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# Efficacy of a Pneumatic Oxygen Conserving Device in the Oxygenation of COPD Patients During Sleep

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**An Abstract Presented to the Faculty of the Graduate School of Lindenwood University in Partial Fulfillment of the Requirements for the Degree of Masters in Health Management**
**Winter 2002**

**Abstract**

For the greater than one million Americans who rely on supplemental oxygen for survival, the vast majority of them struggle with ambulatory oxygen sources which restrict their ability to move freely about within and out of their homes. Liquid oxygen sources can provide the smallest and longest lasting ambulatory oxygen supply. However, the cost of the provision on liquid oxygen has historically been cost prohibitive under our current Medicare reimbursement schedule. The HELiOS™ Oxygen System by Puritan-Bennett a division of Mallinckrodt, has developed an oxygen system, which allows for the smallest, lightest weight and longest lasting oxygen system ever developed. This system was also designed with special considerations for reducing the cost of provision and therefore, more acceptable in today's restraints on Medicare reimbursement.

This study was designed to examine the potential issue of the HELiOS product to effectively oxygenate patients during hours of sleep. In addition, it will discuss the philosophical issues of compliance with oxygen therapy orders when oxygen sources are provided which significantly reduce quality of life issues for the patient. This research showed that of a small sample of 19 subjects, 63% (12 subjects) experienced saturations that were not clinically significantly different from that which they experienced on their current continuous oxygen flow source. Collective data in a two-tailed t-test resulted in a p value of = 0.001, indicating that there is a statistically significant, high probability that the saturation of a randomly chosen oxygen therapy patient's oxygen saturation would not be clinical equal to that of the same patient on continuous flow oxygen. Therefore, this researcher would recommend an overnight oximetry be performed for most all patients who will be converting from continuous flow oxygen to the HELiOS™ Demand Flow Oxygen System during hours of sleep.

# Efficacy of a Pneumatic Oxygen Conserving Device in the Oxygenation of COPD Patients During Sleep

**Ronda Z. Bradley BS, RRT**

**A Thesis Presented to the Faculty of the Graduate School of Lindenwood University in Partial Fulfillment of the Requirements for the Degree of Masters in Health Management**
**Winter 2002**

COMMITTEE IN CHARGE OF CANDIDACY

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Professor of Mathematics: Rita Kottmeyer Ph.D.

Assistant Professor: Suzanne M Nordstrom

Dedication

To the members of EFFORTS (Emphysema Foundation For Our Right To Survive), Patient advocacy group, who has given so many the ambition to accelerate improvements in medical devices. Your passion for improving the quality of life for Long Term Oxygen Therapy patients continues to impact the lives of many worldwide. www.emphysema.net

Acknowledgements

I would like to thank the many people who worked diligently to see this project to its completion. First, to Scott Remes, Engineering Project Manager of Puritan Bennett, Oxygen Division; Your dedication to meeting the needs of patients will always be remembered and alive in the joy of oxygen patients throughout the world who can now experience life outside of their home, thanks to your efforts in the development of HELiOS™. Secondly, to Dr. Thomas Siler, Mitchell Champagne, Sue Townsley and the Staff at the Sleep Disorders Center of St.Joseph Health Care Center in St.Charles, MO. Your tremendous assistance in the completion of this project and your tireless efforts to provide excellence in medical care to your patients is to be commended.
Thank you.

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# Chapter I

## INTRODUCTION

### Home oxygen delivery

There are approximately 1.2 million patients in the United States receiving oxygen therapy. The primary diagnosis requiring treatment with oxygen therapy is Chronic Obstructive Lung Disease (COPD). This disease classification includes patients suffering from Emphysema, Chronic Bronchitis, Bronchiectasis, and Asthma. It is estimated that approximately 200,000 new patients will require oxygen therapy in the United States alone in the year 2000 (Frost, 1999). With the great number of patients receiving and expected to begin receiving oxygen therapy, one would think that this would be an area of great research and development interest to not only physicians but also medical device manufacturers. However, quite the opposite is true. There have been very few comprehensive, definitive studies on the topic. The most recent comprehensive studies were published in 1980 and 1981 (NOTT 1980, MRC1981). There have also been very few breakthrough products developed for the delivery of oxygen therapy in the past 20 years. The products that have been developed do not have a comprehensive scope. These products are primarily comprised of oxygen concentrators, conventional liquid oxygen systems, and oxygen conserving devices to be used with compressed gas tanks (O'Donohue 1997). These products may assist the oxygen provider company by reducing the cost and may slightly improve

portability of the ambulatory oxygen, but they do a very poor job in addressing the issues of all of the stakeholders in the oxygen supply process, including the patient, physician, provider, payer and producer. It is essential that more in-depth research in this area takes place and that manufactures (producers) of medical equipment begin looking for products that meet the requirements of all stakeholders in this process.

In an attempt to create a revolutionary oxygen product that considers the interest of each of the previously mentioned shareholders in the provision of oxygen, Puritan-Bennett has developed a home oxygen delivery device that has the potential to do just that. However, this device as currently designed (PB, 1999) is not without its own set of challenges. This device, for optimum economic efficacy, relies on the use of an oxygen-conserving device to be used on a 24-hour per day basis. Prior to the development of this product there had been few attempts to develop a conserving device to be used during hours of sleep (Cuvelier,1999, Bower, 1988). Those attempts that had been made were either relatively unsuccessful or required a design element which would significantly increase the price of the provision of the device, therefore removing it as a feasible option under the current economic restraints of the third party payer systems, especially Medicare. Secondly, none of the previously attempted designs provided for a mechanism, which would encourage patients to use their oxygen more hours of the day.

The question to be explored in the study of this new device will be; Will this device allow for adequate oxygenation of COPD patients during hours of sleep? This study was designed to examine this question in regards to subjects who have current prescriptions for long term oxygen therapy for supplemental use and would fall into the criteria of supply of low flow oxygen as provided by the study device. It is hypothesized that this device will be effective in oxygenation of 70% of subjects equal to that of continuous flow oxygen and that no subjects will reach an oxygen saturation level that would require intervention.

# Chapter II

## LITERATURE REVIEW

It has been shown that the use of oxygen therapy can increase survival rates for patients with chronic lung disease. The benefit of long-term oxygen therapy was undisputedly proven in the studies of the Medical Research Council of the United Kingdom (MRC, 1981) and the Nocturnal Oxygen Therapy Trials (NOTT, 1980) performed in the United States. The MRC study, which compared several outcome measures of 87 chronically hypoxemic patients suffering from lung disease, observed patients over a minimum of two years. Patients who were equally matched in severity and disease process were divided into two groups. The control group would not receive any oxygen therapy except in acute exacerbation requiring hospitalization. The study group would receive oxygen during the evening and night hours with a mean use time of 15 hours per day. This study showed that subjects in the study group, receiving oxygen therapy for approximately 15 hours per day, had much improved clinical outcomes including an improved survival rate at 24 months of 62% verses the control group with survival rate of only 50% (MRC, 1981).

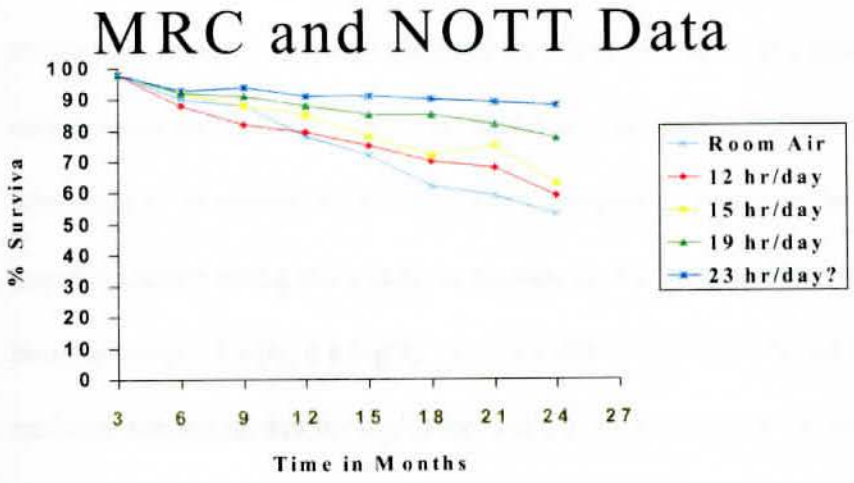
Concurrent with the findings of the MRC study, a similar study was taking place in the United States observing the effects of oxygen therapy on a group of 203 subjects. This study looked at a control group of patients who received

oxygen therapy for approximately 12 hours per day or while sleeping. An equally matched group making up the study group was asked to use their oxygen therapy on a continuous basis. These subjects were provided with portable oxygen equipment that at the time of the study was state of the art and included portable 8-pound liquid oxygen units. The results of this study were similar to the MRC study in that the subjects who used their oxygen therapy more hours per day had much-improved outcomes. The two-year survival of the nocturnal oxygen therapy users was approximately 58% while that of the continuous oxygen therapy group was approximately 78% (NOTT, 1980).

Upon a closer look at the reported data from the NOTT trial, it should be noted that the subjects who were asked to use their oxygen therapy nocturnally were very successful in doing so, with a mean duration of oxygen therapy 12 hours per day. Subsequently, the subjects who were asked to use their oxygen therapy on a continuous basis were not quite as compliant with the request of the investigators. The mean duration of use for these subjects was 19.3 hours per day. The reason for non-compliance was not recorded as an outcome measure of this study (NOTT, 1980). However, upon interview of one of the primary investigators of this study, Dr. Thomas Petty, three primary reasons for non-compliance were recalled in this group. The first reason was that the continuous flow of oxygen had a significant drying effect on the nares of the patients. These patients intermittently removed their oxygen to allow for rest periods to rehydrate the nasal mucosa. The second reason recalled was that the subjects' ears would

become sore from the pulling of the 50-foot nasal cannula used in the home. The subjects would remove the oxygen therapy to allow for rest periods of the skin around the ears and to be free for a period of time from the nuisance of the restricting tubing length. The third reason reported was that the patients did not always use their oxygen therapy when leaving the home. Two major contributors to this non-compliance issue could be the self conciseness of the patients of the use of oxygen due to the appearance of the oxygen equipment, and the effort required to switch to the portable source and the cumbersome equipment needed to do so (Petty, 1999). These findings perplex and concern many clinicians that seek ways to improve compliance and thus improve outcomes of their oxygen therapy patients.

With a mathematical extrapolation it can be estimated that the survival percentage of subjects who were to use their oxygen therapy for up to a 23 hour per day basis would be even more significantly improved than that of the continuous oxygen therapy sub-set of patients observed in the NOTT study. An example of this extrapolation can be seen along with the actual data points of the NOTT and MRC data point sets, in Figure 1. This chart makes a compelling argument that the medical community must find ways to overcome the current objections to oxygen therapy use on a 24-hour basis in order to improve survival outcomes for this group of patients.




(Anals of Internal Medicine 1980, Lancet 1981)

Puritan-Bennett, a subsidiary of Mallinckrodt, Inc. has devised a product to address the primary, known objections of patients to the 24-hour per day use of oxygen therapy. This product is named HELiOS$^{TM}$, which is an acronym for "High Efficiency Liquid Oxygen System". This system combines the use of a very small cryogenic container of oxygen with a pneumatic oxygen-conserving device to allow the patient interface to be a very small, lightweight unit of only 3.4 pounds when full. This unit will last for up to 10 hours for the 2-liter per

patient. The system is designed to allow the user to fill the portable unit in the morning and place it into a waist pack, chest strap, or back pack, fo r up to ten hours of "hands free" oxygen use. Sometime throughout the day the patient would need to "top off" the unit to allow them to move freely inside and outside of the home for the remainder of their hours of mobility. When settling in for the night the patient, continuing to use the same interface, would simply attach connecting tubing up to 100 feet long, from the stationary unit to the portable unit. This would allow the patient to first utilize any remaining oxygen in the portable therefore, not wasting the oxygen remaining in the bottle. When the portable becomes empty during the night, the evaporative gas of the liquid stationary that has been storing all day for nighttime use would then supply the oxygen.

This system design effectively deals with all of the reported objections to the 24-hour compliance issue seen in the NOTT study. The oxygen flow is not continuous at any liter flow greater than one liter per minute of flow. It is only provided during inspiration. This demand oxygen system reduces the drying effect of the nasal mucosa seen with continuous oxygen therapy while continuing to be very effective in oxygenating patients. The ability of patients to utilize the light-weight "hands free" system even while in the home, eliminates the need for the patient to be tethered to a 50 foot tubing which conventionally provides oxygen therapy for patients in their homes from a stationary source. This elimination of the 50-foot supply tubing for use in the home significantly reduces the pulling of the cannula on the patients' ears, reducing the skin irritation seen with

conventional systems. Additional benefits for this include improved freedom from the stationary unit and the elimination of need to change the interface when one wishes to move beyond the 50-foot radius from the stationary. The removal of the need for the supply line also reduces the fall hazard to the patient and others in the home due to the removal of the supply tubing throughout the home. Finally, this state of the art system provides a very small, sleek oxygen interface that has a non-medical appearance (See figure 2). The ease of use should contribute to improved compliance.

The Helios ™ unit incorporates a patented design for the oxygen container. Historically, cryogenic (liquid oxygen) vessels were designed like a bottle. These standard bottles have a neck at the top of the bottle where the evaporation to a gaseous form of the oxygen takes place. This old design requires that the bottle be kept up right in order for the liquid oxygen to remain in proper position in the bottom of the bottle. If the bottle were to tip over on its side, the oxygen container will begin to hiss and vent the oxygen. Within a few minutes the liquid oxygen could actually spill from the container, creating a cold burn hazard to the patient should they touch this material that is at a temperature of approximately minus 300 degrees Fahrenheit (PB, 1987). The new HELiOS ™ container design is built like a tanker truck or a closed soda can. This closed design incorporates a floating tube, which is used to pull up the liquid oxygen into the warming coils for evaporation into the gaseous state. This design allows the container to have excellent tip over characteristics. The vessel is designed to operate in the upright

operate in the upright and horizontal positions. This design is not only beneficial from a safety stand point, but also allows for the most convenient transport of the unit in many configurations, therein reducing the anxiety of the patient during outings from the home (PB, 2000).

Figure 2

(Photograph courtesy of Mallinckrodt, Inc.-Puritan-Bennett product line-St.Louis, MO)

The use of small and very portable oxygen systems, which allow for ease in ambulation for patients, has many benefits in addition to improved compliance.

The positive effects of pulmonary rehabilitation programs with the use of ambulatory oxygen systems have been well documented (Clark 1996, Harris 1996, Dean 1992, Criner 1987). A study by Janssens et.al. published in 1997 showed a direct correlation between distance walked per day with the quality of life score of

patients with chronic pulmonary disease (Janssens, 1997). A second study published in 1991 by Lock et.al. compared the number of hours of ambulation outside of the home for patients who were utilizing liquid oxygen portables weighing approximately 8 lbs. and lasting for about 4 hours to patient who used E-tank sized cylinders of compressed gaseous oxygen in carts weighing approximately 15 pounds and lasting approximately 5 hours. The results of this study showed that those patients who were provided with the liquid oxygen systems ambulated a mean of 23.5 hours per week while the matched group using the gaseous oxygen source only ambulated a mean of 10 hours per week (Lock, 1991).

The overwhelming benefit of the use of liquid oxygen therapy systems begs the question, "Why are all oxygen therapy patients who have the ability and desire to ambulate not provided liquid oxygen systems?" The answer to this question is that there are many other stakeholders involved in the provision of oxygen therapy in the United States. Both the Home Care Company providing the oxygen therapy modality and the third party payer who contributes to the reimbursement for this therapy are significant contributors to the determination of the modality of oxygen provided to patients. Because the majority of oxygen therapy patients are Medicare beneficiaries, the reimbursement by Medicare as the third party payer to the Home Care Company for the provision of the oxygen therapy significantly impacts the type of oxygen provided. The reimbursement of oxygen therapy to the Home Care Company by Medicare is "Modality Neutral" (Petty, 1990). This

means that the Home Care Company is reimbursed the same amount by Medicare for the provision of the oxygen therapy equipment, supplies, and service, with no differentiation for more ambulatory oxygen sources. Compounding this problem is the fact that the reimbursement for oxygen therapy to Home Care Companies by Medicare was reduced by 25% in 1998 and was reduced by an additional 5% in 1999. This was a direct effect of the Balanced Budget Act of 1998. Because conventional liquid oxygen sources require the Home Care Company to send someone out to the home approximately once per week to refill the stationary oxygen vessel, the cost of providing the "service" required with conventional liquid oxygen systems has been cost prohibitive. Oxygen concentrators, requiring only once every three month visits for maintenance are much less expense to provide (PB, 1999). However, oxygen concentrators do not provide for an ambulatory source of oxygen for patients.

In an attempt to reduce the cost of long-term oxygen therapy, (LTOT), conserving devices have been developed which deliver oxygen at the point during inspiration, which is most effective for oxygenation. To this point most oxygen conserving devices have been used to conserve oxygen in portable oxygen systems. This has become a very popular way of providing ambulatory oxygen with a compressed gas tank called and M-6 and can be used in conjunction with an oxygen concentrator to be used while the patient is at home. This system typically allows a 5.5-6 pound system to last for anywhere from 4-6 hours for the typical 2-liter per minute patient. Although this has been found effective in reducing the

cost of the provision of ambulatory oxygen (Stiegmeyer, 1999), this system is not without many drawbacks. Many of these conserving devices used with compressed gas cylinders are very complicated and require significant dexterity by the patient to remove the regulator, open the tank, and remember the sequence in order to initiate the function of the conserving device.

As previously mentioned, the stationary system used with this modality is typically an oxygen concentrator. This is a machine that is powered by electricity. It draws in air from the room. Air is comprised of approximately 21% oxygen, 78% nitrogen, and 1% various other trace gasses. The oxygen concentrator then filters the air through cylinders filled with a molecular sieve, which removes the nitrogen from the air. The remaining oxygen and other trace gases are then compressed and emitted from the oxygen concentrator with flow rates that vary from typically ½ to 5 liters per minute with an oxygen purity of approximately 92-94% pure oxygen (Scanlan, 199). Although this system is very economical for the Home Care Company to provide, it has several negative implications for many patients. First, the concentrator operates from an electrical source. Depending upon the region and electrical prices in the area, the use of a concentrator may increase the electrical bill of the patient from $240 to $300 per year (Petty 1994). There is little to no government assistance or reimbursement for this additional cost. The concentrator also makes noise, which is unacceptable to many patients. An example of the concentrator and compressed gas cylinders can be seen in Figure 3. The use of the concentrator in the home and the small compressed gas

compressed gas cylinders for activity outside the home does not address the need to be tethered to the concentrator by a 50 foot extension tubing while the patient is in their home. It also adds a level of complexity to the desire of the patient to leave their home. Because the patient must discontinue the use of the oxygen concentrator and initiate the use of the compressed gas with conserving device source, the patient may determine that the effort required to leave the home while utilizing the oxygen therapy is simply not worth the effort (Ojile, 1999). They will then either leave the home without the use of their oxygen or worse, not leave home at all.

Figure 3

(Photograph Courtesy of Mallinckrodt, Inc.-Puritan Bennett product line-St.Charles, Mo)

The HELiOS™ oxygen system effectively deals with many of the barriers of oxygen therapy provision. In addition to the many patient benefits that it provides, its patented designed storage system allows it to be as economical as the concentrator and small cylinder option for any ambulatory patient whose current or desired life-style would require at least monthly delivery of small tanks for use during ambulation.

The overall economic benefit of the HELiOS™ system is most prudent if the system can be used by the patient breathing through the portable unit on a 24-hour basis. This creates a significant challenge for this product. To this point, oxygen-conserving devices have primarily been used by patients during ambulation only. The use of various types of conserving devices has been shown to be effective in the oxygenation of the ambulatory patient in several studies (Carter, 1989,Rinow 1986, Braun 1992, Mecikalski, 1984, Stegmaier, 1999). However, a limited number of attempts have been made to utilize oxygen-conserving devices during sleep and have for the most part been unsuccessful in doing so.

The bases of this empirical research will be the attempt to determine the significance to patient outcomes in the use of the HELiOS™ oxygen therapy product on a 24-hour per day basis. The focus of the research will be to determine the implications of the use of this pneumatic oxygen-conserving device during sleep. In order to promote use of these devices on a 24-hour basis, it is first necessary to understand their effectiveness in the oxygenation of patients and specifically patients during sleep.

This study will compare the efficacy of a pneumatic demand device (PDD) to a standard continuous flow system in maintaining oxygenation of subjects with chronic lung disease requiring oxygen therapy during sleep. In a previous trial using a similar Mallinckrodt device, oxygenation was substantially equivalent in 70% of subjects utilizing a similar PDD during sleep when compared with continuous flow oxygen (Sa02 $\pm$ 2%). Subjects who failed to meet the success criterion of no episodes of > five consecutive minutes of oxygen desaturation to less than 90%, were attributed to failure to trigger the device.

In this study, subjects were observed in the sleep lab under full polysomnography for a total of three nights. The first night served as an acclimation night as well as a night to titrate the patient's oxygen to determine actual nocturnal oxygen needs. This acclimation night was also used as a night for screening any patients who suffered from obstructive sleep apnea. The patients were then randomized to either continuous flow oxygen or oxygen via the demand conserving device. Outcome measures from this study included the quality of sleep while utilizing each mode of oxygen therapy. The quality of sleep was quantified in number of minutes spent in REM as well as the number of arousal throughout the entire sleep period. This outcome measure was of interest to determine if the intermittent "puffs" of oxygen or the noise created by the device would arouse patients from sleep or cause them to have a lower quality to sleep.

The second outcome measure to be determined was if the volume of oxygen delivered by the conserving device was adequate to maintain oxygen

saturation equal to that of continuous flow. Any variance greater than 2% saturation points from the mean and lasting for greater than five minutes would be considered a significant decrease in saturation. These episodes of desaturation would of course only be considered to be due to lack of volume of oxygen delivered if they occurred when the patient was consistently triggering the oxygen-conserving device. The third outcome measure was to determine if the patients could maintain saturation equal to continuous flow even in a situation of "failure to trigger" the device. This is of importance because it was hypothesized that the target population for this product, Chronic Obstructive Pulmonary Disease (COPD) patients would experience at least some failure to trigger of the device over the entire sleep period despite its extreme sensitivity. Both the pathophysiology of the COPD patient and previously documented attempts at the use of oxygen conserving devices during sleep would suggest that this might occur (Cuvelier, 1999, Kacmarek, 1990).

COPD patients suffer from a condition that causes air to be trapped within the lungs. This air trapping results in the eventual expansion of the diameter of the chest wall and therefore, loss of the natural, elastic recoil of the chest during the expiratory phase of breathing. This further exacerbates the problem of the air trapping. This increased air trapping begins to press downward on the diaphragmatic muscle. Healthy people rely on the contraction of the diaphragms to drop enough to create a vacuum, which results in a negative pressure to be created. This causes air to flow into the lungs. However, due to the fact the

diaphragms of a COPD patient are flattened from the air trapping, it becomes difficult for the contraction of the diaphragms alone to create enough negative pressure to create an appropriate level of airflow. To compensate for the deficit, COPD patients use what is known as the accessory muscles of respiration to assist in the movement of the chest wall great enough to create a significant negative pressure. The healthy person when over exerted uses these skeletal muscles of the neck, chest wall, and abdomen and a need has been created to breath much more deeply than normal. The need for COPD patients to use their accessory muscles of respiration to create a negative pressure becomes problematic during sleep in the attempt to trigger a demand system of oxygen flow. During deep sleep known as Stage IV and more significantly in REM (Rapid Eye Movement) sleep, the skeletal muscles of the body are in a paralytic state. This total lack of movement of the skeletal muscle of the body is what causes one to feel rested in the morning. This is why the quality of an individual's sleep is often quantified in the time spent in REM. Although the demand oxygen-conserving device being studied needs only a very little negative pressure in order to trigger (0.05 cm $H_2O$), even this minuet amount of pressure may not be created during REM sleep in the COPD patient.

This study is being conducted to explore increased sensitivity for triggering and to provide options for subjects who cannot trigger the device. To date, most studies have shown that oxygenation of subjects with conserving devices is most effective when the majority of the oxygen provided is supplied during the first 0.3 seconds of inspiration (Bliss, 2000). Such devices have been proven effective

during wakeful hours (at rest and exercise) and similar data reproduced in various studies(Braun, 1992, Tiep, 1995). With previously produced and marketed conserving devices, patients were only encouraged to use the device during ambulation outside of the home. However, the HELiOS$^{TM}$ product is designed for use on a continuous basis. This product design is requiring that patients use a conserving device during all activities of daily living, including exercise, rest and sleep. Chapter III of this manuscript will provide the research protocol and design established to evaluate the efficacy of the HELiOS$^{TM}$ oxygen conserving system.

# Chapter III

## Methodology

### Study Rational

This study was designed to examine the efficacy of a Pneumatic Demand Device (PDD) in the oxygenation of subjects with chronic lung disease requiring oxygen therapy during sleep. Previous medical trials have shown that 70% of subjects utilizing a similar PDD during sleep oxygenated as well (Sa02 $\pm$ 2%) as they did while using continuous flow oxygen (Mallinckrodt, 1999). Subjects who failed to meet the success criteria defined as no episodes of > five consecutive minutes of desaturation of < 90%, could be attributed to failure to trigger the device. This study was conducted to explore the possibilities of increasing sensitivity and to provide options for subjects who cannot trigger the device. It has been shown that the use of oxygen during sleep can increase survival rates for subjects with chronic lung disease (MRC, 1981, NOTT, 1980). In attempts to decrease health care spending, devices have been developed to conserve oxygen by delivering the oxygen at the point during inspiration that can most efficiently be utilized for oxygenation. If such devices could be proven to be effective in the oxygenation of sleeping patients, their use on a 24hour per day basis would dramatically reduce the cost of providing

Long Term Oxygen Therapy. To date the majority of studies have shown that oxygenation of subjects with conserving devices are most effective when the majority of the oxygen provided is supplied during the first 0.3 seconds of inspiration (Bower, 1988). Such devices have been proven effective during wakeful hours (at rest and exercise) and replicated in various studies ( Braun, 1992, NPB, 1998).

This study was designed to look at the ability of a PDD to provide oxygenation equal to that of continuous flow during sleep. It is known that the level of oxygenation is altered during sleep. This is thought to be most likely from the recumbent position during sleep decreasing the level of movement in the diaphragm and therefore decreasing the total amount of airflow into the lungs. This problem is exacerbated in the COPD patient due to diaphragmatic fatigue and hyperinflation (Scanlan, 1999). Further concerns have been raised by the display of altered chest wall and muscle excursion during REM sleep in healthy subjects (Becker, 1999). Patients suffering from COPD must utilize accessory muscles for adequate ventilation and thus oxygenation. This makes the sensitivity of conserving devices utilized during sleep key in the efficacy of the unit.

## Study Objectives

The objectives of this sleep study were as follows:

1. To evaluate the ability of a 4:1 pneumatic conserving device to provide equivalent oxygenation of patients as with continuous flow oxygen during sleep.

2. To evaluate the quality of sleep of patients using an oxygen-conserving device compared with their quality of sleep during use of continuous flow oxygen.

3. To compare the performance of a variable flow-conserving device with previously studied PDD and continuous flow oxygen in the oxygenation of patients during sleep.

## Methods

A total of 20 subjects currently utilizing supplemental oxygen were recruited for this study. Patients underwent a pulmonary function test including spirometry, plethysmography, and diffusion measurement to characterize the severity of their COPD. Subjects underwent either 3 or 4 nights of polysomnography recording on consecutive nights. Polysomnography was performed in the sleep lab. The first night served as an acclimation night (Toussaint, 1995). This first night also served as an evaluation for exclusion of subjects with Obstructive or Central Apnea, defined as greater than ten apneas or hypopneas per hour of sleep. During

the acclimation night subjects breathed oxygen per nasal cannula at their previously prescribed liter flow. Adjustments in oxygen prescription were allowed during this evaluation time period to keep oxygen saturations greater than 90%. On the second and third nights the subjects either received oxygen at their regularly prescribed liter flow or they received oxygen per the 4:1 PDD at an equivalent setting to their prescribed liter flow. (See table below). The order for delivery method on the second and third nights will be randomized.

**4:1 and variable flow device, wave form characteristics: Calculations made at 18 breaths/minute with I:E ratio of 1:2.**

**4:1 Technology: Oxygen Usage**

| flow rate (lpm) | bolus size (ml) | tail rate (lpm) | final rate (lpm) | $O_2$ from tank/ breath (ml) | $O_2$ from canula/ breath (ml) |
|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | | |
| 1/8 | 0 | 1/8 | 1/8 | 6.94 | **6.94** |
| 1/4 | 0 | 1/4 | 1/4 | 13.89 | **13.89** |
| 1/2 | 0 | 1/2 | 1/2 | 27.78 | **27.78** |
| 3/4 | 0 | 3/4 | 3/4 | 41.67 | **41.67** |
| 1 | 9 | 0.5 | 0 | 22.70 | **18.26** |
| 1 1/2 | 9 | 0.65 | 0 | 25.48 | **21.04** |
| 2 | 12 | 0.75 | 0 | 30.33 | **25.89** |
| 2 1/2 | 12 | 1 | 0 | 34.96 | **30.52** |
| 3 | 15 | 1.5 | 0 | 47.22 | **42.78** |
| 3 1/2 | 15 | 1.75 | 0 | 51.85 | **47.41** |
| 4 | 15 | 2 | 0 | 56.48 | **52.04** |

Polysomnography was performed in accordance with published guidelines ("Indications and Standards, 1989) and measurements included central and occipital EEG, chin and leg EMG, ECG, snoring sounds, air flow, chest and abdominal respiratory effort, pulse oximetry, and body position. The pulse oximetry waveform was monitored for detection of artifact therefore increasing accuracy of oximetry measurements. A second microphone was placed on the regulator to record sounds associated with the pulse flow of oxygen. This additional microphone was used to determine whether pulses of oxygen were the cause of increased EEG arousals during sleep. All physiologic signals were digitized and stored on a computerized sleep system. (Sandman - NBP) for scoring and analysis. Sleep stages and arousals were scored according to standard criteria.("American Sleep Disorders Asso", 1992). Pulse oximetry measurements were digitized and analyzed to yield values for mean and nadir nocturnal saturations. Additional data was reported includes, number of desaturations and percentage of time spent at a saturation of less than 90%. REM versus Non-REM sleep stage and oxygen saturations will be compared for nights 2 and 3. The effect of body position on pulse oximetry was also taken into account and reported. All subjects were observed during sleep for notation of body position and nasal cannula placement during periods of desaturation.

Control Group and Study Population

Although it is difficult to blind subjects to the delivery device due to the sensation of the "pulse" of oxygen with the demand flow system, no special attempts were made to inform subjects of the device that will be used that specific night.

Subjects served as their own control. Each subject was studied a minimum of three nights with the first night serving as an acclimation as well as a screening study. On the two nights to follow, all subjects were studied one night as a control night at continuous flow and another night on the test device.

Mixed gender subjects > 18 years of age and diagnosed with chronic lung disease were recruited. Subjects must have had previously qualified for Nocturnal Oxygen via the HCFA guidelines and must currently be using between 1 and 4 L/min continuous oxygen as prescribed by their physician. A total of 20 evaluable subjects were to be studied. Subjects were be recruited by the Investigator from area medical practices. Each subject was tested over a 3 to 4 day period. No medications were contraindicated.

Inclusion and Exclusion Criteria

The following were used as enrollment criteria and subjects will be screened by the site research coordinator and sleep lab staff.

6. Subjects must be at least 18 years of age and previously met requirements for oxygen therapy in accordance with the HCFA guidelines.

7. Subjects must currently be utilizing nocturnal oxygen therapy at a prescribed rate between one and four liters per minute.

8. Subject must have a previous diagnosis of Chronic Lung Disease, which must be demonstrated by Pulmonary Function representative of lung disease.

9. Subjects must be willing to comply with the study protocol including testing over 3 to 4 nights.

10. Subjects must exhibit no signs of acute exacerbation of their disease state
including fever or purulent secretions.

6. Subjects' medication regimen must be previously titrated for optimal treatment affect.

7. Subjects must be willing to sign informed consent.

Subjects were to be excluded from this study if they did not meet the specific inclusion criteria, or if:

1. Subject failed to sign an informed consent

2. Subject demonstrated any of the following any time during the study period:

- Unstable or untreated angina
- Recent Myocardial infarction (within four weeks prior to study)
- Acute myocarditis or pericarditis
- Aneurysm of the heart or aorta
- Primary pulmonary hypertension
- Recent systemic or pulmonary embolus (four weeks prior to study)
- A condition in which SpO2 might be invalid (COHb, Sickle cell)
- Untreated or unstable nocturnal asthma symptoms.
- Previously diagnosed/current signs of obstructive or central apnea
- Required oxygen therapy as a life-sustaining measure

Withdraw criteria

Subjects were free to withdraw consent and discontinue participation in the study at any time without prejudice to further treatment. A subject's participation in the study could have been discontinued at anytime during the study at the discretion of the investigator. The following were used as criteria for justifiable reasons for the investigator to remove a patient from the study:

- Their treatment or health would have been compromised by their continued participation in the study.
- Subject or site investigator feels that the subject was not willing or able to continue to participate.
- The subject wishes to discontinue participation

Adverse effects of the study were also an indication for the subject to be taken off of the study. Such indications would include but were not limited to:

- Request from the subject to terminate the study for any reason

- Any signs or symptoms demonstrated by the subject in which the Investigator felt would place the subject in immediate medical danger.

In the event of the need to discontinue any subject's participation in the study, the subject would have been contacted by the investigator and informed of the reason for discontinuation of study. Any adverse events will be immediately reported to the Sponsoring research coordinator and the appropriate information would be provided on the case report form.

Safety Assessment (Risk/Benefit Analysis)

Although there were no direct medical benefits to the study subjects, there may be advances in product technology as a result of this study, which will ultimately benefit patients dependent on LTOT.

A risk to participation in this study was the potential for poor quality of sleep due to non-acclimation to the PDD and/or sleeping in an unfamiliar environment. If a subject fails to trigger the device their saturation may decline. Prior to the sensitivity modifications of this study, 70% of subjects studied triggered the device and saturated well. It was hypothesized that the study modifications would allow for increased sensitivity. However, all subjects were closely monitored in the sleep lab setting and could be reverted to continuous flow therapy, if required. No subject entered into this study required oxygen therapy as a life-sustaining measure.

There are two possible adverse device effects that have been reported in the literature. The first is the potential for the inability of the conserving device to provide oxygen in the volume and delivery method required to oxygenate the patient adequately. (> 88% SaO2 as defined by the established Medicare guidelines for the qualification for need of supplemental oxygen.) Secondly, there is a risk of the inability of the patient to trigger the conserving device, resulting in desaturation, specifically during REM sleep in COPD patients. It is anticipated that either one or both of these effects might occur during the study.

The safety action that is in place for such anticipated adverse device effect is to include extensive monitoring. All patients are to be monitored with full polysomnography, which includes EEG, ECG, EMG, respiratory rate, oxygen saturation, airflow (via pressure transducer), and abdominal movement for effort. Prior to and following each night of study a non-invasive blood pressure assessment will be taken. All subjects are also continually monitored via closed circuit video monitoring.

Data collection

All data for subjects entered into the study was collected digitally. In addition to the digital recording of the polysomnograph, specific data that was reported as primary or secondary outcome measures were

collected on a standard case report form (CRF). All CRFs were collected and used in final analysis of the data.

Efficacy of the study device was determined by two parameters.

1) The mean oxygen saturation of subjects while utilizing the study device as compared with the mean saturations of the same subject during the use of continuous flow.

2) the proportion of patients who fail to tolerate the device. A failure to tolerate the device is defined as a subject who experiences > ten episodes of desaturation to < 90% for greater than 5 minutes.

This protocol and subject informed consent form are reviewed and approved by the Institutional Review Board (IRB) of the testing facility in complying with the requirements of 21 CFR 56 or CPMP/ICH/135/95 Part 5.11 before enrollment of subjects. (See Appendix A )

# Chapter IV

## Data Collection

The data from each subject was accepted for analysis when following the acclimation night, data for the control and the measurement nights had been completed, subject had agreed to continue in the study, and had not exhibited any signs or symptoms of central or obstructive sleep apnea. All subject data that was used in the final data collection process was from subjects who were potential candidates as users of the study product. This criteria included that the subject must have been prescribed continuous oxygen therapy, they could not have a known need for greater than 4 liters per minute of oxygen under any activities of daily living, and must not have been dependent upon oxygen therapy as a means of "life support".

Potential patients who were not enrolled based on screening outcome were not included in the statistical analysis. Data from those patients are reported in screening data listings only. All patients enrolled in this study are included in all data listings of patient characteristics. Only patients that received the test device are included in summary tables of patient safety and efficacy characteristics.

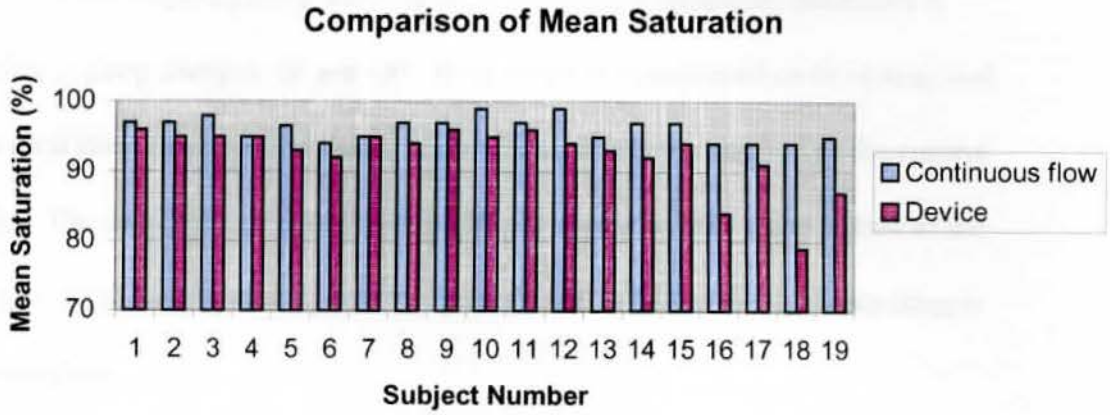
Demographic

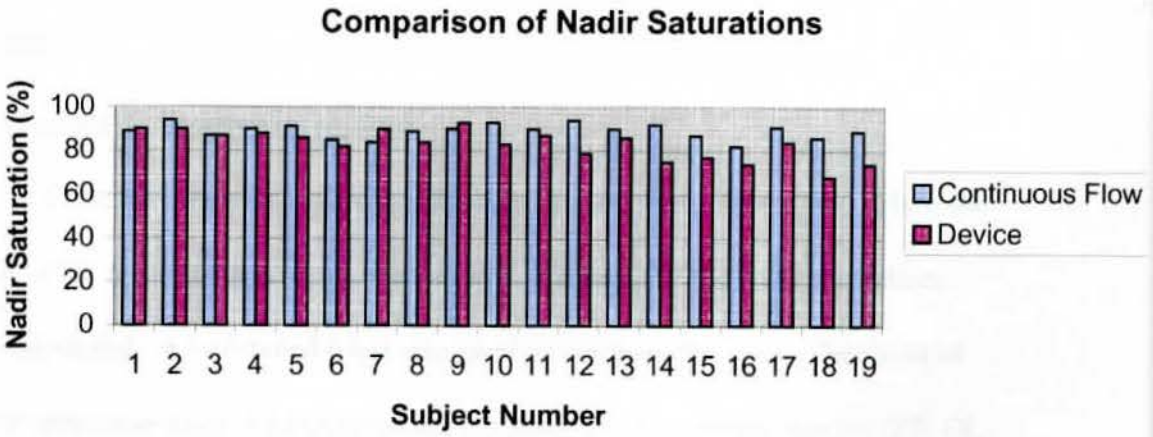
A total of twenty (20) subjects were studied resulting in nineteen (19) evaluable case report forms. One subject's data was excluded when it was discovered that her ambulatory oxygen prescription was greater than 4 liters per minute, which would exclude this subject from candidacy for the current product in evaluation (H300 HELiOS oxygen portable). The data sample included seven (7) male patients. The mean age was 69 years old (range 57-77). All subjects had been previously diagnosed with Chronic Obstructive Lung Disease (COPD) and prescribed oxygen therapy at a rate of 1-4 l/min of continuous flow oxygen for use during sleep and not greater than 4 l/min of oxygen during waking rest or exercise. Mean FEV1 for the study subjects was 47.6 of predicted (21-103% range).

Data Results-Individual Study Comparison

Oxygen Saturation

Twelve (12) of the nineteen (19) patients (63%) experienced both mean and nadir (lowest) oxygen saturation of not greater than $\pm$ 4 oxygen saturation percentage points of variance during the study night when compared with the same measurements during the control night of study. The greatest variance in mean and nadir oxygen saturation was 15 percentage points and 18 percentage points respectively. Bar graphs of the mean saturations as well as the nadir can be seen below.




Of the 7 subjects who had desaturation greater than 4 percentage points from the control night, the average time spent in desaturation of less than 88% was 31 minutes (21-42.5 minutes range).

## Sleep Quality

Two subjects (10%) were reported as having a significant difference in quality of sleep (Subject 16 and 18). Both subjects experienced more arousal and less total sleep time in REM during the study night when compared to the control night. The decrease in quality of sleep did not appear to have a correlation to the trigger of the device but did seem to correlate with a failure to trigger resulting in desaturation.

## Correlation with Pulmonary Function

Data from this small sample set of 19 patients showed no correlation between pulmonary function measures and ability to trigger and/or maintain oxygen saturation during sleep. Correlations attempted included RV/TLC, FEV1, and DIF.

## Data Results-Collective Group Data

Collective data analysis was performed on the group as a whole. Here the mean of the mean oxygen saturations as well as a mean of the nadir saturations was calculated. A two-tailed t-test was used to compare the data. The mean of the oxygen saturation of subjects on the Continuous Flow device was 96.18% ($X_c$ = 98.18) ($SD_c$ =1.64) and the mean of the oxygen saturation of the subjects on the Study Device was 92.42% ($X_d$ = 92.42) ($SD_d$ =4.49) This produced a t*= 3.45 with a p value = 0.001. A large p value ($p > 0.01$) would indicate that the two devices (Continuous flow ($X_c$) and Study Device ($X_d$)) are not statistically, significantly different. Therefore, the fact that the p value was quite small ($p <$

0.001) would indicate that for the group collectively there is a high probability that the two forms of oxygen delivery would be statistically, significantly different.

# Chapter V

## Discussion

This study has raised some questions as to the efficacy of a conserving device such as HELiOS™, examined in this study, to provide an equal level of oxygen saturation as would continuous flow oxygen. HELiOS was very effective in providing oxygen saturation equal to continuous flow in 63% of the subjects studied but did fail to provide equal saturation in 37% of patients studied. This study raises several questions to be discussed.

No immediate harm was found to have occurred in any patients studied, even those whose oxygen saturation dropped for up to 30 minutes. Therefore, if in fact, the patient describes significant benefits in quality of life improvements with the HELiOS™ product and has reported that they are utilizing their oxygen more hours of the day, should these patients not be left on the product? The data from the NOTT and MRC studies only reported that the number of hours per day that the patients remained on their oxygen was a significant contributor to the increased longevity of the patients.

Since the desaturation of all patients seemed to be attributed to the inability to trigger the device and not the volume of oxygen delivered, it could be assumed that the actual problem with the patients was ventilation (depth of respiration) and not necessarily oxygenation as a primary contributor. Here desaturation (lack of appropriate oxygenation) was only the by-product (symptom) of the actual problem, which was ventilation (depth of respiration). This would indicate that the

most effective treatment would be a device that would increase ventilation during Stages IV and REM sleep.

Study Limitation

This study provided a general basis of information regarding the use of one conserving device during hours of sleep. A primary limiting factor of this study is the small sample size used to draw conclusion. Large study populations are typically cost prohibitive in medical device studies. It is the researcher's belief that this is the primary reason why additional studies to find more adaptive and effective medical devices for populations as in this case, the elderly, as well as in the case of medical devices which are primarily used by pediatric patients. Study of a larger sample size would provide much needed data as to the efficacy of this and other devices. This would also provide additional data points, allowing for more accurate determinations if there were in fact, correlations with any pulmonary function values, which could be determined during waking hours.

A second limiting factor in this study was the inability to collect data on the patients end tidal $CO_2$ ($et.CO_2$). The continuous monitoring of $et.CO_2$ would provide additional insight as to the source of these patients' inability to maintain oxygen saturation during hours of sleep. Information about the patients "depth of respiration" during sleep could lead to more effective treatment modalities which would provide for ventilatory support, if in fact this did prove to be the source of the problem for such patients. At the time of this study the patient interfaces to be

used with the type of technology needed to provide this parameter was not available.

Future Study Recommendations

The data from this study does provide some insight into the ability of this conserving device to be used during hours of sleep, the level of desaturation that might be expected in some patients, and as expected, the need for additional study in this area. Several areas of additional study would complement this study.

A more comprehensive study, which provided data as to whether or not this device did increase the number of hours per day that patients, did use their oxygen therapy. This study would also provide data that would allow for analysis as to the significance of the effect of some drop in oxygen saturation at night, if in fact, the patient did use their oxygen therapy more hours of the day. Such a study could be designed similarly to the NOTT 1981 study. Equally matched study groups in disease process and severity would need to be established with patient populations of at least 100 patients per group. The patients would need to be studied for a minimum of 24 months with no less than 500 days of data collected. This was found to be a critical point in the differences in both the MRC and NOTT studies. Such a study would provide much needed insight into the question as to whether or not some desaturation of up to 30 minutes during the hours of sleep could not be off set by increasing the hours of use during the day.

A second study that would provide much needed information for this patient population would be an evaluation of the true cause and effect of oxygen

A second study that would provide much needed information for this patient population would be an evaluation of the true cause and effect of oxygen desaturation at night for COPD patients. A study, which incorporated the continuous monitoring of etCO2, could provide this information. As previously mentioned, at the time of this study, the equipment and interface for this monitoring was not available. However, since the time of this study, such an interface has been developed by Oridion Medical Inc. This product, called the Smart Capnoline® $O_2$, when used with the Microstream® Capnography technology, allows for continuous monitoring of $etCO_2$. The product provides a unique design interface that monitors during both nasal and oral exhalation while providing low flow oxygen therapy. (www.oridion.com) Such a study would provide information that might inform investigators that the patients lack of ability to maintain oxygenation during sleep is actually a function of their inability to ventilate appropriately. Therefore, oxygen supplementation is actually treating the symptom and not the problem. This would open doors for new and better product development of comfortable non-invasive ventilation devices that would treat the actual problem. It could be hypothesized that the development of such products and their effective use would have even a greater impact on the outcomes and longevity of COPD patients.

## Conclusion

using an oxygen conserving device did not seem to be related to the tactile stimulation of the device trigger, but did seem to be related to failure to maintain optimum oxygen saturation. Considering the potential benefit of this single interface oxygen delivery device, this oxygen delivery method should be considered for those patients who can maintain oxygen saturation while using the device. The use of pulse oximetry to evaluate patients for such technology appears to be an effective measure of the subjects' ability to tolerate the device.

Since the release of the HELiOS ™ Oxygen System, several additional devices have been released, which are similarly designed. Although none are known to have any additional clinical or fina ncial benefits, at minimum, there is additional innovation in the area of oxygen therapy delivery. If the development of this device has done nothing more; it has placed a significant mark in the production of oxygen therapy devices. These devices offer care for more than the one million people in the United States that must live with the day-to-day frustrations and limitations of Long Term Oxygen Therapy. Long Term Oxygen Therapy is the only effective treatment for COPD, a disease with no known cure.

## Appendix A

### Title 21, Part 812
Applicability (**Section 812.2)**

(b) *Abbreviated requirements.* The following categories of investigations are considered to have approved applications for IDE's, unless FDA has notified a sponsor under §812.20(a) that approval of an application is required:

(1) An investigation of a device other than a significant risk device, if the device is not a banned device and the sponsor:

(i) Labels the device in accordance with §812.5;

(ii) Obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval;

(iii) Ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, informed consent under Part 50 and documents it, unless documentation is waived by an IRB under §56.109(c);

(iv) Complies with the requirements of §812.46 with respect to monitoring investigations;

(v) Maintains the records required under §812.140(b) (4) and (5) and makes the reports required under §812.150(b) (1) through (3) and (5) through (10);

(vi) Ensures that participating investigators maintain the records required by §812.140(a)(3)(i) and make the reports required under §812.150(a) (1), (2), (5) and (7); and

(vii) Complies with the prohibitions in §812.7 against promotion and other practices.

(2) An investigation of a device other than one subject to paragraph (e) of this section, if the investigation was begun on or before July 16, 1980, and to be completed, and is completed, on or before January 19, 1981.

**Title 21, Part 812**
Definitions (Section 812.3)

(m) *Significant risk device* means an investigational device that:
(1) Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
(2) Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
(3) Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
(4) Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

Reference

American Sleep disorders Association Atlas Task Force: (1992). EEG arousouls:scoring and examples American Sleep Disorders Association atlas task force:EEG arousals:scoring and examples. Sleep 15:173-184.

Becker, H., Piper, A., Flynn, W., McNamara, S., Grunstein, R., Peter, H., Sullivan, C. (1999). Breathing during sleep in patients with nocturnal Desaturation, Am J Respir Cit Care Med, 159:112-118.

Bliss, P., McCoy, R. (2000). Performance of new demand oxygen delivery Systems in a simulation of low flow oxygen use. American Association For Respiratory Care; International Congress 2000. Cincinnati, OH.

Bower, B., Zimmer, D. (1988). Performance of a demand oxygen saver System during rest, exercise, and sleep in hypoxemic patients. Chest, 94(1):77-80.

Braun, S, Spratt, G., Scott, G., Ellersieck, M. (1992). Comparison of six oxygen delivery systems for COPD patients at rest and during exercise, Chest, 102:694-98.

Clark, C., MacKay. (1996). Low intensity peripheral muscle conditioning improves exercise tolerance and breathlessness in COPD, Eur Resp J, 2590-96.

Criner, Celli. (1987). Ventilatory muscle recruitment in exercise with $O_2$ in obstructed patients with mild hypoxemia, J Appl Physiology, 63(1): 195-200.

Carter, R., Tashkin, D., Djahed, B., Hathaway, E., Nicotra, B., Tiep, B.

(1989), Demand oxygen delivery for patients with restrictive lung disease. Chest, 96:1307-11.

Cuvelier, M., Czernichow, V., Portier, B., Simson, D. (1999). Nocturnal efficiency and tolerance of a demand oxygen delivery system in COPD patients with nocturnal hypoxemia. Chest, 116:22-29.

Dean, Brown, Himelman, Donertry, Gold, Stalbarg. (1992). Oxygen may improve dyspnea and endurance in patients with chronic obstructive pulmonary disease and only mild hypoxemia, Am Rev Respir Dis, 146: 941-945.

Harris-Eze, S., Clenens, Z., Gallagher, M. (1996). The roll of hypoximia and pulmonary mechanics in exercise limitations in interstitial lung disease. Am J Resp Crit Care Med, 154:994-1001.

Health Care Financing Administration (HCFA) (2000). Medicare Part B; Reimbursement guidelines 2000 edition.

Indications and standards for cardiopulmonary sleep studies-American Thoracic Society; Medical section of the American Lung Association. (1989). Am Rev Respir Dis, 139:559-68.

Janssens, J.P., Rochet, T., Frey, J.G., Dousse, N., Pichard, C., Tschopp, J., (1991). Exercise related quality of life in patients with long term oxygen therapy. Resp Med, 154(5):591-597.

Kacmarek, R., Mack, C., Dimas, S. (1990). The Essentials of Respiratory Care; Third Edition. St.Louis: Mosby Books, pp 282.

Lock S., Blower G., Prynne M., Wedzicha, J., (1991). Comparison of

liquid and gaseous oxygen for domiciliary portable use. Resp Med, 85: 407-12.

Mallinckrodt, (2000). HELiOS™ instructional video.

Mallinckrodt, (2000). Technical manual HELiOS™ H300.

Mecikalski, M., Shigeoka, J. (1984). A demand valve conservers oxygen in subjects with chronic obstructive pulmonary disease. Chest, 86(5):667-670.

Nocturnal Oxygen Therapy Group (NOTT), (1980). Continuous or nocturnal oxygen therapy in hypoxemic chronic obstructive lung disease: a clinical trial. Ann Internal Med. 93(3):391-98.

O'Donohue, W., Long Term Oxygen Theraphy:Scientific Basis and Clinical Application. New York: Dekker.

Ojile, J. (May 1999). [Interview with Dr. Joseph Ojile]

Petty, T. (October 1999). [Interview with Dr. Thomas Petty]

Petty, T., O'Donohue, W. (1994). Further recommendations for prescribing, reimbursement, technology development and research in long-term oxygen therapy, Summary of the fourth oxygen consensus conference. Am J Respir Crit Care Med. 150:875-877.

Petty, O'Donohue, Gracey Greene, Pierson, Plummer. (1999). Conference report; New problems in supply, reimbursement and certification of medical necessity for long-term oxygen therapy, Summary of the third consensus conference. Am Rev Respir Dis. 142:721-24.

Purittan-Bennett Technical Manual Companion 1000™. (1987) P/N B-

775567-00.

Purittan-Bennett Technical Manual, Aeris 590™. (1999).

Rinow, M., Saltzman, A. (1986). Effectiveness of a new oxygen demand valve in chronic hypoxemia. Chest. 90(2):204-207.

Report of the Medical Research Council Working Party (MRC). (1981). Long term domiciliary oxygen therapy in chronic hypoxemic cor pulmonale complicating chronic bronchitis and emphysema. Lancet. 8222:681-686.

Scanlan, Spearman, Sheldon. (1990). Egan's Fundamentals of Respiratory Care, Fifth Edition. St.Louis: Mosby Books.

Steigmeyer, Lewarski, Milus. (1999). Oxygen conservation devices improve portability and reduce the cost of care for ambulatory home oxygen therapy patients. Resp Care. 44(10).

Tiep, B. (1995). Portable oxygen therapy with oxygen conserving device and methodologies. Arch Chest Dis. 50(1):51-57.

Tiep, Carter, Nicota, Berry, Phyllips, Otsap. (1987). Demand oxygen delivery during exercise. Chest. 91(1):15-20.