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SLEEP DISORDERS

(SAMPLE COPY, NOT FOR RESALE)

Insomnia, Sleep Apnea, Restless Leg Syndrome, Bruxism, Narcolepsy and Sleepwalking

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1. Overview

1.1 Statement of Report

Insomnia, sleep apnea, restless leg syndrome, bruxism, narcolepsy and sleepwalking are all serious sleep disorders that possess negative—and sometimes fatal—health consequences. Often undiagnosed and thus not treated, sleep disorders can not only take a toll on personal health but can also adverse effects on personal relationships and reduce worker productivity. In examining the troubling increase in a variety of sleep disorders, this report will analyze the causes and available treatments for sleep disorder sufferers.

This is a particularly interesting time in the evolution of the sleep disorders market because the blockbuster drugs that have dominated this space are coming off patent protection. There has been a strong push on the part of the major pharmaceutical companies to develop or acquire replacement sources of revenue. Moreover, there are several new drugs that will be released shortly. As such, the need for the major pharmaceutical houses to replace the income from these sources has led to interesting partnerships and acquisitions. These developments as well as non-pharmaceutical treatments are leading to better options for individuals who suffer from sleep disorders on a regular basis.

1.2 About This Report

By purchasing this report, the reader will have:

- An understanding of the most exciting sleep disorders market segments.
- The latest information on leading products and research and development (R&D) initiatives.
- Familiarity with recent developments and their effects on selected markets.
- Knowledge of the sleep disorders market as an area of growth, research and investment.
- An extensive review of the leading companies in the sleep disorders market.

Key questions answered in this report:

- What are the main types of sleep disorders, including insomnia, sleep apnea, restless leg syndrome, bruxism, narcolepsy and sleepwalking, and how are they managed?
- What are the main types of sleep disorders treatments that are currently available?
- Who are the current key players in this marketplace?
- What is the current state of the sleep disorders market?

Additionally, this report contains:

- In-depth profiles of the leading companies providing sleep disorders solutions.
- Detailed analysis of the trends in the sleep disorders marketplace.
- Views on the sleep disorders industry from leading industry experts.
- Analysis of new sleep disorders developments.

Sleep disorders discussed in this report include: sleep apnea (obstructive sleep apnea/hypopnea syndrome, central sleep apnea); restless leg syndrome; periodic limb movement disorder; somnambulism (*e.g.*, sleepwalking), parasomnias (*e.g.*, night terrors, bed-wetting); bruxism (*e.g.*, teeth grinding); narcolepsy; circadian rhythm disorders (*e.g.*, shift-worker sleep disorder); transient sleep disorders, such as those caused by jet lag; and insomnia, which is a symptom caused by a number of neurological and psychiatric disorders.

1.3 Scope of the Report

This analysis primarily focuses on the following sleep disorders:

- Insomnia.
- Sleep apnea.
- Restless leg syndrome.
- Bruxism (teeth grinding).
- Narcolepsy.
- Sleepwalking.

The report discusses products, trends, new developments and compensation issues that are currently affecting or are likely to affect the market soon. Analyses are provided for each of the key companies in the major and minor market segments. The reader should consult other TriMark Publications reports at <http://www.trimarkpublications.com> for a detailed discussion of the important individual market segments that are related to these markets such as the diagnostics, medical devices and pharmaceuticals markets.

1.4 Methodology

The author of this report is an MD with three decades of experience as a medical products industry analyst. He has held many senior level positions in hospitals, healthcare and life sciences organizations and companies. The editor of the report has a PhD in biophysics and has worked as a research assistant professor at the University of Missouri.

Company-specific information is obtained mainly from industry trade publications, academic journals, news and research articles, press releases and corporate websites, as well as annual reports for publicly-held firms. Additionally, sources of information include the non-governmental organizations (NGOs) such as the World Health Organization (WHO) and governmental entities like the U.S. Department of Health and Human Services (HHS) and U.S. federal agencies such as National Institutes of Health (NIH), Food and Drug Administration (FDA) and the Centers of Disease Control and Prevention (CDC). Where possible and practicable, the most recent data available have been used.

Some of the statistical information was taken from Biotechnology Associates' databases and from TriMark's private data stores. The information in this study was obtained from sources that we believe to be reliable, but we do not guarantee the accuracy, adequacy or completeness of any information or omission or for the results obtained by the use of such information. Key information from the business literature was used as a basis to conduct dialogue with and obtain expert opinion from market professionals regarding commercial potential and market sizes. Senior managers from major company players were interviewed for part of the information in this report.

Primary Sources

TriMark collects information from hundreds of Database Tables and many comprehensive multi-client research projects, and Sector Snapshots that we publish annually. We extract relevant data and analytics from TriMark's research as part of this data collection.

Secondary Sources

TriMark uses research publications, journals, magazines, newspapers, newsletters, industry reports, investment research reports, trade and industry association reports, government-affiliated trade releases and other published information as part of its secondary research materials. The information is then analyzed and translated by the Industry Research Group into a TriMark study. The Editorial Group reviews the complete package with product and market forecasts, critical industry trends, threats and opportunities, competitive strategies and market share determinations.

TriMark Publications Report, Research and Data Acquisition Structure

The general sequence of research and analysis activity prior to the publication of every report in TriMark Publications includes the following items:

- Completing an extensive secondary research effort on an important market sector, including gathering all relevant information from corporate reporting, publicly-available data and proprietary databases.
- Formulating a study outline with the assigned writer, including important items, as follows:
 - Market and product segment grouping, and evaluating their relative significance.
 - Key competitors' evaluations, including their relative positions in the business and other relevant facts to prioritize diligence levels and assist in designing a primary research strategy.
 - End-user research to evaluate analytical significance in market estimation.
 - Supply chain research and analysis to identify any factors affecting the market.
 - New technology platforms and cutting-edge applications.
- Identifying the key technology and market trends that drive or affect these markets.
- Assessing the regional significance for each product and market segment for proper emphasis of further regional/national primary and secondary research.
- Completing a confirmatory primary research assessment of the report's findings with the assistance of expert panel partners from the industry being analyzed.

1.5 Executive Summary

In order to put sleep disorders in a proper context, the study begins with an examination of key characteristics of the overall sleep disorders market. The types of disorders, causes of insomnias, parasomnias and their treatments are analyzed, with the additional review of treatments including pharmaceuticals, devices (continuous positive airway pressure or CPAP machines) and others (nutraceuticals, etc.). The report goes on to describe the primary product offerings of the major companies in this market space including major classes of prescription and over-the-counter (OTC) pharmaceuticals. Finally, a review of companies developing treatments for insomnia, sleep apnea, restless leg syndrome, bruxism, narcolepsy and sleepwalking are examined.

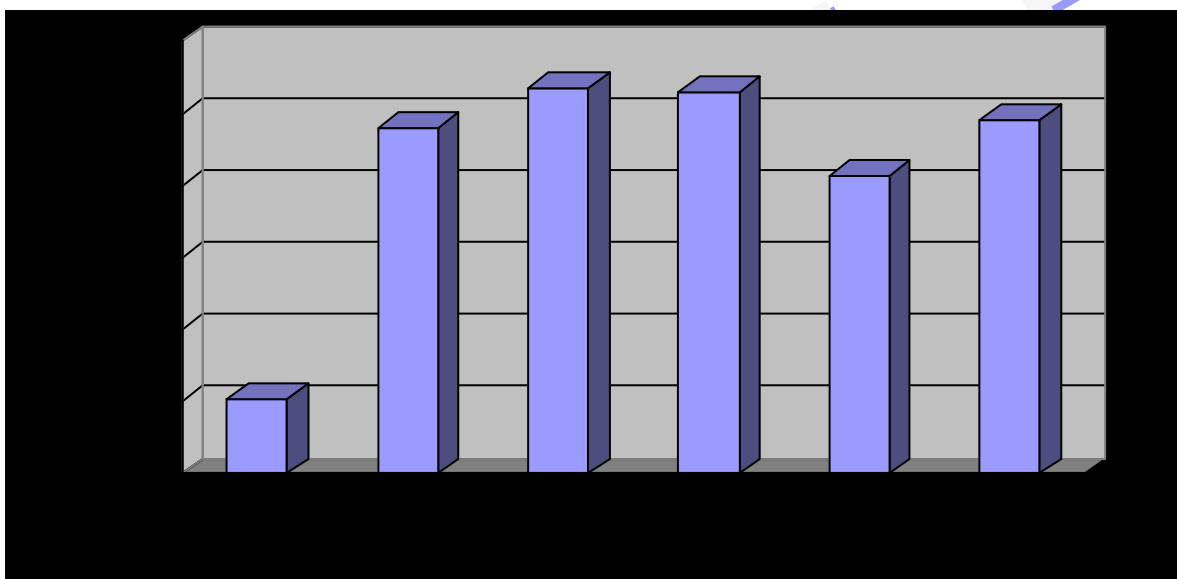
The impact of sleeplessness on a patient's health, and subsequently on the economy, is significant, as indicated by recent studies suggesting a strong link between sleep loss and disease. For example, according to researchers at the University of Chicago, after only three nights of poor quality sleep, young healthy men and women became less sensitive to insulin, resulting in a reduced tolerance to glucose and an increased risk for type 2 diabetes. The decrease in insulin sensitivity was comparable to that caused by gaining █ to █ pounds. Additionally, a study published in the *Archives of Internal Medicine* indicated that women who slept █ hours or less per night over a █-year study period increased their risk of developing coronary heart disease by █%. In addition to health-related costs to the economy, sleeplessness causes highway deaths and an increase in job-related accidents for healthcare workers, law enforcement agents and pilots. Some estimates report that yearly costs related to sleep disorders are \$█ in lost productivity, \$█ in healthcare and \$█ in motor-vehicle accidents, for a total impact on the economy of \$█. This impact will only become greater as the population ages; an older person (over █ years) gets █ to █ times less "deep sleep" as a younger person (less than █ years).

Of a total population of █ Americans, █% are estimated to experience insomnia symptoms or sleep disorders. Companies across U.S. are trying to sell a perfect night's sleep with pills, premium mattresses, high tech pillows, white noise machines, aromatherapy, and more. And it has fast become a \$█ a year industry. As obesity rates climb and Americans age, more people are developing sleep apnea, restless legs syndrome (RLS) and other sleep disorders. There are now █ to █ "sleep labs" in the U.S. These labs perform sleep studies and help design treatment programs for insomniacs and those with sleep apnea and other conditions.

The growing sleep disorders market reached more than \$ [REDACTED] in [REDACTED]. Pfizer and Neurocrine will jointly launch a new product and Sepracor is expected to bring its single-enantiomer product to market, but other companies will see their market share erode significantly. Compared with many other central nervous system (CNS) indications, the pipeline of emerging therapies for sleep disorders is relatively sparse, but established players such as GlaxoSmithKline are developing new products that may expand this market.

The leading drugs in the market for sleep disorders are Ambien CR, Ambien, Lunesta, Rozerem and Sonata. The drawback of Ambien is that it wears off too quickly in some patients. Neurocrine Biosciences, Inc. sees that failing as an opportunity. Neurocrine has created a time-release version of its experimental gamma-aminobutyric acid (GABA) drug, called Indiplon. It also plans to market a short-acting version so that people who wake up in the middle of the night can pop the pill and get a few extra hours of shut-eye without waking up groggy. Several companies, including Sanofi and Aventis are developing drugs patients can take to avoid waking up in the middle of the night. They prevent the brain chemical serotonin from disrupting slumber. Perhaps more radical, some researchers aim to alter the very architecture of sleep. Pfizer has a compound that slows down overactive synapses in the brain, thus prolonging the deepest, most restorative phases of sleep.

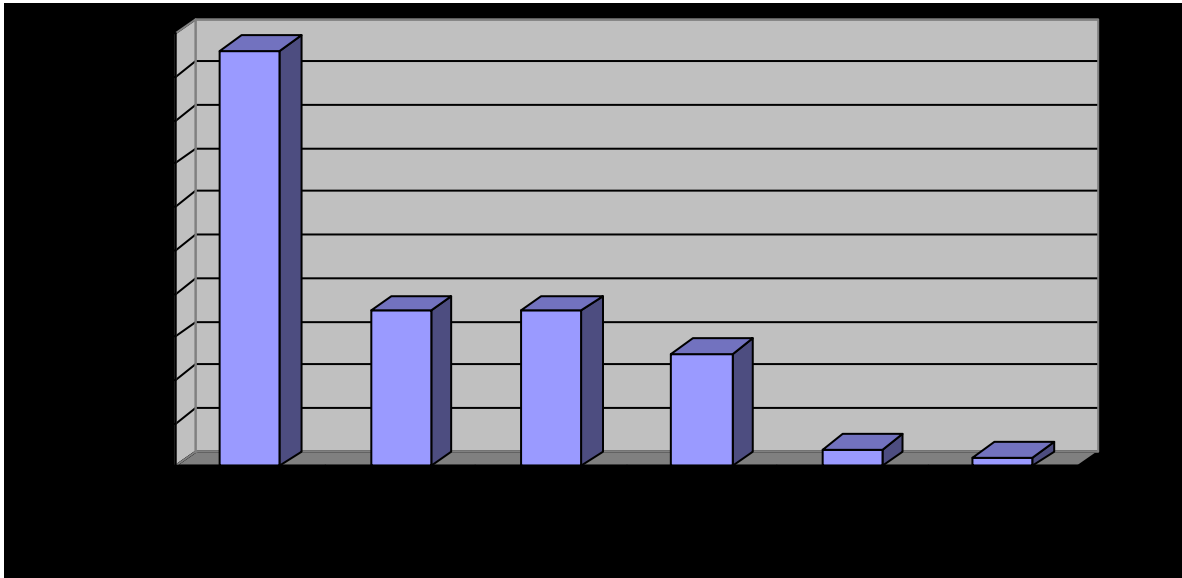
Figure 1.1: Total Market for Leading Sleep Drugs, 2007



Source: [REDACTED]

In [REDACTED], the insomnia market was dominated by Sanofi-Aventis's Ambien, which garnered well over [REDACTED] of the total insomnia market. Sepracor enjoyed a robust market launch of Lunesta due to its novel direct-to-consumer (DTC) campaign. Growth of the brand has recently slowed however, due to the arrival of generic zolpidem products in [REDACTED] and Sanofi-Aventis's increased physician detailing efforts for Ambien CR. Although it has a superior safety and tolerability profile in comparison to other prescription sleep aids, Takeda's Rozerem has suffered commercially from being less efficacious than the non-benzodiazepine and benzodiazepine GABA_A receptor agonist hypnotics.

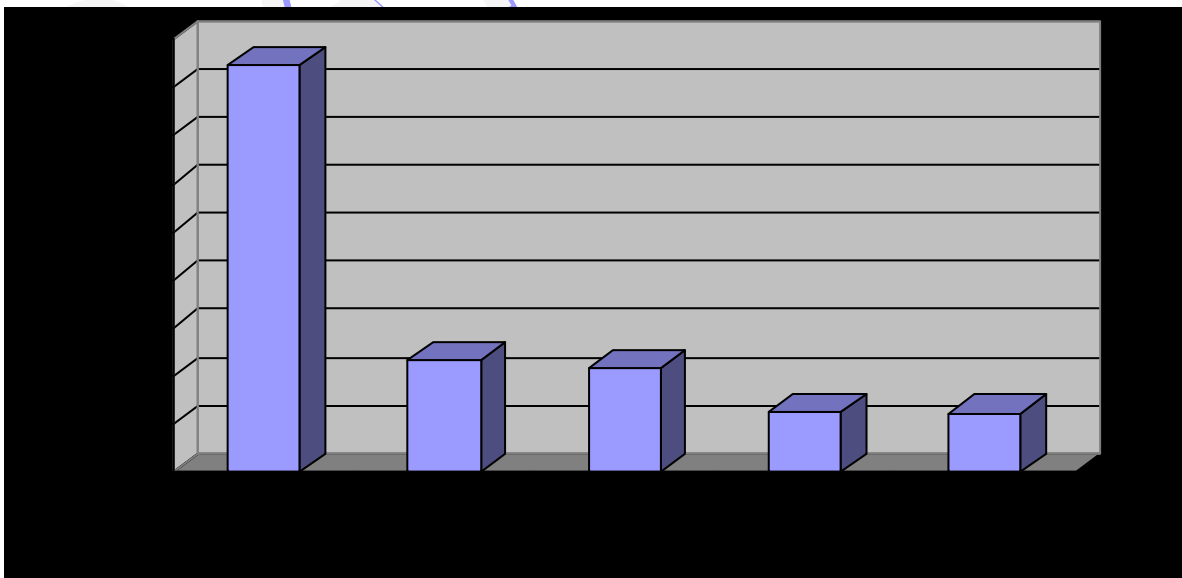
Figure 1.2: Sleep Product's Market Share, 2007



Source: [Redacted]

CPAP is the most effective and widely used method of treating sleep apnea. The CPAP device does not breathe for the individual. One can breathe at a normal rate by using the device. A CPAP device provides air pressure through a face mask to help keep the breathing passage open during sleep. This is a market where the two largest players control about █% of the market. ResMed is a medical device company that focuses particularly on the disorder of sleep disorder breathing. The other company is Respirationics, and it has been acquired by Royal Philips.

Figure 1.3: Percent Market Share of Leading CPAP Devices, 2008



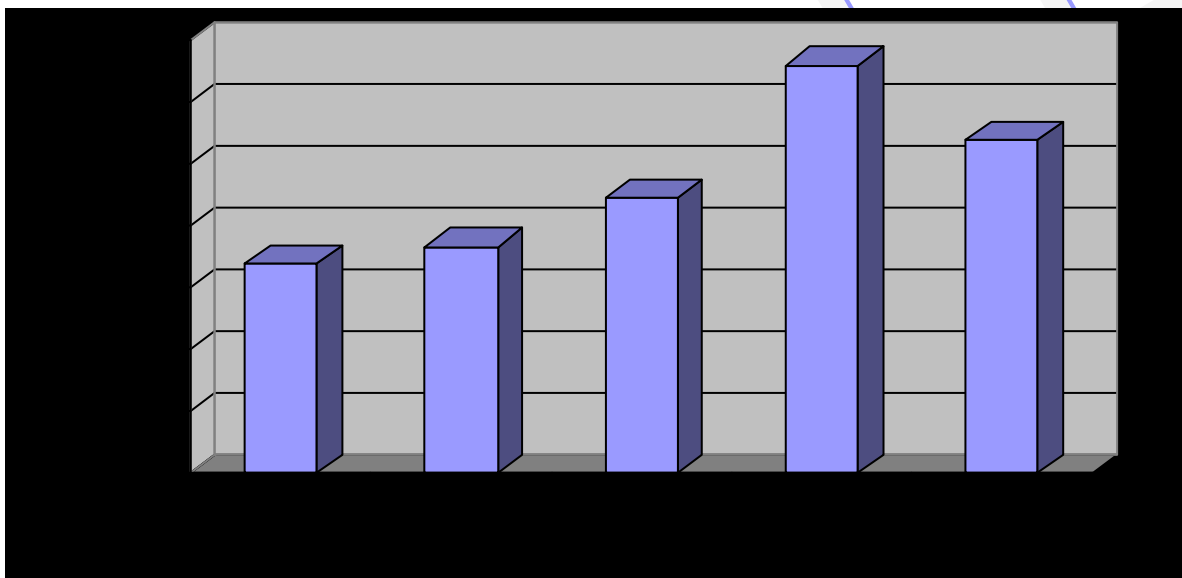
Source: [Redacted]

1.6 U.S. Sleep Market

U.S. sleep market was worth \$ [redacted] in [redacted] and is forecast to grow [redacted] % to [redacted]. The major anti-insomnia drug producers spent \$ [redacted] in [redacted] advertising Ambien CR, Lunesta and Rozerem, producing \$ [redacted] in sales. However, this was down [redacted] % as Ambien came off patent and sales of generics rose. New drugs are in the pipeline. Sleep Labs, which perform studies to diagnose sleep disorders, are estimated to number [redacted]+. The typical lab has revenues of \$ [redacted] and conducts [redacted] studies per year. Labs are located in hospitals, physician’s practices, universities, or are independent. This segment will be worth \$ [redacted] in [redacted]. A [redacted] ruling by the Center for Medicare Services will have a major impact on the field of sleep medicine. Portable devices may now be used for home testing, resulting in uncertainties for sleep labs but boosting the market for CPAP devices—a \$ [redacted] market that’s growing [redacted] % a year to [redacted] and dominated by ResMed and Respiroics. The huge \$ [redacted] mattress market and \$ [redacted] pillows market were being hurt by the recession in [redacted]. Retail sales are to rebound in [redacted]. Premium non-innerspring (air, memory foam) models are selling well.

1.6.1 Sleep Drugs Market in the U.S.

Figure 1.4: U.S. Rx and OTC Sleeping Pills Market, 2003-2007



Source: [redacted]

Americans are consuming sleeping pills at a rapid rate, due to heavy marketing by the drug companies and a belief that a new generation of sleeping pills is safer than their predecessors. Decades ago, barbiturates were the drugs of choice for insomnia, but they are addictive and carry a high risk of death by overdose. In the 1970’s they were largely displaced by benzodiazepines, drugs that include Dalmane and Halcion, which are less prone to overdose but have their own unpleasant side effects, including next-day drowsiness, dependence and withdrawal symptoms. The “Z pills” were developed to overcome such side effects.