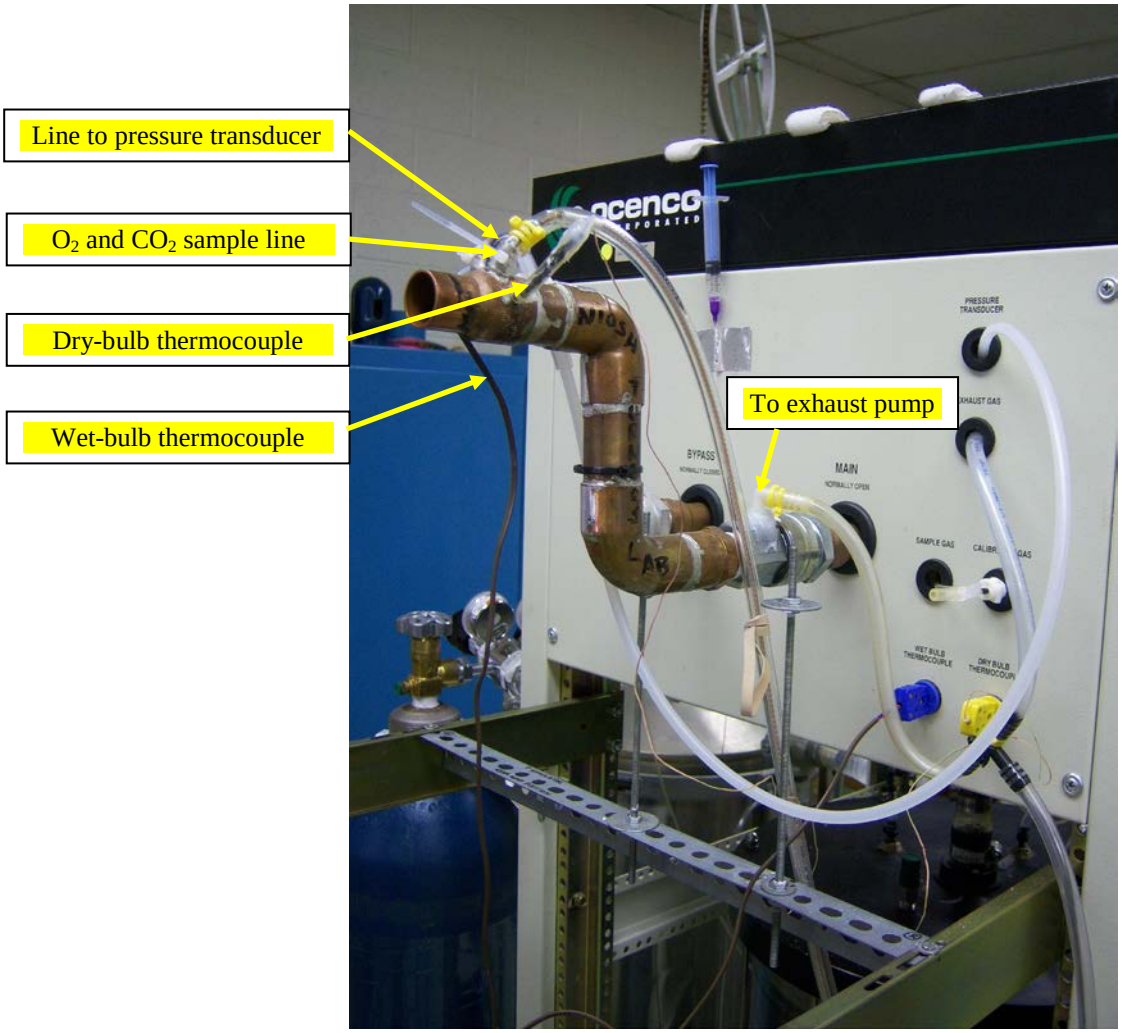

Figure 5. Exposed trachea from ABMS. Head form removed to expose the following sample lines: dry-bulb thermocouple, wet-bulb thermocouple, pressure transducer, exhaust gases, combined O_2 and CO_2 gas sample line.

volume of inhaled CO_2 and O_2 by the breath volume. A more detailed explanation is given in the appendix of the public document by Kyriazi (1986). Deno (1984) provides a description of the development of the ABMS.

3.3 Research Design and Variables

This study used a cross-sectional experimental design with 2x2x3 (surgical mask x exhalation valve x FFR type) factorial analysis of variance. The dependent variables were

average inhaled CO_2 concentration, average inhaled O_2 concentration, peak inhalation pressure, and peak exhalation pressure. Statistics were performed on average inhaled dry-bulb temperature and average inhaled wet-bulb temperature but the differences were very small. In this case, temperature within the FFR was difficult to interpret since heat from a user's face was not available and did not contribute to the temperature within each FFR. For each dependent variable, comparisons between the treatment (SM versus no SM) were performed for FFR with and without exhalation valves and for each type of FFR (cup, horizontal flat-fold, and other flat-fold).

Models of each type of FFR in the U.S. Strategic National Stockpile were selected to represent the SNS (Authorization of Emergency Use of Certain Personal Respiratory Protection Devices; Availability, 2009); in addition, similar models with exhalation valves and other popular models from the market were evaluated. All tests were repeated with a FDA-cleared SM also selected from the SNS. The total number of respirators tested were approximately 15 models x 2 exhalation valve configurations (with and without) x 4 respirator trials x 2 FDA-cleared surgical-mask configurations (with and without) = 240 tests.

Thirty NIOSH-approved disposable FFR models were selected for this investigation. Among the 30 respirator models, 18 were of the cup type, six of the horizontal flat fold type, and six of the other flat fold type. The "other flat-fold" types included three vertical flat fold and three tri-fold respirators. Table 1 provides the grouping among the respirator models for each type and the presence of an exhalation valve. One FDA-cleared flat-fold SM was included as a treatment for comparison among each respirator model and is present in the SNS. The SM used was Medline NON27382 which was also in the SNS (see Figure 3a).

Table 1: Grouping of the FFR Type and Valve

FFR type	FFR without Exhalation Valve	FFR with Exhalation Valve
Cup	3M 1860 (M)†	3M 8211 (O)
	3M 8000 (O)†	3M 8212 (O)
	3M 8210 (O)†	3M 8511 (O)
	Inovel 3002 (M)†	3M 8512 (O)
	AO Safety N9504C (O)*	AO Safety N9505C (O)*
	Crews RPN951 (O)*	Crews RPN952 (O)*
	Gerson 1730 (O)*†	Gerson 1740 (O)*
	Moldex 2200 (M/L)*†	Moldex 2300 (M/L)*
	Moldex-Metrics 2600 (M/L)*	Moldex-Metrics 2700 (M/L)*
Horizontal Flat-fold	Kimberly-Clark 46727 (O)†	Willson N9520FM (M)
	Crews RPFN951 (O)*	Crews RPFN952 (O)*
	San Huei SH2950 (O)*	San Huei SH2950V (O)*
Other Flat-fold	3M 1870 (O)†	Dräger Piccola (O)
	3M 9210 (O)*†	3M 9211 (O)*
	San Huei SH3500 (O)*	San Huei SH3500V (O)*

Respirators are FFR (size)
M = medium size, M/L = medium/large size, O = one-size-fits-all/universal size
* Paired-valve respirators: the same FFR with or without an exhalation valve
† Selected FFR from the Strategic National Stockpile

Each week, FFR testing was preceded by instrument calibration (pressure transducer, and both dry-bulb and wet-bulb thermocouples) and room-air validation studies. The room-air validation studies were performed on the exhaust gases as a means of confirming calibrated metabolic valves, sampling times, and lung volumes. Lung volume was electronically controlled by a stepper motor. The ABMS O_2 and CO_2 analyzers were calibrated using standard calibration gases (15% O_2 and 8% CO_2) before each trial. In addition, the response time (<100 milliseconds) and transport time (<300 milliseconds) were calculated electronically before each trial in these fast-response gas analyzers then used to electronically offset sample time. According to the manufacturers' instructions, respirators

were placed on the head form attached to the trachea of the ABMS. A sealant (Poli-Grip®) was applied to the contact area between the head form and respirator in order to create a seal between the facial surface of the head form with each FFR. The face seal with a NIOSH-approved FFR among human users is assessed with a fit-test. No sealant was used while donning a SM to the FFR since a fit-test is not needed for using surgical masks. FFRs, with and without SM, were tested for a minimum of 5 minutes at each work rate. For the ABMS, minute ventilation, O_2 consumption and CO_2 production change instantaneously between changes in energy expenditures which produce a rapid change (< 1 minute) in measured gas concentrations and steady state.

The breathing frequencies (f), tidal volumes (V_T), minute ventilation rates ($\dot{V}_E$), O_2 consumption rates ($\dot{V}O_2$), CO_2 production rates ($\dot{V}CO_2$), and respiratory quotients (R) programmed into the ABMS are shown in Table 2. These metabolic rates represent a progression from light to very intense energy expenditures. For health care workers, the range of energy expenditure can be from very light (e.g., desk work used for writing patient notes, 1.8 METs; or performing procedures in an operating room, 3 METs) to moderate (e.g., moving patients 34 kilograms or more, 7.5 METs) to very hard (e.g., responding to emergency calls by paramedics, patient care by physical therapists, and emergency calls performed by flight nurses, >10 METs) (Ainsworth et al., 2000). One MET (metabolic equivalent) is equal to a resting metabolic rate, or 3.5 ml of O_2 consumed$\cdot kg^{-1}\cdot min^{-1}$.

The metabolic rates are comparable to a draft international standard (ISO/TS 16876-1) for a person with a body surface area of 1.8 m^2 (1.75 meters in height and 70 kilograms in weight): $\dot{V}O_2$ (STPD): 0.5 $L\cdot min^{-1}$, 0.9 $L\cdot min^{-1}$, 1.5 $L\cdot min^{-1}$, 2.1 $L\cdot min^{-1}$, 2.5 $L\cdot min^{-1}$, and 3.1 $L\cdot min^{-1}$; and $\dot{V}_E$ (BTPS): 16 $L\cdot min^{-1}$, 27 $L\cdot min^{-1}$, 48 $L\cdot min^{-1}$, 66 $L\cdot min^{-1}$, 78 $L\cdot min^{-1}$, and 99

$L \cdot min^{-1}$. In the past (Morris, 1991) as well as in the current standard, $\dot{V}CO_2$ was assigned the same value as $\dot{V}O_2$ because it assumed that the respiratory quotient (R) was equal to 1 or the value was not cited. Throughout the spectrum of normal physical activity, the respiratory quotient will range from 0.80 to >1.0, which is the same as Table 2.

In a randomized fashion, models of FFR and the same models of FFR with the selected SM were evaluated as the test conditions. Flow-weighted average inhaled CO_2 and O_2 concentrations, peak inhaled and exhaled pressures at the mouth, average inhaled wet-bulb, and dry-bulb temperatures were measured by the ABMS, and arithmetic means of these variables were calculated. The data during the last minute of each variable at each level of energy expenditure (Table 2) for each condition (FFR only and FFR with SM) were used for analysis.

Table 2: Metabolic Variables for the ABMS Exercise Protocol

Test Level	f (breath/min)	V_T (Liters, STPD)	$\dot{V}_E$ ($L \cdot min^{-1}$, STPD)	$\dot{V}O_2$ ($L \cdot min^{-1}$, STPD)	$\dot{V}CO_2$ ($L \cdot min^{-1}$, STPD)	R
1	12.9	0.76	9.8	0.5	0.4	0.80
2	19.5	1.30	25.3	1.0	0.8	0.80
3	28.0	1.36	38.0	1.5	1.3	0.87
4	32.6	1.90	62.0	2.0	1.9	0.95
5	34.2	2.05	70.0	2.5	2.5	1.00
6	36.4	2.20	80.0	3.0	3.15	1.05

(f = frequency of breathing; V_T = tidal volume; $\dot{V}_E$ = minute ventilation, expired; $\dot{V}O_2$ = oxygen consumption; $\dot{V}CO_2$ = carbon dioxide production; R = respiratory Quotient)

When all the experimental trials were concluded, an examination of the variances among the trails revealed inconsistencies which required more trials for approximately six

FFR models to improve homogeneity of the results. Two-hundred eighty-one trials were completed, or an average of 4.7 trials for each FFR model tested with and without a SM.

Results included the mean and standard deviation of the following dependent variables for each respirator model tested under conditions with and without a SM: average inhaled CO_2 concentration, average inhaled O_2 concentration, peak inhaled and exhaled pressures at the mouth, average inhaled wet-bulb temperature, and average inhaled dry-bulb temperature. In this investigation, average inhaled temperature (determined by the dry-bulb and wet-bulb temperature measurements) was considered a variable of comfort and does not present a respiratory or metabolic risk compared to the inhaled gases and peak breathing pressures. Limited statistical analyses were performed on temperature because its relevance was limited. No temperature information from the face could be included because the head form was near room temperature and did not sweat. A facial surface temperature less than normal body temperature may have been responsible for FFR temperatures lower than expected. If additional information should become available that suggests that humidity or temperature triggers a larger concern than originally thought, then additional statistical analyses were included.

The research questions were as follows:

Using the ABMS throughout the range of energy expenditures, what were the effects on inhaled CO_2 and O_2 concentrations, and peak inhalation and exhalation pressures caused by:

1. Selected NIOSH-certified FFRs?
2. Selected NIOSH-certified FFRs with exhalation valves?
3. Selected NIOSH-certified FFRs covered with a FDA-cleared SM?

4. Selected NIOSH-certified FFRs with exhalation valves and covered with a FDA-cleared SM?

3.4 Sample Size and Statistical Analyses

Data from a previous NIOSH study that investigated the inhaled CO_2 concentrations in various respirators using the ABMS (Sinkule et al. 2003) were used to determine sample sizes in the current study. The primary measure of interest, for purposes of estimating the study's power, was the minimal fractional inhaled CO_2 concentration (expressed here as a percent). The mean fractional minimal inhaled CO_2 concentration was 0.25%, the within-group, or within-respirator standard deviation (pooled over the different units) was 0.09%. The between-group variability represented 94.4% of the overall variability in CO_2 measurements. For the initial power estimate, the analysis of variance contrast between those with and without a SM will have similar power to the 2-sample t-test with a pooled standard deviation of 0.09% and a sample size of $n = 0.944 \times 96$, which (conservatively) ≈ 90 per group (Neter et al., 1985). The following results give power estimates for different assumptions about the primary difference in minimal inhaled CO_2 concentrations between those tests with and without a SM; all estimates are based on a 1-sided test (which assumes that the CO_2 measurement can only be greater, or the same, with the SM).

CO_2 level (with a SM):	Statistical Power:
0.26%	18.4%
0.27%	43.9%
0.28%	72.3%
0.29%	90.9%
0.30%	98.1%

For example, compared to the fractional minimal inhaled CO_2 concentration within the N95 without a SM, we have a 98.1% probability of a true hypothesis if the difference detected in the minimal inhaled CO_2 concentration of a FFR with a SM is at least 0.05% (the difference in the minimal inhaled CO_2 concentration of a FFR without a SM, 0.25%, and the minimal inhaled CO_2 concentration of a FFR with a SM, 0.30%). The sample size, therefore, of four respirators of each model were tested for 5 minutes at each O_2 consumption rate. Respirators were tested randomly according to type.

Dependent variables (average inhaled CO_2 concentrations, average inhaled O_2 concentrations, and peak inhalation and exhalation pressures) were analyzed using 2x2x3 (SM x exhalation valve x FFR type) factorial analysis of variance (ANOVA). For each dependent variable, comparisons between the treatment (SM versus no SM) were performed for respirators with and without exhalation valves and for each type of respirator (cup, horizontal flat-fold, and other flat-fold). If necessary, the Tukey multiple comparison test was used for all *post hoc* analysis of significant effects. Statistical significance for ANOVA and Tukey analyses was set at $P<0.05$. Data analyses were performed using SPSS, version 18 (SPSS, Inc., Chicago, IL).

4.0 RESULTS

4.1 Respiratory Gases

Results for the average inhaled CO_2 concentration (expressed as percent) among FFR with and without SM are shown in Table 3. Among the six levels of energy expenditure, the average inhaled CO_2 concentrations were higher ($p<0.05$) among the cup FFR with SM compared to cup FFR alone at 0.5 $L \cdot min^{-1}$, 2.5 $L \cdot min^{-1}$, and 3.0 $L \cdot min^{-1}$. The average inhaled CO_2 concentrations were lower ($p<0.05$) among horizontal flat-fold FFR with SM compared to horizontal flat-fold FFR alone at 1.0 $L \cdot min^{-1}$ and 1.5 $L \cdot min^{-1}$. The average inhaled CO_2 concentrations were not different between other flat-fold FFR with and without SM. A significant ($p<0.05$) main effect was observed for average inhaled CO_2 by the following variables: FFR type at $\dot{V}O_2$ of 0.5 $L \cdot min^{-1}$, 1.0 $L \cdot min^{-1}$, and 1.5 $L \cdot min^{-1}$; and, exhalation valve at $\dot{V}O_2$ of 0.5 $L \cdot min^{-1}$, 1.0 $L \cdot min^{-1}$, 1.5 $L \cdot min^{-1}$, 2.0 $L \cdot min^{-1}$, 2.5 $L \cdot min^{-1}$, and 3.0 $L \cdot min^{-1}$. Significant interactions ($p<0.05$) between N95 type and exhalation valve on average inhaled CO_2 concentration were observed for $\dot{V}O_2$ of 0.5 $L \cdot min^{-1}$ only; between FFR type and SM use for $\dot{V}O_2$ of 1.0 $L \cdot min^{-1}$, 2.5 $L \cdot min^{-1}$, and 3.0 $L \cdot min^{-1}$; between FFR with exhalation valves and SM use at $\dot{V}O_2$ of 1.5 $L \cdot min^{-1}$, 2.0 $L \cdot min^{-1}$, 2.5 $L \cdot min^{-1}$, and 3.0 $L \cdot min^{-1}$.

Table 3: Average Inhaled Carbon Dioxide Concentrations (%) Among FFR With and Without SM

Oxygen Consumption, L·min^{-1}	Treatment	Cup (n = 18)	Horizontal Flat-fold (n = 6)	Other Flat-fold (n = 6)
0.5	N95 only	2.49 ± 0.51	3.52 ± 0.93	2.65 ± 0.57
	N95 + SM	2.93 ± 0.38∗	3.14 ± 0.64	3.13 ± 0.40
1.0	N95 only	1.64 ± 0.53	2.87 ± 1.12	1.93 ± 0.66
	N95 + SM	1.98 ± 0.39	2.00 ± 0.44∗	2.01 ± 0.12
1.5	N95 only	2.09 ± 0.82	3.23 ± 1.32	2.31 ± 0.94
	N95 + SM	2.31 ± 0.41	2.30 ± 0.46∗	2.21 ± 0.09
2.0	N95 only	1.43 ± 0.60	1.81 ± 0.82	1.65 ± 0.73
	N95 + SM	1.75 ± 0.33	1.67 ± 0.33	1.58 ± 0.15
2.5	N95 only	1.28 ± 0.57	1.66 ± 0.77	1.52 ± 0.73
	N95 + SM	1.65 ± 0.38∗	1.52 ± 0.26	1.48 ± 0.16
3.0	N95 only	1.52 ± 0.65	1.90 ± 0.87	1.79 ± 0.89
	N95 + SM	1.99 ± 0.33∗	1.75 ± 0.32	1.71 ± 0.22

Values are means ± SD
N95 only = FFR alone, N95 + SM = FFR with SM cover
∗Significantly different from N95 only, $p<0.05$

Results for the average inhaled O_2 concentration (expressed as percent) among FFR with and without SM are in Table 4. Among the six levels of energy expenditure, the average inhaled O_2 concentrations were lower ($p<0.05$) among the cup FFR with SM compared to cup FFR alone at 0.5 L·min^{-1}, 2.5 L·min^{-1}, and 3.0 L·min^{-1}. The average inhaled O_2 concentrations were higher ($p<0.05$) among horizontal flat-fold FFR with SM compared to horizontal flat-fold FFR alone at 1.0 L·min^{-1} and 1.5 L·min^{-1}. The average inhaled O_2 concentrations were not different between other flat-fold FFR with and without SM. A significant ($p<0.05$) main effect was observed for average inhaled O_2 by the following

variables: FFR type at $\dot{V}O_2$ of 0.5 L·min^{-1}, 1.0 L·min^{-1}, and 1.5 L·min^{-1}; and, exhalation valve at $\dot{V}O_2$ of 0.5 L·min^{-1}, 1.0 L·min^{-1}, 1.5 L·min^{-1}, 2.0 L·min^{-1}, 2.5 L·min^{-1}, and 3.0 L·min^{-1}. Significant ($p<0.05$) interactions between FFR type and exhalation valve on average inhaled O_2 concentration were observed for $\dot{V}O_2$ of 0.5 L·min^{-1} only; between FFR type and SM use for $\dot{V}O_2$ of 1.0 L·min^{-1}, 1.5 L·min^{-1}, and 3.0 L·min^{-1}; between FFR with exhalation valves and SM use at $\dot{V}O_2$ of 1.5 L·min^{-1}, 2.0 L·min^{-1}, 2.5 L·min^{-1}, and 3.0 L·min^{-1}.

Table 4: Average Inhaled Oxygen Concentrations (%) Among FFR With and Without SM

Oxygen Consumption, L·min^{-1}	Treatment	Cup (n = 18)	Horizontal Flat-fold (n = 6)	Other Flat-fold (n = 6)
0.5	N95 only	17.40 ± 0.81	16.10 ± 1.14	17.31 ± 0.77
	N95 + SM	16.81 ± 0.54∗	16.52 ± 0.79	16.58 ± 0.67
1.0	N95 only	18.84 ± 0.77	17.30 ± 1.39	18.47 ± 0.89
	N95 + SM	18.39 ± 0.50	18.39 ± 0.55∗	18.29 ± 0.17
1.5	N95 only	18.49 ± 1.04	17.15 ± 1.52	18.22 ± 1.13
	N95 + SM	18.22 ± 0.49	18.25 ± 0.51∗	18.25 ± 0.09
2.0	N95 only	19.33 ± 0.70	18.92 ± 0.84	19.08 ± 0.84
	N95 + SM	18.96 ± 0.37	19.05 ± 0.35	19.05 ± 0.15
2.5	N95 only	19.52 ± 0.65	19.12 ± 0.77	19.26 ± 0.82
	N95 + SM	19.11 ± 0.41∗	19.25 ± 0.28	19.19 ± 0.16
3.0	N95 only	19.32 ± 0.71	18.95 ± 0.83	19.03 ± 0.96
	N95 + SM	18.82 ± 0.38∗	19.06 ± 0.34	18.98 ± 0.23

Values are means ± SD
N95 only = FFR alone, N95 + SM = FFR with SM cover
∗Significantly different from N95 only, $p<0.05$

4.2 Breathing Pressures

Peak inhalation and exhalation pressures are used as measures of breathing resistance. Results for peak exhalation pressure (expressed in mmHg) among FFR with and without SM are in Table 5. Among the six levels of energy expenditure, the peak exhalation pressures were higher ($p<0.05$) among the cup FFR with SM compared to cup FFR alone at 1.5 $L \cdot min^{-1}$, 2.0 $L \cdot min^{-1}$, 2.5 $L \cdot min^{-1}$, and 3.0 $L \cdot min^{-1}$. Peak exhalation pressures were not different between horizontal flat-fold FFR with or without SM, nor between other flat-fold FFR with or without SM. In addition, a significant ($p<0.05$) main effect of SM use and FFR with an exhalation valve on peak exhalation pressure was observed for $\dot{V}O_2$ of 1.5 $L \cdot min^{-1}$, 2.0 $L \cdot min^{-1}$, 2.5 $L \cdot min^{-1}$, and 3.0 $L \cdot min^{-1}$.

Results for peak inhalation pressure among FFR with and without SM are in Table 6. Among the six levels of energy expenditure, the peak inhalation pressures were higher ($p<0.05$) among the cup FFR with SM compared to cup FFR alone at every level of O_2 consumption. Peak inhalation pressures were different between other flat-fold FFR with or without SM at the $\dot{V}O_2$ of 2.0 $L \cdot min^{-1}$, 2.5 $L \cdot min^{-1}$, and 3.0 $L \cdot min^{-1}$. Peak inhalation pressures were not different between horizontal flat-fold FFR with and without SM. In addition, a significant ($p<0.05$) main effect of SM use on peak inhalation pressure was observed for $\dot{V}O_2$ of 1.0 $L \cdot min^{-1}$, 1.5 $L \cdot min^{-1}$, 2.0 $L \cdot min^{-1}$, 2.5 $L \cdot min^{-1}$, and 3.0 $L \cdot min^{-1}$.

The presence of an exhalation valve may affect breathing pressure response. Fifteen of the 30 FFR contained an exhalation valve. The exhalation valve is a flexible dam (usually made of rubber) anchored to a circular frame that is mounted in the wall of the FFR directly in the front of the breathing zone. The circular frame has adequate venting to facilitate the flow of air during exhalation. The valve is anchored with a flexible connection so that it can

passively lift from its frame with positive mask pressure created by exhalation and allow the valve to become seated against the valve frame between breaths. The valve prevents inward leakage of ambient air during exhalation and during the isovolumic period between inhalation and exhalation. Upon negative mask pressure created by inhalation, the flexible dam is pulled into its frame to create a seal and prevent air leak into the FFR mask. Table 7 contains results of peak inhalation and exhalation pressures in FFR with and without exhalation valves compared to FFR with and without SM.

Table 5: Peak Exhalation Pressures (mmH_2O) Among FFR With and Without SM

Oxygen Consumption, $L \cdot min^{-1}$	Treatment	Cup (n = 18)	Horizontal Flat-fold (n = 6)	Other Flat-fold (n = 6)
0.5	N95 only	8 ± 2	7 ± 2	7 ± 4
	N95 + SM	8 ± 2	8 ± 2	9 ± 3
1.0	N95 only	10 ± 3	11 ± 3	9 ± 3
	N95 + SM	12 ± 3	12 ± 3	11 ± 2
1.5	N95 only	14 ± 4	15 ± 3	14 ± 4
	N95 + SM	17 ± 4∗	18 ± 4	17 ± 2
2.0	N95 only	23 ± 7	24 ± 4	22 ± 6
	N95 + SM	29 ± 7∗	30 ± 8	28 ± 4
2.5	N95 only	20 ± 6	21 ± 4	19 ± 5
	N95 + SM	25 ± 6∗	26 ± 6	24 ± 4
3.0	N95 only	24 ± 8	25 ± 4	23 ± 6
	N95 + SM	30 ± 7∗	31 ± 8	29 ± 4

Values are means ± SD
N95 only = FFR alone, N95 + SM = FFR with SM cover
∗Significantly different from N95 only, $p<0.05$

Table 6: Peak Inhalation Pressures (mmH_2O) Among FFR With and Without SM

Oxygen Consumption, $L \cdot min^{-1}$	Treatment	Cup (n = 18)	Horizontal Flat-fold (n = 6)	Other Flat-fold (n = 6)
0.5	N95 only	-6 ± 1	-5 ± 2	-6 ± 2
	N95 + SM	-7 ± 2∗	-6 ± 2	-7 ± 1
1.0	N95 only	-12 ± 2	-12 ± 4	-12 ± 2
	N95 + SM	-15 ± 3∗	-14 ± 5	-14 ± 2
1.5	N95 only	-19 ± 4	-19 ± 6	-18 ± 2
	N95 + SM	-23 ± 5∗	-23 ± 8	-23 ± 3
2.0	N95 only	-35 ± 6	-34 ± 10	-33 ± 3
	N95 + SM	-41 ± 7∗	-43 ± 16	-44 ± 11∗
2.5	N95 only	-35 ± 6	-34 ± 10	-33 ± 3
	N95 + SM	-42 ± 8∗	-44 ± 16	-45 ± 12∗
3.0	N95 only	-41 ± 7	-42 ± 13	-40 ± 3
	N95 + SM	-49 ± 9∗	-54 ± 22	-56 ± 17∗

Values are means ± SD
N95 only = FFR alone, N95 + SM = FFR with SM cover
∗Significantly different from N95 only, $p<0.05$

Table 7: Peak Inhalation and Exhalation Pressures (mmH_2O) Among FFR With and Without Exhalation Valves Between FFR With and Without SM

Oxygen Consumption, $L \cdot min^{-1}$	Treatment	Peak Inhalation Pressure		Peak Exhalation Pressure	
		Plain N95	N95 + EV	Plain N95	N95 + EV
0.5	N95 only	-6 ± 1	-5 ± 2	7 ± 2	8 ± 2
	N95 + SM	-7 ± 2	-7 ± 2*	8 ± 2	8 ± 3
1.0	N95 only	-11 ± 2	-12 ± 3	11 ± 3	10 ± 3
	N95 + SM	-14 ± 3*	-15 ± 4*	13 ± 2*	10 ± 3
1.5	N95 only	-18 ± 3	-20 ± 4	16 ± 4	13 ± 4
	N95 + SM	-22 ± 4*	-24 ± 6*	19 ± 3*	15 ± 3
2.0	N95 only	-33 ± 5	-36 ± 8	27 ± 6	20 ± 5
	N95 + SM	-40 ± 8*	-45 ± 11*	33 ± 6*	25 ± 5*
2.5	N95 only	-33 ± 5	-36 ± 8	23 ± 5	17 ± 5
	N95 + SM	-40 ± 8*	-45 ± 12*	28 ± 5*	22 ± 4*
3.0	N95 only	-39 ± 5	-43 ± 9	27 ± 6	20 ± 6
	N95 + SM	-49 ± 12*	-54 ± 15*	34 ± 6*	26 ± 5*

Values are means ± SD
N95 only = FFR alone, N95 + SM = FFR with SM cover
N95 alone = FFR without exhalation valve, N95 + EV = FFR with exhalation valve
*Significantly different from N95 only, $p<0.05$

4.3 Inhaled Breathing Temperatures

Results for average inhaled dry-bulb temperature (degrees Celsius) among the types of FFR are in Table 8. The dry-bulb temperature for the cup FFR with SM were different from cup N95 without SM at $\dot{V}O_2$ of 1.0 $L \cdot min^{-1}$, 1.5 $L \cdot min^{-1}$, 2.0 $L \cdot min^{-1}$, 2.5 $L \cdot min^{-1}$, and 3.0 $L \cdot min^{-1}$. Average inhaled dry-bulb temperatures were not different between horizontal flat-fold FFR with and without SM, nor between other flat-fold FFR with and without SM. In addition, a

significant ($p<0.05$) main effect of FFR with an exhalation valve and SM use on average inhaled dry-bulb temperature was observed for $\dot{V}O_2$ of 1.5 L·min^{-1}, 2.0 L·min^{-1}, 2.5 L·min^{-1}, and 3.0 L·min^{-1}. Significant ($p<0.05$) interactions between FFR with exhalation valves and SM use on average inhaled dry-bulb temperature at $\dot{V}O_2$ of 1.5 L·min^{-1}, 2.0 L·min^{-1}, 2.5 L·min^{-1}, and 3.0 L·min^{-1}.

Results for average inhaled wet-bulb temperature (degrees Celsius) among the types of FFR are in Table 9. The average inhaled wet-bulb temperature for the cup FFR with SM were different from cup N95 without SM at 1.0 L·min^{-1}, 1.5 L·min^{-1}, 2.0 L·min^{-1}, 2.5 L·min^{-1}, and 3.0 L·min^{-1}. Average inhaled wet-bulb temperatures were not different between horizontal flat-fold FFR with and without SM, nor between other flat-fold FFR with and without SM. In addition, a significant ($p<0.05$) main effect of FFR with an exhalation valve on average inhaled wet-bulb temperature was observed for $\dot{V}O_2$ of 1.0 L·min^{-1}, 1.5 L·min^{-1}, 2.0 L·min^{-1}, 2.5 L·min^{-1}, and 3.0 L·min^{-1}; and, SM use on average inhaled wet-bulb temperature for $\dot{V}O_2$ of 1.5 L·min^{-1}, 2.0 L·min^{-1}, 2.5 L·min^{-1}, 3.0 L·min^{-1}. Significant ($p<0.05$) interactions between FFR with exhalation valves and SM use on average inhaled wet-bulb temperature at $\dot{V}O_2$ of 1.5 L·min^{-1}, 2.0 L·min^{-1}, 2.5 L·min^{-1}, and 3.0 L·min^{-1}.

Table 8: Average Inhaled Dry-Bulb Temperatures (degrees Celsius) Among FFR With and Without SM

Oxygen Consumption, $L \cdot min^{-1}$	Treatment	Cup (n = 18)	Horizontal Flat-fold (n = 6)	Other Flat-fold (n = 6)
0.5	N95 only	29 ± 1	29 ± 1	28 ± 1
	N95 + SM	29 ± 1	30 ± 1	29 ± 1
1.0	N95 only	31 ± 1	32 ± 2	31 ± 1
	N95 + SM	32 ± 1∗	32 ± 1	31 ± 1
1.5	N95 only	32 ± 1	33 ± 2	32 ± 1
	N95 + SM	33 ± 1∗	33 ± 1	32 ± 1
2.0	N95 only	32 ± 1	33 ± 1	32 ± 1
	N95 + SM	33 ± 1∗	34 ± 1	33 ± 1
2.5	N95 only	32 ± 1	32 ± 1	32 ± 1
	N95 + SM	33 ± 1∗	33 ± 1	33 ± 1
3.0	N95 only	32 ± 1	33 ± 1	32 ± 1
	N95 + SM	33 ± 1∗	34 ± 1	33 ± 1

Values are means ± SD
N95 only = FFR alone, N95 + SM = FFR with SM cover
∗Significantly different from N95 only, $p<0.05$

Table 9: Average Inhaled Wet-Bulb Temperatures (degrees Celsius) Among FFR With and Without SM

Oxygen Consumption, $L \cdot min^{-1}$	Treatment	Cup (n = 18)	Horizontal Flat-fold (n = 6)	Other Flat-fold (n = 6)
0.5	N95 only	27 ± 1	27 ± 2	26 ± 1
	N95 + SM	28 ± 1	27 ± 1	27 ± 1
1.0	N95 only	28 ± 1	29 ± 2	28 ± 1
	N95 + SM	29 ± 1∗	30 ± 1	28 ± 1
1.5	N95 only	29 ± 2	30 ± 3	29 ± 1
	N95 + SM	30 ± 1∗	31 ± 1	30 ± 1
2.0	N95 only	29 ± 2	30 ± 3	29 ± 1
	N95 + SM	30 ± 2∗	31 ± 1	29 ± 1
2.5	N95 only	27 ± 2	28 ± 3	28 ± 1
	N95 + SM	29 ± 2∗	30 ± 1	28 ± 1
3.0	N95 only	28 ± 2	29 ± 3	28 ± 1
	N95 + SM	30 ± 2∗	30 ± 1	29 ± 1

Values are means ± SD
N95 only = FFR alone, N95 + SM = FFR with SM cover
∗Significantly different from N95 only, $p<0.05$

5.0 DISCUSSION

5.1 N95 Respirators (FFR) and Surgical Mask Covers (SM)

The purpose of this investigation was to characterize the inhaled breathing gas concentrations and breathing pressures among a representative sample of FFR with and without a SM using the ABMS. Breathing temperatures were examined as an indication of user comfort. The main sample of FFR was changed due to changes in the SNS and the market from the beginning of the investigation, which removed a type of FFR (FFR cup with fit seal) and increased the sample by the FFR added to the SNS. These modifications changed FFR type groupings while maintaining selections with current market conditions.

The Certified Equipment List, maintained by NIOSH, provides the public with information of the NIOSH-approved FFR including NIOSH-approved FFR with expired certifications. The sample used in this investigation represented approximately 10% of the approximately 350 NIOSH-approved FFR. Not all of the NIOSH-approved FFR are sold in the United States. According to a manufacturer, the following four FFR used in this investigation were not sold through distributors in the United States but could be procured through internet sources: San Huei SH2950, San Huei SH2950V, San Huei SH3500, and San Huei SH3500V.

The basis for FFR participation in the SNS was determined by the NIOSH approval. Nine FFRs were FFR models also within the SNS. None of the FFR selected from the SNS

had exhalation valves. If healthcare professionals were to use FFR with exhalation valves and the SM in the event of reduced FFR supplies, the added SM protection could prevent exhaled contamination by the wearer, based on size of the infectious aerosol alone (Rengasamy et.al., 2009).

5.2 Respiratory Gases

Previous research has provided a basis for changes that occur in respiratory gases from respirator use, that is, respirator dead space. Increased dead space causes an increase in tidal volume and respiratory rate (Harber et al., 1982). Sinkule, et.al. (2003) investigated five types of respiratory protection using the ABMS: air-purifying respirators (n = 27), air-supplied respirators (n = 20), gas masks (n = 6), powered air-purifying respirators (n = 11), and FFR (n = 26). Using the same six levels of energy expenditure as the present investigation, FFR produced the highest levels of average inhaled CO_2 concentrations and lowest average inhaled O_2 concentrations for all levels of energy expenditure compared to all other respiratory protective devices examined. Table 3 contains average inhaled CO_2 concentrations among the FFR used in the present investigation. The practical significance of these findings includes the influence of dead-space upon the CO_2 concentrations among horizontal flat-fold FFR, which were larger in comparison than the other types of FFR without a SM. The average inhaled CO_2 concentrations were above the NIOSH STEL of 0.5% among all levels of energy expenditure, without and with SM. Individually, three of the 30 FFR tested without SM produced average inhaled CO_2 concentrations above 4%, which is Immediately Dangerous to Life and Health (IDLH). IDLH is the designation of maximal exposure above which only highly reliable respiratory protection provides maximal worker protection. One FFR (AOSafety Pleats Plus) was withdrawn from the analysis based

upon the exceptionally large average inhaled CO_2 concentration – 5.8% at $\dot{V}O_2$ of 0.5 $L \cdot min^{-1}$. This high level of CO_2 exposure is above the NIOSH Ceiling of 3% and IDLH of 4%. The NIOSH Ceiling is used to describe occupational exposures that shall not be exceeded through any part of the workday (American Conference of Governmental Industrial Hygienists, 2011). The performance of this FFR model was a true outlier that skewed analyses. Manufacturing of this FFR was discontinued through the course of this investigation.

The respirator provides a micro-environment for the exposure pathway of CO_2 (Nieuwenhuijsen, 2006; Checkoway, Pearce, and Kriebel, 2004). The user's exposure to CO_2 concentrations include those from multiple sources; e.g., from the respirator and from others within the room. According to CFR 42 Part 84, the highest inhaled CO_2 concentration permitted for respiratory protection is 2.5% lasting ≤30 minutes for the self-contained breathing apparatus (Approval of Respiratory Protection Devices, 2006b). A standard test procedure (STP) used by NIOSH for the evaluation of negative-pressure air-purifying hooded respirators for escape only contains an inhaled CO_2 concentration threshold of 2.5% for apparatus of 15-30 minutes duration, and 2.0% for an apparatus of 45-60 minutes duration (National Institute for Occupational Safety and Health, 2006). This STP is the only evaluation of inhaled CO_2 and O_2 in human participants among negative-pressure air-purifying respirators, including FFR. Of the FFR in this investigation, average inhaled CO_2 was likely to be lower than 2.0% for levels of energy expenditure at 2.0 $L \cdot min^{-1}$ or greater, both without and with a SM. At levels of energy expenditure of 1.5 $L \cdot min^{-1}$ or lower, average inhaled CO_2 appeared likely to be above 2.0% for all FFR and more so at the lowest level of energy expenditure (rest).

Respiratory rate, tidal volume, and alveolar CO_2 become elevated with inhaled CO_2 concentrations above ambient (Consolazio, Fisher et al., 1947; Schneider and Truesdale, 1922; Patterson et al., 1955). These physiological responses occur to compensate for abnormal diffusion of CO_2 from the blood, due to a decrease in the ratio of alveolar to capillary CO_2 (Schulte, 1964). In addition to the increased rate and depth of breathing, cardiac output will increase to compensate for the additional CO_2 (Schulte, 1964). While inhaling 1 – 2% CO_2 for 17 to 32 minutes, slight increases have been reported in systolic and diastolic blood pressures (Schneider and Truesdale, 1922). Exposures of increased inhaled CO_2 between 2 – 3% have been known to produce sweating, headache and dyspnea for some subjects at rest after several hours (Schneider and Truesdale, 1922). If inhaled CO_2 concentrations occur between 4 – 5%, dyspnea can occur within several minutes and increased blood pressure, dizziness and headache can occur within 15-32 minutes (Patterson et al., 1955; Schneider and Truesdale, 1922; Schulte, 1964). As noted in several of these studies, headaches have been reported at inhaled CO_2 concentrations similar to those found in this investigation. This is consistent with one study which found that 37% of healthcare workers surveyed reported headaches following FFR use (Lim et al., 2006).

A striking unanticipated finding among the horizontal flat-fold FFR was a *reduction* in the average inhaled CO_2 concentration when a SM was applied as an additional layer of protection at $\dot{V}O_2$ of 1.0 and 1.5 $L \cdot min^{-1}$. The high average inhaled CO_2 concentrations among horizontal flat-fold FFR without a SM were caused by the larger respirator dead-space compared to the cup type of FFR or other flat-fold FFR. The additional respirator dead-space was increased by inflating the horizontal flat-fold FFR during exhalation. During inhalation with the horizontal flat-fold, the FFR collapsed against the head form face. The

application of the horizontal flat-fold type of SM -- a glove-to-hand sleeve over the horizontal flat-fold FFR -- restricted the inflation effect during exhalation and reduced the dead-space. The average inhaled CO_2 concentration among cup FFR increased among those with a SM compared to those without the SM at $\dot{V}O_2$ of 0.5, 2.5 and 3.0 $L \cdot min^{-1}$, due to the additional dead space caused by the horizontal flat-fold type of SM. For the other flat-fold FFR, three FFR were of the tri-fold type and three FFR were of the vertical flat-fold type. The orientation of these other flat-fold types on the user's face and other dead space features would affect the average inhaled CO_2 concentrations. With a SM cover, the orientation of the other flat-fold FFR (vertical flat-fold and tri-fold) would change on the user's face. Placing a horizontal flat-fold SM on a vertical flat-fold FFR would require bending the corners/ends of the vertical flat-folds, which likely would decrease the dead space within the FFR. Bending of the folds in tri-folded FFR would be needed with the application of a horizontally flat-folded SM cover, which also would reduce the dead space in the FFR. Any bending or folding of the FFR filter material also compromises the total surface area of the filter media and filtration efficiency. The variability of the average inhaled CO_2 concentration results among the various types of flat-fold FFR combined in the "other flat fold" category contributed to insignificant differences between this type of FFR with and without SM.

The effect of the additional inhaled concentrations of CO_2 would result in physiological changes which would not be seen in an ABMS that does not respond to increased concentrations of CO_2. The effects on humans, therefore, depend on the amount of respirator dead space and the tidal volume of the user. The data used to program the ABMS for the minute ventilation, respiratory rate, O_2 consumption, and CO_2 concentration at each

level of energy expenditure originated from healthy men with body weight between 85-92 kilograms. If the FFR user is smaller by body weight with a concomitant reduction in tidal volume, the effects from the FFR dead space would be greater; higher average inhaled CO_2 concentrations and lower average inhaled O_2 concentrations would be observed (Sinkule and Turner, 2004). In a responding human, the elevated CO_2 concentrations would cause hyperventilation (increased tidal volume and respiratory rate); sweating; headache; dizziness; and, increases in cardiac output, diastolic and systolic blood pressures.

The changes in average inhaled O_2 concentration closely followed the expected reciprocal changes in average inhaled CO_2 concentration, whereas average inhaled O_2 concentration increased in conditions where average inhaled CO_2 concentration decreased and vise versa. One reason for the changes in average inhaled O_2 concentration relative to average inhaled CO_2 concentration is because of the relative displacement of the gases in air; the changes in one gas directly allows for a greater or lesser proportion of the other gases. Like the unanticipated change that occurred among the horizontal flat-fold FFR, where a *reduction* in the average inhaled CO_2 concentration was observed when a SM was applied as an additional layer of protection at $\dot{V}O_2$ of 1.0 and 1.5 $L \cdot min^{-1}$, an *increase* in the average inhaled O_2 concentration also occurred for this select sub-set of FFR. According to CFR 42 Part 84 (Approval of Respiratory Protection Devices, 2006a), a hazardous atmosphere occurs in any O_2-deficient atmosphere of less than a partial pressure of 148 mmHg, or 19.5%. From Table 4, the average inhaled O_2 concentration was below 19.5% for all conditions for all levels of energy expenditure, except for the condition of "N95 only" at the level of O_2 consumption of 2.5 $L \cdot min^{-1}$. The average inhaled O_2 concentration of $\leq$15% occurred in one FFR without SM during the 0.5 and 1.5 $L \cdot min^{-1}$ levels of energy expenditure. In a clinical

trial, inhaled oxygen concentration of 15% caused more time needed to travel a standard distance with the lowest power output measured and coincided with the highest measured capillary blood lactate concentrations when compared to normoxia and hyperoxia (F_IO_2, 100%); caused muscle fatigue, reduced calcium ion released from the sarcoplasmic reticulum, increased minute ventilation by 26%, and decrease O_2 consumption by 10% (Amann et al., 2006). At the threshold partial pressure of O_2 at 132 mmHg (17.4% O_2), symptoms include headache, lightheadedness, drowsiness, muscular weakness, dyspnea on exertion, nausea, and vomiting (Schulte, 1964). Neurological symptoms, such as reduced memory and mental work capacity, auditory and visual disturbances, vertigo, tinnitus, and irritability, may be manifested if O_2 deficiency continues (Schulte, 1964).

5.3 Breathing Pressures

The peak inhalation and exhalation pressures could impact respirator comfort, in addition to inhalation and exhalation temperatures, respirator weight, respirator valves, etc. The increased pressure may cause a decrease in respiratory rate (Harber et al., 1982; Louhevaara, 1984) and tidal volume (Harber et al., 1982). Among older individuals, respiratory rate may not change and tidal volume decreases with increased inspiratory resistance (Louhevaara, 1984). Table 5 (Peak Exhalation Pressures) and Table 6 (Peak Inhalation Pressures) show how the breathing pressures increase with energy expenditure where respiratory rate and tidal volume cause more air flow during inhalation and exhalation. During exhalation, the differences between FFR with and without SM occur only in cup type of FFR. The difference in the group with the largest representation (cup type with 60% of the sample) would explain the variation. No differences between the FFR at the lowest levels of energy expenditure occurred with the lowest tidal volumes and peak flows vis-à-vis half the sample

contained FFR with exhalation valves. In a previous NIOSH investigation of FFR breathing pressures with and without SM using a breathing machine, mean FFR alone and without exhalation valves (three models) at minute ventilations of 1.0 and 1.5 $L \cdot min^{-1}$ with a sinusoidal breathing waveform reported exhalation pressures of 7 and 11 mmH_2O, respectively (Vojtko et al., 2008). From the same report, the mean FFR with a SM at minute ventilations of 1.0 and 1.5 $L \cdot min^{-1}$ and sinusoidal breathing waveform reported mean exhalation pressures of 8 and 12 mmH_2O, respectively. In FFR with exhalation valve (one model), Vojtko reported 4 and 5 mmH_2O, respectively, at 1.0 and 1.5 $L \cdot min^{-1}$ for FFR alone; and, 4 and 6 mmH_2O, respectively, for FFR with SM. The most significant factors contributing to the differences between the data reported from this study and the Vojtko study could be due a larger sample size (30 FFR models versus 4 FFR models) and the difference in the minute ventilation expressed by the Vojtko study (atmospheric temperature and pressure (ATP), ambient) and the present study (STPD). The conversion from ATP to STPD (used from the ABMS) would change minute ventilation from 25 to 22 $L \cdot min^{-1}$ and from 40 to 35 $L \cdot min^{-1}$ (Cotes, Chinn, and Miller, 2006). Thus, the corrected minute ventilations from the manikin data used in the Vojtko et al. (2008) study are lower when adjusted to the same volumetric format used in the present study.

Clinically, it would be important to know when humans find the added pressure from FFR wear intolerable or the point where users detect the added pressure from a SM. Two reports investigated the minimal pressures that can be detected in humans from elastic and non-elastic loads (Bennett et al., 1962; Campbell et al., 1961). Bennett et al. (1962) conducted a study using added restrictive loads to measure the ability to determine the lowest restriction noticeable by humans. Participants were asked to breathe (assuming inhalation

and exhalation were weighted equally) through progressively narrowed tubes (between 2 – 12 $mmH_2O \cdot liter^{-1} \cdot second^{-1}$) which were previously calibrated with a water manometer. The mean 50% level of detection was 6 $mmH_2O \cdot liter^{-1} \cdot second^{-1}$ (BTPS). Bennett reported a non-linear relationship between the pressure and flow characteristics for each load. The relationship between the results from Bennett et al. (1962) and the ranges of pressures in Table 8, the mean exhalation pressures (Table 5), and the mean inhalation pressures (Table 6), can be used to estimate the level of energy expenditure where a SM addition to using a FFR is detected by humans. During exhalation (Table 5), the difference in pressures at the energy expenditure commensurate with the flow rate in the Bennett study (at $\dot{V}O_2$ between 0.5 and 1.0 $L \cdot min^{-1}$ by the ABMS) between FFR and FFR+SM were smaller than the 50% level of detection for each flow. The same comparison analysis among the FFR and FFR+SM during inhalation (Table 6) also demonstrate that the difference in pressures were smaller than the 50% level of detection for the flow at $\dot{V}O_2$ between 0.5 and 1.0 $L \cdot min^{-1}$. These results suggest that the increased pressures resulting from the addition of the SM at the lower levels of energy expenditure used in this investigation would not be detected in humans compared to using the same FFR without a SM. These are the same levels of energy expenditure which occur with a significant portion of activities conducted by healthcare workers.

5.4 Study Limitations

While the ABMS is an accurate, reproducible, functional and useful tool to characterize the metabolic responses that can be produced by the use of respiratory protection, there are

limitations to its use. For negative pressure respiratory protection, such as FFR, elastomeric air-purifying respirators, and gas masks, the ABMS measurements for the respirator's dead space are affected primarily by the minute ventilation, more specifically, tidal volume. As the normal user's tidal volume decreases, the effect from respirator dead space becomes greater. Conversely, the opposite occurs as tidal volume increases, such as that in normal larger persons and exercise. In a field study, smaller healthcare workers (e.g., women) were more likely to experience intolerance for wearing FFR before the end of the shift (Radonovich et al., 2009). The limitation, therefore, is characterizing respiratory protection with a tidal volume specific to the human data used to program the metabolic parameters of the ABMS, or a subset of subjects with a body size of 85-92 kg.

Another limitation for the ABMS is that it does not respond, that is, respiratory protection for the ABMS does not cause changes in breathing times, breathing volumes/depths, or breathing patterns. Humans respond to the changes in the breathing zone from the use of respiratory protection. However, those stimuli produced by the results of using respiratory protection are masked by the human response. The human response was similar to the ABMS measurements in a previous investigation (Sinkule and Turner, 2004). The stimuli from using various forms of respiratory protection, or types of FFR and treatments affecting FFR (e.g., SM), will vary in magnitude. These effects were characterized in this investigation. Some human participants are hyposensitive to CO_2 and metabolic acidosis, and do not respond normally to increased CO_2 concentrations until hyperventilation occurs at exhaustive workloads (Whipp, Davis, and Wasserman, 1989).

Subjective responses from the use of FFR with or without a SM cannot be reported from data using the ABMS. For studies that examined FFR with and without SM,

and did not report inspired gases, the subjective responses included a gender-related reduction in tolerance time (Radonovich et al., 2009); greater comfort using FFR with exhalation valve +SM at 1.7 mile·hour^{-1} treadmill speed compared to 2.5 mile·hour^{-1} (Roberge et al., 2010); and, reduced respiratory rate. The subjective responses reported in FFR + SM studies using human subjects without measuring inhaled gases, however, was limited by a variety of research designs with their own limitations; e.g. subjective tolerance time of the FFR among subjects that included subjects that smoke (Radonovich et al., 2009), a research design that did not allow for stratification based on various physical activities throughout the experimental period (Radonovich et al., 2009), research test participants were not stratified based upon age (Roberge et al., 2010; Radonovich et al., 2009), and reporting mixed (inhaled and exhaled) respiratory gases (Roberge et al., 2010).

The relationship between physical activity and aging is important for the research design as well as its relevance for an aging workforce. Between July, 2007, and March, 2009, the proportion of licensed registered nurses (RN) under the age of 30 in California decreased from 7.6% to 6.9%, and the age range of 50-59 years of age had the largest proportion of RNs for both 2007 (30.3%) and 2009 (29.6%) (Spetz, 2009). The largest difference between 2007 and 2009 occurred in the 60-69 age range, which were 12.7% and 16%, respectively. The health care employee's functional capacity to accomplish their occupational activities increases to approximately age 30, thereafter decreases with increasing age (McArdle et al., 2010). Muscle mass reduction with aging, 40-50% between 25 and 80 years, is the single largest factor that contributes to decreasing muscle strength even among physically active adults (McArdle et al., 2010). Since the physical activities that are possible for health care workers can range from 1.8 METs (sitting and writing) to 7.5

METs (moving/pushing objects 75 pounds+), the effects of engaging with these activities will vary with worker's age (Ainsworth et al., 2000). For women 60-69 years old, 7.5 METs is above the 35th percentile for their predicted maximal aerobic power (American College of Sports Medicine, 2010). When compared to women 20-29 years old, this same amount of work is above the 1 percentile (American College of Sports Medicine, 2010). Physical activities, therefore, are not the same for all workers regardless of their age. The same applies for gender differences as well (American College of Sports Medicine, 2010; McArdle et al., 2010).

5.5 Conclusions

Approximately 10% of commercially-available NIOSH-approved FFR models were examined with and without SM using the ABMS to characterize metabolic responses in an attempt to understand the implications of the recommendation to apply a SM over the FFR to extend the respirator's useful life for healthcare workers. Conclusions for this investigation include the following:

1. generally, average inhaled CO_2 concentration decreased and average inhaled O_2 concentration increased with increasing oxygen consumption in FFR and FFR with SM;
2. peak exhalation pressure and peak inhalation pressure increased with increasing oxygen consumption, but more so in FFR with SM;
3. compared to FFR without SM, higher average inhaled CO_2 concentrations were observed in 4 of 6 workloads among FFR with SM;
4. the addition of the SM to horizontal flat-fold FFR at $\dot{V}O_2$ of 1.0 and 1.5 $L \cdot min^{-1}$ caused a reduction in average inhaled CO_2 concentrations and an

increase in average inhaled O_2 concentrations due to the effects of the (horizontal flat-fold) SM on the FFR dead space; and,

5. the average inhaled CO_2 concentrations were above the NIOSH STEL for all FFR, both without and with SM (Table 10), and the reciprocal changes adversely affected the average inhaled O_2 concentrations for most FFR (<19.5%), also with and without SM (Table 11) .

At the lower levels of energy expenditure, this investigation provided evidence to suggest that the IOM recommendation of adding a SM over FFRs in order to extend the daily duration of FFRs and reduce the consumption of FFRs during a pandemic would produce clinically small changes in inhaled breathing gases and breathing pressures resulting in a minimal effect on physical work performance, and the amount and direction of change is affected by the type of FFR and shape of the SM. In addition, the evidence also indicates possible improvements in inhaled breathing gases caused by the effects in the dead space characteristics of the FFR by the shape of the SM.

5.6 Recommendations for Future Research

Future research may consider human subject testing of various FFR models, adjusted for age and gender, while measuring time-weighted mean inhaled CO_2 and O_2 gas concentrations and comparing the responses to average inhaled CO_2 and O_2 gas concentrations from the ABMS. This proposed research may provide a connection of ABMS results with human subject responses for use in the development of an ABMS-based standard test procedure for evaluating negative-pressure air-purifying respiratory protective devices. Certain special groups also may benefit from exploratory research using the ABMS to evaluate respiratory

protection, e.g. children that use respiratory protection while performing activities in the agricultural industry.

Table 10: Value Ranges for Average Inhaled Carbon Dioxide Concentrations (%) Among FFR With and Without SM

Oxygen Consumption, $L \cdot min^{-1}$	Treatment	Cup (n = 18)	Horizontal Flat-fold (n = 6)	Other Flat-fold (n = 6)
0.5	N95 only	1.57 – 3.48	2.00 – 4.52	2.04 – 3.55
	N95 + SM	2.26 – 3.60	2.30 – 4.00	2.38 – 3.51
1.0	N95 only	1.08 – 3.07	1.29 – 4.47	1.27 – 3.08
	N95 + SM	1.56 – 3.30	1.46 – 2.70	1.86 – 2.13
1.5	N95 only	1.33 – 4.02	1.43 – 5.16	1.35 – 3.71
	N95 + SM	1.90 – 3.52	1.78 – 2.92	2.10 – 2.32
2.0	N95 only	0.81 – 2.69	0.87 – 3.04	0.92 – 2.57
	N95 + SM	1.28 – 2.67	1.28 – 2.07	1.41 – 1.78
2.5	N95 only	0.67 – 2.59	0.77 – 2.89	0.79 – 2.36
	N95 + SM	1.06 – 2.57	1.12 – 1.84	1.33 – 1.67
3.0	N95 only	0 76 – 2.68	0.98 – 3.10	0.89 – 2.97
	N95 + SM	1.56 – 2.66	1.36 – 2.29	1.45 – 2.02

Values are minimum - maximum
N95 only = FFR alone, N95 + SM = FFR with SM cover

Table 11: Value Ranges for Average Inhaled Oxygen Concentrations (%) Among FFR With and Without SM

Oxygen Consumption, $L \cdot min^{-1}$	Treatment	Cup (n = 18)	Horizontal Flat-fold (n = 6)	Other Flat-fold (n = 6)
0.5	N95 only	15.79 – 18.77	14.82 – 17.96	16.09 – 18.27
	N95 + SM	15.81 – 17.57	15.61 – 17.51	15.90 – 17.79
1.0	N95 only	16.75 – 19.62	15.30 – 19.20	16.91 – 19.27
	N95 + SM	16.91 – 18.97	17.61 – 19.01	18.08 – 18.49
1.5	N95 only	16.00 – 19.43	14.80 – 19.12	16.47 – 19.33
	N95 + SM	16.99 – 18.90	17.66 – 18.86	18.15 – 18.39
2.0	N95 only	17.78 – 20.04	17.57 – 19.81	17.94 – 19.85
	N95 + SM	18.11 – 19.43	18.65 – 19.47	18.79 – 19.22
2.5	N95 only	18.10 – 20.20	17.80 – 19.93	18.26 – 20.04
	N95 + SM	18.29 – 19.66	18.92 – 19.61	18.93 – 19.39
3.0	N95 only	18.06 – 20.10	17.70 – 19.73	17.72 – 19.96
	N95 + SM	18.04 – 19.41	18.52 – 19.42	18.59 – 19.29

Values are minimum - maximum
N95 only = FFR alone, N95 + SM = FFR with SM cover

BIBLIOGRAPHY

Ainsworth, B.E., Haskell, W.L., Whitt, M.C., Irwin, M.L., Swartz, A.M., Strath, S.J., O'Brien, W.L., Bassett, D.R., Schmitz, K.H., Emplaincourt, P.O., Jacobs, D.R., & Leon, A.S. (2000). Compendium of physical activities: an update of activity codes and MET intensities. Medicine and Science in Sports and Exercise, 32(9), S498-S516.

Amann, M., Eldridge, M.W., Lovering, A.T., Stickland, M.K., Pegelow, D.F., and Dempsey, J.A. (2006). Arterial oxygenation influences central motor output and exercise performance via effects on peripheral locomotor muscle fatigue in humans. Journal of Physiology, 575 (3), 937-952. doi:10.1113/jphysiol.2006.113936

American College of Sports Medicine (2010). ACSM's Guidelines for Exercise Testing and Prescription. Eighth Edition. Baltimore, MD: Lippincott Williams & Wilkins, 60-104.

American Conference of Governmental Industrial Hygienists (2011). Guide to Occupational Exposure Values. 1330 Kemper Meadow Drive, Cincinnati, OH 45240-4148.

Approval of Respiratory Protection Devices, 42 CFR § 84.2(o)(2)(y) Definitions (2006a).

Approval of Respiratory Protection Devices, 42 CFR § 84.97 Test for carbon dioxide in inspired gas; open- and closed-circuit apparatus; maximal allowable limits (2006b).

Authorization of Emergency Use of Certain Personal Respiratory Protection Devices; Availability (US Department of Health & Human Services), 74 Federal Register. 38644 (2009) Available from http://www.federalregister.gov/articles/2009/08/04/E9-18570/authorization-of-emergency-use-of-certain-personal-respiratory-protection-devices-availability#h-9 (accessed November 2, 2010).

Beeckman, D., Turner, N. and Campbell, D. (1998) Using an automated breathing and metabolic simulator (ABMS) to test the performance of air-purifying respirators, American Industrial Hygiene Conference and Exposition, Atlanta, GA.

Bennett, E.D., Jayson, M.I., Rubenstein, D., & Campbell, E.J. (1962). The ability of man to detect added non-elastic loads to breathing. Clinical Science, 23, 155-62.

Campbell, E.J., Freedman, S., Smith, P.S., & Taylor, M.E. (1961). The ability of man to detect added elastic loads to breathing. Clinical Science, 20, 223-31.

Checkoway, H., Pearce, N., and Kriebel, D. (2004). Characterizing the Workplace Environment. Research Methods in Occupational Epidemiology. Second Edition (pp. 17-57).198 Madison Avenue, New York, New York 10016: Oxford University Press, Inc.

Compressed Gas Association. Fourth Edition.(1999) *Carbon Dioxide*. Kluwer Academic Publishers: Norwell, MA., 295-311.

Consolazio, W.V., Fisher, M.B., Pace, N., Pecora, L.J., Pitts, G.C., & Behnke, A.R. (1947). Effects on man of high concentrations of carbon dioxide in relation to various oxygen pressures during exposures as long as 72 hours. American Journal of Physiology, 151, 479-503.

Cotes, J.E., Chinn, D.J., & Miller, M.R. (2006). Lung function: physiology, measurement and application in medicine. Sixth Edition. page 57, Section 6.6, Standardisation of volumes for temperature and pressure (use of Boyle's and Charles' laws), Chapter 6. Basic Terminology and Gas Laws.; Blackwell Publishing, Inc.:350 Main Street, Malden, Massachusetts 02148-5020.

Deno, N.S. (1984). Automatic Breathing and Metabolic Simulator: The Respiring Robot. Journal of the International Society for Respiratory Protection, 2, 38-51.

Echt, A., Burroughs, G., Lenhart, S., and Booher, D. (1996) Health Hazard Evaluation Report. Cincinnati Sportsmedicine and Orthopaedic Center, Cincinnati, OH: National Institute for Occupational Safety and Health (NIOSH). *HETA* 96-0060-2632.

Harber, P., Tamimie, R.J., Bhattacharya, A., & Barber, M. (1982) Physiologic effects of respirator dead space and resistance loading. Journal of Occupational Medicine, 24, 681-9.

Hogan, M.C., Cox, R.H., & Welch, H.C. (1983). Lactate accumulation during incremental exercise with varied inspired oxygen fractions. Journal of Applied Physiology 55, 1134-1140.

ISO 8996 (1990). Ergonomics – Determination of metabolic heat production. International Organization of Standards.

ISO/TS 16976-1 (draft) (2006). Respiratory protective devices – Human Factors – Part 1: Work rates and physiology. International Organization of Standards.

Johnson, D.F., Druce, J.D., Birch, C., & Grayson M.L. (2009). A Quantitative Assessment of the Efficacy of Surgical and N95 Masks to Filter Influenza Virus in Patients with Acute Influenza Infection. Clinical Infectious Diseases, 49, 275-277.

Kyriazi, N. (1986) Development of an automated breathing and metabolic simulator. Pittsburgh, PA: U.S. Department of the Interior, Bureau of Mines, IC 9110.

Li, Y., Tokura, H., Guo, Y.P., Wong, A.S.W., Wong, T., Chung, J., & Newton, E. (2005). Effects of wearing N95 and surgical facemasks on heart rate, thermal stress and subjective sensations. International Archives of Occupational and Environmental Health, 78, 501-509.

Lim, E.C.H., Seet, R.C.S., Lee, K-H, Wilder-Smith, E.P.V., Chuah, B.Y.S., & Ong, B.K.C. (2006). Headaches and the N95 face-mask amongst healthcare providers. Acta Neurologica Scandinavica, 113, 199-202.

Louhevaara, V.A. (1984). Physiological effects associated with the use of respiratory protective devices - a review. Scandinavian Journal of Work Environment & Health, 10, 275-81.

McArdle, W.D., Katch, F.I., & Katch, V.L. (2010). Physical Activity, Health, and Aging. In: Exercise Physiology: Nutrition, Energy, and Human Performance. Seventh Edition. Baltimore, MD: Lippincott Williams & Wilkins; 831-875.

Morris, L.A. (1991). Dead space and inhaled carbon dioxide levels in respiratory protective equipment. HSE Contract Research Report No. 27.

National Academy of Sciences (2006). Reusability of Facemasks During an Influenza Pandemic: Facing the Flu. The National Academies Press, 500 Fifth Street, N.W., Washington, DC 20001.

National Institute for Occupational Safety and Health (2006). CET-APRS-STP-CBRN-0454: Determination of Human Subject Breathing Gas (HSBG) Concentrations (Carbon Dioxide and Oxygen) for Chemical, Biological, Radiological and Nuclear (CBRN) Air-Purifying Escape Respirator. Retrieved on August 25, 2006 from http://www.cdc.gov/niosh/npptl/stps/pdfs/CET-APRS-STP-CBRN-0454.pdf

National Institute for Occupational Safety and Health. Certified Equipment List. Available from http://www.cdc.gov/niosh/npptl/topics/respirators/cel/default.html (accessed May 13, 2011).

Neter, J., Wasserman, W., & Kutner, M. (1985). Applied Linear Statistical Models. Second Editon. Homewood, IL: Richard D. Irwin, Inc.

Nieuwenhuijsen, M. J. (2006). Introduction to exposure assessment. In Mark J. Nieuwenhuijsen, Editor, Exposure Assessment in Occupational and Environmental Epidemiology (pp. 5-7). Great Clarendon Street, Oxford OX2 6DP: Oxford University Press.

Patterson, J.L., Heyman, H., Battery, L.L. & Ferguson, R.W. (1955). Threshold of response of the cerebral vessels of man to increases in blood carbon dioxide. Journal of Clinical Investigation, 34, 1857-1864.

Radonovich, L.J., Cheng, J., Shenal, B.V., Hodgson, M., & Bender, B.S. (2009). Respirator tolerance in health care workers. Journal of the American Medical Association, 301, 36-38.

Raven, P.B., Dodson, A.T., & Davis, T.O. (1979). The physiological consequences of wearing industrial respirators: A review. American Industrial Hygiene Association Journal, 40, 517-534.

Rengasamy, S., Miller, A., Elmer, B.C., & Shaffer, R.E. (2009). Filtration Performance of FDA-Cleared SMs. Journal of the International Society for Respiratory Protection, 26, 54-70.

Roberge, R.J., Coca, A., Williams, W.J., Palmiero, A.J., & Powell, J.B. (2010). Surgical mask placement over N95 filtering facepiece respirators: physiological effects on healthcare workers. Respirology, 15, 516-21.

Sayers, J.A., Smith, R.E., Holland, R.L., & Keatinge, W.R. (1987). Effects of carbon dioxide on mental performance. Journal of Applied Physiology, 63, 25-30.

Schneider, E.C. & Truesdale, E. (1922). The effects on the circulation and respiration of an increase in the carbon dioxide content of the blood in man. American Journal of Physiology, 63, 155-175.

Schulte, J.H. (1964). Sealed environments in relation to health and disease. Archives of Environmental Health, 8, 438-452.

Sinkule, E. and Turner, N. (2004). Inhaled Carbon Dioxide and Oxygen Concentrations in Three Escape Hood Respirators During Rest and Exercise. Medicine and Science in Sports and Exercise, 36, S245.

Sinkule, E., Turner, N., & Hota, S. (2003). Automated Breathing and Metabolic Simulator (ABMS) CO_2 Test for Powered and Non-Powered Air-Purifying Respirators, Airline Respirators and Gas Masks. American Industrial Hygiene Conference and Exposition, Abstracts, 54.

Spetz, J. (2009). Forecasts of the Registered Nurse Workforce in California. University of California for the California Board of Registered Nursing. Retrieved at http://www.rn.ca.gov/pdfs/forms/forecasts2007.pdf on November 1, 2010.

Vojtko, M.R., Roberge, M.R., Vojtko, R.J., Roberge, R.J., & Landsittel, D.P. (2008). Effect on breathing resistance of a surgical mask worn over a N95 filtering facepiece respirator. Journal of the International Society for Respiratory Protection, 25, 1-8.

Whipp, B.J., Davis, J.A., & Wasserman, K. (1989). Ventilatory control of the 'isocapnic buffering' region in rapidly-incremental exercise. Respiratory Physiology, 76, 357-67.

Yang, Y., Sun, C., & Sun, M (1997). The effect of moderately increased CO_2 concentration on perception of coherent motion. Aviation Space & Environmental Medicine, 68, 187-91.