



THE WEINBERG GROUP®

VIA FEDEX

April 20, 2016

Gayatri R. Rao, M.D., J.D.
Director, Office of Orphan Products Development
Food and Drug Administration
10903 New Hampshire Avenue
WO32-5295
Silver Spring, MD 20993-0002

RE: Request for Orphan Drug Designation for Sodium Oxybate for Extended-Release Oral Suspension (FT218)
Indication: For the treatment of cataplexy and excessive daytime sleepiness in narcolepsy

Dear Dr. Rao:

On behalf of Flamel Ireland Limited (Flamel), enclosed please find two (2) archival, electronic copies (CD) of Flamel's "Request for Orphan Drug Designation" for Sodium Oxybate for Extended-Release Oral Suspension (FT218).

Should any questions arise, please do not hesitate to contact me. I can be reached via telephone at 202.730.4129 or by email at marla.scarola@weinberggroup.com.



Marla Scarola, MS
Senior Consultant
The Weinberg Group Inc.

MES/ms

REQUEST FOR ORPHAN PRODUCT DESIGNATION

SODIUM OXYBATE

FOR THE TREATMENT OF

**CATAPLEXY AND EXCESSIVE DAYTIME
SLEEPINESS IN NARCOLEPSY**

Sponsor:

**Flamel Ireland Limited
Block 10-1 Blanchardstown Corporate Park
Ballycoolin
Dublin 15
Ireland**

U.S. Agent:

**Marla Scarola
Senior Consultant
The Weinberg Group Inc.
1129 Twentieth St. NW, Suite 600
Washington, DC 20036**

April 20, 2016

TABLE OF CONTENTS

1.	REQUEST FOR ORPHAN DESIGNATION.....	3
2.	SPONSOR INFORMATION	4
3.	INDICATION FOR WHICH THE DRUG IS BEING INVESTIGATED	5
4.	SCIENTIFIC RATIONALE FOR THE USE OF SODIUM OXYBATE FOR THIS INDICATION	6
5.	SUPERIORITY OVER A SIMILAR ALREADY-APPROVED SODIUM OXYBATE PRODUCT WITH ORPHAN DRUG STATUS	7
6.	MEDICAL PLAUSIBILITY OF THE POPULATION CHOSEN..	10
7.	REGULATORY STATUS AND MARKETING HISTORY OF SODIUM OXYBATE	11
8.	SUBSTANTIATION OF ORPHAN STATUS	12
9.	REFERENCES	13

1. REQUEST FOR ORPHAN DESIGNATION

Flamel Ireland Limited (Flamel), in accordance with 21 CFR Part 316, requests Orphan Drug Designation (ODD) for sodium oxybate extended-release oral suspension (FT218) for the treatment of cataplexy and excessive daytime sleepiness in narcolepsy. There are fewer than 200,000 patients diagnosed with narcolepsy in the United States.

Sodium oxybate oral solution (Xyrem[®] by Jazz Pharmaceuticals, Inc.) is currently approved for this indication in the US.

2. SPONSOR INFORMATION

Name and Address of Sponsor

Flamel Ireland Limited
Block 10-1 Blanchardstown Corporate Park
Ballycoolin
Dublin 15
Ireland

Primary Contact Person

Marla Scarola
U.S. Agent for Flamel
Phone: 202.730.4129
E-mail: marla.scarola@weinberggroup.com

Trade and Generic Names of the Drug

Generic name: Sodium oxybate

Trade name: A trade name for FT218 has not been established at this time by
Flamel. Jazz Pharmaceuticals markets sodium oxybate oral solution as
Xyrem®.

Manufacturing Information

Manufacture of sodium oxybate drug substance is performed by the following cGMP
compliant Contract Manufacturing Organization (CMO):

(b) (4)

Manufacture of FT218 drug product is performed by the following cGMP compliant
CMO:

(b) (4)

3. INDICATION FOR WHICH THE DRUG IS BEING INVESTIGATED

Flamel is investigating FT218 for the treatment of cataplexy and excessive daytime sleepiness in narcolepsy (i.e., the treatment of narcolepsy).

Narcolepsy is a chronic brain disorder that involves poor control of sleep-wake cycles. People with narcolepsy experience periods of extreme daytime sleepiness and sudden, irresistible bouts of sleep that can strike at any time. These “sleep attacks” usually last a few seconds to several minutes. In addition to daytime sleepiness, other major symptoms may include cataplexy, vivid dream-like images or hallucinations, as well as total paralysis just before falling asleep or just after waking-up. Most individuals also experience disturbed nocturnal sleep, i.e. poor sleep quality that can involve frequent waking during nighttime sleep, a short latency to REM sleep, and other sleep disorders (NINDS 2016).

4. SCIENTIFIC RATIONALE FOR THE USE OF SODIUM OXYBATE FOR THIS INDICATION

Although the mechanism of action is not well understood, the effectiveness of sodium oxybate for treating cataplexy and excessive daytime sleepiness in narcolepsy is well-demonstrated. A review and meta-analysis by Alshaikh et al. (2012) encompassing six randomized, placebo-controlled clinical studies that were reported between 1989 and 2006 showed effectiveness compared to placebo in:

- Reducing weekly cataplexy (-8.46; 95% CI = -15.27, -1.64);
- Reducing sleep attacks (-12.65; 95% CI = -17.72, -1.59);
- Improving performance on the Maintenance of Wakefulness Test (5.18; 95% CI = 2.59, 7.78), and
- Improving Clinical Global Impression (2.42; 95% CI = 1.77, 3.32).

As indicated in Section 7, the FDA has approved sodium oxybate (Xyrem[®]) for use in the treatment of cataplexy and excessive daytime sleepiness in narcolepsy. Further, both the American Academy of Sleep Medicine and the European Federation of Neurological Sciences recommend sodium oxybate as first-line therapy for cataplexy, excessive daytime sleepiness, and disturbed nocturnal sleep in narcolepsy (Swick 2015).

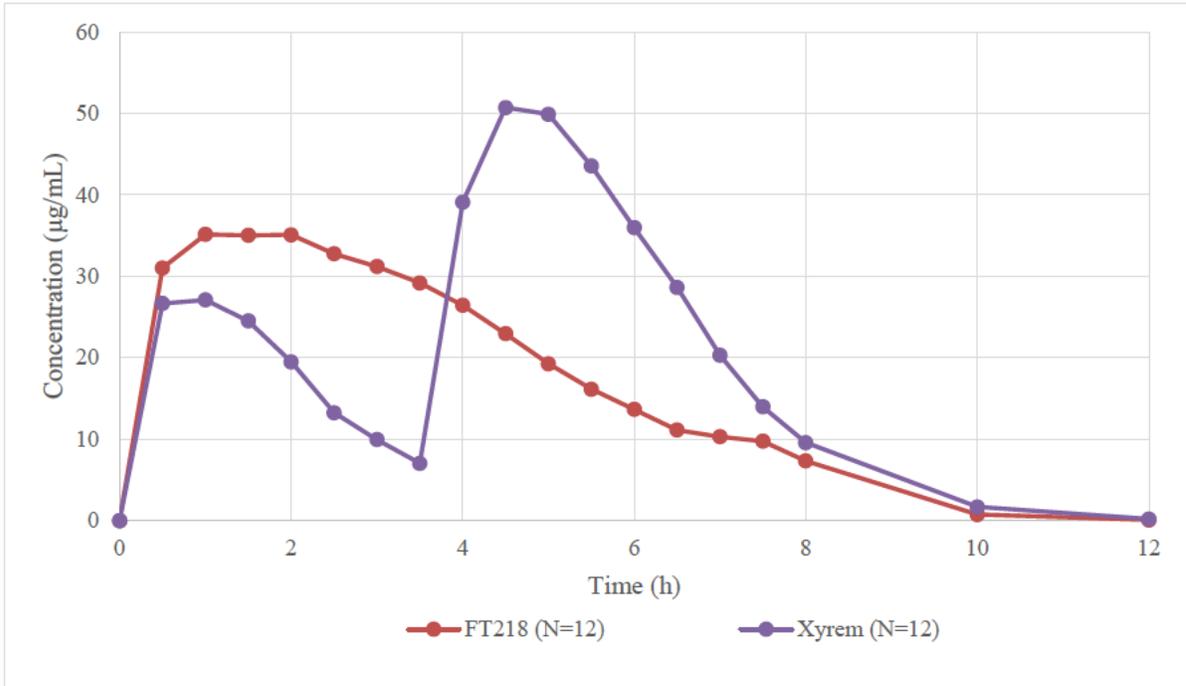
5. SUPERIORITY OVER A SIMILAR ALREADY-APPROVED SODIUM OXYBATE PRODUCT WITH ORPHAN DRUG STATUS

FT218 provides a major contribution to patient care over the approved marketed product, Xyrem[®] (NDA 021196).

Xyrem[®] has a short half-life (0.5 to 1 hour) and a duration of action of only 2 to 4 hours necessitating twice-nightly dosing in order to achieve 6 to 8 hours of nighttime sleep (Mignot 2012). Patients who consume a dose at bedtime are required to awaken and take another dose in the middle of the night. Current labeling for Xyrem[®] states that patients may need to set an alarm to awaken for the second dose. If the window for the second dose (2.5 to 4 hours after the first dose) is missed, patients are instructed to skip the second dose because of the potential negative effects on functioning/alertness the following day.

FT218 is a one-dose sustained release formulation of sodium oxybate that obviates the need for awakening during the night to take a second dose. Comparison of blood levels from sodium oxybate achieved with a single 4.5 g dose of FT218 and split 2.25 g doses of Xyrem[®] (Figure 1) demonstrate the ability of the FT218 formulation to maintain therapeutic blood levels of the drug longer than a single dose of Xyrem[®]. Further, FT218 shows elimination of plasma levels at the end of the night similar to that achieved with Xyrem[®] taken twice, indicating that carryover sedation is unlikely to exceed that of the currently marketed product.

Figure 1: Mean Plasma Sodium Oxybate Concentrations ($\mu\text{g/mL}$) – Time Profiles after a Single Oral Administration of 4.5 g of FT218 or Two 2.25 g Administrations of Xyrem[®]



Although the reduction of twice per night dosing to a single dose does not represent a large magnitude change in the number of doses/day, it represents a substantive improvement in patient care. Individuals suffering from fragmented sleep and an overall sleep deficit consider the elimination of the need to carefully time and wake up for a second nighttime dose to be a substantial advancement in therapy. In a survey of 1,350 individuals impacted by narcolepsy, the results of which were distributed at the September 24, 2013 FDA Meeting on Drug Development for Narcolepsy, responses to a question about an ideal therapy included, “a drug that would provide consistent and adequate control of the daytime sleepiness without the hard crash and one that would require one dose taken at bedtime resulting in 8 hours of restorative sleep” (Unite Narcolepsy 2013). Eliminating this second dose also increases the likelihood that patients will achieve a full 6-8 hours of restorative sleep.

The need to set an alarm for a second nighttime dose also disrupts the sleep of roommates and partners who share a bedroom with an affected individual. For patients aged 16-18 years, a parent or caregiver may be adversely impacted by the need for nighttime dosing and burdened by concern that the patient will not reliably awaken.

Other Advantages of Once per Night Dosing with FT218

In addition to eliminating the obvious disadvantages of: 1) needing to disrupt sleep in order to take a drug that promotes sleep, or 2) the potential for decreased efficacy if the second dose is missed, FT218 may provide other contributions to patient care.

For example, administration of a second nightly dose of Xyrem[®] presents safety risks. The instructions for use direct patients to measure out both nightly doses prior to bedtime and place the second dose near the bed for consumption 2.5 to 4 hours after the first dose. Although a container with child-resistant cap is provided for the second dose, there is the potential for consumption of the product left on a bedside table by a child while the parent is sleeping - if the child-resistant container is not used – or deliberate misuse by another person in the household. Further, because of the rapid onset of effects, individuals are at risk of falls or other accidental injuries if the second dose is not consumed in bed (as is recommended in the label instructions). Lastly, the packaging of product in individual premeasured single-dose sachets lessens and may even eliminate the risk of accidental measurement errors in nightly dose preparations.

Potential Impact on Diversion

Sodium oxybate has a history of illicit use as the “date-rape drug.” This substance has been added to a target’s drink without his/her knowledge in order to incapacitate the individual. In addition to standard precautions to limit access, FT218 will be provided as white granules as opposed to Xyrem[®] which is a clear to slightly opalescent oral solution. The appearance and mouth feel of the white granules could alert the target of the misuse that a substance has been added to his/her drink.

**6. MEDICAL PLAUSIBILITY OF THE POPULATION
CHOSEN**

Not applicable. Sodium oxybate is intended for all patients with cataplexy and excessive daytime sleepiness due to narcolepsy.

7. REGULATORY STATUS AND MARKETING HISTORY OF SODIUM OXYBATE

FT218

FT218 is currently being tested under IND 126,321 for the treatment of cataplexy and excessive daytime sleepiness in narcolepsy. It is not approved or marketed in any country including the US for any indication. No adverse regulatory actions have been taken against FT218 in any country.

Xyrem® (Jazz Pharmaceuticals)

US History

Xyrem® was approved for marketing in the US for the treatment of cataplexy associated with narcolepsy on July 17, 2002 (NDA 021196). The indication was expanded on November 18, 2005 to include the treatment of excessive daytime sleepiness in patients with narcolepsy (NDA 021196; Supplement 005).

Xyrem® has orphan drug status in the US for the treatment of narcolepsy (FDA 2016a).

A Pediatric Written Request has been issued for sodium oxybate in narcolepsy with cataplexy (FDA 2016b).

Rest of World History

Xyrem® is approved for cataplexy and excessive daytime sleepiness in narcolepsy in the European Union, Norway, Switzerland, and Canada (ADIS R&D 2015).

Xyrem® has orphan drug status for treatment of narcolepsy in the European Union (EMA 2010).

Sodium oxybate is approved under the trade name Alcover® in Italy and Austria for use in alcohol withdrawal syndrome (Busardo et al. 2015).

Flamel is not aware of any adverse regulatory actions that have been taken against Xyrem® in any country.

8. SUBSTANTIATION OF ORPHAN STATUS

The National Organization for Rare Diseases reports that narcolepsy affects approximately 1 in 2,000 in the general population (NORD 2016).

The most recent published estimate of prevalence used data from King County in Washington state (Longstreth et al. 2009) The overall prevalence per 100,000 for physician-diagnosed narcolepsy with or without cataplexy was 30.6 (95% CI: 27.6, 33.5). For narcolepsy with cataplexy, the prevalence was 21.8 (95% CI: 18.8, 24.8) per 100,000. A similar study conducted in Olmsted County in Minnesota that attempted to identify all residents with a diagnosis of narcolepsy with cataplexy from 1960 to 1989 estimated a prevalence of 36 per 1000 (95% CI: 25, 50; Silber et al. 2002).

All of the above estimates indicate a prevalence of less than 200,000 in the US.

9. REFERENCES

- Adis R&D Insight. 2015. Sodium oxybate. Adis R&D Insight Report. Accession number 8211. Revised 2 Dec 2015. Cited 4 Apr 2016.
- Alshakaikh MK, Tricco AC, Tashkandi M, mamdani M, Straus SE, BaHammam AS. 2012. Sodium oxybate for narcolepsy with cataplexy: Systematic review and meta-analysis. *J Clin Sleep Med.* 8:451-458.
- Busardò FP, Kyriakou C, Napoletano S, Marinelli E, Zaami S. 2015. Clinical applications of sodium oxybate (GHB): from narcolepsy to alcohol withdrawal syndrome. *Eur Rev Med Pharmacol Sci.* 19(23):4654-4663.
- European Medicines Agency (EMA 2010). Public summary of opinion on orphan designation. Available at:
http://www.ema.europa.eu/docs/en_GB/document_library/Orphan_designation/2009/10/WC500005734.pdf
- Food and Drug Administration (FDA). 2016a. Oxybate. Orphan Drug Designation and Approval database. Product name = oxybate. Available at:
<http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm>
- Food and Drug Administration (FDA). 2016b. Sodium Oxybate. Written requests issued database. Available at:
<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm050002.htm>
- Longstreth WT, Ton TGN, Koepsell T, Gersuk VH, Hendrickson A, Velde S. 2009. Prevalence of narcolepsy in King County, Washington, USA. *Sleep Med.* 10:422-426.
- Mignot EJM. 2012. A practical guide to the therapy of narcolepsy and hypersomnia syndromes. *Neurotherapeut.* 9:739-752.
- National Institute of Neurological Disorders and Stroke (NINDS). 2016. Narcolepsy Fact Sheet. Available at:
http://www.ninds.nih.gov/disorders/narcolepsy/detail_narcolepsy.htm
- National Organization for Rare Disorders (NORD). 2016. Narcolepsy. Available at:
<http://rarediseases.org/rare-diseases/narcolepsy/>
- Silber MH, Krahn LE, Olson EJ, Pankratz VS. 2002. The epidemiology of narcolepsy in Olmsted County, Minnesota: A population-based study. *SLEEP* 25:197-202.
- Swick TJ. 2015. Treatment paradigms for cataplexy in narcolepsy: Past, present, and future. *Nature Sci Sleep.* 7:159-169.
- Unite Narcolepsy. 2013. Patient-Focused Narcolepsy Survey: Interim Analysis as of September 16, 2013. Available at: <http://www.unitenarcolepsy.org/>

TABLE OF CONTENTS

5.3	Exclusivity Claim	3
5.3.1	New Clinical Investigation	3
5.3.2	Orphan Drug Exclusivity	3
5.3.2.1	Risk of Nocturnal Falls and Other Adverse Events Associated with Second Dose	5
5.3.2.2	Patient Experience and Perception of Second Dose	10
5.3.2.3	Risk of Misuse Associated with Second Dose	14
5.3.2.4	Food Effect	15
5.3.2.5	Patient Preference	15
5.3.2.6	Statements from Stakeholders	18
5.3.2.7	Potential Impact on Diversion	18
5.3.2.8	Impact of Salt Content	19
5.3.2.9	Summary	19
5.3.2.10	References	20

LIST OF APPENDICES

- Appendix 1. Certification of Affiliation
- Appendix 2. Statements from Stakeholders

LIST OF TABLES

Table 1:	FAERS Cases in which Second Nightly Dose of Xyrem [®] Resulted in a Fall	6
Table 2:	Cross-Study Comparison of Safety Profiles of Xyrem [®] and FT218	9
Table 3:	Examples of Xyrem [®] Patients Issues Due to a Second Nightly Dose	12
Table 4:	Examples of the Second Dose of Xyrem [®] Negatively Impacting a Partner/Roommate	14
Table 5:	Stated Preference Ratings for Product X and Product Y	18

LIST OF FIGURES

Figure 1:	Mean Plasma GHB Concentration (µg/mL) – Time Profiles after a Single Oral Administration of 6 g of FT218 or Two 3 g Administrations of Xyrem [®] Administered 4 Hours Apart	4
-----------	--	---

1.3. Administrative Information

Figure 2: Volume and Types of Quality of Life Issues Associated with Second Nightly Dose of Xyrem®	12
Figure 3: Most Common Mentions with the Quality of Life Conversations Reviewed	14
Figure 4: Drivers of Overall Product Choice	16
Figure 5: Drivers of Less Anxiety/Stress	17

5.3 Exclusivity Claim

Avadel CNS Pharmaceuticals, LLC (Avadel) hereby claims three (3) years of New Clinical Investigation (NCI) exclusivity under 21 CFR 314.108(b)(4) from the date of approval of this NDA for sodium oxybate for extended-release oral suspension (FT218). Additionally, Avadel hereby claims seven (7) years of orphan drug exclusivity based on its demonstration of clinical superiority for purposes of orphan drug exclusive approval pursuant to 21 USC 360cc(c) and 21 CFR 316.34(c).

These claims for exclusivity are based upon the below information.

5.3.1 New Clinical Investigation

In support of this NDA, Avadel has conducted a new clinical investigation which meets the definition as provided in 21 CFR 314.108(a). Avadel¹ completed a Phase 3 efficacy and safety study: [CLFT218-1501](#). The results of this investigation have not been relied on by the FDA to demonstrate substantial evidence of effectiveness of a previously approved drug product for any indication, or of safety for a new patient population, and do not duplicate the results of another investigation that was relied on by the Agency to demonstrate the effectiveness or safety in a new patient population of a previously approved drug product.

5.3.2 Orphan Drug Exclusivity

On January 8, 2018, Avadel was granted orphan drug designation for sodium oxybate for extended-release oral suspension for treatment of narcolepsy (DRU-2016-5302). The designation was granted based on the plausible hypothesis that FT218 may be clinically superior to the same drug(s) already approved for the same indication. In this submission, Avadel hereby provides its demonstration of clinical superiority for purposes of orphan drug exclusive approval pursuant to 21 USC 360cc(c) and 21 CFR 316.34(c). Avadel argues that the once-nightly dosing regimen of FT218 provides a significant therapeutic advantage over and above the currently approved twice-nightly formulations of sodium oxybate by providing both greater safety and a major contribution to patient care (MC-to-PC).

Sodium oxybate is approved in the United States (U.S.) as Xyrem[®] (sodium oxybate) oral solution (NDA 021196) and Xywav[®] (calcium, magnesium, potassium, and sodium oxybates) oral solution (NDA 212690) for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy. The primary difference between these products is that Xyrem[®] bears a warning regarding use in patients sensitive to high sodium intake due to its salt content and Xywav[®] does not bear this warning. However, both currently approved sodium oxybate formulations require a twice-nightly dosing regimen, once at bedtime and once again 2.5-4 hours later in the middle of the night. This twice-nightly dosing regimen disrupts continuous sleep, can result in poor compliance (which can lead to worsening efficacy and quality of life), is associated with additional adverse events (AEs) in the middle of the night, (both resulting from waking up from a deep sleep state and from causing a second, high C_{max}),

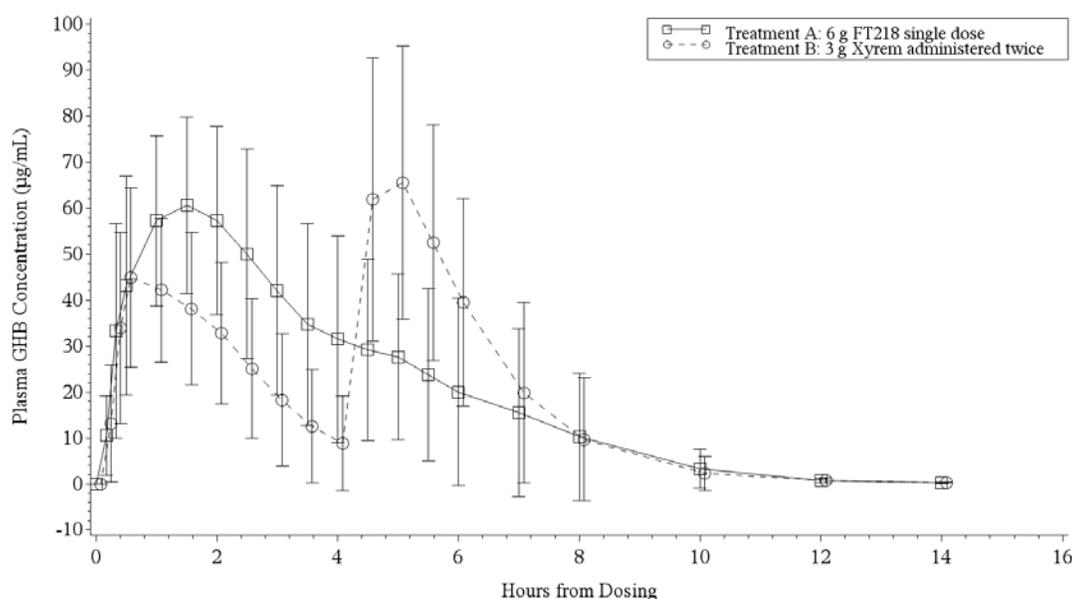
¹ Please note that the Sponsor of the study, Flamel Ireland Limited dba Avadel Ireland, and the applicant named in this filing, Avadel CNS Pharmaceuticals, LLC, are both wholly owned subsidiaries of Avadel Pharmaceuticals plc. Please see Certification of Affiliation in [Appendix 1](#).

1.3. Administrative Information

and is highly inconvenient for both patients and their partners or roommates who may also experience disrupted sleep.

FT218 is a once-nightly extended-release formulation of sodium oxybate that obviates the need for awakening during the night to take a second dose. Comparison of blood levels from sodium oxybate achieved with a single 6 g dose of FT218 and split 3 g doses of Xyrem[®] (Figure 1) demonstrate that once-nightly FT218 has equivalent exposure to twice-nightly Xyrem[®] with similar morning plasma levels (C_{8h}) and variability to twice-nightly Xyrem[®].

Figure 1: Mean Plasma GHB Concentration ($\mu\text{g/mL}$) – Time Profiles after a Single Oral Administration of 6 g of FT218 or Two 3 g Administrations of Xyrem[®] Administered 4 Hours Apart



Source: [Figure 14.2.2.1 PKFT218-1801](#)

Error bars indicate standard error.

Treatment B is shifted to the right for ease of reading.

The efficacy of FT218 in the treatment of EDS and cataplexy associated with narcolepsy was evaluated in a Phase 3 study conducted under Special Protocol Assessment (SPA) Agreement (CLFT218-1501, the REST-ON study). All three FT218 doses tested (9 g, 7.5 g, and 6 g) showed significant improvement compared to placebo on the three co-primary endpoints of Maintenance of Wakefulness Test (MWT), Clinical Global Impression-Improvement (CGI-I), and mean change in weekly cataplexy attacks, results which are consistent with the known efficacy of twice-nightly sodium oxybate. FT218 obviates the need for middle-of-the-night awakening for a second nightly dose and eliminates the second, high C_{max} , which results in both greater safety through a reduction in significant adverse effects, and a major contribution to patient care through improved convenience, compliance, and quality of life.

5.3.2.1 Risk of Nocturnal Falls and Other Adverse Events Associated with Second Dose

Administration of a second nightly dose of sodium oxybate presents potential safety risks. First, forcibly waking up from a sodium oxybate-induced deep sleep poses additional safety risks as one may get out of bed, ambulate, and fall with subsequent injury resulting from a drug-induced groggy or stuporous state. Secondly, because of the rapid onset of effects, individuals are at risk of falls or other accidental injuries if the second dose is not consumed in bed (as is recommended in the label instructions). This risk was acknowledged by the FDA in a 2013 review of the Xyrem[®] post-marketing data and was addressed by revision to the labeling language to address the risk of nocturnal falls. The label was updated to specify that patients should remain in bed following ingestion of the second dose; the prior version of the label already included these instructions with respect to the first dose.

The FDA Adverse Event Reporting System (FAERS) database was searched for Xyrem[®] (sodium oxybate) to retrieve cases in which a patient fell after the second dose of Xyrem[®]. For the time period from January 1, 2003 to June 30, 2020, there were a total of 52,483 Xyrem[®] cases in the FAERS database. Through the Freedom of Information Act (FOIA), Avadel requested MedWatch forms for individual cases related to falls and fracture with event dates ranging from 2016-2019. All cases requested were determined to be serious, indicated that Xyrem[®] was the suspect product and were reported by healthcare professionals. The first Avadel request for 12 Xyrem[®] cases was submitted on November 4, 2019. Monthly requests for 12 additional Xyrem[®] cases were subsequently submitted every month through August 2020 for a total of 10 requests (120 cases) submitted. The last request was submitted on August 1, 2020.

The following criteria were used to select cases of potential interest:

1. Xyrem[®] was the only suspect product.
2. All cases had reported reaction of fall.
3. Most cases had at least one other reported reaction in addition to fall with many including a fracture or some other type of injury.
4. All cases occurred in the last 5 years (i.e., to ensure that the 2013 labeling revision to strengthen the language around staying in bed after dosing had been implemented).

Of the 52,483 Xyrem[®] cases in the FAERS database, 2056 cases included a reported reaction of fall. Due to the limitation of number of cases that could be requested per month, a total of 120 cases in which a fall was a reported reaction were requested and received. The Initial FDA Receipt date in FAERS for the 120 cases which Avadel received ranged from March 28, 2016 to June 30, 2020. Of the 120 cases, there were 14 (11.67%) received in which a patient experienced a fall after the second dose of Xyrem[®]. [Table 1](#) includes a summary of the relevant cases that demonstrated falls in the middle of the night related to the second dose of Xyrem[®]. Although this is a relatively small number of cases, falling as a result of the second dose was integral to a large percent of the cases analyzed and, given the large number of post-marketing reports, constitutes a serious safety concern that can be avoided with FT218.

1.3. Administrative Information

Table 1: FAERS Cases in which Second Nightly Dose of Xyrem® Resulted in a Fall

Case ID	Narrative from Case Report
15042765	A 62-year-old female fell and broke her wrist after her 2 nd dose of Xyrem® (sodium oxybate) from sleepwalking. The patient discontinued Xyrem®. There were no other pre-existing medical conditions or medications which might have contributed to the events. The nurse assessed the events of sleepwalking, broke her wrist and fall as related to the use of Xyrem®.
15452509	A 44-year-old female fell and broke three bones in her face after taking her second dose of 4.25 g of Xyrem® (sodium oxybate) for narcolepsy with cataplexy at 7:00 AM which was before she normally got up. She had gotten out of bed to go to the bathroom and tripped on some boxes on the way, fell and broke three bones in her face. She was in the hospital for several days and got stitches. She discontinued taking Xyrem® because of the incident. Preexisting conditions or medications that might have contributed to the events were polypharmacy (pain medications) and that she might have taken an extra Xyrem® dose. The physician assessed the events of three broken bones in her face and fall as related to Xyrem® use.
15906083	A 61-year-old female taking Xyrem® (sodium oxybate) for narcolepsy with cataplexy was dizzy and passed out at 3:00 AM one morning. She reported she lost consciousness when she passed out. Xyrem® was withdrawn after the incident. A physician assistant stated that the event of passed out might possibly be related to the use of Xyrem® therapy but was unsure.
12971147	A 55-year-old female taking Xyrem® (sodium oxybate) for narcolepsy experienced sleep walking after her second dose of Xyrem®, fell and fractured her ankle. Her physician changed her dose to one dose at bedtime since she was sleep walking after her second dose.
15452474	A 44-year-old female taking Xyrem® (sodium oxybate) for narcolepsy with cataplexy fell when she got out of bed in the middle of the night. When she fell, she broke her nose and was taken to the emergency room. The physician had decreased the patient's dose from 4.5 g twice nightly to 3.75 g/3 g nightly due to the event.
15906079	A female taking Xyrem® (sodium oxybate) for obstructive sleep apnea frequently fell in the bathroom or out of bed shortly after taking her second dose of Xyrem®. She stopped taking Xyrem® after she fell out of bed and broke her collar bone. She now had an inspire device implanted.
16882434	An 87-year-old female taking Xyrem® (sodium oxybate) for narcolepsy with cataplexy got up to go to the bathroom in the middle of the night and her legs got twisted under her and she fell and broke her arm. She went to the hospital and indicated that it had nothing to do with Xyrem®. She confirmed Xyrem® stopped her from having cataplexy and continued taking Xyrem®. A physician medically confirmed the events of legs got twisted under her, fall and broke an arm but did not feel events were caused by Xyrem®.
17166815	A 52-year-old female taking Xyrem® (sodium oxybate) for narcolepsy with cataplexy reported that she had a pretty nasty fall. She went to the bathroom after taking Xyrem®, was out of it and her husband had to pick her up off the floor. She broke the orbit underneath her eye, had a concussion and went to the emergency room. The events were medically confirmed by a physician. Xyrem® was withdrawn due to the events. The physician considered the events of fall, broke the orbit underneath her eye and concussion to be related to Xyrem®.
17105135	A 60-year-old female taking Xyrem® (sodium oxybate) started 4.5 g Xyrem® twice nightly for narcolepsy. She fell three times in the night in one month. Following one fall, she hit her face. It was thought that the patient falls might have been because she got out of bed soon after taking Xyrem®.

Table 1: FAERS Cases in which the Second Nightly Dose of Xyrem® Resulted in a Fall (Continued)

Case ID	Narrative from Case Report
12498787	A 75-year-old male started taking Xyrem® (sodium oxybate) oral solution at 2.25 g twice nightly for narcolepsy with cataplexy and then was increased to 3 g twice nightly. He usually got up in the middle of the night before the second dose of Xyrem® to use the bathroom however, on one night, he took the second dose, but he did not go back to bed immediately. He did not quite make it to his bed, fell and hit his shoulder on the way down breaking his clavicle.
12935212	A 62-year-old female patient taking Xyrem® (sodium oxybate) fell in the middle of the night and broke her ribs and possibly her tibia.
17613007	A 60-year-old female taking Xyrem® (sodium oxybate) for narcolepsy reported she fell overnight because she had neuropathy in her feet. She further reported that she used to fall during the day because she had chronic immune demyelinating polyneuropathy. She had taken her medication and got up to use the restroom and she was not clear headed. She indicated that Xyrem® made her “head feel goofy.” She reported that she had missed a couple of doses because if she did not take the medicine right when she woke up, she doze back off without taking it as she still had some effect from the first dose. She considered the events of Xyrem® makes “head feel goofy” and fell/falls sometimes during the day related to Xyrem®.
17808644	A 24-year-old female taking Xyrem® (sodium oxybate) for narcolepsy took her first dose at 10:00 PM one evening and then reported she had an accident after her second Xyrem® dose at 1:45 AM. Sometime between 6:00-6:30 AM, she got up to go to bathroom, was dizzy and holding onto the bathroom counter and passed out. She reported that she fell and broke both bones in her right leg. She assessed the event of broke both bones in her right leg, fell, dizzy and passed out to be related to Xyrem®. Xyrem® was withdrawn for the event of passed out.
17887464	A 66-year-old female taking Xyrem® (sodium oxybate) for narcolepsy with cataplexy reported her balance was bad, that she fell down a flight of stairs and more than once fell off the toilet when she went to get up to go to the bathroom. She also reported that she had “blood on the brain,” dislocated her shoulder and had a cut on her foot. Due to these events, she would only take one dose of Xyrem® per night. She reported she fell off the toilet because she fell asleep on the toilet. On two occasions, she thought she was sitting on the toilet but was sitting on the tub and fell into the tub. She fell off the toilet too many times to count. Once she fell and broke the shower doors and another time, she moved the whole toilet when she fell off. The patient once could not find her way out of the bedroom and ended up in the closet. She wears depends now due to not knowing she was going to the bathroom while she was asleep. Xyrem® dose was decreased due to the events.

In the real-world study mentioned above, Side Effects and Safety was the second highest conversation volume among Second Dose conversation themes after Quality of Life and was the most negative in regard to patient sentiment across all discussions. The context topic of “Falling” was mentioned six times within Side Effects and Safety. These articles with mentions of falling included three in which Xyrem® patients fell and suffered from physical injury, and three in which patients almost fell. One patient reported while using the restroom before taking his/her second dose, he/she fell asleep and hit his/her eyebrow on the granite bathroom counter, leading to stitches and scarring. Another article reported that a Xyrem® patient had lacerated both his/her chin and eyebrow when getting up in the middle of the night. The third case was from a Xyrem® patient who tried to stay awake after taking a dose of Xyrem®, went to the

kitchen at 2:00 AM, fell and lacerated his/her forehead, and never realized it until he/she woke up again several hours later with his/her pillows covered in blood. Additionally, other patients did not fall but almost fell. One said, “before the second dose I had to pee and felt dizzy walking, I had my friend walk with me.” Another said, “a couple of times I’ve had close calls with falling over and catching myself before I hit my head on something.” The last said, “when I got out of bed, I had to hold on to everything possible so I didn’t fall because I was soooo dizzy.” Additionally, another patient in this study did not mention falling but, when describing the second dose, stated, “if you’ve ever been wonky and confused after anesthesia, that’s pretty much what it can feel like waking up for that second dose.”

The data and safety reports above clearly demonstrate that Xyrem[®] patients continue to suffer from significant adverse events related to having to wake up to take the requisite second dose.

In addition, a meta-analysis of six studies conducted to assess the pharmacokinetics of FT218 in healthy volunteers found that, in general, known adverse events associated with sodium oxybate (i.e., neurological and gastrointestinal) occurred close to T_{max} , around the C_{max} period (approximately 1.5-2.0 hours after dosing) (Seiden et al. 2020). Across all doses of FT218, approximately 70% of AEs occurred around C_{max} . The most frequent system organ class (SOC) for AEs around C_{max} for FT218 were nervous system disorders followed by gastrointestinal disorders, which are the most common AEs associated with twice-nightly sodium oxybate. Since it appears that the AEs were related to C_{max} and FT218 has only one C_{max} compared to twice-nightly sodium oxybate, FT218 is expected to have more favorable safety profile compared to twice-nightly dosing by avoiding a second C_{max} and the types of AEs described above. It was also demonstrated that there is a correlative relationship between C_{max} and incidence of nausea and vomiting with twice-nightly sodium oxybate (Chen et al. presented at World Sleep 2019). In two relative bioavailability studies comparing FT218 to EU-sourced Xyrem[®], FT218 had a C_{max} that was below bioequivalence criteria compared to twice-nightly sodium oxybate. In a bioequivalence study comparing FT218 to U.S.-sourced Xyrem[®], C_{max} was within bioequivalence criteria. Based on this and the single C_{max} , FT218 should have a lower incidence of adverse events compared to twice nightly sodium oxybate.

Comparing rates of adverse events from the REST-ON study to prior data from twice-nightly sodium oxybate pivotal trials, these PK differences appear to translate clinically with FT218 having lower rates of well-known sodium oxybate adverse events compared to twice-nightly sodium oxybate. In the REST-ON study, well-established sodium oxybate-associated AEs such as nausea, dizziness, vomiting, somnolence, and tremor occurred at low rates across each dose of FT218. Rates of these adverse reactions appeared to occur at lower rates than seen with twice-nightly sodium oxybate (see Table 2).

The incidence of nausea as an AE occurred in approximately 8% at FT218 4.5 g, 9% at 6 g, 8% at 7.5 g, and 4% at 9 g, and as an adverse reaction occurred at approximately 6% at the 4.5 g dose, 8% at 6 g, 7% at the 7.5 g dose, and 1% at the 9 g dose. In one Xyrem[®] study, nausea occurred at 15% at 6 g and 34% at 9 g, while another study reported nausea in 12% at 4.5 g, 16% at 6 g, and 27% at 9 g; a third trial reported nausea in 22% of subjects on the 9 g dose (U.S. Xyrem[®] Multicenter Study Group 2002; Xyrem[®] International Study Group 2005; Black and Houghton 2006). Nausea as an adverse reaction was reported in the Xyrem[®] label at 8% with Xyrem[®] 4.5 g, 13% at 6 g, and 20% at 9 g (Xyrem[®] Prescribing Information 2020).

1.3. Administrative Information

Similarly, AEs of vomiting occurred in approximately 4% of subjects with FT218 4.5 g, 5% at 6 g, 8% at 7.5 g, and 9% at 9 g, while adverse reactions of vomiting occurred in 3% at 4.5 g, 3% at 6 g, 6% at 7.5 g, and 5% at 9 g. Published pivotal studies with Xyrem[®] demonstrated vomiting in 6% at 6 g and 11% at 9 g in one study and 13% at 9 g in another study (U.S. Xyrem[®] Multicenter Study Group 2002; Black and Houghton 2006), while the Xyrem[®] label lists vomiting as an adverse reaction at 2% with 4.5 g, 4% with 6 g, and 11% with 9 g (Xyrem[®] Prescribing Information 2020).

A similar pattern was seen with dizziness, as rates with FT218 as an AE were 6% at 4.5 g, 4% at 6 g, 6% at 7.5 g, and 9% at 9 g. With Xyrem[®], dizziness occurred as an AE in 30% of subjects at 6 g and 34% at 9 g in one study, 12% at 4.5 g, 16% at 6 g, and 24% at 9 g in another study, and 7% at 9 g in a third study (U.S. Xyrem[®] Multicenter Study Group 2002; Xyrem[®] International Study Group 2005; Black and Houghton 2006). Dizziness as an adverse reaction occurred in 6% of subjects at FT218 4.5 g, 4% at 6 g, 6% at 7.5 g, and 5% at 9 g, compared to 9% at 4.5 g, 11% at 6 g, and 15% at 9.0 g with Xyrem[®], according to the label (Xyrem[®] Prescribing Information 2020). Somnolence and tremor also occurred at lower rates than with published pivotal trials of Xyrem[®] as well as the Xyrem[®] label for both AEs and adverse reactions.

AEs of feeling drunk only occurred in one subject on FT218 at the 4.5 g dose level. This Preferred Term (PT) would likely capture AEs of feeling “hungover” from the study drug the next morning. Per the Xyrem[®] label, this occurred as an adverse reaction in 3% of patients on the 9 g dose (Xyrem[®] Prescribing Information 2020). Other important labeled AEs with Xyrem[®], such as disturbance of attention and disorientation, occurred in zero to one patient with FT218, well lower than the frequencies seen with Xyrem[®].

Table 2: Cross-Study Comparison of Safety Profiles of Xyrem[®] and FT218

Adverse Reaction/Event	FT218				Xyrem [®]		
	4.5 g	6 g	7.5 g	9 g	4.5 g	6 g	9 g
Nausea (adverse event)							
CLFT218-1501 (REST-ON)	8%	9%	8%	4%	-	-	-
Xyrem [®] Multicenter Study Group 2002	-	-	-	-	-	15%	34%
Xyrem [®] Multicenter Study Group 2005a	-	-	-	-	12%	16%	27%
Black and Houghton 2006	-	-	-	-	-	22%	-
Nausea (adverse reaction)							
CLFT218-1501 (REST-ON)	6%	8%	7%	1%	-	-	-
Xyrem [®] Label	-	-	-	-	8%	14%	20%
Vomiting (adverse event)							
CLFT218-1501 (REST-ON)	4%	5%	8%	9%	-	-	-
Xyrem [®] Multicenter Study Group 2002	-	-	-	-	-	6%	11%
Black and Houghton 2006	-	-	-	-	-	-	13%

Table 2: Cross-Study Comparison of Safety Profiles of Xyrem® and FT218 (Continued)

Adverse Reaction/Event	FT218				Xyrem®		
	4.5 g	6 g	7.5 g	9 g	4.5 g	6 g	9 g
Vomiting (adverse reaction)							
CLFT218-1501 (REST-ON)	3%	3%	6%	5%	-	-	-
Xyrem® Label	-	-	-	-	2%	4%	11%
Dizziness (adverse event)							
CLFT218-1501 (REST-ON)	6%	4%	6%	9%	-	-	-
Xyrem® Multicenter Study Group 2002	-	-	-	-	-	30%	34%
Xyrem® Multicenter Study Group 2005a	-	-	-	-	12%	16%	24%
Black and Houghton 2006	-	-	-	-	-	-	7%
Dizziness (adverse reaction)							
CLFT218-1501 (REST-ON)	6%	4%	6%	5%	-	-	-
Xyrem® Label	-	-	-	-	9%	11%	15%
Somnolence (adverse reaction)							
CLFT218-1501 (REST-ON)	0%	1%	2%	4%	-	-	-
Xyrem® Label	-	-	-	-	1%	3%	8%
Tremor (adverse reaction)							
CLFT218-1501 (REST-ON)	1%	1%	1%	1%	-	-	-
Xyrem® Label	-	-	-	-	0%	2%	5%
Feeling “drunk” (adverse event)							
CLFT218-1501 (REST-ON)	1%	0%	0%	0%	-	-	-
Xyrem® Label	-	-	-	-	0%	<1%	3%

This was also evident in the real-world study capturing Xyrem® patient topics and sentiments. “Nausea” and “Vomiting” were context topics within Side Effects and Safety that were driven by patient stories about feeling either nauseous or vomiting after taking the Second Dose, which has a higher C_{max} than the first dose. One Xyrem® patient noted that he/she stopped taking Xyrem® due to vomiting and being physically unable to take his/her second dose. Another stated, “Usually after my second dose I wake up feeling like I’m going to throw up. Last night was the first night I actually did.”

5.3.2.2 Patient Experience and Perception of Second Dose

Individuals suffering from fragmented sleep and an overall sleep deficit consider the elimination of the need to carefully time and wake up for a second nighttime dose to be a substantial advancement in therapy. In a survey of 1350 individuals impacted by narcolepsy, the results of which were distributed at the September 24, 2013 FDA Meeting on Drug Development for Narcolepsy,

responses to a question about an ideal therapy included, “a drug that would provide consistent and adequate control of the daytime sleepiness without the hard crash and one that would require one dose taken at bedtime resulting in 8 hours of restorative sleep” (Unite Narcolepsy 2013).

Twice-nightly sodium oxybate has a short half-life (0.5-1 hour) and a duration of action of only 2-4 hours, necessitating twice-nightly dosing in order to achieve 6-8 hours of nighttime sleep (Mignot 2012). Patients who consume a dose at bedtime are required to awaken and take another dose in the middle of the night. Current labeling for twice-nightly sodium oxybate states that patients may need to set an alarm to awaken for the second dose. If the window for the second dose (2.5-4 hours after the first dose) is missed, patients are instructed to skip the second dose because of the potential substantial negative effects of a late second dose on functioning/alertness the following day.

Avadel conducted a study to gain insight on the experiences and the scale of impacts to patients and caregivers specifically tied to the second requisite nightly Xyrem[®] dose (Second Dose). Publicly available digital Xyrem[®] and narcoleptic-related data from an approximately two-year period (September 1, 2017 to October 15, 2019) was collected from both Clearnet (accessible by the public through standard browsers, such as Chrome) and Dark Web sources, including blogs, forums, message boards, social media outlets, OpenFDA, and more. These data were processed and analyzed with industry and academia-accepted techniques, including, but not limited to, Latent Dirichlet Allocation (LDA) and advanced propriety algorithms. Publicly available, U.S.-based English and Spanish language digital conversation data with mentions of narcolepsy and Xyrem[®] resulted in a total of 231,873 articles. After a secondary data-cleansing phase to ensure quality insights conducive to a high standard of data science and analytics, a total of 102,852 relevant articles were identified within the narcolepsy landscape. From within this dataset of 102,852 articles, 259 articles with consumers specifically discussing the Second Dose were identified. A data collection limited and targeted in scope within forum media, where the majority of Second Dose articles had originally been identified, was also completed from the period of January 1, 2017 to August 30, 2017, resulting in 33 additional Second Dose articles being identified. These two Second Dose datasets made available a total of 292 consumer Second Dose articles for full analysis. The Second Dose discussion dataset was categorized into three primary conversation themes: Side Effects and Safety, Quality of Life, and Misuse and Abuse. “Trouble Waking up for Second Dose” was the most voluminous topic among Quality of Life conversation (Figure 2). In these discussions, patients expressed how difficult it was for them to wake up in time for the Second Dose, often noting the use of specialized alarms and lights needed to make sure they had the best chance of waking up. “Missing Second Dose” was the second most voluminous topic, with mentions of times where consumers did not wake up and missed their second dose completely. Table 3 shows examples of patients’ and partners’ comments on the difficulty of taking the second dose and consequences that result from not taking it. There were additional comments on this topic, but not all were included due to redundancy. Many of these patients noted that their narcolepsy symptoms felt worse the next day after missing their second dose. In all of the studies demonstrating the efficacy of Xyrem[®] on cataplexy and EDS in narcolepsy, patients took both nightly doses, but in the real-world setting, many patients are non-compliant with the second dose of Xyrem[®], which is likely to result in decreased efficacy and a poorer quality of life. By eliminating the middle-of-the-night dosing, FT218 avoids this problem and the associated consequences of missing the second dose.

Figure 2: Volume and Types of Quality of Life Issues Associated with Second Nightly Dose of Xyrem®

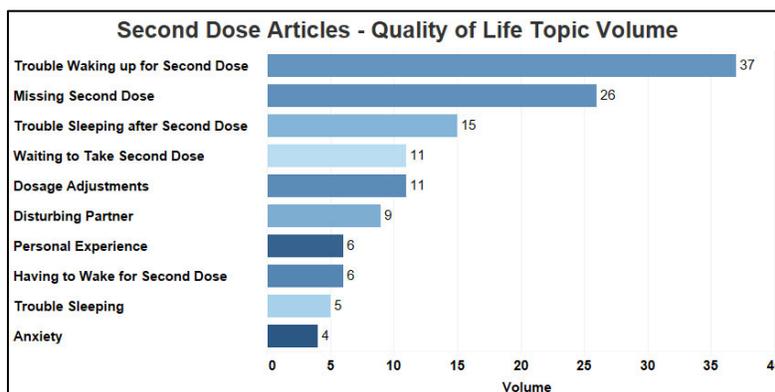


Table 3: Examples of Xyrem® Patients Issues Due to a Second Nightly Dose

<p>“I struggle immensely with waking up to take a second dose and am at the point where I only take the first one and don’t bother preparing the second”</p>
<p>“I slept through my 3:30 am dose and woke up at 5:00 am, unable to dose again since work started in four hours”</p>
<p>“I’m now on the fourth night in a row where I’ve missed my second dose. Basically I’m turning off my phone alarm without taking the dose. I’m not consciously making this choice and have absolutely no memory of doing so.”</p>
<p>“I often sleep through my alarm for the second dose. It knocks me out for a solid 5 hours which is great because I haven’t slept that well in a very long time, but I can’t seem to get myself up to take the second dose. I end up waking about five hours after dose one with not enough time to take the second dose and be able to get up when I need to in the morning.”</p>
<p>“At least once a week I sleepily snooze or turn off my alarm to take my second dose without consciously realizing it went off. By the time I naturally wake up it’s far too late to take it and be awake for work, but way too early to get up and get ready.”</p>
<p>“I sleep through 9 alarms (much to the chagrin of my husband) including a vibrating wristwatch and my cell phone alarm. Last night, my husband got home from work shortly before my dose, and tried waking me up for it after I slept through my alarms”</p>
<p>“So today’s gonna suck either slept through my Xyrem® alarm or never set it last night. Either way, I can't take my second dose, it's too close to when I need to be up and too far from my first dose. I'm gonna be a zombie, but, I have to power through.”</p>
<p>“Sounds promising (response to a once-nightly sodium oxybate). Can’t wait! I still struggle to wake up half the time for my second dose of Xyrem® when then leaves me waking up wide awake from the rebound an awkward 2-3 hours before my alarm.”</p>

Table 3: Examples of Xyrem® Patients Issues Due to a Second Nightly Dose (Continued)

<p>“I started sleeping thru my second dose alarm, missing it, and waking up at awkward hours where I couldn't take my second dose in time to get up for work”</p>
<p>“The hardest part of Xyrem® for me is waking up after 4-5 hours and not knowing how the hell I managed to miss my second dose, and knowing that it's too late to try. This is the worst.”</p>
<p>“I'm fairly convinced that I'm going to have to incorporate a jump starter and testicular electrodes into my alarm to guarantee waking up for my second dose some nights.”</p>
<p>“I am having a lot of trouble waking up to take my second dose of Xyrem®. Nothing I try seems to work.”</p>
<p>“My girlfriend has narcolepsy and takes Xyrem® which requires her to wake up around 2 am to take a 2nd dose. However, lately she has had trouble sleeping through her alarm and missing her second dose which leaves her tired throughout the day.”</p>
<p>“I was finding it impossible to wake up for my second dose and was extremely groggy in the mornings.”</p>
<p>“I failed to wake up for my second dose 99% of the time and on the rare times I did wake up for it I'd feel completely hungover/drunk by the time I got up for work 4-5 hours after it.”</p>
<p>“I'm having the darnedest time waking up for the second dose. It's not that I don't wake up from the pillow alarm clock but I half asleep turn it off every time without taking the meds.”</p>

The need to set an alarm for a second nighttime dose also disrupts the sleep of roommates and partners who share a bedroom with an affected individual. A parent or caregiver may be adversely impacted by the need for nighttime dosing and burdened by concern that the patient will not reliably awaken. The real-world study showed that although most of the Quality of Life topics were directly linked to patients using Xyrem®, the topic “Disturbing Partner” focused on the effects that having to wake up in the middle of the night had on patients’ partners. The discussions with this topic focused primarily on requests for advice from other Xyrem® patients on how not to wake up their partners when they awakened for the Second Dose, as well as requests for advice from the disturbed partners themselves. Of the 292 cases reviewed, there were six (6) instances where patients voiced that their bed partner or roommates were negatively impacted by their need to set an alarm to wake up for the second dose of Xyrem® or asked for advice on how to limit the impact on their bed partner. [Table 4](#) describes patient’s or partner’s direct statements on this topic. Additionally, one patient asked, “As a single person, I wonder who is possibly going to put up with my 2am Xyrem® alarm?” Within the Quality of Life conversations that were reviewed as part of this study, the word “partner” had the most mentions followed by “Family” and “Anxiety” topics ([Figure 3](#)). Therefore, not only does waking up in the middle of the night affect the patient, it also decreases the quality of life of their bedpartner. A once-nightly formulation of sodium oxybate would eliminate this issue for partners and caregivers.

Table 4: Examples of the Second Dose of Xyrem® Negatively Impacting a Partner/Roommate

<p>“Those of you that take Xyrem® and have significant others: how do take your 2nd dose without making your bedmate want to kill you?”</p>
<p>“My husband wakes up at the drop of a dime and it has taken years to realize I’m under the influence and gently ask if I’m awake, need the bathroom, a drink, help getting back to bed. His first reaction used to be anger that I woke him up.”</p>
<p>“I don’t want to wake my fiancé up every night with my alarm. What Xyrem® tips do you have?”</p>
<p>“At this point, the only settings that wake me up at all also wake my roommates (I’m a student living off-campus with some friends), who are very understanding of the fact that I need to wake up to take my second dose, but also need their own sleep. I feel so bad about potentially waking them up that I’ve basically stopped trying to take me second dose at all - I just take the first one when I go to bed, which is helpful but nowhere near as effective as two doses was.”</p>
<p>“My boyfriend has been taking it for a couple years now, and still needs an alarm to wake up for the second dose... hence I wake up every night around 2-3am. I could sleep through it before, but now he’ll unconsciously snooze the alarm for long enough to get me up. Plus, he usually sets a “backup” as well and almost always forgets to turn it off after taking his second dose. I tend to get really pissed off in my half awake state and have a harder and harder time going back to sleep because of those angry feelings. I feel bad complaining because I know he was so tired all the time for years, but now I’m tired all the time and today feels like I’ve hit bottom. I’m trying not to fall asleep at my desk as I write this.”</p>

Figure 3: Most Common Mentions with the Quality of Life Conversations Reviewed

Reference Topic	Number of Mentions
Partner (Wife, Husband, Girlfriend, Boyfriend, Roommate)	32
Family (Parents, Mom/Mother, Dad/Father, Children/Kid)	27
Anxiety	16
Job (Work)	12
Depression	9
Lifestyle	7
Stress	7

5.3.2.3 Risk of Misuse Associated with Second Dose

The twice-nightly sodium oxybate instructions for use direct patients to measure out both nightly doses prior to bedtime and place the second dose near the bed for consumption 2.5-4 hours after the first dose. Although a container with child-resistant cap is provided for the second dose, there is the potential for consumption of the product left on a bedside table by a child while the

parent is sleeping (if the child-resistant container is not used) or deliberate misuse by another person in the household. The real-world study that evaluated 292 patient reports associated with the second dose of Xyrem[®] identified one report where a Xyrem[®] patient's roommate stole their medication. There were also two reports of patients who took both doses of Xyrem[®] at bedtime, not realizing they had already taken their previous dose.

5.3.2.4 Food Effect

Avadel conducted a food effect study (PKFT218-1603) to assess the effect of food on FT218 administered at 6 g in healthy volunteers. The least squares geometric means ratios for AUC_{0-t} and AUC_{0-inf} were 86% for both parameters in the fed vs. fasted state, and the associated 90% CI for AUC_{0-t} was not contained in the standard equivalence limits of 80.0-125.0%, while the AUC_{0-inf} was contained within the standard equivalence limits (79.91-92.62% and 80.01-92.67%, respectively), meaning the AUC is only slightly decreased by food. The least squares geometric means ratio for C_{max} was 66.74%, with the associated 90% CI lower and upper limit of 58.20% and 76.54%, corresponding to a more pronounced decrease on C_{max} . Based on these results, there appears to be a greater food effect with Xyrem[®] than with FT218, as Xyrem[®]'s AUC_{0-inf} was 63% in the fed vs. fasted state and C_{max} was 41% in the fed compared to the fasted state, both not being contained in the standard equivalence limits of 80.0-125.0%. The Xywav[®] label indicates that administration of Xywav[®] immediately after a high-fat meal resulted in a mean reduction in C_{max} by 33%, and mean reduction in AUC by 16%. Both the Xyrem[®] and Xywav[®] labels instruct patients to take the first nightly dose at least two hours after eating. In the real-world study that evaluated 292 patient conversations on the internet, there were some instances where patients said they ate too close to the time they took Xyrem[®] and felt it did not work as well and their symptoms were worse the next day. For example, one patient stated, "My Xyrem[®] is up to 50% less effective if I don't take it on a completely empty stomach." Given that both exposure and maximum concentration would be higher if taken shortly after eating with FT218 compared to twice-nightly Xyrem[®], FT218's favorable pharmacokinetic profile, with a reduced food effect and subsequent impact on blood levels, could also result in greater efficacy and improved quality of life.

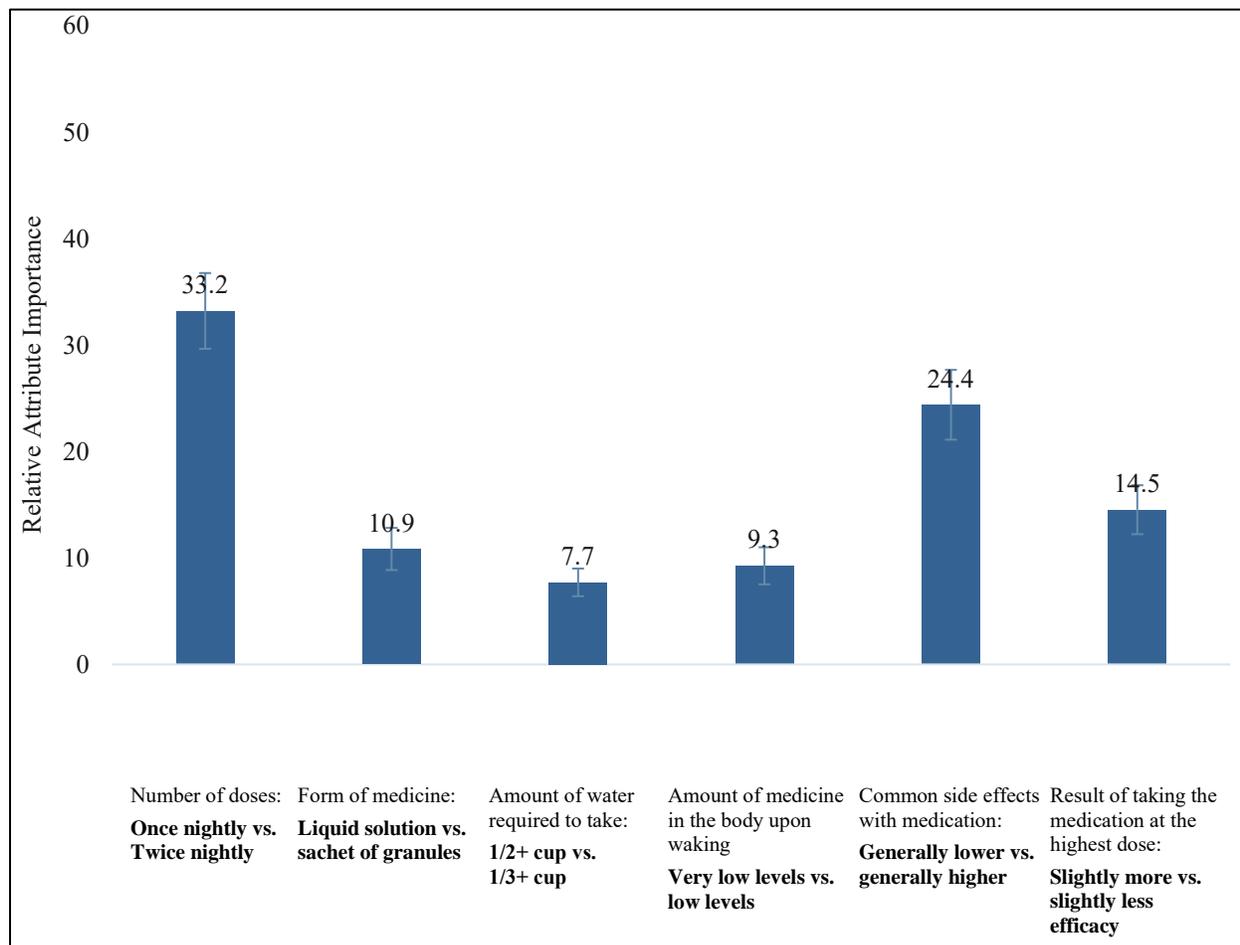
5.3.2.5 Patient Preference

To evaluate the preference of FT218 compared to twice-nightly sodium oxybate, Avadel conducted a Discrete Choice Experiment (DCE) to quantitatively characterize the preferred treatment attributes of narcolepsy patients. A 30-minute web-based survey of n=75 narcolepsy patients (past and current sodium oxybate users) was designed to characterize and quantify preferred narcolepsy treatment attributes from the perspective of narcolepsy patients. This study was reviewed and approved by a U.S. Institutional Review Board. The study also examined the burden of illness in narcolepsy and patient satisfaction with existing treatments.

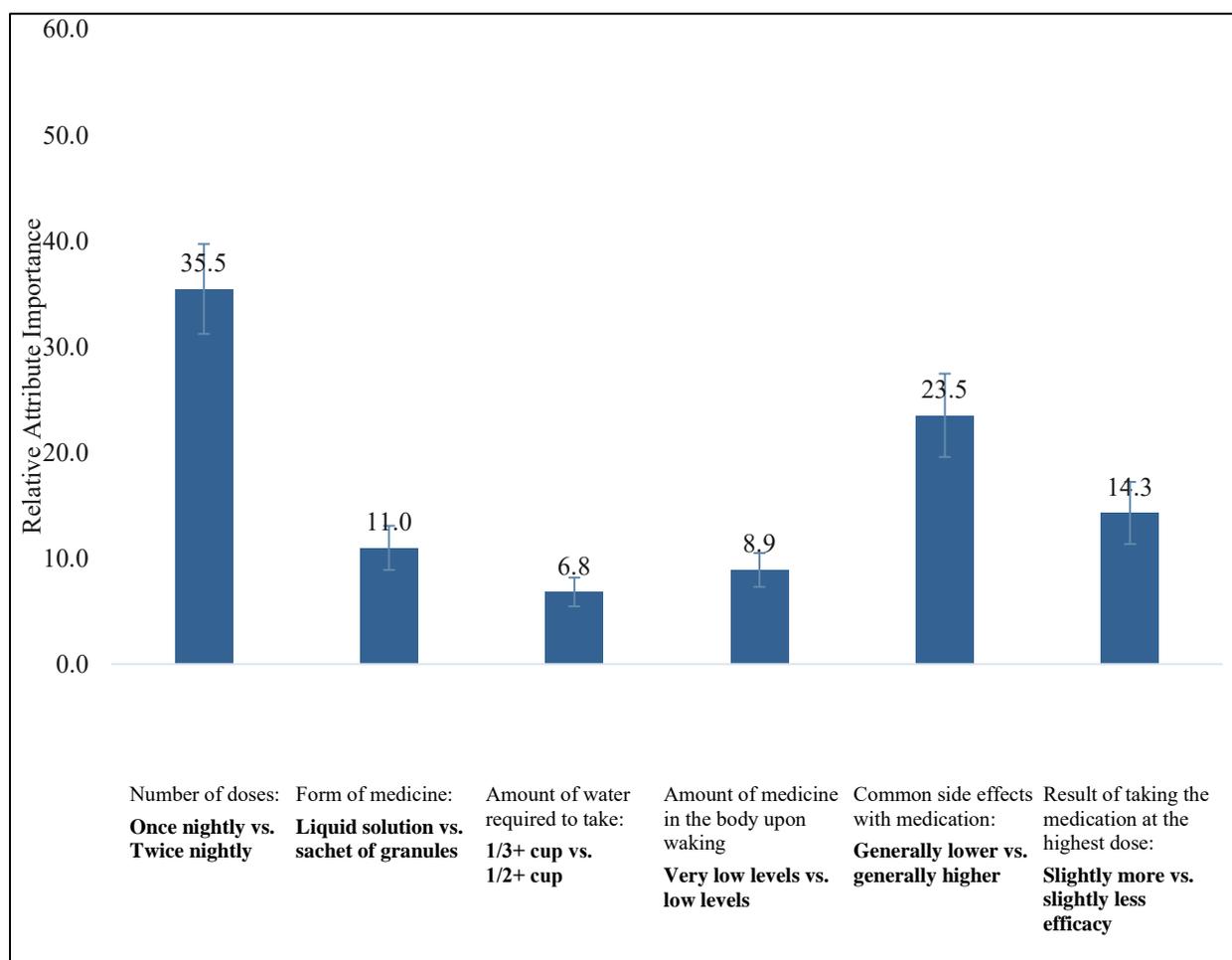
The relative preference of treatment attributes was examined via a DCE and a rating exercise. In the DCE, dosing frequency (once nightly vs. twice nightly) was the single most important attribute when selecting a narcolepsy treatment (relative attribute importance = 33.2), and degree of side effects experienced with the medication was found to be the second most important driver of product choice (relative attribute importance = 24.4) (Figure 4). Patients preferred a once-nightly product over a similar twice-nightly product overall. The most common reasons for

overall product preference were lack of need to wake up in the middle of the night to take second dose (48%), fewer side effects (46%), and ease of taking/handling (32%).

Figure 4: Drivers of Overall Product Choice



When asked to pick which treatment they are more likely to take exactly as directed and with which treatment they expect to experience less stress and anxiety, patients also preferred the once-nightly product. The number of doses for a product was the most important driver of reduced anxiety/stress (relative attribute importance = 35.5), and once-nightly dosing was strongly preferred over twice-nightly dosing with a relative preference weight of +92.5. Side effects related to the medication (relative attribute importance = 23.5) was the second most important driver of reduced anxiety/stress (Figure 5).

Figure 5: Drivers of Less Anxiety/Stress

Patients also rated their preference between two hypothetical narcolepsy product profiles: Product X, a once-nightly product similar to FT218, and Product Y, a twice-nightly product similar to Xyrem[®]. Product X (mean rating=7.5) was consistently preferred over Product Y (mean rating=4.3) overall, and this mean preference was statistically significant at α of <0.05 (Table 5). Many patients noted that they preferred Product X over Product Y due to its once-nightly dosing schedule, and therefore, “lower risk of falling because sleep is not interrupted,” or “it won’t disturb me or my bed partner.” Furthermore, satisfaction with physical safety (i.e., reduced risk of nighttime falls) was rated significantly higher for Product X vs. Product Y. Taken together, these results suggest substantial unmet need for a safer treatment that patients can take once a night, like FT218.

Table 5: Stated Preference Ratings for Product X and Product Y

Attribute	Mean Rating ¹	
	Product X ²	Product Y ²
Overall level of preference	7.5	4.3
Likelihood to take as directed	7.9	5.9
Likelihood to experience stress/anxiety with taking	4.5	5.9

¹ For each product, patients were asked to rate their level of preference overall (measured on a scale of 1-9, where 1=not at all preferred and 9=strongly preferred), likelihood to take the product exactly as directed, and likelihood to experience anxiety/stress when thinking about the treatment (measured on a scale of 1-9, where 1=least likely and 9=most likely)

² The Product X profile contained a safety, efficacy, and administration profile similar to that of FT218, while the Product Y profile contained a safety, efficacy, and administration profile similar to that of Xyrem[®].

Bolded value represents a statistically significant difference between Product X and Product Y profiles shown at α of <0.05

5.3.2.6 Statements from Stakeholders

To support the request for orphan designation, Avadel collected letters from four Key Opinion Leaders (KOLs) in the field of narcolepsy describing their experiences with narcolepsy patients and how they expect a reduction in dosing frequency to impact their patients. The letters speak to the real-life difficulties that narcolepsy patients encounter when being treated with twice-nightly sodium oxybate and the expected positive impact that a once-nightly formulation would offer. The KOL letters are provided in [Appendix 2](#) for Agency consideration.

More recently, Avadel obtained letters of support from two patient advocacy groups, Wake Up Narcolepsy Inc. and Project Sleep, as well as a patient with narcolepsy and her caregiver. These letters (provided in [Appendix 2](#)) further describe the negative impact of the twice-nightly sodium oxybate dosage regimen on patients and caregivers as well as the anticipated benefits of a once-nightly formulation. Avadel also recently obtained letters of support from additional KOLs and sleep specialists who were investigators in the REST-ON study (provided in [Appendix 2](#)).

5.3.2.7 Potential Impact on Diversion

Sodium oxybate has a history of illicit use as a “date-rape drug.” This substance has been added to a target’s drink without his/her knowledge in order to incapacitate the individual. In addition to standard precautions to limit access, including through the FT218 Risk Evaluation and Mitigation Strategy (REMS), FT218 will be provided as white granules as opposed to twice-nightly sodium oxybate which is a clear to slightly opalescent oral solution. The appearance of FT218 (cloudy in solution) and gritty consistency in the mouth of the white granules should alert a target that a substance has been added to his/her drink. Avadel’s [Study PKFT218-1601](#) included questionnaires on taste, grittiness, and similar attributes. FT218 was reported to be salty and bitter. FT218 was described as gritty by 97% of participants while only 4% described Xyrem[®] as gritty. Xyrem[®] was found to be smooth by 93% of subjects compared to 19% for FT218.

5.3.2.8 Impact of Salt Content

Xywav[®], a recently approved twice-nightly sodium oxybate formulation, has a lower salt content than the previously approved formulation of Xyrem[®]. Avadel acknowledges that FT218 has a salt content commensurate with that of Xyrem[®], ranging from 820-1,641 mg depending on the dose. According to a recent review ([Avidan and Kushida 2020](#)) in which a critical evaluation of the literature was conducted to examine the relationship between cardiovascular (CV) risk and sodium intake, narcolepsy, and sodium oxybate exposure, the findings suggested that increased CV risk is associated with extremes of daily sodium intake, and that narcolepsy is associated with comorbidities that may increase CV risk in some patients. However, data from studies regarding sodium oxybate use in patients with narcolepsy have shown a very low frequency of CV side effects (e.g., hypertension) and no overall association with CV risk. In the absence of data that specifically address CV risk with sodium oxybate based on its sodium content, the clinical evidence to date suggests that sodium oxybate treatment does not confer additional CV risk in patients with narcolepsy. Overall, the documented safety, efficacy, and quality of life issues related to the second dose of twice-nightly sodium oxybate present a greater risk to patients than sodium content, and each of these greater risks is significantly improved and addressed with the once-nightly formulation of FT218.

5.3.2.9 Summary

The once-nightly dosing regimen of FT218 is clinically superior to the currently approved twice-nightly formulations of Xywav[®] and Xyrem[®] and provides a major contribution to patient care (MC-to-PC). As evidenced by the letters provided in [Appendix 2](#), this view is shared by prominent clinicians in the field of narcolepsy, patient advocacy groups, and actual patients and caregivers living with narcolepsy. The option of a narcolepsy treatment with a once-nightly dosing regimen removes the disruption to sleep and increased risk of adverse events associated with waking to take a second dose. This risk is evidenced by the strengthening of the Xyrem[®] label post-approval to account for the risk of falls when patients do not remain in bed following the ingestion of their doses. Also, given the correlation between C_{max} and adverse events such as nausea and vomiting, the existence of a second C_{max} for the twice-nightly products may increase the risk of these events as well. Data from the REST-ON study demonstrated that well-known sodium oxybate-associated adverse events occurred at lower rates with FT218 than seen in previous Xyrem[®] pivotal studies. Once-nightly FT218 allows patients and their spouses/partners to remove the anxiety and disruption related to waking for a second dose each night. Further, the reported difficulties in waking for a second dose results in many cases of missed doses. This lack of adherence to the dosing regimen impacts the efficacy and quality of life of the treatment for the patient. Furthermore, data from the discrete choice experiment conducted in current or previous twice-nightly sodium oxybate users clearly shows a preference for a once-nightly sodium oxybate compared to the twice-nightly product.

FT218 offers narcolepsy patients an effective and safe once-nightly alternative to the disruptive and problematic twice-nightly dosing regimen. In addition to avoiding the potential safety and quality-of-life issues related to the second dose, FT218 also allows dosing flexibility without a food effect and obviates the need for an unattended dose of a controlled substance to be left out on a bedside table risking inadvertent or deliberate misuse. Also, the likelihood of FT218's use as an illicit substance to incapacitate an unknowing individual is expected to be lessened based on feedback on easily detectable taste and mouthfeel of the drug product.

5.3.2.10 References

- Avidan AY, Kushida CA. 2020. The sodium in sodium oxybate: is there any cause for concern? *Sleep Medicine* 75:497-501.
- Black J, Houghton WC. 2006 Sodium oxybate improves excessive daytime sleepiness in narcolepsy. *Sleep*. 29(7):939-946.
- Chen C, Skowronski R, Jenkins J, Zomorodi K. 2019. Pharmacokinetics, relative bioavailability, and food effect of JZP-258 and sodium oxybate: results of two phase 1, open-label, randomized crossover studies in healthy volunteers. Presented at: World Sleep Meeting Sep 2019; Vancouver, British Columbia, Canada.
- Mignot EJM. 2012. A practical guide to the therapy of narcolepsy and hypersomnia syndromes. *Neurotherapeut*. 9(4):739-752.
- Seiden D, Grassot J, Monteith D, Dubow J. 2020. The pharmacokinetic adverse event relationship for FT218, a once-nightly sodium oxybate formulation. *Sleep*. 43(1):A282-A283.
- Unite Narcolepsy. 2013. Patient-Focused Narcolepsy Survey: Interim Analysis as of September 16, 2013. Cited 10 Nov 2020.
- U.S. Xyrem Multicenter Study Group. 2002. A randomized, double blind, placebo-controlled multicenter trial comparing the effects of three doses of orally administered sodium oxybate with placebo for the treatment of narcolepsy. *Sleep*. 25(1):42-49.
- Xyrem® International Study Group. 2005. A double-blind, placebo-controlled study demonstrates sodium oxybate is effective for the treatment of excessive daytime sleepiness in narcolepsy. *J Clin Sleep Med*. 1(4):391-397.
- Xyrem® Prescribing Information. 2020. Palo Alto, CA: Jazz Pharmaceuticals, Inc.

APPENDIX 1. CERTIFICATION OF AFFILIATION



10 November 2020

Eric Bastings, M.D.
Acting Director, Division of Neurology 1
Food and Drug Administration
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Re: **Certification of Support for Clinical Investigations**

To whom it may concern:

Avadel CNS Pharmaceuticals LLC is affiliated with Flamel Ireland Ltd (d/b/a/ Avadel Ireland Ltd) as members of a consolidated group. Both companies are under the management and are wholly owned subsidiaries of Avadel Pharmaceuticals plc, a publicly traded company on the NASDAQ under the ticker symbol AVDL. A list of the subsidiaries of Avadel Pharmaceuticals plc is included as Exhibit 21.1 of the 2019 Avadel Pharmaceuticals plc 10-K that was filed with the US Securities Exchange Commission on March 16th of 2020.

Avadel Pharmaceuticals plc and its subsidiaries have provided all of the support for the clinical investigations essential to the approval of NDA 214755. We believe the FDA should consider the applicant to have conducted or sponsored the clinical investigations because all of the studies were performed by and within the Avadel Pharmaceuticals plc family of companies.

Sincerely,

A large grey rectangular box redacting the signature of the sender.

Craig P. Dull, CPA
Assistant Controller

APPENDIX 2. STATEMENTS FROM STAKEHOLDERS

(b) (6)

October 6, 2017

Office of Orphan Products Development
Food & Drug Administration, WO325295
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: Orphan drug status of once nightly dosing of sodium oxybate

Dear Team:

I would like to pass along my views on the importance of sodium oxybate as a treatment option for patients with narcolepsy. You are undoubtedly familiar with sodium oxybate which has been FDA approved for some time as a key option for the management of a variety of symptoms including excessive daytime sleepiness and cataplexy for patients with narcolepsy. This medication represents a critical offering on the menu of treatment options. It is not uncommon for patients with narcolepsy, in part because of insurance preauthorization issues, to have tried a variety of therapeutic agents including modafinil, armodafinil, and a variety of stimulants before being placed on sodium oxybate. Once on this medication in my experience as a clinician and clinical research they typically report functioning better than they had done previously on any of the alternatives.

One major issue though is the twice nightly dosing regimen. This presents a number of significant challenges. The patients are instructed to set an alarm to awaken them so they can take the second dose at a designated time partway through the night. This is a tricky process because if the alarm awakens them out of deep sleep it can trigger a sleep walking or similar non-REM parasomnia behavior. Sometimes patients will wake up spontaneously and take this second dose but forget to turn off the alarm. The alarm then can trigger non-REM parasomnia during the second part of the night after the patient has taken the second dose. I have personally worked with numerous patients who experienced parasomnias associated with sodium oxybate and the use of an alarm.

Many of the patients who are appropriate for sodium oxybate are adolescents and young adults. The need to develop a system where they can take a second dose is challenging. Parents are often involved when the patients live at home. The need to measure out a liquid medication with a syringe and dilute it in water takes practice and precision. However, once patients live independently, whether it is in a dorm setting or other setting, devising a system to take the second dose is tricky. This challenge is compounded by the need to safeguard this medication from being diverted. Patients are generally

instructed to have the second dose handy so they can quickly take it during the middle of the night without needing to get out of bed placing them at risk for falling. However, in a dorm or other shared living accommodation this makes it difficult to secure the medication during the night. In a home situation, having the second dose accessible creates the risk of children, pets and others getting into the medication.

In my opinion, there is a great need for a once nightly sodium oxybate product. I am very pleased that such a product has been developed and is currently under testing in clinical trials in the U.S. and abroad. I hope that this product can be considered for orphan status as was the original twice nightly sodium oxybate. This new formulation will present important advantages over the currently available form.

My background is that I am a Professor of Psychiatry at the Mayo Clinic. I have been involved in Sleep Medicine for over 20 years. My practice and research interests have centered on the needs of patients with narcolepsy or similar primary disorders of hypersomnia. I work as a clinician in a high volume Center for Sleep Medicine at the Mayo Clinic in Arizona. I also work closely with my colleagues at 11 other centers for sleep medicine within the Mayo Clinic system. We have had a favorable experience with sodium oxybate with the exception of the challenges described here, many of which are in large part related to the twice nightly dosing.

I hope that this information is helpful to you as you review the application for orphan status.

Sincerely,

Lois E. Krahn, M.D.

Professor of Psychiatry
Mayo Clinic Center for Sleep Medicine

LEK/bjw

Yale SCHOOL OF MEDICINE

Department of Internal Medicine

MEIR KRYGER, MD, FRCPC
Program Director, Sleep Medicine
Section of Pulmonary, Critical Care
and Sleep Medicine
PO Box 208057
New Haven, CT 06520-8057
Tel: (203) 932-5711 x ^{(b) (6)}
Fax: (203) 875-3634
Meir.kryger@yale.edu
www.medicine.yale.edu

24 August 2017

Office of Orphan Products Development
Food and Drug Administration
WO32-5295
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: Once a night dosing of sodium oxybate would be a major contribution to patient care in patients with narcolepsy.

To whom it may concern:

I am a professor of medicine at Yale School of Medicine. I am chief editor of the most widely used textbook used in sleep medicine, *The Principles and Practice of Sleep Medicine*, which is in its sixth edition. I have published more than 200 peer reviewed articles and book chapters. I have served as president of both the Canadian Sleep Society and the American Academy of Sleep Medicine, and has served as Chair of the Board of Directors of the National Sleep Foundation. I have received the Lifetime Achievement Awards from the Canadian Sleep Society, the National Sleep Foundation, and the Mary Carskadon Outstanding Educator Award. I write this letter not as an academic but as a clinician who has treated hundreds of narcolepsy patients in my 40 year career.

It has been known since 1979 that gamma-hydroxybutyrate, later reformulated in about 2000 as sodium oxybate, has a beneficial effect on patients with narcolepsy-cataplexy. From those early days, it was also apparent that the compound, in order to be optimally effective, had to be taken twice during the night. Prior to the availability of a pharmaceutical grade compound, we had the product prepared by our hospital pharmacists. This was very cumbersome. Patients were provided containers of liquid product. They used a syringe to precisely measure the amount of liquid to be taken. Many patients prepared both doses and kept them at the bedside. The fact that patients had to awaken in the middle of the night to take the second dose was an issue. A liquid preparation, carried in a bottle made



transportation very problematic. This cumbersome treatment has not changed in about 40 years!

I have asked the manufacturer of sodium oxybate many, many times about having a once nightly pre-measured non-liquid formulation, because my patients have had issues with the current preparation:

- Sleeping through the night and not taking the second dose, making the treatment suboptimal.
- Awakening too late to take the second dose (4 hours until leaving the bed are needed for the second dose).
- Others in the home are disrupted by alarms in the middle of the night.
- Patients are fearful that the second dose, if prepared in advance may be ingested by a child
- Risk of falls if the patient gets out of bed to prepare the second dose.
- Measurement errors when using the syringe
- Accidental overdose if both doses are prepared at bedtime and the patient doesn't remember having taken the first dose. (this has happened to 2 of my patients in the last couple of years).

Many of my patients are college students who travel home, or abroad and travelling with bottles of liquid medications are problems at security at airports.

I believe that a formulation, shown to be effective, that is pre-measured, that can be taken once nightly would be a major contribution to patient care over Xyrem . it would be safer and more effective.

Sincerely,

[REDACTED]

Meir Kryger, MD, FRCPC
Professor, Yale School of Medicine
Pulmonary, Critical Care and Sleep Medicine
Fellowship Program Director, Sleep Medicine

1. Broughton, R., and M. Mamelak. "The Treatment of Narcolepsy-Cataplexy with Nocturnal Gamma-Hydroxybutyrate." *Can J Neurol Sci* 6.1 (1979): 1-6.
2. "A Randomized, Double Blind, Placebo-Controlled Multicenter Trial Comparing the Effects of Three Doses of Orally Administered Sodium Oxybate with Placebo for the Treatment of Narcolepsy." *Sleep* 25.1 (2002): 42-9.





DEPARTMENT OF SLEEP DISORDERS MEDICINE
Sleep Disorders & Research Center

2799 West Grand Blvd, CFP-3
Detroit, MI 48202-2689
(313) 916-4417 Office

August 29, 2017

Gayatri R. Rao, M.D., J.D.,
Director for the Office of Orphan Products Development (OOPD)
Food and Drug Administration

Dear Dr. Rao

My name is Thomas Roth and I direct the Sleep Disorders Center at Henry Ford Hospital. I also hold academic appointments at both Wayne State and the University of Michigan Schools of Medicine. I serve as a consultant to several pharmaceutical companies including those with drugs for the treatment of narcolepsy (e.g. Flamel, Jazz and Cephalon) and I was integrally involved in the design of Flamel's ongoing Phase 3 study of extended release sodium oxybate for the treatment of narcolepsy. In the past, I have also served on panels for the FDA Division of Neurology Products.

I am writing this letter to support Flamel's application for receiving orphan drug status for their narcolepsy therapy, currently under development, extended release sodium oxybate.

Narcolepsy is a CNS disorder affecting about 0.05% of the population. It has a myriad of symptoms including excessive daytime sleepiness, cataplexy, hypnagogic hallucinations, sleep paralysis and disturbed sleep. The primary therapies are stimulants for the sleepiness and REM suppressing drugs (e.g. SSRIs) for the auxiliary symptoms. Currently sodium oxybate is used to treat all narcolepsy symptoms including disturbed nocturnal sleep. While sodium oxybate is commonly used to treat the disturbed sleep of narcolepsy patients, and there are many articles supporting this, improving disturbed sleep is not an indication approved by the FDA.

Xyrem was granted orphan drug status based on the prevalence of narcolepsy. Xyrem has a short half-life (0.5 to 1 hour) and a duration of only 2-4 hours. Thus, directions for the use of Xyrem call for patients to awaken after four hours to take a second dose of medication. Patients report that the second dose is both



DEPARTMENT OF SLEEP DISORDERS MEDICINE
Sleep Disorders & Research Center

2799 West Grand Blvd, CFP-3
Detroit, MI 48202-2689
(313) 916-4417 Office

inconvenient and problematic. At an FDA hearing on narcolepsy, patients reported the desire “for a once a night sodium oxybate, a drug that would provide consistent and adequate control of the daytime sleepiness without the hard crash and one that would require one dose taken at bedtime resulting in 8 hours of restorative sleep” (Unite Narcolepsy 2013). Flamel has developed a sustained release formulation of sodium oxybate (FT218) with the aim of having a once nightly formulation of sodium oxybate for the treatment of narcolepsy (i.e. indicated for the treatment of excessive daytime sleepiness and cataplexy. To that end Flamel is carrying out trials to support this indication. PK data presented on this formulation show that the once a night formulation as compared to two doses of the current approved formulation show similar AUCs and similar blood levels at the end of the night.

There are several reasons why such a formulation, if proven to be safe and effective, would provide a substantial step forward for narcolepsy patients. These advantages were reported to me from discussions with sleep disorder clinicians as well as patients with narcolepsy and their family members. The results of a survey of 16 patients is provided as an attachment to this letter.

From a convenience point of view, patients report that the waking up for the second dose further fragments their already disturbed sleep. Also, patients do not like leaving a second dose on their night stand. Patients report this is especially a problem if they have children or pets in the home, when traveling and staying in a hotel, and especially for their children in a dormitory. Finally, patients report that the use of an alarm clock to arise and take the second dose is disturbing to their bed partner and occasionally to others in the home.

From a safety point of view, there is concern with failing to wake up on time and taking the second dose too late resulting in impaired alertness the next day. Also, after the night time awakening patients often go to the bathroom (because of the amount of water consumed with the two doses) and get injured due to falls. They do this despite the fact that the label says to take the dose while in bed. In meetings with patients with narcolepsy, injury due to bathroom trips after the second dose is not an uncommon experience .

From an efficacy point of view, patients often awaken too late and do not take the second dose resulting in a significant reduction in alertness the next day. Finally a single nightly dose will result in consistent blood levels every night as they are not dependent on when the patient takes each of the two doses.



DEPARTMENT OF SLEEP DISORDERS MEDICINE
Sleep Disorders & Research Center

2799 West Grand Blvd, CFP-3
Detroit, MI 48202-2689
(313) 916-4417 Office

For all of the above reasons, I strongly support the FDA granting orphan drug status to Flamel for FT218.

Cordially,



Thomas Roth PhD

Director, Sleep Medicine

Henry Ford Hospital

Clinical Professor, Department of Psychiatry

University of Michigan College of Medicine

Professor Department of Psychiatry

Wayne State University School of Medicine

Sodium Oxybate Dosing Questions

16 completed

1. Is leaving your middle of the night (second dose) of sodium oxybate out during the night a concern for you ?

Not at all 1 2 3 4 5 6 7 8 9 Very Much

Result: 4.5 ± 3.1

2. Do you ever forget or sleep through the night and thereby not take your middle of the night sodium oxybate dose

Never 1 2 3 4 5 6 7 8 9 Often

Result: 5.3 ± 2.2

3. How often have you taken your second dose of sodium oxybate later than planned or too close to the time you plan to get up?

Never 1 2 3 4 5 6 7 8 9 Often

Result: 5.5 ± 2.1

4. Have you ever experienced amnesia or loss of balance before or after taking your middle of the night dose of sodium oxybate

Never 1 2 3 4 5 6 7 8 9 Often

Result: 5.2 ± 3.1

5. Would a once a night formulation of sodium oxybate help with your medication compliance

No 1 2 3 4 5 6 7 8 9 Yes

Result: 8.7 ± 1.1

6. Would a once a night formulation of sodium oxybate make you feel safer?

No 1 2 3 4 5 6 7 8 9 Yes

Result: 8.7 ± 1.0

7. Would a once a night formulation of sodium oxybate be more convenient

No 1 2 3 4 5 6 7 8 9 Yes

Result: 8.9 ± 0.3

8. Would a once a night formulation of sodium oxybate be beneficial to the narcolepsy community

No 1 2 3 4 5 6 7 8 9 Yes

Result: 8.7 ± 1.0

Todd J. Swick, M.D.

Fellow of the American Academy of Neurology

Fellow of the American Academy of Sleep Medicine

Sleep Medicine/Neurology

7500 San Felipe, Suite 525

Phone: (713) 465-9282

Houston, Texas 77063

Fax: (713) 465-9248

tswick@houstonssleepcenter.com

September 12, 2017

Office of Orphan Products Development
Food and Drug Administration
WO32-5295
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Re: Once a night dosing of sodium oxybate and its advantages over the only other available formulation that requires twice nightly dosing regimen (Xyrem®).

To whom it my concern:

I have been practicing sleep medicine with a sub-specialty in diseases of central hypersomnolence of which narcolepsy with and with cataplexy are the prime examples for the past 35 years. I am board certified by the American Board of Sleep Medicine and the American Board of Psychiatry and Neurology in Adult Neurology and Sleep medicine. In 2014, I was awarded the Robert Clark Medal for Physician of the Year by the National Narcolepsy Network, the national advocacy group for patients with narcolepsy. I was involved in the original pivotal trials of Xyrem® that were presented to the FDA at the time of its initial approval for the treatment of cataplexy and subsequently for its secondary indication for EDS with or without cataplexy.

I am currently caring for >100 patients who are currently taking Xyrem® and have seen a remarkable improvement in these patients lives because of this innovative medication. However, over the past 15 years practical issues have arisen vis-a-vie issues related to having to take two nightly doses of sodium oxybate.

My practice is restricted to ambulatory/home based patients. The patients are instructed to prepare the two doses of sodium oxybate **prior to getting into bed for the night** to avoid any rapid onset of sleep. I have had patients take the first dose without preparing the second dose, accidentally spilling the second dose and in a few cases waking up after only 30-60 minutes and thinking that the 3-4-hour drug free time has elapsed and take the “second dose”.

I have had other patients wake up for the second dose and “raid the refrigerator” to “get a snack” at the time of the second dose (either before or after taking the dose) and then wonder why the efficacy of the drug has diminished after several weeks of this behavior. (Food greatly decreases the absorption of the drug from the GI tract.)

In more serious situations, the patient takes the second dose and then decides to use the rest room and falls asleep either standing in front of the commode or while sitting down resulting in minor head/neck injuries.

These situations will go a long way to be obviated using a once night sodium oxybate preparation.

September 12, 2017

There are also so practical considerations for a once nightly dosing regimen:

1. Easier transportation of the drug before reconstitution (this is particularly advantageous when traveling by plane in terms of carrying liquids).
2. There are people who sleep through alarms and miss the second dose thus greatly diminishing the overall efficacy of the treatment.
3. The alarms themselves cause disruption to bedmates, roommates and others who might hear or interact with the alarms.
4. Risk of psychomotor impairment when waking up for the second dose and running the risk of falling and/or in other ways injuring themselves.
5. Dosing errors in terms of drawing up the correct amount of sodium oxybate in the dispenser syringe.
6. Accidental overdose when the patient accidentally took both doses at the beginning of the night and then taking an additional dose 3-4 hours after the mistaken first "double-dose".

I believe a once-nightly dosing of sodium oxybate would increase patient compliance and greatly decrease the above enumerated problems. In treating patient with narcolepsy for the past 15 years I have seen every one of these issues.

To summarize, I believe that a once-nightly formulation of sodium oxybate would be greeted with much enthusiasm by the narcolepsy community and obviate the issues outline above.

Sincerely,


Todd J. Swick, M.D.
Diplomate, American Board of Sleep Medicine

TJS: ts
T: 9/12/17



August 21, 2020

Office of Orphan Products Development
Food & Drug Administration, WO325295
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: Orphan drug status of once nightly dosing of Sodium Oxybate

Dear Orphan Products Development Team:

Wake Up Narcolepsy writes to you in support of the once-nightly dosing of Sodium Oxybate as a treatment option for people with narcolepsy. This letter contains recommendations from two staff members (Claire Crisp and (b) (6)) who are also parents/caregivers to people with narcolepsy.

Wake Up Narcolepsy, Inc is a 501 (c)(3) not for profit patient advocacy organization (based in the US) that was founded in 2009 to provided funds for narcolepsy research and to provide support for individuals with narcolepsy and their families. To date, we have raised almost 1 million USD and have expanded our mission to include patient services by way of support and education and to raise narcolepsy awareness within the sleep space and the wider population at large. Wake Up Narcolepsy (WUN) also works closely with leading pharmaceutical companies to recruit patients for clinical trials, facilitate drug development and communicate medication options to families affected by narcolepsy. In particular, we have partnered with Avadel at both patient-focused and industry conferences and fully support the once-nightly dosing of sodium Oxybate as a significant improvement in terms of safety, management of symptoms and quality of life for people with narcolepsy.

Claire Crisp, Grad. Phys. SRP. MCSP

My background is that I have worked as the Executive Director for Wake Up Narcolepsy for almost 3 years, have over 10 years of experience as a caregiver to a person with narcolepsy, and am an advocate for people with narcolepsy and their caregivers. As an author, my book *Waking Mathilda- a Memoir of Childhood Narcolepsy*, published in 2017 (Palace Gate Press), has sold over 2,000 copies worldwide. Our family's journey with narcolepsy has been reported in the national news (UK and US), featured on radio, cited in academic papers and the book is used as a teaching tool for

employees at pharmaceutical companies. I am also the host of the Narcolepsy 360 podcast which is about to begin its 3rd season. My role at WUN extends to direct patient support, global awareness campaigns, providing educational resources and facilitating patient recruitment for clinical trials.

The proposed once nightly Sodium Oxybate offers a critical improvement on the current twice nightly regime for both people with narcolepsy and their caregivers for the following reasons:

Many people with narcolepsy require supervision in taking the second dose due to the crucial time delay required between the two doses. In my experience my daughter has needed vigilant supervision to ensure there is a 3-hour distance between the two doses. I am sure you are aware of the serious consequences of consuming both doses too close together. For this reason, my husband and I have administered the second dose of Sodium Oxybate around 2/3am every night for the last 10 years. Having tried several safety devices, we are still sufficiently concerned re. the timing of the second dose to still need to supervise our daughter. It is well documented that sleep deprivation has long-term serious health effects, some of which we are already experiencing. During especially exhausting seasons we have sought additional night care in the way of nurses, nuns and willing friends to do what in our home we call 'the night shift.'

In addition, many people on Sodium Oxybate currently experience night wanderings and sleep related eating disorders (SRED). This is true of my daughter who also attempts to leave the house and eats before taking the second dose, thus rendering it partially ineffective. Over time, these night wakings have led to her gaining significant weight and compromised not only her safety but that of our family on nights where she attempts to unlock doors. Mathilda has fallen in the night, needed help using the bathroom and cut herself with knives attempting to chop up food. In the morning, she recalls none of these activities.

Still, Sodium Oxybate has remained a good medication of choice in that it effectively treats much of her excessive daytime sleepiness and around 80% of her cataplexy. For this reason, and having weighed up other medication options, she has continued with the twice nightly Sodium Oxybate for 10 years now. Our current concerns revolve around how our daughter will be able to live independently given her current medication regime.

The impact from a safety perspective of the once a night Sodium Oxybate cannot be overstated. In addition, as a parent/caregiver, there are many health benefits to her taking a single dose, not to mention peace of mind.

More broadly and for many of the same reasons listed above, people with narcolepsy (and their caregivers) have been eagerly anticipating the once a night Sodium Oxybate as a solution to issues they have with the second dose. While I have given a personal account of these challenges, I am confident they reflect the very significant burden that people with narcolepsy face every night.

(b) (6), PhD

Throughout the last almost three years of working as the (b) (6) for Wake Up Narcolepsy, I have had the opportunity to work alongside and support many individuals with narcolepsy in the community and their families. During this time, I have spoken with multiple patients who need Sodium Oxybate to have some semblance of a "normal" life. Unfortunately, due to the constraints of the current Sodium Oxybate that is available to individuals with narcolepsy, some of these patients are not able to take it and thereby not living their "best" life. I would like to take the opportunity to share with you some of the stories and the reasons that the narcolepsy community would greatly benefit from a once-nightly dosing option.

As a parent of a ten-year-old child with narcolepsy and severe cataplexy, who has lived more than half of his life with this diagnosis, I am in support of granting Orphan Drug status of the once nightly dosing of Sodium Oxybate. My son started taking Sodium Oxybate at age 5, after a six-month diagnostic process. As a young child, there was no way that he would be able to wake up and give himself the second dose of medication in the middle of the night. In fact, many adults have issues with this same task and tend to sleep through their alarms or need another individual to come and wake them up for the second dose. What that means for a parent or caregiver of a person with narcolepsy is that sleeping through an entire night ceases to exist. For our family, we spent five years with either myself or my husband sleeping in a second bed next to my son to provide the middle of the night dose in an effort to ensure the rest of the family was not woken up with alarms and movement. Without doing so, we would have had a household of four (rather than just two) that now had consistent fragmented sleep. Research has shown us that fragmented sleep can cause sleep deprivation, daytime sleepiness, mood swings, weight gain, decreases in psychomotor performance, and many other health problems. Requiring a person with narcolepsy (and his/her immediate family) to wake up in the middle of the night, every single night, in order to receive optimum benefit of a medication is often a deterring factor for individuals when seeking treatment.

In addition to waking up in the middle of every night to take Sodium Oxybate, there are also concerns with the preparation of the current medication. A person with narcolepsy or caregiver has two options when mixing the medication for each night, both of which present some major hazards. A person can either make up both doses at one time or they can make the first dose before bed and make the second dose in the middle of the night. When making both doses at one time, it becomes an automatic behavior (after doing it for so long) that oftentimes the person can zone out while mixing the doses. Personally, I have had to dump multiple doses of Sodium Oxybate down the kitchen drain because I couldn't remember if I put the medication in both bottles or if accidentally put both doses in one bottle. For those who make the second dose in the middle of the night, sleep deprivation can cause accidents in the dosing whether it is remembering if you added the medication or accidentally added it twice because you did not remember already adding it. The once-nightly Sodium Oxybate will be a game-changer in this regard. It is a medication that only has to be mixed one time and then taken. That will also decrease the instances of individuals taking the medication for the first time, then forgetting they took it and accidentally taking the second dose shortly after.

I have spoken with many individuals who have expressed a concern because either they, as an individual with narcolepsy, or their child, as a caregiver to a person with narcolepsy, have woken up after only an hour of sleep from a dream that it was time for the second dose. This has resulted in over-dosing since the current Sodium Oxybate is not time-released and kicks in immediately. In an effort to counteract this possibly, many people purchase kitchen timer lock boxes to store the second dose in the middle of the night. However, this too comes with its own issues. Traveling with medication is difficult enough but adding special lock boxes to the mix make it even more of a hassle. Additionally, when the box unlocks in the middle of the night, the soft noise it makes often awakes the person with narcolepsy and they take the dose right away. However, if you set the box not to unlock until the exact time they are supposed to take the medication, and the person wakes up five -minutes early, they can fall back to sleep waiting for the box and miss the second dose entirely (as the next time they wake up it may very well be too late to take it and still be able to get up in the morning).

Furthermore, many patients are not willing to mix the medication with water alone and opt for something to help disguise the saltiness. While that is not a problem for the initial dose, as the person with narcolepsy can take the dose and then brush his/her teeth, it is an issue for the second dose. Consistently drinking potentially sugary drinks in the middle of the night can cause teeth issues for the individual. Another concern is that many people on the twice a night Sodium Oxybate

wake up famished in the middle of the night and eat between doses. Not only does this cause the medication to metabolize differently and often makes it not as effective, but it also creates issues with weight gain due to the nightly eating.

All of the issues described are just a small amount of the reasons why the narcolepsy community needs access to a once-nightly Sodium Oxybate option. As a parent, I can tell you that this medication will help us to regain a semblance of normal in our nightly lives. This option will allow more individuals to be optimally treated and will create better outcomes for individuals with narcolepsy and their families.

Respectfully,

(b) (6)

P. MCSP

(b) (6), PhD

Wake Up Narcolepsy



August 20, 2020

Janet Maynard, M.D., M.H.S
Director
Office of Orphan Products Development
Food and Drug Administration
WO32-5295
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Andrea Furia-Helms
Director
Patient Affairs Staff
Food and Drug Administration
WO32-3126
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Dear Directors Maynard and Furia-Helms,

Thank you for your leadership at the Food and Drug Administration (FDA) and for your efforts to fully incorporate patient needs and the patient perspective into regulatory review. I write today on behalf of the sleep disorders community as the President and CEO of Project Sleep to request fair and fast consideration of FT218 as a potential treatment of excessive daytime sleepiness and cataplexy in patients with narcolepsy.

Believing in the value of sleep, Project Sleep aims to improve public health by educating individuals about the importance of sleep health and sleep disorders. Project Sleep educates and empowers individuals using events, campaigns, and programs to bring people together and talk about sleep as a pillar of health. Project Sleep also works to educate policymakers and regulators about the unique needs of the sleep community to advance research and public health, facilitate the development of innovative therapies, and ensure proper coverage and care for people living with sleep disorders.

Narcolepsy, particularly narcolepsy with cataplexy, is a serious neurological condition. Functionality varies greatly based on many factors, including the 24-hour nature of the condition and the highly complex nature of managing multiple major symptoms both day and night. Currently, treatment options are extremely limited and people with narcolepsy have numerous challenges with available therapies due to the highly personalized nature of the condition.

Project Sleep applauds the FDA for its strong commitment to patient-focused drug development. In furtherance of the FDA's patient-focused approach, we would like to highlight dosing frequency and treatment adherence as critical factors in evaluating nighttime treatments like FT218.

For people managing serious chronic conditions like narcolepsy in the real world and over the long term, one's ability to adhere to a particular treatment regimen directly impacts one's outcomes. Researchers have looked at the effects of dosing frequency on treatment adherence in chronic diseases, finding higher rates of adherence in patients using less frequently dosed medications.¹ These studies often look at the differences between once-daily versus twice or thrice-daily regimens, with one major literature review indicating that in studies comparing once-

¹ Saini SD, Schoenfeld P, Kaulback K, Dubinsky MC. Effect of medication dosing frequency on adherence in chronic diseases. Am J Manag Care. 2009;15(6):e22-e33. Published 2009 Jun 1.



daily versus twice-daily dosing, patients receiving once-daily dosing had 2% to 44% more adherent days compared with patients receiving twice-daily dosing, with most studies clustering around 13% to 26%.²

While these studies are not specific to narcolepsy and do not speak to treatments administered at nighttime, we believe that the challenges surrounding dosing frequency and treatment adherence for daytime medications would be similar, if not even more exaggerated, for nighttime medications. As narcolepsy is a neurological condition that impairs the brain's ability to regulate the sleep/wake cycle, dosing frequency for a nighttime medication for this particular patient population is of particular significance.

Thus, Project Sleep believes that a simplified nighttime dosing regimen is essential to improve treatment adherence and outcomes for people with narcolepsy. Further, such an advancement would also likely have impacts on quality of life and quality of sleep for patients, bed partners and caregivers.

The FDA's leadership in ensuring people with narcolepsy have access to a variety of impactful orphan therapies is deeply appreciated. Thank you for your time and for your consideration of my request. Please let me know if you have any questions or if you would like to discuss the contemporary treatment needs of the narcolepsy community further.

Sincerely,



Julie Flygare, JD
President & CEO
Project Sleep
www.project-sleep.com

² Ibid.

November 4, 2020

Office of Orphan Products Development
Food & Drug Administration, WO325295
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: Consideration of once-nightly sodium oxybate (FT218) for Orphan Drug status as a treatment for narcolepsy

To whom it may concern,

I am a 31-year-old Narcoleptic patient and current twice-nightly sodium oxybate user who would like to pass on my views on the great importance of a once-nightly sodium oxybate treatment option for my condition. I have been taking Xyrem, the twice-nightly option for the past 16 years (since age 15) and while it has made a world of difference in my quality of life and ability to function, I am very familiar with the significant downsides and ongoing threat to my safety it poses. I have stayed on it up to this point only because there were no other options available and I was desperate for the benefits no other treatments came close to providing.

There are many issues with the twice-nightly dosing regimen. Patients like me are to prepare both doses before bedtime so the second one is handy to take upon awakening (usually through an alarm) partway during the night at a designated time. This can be tough to get right, and I often find myself taking the second dose too late or forgetting if I took it. Or, in my sleepiness and foggy state come bedtime I accidentally take both doses at once forgetting I've already taken one. This has led to a family member having to rush to check on my breathing, etc. or an ambulance being called as a double dose at once can be very dangerous.

In addition to this, I am triggered to sleepwalk in this half-awake state between doses with no recollection of it come morning. I often wake up with bruises from wandering around and bumping into things. I have been found attempting to leave the house or holding knives or other potentially dangerous items around the house. More than anything I am prone to sleep eating when I awake to take my second dose (sometimes even inedible/dangerous substances or things like pet food). As a result, I have struggled with my weight for years and often wake up feeling sick and nauseated. Lastly, I will say the current liquid form of this drug is extremely inconvenient and difficult to travel with or receive without leaking bottles. The once-nightly extended release granules would offer an advantage in this regard.

So, in my opinion, a once-nightly sodium oxybate option is extremely important for many patients like myself who have come to rely on this type of drug to better function in our everyday lives. It would also provide great peace of mind to our families and those who care for us. I am very grateful this safer and more convenient alternative product (FT218) has been developed and is currently being reviewed by the FDA. I hope that my perspective as a patient has been helpful to you as you review this orphan drug application.

Sincerely,

DocuSigned by:

A grey rectangular box containing a blue DocuSigned logo on the left and large red text "(b) (6)" in the center.

(b) (6)

Narcolepsy Patient
Current Sodium Oxybate User (twice nightly)

(b) (6)

November 4, 2020

Office of Orphan Products Development
Food and Drug Administration, WO325295
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: Consideration of once-nightly sodium oxybate (FT218) for Orphan Drug status as a treatment for narcolepsy

To whom it may concern:

I would like to express my views on the importance of once (FT218) vs. twice (Xyrem) nightly sodium oxybate as a meaningful treatment contribution to narcolepsy patient care. My name is (b) (6) and I am the mother of a 31-year-old narcoleptic daughter, (b) (6) has suffered from narcolepsy with cataplexy for 20 years, since the age of 11. She and I have served on the Avadel patient advisory board for the past 4 years, offering patient and parent perspectives on the benefit of a once-nightly sodium oxybate for treatment of narcolepsy. (b) (6) has been taking twice-nightly Xyrem for almost 15 years. It has proven to be a vitally effective drug in controlling her symptoms. However, the twice-nightly dosing has caused significant issues to both her physical safety and her psychological wellbeing.

Narcolepsy causes terribly fragmented sleep; and waking up to take a second dose of medication only further impairs her ability to obtain restorative sleep. The twice-nightly Xyrem causes a sudden rapid onset of sleep, while the once-nightly FT218 will be a slow time released drug, thus allowing for better sleep consolidation and more restorative rest.

Another benefit of FT218 is that it would greatly reduce the incidence of a potentially dangerous accidental overdose. On a recent occasion (b) (6) had forgotten that she had taken her first dose of Xyrem. In her state of impaired cognition from that first dose, she immediately took her second dose. I sat by her bedside for several hours watching her breathe until the medication wore off. I was petrified of a potential disaster that night, and this fear lingers in the back of mind ever since. A once-nightly option would eliminate this situation.

(b) (6) often wanders between her two Xyrem doses, which has resulted in nighttime falls as well as compulsive overeating during the night. Food decreases the effectiveness of her second dose of Xyrem, as it decreases absorption of the drug. As a result, (b) (6) has on more than one occasion gained 50 pounds from this nighttime eating. This has caused profound detriment not only to her physical health but to her emotional well-being and self-esteem as well. When the Xyrem isn't properly absorbed it loses effectiveness, resulting in an increase of (b) (6) hypnagogic hallucinations. She will scream out in terror, waking others in the home and evoking significant emotional distress on the family. (b) (6) will use the bathroom between her two Xyrem doses, which often results in falling and stumbling in her state of disorientation. This is also disruptive to other family members and has caused her minor injuries over the years as well.

Another difficulty with twice-nightly sodium oxybate has to do with traveling. When in a strange hotel room, her disorientation causes her to really wander in between doses, and she has been found trying to open the hotel room door to wander the halls. This makes it difficult for her travel companions, but also undermines (b) (6)'s confidence to travel alone. A once-nightly dose of FT218 would eliminate her fears of wandering in strange places during the night and encourage her independence and self-confidence to care for her own basic sleep needs.

I strongly encourage the FDA to consider priority review of FT218 for orphan drug status so that (b) (6), and so many other twice-nightly sodium oxybate users like her, can avail herself of this new once-nightly drug. The overall health benefits would be tremendous, including consolidation of sleep and resetting her biological clock to sleep longer through the night. In addition, FT218 would be a much safer drug in preventing nighttime sleep walking, overeating, and potentially dangerous self-injury. Most importantly would be the sense of independence it would give (b) (6) to manage her own sleep. This independence would boost her self-esteem by allowing her to travel and live alone without fear of self-injury or incidents in the middle of the night. This overall change in her quality of life would be a major improvement for her and for others suffering from narcolepsy. Thank you for your consideration in granting FT218 priority review and orphan drug status.

(b) (6)

October 12, 2020

Office of Orphan Products Development
Food and Drug Administration
WO32-5295
10903 New Hampshire Avenue
Silver Spring, MD 20993*0002

To whom it may concern:

I am a neurologist and professor of psychiatry at the Stanford University Medical Center. I serve as Division Chief and Medical Director of Stanford Sleep Medicine, and have been evaluating and managing patients with sleep disorders since 1990. I have been conducting basic and clinical research on sleep for longer than that time, with my initial research focused on cataplectic attacks in canines and humans with narcolepsy starting in 1977. I have served as president of the World Sleep Federation and the American Academy of Sleep Medicine, and as founding president of the World Sleep Society and California Sleep Society. I have served as chair of the Standards of Practice Committee of the American Academy of Sleep Medicine and am currently chair of the International Sleep Medicine Guidelines Committee of the World Sleep Society. I have authored or edited over 250 publications; also authored or edited six books, including serving as editor-in-chief of the largest publication on the field of sleep to date, the Encyclopedia of Sleep (4 volumes, 429 chapters, 748 authors), and serves as editor-in-chief of the journal Sleep Science and Practice. I am a past recipient of the highest professional awards in the field of sleep medicine, the American Academy of Sleep Medicine's Nathaniel Kleitman Distinguished Service Award and the World Sleep Society's Distinguished Service Award. I write this letter not as an academic researcher but as a clinician who has treated hundreds of patients with narcolepsy.

Sodium oxybate is the primary treatment option for patients with narcolepsy, since it is highly effective in managing the most difficult symptoms of narcolepsy: cataplexy and excessive daytime sleepiness. This medication is clearly superior to other treatments prescribed to patients with narcolepsy, which include stimulants, such as modafinil and dextroamphetamine, and anticataplectic medications, such as certain antidepressants. The availability of sodium oxybate offers advantages over these medications since you typically need to only prescribe this medication (instead of two different classes of medication) and has less of the adverse effects of these other medications.

Although sodium oxybate is clearly an advantageous medication to prescribe to patients with narcolepsy, the problem is that twice nightly dosing is problematic. There are several difficulties with this approach. The main difficulty is the patient needs to awaken in the middle of the night

in order to take the second dose. If the patient is awakened in the middle of deep sleep, i.e., N3 sleep, there is a good chance that they will have sleep inertia, which is the grogginess and confusion upon awaking. In a severe episode, the patient may lash out at his/her bedpartner or it may transition into a sleepwalking or sleep terror episode. Injury to the patient and/or bedpartner would be possible in any of these scenarios. This is especially a problem in adolescents and young adults. These patient populations have greater sleep need and higher sleep depth in the first half of the night. Such patients would have more difficulty waking up to take the second dose of the medication, and would be at greater risk for these NREM parasomnias (i.e., unusual behaviors during sleep, such as the confusional arousals, sleepwalking, and sleep terrors, as mentioned above). I have had the experience of managing these patients with narcolepsy whom have had difficulty waking up in the middle of the night to take this second dose or completely ignoring their alarms and not taking this dose.

In my opinion, there is a tremendous need for a once nightly sodium oxybate product. I am enthused that such a product has been developed and the pivotal Phase III REST-ON clinical trial of FT218 for excessive daytime sleepiness and cataplexy in patients with narcolepsy has recently been completed with the topline data released. I hope that this product can be considered for orphan status as was the original twice nightly sodium oxybate. As discussed earlier, this new formulation presents important advantages over the currently available product.



Clete A. Kushida, M.D., Ph.D.
Division Chief and Medical Director, Stanford Sleep Medicine
Director, Stanford Center for Human Sleep Research
Professor, Department of Psychiatry and Behavioral Sciences,
Stanford University Medical Center

October 20, 2020

Office of Orphan Products Development, FDA
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: Orphan drug status of once nightly dosing formulation of sodium oxybate (FT218)

To whom it may concern:

I strongly support the FDA granting orphan drug status to Avadel's once a night dosing formulation of sodium oxybate also known as FT218. The currently available formulation of sodium oxybate requires twice a night dosing which often poses a challenge for narcoleptics and their families. Narcolepsy, as you know, places a significant burden on functioning, psychological status, relationships and overall health.

Twice a night dosing evokes the following concerns:

- Under or overdosing as a result of patients' inability to awaken for the second dose. Or waking with too few hours remaining in bed (must have 4 hours in bed after second dose to reduce risk of adverse events).
- Patients wake for the 2nd dose groggy and posturally unstable therefore increasing risk for falls.
- Parents have concerns about the 2nd dose being accidentally diverted to a child or roommate.
- Family members sleep is often disrupted due to the 2nd dosing.

As a sleep researcher for 35 years I have been principle investigator on all drug treatment trials related to narcolepsy including but not limited to modafinil, armodafinil, sodium oxybate (twice a night and single dose formulations, solriamfetol, and pitolisant). There are other drugs in development in our lab which are promising. In addition to my professional experience with this population, my mother-in-law was narcoleptic and I personally saw the struggles with getting adequate treatment for her disease. Of all of the drugs currently available for treating narcolepsy, sodium oxybate demonstrates the highest degree of efficacy for reducing excessive sleepiness and cataplexy. It is considered a first line treatment. Having a once a night formulation would be a huge improvement over the twice, nightly dosing, reducing the complexity of managing this highly effective drug.

I urge you to consider doing what you can to expedite the orphan drug process making this formation available to patients at the earliest date possible. The clinical trials with FT 218 have demonstrated efficacy equivalence and with adverse events similar to twice a night dosing. Having an additional treatment option for narcolepsy will undoubtedly improve patient outcomes. I appreciate your consideration of this important matter.

Best regards


Russell Rosenberg, Ph.D.
Chief Science Officer and CEO

Address

5887 Glenridge Drive NE, Suite 400
Atlanta, GA 30328

Phone

(404) 851-9934

Fax

(404) 851-8458

TABLE OF CONTENTS

5.3	Exclusivity Claim – Supplemental Information in Demonstration of Clinical Superiority of FT218	2
5.3.1	FT218 Reduces Adverse Events Associated with Currently Approved Twice-Nightly Sodium Oxybate and Provides Improved Quality of Life through Uninterrupted Nighttime Sleep	3
5.3.2	FT218 Eliminates the Need for Forced Nighttime Awakenings and Provides Improved Sleep Architecture, which Is Associated with a Reduction in Cardiovascular Risk.....	5
5.3.2.1	Sleep Disturbance and Circadian Disruptions are Associated with Cardiovascular Risk.....	6
5.3.2.2	The Evidence of Reduction in Cardiovascular Risk from Consolidated Nighttime Sleep Has Clinical Significance for All Patients with Narcolepsy, Regardless of Sodium Sensitivity	8
5.3.3	FT218 Is Clinically Superior to Xywav [®] and Xyrem [®]	9
References	10

5.3 Exclusivity Claim – Supplemental Information in Demonstration of Clinical Superiority of FT218

As the Agency is aware, sodium oxybate has been approved in the United States as Xyrem[®] (sodium oxybate) oral solution (NDA 021196) and Xywav[®] (calcium, magnesium, potassium, and sodium oxybates) oral solution (NDA 212690) for the treatment of cataplexy and excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy. On June 24, 2021, Xywav[®] was found to be clinically superior to Xyrem[®] on the basis of greater safety, as the Agency determined that differences in the sodium content of the two products at the recommended doses was clinically meaningful in reducing cardiovascular morbidity in a substantial proportion of patients for whom the drug is indicated. However, both Xyrem[®] and Xywav[®] still require twice-nightly dosing, once at bedtime and once again in the middle of the night 2.5 to 4 hours later.

As discussed in Avadel CNS Pharmaceuticals, LLC's (Avadel's) NDA 214755 for Sodium Oxybate for Extended-Release Oral Suspension (FT218) ([1.3.5.3.2 Exclusivity Claim – Orphan Drug Exclusivity](#)), the once-nightly dosing regimen of FT218 provides a significant therapeutic advantage over and above the currently approved twice-nightly formulations of sodium oxybate, by providing both greater safety and a major contribution to patient care. Specifically, Avadel previously demonstrated that the twice-nightly dosing regimen, which disrupts continuous sleep by requiring a forced awakening for patients to get up and take the second dose, can result in poor compliance (which can lead to worsening efficacy and quality of life); is associated with additional adverse events (AEs) in the middle of the night (both resulting from waking up from a deep sleep state and from a second drug concentration peak that occurs in the middle of the night, which is also the C_{max} for the drug); and is highly disruptive for both patients and their partners or roommates, who may also experience disrupted sleep due to the patient's need for a middle-of-the-night alarm.

Following FDA's recent determination that Xywav[®] is clinically superior to Xyrem[®] on the basis of greater safety, Avadel submits this supplemental information to further demonstrate the clinical superiority of FT218 over both Xywav[®] and Xyrem[®].¹ Specifically, this submission provides updated clinical data in support of Avadel's prior submission and also provides additional information demonstrating that disrupted sleep and disordered sleep architecture – such as that required for effective dosing of Xywav[®] and Xyrem[®] – is associated with an increased risk of cardiovascular disease. By eliminating the necessity of a forced awakening for patients to take a second dose in the middle of the night, FT218 offers greater sleep consolidation and improved sleep architecture for narcolepsy patients, providing both greater safety and a major contribution to patient care.

¹ We note that, based on applicable legal and regulatory precedent, as will be discussed in a forthcoming letter to the Office of Orphan Products Development and the Office of the Chief Counsel, the Xywav[®] orphan drug exclusivity should not block approval or orphan drug exclusivity for FT218. As a result of FDA's finding of clinical superiority for Xywav[®], FT218 is no longer the "same drug" as Xywav[®]. Accordingly, FT218 is not blocked from approval by the Xywav[®] orphan drug exclusivity, and Avadel need only demonstrate the clinical superiority of FT218 over Xyrem[®] in order to receive its own period of orphan drug exclusivity for FT218. However, we make this additional submission for the convenience of FDA in consideration of its ongoing review, in order to definitively demonstrate the clinical superiority of FT218 over both currently approved twice-nightly sodium oxybate products.

5.3.1 FT218 Reduces Adverse Events Associated with Currently Approved Twice-Nightly Sodium Oxybate and Provides Improved Quality of Life through Uninterrupted Nighttime Sleep

As part of Avadel’s prior demonstration of clinical superiority for FT218 ([1.3.5.3.2 Exclusivity Claim – Orphan Drug Exclusivity](#)), Avadel showed the negative impact to sleep quality of the currently approved twice-nightly dosing regimen for sodium oxybate. Both Xywav[®] and Xyrem[®] have the same dosing regimen, which requires interrupted nighttime sleep for administration in compliance with labeled instructions. The necessity of a forced sleep disruption underscores the inherent harm of twice-nightly dosing for narcolepsy patients.

As discussed in the FT218 NDA, Avadel is conducting an ongoing open label extension/switch study ([CLFT218-1901](#)) known as RESTORE. The purposes of this study include assessing the long-term safety and tolerability of FT218, evaluating long-term efficacy in patients who completed Avadel’s REST-ON study, determining preference for FT218 or twice-nightly sodium oxybate in switch patients, and assessing the prior nocturnal experience with the second nightly sodium oxybate dose in switch patients. Currently, there are 67 patients enrolled in the study, 56 of which are switch patients from twice-nightly sodium oxybate to FT218 (including both Xyrem[®] and Xywav[®] switches). As this is an open label study, Avadel has conducted an interim analysis to look at twice-nightly patients’ prior experience with the second dose as well as preference for FT218 compared to twice-nightly sodium oxybate after three months of stable dosing on FT218. The current analysis is of 53 patients who have completed a [nocturnal questionnaire](#) that asked 18 questions related to their experience with the twice-nightly sodium oxybate dosing regimen over the last three months.²

Thus far, the study has found that 92% of twice-nightly patients answered that they had gotten out of bed after awakening to take their second dose of sodium oxybate. Of the patients who had gotten out of bed, 6% had a fall after awakening to take the second nightly dose, and of the patients who had a fall, 66% (2 of 3) injured themselves. In addition, 32% percent of patients reported experiencing other adverse events besides falls in the middle of the night after taking the second dose – 23% of patients answered that they experienced nausea and/or vomiting after taking the second nightly dose, and 8% of patients actively took precautionary measures (e.g., putting up gates to prevent sleep walking) in an attempt to prevent possible negative effects associated with awakening to take the second nightly dose.

In addition, the interim data from RESTORE confirm that many patients in the real-world setting are noncompliant with the requirement for a second dose, which is likely to result in decreased efficacy and a poorer quality of life. For example, the interim data shows that over the last three months, 21% of twice-nightly sodium oxybate patients intentionally missed their second nightly dose at least once, and 64% of patients missed it unintentionally (e.g., slept through the alarm). Of the patients who unintentionally missed their second dose at least once, 85% of patients

² We note that both Congress and FDA have emphasized the value of patient experience data – like that assessed in the RESTORE study and other studies discussed in this submission – in the Agency’s regulatory decision-making. See 21st Century Cures Act, Pub. L. 114-255 Sections 3001 and 3004 (2016); Eastern Research Group, Inc., *Final Report on the Assessment of the Use of Patient Experience Data in Regulatory Decision-Making* (June 18, 2021), <https://fda.report/media/150405/Assessment-of-the-Use-of-Patient-Experience-Data-in-Regulatory-Decision-Making.pdf> (FDA-commissioned third-party assessment of FDA’s use of patient experience data, required by the 21st Century Cures Act).

1.3. Administrative Information

answered that their narcolepsy symptoms were worse the next day. Consistent with this trend of dosing noncompliance, 4% of patients reported combining their first and second dose, posing a significant safety risk. Overall, 21% of patients stated they experienced anxiety related to their second nightly dose of sodium oxybate. These data underscore Avadel's previous showing, in which "Trouble Waking up for Second Dose" was the most voluminous topic discussed among "Quality of Life" conversations examined in Avadel's study of 292 consumer second-dose articles.³ In this study, "Missing Second Dose" was the second most voluminous topic, with numerous mentions of times where consumers did not wake up and missed their second dose completely.⁴

Finally, the interim RESTORE data show an overall patient preference for the benefits of once-nightly dosing, underscoring the improvement to patient care associated with FT218. As of the time of the interim analysis, 30 switch patients had completed three months of stable dosing on FT218 and completed the patient preference questionnaire. All but two patients (93%) preferred once-nightly FT218 to twice-nightly sodium oxybate. A total of seven switch patients dropped out prior to answering the preference questionnaire, but even if we assumed a worst-case scenario that all patients who dropped out would have preferred twice-nightly sodium oxybate to once-nightly FT218, 76% of patients would still have preferred FT218.⁵

When analyzing data from the four Xywav[®] patients who completed the questionnaire, results were consistent with those on Xyrem[®] and the overall group. Two of the four Xywav[®] patients got out of bed after awakening to take the second dose. One of the four Xywav[®] patients experienced nausea/vomiting with the second nightly dose. Three of the four Xywav[®] patients also unintentionally missed the second dose at least once, and all three felt worse the next day. One Xywav[®] patient experienced anxiety related to the second nightly dose. Another Xywav[®] patient answered that he/she had taken the second dose later than scheduled and then felt groggy/unsteady the next morning. Three of the four Xywav[®] patients found the second nightly dose somewhat inconvenient, while one patient found it not at all convenient.

³ See [Exclusivity Claim 1.3.5.3.2.2: Patient Experience and Perception of Second Dose](#).

⁴ See [Exclusivity Claim Figure 2: Volume and Types of Quality of Life Issues Associated with Second Nightly Dose of Xyrem[®]](#); see also [Exclusivity Claim Table 3: Examples of Xyrem[®] Patients Issues Due to a Second Nightly Dose](#) (providing quotes of real-world patient experiences with Xyrem[®] impacting sleep quality), [Exclusivity Claim Table 4: Examples of the Second Dose of Xyrem[®] Negatively Impacting a Partner/Roommate](#) (providing quotes of real-world patient experiences with Xyrem[®] impacting the sleep quality of a partner or roommate).

⁵ We note that these data are consistent with data FDA previously reviewed as part of the September 24, 2013 FDA Narcolepsy Public Meeting on Patient-Focused Drug Development, where results from a survey of 1350 individuals impacted by narcolepsy were reported; in response to a question about an ideal therapy, patients stated: "a drug that would provide consistent and adequate control of the daytime sleepiness without the hard crash and one that would require one dose taken at bedtime resulting in eight hours of restorative sleep." See [Exclusivity Claim 1.3.5.3.2.2: Patient Experience and Perception of Second Dose](#). The data are also consistent with the results of Avadel's Discrete Choice Experiment (DCE), which found that dosing frequency (once-nightly versus twice-nightly) was the single most important attribute when selecting a narcolepsy treatment, and degree of side effects experienced with the medication was the second most important driver of product choice; patients preferred a once-nightly product over a similar twice-nightly product overall and these results were statistically significant. See [Exclusivity Claim 1.3.5.3.2.5: Patient Preference](#). This abundance of data makes clear that individuals suffering from fragmented sleep and an overall sleep deficit consider the elimination of the need to carefully time and wake up for a second nighttime dose to be a substantial advancement in therapy.

The RESTORE study interim patient preference data is underscored by Avadel's recent market analysis, which found that up to 50% of narcolepsy patients who are offered twice-nightly sodium oxybate refuse it. In May-June 2021, Avadel collected data from 100 physicians (48 sleep medicine practitioners, 23 psychiatrists, and 29 neurologists) who have experience in prescribing Xyrem[®] and/or Xywav[®] and represent academic, community, and private practice, and these healthcare provider responses provide an insightful picture of both patient and clinician concerns. When asked whether having to take a sodium oxybate treatment twice a night significantly limited the number of patients willing to accept the prescription, 43% of responders strongly agreed. When asked to rate unmet needs in current narcolepsy management, impact on disrupted/disturbed nighttime sleep was the highest rated unmet need at 56%. In addition, with the potential introduction of a once-nightly sodium oxybate therapy, the physicians indicated that approximately 50% more patients would be treated with an oxybate therapy. Moreover, although having a lower sodium therapy has only been an option since this year, out of 18 specific attributes, lower sodium ranked last (46%) for factors in making treatment decisions for narcolepsy patients compared to 77% for compliance (7/18) and 86% for impact on EDS (1/18). These results are consistent with the feedback Avadel has received from patients and continue to demonstrate the significant unmet need that a once-nightly sodium oxybate could offer to patients with narcolepsy.

In sum, Avadel's ongoing data collection further supports its prior showing that FT218's once-nightly dosing regimen provides both greater safety and a major contribution to patient care over twice-nightly sodium oxybate.

5.3.2 FT218 Eliminates the Need for Forced Nighttime Awakenings and Provides Improved Sleep Architecture, which Is Associated with a Reduction in Cardiovascular Risk

FT218's once-nightly formulation is designed to give patients a full and continuous night of sleep and address the issues of missing or waking up late for a second dose. FT218's clinical study results demonstrate improved sleep architecture for narcolepsy patients – i.e., less disturbed nocturnal sleep and fewer arousals compared to placebo – and this benefit is experienced without a forced nighttime awakening to achieve complete dosing. For this submission, Avadel has conducted an additional comprehensive literature review, which demonstrates a clear association between cardiovascular risk and sleep disturbance/interruption. As discussed below, by providing consolidated nighttime sleep with once-nightly dosing, FT218 stands to provide a sodium oxybate treatment option with reduced cardiovascular risks for the narcolepsy patient population, underscoring the greater safety of a once-nightly product.

5.3.2.1 Sleep Disturbance and Circadian Disruptions are Associated with Cardiovascular Risk

As presented in the NDA, data from Avadel's REST-ON trial shows that patients on FT218 experience significant reductions in disturbed nocturnal sleep, significant decreases in the number of arousals, and significant improvement in sleep quality and the refreshing nature of sleep.⁶ Twice-nightly sodium oxybate products have also demonstrated efficacy on the cardinal symptoms of narcolepsy, but only when patients take both doses (Roth et al. 2017). As discussed above, the interim results of the RESTORE study indicate that patients on twice-nightly sodium oxybate frequently miss their second dose, which is likely to result in worsened sleep architecture and impaired sleep quality. By eliminating the forced awakenings and dosing compliance issues associated with currently approved sodium oxybate formulations, FT218 offers more consolidated nighttime sleep, with the potential to decrease cardiovascular risk for a large portion of narcolepsy patients.

The association between habitual sleep interruption and cardiovascular risk is clearly demonstrated in the clinical literature. For example, a multinational, double-blind, placebo-controlled trial evaluating 13,026 individuals with 30 days or less of acute coronary syndrome observed that obstructive sleep apnea and shift work are associated with an increased risk of cardiovascular events (Barger et al. 2017). Results obtained with a median follow-up of 2.5 years demonstrated that patients who screened positive for obstructive sleep apnea had a 12% higher risk of major coronary events than those who did not screen positive ($p=0.04$). Overnight shift work (≥ 3 night shifts/week for ≥ 1 year) was also associated with a 15% higher risk of major coronary events ($p=0.01$). The presence of multiple sleep-related risk factors (risk of obstructive sleep apnea, short sleep duration, or circadian disruption associated with shift work) led to an additive increase in risk, and individuals with all three sleep-related risk factors had a two-fold higher risk of major coronary events ($p<0.0001$).

The combination of poor sleep quality and short sleep duration in relation to cardiovascular risk has also been reported in the literature. A study of 4994 patients reporting insomnia or poor sleep observed that poor sleep quality in combination with short sleep duration as assessed by polysomnography resulted in a 29% higher risk of cardiovascular disease (Bertisch et al. 2018). Another study of 6683 individuals with no history of cardiovascular disease reported that short sleepers with poor sleep quality had a 63% higher risk of cardiovascular disease and a 79% higher risk of coronary heart disease (Hoeveraar-Blom et al. 2011).

The impact of routine circadian disruptions on cardiovascular risk is further evident in the cardiovascular risk associated with sleep disorders that result in interrupted sleep, such as restless leg syndrome (RLS) and periodic limb movements in sleep (PLMS), conditions that FDA has estimated occur in about half of patients with narcolepsy (Farkas 2013). A review of large prospective studies assessing nocturnal blood pressure observed that even small changes in nocturnal blood pressure due to interrupted sleep can alter cardiovascular risk significantly and have the potential to substantially alter cardiovascular morbidity and mortality (Calhoun and Harding 2010). Epidemiological studies have also demonstrated a statistically significant,

⁶ See 2.7.3.2.1 Summary of Clinical Efficacy – CLFT218-1501.

independent association between arousals from sleep, including from RLS or PLMS, and an increased risk of cardiovascular disease and mortality ([Jackson et al. 2015](#)).

Moreover, sleep disturbance presents elevated risks of cardiovascular disease in populations with preexisting conditions, such as individuals with Type 2 diabetes, which FDA has stated is connected to the molecular basis of narcolepsy ([Farkas 2013](#)). A review of 36,058 individuals with new-onset Type 2 diabetes aged 40 or younger observed that over a mean follow up period of 7 years, sleep disturbance was significantly associated with an increased risk of cardiovascular disease and all-cause mortality in such patients ([Choi and Choi 2020](#)). Women and middle-aged adults with Type 2 diabetes reporting sleep disturbance had a significantly higher risk of cardiovascular disease than those without, and the risk of all-cause mortality significantly increased in men and older adults with sleep disturbance than those without sleep disturbance.

Habitual sleep disturbance is also associated with an increased risk of heart attack, stroke, and coronary artery disease. Data from 138,201 individuals collected from the 2006 Behavioral Risk Factor Surveillance System, a U.S.-wide telephone interview survey conducted by the Centers for Disease Control and Prevention, was analyzed to observe statistically significant associations between sleep duration and obesity, myocardial infarction, and coronary artery disease in fully adjusted models that took into account physical health ([Grandner et al. 2012](#)). A 2018 literature review analyzing the association between circadian rhythm disorders and stroke reported a cohort study of 80,108 nurses where rotating night shift work was associated with a 4% increased risk of ischemic stroke for every 5 years of exposure, after adjusting for standard vascular risk factors ([Koo et al. 2018](#); [Brown et al. 2009](#)). This literature review observed that the sleep disturbance caused by night shift work is associated with significant interference with the endogenous decline of blood pressure during rest, resulting in abnormally elevated blood pressure during the period of disturbance that persists into the following day. Further, a separate cohort study evaluating 52,599 individuals observed that sleep duration trajectories with lower or unstable patterns may be associated with risks of first cardiovascular events and all-cause mortality ([Wang et al. 2020](#)). A cross-sectional data analysis of 36,480 Brazilian adults also observed that sleep disturbance was associated with decreased cardiovascular health ([Velazquez-Melendez et al. 2021](#)). The association between sleep disturbance and increased cardiovascular risk was further observed in a study evaluating 4104 Canadian adolescents, where multivariable regression models reported that a higher sleep disturbance score was associated with increased odds of being at high cardiovascular risk, increased odds of hypertension, and increased odds of elevated non-high density lipoprotein (HDL) cholesterol ([Narang et al. 2012](#)).

Finally, poor sleep architecture as a result of nighttime awakenings has been shown to be associated with a higher risk of cardiovascular disease. In a study of 3565 patients where sleep architecture was monitored by polysomnography with concomitant blood pressure measurements, the authors found that reduced REM sleep was associated with higher visit-to-visit blood pressure variability and associated increased risk of cardiovascular disease, independent of potential confounders including other sleep characteristics (like total sleep time and obstructive sleep apnea) ([Liu et al. 2020](#)). Changes in sleep quality overall have also been shown to result in increased blood pressure during the following days ([Jafari 2017](#)). In a study of 6184 participants across the U.S. where sleep regularity was assessed by actigraphy and patients were monitored for a five-year follow-up period, irregular sleep duration and timing was identified as an independent risk factor for cardiovascular disease, where individuals who had the most irregular sleep had a more than two-fold increase in the risk of developing cardiovascular

disease over the follow-up period, independent of other risk factors (Huang et al. 2020). An additional study of sleep architecture in hemodialysis patients also showed that reduction of REM sleep latency is associated with a higher rate of new-onset cardiovascular disease events (Shoji et al. 2021). Frequent nighttime awakening and decreased REM sleep has also been consistently linked to prevalent and incident atrial fibrillation (Christensen 2018).

These studies collectively demonstrate the clear association between sleep disruption and cardiovascular risk. This risk remains a concern for all intended patient populations reliant upon Xyrem[®] and Xywav[®] that, out of necessity, must accept the twice-nightly dosing regimen. This dosing regimen and its forced awakenings will *never* allow patients to have normal sleep architecture, increasing the cardiovascular risk indefinitely. However, FT218's unique pharmacokinetic profile makes sleep architecture more normal, with increasing doses leading to increased scores on the Maintenance of Wakefulness Test (MWT) and Epworth Sleep Scale (ESS).⁷ As a result, sleep architecture for patients on FT218 is increasingly normalized over time, posing a potential reduction in cardiovascular risk, and improvement in quality of life, through consolidated nighttime sleep.

5.3.2.2 The Evidence of Reduction in Cardiovascular Risk from Consolidated Nighttime Sleep Has Clinical Significance for All Patients with Narcolepsy, Regardless of Sodium Sensitivity

On June 24, 2021, Xywav[®] was found to be clinically superior to Xyrem[®] on the basis of greater safety based on an FDA finding that the differences in the sodium content of the two products at the recommended doses was clinically meaningful in reducing cardiovascular morbidity in a substantial proportion of patients for whom the drug is indicated. Based on correspondence between Avadel and the Office of Orphan Products Development (OOPD), we understand this determination was based on a recent publication by the National Academies of Sciences, Engineering, and Medicines (National Academies) regarding dietary reference intakes for sodium and potassium, and the most recent dietary guidelines published by the U.S. Department of Agriculture (USDA), both of which recommend daily salt intake restrictions for the general U.S. adult population. These resources were sufficient to find clinical superiority of Xywav[®] on the basis of greater safety due to the lower sodium content, despite a lack of clinical or real-world evidence showing that the sodium content of Xyrem[®] increases cardiovascular risks in patients with narcolepsy.

Unlike OOPD's reliance on the National Academies and USDA resources to establish a link between reduced sodium content and greater safety as a general matter, Avadel has relied on data specific to twice-nightly sodium oxybate products in demonstrating that once-nightly FT218 provides greater safety than both Xyrem[®] and Xywav[®].⁸ Moreover, as set forth in this

⁷ See [NDA 2.7.3.2.1 Summary of Clinical Efficacy – CLFT218-1501](#).

⁸ See [Exclusivity Claim 1.3.5.3.2.1: Risk of Nocturnal Falls and Other Adverse Events Associated with Second Dose](#) (describing Avadel's review of the FDA Adverse Event Reporting System (FAERS) database for cases of patient falls and other AEs associated with awakening for the second nightly dose of Xyrem[®]); [Exclusivity Claim 1.3.5.3.2.2: Patient Experience and Perception of Second Dose](#) (describing Avadel's literature study of patient experiences and perceptions associated with the second nightly Xyrem[®] dose); [Exclusivity Claim 1.3.5.3.2.6 & Appendix 2: Statements from Stakeholders](#) (providing statements from key opinion leaders, patient advocacy

submission, the association between sleep disruption (such as forced nighttime awakenings) and cardiovascular risk has been well-established in the clinical literature, with numerous studies of large patient populations observing statistically significant associations between habitual sleep disturbance/poor sleep architecture and cardiovascular risk. Together, this expansive scientific dataset demonstrates evidence of the increased cardiovascular risk inherent to the twice-nightly dosing regimen of Xywav[®] and Xyrem[®].

Importantly, the evidence underlying the clear association between impaired sleep quality and increased cardiovascular risk has clinical significance for the entire narcolepsy patient population, not just those who are sodium-sensitive. As FDA is aware, the Xyrem[®] label bears a warning regarding use in patients sensitive to high sodium intake, which states: “Xyrem has a high salt content. In patients sensitive to salt intake (e.g., those with heart failure, hypertension, or renal impairment), consider the amount of daily sodium intake in each dose of Xyrem” (Xyrem Prescribing Information 2020). While the Xywav[®] label was not required to bear this warning, the continued warning on the Xyrem[®] label in lieu of a contraindication for sodium-sensitive patients represents FDA’s conclusion that while the sodium content of Xyrem[®] may be of concern for sodium-sensitive patients, use of Xyrem[®] may still be appropriate for these patients, as well as for the non-sodium-sensitive population. It follows, then, that a once-nightly product, which poses potential cardiovascular benefits through consolidated nighttime sleep to all patients, regardless of sodium sensitivity, stands to provide a clinically significant improvement to overall patient safety. Additionally, since the sleep interruption required for the second dose of Xywav[®] and Xyrem[®] is also often experienced by patients’ partners, roommates, and other caregivers who may be assisting patients with properly administering the second dose, FT218’s ability to provide uninterrupted, restful sleep has the potential to decrease the cardiovascular risk of both patients and these other impacted individuals, offering a much broader benefit than the population potentially benefitting from the lower sodium content of Xywav[®].

5.3.3 FT218 Is Clinically Superior to Xywav[®] and Xyrem[®]

The once-nightly dosing regimen of FT218 is clinically superior to the currently approved twice-nightly formulations of Xywav[®] and Xyrem[®] by providing both greater safety and a major contribution to patient care. The option of a sodium oxybate treatment with a once-nightly dosing regimen removes the necessity of disrupted sleep and disordered sleep architecture associated with a forced awakening to take a second nightly dose and frequent noncompliance with the second dose, posing a potential cardiovascular safety benefit across the entire patient population. The interruption of sleep that is required for proper administration of Xywav[®] and Xyrem[®] negatively impacts not only the quality of life of patients, but also partners and roommates, all burdened by the twice-nightly dosing schedule that presents a cumulative increased cardiovascular risk. Furthermore, data from the ongoing RESTORE study shows a solid patient preference for FT218 compared to twice-nightly products, underscoring how once-nightly FT218 provides patients with improved sleep quality for a more restful, restorative sleep. Avadel has demonstrated the clear clinical superiority of FT218 warranting orphan drug exclusivity upon approval.

groups, and other stakeholders in the narcolepsy field regarding the negative impact of twice-nightly sodium oxybate formulations and the anticipated benefits of a once-nightly option).

References

- L. Barger, et al. (2017), *Short Sleep Duration, Obstructive Sleep Apnea, Shiftwork, and the Risk of Adverse Cardiovascular Events in Patients after an Acute Coronary Syndrome*, J. Am. Heart Assoc. 6: e006959
- S. Bertisch, et al. (2018), *Insomnia with Objective Short Sleep Duration and Risk of Incident Cardiovascular Disease and All-Cause Mortality: Sleep Heart Health Study*, Sleep J. 41(6): 1-9
- D. Brown, et al. (2009), *Rotating Night Shift Work and the Risk of Ischemic Stroke*, Am. J. Epidemiol. 169(11): 1370-1377
- D. Calhoun and S. Harding (2010), *Sleep and Hypertension*, Chest 138(2): 434-443
- M. Christensen (2018), *Sleep Characteristics that Predict Atrial Fibrillation*, Heart Rhythm 15(9): 1289-1295
- Y. Choi and J. Choi (2020), *Association of Sleep Disturbance with Risk of Cardiovascular Disease and All-Cause Mortality in Patients with New-Onset Type 2 Diabetes: Data from the Korean NHIS-HEALS*, Cardiovasc. Diabetol. 19: 61-68
- R. Farkas (2013), "Background on Narcolepsy and Therapeutic Options," Presentation at the FDA Neurology Public Meeting on Patient-Focused Drug Development, Sept. 24, 2013
- M. Grandner, et al. (2012), *Sleep Disturbance Is Associated with Cardiovascular and Metabolic Disorders*, J. Sleep Res. 21: 427-433
- M. Hoevenaar-Blom, et al. (2011), *Sleep Duration and Sleep Quality in Relation to 12-Year Cardiovascular Disease Incidence: The MORGEN Study*, Sleep 34(11): 1487-1492
- T. Huang, et al. (2020), *Sleep Irregularity and Risk of Cardiovascular Events: The Multi-Ethnic Study of Atherosclerosis*, J. Am. Coll. Cardio. 75(9): 991-999
- C. Jackson, et al. (2015), *Sleep as a Potential Fundamental Contributor to Disparities in Cardiovascular Health*, Ann. Rev. Public Health 36: 417-440
- B. Jafari (2017), *Sleep Architecture and Blood Pressure*, Sleep Med. Clin. 12: 161-166
- D. Koo, et al. (2018), *Sleep Disturbances as a Risk Factor for Stroke*, J. Stroke 20(1): 12-32
- X. Liu, et al. (2020), *Visit-to-Visit Blood Pressure Variability and Sleep Architecture*, J. Clin. Hypertens. 23: 323-330
- I. Narang, et al. (2012), *Sleep Disturbance and Cardiovascular Risk in Adolescents*, CMAJ 184(17): E913-E920
- T. Roth, et al. (2017), *Effect of Sodium Oxybate on Disrupted Nighttime Sleep in Patients with Narcolepsy*, J. Sleep Research 26: 407-414

1.3. Administrative Information

S. Shoji, et al. (2021), *REM Sleep Latency as an Independent Risk for Cardiovascular Events in Hemodialysis Patients*, *Physiological Reports* 9: e14837

G. Velazquez-Melendez, et al. (2021), *Association of Self-Reported Sleep Disturbances with Ideal Cardiovascular Health in Brazilian Adults: A Cross-sectional Population-Based Study*, *Sleep Health* 7: 183-190

Y. Wang, et al. (2020), *Association of Longitudinal Patterns of Habitual Sleep Duration with Risk of Cardiovascular Events and All-Cause Mortality*, *JAMA Net. Open* 3(5): e205246

Xyrem Prescribing Information (Rev. Sept. 2020)



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Office of Orphan Products Development
Food and Drug Administration
10903 New Hampshire Avenue
WO32-5295
Silver Spring, MD 20993

May 9, 2016

The Weinberg Group Inc.
1129 Twentieth St., NW, Suite 600
Washington, DC 20036

Attention: Marla Scarola, MS
Senior Consultant

Dear Ms. Scarola:

This letter acknowledges receipt of your orphan-drug designation request submitted on behalf of Flamel Ireland Limited pursuant to section 526 of the Federal, Food, Drug, and Cosmetic Act (21 U.S.C. 360bb) for the following:

Name: sodium oxybate for extended-release oral suspension

Disease or Condition: Treatment of cataplexy and excessive daytime sleepiness in narcolepsy.

Date of request: April 20, 2016

Date of receipt: April 20, 2016

Designation request number: 16-5302

We will correspond with you after we have completed our review of the request.

All communications concerning the request should be identified with the above designation request number. If you have any questions, please call me at 301-796-8685 or alternatively at 301-796-8660.

Sincerely,


Mary L. Grice
Designation Coordinator

cc:

OOPD/File # 16-5302
OOPD/Chron

History:
Jdb5/9/16
ACKNOWLEDGEMENT



**DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Office of Orphan Products Development**

Exclusivity Memorandum

Date:	See electronic signature date
From:	Roberta Szydlo, RPh, MBA, Senior Program Management Officer
Through:	Henry Startzman III, MD, Director, Orphan Drug Designation Program Aaron Friedman, JD, Associate Director for Policy
To File #:	DRU-2016-5302
Name of drug or biologic:	Lumryz (sodium oxybate) for extended-release oral suspension
Orphan designation:	Treatment of narcolepsy
Designation date:	01/08/2018
Sponsor name:	Flamel Ireland Limited dba Avadel Ireland
NDA, sNDA, BLA, or sBLA #:	NDA 214755
Approval date:	05/01/2023
Approved indication:	Treatment of cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy

Is the approval within scope of designation?	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>		
Comments:	The approved indication for Lumryz above is within the scope of the orphan-drug designation for the treatment of narcolepsy.		
Has the same drug or biologic been previously approved?	Yes <input type="checkbox"/> No <input type="checkbox"/>	Is the drug or biologic a New Molecular Entity (NME) or New Biological Entity (NBE)?	Yes <input type="checkbox"/> No <input type="checkbox"/>
Comments:	See appended memo and consults for analysis regarding Lumryz's eligibility for its own term of ODE. We note that the appended documents also address Lumryz's approvability in light of Xywav's unexpired ODE, but the analysis also includes FDA's decision regarding Lumryz's eligibility for its own term of ODE.		
Has the same drug or biologic already been approved for the same indication?	Yes <input type="checkbox"/> No <input type="checkbox"/>		
Comments:	See appended memo and consults for analysis regarding Lumryz's eligibility for its own term of ODE. We note that the appended documents also address Lumryz's approvability in light of Xywav's unexpired ODE, but the analysis also includes FDA's decision regarding Lumryz's eligibility for its own term of ODE.		
Has clinical superiority been demonstrated?	Yes <input type="checkbox"/> No <input type="checkbox"/> Not Applicable <input type="checkbox"/>		
Comments:	See appended memo and consults for analysis regarding Lumryz's eligibility for its own term of ODE. We note that the appended documents also address Lumryz's approvability in light of Xywav's unexpired ODE, but the analysis also includes FDA's decision regarding Lumryz's eligibility for its own term of ODE.		
Recommendation:	Recognize Exclusivity: Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Lumryz (sodium oxybate) for extended-release oral suspension is eligible for orphan-drug exclusivity for the treatment of cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy.		

Additional comments (optional):
--



Office of Orphan Products Development
Food and Drug Administration
10903 New Hampshire Avenue
WO32-5271
Silver Spring, MD 20993

ProPharma Group
1129 20th Street Northwest
Suite 600
Washington, DC 20036

Attention: Marla Scarola, MS
US Agent for Flamel Ireland Limited dba Avadel Ireland
marla.scarola@propharma.com

Re: Orphan-drug designation DRU-2019-7038

Dear Ms. Scarola:

This letter refers to your oxybate drug that was designated as a drug for a rare disease or condition pursuant to section 526 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360bb) on January 8, 2018, for “treatment of narcolepsy.” We also refer to the letter from the Center for Drug Evaluation and Research, dated May 1, 2023, approving New Drug Application (NDA 214755) for Lumryz (sodium oxybate).

Lumryz is eligible for seven years of orphan-drug exclusive approval pursuant to section 527 of the FD&C Act (21 U.S.C. 360cc) for *treatment of cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy*. The period of exclusive approval expires seven years after May 1, 2023, the date of approval of the NDA 214755. The scope of orphan-drug exclusive approval is described under 21 CFR 316.31.

In accordance with section 527(e)(2) of the FD&C Act (21 U.S.C. 360cc(e)(2)), FDA’s summary of the clinical superiority finding will be posted at <https://www.fda.gov/orphan>.

It is the sponsor’s responsibility to assure the availability of sufficient quantities of this drug to meet the needs of patients. Failure to do so could result in the withdrawal of the drug’s exclusive approval as stipulated under 21 CFR 316.36(b).

Flamel Ireland Limited dba Avadel Ireland

Should you have any questions, please contact our office by phone at 301-796-8660 or by email at orphan@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Director
Office of Orphan Products Development



Sandra Retzky

Digitally signed by Sandra Retzky

Date: 5/1/2023 12:08 PM EDT
GUID: 51403



THE WEINBERG GROUP®

VIA FEDEX

July 24, 2017

Gayatri R. Rao, M.D., J.D.
Director, Office of Orphan Products Development
Food and Drug Administration
10903 New Hampshire Avenue
WO32-5295
Silver Spring, MD 20993-0002

RECEIVED

JUL 24 2017

Office of Orphan
Products Development

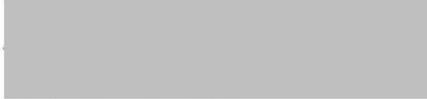
**RE: Designation request # 16-5302: Sodium Oxybate for Extended-Release Oral Suspension (FT218) for the treatment of cataplexy and excessive daytime sleepiness in narcolepsy
SN0002: Request for Extension**

Dear Dr. Rao:

On behalf of Flamel Ireland Limited doing business as Avadel Ireland (Avadel), we respectfully request an extension to the pending Request for Orphan Drug Designation for Sodium Oxybate for Extended-Release Oral Suspension (FT218) for the treatment of cataplexy and excessive daytime sleepiness in narcolepsy (please refer to Designation request # 16-5302). The pending application is scheduled to be withdrawn on August 23, 2017. With a Phase 3 trial underway, Avadel has developed relationships with a number of Key Opinion Leaders (KOLs) in the field of narcolepsy. We are currently preparing an amendment to the designation request presenting the opinions of the KOLs regarding FT218's superiority over a similar already-approved sodium oxybate product with orphan drug status. We request a four-month extension allowing for a response by December 23, 2017.

Should any questions arise, please do not hesitate to contact me. I can be reached via telephone at 202.730.4129 or by email at marla.scarola@weinberggroup.com.

Very truly yours,


Marla Scarola, MS
Senior Consultant
The Weinberg Group Inc.

MES/ms



VIA FEDEX

October 13, 2017

RECEIVED

OCT 13 2017

Office of Orphan
Products Development

Gayatri R. Rao, M.D., J.D.
Director, Office of Orphan Products Development
Food and Drug Administration
10903 New Hampshire Avenue
WO32-5295
Silver Spring, MD 20993-0002

**RE: Orphan Drug Designation #16-5302
Request for Orphan Drug Designation for Sodium Oxybate for Extended-Release Oral Suspension (FT218)
Indication: For the treatment of cataplexy and excessive daytime sleepiness in narcolepsy**

Dear Dr. Rao:

On behalf of Flamel Ireland Limited dba Avadel Ireland (Avadel), enclosed please find two (2) archival, electronic copies (CD) of an amendment to Avadel's "Request for Orphan Drug Designation" for Sodium Oxybate for Extended-Release Oral Suspension (FT218), originally submitted on April 20, 2016. Avadel also makes reference to the amendment submitted on May 13, 2016, the Office of Orphan Products Development's (OOPD's) response dated August 23, 2016 that orphan status was not granted, and the request for an extension submitted on July 21, 2017.

In the original request, Avadel argued that FT218 provides a major contribution to patient care over the similar already-approved sodium oxybate product (Xyrem®, NDA 021196). In the response to the request, OOPD acknowledged that the proposed dosing regimen of FT218 is more convenient to the patient and/or caregivers than that of Xyrem®. However, the reduction in dosing frequency was not considered a major contribution to patient care. Avadel is now submitting letters from four Key Opinion Leaders (KOLs) in the field of narcolepsy describing their experiences with narcolepsy patients and how they expect a reduction in dosing frequency to impact their patients. The following attachments are provided:

- Letter from Dr. Lois Krahn
- Letter from Dr. Meir Kryger
- Letter from Dr. Thomas Roth
- Patient survey from Dr. Thomas Roth
- Letter from Dr. Todd Swick
- CV of Dr. Lois Krahn

Gayatri Rao, M.D., J.D.

October 13, 2017

Page 2

- CV of Dr. Meir Kryger
- CV of Dr. Thomas Roth
- CV of Dr. Todd Swick

On the basis of these KOL letters, Avadel respectfully requests that OOPD reconsider the determination that FT218 does not provide a major contribution to patient care over Xyrem®.

Should any questions arise, please do not hesitate to contact me. I can be reached via telephone at 202.730.4129 or by email at marla.scarola@weinberggroup.com.

Very truly yours,



Marla Scarola, MS
Senior Consultant
The Weinberg Group Inc.

MES/al

Enclosures



Curriculum Vitae and Bibliography

Lois F Krahn MD

(b) (6)

Present Academic Rank and Position

- Consultant** - Division of Adult Psychiatry, Department of Psychiatry & Psychology, Mayo Clinic, Scottsdale, Arizona 2003 - Present
- Consultant (Joint Appointment)** - Division of Pulmonary Medicine, Department of Internal Medicine, Mayo Clinic, Scottsdale, Arizona 2003 - Present
- Professor of Psychiatry** - Mayo Clinic College of Medicine and Science 04/2006 - Present
- Chair** - Mayo Clinic Arizona Committees, Executive Operations Team - Arizona, Personnel Committee, Mayo Clinic, Scottsdale, Arizona 2009 - Present
- Chair** - Education Committee, Division of Education Services, Department of Administration, Mayo Clinic, Scottsdale, Arizona 2010 - Present
- Director** - Division of Education Services, Department of Administration, Mayo Clinic, Scottsdale, Arizona 08/2010 - Present
- Arizona Ombudsman** - Department of Education Administration, Mayo Clinic College of Medicine and Science, Scottsdale/Phoenix, Arizona 2013 - Present

(b) (6)

Certification

Board Certifications

American Board of Psychiatry and Neurology (ABPN)

- Psychiatry 1994 - 2013
- Psychiatry/Addiction Psychiatry 1997 - 2007
- Psychiatry/Geriatric Psychiatry 1995 - 2014

Psychiatry/Psychosomatic Medicine	2005 - 2015
Psychiatry/Sleep Medicine	2007 - 2017

American Board of Sleep Medicine

Sleep Medicine	1997 - Present
----------------	----------------

National Board of Medical Examiners (NBME)

Diplomate	1990 - Present
-----------	----------------

Mayo Clinic Quality Academy

Mayo Clinic Quality Fellow: Bronze Level Certification	2010
--	------

Licensure

Virginia	(Medical)	07/1989 - 1991
District of Columbia	(Medical)	01/1991 - 1992
Maryland	(Medical)	07/1991 - 1992
Minnesota	(Medical)	09/1992 - Present
Florida	(Medical)	10/1995 - Present
Arizona	(Medical)	01/2003 - Present

Honors and Awards

Hugh H. Hussey Award for excellence in medical student training by a Resident in Psychiatry - Georgetown University School of Medicine	1992
Research Award for Outstanding Resident Paper, "Sleep Assessment of Psychiatric Inpatients: Correlation of Patient Subjective Report, Nursing Assessment, and Wrist Actigraphy Recording" - Academy of Psychosomatic Medicine	1993
Dista Fellowship Award - Society of Biological Psychiatry	1994
Howard Rome Academic Writing Award presented annually to the author of the best paper written by a Mayo Graduate School of Medicine Psychiatry Resident - Awarding Organization	1994
New Investigator Travel Award - National Institute of Mental Health sponsored New Clinical Drug Evaluation Unit (NCDEU) Meeting	1994
Teacher of the Year - Department of Psychiatry & Psychology, Mayo Clinic	1995
Junior Faculty Award - Association for Academic Psychiatry	1996
Teacher of the Year - Department of Psychiatry & Psychology, Mayo Clinic	1997
Exemplary Psychiatrist Award - National Alliance for the Mentally Ill	1998
Teacher of the Year - Department of Psychiatry & Psychology, Mayo Clinic	1999
Teacher of the Year "Hall of Fame" - Mayo Clinic	1999
Regional Teaching Award - Association for Academic Psychiatry	2000
11th Annual Nancy C.A. Roeske Certificate of Recognition for Excellence in Medical School Teaching - American Psychiatric Association	2001
Regional Teaching Award, Region VIII - Academy of Academic Psychiatry	2001
Faculty Service Award - Mayo Medical School, Mayo Clinic College of Medicine	2002
Distinguished Educator Award - Department of Psychiatry & Psychology, Mayo Clinic	2003
MacMillan Leadership Scholarship - Whitney E. and Elizabeth S. MacMillan Management Scholars Program, Mayo Foundation	2004 - 2006
Faculty Service Award - Mayo Medical School, Mayo Clinic College of Medicine	2008

Bibliography

Peer-reviewed Articles

1. Cohen CG, **Krahn L**, Wise TN, Epstein S, Ross R. Delusions of disfigurement in a woman with acne rosacea. *Gen Hosp Psychiatry*. 1991 Jul; 13(4):273-7. PMID:1831428
2. **Krahn LE**, Goldberg RL. Psychotropic medications and the skin. *Adv Psychosom Med*. 1994; 21:90-106. PMID:7801829
3. Zimmermann RC, **Krahn L**, Klee G, Delgado P, Ory SJ, Lin SC. Inhibition of presynaptic catecholamine synthesis with alpha-methyl-para-tyrosine attenuates nocturnal melatonin secretion in humans. *J Clin Endocrinol Metab*. 1994 Oct; 79(4):1110-4. PMID:7962283 DOI:10.1210/jcem.79.4.7962283
4. Epstein SA, **Krahn L**, Clauw DJ, Gomes AP, Weigert S, Goldberg RL. Psychiatric aspects of the eosinophilia-myalgia syndrome. *Psychosomatics*. 1995 Jan-Feb; 36(1):22-5. PMID:7871130
5. **Krahn LE**, Rummans TA, Sharbrough FW, Jowsey SG, Cascino GD. Pseudoseizures after epilepsy surgery. *Psychosomatics*. 1995 Sep-Oct; 36(5):487-93. PMID:7568657
6. Rummans TA, Evans JM, **Krahn LE**, Fleming KC. Delirium in elderly patients: evaluation and management. *Mayo Clin Proc*. 1995 Oct; 70(10):989-98. PMID:7564554 DOI:10.1016/S0025-6196(11)64380-2
7. Chabolla DR, **Krahn LE**, So EL, Rummans TA. Psychogenic nonepileptic seizures. *Mayo Clin Proc*. 1996 May; 71(5):493-500. PMID:8628032 DOI:10.1016/S0025-6196(11)64094-9
8. Zimmermann RC, **Krahn L**, Klee G, Lu PY, Ory SJ, Lin SC. The impact of gender on alpha-methyl-para-tyrosine mediated changes in prolactin secretion and 6-hydroxymelatonin sulfate excretion. *Psychoneuroendocrinology*. 1996 Jul; 21(5):469-78. PMID:8888369
9. **Krahn LE**, Lu PY, Klee G, Delgado PR, Lin SC, Zimmermann RC. Examining serotonin function: a modified technique for rapid tryptophan depletion. *Neuropsychopharmacology*. 1996 Oct; 15(4):325-8. PMID:8887985 DOI:10.1016/0893-133X(95)00273-G
10. Reeves AL, So EL, Sharbrough FW, **Krahn LE**. Movement disorders associated with the use of gabapentin. *Epilepsia*. 1996 Oct; 37(10):988-90. PMID:8822698
11. **Krahn LE**, Rummans TA, Peterson GC. Psychiatric implications of surgical treatment of epilepsy. *Mayo Clin Proc*. 1996 Dec; 71(12):1201-4. PMID:8945496 DOI:10.1016/S0025-6196(11)64706-X
12. MacMorran WS, **Krahn LE**. Adverse cutaneous reactions to psychotropic drugs. *Psychosomatics*. 1997 Sep-Oct; 38(5):413-22. PMID:9314710
13. **Krahn LE**, Lee J, Richardson JW, Martin MJ, O'Connor MK. Hypokalemia leading to torsades de pointes. Munchausen's disorder or bulimia nervosa? *Gen Hosp Psychiatry*. 1997 Sep; 19(5):370-7. PMID:9328782
14. **Krahn LE**, Reese MM, Rummans TA, Peterson GC, Suman VJ, Sharbrough FW, Cascino GD. Health care utilization of patients with psychogenic nonepileptic seizures. *Psychosomatics*. 1997 Nov-Dec; 38(6):535-42. PMID:9427850
15. **Krahn LE**, Lin SC, Wisbey J, Rummans TA, O'Connor MK. Assessing sleep in psychiatric inpatients: nurse and patient reports versus wrist actigraphy. *Ann Clin Psychiatry*. 1997 Dec; 9(4):203-10. PMID:9511943
16. Sutor B, Rummans TA, Jowsey SG, **Krahn LE**, Martin MJ, O'Connor MK, Philbrick KL, Richardson JW. Major depression in medically ill patients. *Mayo Clin Proc*. 1998 Apr; 73(4):329-37. PMID:9559036

17. Zimmermann RC, **Krahn L**, Rahmanie N, Sauer MV. Prolonged inhibition of presynaptic catecholamine synthesis does not alter leptin secretion in normal-weight men women. *Hum Reprod*. 1998 Apr; 13(4):822-825. PMID:9619531
18. **Krahn LE**, Santoscoy G, Van Loon JA. A schizophrenic patient's attempt to resume dialysis following renal transplantation. *Psychosomatics*. 1998 Sep-Oct; 39(5):470-3. PMID:9775708
19. **Krahn LE**, Maraganore DM, Michels VV. Childhood-onset schizophrenia associated with parkinsonism in a patient with a microdeletion of chromosome 22. *Mayo Clin Proc*. 1998 Oct; 73(10):956-9. PMID:9787744 DOI:10.4065/73.10.956
20. Takahashi PY, **Krahn L**. Case report: delusions of parasitosis as an unusual presenting feature of dementia. *Ann Long-Term Care*, 1999; 7(4):153-155.
21. **Krahn LE**, Lin SC, Klee GG, Lu PY, Ory SJ, Zimmermann RC. The effect of presynaptic catecholamine depletion on 6-hydroxymelatonin sulfate: a double blind study of alpha-methyl-para-tyrosine. *Eur Neuropsychopharmacol*. 1999 Jan; 9(1-2):61-6. PMID:10082229
22. Goodman JA, **Krahn LE**, Smith GE, Rummans TA, Pileggi TS. Patient satisfaction with electroconvulsive therapy. *Mayo Clin Proc*. 1999 Oct; 74(10):967-71. PMID:10918861 DOI:10.4065/74.10.967
23. **Krahn LE**, Boeve B, Olsen E, Herold D, Silber M. A standardized test for cataplexy. *Sleep Med*. 2000; 1:125-30. PMID:10767653
24. **Krahn LE**. Current issues in diagnosis and treatment of narcolepsy. *Directions in Psychiatry*. 2000; 20:255-64. PMID:0
25. Saad DA, Black JL 3rd, **Krahn LE**, Rummans TA. ECT post eye surgery: two cases and a review of the literature. *J ECT*. 2000 Dec; 16(4):409-14. PMID:11314879
26. Gursky JT, **Krahn LE**. The effects of antidepressants on sleep: a review. *Harv Rev Psychiatry*. 2000 Dec; 8(6):298-306. PMID:11133824
27. **Krahn LE**, Gleber E, Rummans TA, Pileggi TS, Lucas DL, Li H. The effects of electroconvulsive therapy on melatonin. *J ECT*. 2000 Dec; 16(4):391-8. PMID:11314877
28. **Krahn LE**, Moore WR, Altchuler SI. Narcolepsy and obesity: remission of severe cataplexy with sibutramine. *Sleep Med*. 2001 Jan; 2(1):63-5. PMID:11152984
29. **Krahn LE**, Hanson CA, Pileggi TS, Rummans TA. Electroconvulsive therapy and cardiovascular complications in patients taking trazodone for insomnia. *J Clin Psychiatry*. 2001 Feb; 62(2):108-10. PMID:11247094
30. **Krahn LE**, Black JL, Silber MH. Narcolepsy: new understanding of irresistible sleep. *Mayo Clin Proc*. 2001 Feb; 76(2):185-94. PMID:11213307 DOI:10.1016/S0025-6196(11)63126-1
31. Worrel LM, **Krahn LE**, Sletten CD, Pond GR. Treating fibromyalgia with a brief interdisciplinary program: initial outcomes and predictors of response. *Mayo Clin Proc*. 2001 Apr; 76(4):384-90. PMID:11322354 DOI:10.4065/76.4.384
32. Zimmermann RC, **Krahn LE**, Klee GG, Ditkoff EC, Ory SJ, Sauer MV. Prolonged inhibition of presynaptic catecholamine synthesis with alpha-methyl-para-tyrosine attenuates the circadian rhythm of human TSH secretion. *J Soc Gynecol Investig*. 2001 May-Jun; 8(3):174-8. PMID:11390253
33. **Krahn LE**, Hansen MR, Shepard JW. Pseudocataplexy. *Psychosomatics*. 2001 Jul-Aug; 42(4):356-8. PMID:11496028

34. Black JL, **Krahn LE**, Jalal SM. Voltage-gated calcium channel gamma 2 subunit gene is not deleted in velo-cardio-facial syndrome. *Mol Psychiatry*. 2001 Jul; 6(4):461-4. PMID:11443534 DOI:10.1038/sj.mp.4000868
35. Malik S, Boeve BF, **Krahn LE**, Silber MH. Narcolepsy associated with other central nervous system disorders. *Neurology*. 2001 Aug 14; 57(3):539-41. PMID:11502932
36. Augustine K, Cameron B, Camp J, **Krahn L**, Robb R. An immersive simulation system for provoking and analyzing cataplexy. *Stud Health Technol Inform*. 2002; 85:31-7. PMID:15458056
37. Silber MH, **Krahn LE**, Olson E. Diagnosing narcolepsy: validity and reliability of new diagnostic criteria. *Sleep Med*. 2002; 3:109-13. PMID:14592228
38. **Krahn LE**. Enigmatic patients: factitious disorder with physical symptoms. *Directions in Psychiatry*. 2002; 22:217-23. PMID:0
39. **Krahn LE**. Excessive daytime sleepiness: a psychiatric perspective. *Current Psychiatry*. 2002; 1(1):49-57. PMID:0
40. **Krahn LE**, Boeve BF, Oliver L, Silber MH. Hypocretin (orexin) and melatonin values in a narcoleptic-like sleep disorder after pinealectomy. *Sleep Med*. 2002; 3(6):521-3. PMID:14592149
41. **Krahn LE**, Hansen MR, Tinsley JA. Psychiatric residents' exposure to the field of sleep medicine: A survey of psychiatric program directors. *Academic Psychiatry*. 2002; 26:253-6. PMID:12824128
42. Lapid MI, Hall-Flavin DK, Cox LS, Lichty EJ, **Krahn LE**. Smokeless tobacco use among addiction patients: a brief report. *J Addict Dis*. 2002; 21(2):27-33. PMID:11916370
43. **Krahn LE**, Bostwick JM, Sutor B, Olsen MW. The challenge of empathy: a pilot study of using standardized patients to teach introductory psychopathology to medical students. *Academic Psychiatry*. 2002; 26:26-30. PMID:11867425
44. Silber MH, **Krahn LE**, Olson EJ, Pankratz VS. The epidemiology of narcolepsy in Olmsted County, Minnesota: a population-based study. *Sleep*. 2002 Mar 15; 25(2):197-202. PMID:11902429
45. Kung S, Mueller PS, Geda YE, **Krahn LE**. Delirium resulting from paraneoplastic limbic encephalitis caused by Hodgkin's disease. *Psychosomatics*. 2002 Nov-Dec; 43(6):498-501. PMID:12444235
46. **Krahn LE**, Pankratz VS, Oliver L, Boeve BF, Silber MH. Hypocretin (orexin) levels in cerebrospinal fluid of patients with narcolepsy: relationship to cataplexy and HLA DQB1*0602 status. *Sleep*. 2002 Nov 1; 25(7):733-6. PMID:12405608
47. Black JL 3rd, **Krahn LE**, Pankratz VS, Silber M. Search for neuron-specific and nonneuron-specific antibodies in narcoleptic patients with and without HLA DQB1*0602. *Sleep*. 2002 Nov 1; 25(7):719-23. PMID:12405606
48. **Krahn LE**. Factitious disorder: managing patients who intend to be ill. *Current Psychiatry*. 2003; 2:47-56. PMID:0
49. **Krahn LE**. Out of the pipeline: Sodium Oxbate. *Current Psychiatry*. 2003; 2:123-6.
50. Cox LS, Patten CA, **Krahn LE**, Hurt RD, Croghan IT, Wolter TD, Schroeder DR, Tri D, Offord KP. The effect of nicotine patch therapy on depression in nonsmokers: a preliminary study. *J Addict Dis*. 2003; 22(4):75-85. PMID:14723479
51. Korndorfer SR, Lucas AR, Suman VJ, Crowson CS, **Krahn LE**, Melton LJ 3rd. Long-term survival of patients with anorexia nervosa: a population-based study in Rochester, Minn. *Mayo Clin Proc*. 2003 Mar; 78(3):278-84. PMID:12630579 DOI:10.4065/78.3.278

52. **Krahn LE**, Li HZ, O'Connor MK. Patients who strive to be ill: Factitious disorder with physical symptoms. *Am J Psychiatry*. 2003 Jun; 160(6):1163-8. PMID:12777276
53. **Krahn LE**. Sleep disorders. *Semin Neurol*. 2003 Sep; 23(3):307-14. PMID:14722826 DOI:10.1055/s-2003-814742
54. **Krahn LE**. Help night shift workers sleep properly. *Current Psychiatry*. 2004; 3. PMID:0
55. Nelson TK, **Krahn LE**. Treating affective illness in chronic pain: Comorbidity presents treatment challenges and opportunities. *Current Psychiatry*. 2004; 3(5):51-67. PMID:0
56. Kotagal S, **Krahn LE**, Slocumb N. A putative link between childhood narcolepsy and obesity. *Sleep Med*. 2004 Mar; 5(2):147-50. PMID:15033134 DOI:10.1016/j.sleep.2003.10.006
57. **Krahn LE**, Gonzalez-Arriaza HL. Narcolepsy with cataplexy. *Am J Psychiatry*. 2004 Dec; 161(12):2181-4. PMID:15569886 DOI:10.1176/appi.ajp.161.12.2181
58. **Krahn LE**. Out of the pipeline Eszopiclone. *Current Psychiatry*. 2005; 4(2):222-5. PMID:0
59. **Krahn LE**. Psychiatric disorders associated with disturbed sleep. *Semin Neurol*. 2005 Mar; 25(1):90-6. PMID:15798941 DOI:10.1055/s-2005-867077
60. Black JL 3rd, Silber MH, **Krahn LE**, Fredrickson PA, Pankratz VS, Avula R, Walker DL, Slocumb NL. Analysis of hypocretin (orexin) antibodies in patients with narcolepsy. *Sleep*. 2005 Apr; 28(4):427-31. PMID:16171287
61. Auger RR, Goodman SH, Silber MH, **Krahn LE**, Pankratz VS, Slocumb NL. Risks of high-dose stimulants in the treatment of disorders of excessive somnolence: a case-control study. *Sleep*. 2005 Jun; 28(6):667-72. PMID:16477952
62. Wall CA, Rummans TA, Aksamit AJ, **Krahn LE**, Pankratz VS. Psychiatric manifestations of Creutzfeldt Jakob disease: A 25-year analysis. *Journal of Neuropsychiatry & Clinical Neurosciences*. 2005 Fal; 17(4):489-95. PMID:0
63. Black JL 3rd, Silber MH, **Krahn LE**, Avula RK, Walker DL, Pankratz VS, Fredrickson PA, Slocumb NL. Studies of humoral immunity to preprohypocretin in human leukocyte antigen DQB1*0602-positive narcoleptic subjects with cataplexy. *Biol Psychiatry*. 2005 Sep 15; 58(6):504-9. PMID:16043129 DOI:10.1016/j.biopsych.2005.04.026
64. **Krahn LE**, DiMartini A. Psychiatric and psychosocial aspects of liver transplantation. *Liver Transpl*. 2005 Oct; 11(10):1157-68. PMID:16184540
65. **Krahn LE**. Reevaluating spells initially identified as cataplexy. *Sleep Med*. 2005 Nov; 6(6):537-42. PMID:15994123
66. **Krahn LE**, Lymp JF, Moore WR, Slocumb N, Silber MH. Characterizing the emotions that trigger cataplexy. *J Neuropsychiatry Clin Neurosci*. 2005 Winter; 17(1):45-50. PMID:15746482 DOI:10.1176/jnp.17.1.45
67. Morgenthaler TI, Olson EJ, Gay P, Decker PA, Herold D, Moore W, Silber MH, **Krahn L**. Effect of a targeted obstructive sleep apnea consult to improve access and quality at a sleep disorders center. *J Clin Sleep Med*. 2006 Jan 15; 2(1):49-56. PMID:17557437
68. Caselli RJ, Chen K, Bandy D, Smilovici O, Boeve BF, Osborne D, Alexander GE, Parish JM, **Krahn LE**, Reiman EM. A preliminary fluorodeoxyglucose positron emission tomography study in healthy adults reporting dream-enactment behavior. *Sleep*. 2006 Jul; 29(7):927-33. PMID:16895260
69. Moore WR, Silber MH, Decker PA, Heim-Penokie PC, Sikkink VK, Slocumb N, Richardson JW, **Krahn LE**.

- Cataplexy Emotional Trigger Questionnaire (CETQ)--a brief patient screen to identify cataplexy in patients with narcolepsy. *J Clin Sleep Med*. 2007 Feb 15; 3(1):37-40. PMID:17557451
70. Martin KA, **Krahn LE**, Balan V, Rosati MJ. Modafinil's use in combating interferon-induced fatigue. *Dig Dis Sci*. 2007 Apr; 52(4):893-6. Epub 2007 Feb 21. PMID:17318387 DOI:10.1007/s10620-006-9519-0
 71. Martin KA, **Krahn LE**, Balan V, Rosati MJ. Selective serotonin reuptake inhibitors in the context of hepatitis C infection: reexamining the risks of bleeding. *J Clin Psychiatry*. 2007 Jul; 68(7):1024-6. PMID:17685737
 72. Driver-Dunckley ED, Noble BN, Hentz JG, Evidente VG, Caviness JN, Parish J, **Krahn L**, Adler CH. Gambling and increased sexual desire with dopaminergic medications in restless legs syndrome. *Clin Neuropharmacol* 2007 Sep-Oct; 30 (5):249-55 PMID:17909302 DOI:10.1097/wnf.0b013e31804c780e
 73. **Krahn LE**, Miller BW, Bergstrom LR. Rapid resolution of intense suicidal ideation after treatment of severe obstructive sleep apnea. *J Clin Sleep Med*. 2008 Feb 15; 4(1):64-5. PMID:18350966 PMCID:2276837
 74. **Krahn LE**, Bostwick JM, Stonnington CM. Looking toward DSM-V: should factitious disorder become a subtype of somatoform disorder? *Psychosomatics*. 2008 Jul-Aug; 49(4):277-82. PMID:18621932 DOI:10.1176/appi.psy.49.4.277
 75. Eleid MF, **Krahn LE**, Agrwal N, Goodman BP. Carisoprodol withdrawal after internet purchase. *Neurologist* 2010 Jul; 16 (4):262-4 PMID:20592570 DOI:10.1097/NRL.0b013e3181aa917e
 76. Bright RP, Civalier KM, **Krahn L**. Reliability of self-reported nicotine use as determined by serum cotinine levels in patients referred for liver transplantation. *Psychosomatics*. 2010 Sep-Oct; 51(5):395-400. PMID:20833938 DOI:10.1176/appi.psy.51.5.395
 77. Bright RP, **Krahn L**. Depression and suicide among physicians. *Current Psychiatry*. 2011; 10(4):16-30.
 78. Chopra A, Selim B, Silber MH, **Krahn L**. Para-suicidal amnesic behavior associated with chronic zolpidem use: implications for patient safety. *Psychosomatics*. 2013 Sep-Oct; 54(5):498-501. Epub 2013 Jan 22. PMID:23352047 DOI:10.1016/j.psym.2012.10.012
 79. **Krahn LE**, Hershner S, Loeding LD, Maski KP, Rifkin DI, Selim B, Watson NF. Quality measures for the care of patients with narcolepsy. *J Clin Sleep Med* 2015 Mar 15; 11 (3):335 PMID:25700880 PMCID:4346654 DOI:10.5664/jcsm.4554
 80. Bright RP, **Krahn L**. Value-added education: enhancing learning on the psychiatry inpatient consultation service. *Acad Psychiatry*. 2015 Apr; 39(2):212-4. Epub 2014 Nov 01. PMID:25361627 DOI:10.1007/s40596-014-0236-2
 81. **Krahn LE**, Tovar MD, Miller B. Are Pets in the Bedroom a Problem? *Mayo Clin Proc* 2015 Dec; 90 (12):1663-5 Epub 2015 Oct 23 PMID:26478564 DOI:10.1016/j.mayocp.2015.08.012

Books

1. Kramlinger K, **Krahn LE**. *Mayo Clinic on Depression*. Kramlinger K, Wells L, Sutor B, Krahn L. Rochester, MN: Mayo Clinic 2001.
2. Silber MH, **Krahn LE**, Morgenthaler TI. *Sleep medicine in clinical practice*. London: Taylor & Francis; 2004. 392 p.
3. Hodgson H, **Krahn L**. *Smiling through your tears: anticipating grief*. North Charleston: BookSurge; 2004. 190 p.
4. Silber MH, **Krahn LE**, Morgenthaler TI. *Sleep medicine in clinical practice*. Silber MH; Krahn LE; Morgenthaler TI. 2nd ed. New York: Informa Healthcare; 2010.

5. **Krahn LE**, Silber MH, Morgenthaler TI. Atlas of sleep medicine. New York: Informa Healthcare; 2011.

Book Chapters

1. **Krahn LE**, Richardson JW. Sleep disorders in the medically ill. In: Stoudemire A, et al, editors. Psychiatric Care of the Medical Patient. Second Edition. Oxford: Oxford University Press; 2000. p. 683-97.
2. **Krahn LE**. Psychiatry. In: Habermann TM, editor. Mayo Clinic internal medicine board review, 2002-2003. 5th Edition. Philadelphia: Lippincott Williams & Wilkins; 2002. p. 835-57.
3. **Krahn LE**. Sleep disorders. In: Hensrud D. Clinical Preventive Medicine, 2ed. AMA Press; 2002.
4. Bostwick JM, Philbrick KL, **Krahn LE**. Identify the resident at risk a took kit for today's chief medical resident. In: Ficolora RD. Internal Medicine. 2004.
5. Slattery MJ, **Krahn LE**. Psychiatry. In: Habermann TM, editor. Mayo Clinic internal medicine board review, 2004-2005. Philadelphia: Lippincott Williams & Wilkins; 2004. p. 823-45.
6. **Krahn LE**. Sleep disorders. In: Lang RS, Hensrud DD, editors. Clinical preventive medicine. 2nd Edition. Chicago: American Medical Association; 2004. p. 125-33.
7. **Krahn LE**, Richardson JW. Sleep disorders. In: Levenson JL, editor. The American Psychiatric Publishing textbook of psychosomatic medicine. 1st Edition. Washington, DC: American Psychiatric Pub.; 2005. p. 335-57.
8. **Krahn LE**, Jowsey SG. Psychiatry. In: Habermann TM, editor. Mayo Clinic internal medicine review, 2006-2007. 7th Edition. Rochester: Mayo Clinic Scientific Press; 2006. p. 805-24.
9. **Krahn LE**. Circadian rhythm disorders. In: Pagel JF, Pandi-Perumal SR, editors. Primary care sleep medicine: a practical guide. Totowa: Humana Press; 2007. (Current Clinical Practice.). p. 261-74.
10. **Krahn LE**. Clinical features, diagnosis, and treatment of narcolepsy. In: Pagel JF, Pandi-Perumal SR, editors. Primary care sleep medicine: a practical guide. Totowa: Humana Press; 2007. (Current Clinical Practice.). p. 231-6.
11. **Krahn LE**. Insomnia: differential pearls. In: Barkoukis TJ, Avidan AY, editors. Review of sleep medicine. 2nd Edition. Philadelphia: Butterworth-Heinemann/Elsevier; 2007. p. 95-104.
12. **Krahn LE**. Mental disorders associated with disturbed sleep. In: Pagel JF, Pandi-Perumal SR, editors. Primary care sleep medicine: a practical guide. Totowa: Humana Press; 2007. (Current Clinical Practice.). p. 237-45.
13. **Krahn LE**, Jowsey SG. Psychiatry. In: Habermann TM, Ghosh AK, editors. Mayo Clinic internal medicine: concise textbook. Rochester: Mayo Clinic Scientific Press; 2008. p. 707-24.
14. **Krahn LE**, Morgenthaler TI. Animals and sleep. In: Krahn LE; Silber MH; Morgenthaler TI editor. Atlas of sleep medicine. New York: Informa Healthcare; 2011. p. 25-9.
15. **Krahn LE**. Circadian rhythm sleep disorders: physiology of the circadian clock. In: Krahn LE; Silber MH; Morgenthaler TI editor. Atlas of sleep medicine. New York: Informa Healthcare; 2011. p. 131-44.
16. **Krahn LE**. Cross-cultural aspects of sleep. In: Krahn LE; Silber MH; Morgenthaler TI editor. Atlas of sleep medicine. New York: Informa Healthcare; 2011. p. 13-24.
17. **Krahn LE**. Insomnia. In: Krahn LE; Silber MH; Morgenthaler TI editor. Atlas of sleep medicine. New York: Informa Healthcare; 2011. p. 100-16.

18. **Krahn LE.** Sleep disorders. In: Levenson JL. The American Psychiatric Publishing textbook of psychosomatic medicine: psychiatric care of the medically ill. 2nd ed. Washington, DC: American Psychiatric Publishing, Inc.; 2011. p. 335-59.

Editorials

1. **Krahn LE.** Recognizing an opportunity: screening for alcohol disorders after motor vehicle crashes. *Mayo Clin Proc.* 2000 Mar; 75(3):229-30.
2. **Krahn LE.** Factitious disorders with physical. *Evidence and Experience in Psychiatry.* 2005.
3. **Krahn LE.** Insomnia supplements (series of 4). *OB/GYN Times.* 2005.
4. **Krahn LE.** Understanding the needs of older patients with narcolepsy. *Sleep Med* 2016 Oct; 26:85 Epub 2016 Sept 30

Commentaries

1. Vargas HE, **Krahn L.** The transplantation candidate with alcohol misuse: the selection minefield. *Liver Transpl.* 2008 Nov; 14(11):1559-60. PMID:18975287 DOI:10.1002/lt.21604

Audio/Video/CD-ROM/etc.

1. **Krahn LE.** Drugs for Shyness. *Mayo Clinic Health Oasis,* 2000 Apr.
2. **Krahn LE.** Mayo Clinic office visit: Sleep issues. *Mayo Clinic Women's Healthsource.* 2003; 7(8 suppl 1-2).
3. **Krahn LE.** Sleep Issues. *Mayo Clinic Women's Healthsource Office Visit.* 2003Aug.
4. **Krahn LE.** New strategies for coping with shift work. *Current Psychiatry.* 2004.

Letters

1. **Krahn LE,** Rummans TA, Sharbrough FW, Jowsey SG, Cascino GD. Use of caffeine in medically refractory seizure patients. *Neuropsychiatry Neuropsychol Behav Neurol.* 1994 Apr; 7:136.
2. Chabolla DR, **Krahn LE,** Rummans TA, So EL. Dynamic psychotherapy for psychogenic nonepileptic seizures - response. *Mayo Clin Proc.* 1996 Nov; 71(11):1125. PMID:8917304 DOI:
3. **Krahn LE.** Paranoid schizophrenia--malingering or factitious disorder. *Am J Psychiatry.* 1997; 154(11):1599-601. PMID:9356571 DOI:
4. **Krahn LE,** Sutor B, Bostwick JM. Conveying emotional realism: a challenge to using standardized patients. *Acad Med.* 2001 Mar; 76(3):216-7. PMID:11242566 DOI:
5. Black JL, Avula RK, Walker DL, Silber MH, **Krahn LE,** Pankratz VS, Fredrickson PA, Slocumb NL. HLA DQB1*0602 positive narcoleptic subjects with cataplexy have CSF IgG reactive to rat hypothalamic protein extract. *Sleep.* 2005 Sep 1; 28(9):1191-2. PMID:16268389 DOI:
6. Civalier KA, **Krahn LE,** Agrwal N. Repeated episodes of neutropenia triggered by mirtazapine. *Psychosomatics* 2009 May-Jun; 50 (3):299-300 PMID:19567774 DOI:10.1176/appi.psy.50.3.299
7. **Krahn LE,** Martin KA, Silber MH. Narcoleptic patients' perceptions of nicotine. *J Clin Sleep Med.* 2009 Aug 15; 5(4):390. PMID:19968021 DOI:

Abstracts

1. Zimmerman RC, **Krahn L**, Klee GG, Lin SC, Ory SJ. Alpha-methylparatyrosine (AMPT) induced changes in noradrenergic transmission do not induce symptoms encountered in premenstrual syndrome (pms) in the early follicular phase of the menstrual cycle in healthy women. (Abstract no. 0-058). American Fertility Society Abstracts. 1994; (Suppl):S29.
2. **Krahn LE**, Zimmermann R, Klee G, Ory S, Lin S. Alpha-Methyl-Para-Tyrosine on Prolactin and Melatonin Secretion in Humans. *Psychopharmacology Bulletin*. Vol. 30, 1994.
3. **Krahn LE**, Lin SC, Klee G, Delgado P, Zimmerman RC. Melatonin: a novel marker to characterize presynaptic catecholamine depletion. *Biol Psychiatry*. 1994; 35(9):668.
4. **Krahn LE**, Lin S, Hauri P, Rummans T, O'Connor MK. Sleep assessment of psychiatric inpatients: correlation of patient subjective report, nursing assessment, and wrist actigraphy recording. *Psychosomatics*. 1994; 34(2):214.
5. **Krahn LE**, Rummans T, Sharbrough F, Jowsey S, Cascino G, Trenerry M. Use of caffeine in medically refractory seizure patients. *Psychosomatics*. 1994; 34(2):187.
6. Reese M, **Krahn L**, Rummans T, Peterson G, Suman V, Sharbrough F, Cascino G. Health Care Utilization in Patients Previously Diagnosed with Non-Epileptic Seizures. *Psychosomatics*. 37(2):186-187, 1995.
7. Reese MM, **Krahn LE**, Rummans TA, Peterson GC, Suman VJ, Sharbrough FW, Cascino GD. Health care utilization in patients previously diagnosed with nonepileptic seizures. (Abstract 4.42). *Epilepsia*. 1995; 36(Suppl 4):105.
8. Stockard J, **Krahn LE**, O'Connor M, Pileggi T, Rummans T. Ictal and Interictal EEG Markers of Seizure Inhibition Predict and Index Antidepressant Efficacy of Electroconvulsive Therapy. American Electroencephalographic Society Annual Meeting, 1995.
9. **Krahn LE**, Rummans T, Peterson G, Cascino G, Sharbrough F. Pilot study of psychosocial outcome of epilepsy surgery for patients with a lifetime prevalence of depressive spectrum disorders. *Psychosomatics*. 1995; 35(2):178.
10. Peterson GC, **Krahn LE**, Rummans TA, Cascino GD, Sharbrough FW. Psychosocial outcome of epilepsy surgery for patients with depressive disorders: a pilot study. (Abstract no. 4.45). *Epilepsia*. 1995; 36(Suppl 4):105.
11. Lu P, **Krahn LE**, Lin S, Klee G, Ory S, Zimmermann R. The Impact of Gender on Alpha-Methyl-Para-Tyrosine Mediated Changes in Prolactin and Melatonin Secretion. Society for Gynecologic Investigation, 1995.
12. **Krahn LE**, Lu PY, Klee GG, Lin SC, Zimmerman RC. Examining serotonin function: a modified technique for rapid tryptophan depletion. *Biol Psychiatry*. 1996; 37(9):659.
13. Lu P, **Krahn LE**, Lin S, Klee G, Ory S, Zimmermann R. Ovarian Androgen Production is Not Affected by Sympathetic Nervous System (SNS) Suppression With Alpha-Methyl-Para-Tyrosine (AMPT). *Fertility and Sterility*, 1996.
14. **Krahn LE**, Zimmermann R, Klee G, Lin S, Sauer M. The effect of catecholamine depletion on thyrotropin secretion. *Biol Psychiatry*. 1996; 39(7):592.
15. Zimmermann RC, Rahmanie A, **Krahn L**, Ferin M, Sauer MV. Inhibition of norepinephrine synthesis with alpha-methyl-para-tyrosine does not alter leptin secretion. (Abstract O 027). *Fertil Steril*. 1997; S14.
16. **Krahn LE**, Rummans T, Ryan D, O'Connor M. Use of electroconvulsive therapy for depression coexisting with congestive heart failure. *Psychosomatics*. 1997; 38(2):192.

17. **Krahn LE**, Grewal R, O'Connor M. Factitious disorders with physical symptoms in a tertiary care setting: confrontation and willingness to accept psychiatric treatment. *Psychosomatics*. 1998; 39(2):211-2.
18. Goodman J, **Krahn LE**, Smith G, Rummans T, Pileggi T. Patient satisfaction with electroconvulsive therapy. *J ECT*. 1998; 14(2):136-7.
19. Gleber E, **Krahn L**, Rummans T, Pileggi T, Lucas D. Changes in urinary levels of melatonin metabolite in responders to ECT for depression. (Abstract 332). *Biol Psychiatry*. 1998 Apr 15; 43(8S Suppl).
20. **Krahn LE**, Boeve BF, Olson EJ, Herold DL, Silber MH. Physiologic changes in cataplexy provoked by humorous videotapes. *Sleep*. 1999; 22(Suppl):S155.
21. **Krahn LE**, Silber M. Cataplexy in the elderly. *Sleep*. 2000; 23(Suppl 2):A307.
22. Malik S, Silber M, Boeve BF, **Krahn LE**. Symptomatic (secondary) narcolepsy: does it occur? *Sleep*. 2000; 23(Suppl 2):A302.
23. Saad DA, **Krahn LE**. Treating dementia and depression with antibiotics: psychiatric issues in CNS whipple disease. 47th Annual Meeting of the Academy of Psychosomatic Medicine, Palm Springs, CA. 2000 Nov:17-8.
24. **Krahn LE**, Carmichael SW, Pittlekow MR, Windebank AJ. Required medical student research. *Innovations in Medical Education (AAMC)* 2001; 26:178.
25. Black JL, **Krahn LE**, Silber MH. A pilot study of serologic markers of autoimmunity in patients with narcolepsy. (Abstract 559.K). *Sleep*. 2001 Apr 15; 24(Abstract Suppl):A318-A319.
26. Silber MH, **Krahn LH**, Olson EJ, Pankratz VS. Epidemiology of narcolepsy in Olmsted County, Minnesota: a population-based study. (Abstract 158.K). *Sleep*. 2001 Apr 15; 24(Abstract Suppl):A98.
27. Gowda A, **Krahn LE**, Slocumb N, Lymp J, Moore W, Silber MH. Experiences that trigger cataplexy. (Abstract 573.K). *Sleep*. 2001 Apr 15; 24(Abstract Suppl):A327.
28. Roger ER, Silber MH, **Krahn LE**. Narcolepsy, cataplexy, and aging. (Abstract 558.K). *Sleep*. 2001 Apr 15; 24(Abstract Suppl):A318.
29. **Krahn LE**, Hansen MR, Tinsley JA. Psychiatric resident exposure to sleep medicine: a survey of psychiatric program directors. (Abstract 739.S). *Sleep*. 2001 Apr 15; 24(Abstract Suppl):A416-A417.
30. **Krahn LE**, Boeve BF, Oliver L, Silber MH. CSF hypocretin (orexin) levels in narcolepsy with and without ataplexy. *Sleep*. 2002; 25(Suppl):A234.
31. **Krahn LE**, Oliver LK, Pankratz VS, Boeve BF, Silber MH. CSF hypocretin (orexin) levels in narcolepsy with and without cataplexy. *Sleep*. 2002; 25(abstr suppl):A235-6.
32. Kotagal S, Kubas S, **Krahn LE**. Delayed sleep phase syndrome in adolescents: perspectives on psychosocial outcomes. *Sleep*. 2002; 25(Suppl):A17.
33. **Krahn LE**, Lymp J, Moore W, Silber MH. Identifying cataplexy: exploring the mind-body nterface. *Sleep*. 2002; 25(Suppl):A235.
34. **Krahn LE**, Boeve BF, Oliver LK, Silber MH. Secondary narcolepsy with normal CSF hypocretin (orexin) levels. *Sleep*. 2002; 25(abstr suppl):A234-5.
35. **Krahn LE**, Lymp JF, Moore WR, Silber MH. Identifying cataplexy: exploring the mind-body interface (Abstract 420). *Biol Psychiatry*. 2002 Apr 15; 51(8S):144S.

36. **Krahn LE.** The patient perspective of pre-clinical medical school education. *Teaching and Learning in Medicine.* 2003.
37. Silber MH, **Krahn LE**, Slocumb NL. Clinical and polysomnographic findings of narcolepsy with and without cataplexy: a population-based study (Abstract 0711.K). *Sleep.* 2003 May 15; 26(Abtract Suppl):A282-3.
38. **Krahn LE**, Kubas SM, Pankratz VS, Harris AM, Kotagal S. Long-term outcome of adolescents with delayed sleep phase disorder (Abstract 0283.E). *Sleep.* 2003 May 15; 26(Abtract Suppl):A115.
39. Boeve BF, **Krahn LE**, Silber MH, Oliver L, Parisi JE, Dickson DW, Ferman TJ, Smith GE, Tangalos EG, Petersen RC. Normal CSF hypocretin-1 levels in autopsy-proven Alzheimer's disease =+ Lewy body disease (Abstract 0887.O). *Sleep.* 2003 May 15; 26(Abtract Suppl):A352-3.
40. Young TJ, Silber MH, **Krahn LE**, Slocumb NL. HLA DQB1*0602 status is related to CSF hypocretin-1 levels in narcoleptic patients without cataplexy. *Sleep.* 2004; 27(Suppl S):242.
41. Kotagal S, Silber MH, **Krahn LE**, Boeve BF, Althuler SI, Moore WR. Response of narcolepsy-cataplexy to treatment with sodium oxybate. *Sleep.* 2004; 27(Suppl S):237-8.
42. Auger R, Goodman SH, Silber MH, **Krahn LE**, Slocumb NL. Risks of high dose stimulant use for disorders of excessive somnolence: A case-control study. *Sleep.* 2004; 27(Suppl S):241.
43. Lee EK, **Krahn LE.** Sleep learning and education evaluation for psychiatry: a SLEEP study. *Sleep.* 2004; 27(Suppl S):375.
44. Lee EK, **Krahn LE.** Sleep learning and education for psychiatry: A sleep study. *Sleep.* 2004.
45. Silber MH, **Krahn LE**, Slocumb NL. Distribution of age of onset of narcolepsy (Abstract 0661). *Sleep.* 2005; 28(Suppl):A222.
46. Black JL, Avula RK, Walker DL, Silber MH, **Krahn LE**, Pankratz V, Fredrickson PA, Slocumb NL. Screening of HLA DQB1*0602 positive narcoleptics' serum for immunoreactivity to rat hypothalamus protein extract using ELISA (Abstract 0644). *Sleep.* 2005; 28(Suppl):A216.
47. Black JL, Silber MH, **Krahn LE**, Avula RK, Walker DL, Pankratz V, Fredrickson PA, Slocumb NL. Studies of humoral immunity to preprohypocretin in HLA DQB1*0602 positive narcoleptics with cataplexy (Abstract 0637). *Sleep.* 2005; 28(Suppl):A214.
48. Lee EK, Silber MH, **Krahn LE**, Slocumb NL. The relationship between psychiatric disorders and cerebrospinal fluid hypocretin levels in narcolepsy (Abstract 0646). *Sleep.* 2005; 28(Suppl):A217.
49. Black JL, Silber MH, **Krahn LE**, Avula RK, Walker DL, Pankratz VS, Fredrickson PA, Slocumb NL. Studies of humoral immunity to preprohypocretin in HLA DQB1*0602 positive narcoleptics and cataplexy (Abstract 121). *Biol Psychiatry.* 2005 Apr; 57(8S):35S.
50. Moore WR, Silber MH, Heim-Penokie PC, Sikkink VK, Slocumb N, Decker PA, Richardson JW, **Krahn LE.** Cataplexy emotional trigger questionnaire (CETQ) can a brief patient survey identify cataplexy in patients with narcolepsy? (Abstract 0634). *Sleep.* 2005 Jun; 28(Suppl):A213.
51. **Krahn LE.** REM sleep: suppression by a monoamine oxidase inhibitor vs rebound after CPAP initiation (Abstract P 190). *Sleep Med.* 2005 Oct; 6(Suppl 2):S203.
52. Black JL, Silber MH, **Krahn LE**, Walker DL, Avula RK, Pankratz V, Fredrickson PA, Slocumb NL. Studies of humoral immunity to hypocretin receptor 1 and 2 in HLA and DQB1*0602 positive narcoleptics with cataplexy

(Abstract 0647). *Sleep*. 2006; 29(Suppl):A219.

53. **Krahn L**, Martin KA, Silber MH. Narcolepsy and nicotine: A preliminary examination. *Sleep*. 2008; 31(Suppl S):A217.
54. **Krahn L**, Martin KA. Narcolepsy and nicotine. *J Sleep Res*. 2008 Dec; 17(Suppl 1):99.
55. **Krahn L**, Rogers ER. Self-management techniques for Eds in narcolepsy. *Sleep*. 2009; 32(Suppl S):A244.
56. Biernacka J, Veldic M, McElroy SL, Crow S, Sharp A, Benitez J, Rummans T, **Krahn L**, Mrazek D, Post RM, Altshuler LL, Suppes T, Frye MA. The genomics of treatment emergent mania: The Mayo Clinic Individualized Medicine Biobank for Bipolar Disorder. *Bipolar Disord*. 2009 Jun; 11(Suppl 1):20-1.
57. **Krahn LE**, Claypool D, Clayton C. Inflight medical emergencies in airline passengers using hypnotics. *Sleep*. 2010; 33(Suppl S):A508.
58. **Krahn L**. Medical team acceptance of online cognitive behavioral therapy for chronic insomnia at an integrated academic medical centre. *J Psychosom Res*. 2013 Jun; 74(6):550.
59. **Krahn LE**. Pets in the bedroom: a survey of American patients. *J Sleep Res*. 2014 Sep; 23:157.
60. **Krahn L**. Home sleep environment: Are pets in the bedroom beneficial or detrimental? *Journal Of Sleep Research* 2016 Sep; 25 (Suppl 1):235

Book Reviews

1. **Krahn LE**. Review of Stress, the Immune System, and Psychiatry. Edited by B.E. Leonard, K. Miller, Wiley, 1995. *Mayo Clin Proc*. 1996; 71:214.
2. **Krahn LE**. Review of Progress in Clinical Psychiatry One. *Mayo Clin Proc*. 1998; 73(2):198.
3. **Krahn LE**. Review of Clinical Components to Sleep Medicine. *Sleep Medicine*. 2001; 2:85.
4. **Krahn LE**. Sleep Medicine. Lee-Chiong TL, Sateia MJ, Carskadon MA, eds. *Mayo Clin Proce*. 2003;78:121.
5. **Krahn LE**. Psychiatric disorders associated with disturbed sleep. *Sleep Medicine*. 2005.
6. **Krahn LE**. The clinical features, diagnosis and treatment of narcolepsy. *Sleep Medicine*. 2005.

* Indicates that the primary author was a mentee of this author.

Date of Revision: July 12, 2017

Name: Meir Kryger, M.D. FRCPC

Appointment: Professor, Department of Internal Medicine, Section of Pulmonary, Critical Care and Sleep Medicine, Clinician-Educator Track; tenured

Clinical Professor in the Division of Primary Care / Health Systems in Nursing. Courtesy Faculty of the Yale School of Nursing. (September 19,2014)

Yale Program of Sleep Medicine, Director of Sleep Fellowship

Yale Program of Sleep Medicine, Director of Education

Staff Physician, VA Connecticut Healthcare System

(b) (6)

(b) (6)

Yale University

Member of Board of Permanent Officers
Fellow – Pierson College
Fellowship Sleep Program Director

Board Certifications

1976	ABIM Internal Medicine
1976	ABIM Pulmonary Medicine
1976	Fellow of Royal College of Physicians and Surgeons of Canada (Internal Medicine)
1997	Fellow of the American Board of Sleep Medicine
2010	ABIM Sleep Medicine Certification

Professional Honors and Recognition

International

2017	Academy of Applied Myofunctional Sciences <i>De Materia Medica</i> Award, for Lifetime Achievement and Significant Precedent Through Publishing.
2016	American Academy of Dental Sleep Medicine, Pierre Robin Academic Award
2014	Short Listed - British Medical Association Book Awards. Atlas of Clinical Medicine 2E. Internal Medicine category (Highly Commended).

- 2014 National Sleep Foundation Lifetime Achievement Award
- 2013 Sleep Research Society Mary Carskadon Outstanding Educator Award
- 2011 Canadian Sleep Society Distinguished Scientist Award, presented September, 2011, in Quebec City, Canada, as part of World Association of Sleep Medicine/Canadian Sleep Society Joint Congress
- 2004 Associated Professional Sleep Societies Award for Educational Excellence
- 1997 WHO Worldwide Project on Sleep and Health, Committee Member
- 1996 William C. Dement Award for Academic Achievement, American Sleep Disorders Association
- 1992-present Editorial Board, Associate editor, Journal SLEEP
- 2006-present Editorial Board, Journal of Clinical Sleep Medicine
- 2015-present Editorial Board, and Art Director, Sleep Health

National

- 2008-2009 Chairman, Board of Directors, National Sleep Foundation
- 2003 Chair, Congress on Sleep, Health and Aging, at The Institutes of Science, Washington DC, sponsored by National Sleep Foundation, NIA, NIMH, NCSDR, AAMC, CIHR. March 30, 2003
- 1994 Master Lecture, American College of Chest Physicians Annual Meeting. "Sleep and the Heart"
- 1993-1994 President, American Academy of Sleep Medicine
- 1990-1993 President, Canadian Sleep Society
- 1974-1976 American Lung Association Fellowship

Regional

- 2000 Nominated Teacher of the Year (Med 1), University of Manitoba
- 1994 Inaugural George Ferguson Lecturer, Saskatchewan Thoracic Society

Yale School of Medicine: 2nd year Case Workshop. Case Workshop
Yale Hall of Graduate Studies, Sleep Workshop, September 28
Yale Alumni College. Sleep in Art and Literature. Rye NY-March 9
Yale Alumni College. The Science of Sleep. Rye NY-March 16.
Yale Alumni College. Sex Hormones and Sleep. Rye NY-March 23.
Yale Alumni College. Is there a Sleep Problem? Rye NY-March 30
Yale Alumni College. Can't Sleep, Can't Stay Awake. Rye NY-April 6.
Yale Alumni College. You have a Sleep problem. Now What? Rye NY-April 13.
Yale Sleep Medicine Fellowship Bootcamp lectures, June 3
Stanford, Hypersomnia Symposium, Medical Causes of Sleepiness, July 11
Yale Alumni College. Sleep in Art and Literature. NEW HAVEN-October 5.
Yale Alumni College. The Science of Sleep. NEW HAVEN-October 12.
Yale Alumni College. Sex Hormones and Sleep. NEW HAVEN-October 19.
Yale Alumni College. Is there a Sleep Problem? NEW HAVEN-October 26.
Lecture and Seminar on Sleep to Davenport and Pierson freshman counsellors – October 26
Yale Alumni College. Can't Sleep, Can't Stay Awake. NEW HAVEN-November 2.
Yale Alumni College. You have a Sleep problem. Now What? NEW HAVEN-November 9.
Update in Sleep Medicine, Sleep in Art and Literature, St Louis, October 25
Mystery of Sleep Lecture. Dickens Day Event. April 2016
Various lectures and facilitating State Sleep lectures

Publications

Peer Reviewed research

1. Hogg W, Brunton J, **Kryger M**, Brown R, Macklem PT: Gas diffusion across collateral channels. J Appl Physiol 1972; 33:568.
2. **Kryger M**. Quesney LF, Holder D, Gloor P, Maclead P: The sleep deprivation syndrome of the obese patient. Am J Med 1974; 56:531.
3. **Kryger M**: Authors Reply: The interaction of the drive to breathe and sleep in the Pickwickian Syndrome. Sleep Reviews 1974; 74X:R74-131.
4. **Kryger M**, Martin RR, Macklem PT, Anthonisen NR: Effect of gas density and expiratory flow on "closing volumes". J Appl Physiol 1974; 37:831.

5. **Kryger M**, Yacoub O, Anthonisen NR: Effect of inspiratory resistance on occlusion pressure in hypoxia and hypercapnia. *Res Physiol* 1975; 24:241.
6. Anthonisen NR, Utz G, **Kryger M**, Urbanetti JS: Exercise tolerance at 4 and 6 ATA. *Undersea Biomedical Research* 1976; 3:95-102.
7. Doekel RC, Zwillich CW, Scoggin CH, **Kryger MH**, Weil JV: Clinical semi-starvation: Depression of hypoxic ventilatory response. *New Engl J Med* 1976; 295:358-361.
8. **Kryger M**, Yacoub O, Dosman J, Macklem PT, Anthonisen NR: Effect of meperidine on occlusion pressure responses to hypercapnia and hypoxia with and without external inspiratory resistance. *Am Rev Resp Dis* 1976; 114:341-346.
9. Yacoub O, Doell D, **Kryger MH**, Anthonisen NR: Depression of hypoxic ventilatory response by N2O. *Anesthesiology* 1976; 45(4):385-9.
10. **Kryger M**, Weil J, Grover R: Chronic Mountain Polycythemia: A Disorder of the Regulation of Breathing during Sleep? *Chest* 1978; 73S:303S-304S.
11. Dreisin RB, Albert RK, Talley PA, **Kryger MH**, Scoggin CH, Zwillich CW: Flexible fiberoptic bronchoscopy in the teaching hospital. *Chest* 1978; 74:144-149.
12. **Kryger M**, McCullough RE, Collins D, Scoggin C, Weil JV, Grover RF: Treatment of excessive polycythemia of high altitude with respiratory stimulant drugs. *Am Rev Resp Dis* 1978; 117:455.
13. **Kryger M**, Aldrich F, Reeves JT, Grover RF: Diagnosis of airflow obstruction at high altitude. *Am Rev Resp Dis* 1978; 117:1055.
14. **Kryger M**, McCullough R, Doekel R, Collins D, Weil J, Grover RF: Excessive polycythemia of high altitude: Role of ventilatory drive and lung disease. *Am Rev Resp Dis* 1978; 118:659.
15. **Kryger M**, Glas R, Jackson D, McCullough RE, Scoggin C, Grover RF, Weil JV. Impaired oxygenation during sleep with excessive polycythemia of high altitude: improvement with respiratory stimulation. *Sleep* 1978;1 :3.
16. Scoggin CH, Doekel RD, **Kryger MH**, Zwillich CW, Weil JV: Familial aspects of decreased hypoxic drive in endurance athletes. *J Appl Physiol* 1978; 44:464-468.
17. McCullough RG, **Kryger M**: Treatment of chronic mountain sickness with medroxyprogesterone acetate. Analyzer, *J Nat Soc for Cardiopul Technology* 1978; 8:4.
18. Weil J, **Kryger M**, Scoggin C: Breathing and oxygenation in sleep during acute high altitude exposure. *The Hypoxia Symposium* 1979. The Arctic Institute of North America.
19. **Kryger M**, John HK, Vogel S. Karger, Basel. Breathing at high altitude: lessons learned and application to hypoxemia at sea level. In: *Advances in Cardiology* 1980;27:11-16.

20. Mezon B, West P, Maclean JP, **Kryger M**. Sleep apnea in acromegaly. *Am J Med* 1980; 69:615.
21. Mezon B, West P, Israels J, **Kryger M**. Sleep breathing abnormalities in kyphoscoliosis. *Am Rev Resp Dis* 1980; 122:617.
22. Fleetham JA, Mezon B, West P, Bradley CA, Anthonisen NR, **Kryger M**. Chemical control of ventilation and sleep arterial oxygen desaturation in COPD patients. *Am Rev Resp Dis* 1980; 122:583.
23. Fleetham JA, Bradley CA, **Kryger MH**, Anthonisen NR. The effect of low flow oxygen therapy on the chemical control of ventilation in patients with hypoxemic COPD. *Am Rev Respir Dis* 1980; 122(6):833-840.
24. **Kryger MH**, Acres JC, Brownell L. A syndrome of sleep, stridor, and panic. *Chest* 1981; 80:768.
25. Acres JC, **Kryger MH**. Upper airway obstruction. *Chest* 1981; 80:207-211.
26. Acres JC, Sweatman P, West P, Brownell L, **Kryger MH**. Breathing during sleep in parents of sudden infant death syndrome victims. *Am Rev Resp Dis* 1982; 125:163-166.
27. Acres JC, **Kryger MH**. Assessment of the chemical control of ventilation. *Medicine North American* 1982 Mar; 21(Pt 1).
28. **Kryger MH**, Mezon BJ, Acres JC, West P, Brownell L. Diagnosis of sleep breathing disorders in a general hospital. *Arch Intern Med* 1982; 142:956-958.
29. Fleetham J, West P, Mezon B, Conway W, Roth T, **Kryger M**. Sleep, arousals, and oxygen desaturation in chronic obstructive pulmonary disease. The effect of oxygen therapy. *Am Rev Resp Dis* 1982; 126:429-433.
30. Brownell LG, West P, Sweatman P, Acres JC, **Kryger MH**. Protriptyline in obstructive sleep apnea. *NEJM* 1982; 307:1037-1042.
31. Perez-Padilla R, **Kryger MH**. What happens to lung patients when they fall asleep? *J Resp Dis* 1982 Apr.
32. Loveridge B, West P, Anthonisen NR, **Kryger MH**. Single-position calibration of the respiratory inductance plethysmograph. *J Appl Physiol Respirat Environ Exercise Physiol* 1983; 55(3):1031-1034.
33. Perez-Padilla R, West P, **Kryger MH**. Sighs during sleep in adult humans. *Sleep* 1983; 6(3):234.
34. **Kryger MH**. Sleep apnea - from the needles of Dionysius to continuous positive airway pressure. *Arch Int Med* 1983; 143:2301.
35. Brownell LG, Perez-Padilla R, West P, **Kryger MH**. The role of protriptyline in obstructive sleep apnea. *Bull Europ Physiopath Resp* 1983; 19:621.
36. West P, **Kryger MH**. Continuous monitoring of respiratory variables during sleep by microcomputer. *Meth Inform Med* 1983; 22:198-203.

37. West P, **Kryger MH**, Loveridge B. Non-invasive monitoring of respiration by microcomputer. In Procs. IEEE "Frontiers of Engineering in Medicine" Conference, Columbus, Ohio, September 1983 pp 389-394.
38. Loveridge B, West P, Anthonisen NR, **Kryger MH**. Breathing patterns in patients with chronic obstructive pulmonary disease. *Am Rev Resp Dis* 1984; 130:730-33.
39. Perez-Padilla R, West P, Lertzman M, **Kryger MH**. Breathing during sleep in patients with interstitial lung disease. *Am Rev Resp Dis* 1985; 132(2):224.
40. **Kryger MH**. Sleep in restrictive lung disorders. *Clin Chest Med* 1985; 6(4):675-678.
41. **Kryger MH**, Grover RT. Polycythemia of Chronic Mountain Sickness In: *Archivos de Biologia Andina* 1984; 13(1-4):35-40.
42. Brownell LG, West P, **Kryger MH**. Breathing during sleep in normal pregnant women. *Am Rev Respir Dis* 1986; 133:38-41.
43. Loveridge B, West P, **Kryger MH**, Anthonisen NR. Alteration in breathing pattern with progression of chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1986; 134:930-934.
44. Light RB, Perez-Padilla R, **Kryger MH**. Perfluorochemical artificial blood as a volume expander in hypoxemic respiratory failure in dogs. *Chest* 1987; 92:444-449.
45. Perez-Padilla R, Conway W, Roth T, Anthonisen NR, **Kryger MH**. The clinical spectrum of hypoxemic COPD: sleep and hemodynamic studies. *Sleep* 1987; 10(3):216-223.
46. George CF, **Kryger MH**. Oxygenation in tonic and phasic REM in patients with COPD. *Sleep* 1987; 10(3):234-243.
47. West P, George CF, **Kryger MH**. Dynamic in vivo response characteristics of three oximeters: Hewlett-Packard 47201A, Biox III, and Nellcor N-100. *Sleep* 1987; 10(3):263-271.
48. Easton PA, West P, Meatherall RC, Brewster JF, Lertzman M, **Kryger MH**. The effect of excessive ethanol ingestion on sleep in severe chronic obstructive pulmonary disease. *Sleep* 1987; 10(3):224-233.
49. George CF, Millar T, **Kryger MH**. Trial of a dopaminergic antidepressant in obstructive sleep apnea. *Sleep* 1987; 10(2):180-183.
50. Perez-Padilla R, West P, **Kryger MH**. Snoring in normal young adults. *Sleep* 1987; 10(3):249.
51. George CF, **Kryger MH**. Sleep in restrictive lung disease (invited review). *Sleep* 1987; 10(5):409-418.
52. Raetzo MA, Junod AF, **Kryger MH**. Effect of aminophylline and relief from hypoxia on central sleep apnea due to medullary damage. *Bull Eur Physiopathol Respir* 1987; 23:171-175.
53. George CF, Nickerson PW, Hanly PJ, Millar TW, **Kryger MH**. Sleep apnea patients have more automobile accidents. *Lancet* 1987; 8556(II):447.

54. George CF, Millar TW, **Kryger MH**. Identification and quantification of apneas by computer based analysis of SaO₂. *Am Rev Respir Dis* 1988; 137:1238-1240.
55. Conway WA, **Kryger MH**, Timms RM, Williams GW. Clinical significance of sleep desaturation in hypoxemic chronic obstructive pulmonary disease: studies in 130 patients. *Henry Ford Hospital Medical Journal* 1988; 36(1):16-23.
56. He J, **Kryger MH**, Zorick FJ, Conway W, Roth T. Mortality and apnea index in obstructive sleep apnea: experience in 385 male patients. *Chest* 1988; 94(1):9-14.
57. George CF, Millar TW, **Kryger MH**. Sleep apnea and body position during sleep. *Sleep* 1988; 11(1):90-99.
58. Savoy J, **Kryger MH**. Respiratory disorders in sleep. *Medicine North America* 1988; 23:4405-4411.
59. Hanly P, Millar TW, Steljes DG, Baert R, Frais M, **Kryger MH**. Respiration and abnormal sleep in patients with congestive heart failure. *Chest* 1989; 96(3):480-488.
60. Hanly P, George CF, Millar TW, **Kryger MH**. Heart rate response to breath-hold, Valsalva and Mueller maneuvers in obstructive sleep apnea. *Chest* 1989; 95:735-9.
61. Savoy J, Louis M, **Kryger MH**, Forster A. Respiratory response to histamine- and methylcholine-induced bronchospasm in nonsmokers and asymptomatic smokers. *Eur Respir J* 1988; 1:209-216.
62. George CF, **Kryger MH**. Management of Sleep Apnea. *Semin Resp Med* 1988; 9(6):569-576.
63. Hanly P, Millar TW, Steljes DG, Baert R, Frais M, **Kryger MH**. The effect of oxygen on respiration and sleep in patients with congestive heart failure. *Ann Intern Med* 1989; 111(10):777-782.
64. George CF, Millar TW, Hanly PJ, **Kryger MH**. The effect of L-tryptophan on daytime sleep latency in normals (correlation with blood levels). *Sleep* 1989; 12(4):345-354.
65. **Kryger MH**. Sleep apnoea: missing the forest for the trees. *Q J Med.* 1989; 72(267):575-577.
66. **Kryger MH**, Hanly PJ. Cheyne-Stokes respiration in cardiac failure. *Prof Clin Biol Res.* 1990; 345:215-224.
67. Roth T, Roehrs T, **Kryger M**. Mortality in obstructive sleep apnea. *Prog Clin Biol Res.* 1990; 345:347-351.
68. Singh SM, George CFP, **Kryger MH**, Jung JH. Genetic Heterogeneity in Narcolepsy. *Lancet* 1990; 335:726-727.
69. Steljes DG, **Kryger MH**, Kirk BW, Millar TW. Sleep in postpolio syndrome. *Chest* 1990; 98:133-140.
70. Millar TW, Hanly PJ, Hunt B, Frais M, **Kryger MH**. The entrainment of low frequency breathing periodicity. *Chest* 1990; 98:1143-1148.
71. Avital A, Steljes DG, Pasterkamp H, **Kryger M**, Sanchez I, Chernick V: Sleep quality in children with asthma treated with theophylline or cromolyn sodium. *The Journal of Pediatrics* 1991 Dec; 119(6):979-84.

72. **Kryger MH**, Millar T. Cheyne Stokes Respiration: Stability of interacting systems in heart failure. *Chaos* 1991; 3:265.
73. **Kryger MH**, Steljes D, Woon-Chee Y, Mate E, Smith SA, Mahowald M. Central sleep apnoea in congenital muscular dystrophy. *J Neurol Neurosurg Psychiatry* 1991; 54(8):710-712.
74. Avital A, Sanchez I, Holbrow J, **Kryger M**, Chernick V: Effect of theophylline on lung function tests, sleep quality and nighttime SaO₂ in children with cystic fibrosis. *Am Rev Respir Dis* 1991; 144:1245-49.
75. **Kryger MH**, Pouliot Z, Steljes D, Neufeld H, Odyanski T. Subjective versus objective evaluation of hypnotic efficacy: Experience with Zolpidem. *Sleep* 1991; 14(5):399-407.
76. Buckle P, **Kryger MH**, Kerr P, Pouliot Z, Millar T. Polysomnography in acutely ill intensive care unit patients. *Chest* 1992; 102:288-91.
77. Kerr P, Shoenut JP, Millar T, Buckle P, **Kryger MH**. Nasal CPAP reduces gastroesophageal reflux in obstructive sleep apnea syndrome. *Chest* 1992; 101:1539-44.
78. Buckle P, Millar T, **Kryger MH**. The effect of short-term nasal CPAP on Cheyne-Stokes respiration in congestive heart failure. *Chest* 1992; 102:31-35.
79. Kerr P, Millar T, Buckle P, **Kryger MH**. The importance of nasal resistance in obstructive sleep apnea syndrome. *J Otolaryngol* 1992; 21(3):189-95.
80. Millar TW, Hanly P, **Kryger MH**. Short technical note: quantification of periodic breathing: preliminary studies. *Sleep* 1992; 15(4):364-70.
81. Stein MB, Enns MW, **Kryger MH**. Sleep in nondepressed patients with panic disorder: II. Polysomnographic assessment of sleep architecture and sleep continuity. *J Affective Disord* 1993; 28:1-6.
82. Biberdorf DJ, Steen R, Millar TW, **Kryger MH**. Benzodiazepines in congestive heart failure: effects of temazepam on arousability and Cheyne-Stokes respiration. *Sleep* 1993; 16(6):529-38.
83. Kerr P, Shoenut JP, Steens RD, Millar T, Micflikier AB, **Kryger MH**. Nasal CPAP: A new treatment for nocturnal gastroesophageal reflux. *J Clin Gastroenterol* 1993; 17(4):276-80.
84. Steens RD, Pouliot Z, Millar TW, **Kryger MH**, George CF. Effects of zolpidem and triazolam on sleep and respiration in mild to moderate chronic obstructive pulmonary disease. *Sleep* 1993; 16(4):318-26.
85. Alvaro RE, De-Almeida V, Kwiatkowski K, Cates D, **Kryger MH**, Rigatto H. A developmental study of the dose-response curve of the respiratory sensory reflex. *Am Rev Respir Dis*. 1993; 148(4 Pt 1):1013-1017.
86. Gall R, Isaac L, **Kryger MH**. Quality of life in mild obstructive sleep apnea. *Sleep* 1993; 16(8 Suppl):S59-S61.

87. Shoenut JP, Kerr P, Micflikier AB, Yamashiro Y, **Kryger MH**. The effect of nasal CPAP on nocturnal reflux in patients with aperistaltic esophagus. *Chest* 1994; 106(3):738-41.
88. Yamashiro Y, **Kryger MH**. Acute effect of nasal CPAP on periodic limb movements associated with breathing disorders during sleep. *Sleep* 1994 Mar; 17(2):172-5.
89. Steens RD, Millar TW, Su X, Biberdorf D, Buckle P, Ahmed M, **Kryger MH**. Effect of inhaled 3% CO₂ on Cheyne-Stokes respiration in congestive heart failure. *Sleep* 1994 Feb; 17(1):61-8.
90. Yamashiro Y, **Kryger MH**. Acute effect of nasal continuous positive airway pressure on periodic limb movements associated with breathing abnormalities during sleep. *Sleep* 1994; 17: 172-5.
91. Yamashiro Y, **Kryger M**. CPAP titration for sleep apnea using split-night protocol. *Chest* 1995; 107:62-66.
92. Wilkins MA, Xiao-Ling S, Palayew M, Bolli P, McKenzie JK, Yamashiro Y, **Kryger MH**. The effects of posture change and continuous positive airway pressure on cardiac natriuretic peptides in congestive heart failure. *Chest* 1995 April; 107: 909-915.
93. Ahmed M, Serrette C, **Kryger MH**, Anthonisen NR. Ventilatory instability in patients with congestive heart failure and nocturnal Cheyne-Stokes breathing. *Sleep* 1994; 17:527-523.
94. Walker S, Fine A, **Kryger MH**. Sleep Complaints are Common in a Dialysis Unit. *American Journal of Kidney Diseases*, Vol 26, No 5, 1995: pp 751-756.
95. Yamashiro Y, **Kryger MH**. Nocturnal Oximetry: Is It a Screening Tool for Sleep Disorders? 1995. *Sleep*, 18(3): 167-171.
96. Stein MB, Millar TW, Larsen DK, **Kryger MH**. Irregular breathing during sleep in patients with panic disorder. *Am J Psychiatry* 1995; 152:1168-73.
97. Yamashiro Y, Chodirker BN, Hobson D, **Kryger MH**. A familial awake movement disorder mimicking restless legs in a sleep apnea patient. *Sleep* 1995; 18:604-607.
98. Enns M, Stein M, **Kryger M**. Successful treatment of co-morbid panic disorder and sleep apnea with continuous positive airway pressure. *Psychosomatics*, 36(6):585-586, 1995.
99. Shoenut P, Yamashiro Y, Orr WC, Kerr P, Micflikier AB, **Kryger MH**. The effect of severe gastroesophageal reflux on sleep stage in patients with an aperistaltic esophagus. *Digestive dis and sci* 1996; 41(2):372-376.
100. Walker S, Fine A, **Kryger MH**. L-dopa/carbidopa for nocturnal movement disorders in uremia. *Sleep* 19(3):214-218, 1996.
101. Sharma S, Wali S, Pouliot Z, Peters M, Neufeld H, **Kryger M**. Treatment of obstructive sleep apnea with a self-titrating continuous positive airway pressure (CPAP) system. *Sleep* 19(6):497-501, 1996.

102. **Kryger M**, Roos L, Delaive K, Walld R, Horrocks J. Utilization of health care services in patients with severe obstructive sleep apnea. *Sleep* 19(9):S111-S116, 1996.
103. Pouliot Z, Peters M, Neufeld H, **Kryger MH**. Using self-reported questionnaire data to prioritize OSA patients for polysomnography. *Sleep* 20(3):232-236, 1997.
104. Broughton RJ, Fleming JAE, George CFP, Hill JD, **Kryger MH**, Moldofsky H, Montplaisir, Morehouse RL, Moscovitch A, Murphy WF. Randomized, double-blind, placebo-controlled crossover trial of modafinil in the treatment of excessive daytime sleepiness in narcolepsy. *Neurology* 49:444-451, 1997.
105. **Kryger MH**. Controversies in sleep medicine: terminology and definitions in sleep-disordered breathing [editorial] *Sleep* 1997 Dec;20(12):1208.
106. Wali SO, Bahammam AS, Massaeli H, Pierce GN, Iliskovic N, Singal PK, **Kryger MH**. Susceptibility of LDL to oxidative stress in obstructive sleep apnea. *SLEEP* 21(3):290-297, 1998.
107. Pieta J, Millar T, Zacharias J, Fine A, **Kryger MH**. Effect of Pergolide on Restless Legs and Leg Movements in Sleep in Uremic Patients. *Sleep* 1998 Sep 15; 21(6):617-22.
108. Leslie WD, Wali S, **Kryger M**. Blood flow of the middle cerebral artery with sleep-disordered breathing: correlation with obstructive hypopneas (letter). *Stroke* 1999 Jan;30(1):188-90
109. Ronald J, Delaive K, Roos L, Manfreda J, **Kryger MH**. Obstructive sleep apnea patients use more health care resources ten years prior to diagnosis. *Sleep*, 1999 22(2):225-9.
110. Bahammam AS, Tate R, Manfreda J, **Kryger MH**. Sleep in the upper airway resistance syndrome: Effect of nasal dilation, sleep stage, and sleep position. *Sleep*. 1999; 22:592-8.
111. Bahammam AS, Ronald J, Delaive K, Roos L, Manfreda J, **Kryger MH**. Health Care Utilization In Obstructive Sleep Apnea Syndrome Patients Two Years After Diagnosis and Treatment. *Sleep*. 1999; 740-47.
112. Skomro RP, **Kryger MH**. Clinical presentations of obstructive sleep apnea syndrome. *Progress in Cardiovascular Diseases* 1999; 41(5):331-40.
113. Banno, K., Delaive, K., Walld, R., Kryger, M.H. Restless legs syndrome in 218 patients: associated disorders. *Sleep Medicine* 2000; Vol. 1, No. 3: 221-2.
114. Skromo RP, Ludwig S, Salamon E, **Kryger MH**. Sleep Complaints and Restless legs Syndrome in Adult Type 2 Diabetics. *Sleep Medicine*. 2001; 2:417-422.
115. Berg G, Delaive K, Manfreda J, Walld R, **Kryger MH**. The use of health care resources in obesity-hypoventilation syndrome. *Chest*. 2001; 120:377-383.
116. Brown DJ, Kerr P, **Kryger M**. Radiofrequency tissue reduction of the palate in patients with moderate sleep-disordered breathing. *J of Otolaryngol* 2001; 30:193-8.

117. Otake K, Delaive K, Walld R, Manfreda J, **Kryger MH**. Cardiovascular Medication Use In Undiagnosed Obstructive Sleep Apnea Patients. *Thorax* 2002; 57:417-422.
118. Smith R, Ronald J, Delaive K, Walld R, Manfreda J, **Kryger MH**. What are Obstructive Sleep Apnea Patients Being Treated For Prior to OSAS Diagnosis? *Chest*. 2002 Jan; 121(1):164-72.
119. **Kryger MH**, Walld R, Manfreda J. What are Narcolepsy Patients being treated for prior to confirmation of their diagnosis. *Sleep*. 2002 Feb 1; 25(1):36-41.
120. **Kryger M**, Otake K, Foerster J. Low body stores of iron and restless legs syndrome: A correctable cause of insomnia in adolescents and teenagers. *Sleep Medicine* 2002. Mar; 3: 127 - 132.
121. Pouliot Z, Peters M, Neufeld H, Delaive K, **Kryger MH**. Sleep Disorders in a Military Population. 2003 *Military Medicine* 168:7-10.
122. **Kryger MH**, Shepertycky M, Foerster J, Manfreda J. Sleep disorders in repeat blood donors. *Sleep*. 2003 Aug 1; 26(5):625-6.
123. Sassani A, Findley LJ, **Kryger M**, Goldlust E, George C, Davidson TM. Reducing motor-vehicle collisions, costs, and fatalities by treating obstructive sleep apnea syndrome. *Sleep*. 2004 May 1; 27(3):453-8.
124. Shepertycky MR, Banno K, **Kryger MH**. Differences between men and women in the clinical presentation of patients diagnosed with obstructive sleep apnea syndrome. *Sleep*. 2005; 28:309-14.
125. Banno K, Al Sabbagh A, Delaive K, Higami S, **Kryger MH**. Experience in using split-day studies for suspected obstructive sleep apnea syndrome. *Respir Med*. 2005; 99:1334-9.
126. Banno K, **Kryger MH**. Use of polysomnography with synchronized digital video recording to diagnose pediatric sleep breathing disorders. *CMAJ*. 2005; 173:28-30.
127. Banno K, Hobson DE, **Kryger MH**. Long-term treatment of sleep breathing disorder in a patient with Huntington's disease. *Parkinsonism Relat Disord*. 2005; 11:261-4.
128. Albarrak M; Banno K; Sabbagh AA, Delaive K, Walld R, Manfreda J, **Kryger MH**. Utilization of healthcare resources in obstructive sleep apnea syndrome: a 5-year follow-up study in men using CPAP. *Sleep* 2005; 28: 1306-1311.
129. Kapsimalis F, Richardson G, Opp MR, **Kryger M**. Cytokines and normal sleep. *Curr Opin Pulm Med*. 2005 Nov; 11(6):481-4.
130. Singh H, Pollock R, Uhanova J, **Kryger M**, Hawkins K, Minuk GY. Symptoms of obstructive sleep apnea in patients with nonalcoholic fatty liver disease. *Dig Dis Sci*. 2005; 50:2338-43.
131. Banno K, Walld R, **Kryger MH**. Increasing obesity trends in patients with sleep-disordered breathing referred to a sleep disorders center. *J Clin Sleep Med* 2005 Oct 15; 1(4):364-6.

132. Banno K, Okamura K, **Kryger MH**. Adaptive servo-ventilation in patients with idiopathic Cheyne-Stokes breathing. *J Clin Sleep Med* 2006 Apr 15; 2(2):181-6.
133. Vagiakis E, Kapsimalis F, Lagogianni I, Perraki H, Minaritzoglou A, Alexandropoulou K, Roussos C, **Kryger M**. Gender differences on polysomnographic findings in Greek subjects with obstructive sleep apnea syndrome. *Sleep Med* 2006 Aug; 7(5):424-30.
134. Banno K, Manfreda J, Walld R, Delaive K, **Kryger MH**. Healthcare utilization in women with obstructive sleep apnea syndrome 2 years after diagnosis and treatment. *Sleep* 2006 Oct 1; 29(10):1307-11.
135. **Kryger M**, Wang Weigand S, Roth T. Safety of ramelteon in individuals with mild to moderate obstructive sleep apnea. *Sleep Breath* 2007 Sep; 11(3):159-64.
136. **Kryger M**, Wang-Weigand S, Zhang J, Roth T. Effect of Ramelteon, a selective MT (1)/MT (2)-receptor agonist, on respiration during sleep in mild to moderate COPD. *Sleep Breath*. 2008 Aug; 12(3):243-50.
137. Kapsimalis F, Varouchakis G, Manousaki A, Daskas S, Nikita D, **Kryger M**, Gourgoulialis K. Association of sleep apnea severity and obesity with insulin resistance, C-reactive protein, and leptin levels in male patients with obstructive sleep apnea. *Lung*. 2008 Jul-Aug; 186(4):209-17.
138. **Kryger M**, Wang-Weigand S, Zhang J, Roth T. Effect of ramelteon, a selective MT (1)/MT (2)-receptor agonist, on respiration during sleep in mild to moderate COPD. *Sleep Breath*. 2008 Aug; 12(3):243-50.
139. **Kryger M**, Roth T, Wang-Weigand S, Zhang J. The effects of ramelteon on respiration during sleep in subjects with moderate to severe chronic obstructive pulmonary disease. *Sleep Breath*. 2009 Mar; 13(1):79-84. Epub 2008 Jun 27.
140. Kapsimalis F, **Kryger M**. Sleep breathing disorders in the U.S. female population. *J Womens Health (Larchmt)*. 2009 Aug; 18(8):1211-9.
141. Banno K, Ramsey C, Walld R, **Kryger MH**. Expenditure on health care in obese women with and without sleep apnea. *Sleep*. 2009 Feb 1; 32(2):247-52.
142. **Kryger M**, Berry RB, Massie CA. Long-term use of a nasal expiratory positive airway pressure (EPAP) device as a treatment for obstructive sleep apnea (OSA). *J Clin Sleep Med*. 2011 Oct 15;7(5):449-53B.
143. Kushida CA, Berry R, Blau A, Crabtree T, Fietze I, **Kryger MH**, et. al. Positive Airway Pressure Initiation: A Randomized Controlled Trial to Assess the Impact of Therapy Mode and Titration Process on Efficacy, Adherence, and Outcomes. *Sleep*. 2011 Aug 1;34(8):1083-92.
144. Bouloukaki I, Kapsimalis F, Mermigkis C, **Kryger M**, Tzanakis N, Panagou P, et. Al. Prediction of obstructive sleep apnea syndrome in a large Greek population. *Sleep Breath*. 2011 Dec;15(44): 657-64,
145. Berry RB, **Kryger MH**, Massie CA. A novel nasal expiratory positive airway pressure (EPAP) device for the treatment of obstructive sleep apnea: a randomized controlled trial. *Sleep*. 2011 Apr 1;34(4):479-85.

146. Yamashiro Y, **Kryger M**. Is laryngeal descent associated with increased risk for obstructive sleep apnea? *Chest*. 2012 Jun;141(6):1407-13.
147. Berry RB, Kushida CA, **Kryger MH**, Soto-Calderon H, Staley B, Kuna ST. Respiratory event detection by a positive airway pressure device. *Sleep*. 2012 Mar1;35(3):361-7.
148. **Kryger M**, Eiken T, Qin L. The use of combined thermal/pressure polyvinylidene fluoride film airflow sensor in polysomnography. *Sleep Breath*. 2013. Dec;17(4):1267-73.
149. Kushida CA, Halbower AC, **Kryger MH**, Pelayo R, Assalone V, Cardell CY, Huston S, Willes L, Wimms AJ, Mendoza J. Evaluation of a new pediatric positive airway pressure mask. *J Clin Sleep Med*. 2014 Sep 15;10(9):979-84
150. Mutter TC, Chateau D, Moffatt M, Ramsey C, Roos LL, **Kryger M**. A matched cohort study of postoperative outcomes in obstructive sleep apnea: could preoperative diagnosis and treatment prevent complications? *Anesthesiology*. 2014. Oct;121(4):707-18.
151. Sun H, Palcza J, Rosenberg R, **Kryger M**, Siringhaus T, Rowe J, Lines C, Wagner JA, Troyer MD. Effects of suvorexant, an orexin receptor antagonist, on breathing during sleep in patients with chronic obstructive pulmonary disease. *Respir Med*. 2015 Mar;109(3):416-26
152. Javaheri S, Winslow D, McCullough P, Wylie P, **Kryger MH**. The Use of a Fully Automated Automatic Adaptive Servoventilation Algorithm in the Acute and Long-term Treatment of Central Sleep Apnea. *Chest*. 2015 Dec 1;148(6):1454-61.
153. Sun H, Palcza J, Card D, Gipson A, Rosenberg R, **Kryger M**, Lines C, Wagner JA, Troyer MD. Effects of Suvorexant, an Orexin Receptor Antagonist, on Respiration during Sleep In Patients with Obstructive Sleep Apnea. *J Clin Sleep Med*. *J Clin Sleep Med*. 2016;12(1):9-17.
154. **Kryger M**. Jack London's Sleep. *J Clin Sleep Med*. 2016 Nov 15;12(11):1545-1547.
155. Weiss P, **Kryger M**. Positive Airway Pressure Therapy for Obstructive Sleep Apnea. *Otolaryngol Clin North Am*. 2016 Dec;49(6):1331-1341.

Books

1. *Pathophysiology of Respiration*, **Kryger M.**, Editor. John Wiley & Sons, New York, 1981.
2. *Sleep Disorders*. Chest Clinics of North America, **Kryger M.**, Editor. W. B. Saunders Publishing Co. Ltd., Philadelphia, 1985.

3. *Pathophysiology of Respiration* (Japanese Edition), **Kryger M. H.**, Editor. Nishimura Co. Ltd. Tokyo, Japan, 1986.
4. *Principles and Practice of Sleep Medicine*. **M. Kryger**, T. Roth, WC Dement. WB Saunders Co., Philadelphia, 1989.
5. *Introduction to Respiratory Medicine*. **Kryger M.**, Editor. Churchill Livingstone, New York, 1990.
6. *Principles and Practice of Sleep Medicine, 2nd ed.* **M. Kryger**, T. Roth, WC Dement. WB Saunders Co., Philadelphia, 1994.
7. *Principles and Practice of Sleep Medicine in the Child*. R Ferber, **M. Kryger**. WB Saunders Co., Philadelphia, 1995.
8. *Principles and Practice of Sleep Medicine, 3rd ed.* **M. Kryger**, T. Roth, WC Dement. WB Saunders Co., Philadelphia, 2000.
9. *A Woman's Guide to Sleep Disorders*. **Kryger M.** McGraw Hill. New York, 2004. (In Canada, Can't Sleep, Can't Stay Awake. HarperCollins Canada. Toronto, 2004.
10. *Principles and Practice of Sleep Medicine, 4th ed.* **M. Kryger**, T. Roth, WC Dement (eds). Elsevier. Philadelphia, 2005.
11. *Principles and Practice of Pediatric Sleep Medicine*. Sheldon S, Ferber R, **Kryger M** (eds). Elsevier. Philadelphia, 2005.
12. *Atlas of Clinical Sleep Medicine*. **M. Kryger**. Elsevier. Philadelphia, 2010.
13. *Principles and Practice of Sleep Medicine, 4th ed. (Simplified Chinese Translation)* **M. Kryger**, T. Roth, WC Dement (eds). Elsevier. Singapore, 2010.
14. *Principles and Practice of Sleep Medicine, 5th ed.* **M. Kryger**, T. Roth, WC Dement (eds). Elsevier. Philadelphia, 2011.
15. *Kryger's Sleep Medicine Review*. **Kryger MH**, Rosenberg R, Pegram V, Martin L. Elsevier. Philadelphia, 2011.
16. *The Mystery of Sleep*. **Kryger M.** (ebook) – www.krygerbooks.com. 2012, Revised 2015.
17. *Principles and Practice of Pediatric Sleep Medicine 2 E*. Sheldon S, Ferber R, Gozal D, **Kryger M** (eds). Elsevier. Philadelphia, 2014.
18. *Atlas of Clinical Sleep Medicine 2E*. **Kryger M**, Avidan A, Berry R. Elsevier. Philadelphia, 2014.

19. *Atlas Clínico de Medicina do Sono*. (Portuguese translation of above). **Kryger M**, Avidan A, Berry R. Elsevier. Rio de Janeiro, 2015.
20. *Kryger's Sleep Medicine Review*. **Kryger MH**, Rosenberg R, Kirsch D, Martin L. Elsevier. Philadelphia, 2015.
21. *Principles and Practice of Sleep Medicine, 6th ed*. **M. Kryger**, T. Roth, WC Dement (eds). Elsevier. Philadelphia, 2016.
22. *Sleep Breathing Disorders*. **M. Kryger**. Elsevier. Philadelphia, in Press 2016.
23. *The Mystery of Sleep*. **Kryger M**. Yale University Press, New Haven, CT. 2017.

Book Chapters, Reviews (Peer reviewed) editorials, letters

1. **Kryger M**, Bode F, Antic R, Anthonisen N: Diagnosis of obstruction of the upper and central airways. *Am J Med* 1976; 61:85-93.
2. Zwillich C, **Kryger M**, Weil J: Hypoventilation: consequences and management in advances in internal medicine. Year Book Medical Publishers, Chicago 1978; 23:287-306 G. Stollerman, Ed.
3. Weil JV, **Kryger M**, Scoggin C: Sleep and Breathing at High Altitude. In *Sleep Apnea Syndromes*, Alan R Liss Inc. New York 1978 (Eds. Christian Guilleminault and William C. Dement).
4. Weil JV, **Kryger M**, Scoggin C: Sleep and Breathing at High Altitude. In *Sleep Apnea Syndromes*, Alan R Liss Inc. New York 1978 (Eds. Christian Guilleminault and William C. Dement).
5. **Kryger M**. Sleep-related Apnea. *Chest* 1979; 76:242.
6. **Kryger MH**. Central Apnea. *Arch Intern Med* 1982;142:1793.
7. Fleetham JA, **Kryger MH**. Sleep disorders in chronic airflow obstruction. *Medical Clinics of North America* 1981; 65(3):549.
8. **Kryger MH**. Abnormal control of breathing. In: *Pathophysiology of Respiration*, **Kryger M** (ed.). J Wiley Publishers 1981; 103-122.
9. **Kryger MH**. The pleural space. In: *Pathophysiology of Respiration*, **Kryger M** (ed.). J. Wiley Publishers 1981; 123-134.
10. **Kryger MH**. Respiratory Failure 1: Oxygen. In: *Pathophysiology of Respiration*, **Kryger M** (ed.). J. Wiley Publishers 1981; 165-204.
11. **Kryger MH**. Respiratory Failure 2: Carbon Dioxide. In: *Pathophysiology of Respiration*, **Kryger M** (ed.) J. Wiley Publishers 1981; 205-220.

12. **Kryger MH**. Respiratory Failure 3: The Patient. In: Pathophysiology of Respiration, **Kryger M** (ed.). J. Wiley Publishers 1981; 221-230.
13. Chernick V, **Kryger MH**. Pediatric Lung Disease. In: Pathophysiology of Respiration, **Kryger M** (ed.). J. Wiley Publishers 1981; 259-268.
14. **Kryger MH**. Lung Cancer. In: Pathophysiology of Respiration, **Kryger M** (ed.). J. Wiley Publishers 1981; 269-278.
15. **Kryger MH**. High Altitude. In: Pathophysiology of Respiration, **Kryger M** (ed.). J. Wiley Publishers 1981; 299-306.
16. Anthonisen NR, **Kryger MH**. Ventilatory and arousal responses to hypoxemia in sleep. [Editorial] Am Rev Resp Dis 1982;126:1-2.
17. Grover RF, **Kryger MH**. Polycythemia of chronic mountain sickness. In adjustment to high altitude. EC Chamberlayne, PG Condliffe editors. NIH Pub # 83-2496:1983; 37-42.
18. Savoy J, **Kryger MH**. Differential diagnosis of upper-airway obstruction. Prac Card 1984; 10(4):151.
19. Perez-Padilla R, **Kryger MH**. Upper airway obstruction. In: Cherniack RM, Brain MC, Bayless TM eds. Current Therapy in Internal Medicine. Toronto: BC Decker Inc., 1984:737-741.
20. Perez-Padilla R, **Kryger MH**. Upper airway obstruction. In: Cherniack RM, ed. Current Therapy of Respiratory Disease. Toronto: BC Decker Inc., 1984:8-13.
21. Savoy J, **Kryger MH**. Respiratory disorders in sleep. Medicine North America 1985; 22:2977-82.
22. **Kryger MH**. Fat, sleep and Charles Dickens: literary and medical contributions to the understanding of sleep apnea. Clin Chest Med 1985; 6(4):555-562.
23. George CF, **Kryger MH**. Sleep and control of heart rate. Clin Chest Med 1985; 6(4):595-602.
24. West P, **Kryger MH**. Sleep and respiration: methodology and terminology. Clin Chest Med 1985; 6(4):691-712.
25. **Kryger MH**, White DP, Zwillich CW, Robinson RW, Guilleminault C. Sleep and respiration: a postscript. Clin Chest Med 1985; 6(4):713-718.
26. **Kryger MH**. Is it really so bad to snore? J Resp Dis 1986; 7(2):11.
27. Perez-Padilla R, **Kryger MH**. Upper airway obstruction. Current Therapy of Respiratory Disease, R. Cherniack Editor. B. C. Dekker, 1986.
28. George CF, **Kryger MH**. Tracheostomy for sleep apnea. Lancet 1986 Feb; 8.
29. Anthonisen NR, **Kryger MH**. Sleep and breathing in patients with lung disease. In: Breathing Disorders of Sleep, Edelman NH and Santiago TV, eds. Churchill Livingstone, 1986, pp 205-224.

30. **Kryger MH**. Machine Language. Chest Soundings, a bulletin of the ACCP. August, 1986.
31. Perez-Padilla R, **Kryger MH**. Upper Airway Obstruction. In: Current Therapy in Internal Medicine - 2, Bayless TM, Brain MC, Cherniack RM, eds. B. C. Decker Inc., Philadelphia, PA., 1987.
32. George CF, **Kryger MH**. Sleep in Chronic Obstructive Lung Disease. In: Chronic Obstructive Pulmonary Disease: Current Concepts, Petty TL and Hodgkin J, (eds) W. B. Saunders Co., Philadelphia, 1987.
33. **Kryger MH**. Sleep and heart failure. Eur J Respir Dis 1990; 3:1103-1104.
34. George CF, **Kryger MH**. Sleep and sleepiness and the pulmonologist. In: Current Pulmonology, Simmons DH (ed). Year Book Medical Publishers: Chicago, 1990.
35. **Kryger MH**, Hanly PJ. Cheyne-Stokes respiration in cardiac failure. In: Sleep and Respiration, Issa FG, Suratt PM, Remmers JE (eds). Wiley-Liss Publishers: New York, 1990.
36. Roth T, Roehrs T, **Kryger M**. Mortality in Obstructive Sleep Apnea. In: Sleep and Respiration, Issa FG, Suratt PM, Remmers JE (eds). Wiley-Liss Publishers: New York, 1990.
37. **Kryger MH**. Introduction to Respiratory Pathophysiology. In: **Kryger MH**, editor. Introduction to Respiratory Medicine, 2E. New York: Churchill Livingstone, 1990: 1-5.
38. **Kryger MH**. Abnormal Control of Breathing and Sleep Disorders. In: **Kryger MH**, editor. Introduction to Respiratory Medicine, 2E. New York: Churchill Livingstone, 1990: 109-31.
39. **Kryger MH**. Respiratory Failure 1: Oxygen. In: **Kryger MH**, editor. Introduction to Respiratory Medicine, 2E. New York: Churchill Livingstone, 1990: 169-209.
40. **Kryger MH**. Respiratory Failure 2: Carbon Dioxide. In: **Kryger MH**, editor. Introduction to Respiratory Medicine, 2E. New York: Churchill Livingstone, 1990: 211-26.
41. **Kryger MH**. The Lung in Acid-Base Regulation. In: **Kryger MH**, editor. Introduction to Respiratory Medicine, 2E. New York: Churchill Livingstone, 1990: 237-65.
42. Chernick V, **Kryger MH**. Pediatric Lung Disease. In: **Kryger MH**, editor. Introduction to Respiratory Medicine, 2E. New York: Churchill Livingstone, 1990: 267-76.
43. **Kryger MH**. High Altitude. In: **Kryger MH**, editor. Introduction to Respiratory Medicine, 2E. New York: Churchill Livingstone, 1990: 321-29.
44. George CF, **Kryger MH**. Sleep and Sleepiness and the Pulmonologist, In Simmons DH, Current Pulmonology. 11: 1-18, Chicago, Year Book Medical Publishers, Inc, 1990.
45. **Kryger MH**. The management of obstructive sleep apnea. Clin Chest Med 1992; 13(3):481-92.
46. Yamashiro Y, **Kryger MH**. Review: Sleep in heart failure. Sleep 1993; 16(6):513-23.
47. **Kryger MH**. Snoring: a public health hazard? Chest 1993;104(1):2-3.

48. **Kryger MH**, Roth T, Carskadon M. Circadian Rhythms in Humans: An Overview. In: **Kryger MH**, Roth T, Dement WC, editors. Principles and Practice of Sleep Medicine, 2E. Philadelphia: W.B. Saunders Co., 1994: 301-8.
49. **Kryger MH**. Management of Obstructive Sleep Apnea: Overview. In: **Kryger MH**, Roth T, Dement WC, editors. Principles and Practice of Sleep Medicine, 2E. Philadelphia: W.B.Saunders Company, 1994: 736-47.
50. **Kryger MH**. Restrictive Lung Diseases. In: **Kryger MH**, Roth T, Dement WC, editors. Principles and Practice of Sleep Medicine, 2E. Philadelphia: W.B.Saunders Company, 1994: 769-75.
51. **Kryger MH**. Monitoring Respiratory and Cardiac Function. In: **Kryger MH**, Roth T, Dement WC, editors. Principles and Practice of Sleep Medicine, 2E. Philadelphia: W.B.Saunders Company, 1994: 984-93.
52. Yamashiro Y, **Kryger MH**. Why should sleep apnea be diagnosed and treated. Clin Pulm Med 1994; 1: 250-9.
53. Wali SO, **Kryger M**. Medical Treatment of Sleep Apnea, Current Opinion in Pulmonary Medicine 1995, 1:498-503.
54. Lertzman M, **Kryger M**. Fitness to drive in the elderly (letter). Lancet 1995; 345:64.
55. Wali SO, Lertzman M, **Kryger M**. Crashes and Violations among Older Drivers (Letter). Ann Intern Med 1995 Jun; 122(11):885.
56. Lertzman M, Wali SO, **Kryger M**. Sleep Apnea a Risk Factor for Poor Driving, CMAJ. 1995; 153 (8): 1063.
57. **Kryger M**. Sleep apnoea and the misuse of evidence-based medicine. Lancet 349(9054), 803-804, 1997.
58. **Kryger M**, Salva P. Polysomnographic comparisons of zolpidem and benzodiazepines in healthy volunteers and insomniacs. In: Freeman H, Puech AJ, Roth T (Eds). Zolpidem: an update of its pharmacological properties and therapeutic place in the management of insomnia. Elsevier: Paris, 1996, pp 141-148.
59. Kryger, M.H., George, F.P. Differential Diagnosis and Evaluation of Sleepiness: Fishman's Pulmonary Diseases & Disorders, 3rd Edition; Fishman, A.P., Published by McGraw-Hill 1998; Chapter 103, p. 1639.
60. Bahammam A, **Kryger MH**. Decision making in obstructive sleep-disordered breathing. Putting it all together. Otolaryngol Clin North Am. 1999 Apr; 32(2):333-48.
61. Bahammam A, **Kryger MH**. Decision making in obstructive sleep-disordered breathing. Putting it all together. Clin Chest Med 19(1):87-97, 1998.
62. Kryger, MH. Diagnosis and Management of Sleep Apnea Syndrome. Clinical Cornerstone 2000; Vol. 2, No. 5: 39-47.

63. **Kryger M.** Management of Sleep Apnea Hypopnea Syndrome: Overview. In, Principles and Practice of Sleep Medicine, 3rd ed. M. Kryger, T. Roth, WC Dement. WB Saunders Co., Philadelphia, 2000.
64. **Kryger M.** Restrictive lung disorders. In, Principles and Practice of Sleep Medicine, 3rd ed. M. Kryger, T. Roth, WC Dement. WB Saunders Co., Philadelphia, 2000.
65. **Kryger M.** Cardiorespiratory monitoring. In, Principles and Practice of Sleep Medicine, 3rd ed. M. Kryger, T. Roth, WC Dement. WB Saunders Co., Philadelphia, 2000.
66. Kapsimalis F, **Kryger MH.** Gender and obstructive sleep apnea syndrome, part 1: Clinical features. *Sleep.* 2002 Jun 15; 25(4):412-9.
67. Kapsimalis F, **Kryger MH.** Gender and obstructive sleep apnea syndrome, part 2: mechanisms. *Sleep.* 2002 Aug 1; 25(5):499-506.
68. Shepertycky M, Al-Barrak M, **Kryger MH.** Morbidity and mortality in obstructive sleep apnea syndrome 1: Effect of treatment on cardiovascular morbidity. *Sleep and Biological Rhythms* 2003; 1: 15–28.
69. Al-Barrak Shepertycky MM, **Kryger MH.** Morbidity and mortality in obstructive sleep apnea syndrome 2: Effect of treatment on neuropsychiatric morbidity and quality of life. *Sleep and Biological Rhythms* 2003; 1: 65-74.
70. Banno K, **Kryger MH.** Factors limiting access to services for sleep apnea patients (editorial). *Sleep Med Rev.* 2004 Aug;8(4):253-5.
71. Orr WC, Heading R, Johnson LF, **Kryger M.** Sleep and its relationship to gastro-oesophageal reflux. *Aliment Pharmacol Ther.* 2004; 20 Suppl 9:39-46.
72. Phillips B. **Kryger MH.** Management of obstructive Sleep Apnea Hypopnea Syndrome: Overview. In M. Kryger, T. Roth, WC Dement (eds). Principles and Practice of Sleep Medicine, 4th ed. Elsevier. Philadelphia, 2005.
73. **Kryger MH.** restrictive lung disorders. In M. Kryger, T. Roth, WC Dement (eds). Principles and Practice of Sleep Medicine, 4th ed. Elsevier. Philadelphia, 2005.
74. Hirshkowitz M, **Kryger MH.** Monitoring techniques for evaluating suspected sleep-disordered breathing. In M. Kryger, T. Roth, WC Dement (eds). Principles and Practice of Sleep Medicine, 4th ed. Elsevier. Philadelphia, 2005.
75. **Kryger M.** Differential diagnosis of pediatric sleep disorders. Principles and Practice of Pediatric Sleep Medicine. Sheldon S, Ferber R, **Kryger M** (eds). Elsevier. Philadelphia, 2005.
76. Banno K, **Kryger MH.** Sleep disorders in older people. *Aging Health* 2005;1: 449–457.
77. **Kryger MH,** Neubauer DN, Bunn WB 3rd, Bridges J, Rosekind MR. Awakening insomnia management: A collaborative approach to improved care. *Manag Care* 2006 Sep; 15(9 Suppl 6):1-17.

78. Banno K, **Kryger MH**. Sleep apnea: clinical investigations in humans. *Sleep Med* 2007 Jun;8(4):400-26.
79. Kapsimalis F, Basta M, Varouchakis G, Gourgoulianis K, Vgontzas A, **Kryger M**. Cytokines and pathological sleep. *Sleep Med* 2007 Nov 15.
80. Mokhlesi B, **Kryger MH**, Grunstein RR. Assessment and management of patients with obesity hypoventilation syndrome. *Proc Am Thorac Soc*. 2008 Feb 15;5(2):218-25.
81. Kryger, M.H., George, F.P. *Differential Diagnosis and Evaluation of Sleepiness: Fishman's Pulmonary Diseases & Disorders*, 4rd Edition; Fishman, A.P., Published by McGraw-Hill 2008; Chapter 98, p. 1737.
82. Paul KN, Turek FW, **Kryger MH**. Influence of sex on sleep regulatory mechanisms. *J Womens Health*. 2008 Sep; 17(7):1201-8.
83. Lee KA, **Kryger MH**. Women and sleep. *J Womens Health*. 2008 Sep;17(7):1189-90.
84. **Kryger MH**. History of Sleep Medicine. *Atlas of Clinical Sleep Medicine*. Elsevier, Philadelphia. Elsevier, Philadelphia. 2010
85. **Kryger MH**. Physical Examination in Sleep Breathing Disorders. *Atlas of Clinical Sleep Medicine*. Elsevier, Philadelphia. Elsevier, Philadelphia. 2010
86. **Kryger MH**. The Overlap Syndromes. *Atlas of Clinical Sleep Medicine*. Elsevier, Philadelphia. Elsevier, Philadelphia. 2010.
87. **Kryger MH**. Sleep in Thyroid Disease. *Atlas of Clinical Sleep Medicine*. Elsevier, Philadelphia. Elsevier, Philadelphia. 2010.
88. **Kryger MH**. Sleep in Acromegaly. *Atlas of Clinical Sleep Medicine*. Elsevier, Philadelphia. Elsevier, Philadelphia. 2010.
89. Hirshkowitz M, **Kryger MH**. Gallery of Polysomnographic Recordings. *Atlas of Clinical Sleep Medicine*. Elsevier, Philadelphia. Elsevier, Philadelphia. 2010.
90. Masa J, **Kryger MH**. Restrictive Lung Disease. In **Kryger MH**, Roth T, Dement WC eds. *Principles and Practice of Sleep Medicine 5E*. Elsevier, Philadelphia. 2011.
91. Phillips B, **Kryger MH**. Management of Obstructive Sleep Apnea-Hypopnea Syndrome. In **Kryger MH**, Roth T, Dement WC eds. *Principles and Practice of Sleep Medicine 5E*. Elsevier, Philadelphia. 2011.
92. **Kryger MH**. Sleep Medicine. The shot heard around the world. *J Clin Sleep Med*. *J Clin Sleep Med*. 2012 Apr 15;8(2):117-8.
93. **Kryger MH**. Charles Dickens: "What a gain it would have been to physic if one so keen to observe and facile to describe had devoted his powers to the medical art". *J Clin Sleep Med*. 2012 Jun 15;8(3):333-8.

94. Won CH, **Kryger M**. Sleep in patients with restrictive lung disease. Clin Chest Med. 2014 Sep;35(3):505-12.
95. Sen, M, **Kryger, M.H.**. Differential Diagnosis and Evaluation of Sleepiness: Fishman's Pulmonary Diseases & Disorders, 5th Edition; Fishman, A.P., Published by McGraw-Hill (2015).
96. Won C, Michaud G, **Kryger M**. Upper Airway Obstruction in Adults: Fishman's Pulmonary Diseases & Disorders, 5th Edition; Fishman, A.P., Published by McGraw-Hill (2015).
97. Knauert M, Naik S, Gillespie WB, **Kryger M**. Clinical consequences and economic costs of untreated obstructive sleep apnea syndrome. World Journal of Otorhinolaryngology-Head and Neck Surgery (2015) 1, 17-27.
98. **Kryger, MH**. Noon: Rest from Work, after Jean-François Millet by Vincent van Gogh. Sleep Health. 2015; 1, (1) 3-4.
99. **Kryger, M H** Sleep's embrace. Sleep Health. 2015; 1, (2), 84.
100. **Kryger, H**. Henri Matisse: an image of sleep in a time of turmoil. Sleep Health. 2015; 1, (3), 143-144.
101. Mansfield D, **Kryger MH**. Regulating danger on the highways: hours of service regulations Sleep Health. 2015; 1 , (4), 311 – 313.
102. **Kryger, M H**. Entering a dream. Sleep Health. 2015 ; 1, (4), 225
103. **Siegel I, Kryger MH**. The Enigma of the Sleeping Girl. Sleep Health. 2016 ; 2, (2), 85
104. **Kryger MH, Siegel I**. Surrealistic sleep. Sleep Health. 2017 Feb;3(1):1-2.
105. Miner B, **Kryger MH**. Sleep in the Aging Population. Sleep Med Clin. 2017. Mar;12(1):31-38.
106. **Kryger MH, Siegel I**. Sleep under a mother's protective gaze. Sleep Health.2017 Apr;3(2):71-72.
107. **Kryger MH, Siegel I**. Painting a dream: Le Rêve-Pablo Picasso. Sleep Health. 2017 Jun;3(3):134-135.
108. **Kryger MH, Siegel I**. Sleep in enchanted colors. Sleep Health. 2017 Aug;3(4):223-224.
109. **Kryger MH, Siegel I**. The power of sleep. Sleep Health. 2017 Oct;3(5):307-308.

Case Reports

1. **Kryger M**, Levin D: Bronchial adenoma in a young man. Clinical Notes on Respiratory Disease 1977; 16:15-16.
2. Meller D, Fraser I, **Kryger M**. Hyperglycemia in anticholinesterase poisoning. CMAJ 1981; 124:745.

3. **Kryger MH**. Diagnosing sleep breathing disorders. *BronkoScope* 1983;1(4):4.
4. Gallagher CG, Stark R, Teskey J, **Kryger M**. Atypical manifestations of pulmonary adenoid cystic carcinoma. *Br. J. Dis Chest* 1986;80:396.
5. Buckle P, Kerr P, **Kryger MH**. Nocturnal cluster headache associated with sleep apnea. *A. Sleep* 1993; 16(5):487-89.
6. Banno K, Okamura K, **Kryger MH**. Hyperthyroidism in a patient referred for an assessment of obstructive sleep apnea syndrome. *Sleep Med* 2006 Mar;7(2):195-6.

Guidelines

1. **Kryger M**, Member of Respiratory-Related Sleep Disorders Committee of Diagnostic Classification Steering Committee. *The International Classification of Sleep Disorders: Diagnostic and Coding Manual*. ASDA Rochester MN. 1990.
2. ATS Task Force (M Kryger, member). Sleep apnea, sleepiness and driving risk. Official statement of the American Thoracic Society. *Am Rev Respir Dis* 1994; 150:1643-73.
3. **Kryger M**. Sleep Apnea: Science Base, Magnitude of the Problem, Symptoms, and treatment. National Institutes of Health, National Heart, Lung, and Blood Institute 1994 Jun. Report No.: NIH-NHLBI-3800-11-15.
4. Dinges D, Ball E, Fredrickson P, Kiley J, **Kryger MH**, Richardson GS, Rogus S, Sheldon S, Wooten V, Zepf B. Recognizing problem sleepiness in your patients. National center on sleep disorders research working group. *Am Fam Physician* 1999 Feb 15;59(4):937-44
5. **Kryger M**, Lavie P, Rosen R. Recognition and Diagnosis of Insomnia. *Sleep* 1999; 22(3) S421-26.
6. **Kryger M**, Monjan A, Bliwise D, Ancoli-Israel S. Sleep, health, and aging. Bridging the gap between science and clinical practice. *Geriatrics*. 2004 Jan; 59:24-6, 29-30.
7. **Kryger M**. Sleep, health, and aging. Introduction to National Sleep Foundation and National Institute on Aging Congress on Aging. *Geriatrics*. 2004 Jan; 59:23.
8. Fleetham J, Ayas N, Bradley D, Ferguson K, Fitzpatrick M, George C, Hanly P, Hill F, Kimoff J, **Kryger M**, Morrison D, Series F, Tsai W. Canadian Thoracic Society guidelines: diagnosis and treatment of sleep disordered breathing in adults. *Can Respir J* 2006 Oct; 13(7):387-92.
9. Fleetham J, Ayas N, Bradley D, Ferguson K, Fitzpatrick M, George C, Hanly P, Hill F, Kimoff J, **Kryger M**, Morrison D, Series F, Tsai W. [Practice Guidelines of the Canadian Thoracic Society on the diagnosis and treatment of sleep respiratory problems of adults] *Can Respir J* 2007 Jan-Feb;14(1):31-6.
10. Penzel T, Hirshkowitz M, Harsh J, Chervin RD, Butkov N, **Kryger M**, Malow B, Vitiello MV, Silber MH, Kushida CA, Chesson AL Jr. Digital analysis and technical specifications. *J Clin Sleep Med* 2007 Mar 15; 3(2):109-20.

11. Silber MH, Ancoli Israel S, Bonnet MH, Chokroverty S, Grigg Damberger MM, Hirshkowitz M, Kapen S, Keenan SA, **Kryger MH**, Penzel T, Pressman MR, Iber C. The visual scoring of sleep in adults. *J Clin Sleep Med* 2007 Mar 15; 3(2):121-31.
12. Bloom HG, Ahmed I, Alessi CA, Ancoli-Israel S, Buysse DJ, **Kryger MH**, Phillips BA, Thorpy MJ, Vitiello MV, Zee PC. Evidence-based recommendations for the assessment and management of sleep disorders in older persons. *J Am Geriatr Soc.* 2009 May; 57(5):761-89.
13. Kuna ST, Badr MS, Kimoff RJ, Kushida C, Lee-Chiong T, Levy P, McNicholas WT, Strollo PJ Jr; ATS/AASM/ACCP/ERS Committee on Ambulatory Management of Adults with OSA (MH Kryger is listed as Collaborator). An official ATS/AASM/ACCP/ERS workshop report: Research priorities in ambulatory management of adults with obstructive sleep apnea. *Proc Am Thorac Soc.* 2011 Mar; 8(1):1-16.

Software

Kryger MH. KSTATS. Interactive statistics for KnowledgeMan. Retrieval Technology Publishers. Chelmsford, Mass., 1986.

Kryger MH. *Journey Into Sleep*, An Interactive CD based program about sleep and its disorders

CURRICULUM VITAE

Thomas Roth, Ph.D.
 Chief, Division Head
 Sleep Disorders and Research Center
 Henry Ford Hospital
 2799 West Grand Blvd, CFP-3
 Detroit, Michigan 48202-2691
 Phone: (313) 916-5171
 Fax: (313) 916-5167

(b) (6)

Relevant Work Experience

- 2014-Present Consulting Professor and Advisor, Division of Public Mental Health and Public Sciences, Stanford Medicine, Stanford, California
- 2003-Present Professor, Department of Psychiatry, Wayne State University - School of Medicine, Detroit, Michigan
- 1979-Present Clinical Professor, Department of Psychiatry, University of Michigan School of Medicine, Ann Arbor, Michigan
- 1978-Present Director, Sleep Disorders and Research Center, Henry Ford Health System, Detroit, Michigan
- 1995-2003 Director of Research, Henry Ford Health Sciences Center, Detroit, Michigan
- 1995-2003 Adjunct Professor, Department of Psychiatry, Wayne State University - School of Medicine, Detroit, Michigan
- 1978-2003 Division Head, Henry Ford Hospital Sleep Disorders and Research Center, Department of Psychiatry, Detroit, Michigan
- 1977-1978 Co-Director, Sleep Disorders Center, Cincinnati General Hospital, Cincinnati, Ohio
- 1976-1978 Associate Professor of Psychology, Department of Psychiatry, College of Medicine, University of Cincinnati, Cincinnati, Ohio
- 1976-1978 Adjunct Associate Professor of Psychology, Department of Psychology, University of Cincinnati, Cincinnati, Ohio
- 1976-1978 Associate Professor of Psychology, Department of Psychology, Xavier University, Cincinnati, Ohio

- 1972-1978 Co-Director, Sleep Research Laboratory, Veterans Administration Hospital, Cincinnati, Ohio
- 1972-1976 Assistant Professor of Psychology, Department of Psychiatry College of Medicine, University of Cincinnati, Cincinnati, Ohio
- 1970-1972 Research Associate, Department of Psychiatry, College of Medicine, University of Cincinnati, Cincinnati, Ohio
- 1969-1970 Research Assistant, Sleep and Dream Laboratory, Department of Psychiatry, Veterans Administration Hospital, Cincinnati, Ohio
- 1967-1969 Teaching Assistant, Experimental Psychology, University of Cincinnati, Cincinnati, Ohio
- 1967-1968 Research Associate, Department of Community Planning, University of Cincinnati
- 1965-1967 Research Assistant, Department of Pharmacology, College of Medicine, Howard University
- 1965-1967 Teaching Assistant, Introductory and Experimental Psychology, Howard University

Elected Offices

- Chairman, Advisory Board, National Center on Sleep Disorders Research, NHLBI, 1994-1996
- President, Sleep Research Society, 1994-1995
- Chairman, 2nd International Congress, World Federation of Sleep Research Societies, 1993-1995
- Governing Board, World Federation of Sleep Research Societies, 1990-2002
- President-Elect, Sleep Research Society, 1993-1994
- President, National Sleep Foundation, 1990-1993
- Chairman, Scientific Program Committee, Association of Professional Sleep Societies, 1986-1993
- Member, Board of Directors, Association of Professional Sleep Societies, 1986-1992
- Member, Executive Committee, Association of Sleep Disorders Centers, 1984-1989
- Member, Executive Committee, Sleep Research Society, 1986-1995
- Past President, American Academy of Sleep Medicine (formerly Association of Sleep Disorders Centers), 1988-1989
- President, American Academy of Sleep Medicine (former Assoc of Sleep Disorders Centers), 1987-1988
- President, Sleep Research Society (former Assoc for the Psychophysiological Study of Sleep), 1978-1981
- Chairman, Polysomnography Accreditation Committee, American Academy of Sleep Medicine, 1976-1978

Executive Secretary Treasurer, American Academy of Sleep Medicine, 1976-1978

Member, Executive Committee, Association for the Psychophysiological Study of Sleep, 1975-1977

Honors and Awards

Awarded Annual Lecture, Thomas Roth Lecture of Excellence, Associated Professional Sleep Societies, Sleep 2014.

Mary Carskadon Outstanding Educator Award, Sleep Research Society, Boston, Massachusetts, 2012.

Distinguished Scientist Award, Henry Ford Medical Group Board of Governors, October 2006

Founder Award, Sleep Research Society, Chicago, 2005

American Men & Women of Science: A Biographical Directory of Today's Leaders in Physical, Biological, and related Sciences. Ed. Katherine H. Nemej, Pamela M. Kalte, and Noah Schusterbauer. Vol. 6. 22nd ed. Detroit: Gale, 2005.

Significant Early Contributor Award of the Sleep Research Society, 2003

Lifetime Achievement Award, National Sleep Foundation, April 2002

Worldwide Service Award, World Federation of Sleep Research Societies, Third International Congress, Dresden, Germany, 1999.

Distinguished Scientist Award, Sleep Research Society, New Orleans, Louisiana, 1998

C.J. Stringer, M.D., Endowed Memorial Lectureship Speaker, Michigan Thoracic Society Scientific Lessons, 1997.

Nathaniel Kleitman Award of The American Sleep Disorders Association, 1990.

Rush Bronze Award, American Psychiatric Association Meeting, Toronto, May, 1977. Scientific Exhibit, "Evaluation of Hypnotics in Various Patient Populations".

Committee Memberships – Institutional

Chair, Intellectual Property Committee, 2001

Member, Salary Appeals Committee, 2000-2008

Member, Scientist Tract, Appointments and Promotions Committee, 2000

Vice President Medical Affairs/CEO Medical Group Search, 1999

Chief of Pulmonary Medicine Search, 1999

Chair, Biostatistics Search, 1999

Member, Credentials Committee, Henry Ford Hospital, Detroit, MI, 1998

Member, Chair Search Committee Department of Medicine, 1998

Cancer Steering Committee, Henry Ford Hospital, Detroit, MI 1997-2003

Executive Research Directors, Wayne State University, Detroit, MI 1996-2003

Chairman, Research Committee, Henry Ford Hospital, Detroit, MI 1995-2003

Vice Chairman, Intellectual Property Committee, Henry Ford Hospital, Detroit, MI 1995-2003

Member, Academic Council, Henry Ford Health System, 1995-2000

Member, Health Sciences Center Steering Committee, 1995-2000

Chairman, Promotion and Tenure Committee, Department of Psychiatry, Case Western Reserve University/Henry Ford Health Sciences Center, Detroit, MI, 1994-1996

Member, Research Committee, Henry Ford Hospital, Detroit, Michigan, 1985-1989

Chairman, Research Committee, Department of Psychiatry, Henry Ford Hospital, Detroit, MI, 1978-1988

Member, Executive Committee, Department of Psychiatry, Henry Ford Hospital, Detroit, MI, 1978-2001

Member, General Clinical Research Center Committee, Henry Ford Hospital, Detroit, MI, 1979-1982

Member, Residency Training Committee, Department of Psychiatry, Henry Ford Hospital, Detroit, MI, 1979-1982

Member, Research and Education Committee, Veterans Administration Hospital, Cincinnati, Ohio, 1976-1978

Member, Faculty Committee on Human Research, College of Medicine, University of Cincinnati, 1975-1977

Chairman, Research Committee, Xavier University, Cincinnati, Ohio, 1972-1977

Member, Research Committee, Department of Psychiatry, College of Medicine, University of Cincinnati, 1972-1977

Committee Memberships – National

Member, Editor-in-Chief Search Committee, Journal Sleep & Health, National Sleep Foundation, 2014

Member, Revenue Workgroup, Sleep Research Society, 2014

Member, Awards Committee, Sleep Research Society, 2012-

Advisor, DSM-V Task Force, 2011-

Member, Scientific Program Committee, World Federation of Sleep Research Societies (WFSRS), Third International Congress, 1998-1999

Chairman, Scientific Advisory Committee, National Narcolepsy Registry, National Sleep Foundation, 1997-2002

Chairman, Health and Scientific Advisory Committee, National Sleep Foundation, 1996-2002

Chairman, World Health Organizational Committee, Sleep Disorders Program, 1995-2002

Member, NHTSA/National Center on Sleep Disorders Research Expert Panel on Driver Fatigue and Sleepiness, 1997-1998

Member, National Center on Sleep Disorders Research Expert Panel on Insomnia, 1997-1998

Member, Expert Panel Membership, National Health, Lung, and Blood Institute Special Emphasis Panel, 1997

Chairman, Executive Committee, National Sleep Foundation, 1996-1998

Member, Association of Professional Sleep Societies Program Committee, 1994-1996

Member, Sleep Apnea Association Grant Review Committee, 1993-1995

Member, Research Committee, American Sleep Disorders Association, 1993

Board of Directors, American Sleep Apnea Association, 1990-1993

American Thoracic Society/American Sleep Disorders Association Committee on Sleep Disorders Training, 1990-1993

Member, Education Committee, American Sleep Disorders Association, 1988-1992

Member, Grant Review Committee, Association of Sleep Disorders Centers, 1986-1992

Chairman, Fellowship Trainee Grant Committee, World Federation of Sleep Research Societies, 1990

Member, Diagnostic Classification Steering Committee of the American Sleep Disorders Association, 1987-1990

Chairman, Development Committee, Association of Sleep Disorders Centers, 1982-1985

Chairman, Psychopharmacology Committee, Association for the Psychophysiological Study of Sleep, 1976-1986

Member, Finance Committee, American Sleep Disorders Association, 1985-1988

Chairman-Midwest Region, Accreditation Committee, Association of Sleep Disorders Centers, 1983-1985

Member, Physicians Syllabus Subcommittee, Project Sleep; The National Program on Insomnia and Sleep Disorders. United States Department of Health, Education and Welfare, 1979-1981

Member, Joint Coordinating Council, Project Sleep; The National Program on Insomnia and Sleep Disorders. United States Department of Health, Education and Welfare, 1979-1981

Member, Education Committee, Association of Sleep Disorders Centers, 1976-1981

Member, State of Ohio Ethical Review Committee, 1976-1978

Professional Societies

Sleep Research Society (formerly Association for the Psychophysiological Study of Sleep)

American Academy of Sleep Medicine (formerly Association of Sleep Disorders Centers)

American Psychological Association

New York Academy of Sciences

Psychonomic Society

American Association for the Advancement of Science

Clinical Sleep Society

Canadian Sleep Society

International Society for CNS Clinical Trials and Methodology

Scientific Review Activities

EDITOR-IN-CHIEF

Journal Sleep, 1997-2002

ASSOCIATE EDITOR

Sleep Online

Human Psychopharmacology

International Journal of Sleep and Wakefulness

Sleep Medicine

EDITORIAL BOARDS

Advances in Therapy
Behavioral Sleep Medicine
CNS Neuroscience and Therapeutics
International Journal of Sleep Disorders
Mind & Brain, the Journal of Psychiatry
Sleep

Sleep Medicine
Stress and Health
Oren CNS Journal

Anxiety
Clinical Investigation
European Neurological Journal
International Scholarly Research Network Addiction
Open Sleep
Sleep Health
Sleep and Hypnosis
Sleep Reviews
Stress Medicine

OMBUDSMAN

Journal of Sleep Health

ADVISORY BOARDS

Medscape Neurology

REVIEWER

Abnormal Psychology

Accident Analysis & Prevention

Archives of General Psychiatry

Behavioral Sleep Medicine

Comprehensive Psychiatry

Chest

Drugs

European Journal of Psychiatry

Journal of Clinical Psychopharmacology

Journal of the American Medical Association

Journal of Nervous and Mental Disease

Lancet

Mayo Clinic Proceedings

Pharmacotherapy

Sleep

The Medical Letter

American Review of Respiratory Disease

Archives of Internal Medicine

Biological Psychiatry

British Journal of Pharmacology

Clinical Clinical Psychiatry

Journal of the American Geriatric Society

Journal of Biological Rhythms

Journal of Neuroscience

Laryngoscope

New England Journal of Medicine

Neuropsychopharmacology

Psychopharmacology

Other Research Activities

Reviewer, European Science Foundation, 2015-

Member, Advisory Board, Orun CNS Network, 2014-2016

International Forum on Mood and Anxiety Disorders, Member Scientific Committee, 2011-

Presenter: FDA/PERI Workshop on Safety and Efficacy of Hypnotic Drugs, May 10-11, 2011

Director: Sleep Research Society Course on Development of Sleep Promoting Agents, New York, 2008

CDC Special Study Section on Sleep, 2007

Institute of Medicine, Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem, 2006

Planning Committee NIH, The Assessment of Treatment Efficacy, NIH State-of-the-Science Conference on Manifestations and Management of Chronic Insomnia in Adults, 2005

Co-Chair, National Institute of Health Workshop on Neurobiology of Sleep and Waking, September 10-11, 2001

Sleep Meeting , Abstract reviewer 1995 – present

NIH Peer Review Consultant, 1995-Present

Associate Editor, Time Life Medical, 1995-1997

Office of Motor Carriers' Peer Review of Commercial Driver Fatigue Research, Peer Review Report of Commercial Driver Sleep Apnea Research, 1997

Office of Motor Carriers' Peer Review of Commercial Driver Fatigue Research, US Department of Transportation, 1995

Reviewer, Drug Evaluations, American Medical Association, 1991-1992

Chairperson, World Psychiatric Association Task Force on Hypnotics, 1992

Consultant, U.S. Food and Drug Administration Psychopharmacology Advisory Committee, 1992

Ad Hoc Reviewer, The Wellcome Trust, 1993-Present

Ad Hoc Reviewer, British Columbia Health Research Foundation, 1991

Member, United States Department of Transportation Committee on Psychiatric Disorders and Commercial Drivers, 1990

Member, Special Study Section-NIH, (review sleep research proposals) 1983, '84, '87, '88, '89, '90, '93, '95, 2006, '07, '08

Faculty, National Multi-Site Training Program for Basic Sleep Research, 1987-Present

Member, Grant Review Panel, American Narcolepsy Association, 1987-1991

Member, Scientific Advisory Board, Center for Narcolepsy, 1985-Present

Consultant Member, Orphan Products Development IRG, Food and Drug Administration, 1984-1990, '95

Consultant, Board of Scientific Counselors, NIMH, 1989

Member, VA Merit Review Board for Neurobiology, 1989

Chairman, Special Study Section, NIH, (review of sleep research proposals) 1985, 1986, 1988, 1989

Ad Hoc Reviewer, Medical Research Council of Canada, 1986-1988, 1996

Ad Hoc Reviewer, Ministry of Health, Ontario, Canada, 1986-1988

Ad Hoc Member, Neurology A Study Section, NIH, 1981, 1983

Co-Chairman, Project Sleep Consensus Workshop on Insomnia, 1981

Selected Presentations

Inaugural Thomas Roth Lecture of Excellence, Associated Professional Sleep Societies, Sleep 2014.

Keynote Lecture, Association of Professional Sleep Society, Baltimore, 2013

The Assessment of Treatment Efficacy, NIH State-of-the-Science Conference on Manifestations and Management of Chronic Insomnia in Adults, 2005

Key Note Lecture, Hellenic Sleep Research Society, Athens, Greece, 1999

Key Note Lecture, Annual Meeting of the South Africa Sleep Society, 1998

Key Note Lecture Sleep Wake Disorders of Canada, 1997

8th International Rappaport Symposium, 2nd Annual Meeting of the Israel Sleep Research Society, Sleep Medicine, Challenges for the 21st Century, Zichron Yaacov, Israel, 1997

Sleep and Sleep Disorders: From Molecular to Behavior, The 9th Takeda Science Foundation Symposium on Bioscience, Kyoto, Japan, 1996

National Institutes of Health Technology Assessment Conference Statement: Assessment and Methodological Problems in the Evaluation of Insomnia Treatment, October, 1995

NTSB/NASA Ames Fatigue Symposium, 1995

NIH Technology Assessment Conference, Integration of Behavioral and Relaxation Approaches into the Treatment of Chronic Pain and Insomnia, Assessment and Methodological Problems Specific to the Evaluation of Insomnia, 1995

Principal Lecture, Founding Congress of Sleep Research Societies, Cannes, France, 1991

Keynote Address, Annual Meeting of Japanese Sleep Society, 1990

Keynote Address, Annual Meeting of British Sleep Society, 1990

National Institute of Neurological Disorders and Stroke, Consensus Workshop on Narcolepsy, 1990

National Institute of Aging Consensus Conference on Sleep Disorders of Older People, 1990

American Thoracic Society Consensus Conference on Indications and Standards for Cardiopulmonary Sleep Studies, 1989

National Institute of Heart, Lung, and Blood Consensus Conference on Sleep Disordered Breathing, 1988

National Institute of Mental Health Consensus Conference on Drugs and Insomnia, 1984

Scientific Exhibits

Roth T, Dement W, Buysse D, Walsh J, Simon W, Simon R, Young T: Sleep and Its Influence on Physicians Quality of Life and Treatment Practices, American Family Practice, New Orleans, Louisiana, 1997

Roth T, Zorick F, Roehrs T, and Wittig R: Insomnia Treatment: A New Pharmacological Approach. American Psychiatric Association Annual Meeting, Toronto, Canada, 1982

Roth T, Zorick F, Brane A, and Wittig R: Effects of Antidepressant Therapy on Sleep, Depression and Nocturnal Cardiac Functioning. American Psychiatric Association Annual Meeting, New Orleans, Louisiana, 1981

Kramer M, Roth T, Salis P and Zorick F: Assessment of Side Effects of Anti-Psychotic Agents, 1978

Roth T, and Kramer M: Evaluation of Hypnotics in Various Patient Populations, 1977

DATA MONITORING BOARDS

Neurogen Chair Data Safety Monitoring Board NG2-73-205, 2003

Pharmacia Chair Ropinirole Safety Monitoring Board for Sudden Sleep Onset, 2008

Actelion Chair Data Monitoring Board AC-078A201 and AC-078A202, 2017

ORIGINAL ARTICLES

1. Pradhan SN, Beer B, Roth T, Dutta SN: Some Behavioral Effects of Ditrane (JB329) in Rats. *Arch Intl Pharm Ther* 170: 264-275, 1967. PMID: 6076580
2. Pradhan S, Roth T: Comparative Behavioral Effects of Several Anticholinergic Agents in Rats. *Psychopharm* 12: 358-366, 1968. PMID: 5652217
3. Brunner RL, Roth T, Rossi RR: Age Differences in the Development of the Conditioned Emotional Response. *Psychonomic Sci* 21(3): 135-136, 1970.
4. Brunner RL, Rossi RR, Stutz RM, Roth TG: Memory Loss Following Posttrial Electrical Stimulation of the Hippocampus. *Psychonomic Sci* 18(3): 159-160, 1970.
5. Kramer M, Trinder J, Roth T: Dream Content Analysis of Male Schizophrenic Patients. *Canad Psychiat Association J* 17: SS251-SS257, 1972. PMID: 5052064
6. Roth T, Kramer M, Trinder J: The Effect of Noise During Sleep on the Sleep Patterns of Different Age Groups. *Canad Psychiat Association J* 17: SS197-SS201, 1972. PMID: 5042899
7. Butcher RE, Brunner RL, Roth T, Kimmel CA: A Learning Impairment Associated with Maternal Hypervitaminosis-A in Rats. *Life Sci* 11(Part I): 141-145, 1972. PMID: 4675888
8. Orenstein HB, Schumsky DA, Roth T, Brunner R: Spontaneous Recovery and Generalization of Extinction. *J Gen Psych* 86: 173-180, 1972.
9. Kramer M, Blackwell B, Roth T, Wray M: Metiapine in Acute Schizophrenic Patients. *Curr Ther Res* 15(7): 465-469, 1973. PMID: 4198308
10. Kramer M, Roth T: A Comparison of Dream Content in Laboratory Dream Reports of Schizophrenic and Depressive Patient Groups. *Compr Psychiat* 14(4): 325-329, 1973. PMID: 4353392
11. Roth T, Kramer M, Schwartz JL: Triazolam: A Sleep Laboratory Study of a New Benzodiazepine Hypnotic. *Curr Ther Res* 16(2): 117-123, 1974. PMID: 4218805
12. Kramer M, Roth T: The Sleep Clinic. *Cincinnati J Med* 55(9): 173-175, 1974.
13. Schwartz JL, Kramer M, Roth T: Triazolam: A New Benzodiazepine Hypnotic and Its Effect on Mood. *Curr Ther Res* 16(9): 964-970, 1974. PMID: 4214671
14. Kramer M, Roth T, Trinder J: Dreams and Dementia: A Laboratory Exploration of Dream Recall and Dream Content in Chronic Brain Syndrome Patients. *Intl J Aging and Human Develop* 6(2): 169-178, 1975. PMID: 166041
15. Kramer M, Roth T, Goldstein S, Ryan MS, Blackwell B: A Double-Blind Evaluation of Metiapine in Hospitalized Acute Schizophrenics. *Curr Ther Res* 18(6): 839-848, 1975. PMID: 2450
16. Kramer M, Roehrs T, Roth T: Mood Change and the Physiology of Sleep. *Comp Psychiat* 17(1): 161-165, 1976. PMID: 174865
17. Roth T, Kramer M, Lutz T: The Nature of Insomnia: A Descriptive Summary of a Sleep Clinic Population. *Compr Psychiat* 17(1): 217-220, 1976. PMID: 1248235

18. Roth T, Kramer M, Lutz T: Intermediate Use of Triazolam: A Sleep Laboratory Study. *J Intl Med Res* 4(1): 59-63, 1976. PMID: 16793
19. Kramer M, Hlasny R, Jacobs G, Roth T: Do Dreams Have Meaning? An Empirical Inquiry. *Amer J. Psych* 133(7): 778-781, 1976. PMID: 180818
20. Roth T, Kramer M, Roehrs T: Mood Before and After Sleep. *Psych J Univ Ottawa* 1(3): 123-127, 1976.
21. Kramer M, Roth T, Palmer T: The Psychological Nature of the "REM" Dream. I. A Comparison of the REM Dream Report and T.A.T. Stories. *Psychiat J Univ Ottawa* 1(3): 128-135, 1976.
22. Roth T, Kramer M, Lutz T: The Effects of Sleep Deprivation on Mood. *Psychiat J Univ Ottawa* 1: 136-139, 1976.
23. Roth T, Kramer M, Lutz T: The Effects of Hypnotics on Sleep, Performance and Subjective State. *Drugs Exptl Clin Res* 1(1-2): 279-286, 1977.
24. Roth T, Kramer M, Lutz T: The Effects of Triazolam (.25mg) on the Sleep of Insomniac Subjects. *Drugs Exptl Clin Res* 1(1-2): 271-277, 1977.
25. Kramer M, Roth T: Dream Translation. *Israel Ann Psychiat Rel Disc* 15(4): 336-351, 1977. PMID : 273011
26. Roth T, Kramer M, Zorick F: Disorders of Sleep: Diagnosis and Treatment. *Therap Cons* 8(4-6): 1-5, 1977.
27. Karacan I, Orr WC, Roth T, Kramer M, Shurley JT, Thornby JI, Bingham SF, Salis PJ: Establishment and Implementation of Standardized Sleep Laboratory Data Collection and Scoring Procedures. *Psychophysiol* 15(2): 173-179, 1978. PMID: 652912
28. Kramer M, Roth T, Salis PJ, Zorick FA, Blackwell B: Relative Efficacy and Safety of Loxapine Succinate (Loxitane) and Thioridazine Hydrochloride (Mellaril) in the Treatment of Acute Schizophrenia. *Curr Ther Res* 23(5): 619-631, 1978.
29. Sherrick MF, Brunner RL, Roth TG, Dember WN: Rats' Sensitivity to Their Direction of Movement and Spontaneous Alternation Behaviour. *Quar J Exp Psych* 31: 83-93, 1979. PMID: 424507
30. Zorick FJ, Salis PJ, Roth T, Kramer M: Narcolepsy and Automatic Behavior: A Case Report. *J Clin Psychiat* 40(4): 67-73, 1979. PMID: 422531
31. Kramer M, Roth T: The Stability and Variability of Dreaming. *Sleep* 1: 319-325, 1979. PMID: 228375
32. Roth T, Piccione P, Salis P, Kramer M, Kaffeman M: Effects of Temazepam, Flurazepam, and Quinalbarbitone, on Sleep, Psychomotor and Cognitive Function. *Brit J Clin Pharmacol* 8(1): 47S-54S, 1979. PMID: 41542
33. Tietz EI, Roth T, Zorick FJ, Saab P, Kramer M: The Effect of 15 and 20 mg of Quazepam (Sch-16134) on the Sleep of Chronic Insomniacs. *Curr Therap Res* 26(6)(1): 894-899, 1979.
34. Roth T, Tietz EI, Kramer M, Kaffeman M: The Effect of a Single Dose of Quazepam (Sch-16134) on the Sleep of Chronic Insomniacs. *J Intl Med Res* 7: 583-587, 1979. PMID: 42593

35. Hartse KM, Roth T, Piccione PM, Zorick FJ: Rebound Insomnia. *Science* 208: 423, 1980. PMID: 6102800
36. Zorick F, Roth T, Kramer M, Flessa H: Exacerbation of Upper-Airway Sleep Apnea by Lymphocytic Lymphoma. *Chest* 77(5): 689-690, 1980. PMID: 6892693
37. Roth T, Hartse KM, Zorick FJ, Kaffeman ME: The Differential Effects of Short- and Long-acting Benzodiazepines upon Nocturnal Sleep and Daytime Performance. *Drug Res* 30(I), 5a: 891-894, 1980. PMID: 6106491
38. Piccione P, Zorick F, Lutz T, Grissom T, Kramer M, Roth T: The Efficacy of Triazolam and Chloral Hydrate in Geriatric Insomniacs. *J Intl Med Res* 8(5): 361-367, 1980. PMID: 6106611
39. Roth T, Hartse KM, Saab PG, Piccione PM, Kramer M: The Effects of Flurazepam, Lorazepam, and Triazolam on Sleep and Memory. *Psychopharmacology* 70: 231-237, 1980. PMID: 6108588
40. Roth T, Hartse KM, Zorick F, Conway W: Multiple Naps and the Evaluation of Daytime Sleepiness in Patients with Upper Airway Sleep Apnea. *Sleep* 3(3/4): 425-439, 1980. PMID: 6111835
41. Johnson BW, Kramer M, Bonnet M, Roth T, Jansen T: The Effect of Ketazolam on Ocular Motility during REM Sleep. *Curr Therap Res* 28(5): 1980.
42. Roth T, Zorick F: Pharmacological Approaches to the Treatment of Sleep Disorders. *Psiquiatria Clinica* 1(4): 221-224, 1980.
43. Roth T, Zorick F, Sicklesteel J, Stepanski E: Effects of Benzodiazepines on Sleep and Wakefulness. *Br J Clin Pharmacology* 11: 31S-35S, 1981. PMID: 6133532
44. Moore S, Bonnet M, Kramer M, Roth T: A Dose-Response Study of the Hypnotic Effectiveness of Ketazolam in Normal Subjects. *Curr Ther Res* 29(5): 704-713, 1981.
45. Kramer M, Roth T, Arand D, Bonnet M: Waking and Dreaming Mentation: A Test of their Interrelationship. *Neuroscience Letters* 22: 83-86, 1981. PMID: 7219895
46. Stepanski E, Roehrs T, Saab P, Zorick F, Roth T: Readaptation to the Laboratory in Long-Term Sleep Studies. *Bull Psychonomic Soc* 17(5): 224-226, 1981.
47. Zorick FJ, Roth T, Hartse KM, Piccione PM, Stepanski EJ: Evaluation and Diagnosis of Persistent Insomnia. *Am J Psychiatry* 138(6): 769-773, 1981. PMID: 72464806
48. Piccione P, Tallarigo R, Zorick F, Wittig R, Roth T: Personality Differences Between Insomniac and Non-Insomniac Psychiatry Outpatients. *J Clin Psychiatry* 42(7): 261-263, 1981. PMID: 7240111
49. Conway W, Victor L, Magilligan D, Fujita S, Zorick F, Roth T: Adverse Effects of Tracheostomy for Sleep Apnea. *J Amer Med Assoc* 246(4): 347-350, 1981. PMID: 7241781
50. Karacan I, Orr W, Roth T, Kramer M, Thornby J, Bingham S, Kay D: Dose-Related Effects of Flurazepam on Human Sleep-Waking Patterns. *Psychopharm* 73: 332-339, 1981. PMID: 6789354
51. Karacan I, Orr W, Roth T, Kramer M, Thornby J, Bingham S, Kay D: Dose-Related Effects of Phenobarbitone on Human Sleep-Waking Patterns. *Brit J Clin Pharm* 12: 303-313, 1981. PMID: 7295460

52. Roth T, Zorick F: Insomnia: Taking a Rational Approach to an Everyday Problem. *Consultant* 21(10): 203-213, 1981.
53. Tietz EI, Roth T, Zorick F, Piccione P, Kramer M: The Acute Effects of Quazepam on the Sleep of Chronic Insomniacs. *Drug Res* 31(II), (11): 1963-1966, 1981. PMID: 6119098
54. Fujita S, Conway W, Zorick F, Roth T: Surgical Correction of Anatomic Abnormalities in Obstructive Sleep Apnea Syndrome: Uvulopalatopharyngoplasty. *Otolaryngol Head Neck Surg* 89: 923-934, 1981. PMID: 6801592
55. Bonnet M, Kramer M, Roth T: A Dose Response Study of the Hypnotic Effectiveness of Alprazolam and Diazepam in Normal Subjects. *Psychopharmacology* 75: 258-261, 1981. PMID: 6798616
56. Coleman RM, Roffwarg HP, Kennedy SJ, Guilleminault C, Cinque J, Cohn MA, Karacan I, Kupfer DJ, Lemmi H, Miles LE, Orr WC, Phillips ER, Roth T, Sassin JF, Schmidt HS, Weitzman ED, Dement WC: Sleep-Wake Disorders Based on a Polysomnographic Diagnosis - A National Cooperative Study. *JAMA* 247(7): 997-1003, 1982. PMID:7057593
57. Conway WA, Zorick F, Piccione P, Roth T: Protriptyline in the Treatment of Sleep Apnea. *Thorax* 37: 49-53, 1982. PMID: 7071794
58. Roehrs T, Lineback W, Zorick F, Roth T: Relationship of Psychopathology to Insomnia in the Elderly. *J Amer Ger Soc* 30(5): 312-315, 1982. PMID: 7077007
59. Roth T, Zorick F, Wittig R, Roehrs T: Pharmacological and Medical Considerations in Hypnotic Use. *Sleep* 5(S1): S46-S52, 1982. PMID: 6125025
60. Blumer D, Zorick F, Heilbronn M, Roth T: Biological Markers for Depression in Chronic Pain. *J Nervous and Mental Dis* 170(7): 425-428, 1982. PMID: 7086402
61. Wittig RM, Zorick FJ, Blumer D, Heilbronn M, Roth T: Disturbed Sleep in Patients Complaining of Chronic Pain. *J Nervous and Mental Dis* 170(7): 429-431, 1982. PMID: 7086403
62. Roehrs T, Zorick F, Kaffeman M, Sicklesteel J, Roth T: Flurazepam for Short-Term Treatment of Complaints of Insomnia. *J Clin Pharmacol* 22: 290-296, 1982. PMID: 7107976
63. Fleetham J, West P, Mexon B, Conway W, Roth T, Kryger M: Sleep, Arousals and Oxygen Desaturation in Chronic Obstructive Pulmonary Disease. *Am Rev Respir Dis* 126: 429-433, 1982. PMID: 7125332
64. Roth T, Zorick F, Wittig R, McLenaghan A, Roehrs T: The Effects of Doxepin HCl on Sleep and Depression. *J Clin Psychiat* 43(9): 366-368, 1982. PMID: 7118845
65. Hartse KM, Roth T, Zorick F: Daytime Sleepiness and Daytime Wakefulness: The Effect of Instruction. *Sleep* 5(S2): S107-S118, 1982. PMID: 7156646
66. Roth T, Roehrs T, Zorick F: Sleepiness: Its Measurement and Determinants. *Sleep* 5(S2): S128-S134, 1982. PMID: 6760333
67. Zorick F, Roehrs T, Koshorek G, Sicklesteel J, Hartse K, Wittig R, Roth T: Patterns of Sleepiness in Various Disorders of Excessive Daytime Somnolence. *Sleep* 5(S2): S165-S174, 1982. PMID: 7156651

68. Stepanski E, Zorick F, Kaffeman M, Sicklesteel J, Roth T: Effets de l'administration chronique de triazolam 0.50mg sur le sommeil des insomniaques. *La Nouvelle Presse Medicale* 11(40): 2987-2990, 1982. PMID: 6128721
69. Roth R, Roehrs TA, Zorick FJ: Pharmacology and Hypnotic Efficacy of Triazolam. *Pharmacotherapy* 3(3): 137-148, 1983. PMID: 6136026
70. Bliwise D, Seidel W, Karacan I, Mitler M, Roth T, Zorick F, Dement W: Daytime Sleepiness as a Criterion in Hypnotic Medication Trials: Comparison of Triazolam and Flurazepam. *Sleep* 6(2): 156-163, 1983. PMID: 6136085
71. Wittig R, Zorick F, Roehrs T, Sicklesteel J, Roth T: Narcolepsy in a 7-Year Old Child. *J Pediatrics* 102(5): 725-727, 1983. PMID: 6842331
72. Roehrs T, Zorick F, Lord N, Koshorek GL, Roth T: Dose-Related Effects of Estazolam on Sleep of Patients With Insomnia. *J Clin Psychopharm* 3(3): 152-156, 1983. PMID: 6135720
73. Roehrs T, Zorick F, Sicklesteel J, Wittig R, Roth T: Age-Related Sleep-Wake Disorders at a Sleep Disorder Center. *J Amer Geriat Soc* 31(6): 364-370, 1983. PMID: 6853947
74. Wittig R, Zorick F, Piccione P, Sicklesteel J, Roth T: Narcolepsy and Disturbed Nocturnal Sleep. *Clin Electroencephalog* 14(3): 130-134, 1983. PMID: 6616886
75. Roehrs T, Zorick FJ, Sicklesteel JM, Wittig RM, Hartse KM, Roth T: Effects of Hypnotics on Memory. *J Clin Psychopharmacol* 3(5): 310-313, 1983. PMID: 6630591
76. Hauri P, Roth T, Sateia M, Zorick F: Sleep Laboratory and Performance Evaluation of Midazolam in Insomniacs. *Brit J of Clin Pharm* 16: 109S-114S, 1983. PMID: 6138061
77. Zorick F, Roehrs T, Conway W, Fujita S, Wittig R, Roth T: Effects of Uvulopalatopharyngoplasty on the Daytime Sleepiness Associated With Sleep Apnea Syndrome. *Bull Europe Physiopath Resp* 19: 600-603, 1983. PMID: 6652267
78. Roehrs T, Zorick F, Sicklesteel J, Wittig R, Roth T: Excessive Daytime Sleepiness Associated With Insufficient Sleep. *Sleep* 6(4): 319-325, 1983. PMID: 6665394
79. Ancoli-Israel S, Kripke D, Zorick F, Roth T: Effects of a Single Dose of Flurazepam on the Sleep of Healthy Volunteers. *Drug Res* 34(I): 99-100, 1984. PMID: 6538429
80. Wittig RM, Romaker A, Zorick FJ, Roehrs TA, Conway WA, Roth T: Night-to-Night Consistency of Apneas during Sleep. *Am Rev Respir Dis* 129: 244-246, 1984. PMID: 6696325
81. Roehrs T, Zorick F, Koshorek GL, Wittig R, Roth T: Effects of Acute Administration of Brotizolam in Subjects with Disturbed Sleep. *Br J Clin Pharmacology* 16: 371S-376S, 1983. PMID: 6661383
82. Stepanski E, Lamphere J, Badia P, Zorick F, Roth T: Sleep Fragmentation and Daytime Sleepiness. *Sleep* 7(1): 18-26, 1984. PMID: 6718922
83. Roehrs TA, Tietz EI, Zorick FJ, Roth T: Daytime Sleepiness and Antihistamines. *Sleep* 7(2): 137-141, 1984. PMID: 6146180
84. Seidel WF, Roth T, Roehrs T, Zorick F, Dement WC: Treatment of a 12-Hour Shift of Sleep Schedule with Benzodiazepines. *Science* 224: 1262-1264, 1984. PMID: 6729454

85. Roehrs T, Zorick F, and Roth T: Sleep Disorders in the Elderly. *Ger Med Today* 3(6): 76-86, 1984.
86. Roehrs T, Lamphere J, Paxton C, Wittig R, Zorick F, Roth T: Temazepam's Efficacy in Patients with Sleep Onset Insomnia. *Brit J Clin Pharmacology* 17: 691-696, 1984. PMID: 6146327
87. Rosenthal L, Roehrs T, Sicklesteel J, Zorick F, Wittig R, Roth T: Periodic Movements during Sleep, Sleep Fragmentation, and Sleep-Wake Complaints. *Sleep* 7(4): 326-330, 1984. PMID: 6515247
88. Roth T, Roehrs T, Wittig R, Zorick F: Benzodiazepines and Memory. *Brit J Clin Pharmacology* 18: 45S-49S, 1984. PMID: 6151849
89. Fujita S, Conway W, Sicklesteel J, Wittig R, Zorick F, Roehrs T, Roth T: Evaluation of the Effectiveness of Uvulopalatopharyngoplasty. *Laryngoscope* 95(1): 70-74, 1985. PMID: 3965833
90. Nicholson AN, Pascoe PA, Roehrs T, Roth T, Spencer MB, Stone BM, Zorick F: Sustained Performance With Short Evening and Morning Sleeps. *Aviat Space Environ Med* 56: 105-114, 1985. PMID: 3985887
91. Roth T, Hauri P, Zorick F, Sateia M, Roehrs T, Kipp J: The Effects of Midazolam and Temazepam on Sleep and Performance When Administered in the Middle of the Night. *J Clin Psychopharm* 5(2): 66-69, 1985. PMID: 2859305
92. Roehrs T, Vogel G, Vogel F, Wittig R, Zorick F, Paxton C, Lamphere J, Roth T: Eligibility Requirements in Hypnotic Trials. *Sleep* 8(1): 34-39, 1985. PMID: 3992107
93. Nicholson AN, Roth T, Stone BM: Hypnotics and Aircrew. *Aviat Space Environ Med* 56: 299-302, 1985. PMID: 3994611
94. Roth T, and Roehrs T: Determinants of Residual Effects of Hypnotics. *Accid Anal Prev* 17(4): 291-296, 1985. PMID: 4096793
95. Wittig R, Zorick F, Roehrs T, Paxton C, Lamphere J, Roth T: Effects of Temazepam Soft Gelatin Capsules on the Sleep of Subjects With Insomnia. *Curr Therap Res* 38(1): 15-22, 1985.
96. Roth T, Zorick F, Roehrs T, Wittig R: Sleep Disorders: Excessive Daytime Sleepiness. *Therapaeia* 8: 6-14, 1985.
97. Conway W, Fujita S, Zorick F, Sicklesteel J, Roehrs T, Wittig R, Roth T: Uvulopalatopharyngoplasty: One Year Followup. *Chest* 88: 385-387, 1985. PMID: 4028849
98. Roehrs T, Conway W, Wittig R, Zorick F, Sicklesteel J, Roth T: Sleep-Wake Complaints in Patients with Sleep-Related Respiratory Disturbances. *Am Rev Respir Dis* 132: 520-523, 1985. PMID: 4037527
99. Roehrs T, Zorick F, Wittig R, Roth T: Efficacy of a Reduced Triazolam Dose in Elderly Insomniacs. *Neurobiology of Aging* 6: 293-296, 1985. PMID: 4088425
100. Zorick F, Roehrs T, Wittig R, Lamphere J, Sicklesteel J, Roth T: Sleep-Wake Abnormalities in Narcolepsy. *Sleep* 9(1): 189-193, 1986. PMID: 3704441
101. Roehrs T, Zorick F, Wittig R, Paxton C, Sicklesteel J, Roth T: Alerting Effects of Naps in Patients with Narcolepsy. *Sleep* 9(1): 194-199, 1986. PMID: 3704442

102. Roehrs T, Kribbs N, Zorick F, Roth T: Hypnotic Residual Effects of Benzodiazepines with Repeated Administration. *Sleep* 9(2): 309-316, 1986. PMID: 2905824
103. Lamphere J, Roehrs T, Zorick F, Koshorek G, Roth T: Chronic Hypnotic Efficacy of Estazolam. *Drugs Exptl Clin Res* XII(8): 687-692, 1986. PMID: 2875857
104. Roehrs T, Vogel G, Vogel F, Wittig R, Zorick F, Paxton C, Lamphere J, Roth T: Dose Effects of Temazepam Tablets on Sleep. *Drugs Exptl Clin Res* XII(8): 693-699, 1986. PMID: 2875858
105. Roehrs T, Zorick F, Wittig R, Roth T: Dose Determinants of Rebound Insomnia. *Br J Clin Pharmac* 22: 143-147, 1986. PMID: 3530302
106. Lumley M, Roehrs T, Zorick F, Lamphere J, Roth T: The Alerting Effects of Naps in Sleep-Deprived Subjects. *Psychophysiology* 23(4): 403-408, 1986. PMID: 3774925
107. Seidel WF, Cohen SA, Bliwise NG, Roth T, Dement WC. Dose-Related Effects of Triazolam and Flurazepam on a Circadian Rhythm Insomnia. *Clin Pharmacol Ther* 40(3): 314-320, 1986. PMID: 3742936
108. Nicholson AN, Pascoe PA, Spencer MB, Stone BM, Roehrs T, Roth T: Sleep After Transmeridian Flights. *The Lancet*: 1205-1208, Nov 1986. PMID: 2877336
109. Carskadon M, Dement WC, Mitler MM, Roth T, Westbrook PR, Keenan S: Guidelines For The Multiple Sleep Latency Test (MSLT): A Standard Measure of Sleepiness. *Sleep* 9(4): 519-524, 1986. PMID: 3809866
110. Wittig RM, Zorick FJ, Roth T: A Cure for Santa's Sleep Apnea. *The Lancet* No. 8521/22, Vol II: 1464, 1986. PMID: 2878315
111. Roth T, Roehrs TA, Stepanski EJ, Zorick FJ: Antihistamines and Daytime Sleepiness. *J of Resp Dis* 7, March 1987.
112. Cameron OG, Curtis GC, Zelnik T, McCann D, Roth T, Guire K, and Huber-Smith, M: Circadian Fluctuation of Plasma Epinephrine in Supine Humans. *Psychoneuroendocrinology* 12(1): 41-51, 1987. PMID: 3588812
113. Perez-Padilla R, Conway W, Roth T, Anthonisen N, George C, Kryger M: Hypercapnia and Sleep O₂ Desaturation in Chronic Obstructive Pulmonary Disease. *Sleep* 10(3): 216-223, 1987. PMID: 3629083
114. Stepanski EJ, Lamphere J, Roehrs T, Zorick F, Roth T: Experimental Sleep Fragmentation in Normal Subjects. *Intern J Neurosci* 33: 207-214, 1987. PMID: 3596950
115. Lumley M, Roehrs T, Asker D, Zorick F, Roth T: Ethanol and Caffeine Effects on Daytime Sleepiness/Alertness. *Sleep* 10(4): 306-312, 1987. PMID: 3659729
116. Roth T, Roehrs T, Koshorek G, Sicklesteel J, Zorick F: Sedative Effects of Antihistamines. *J Allergy Clin Immunol* 80(1): 94-98, 1987. PMID: 2885356
117. Roth T, Zorick F, Roehrs T: The Interaction of Daytime Sleepiness and Sedative Properties of Drugs. *Psychopharm Bulletin* 23(3): 440-443, 1987. PMID: 3432513
118. Levine B, Roehrs T, Stepanski E, Zorick F, Roth T: Fragmenting Sleep Diminishes its Recuperative Value. *Sleep* 10(6): 590-599, 1987. PMID: 3432859

119. Levine B, Roehrs T, Zorick F, Roth T: Daytime Sleepiness in Young Adults. *Sleep* 11(1): 39-46, 1988. PMID: 3363268
120. Stepanski EJ, Zorick FJ, Roehrs TA, Young DK, Roth T: Daytime Alertness in Patients with Chronic Insomnia Compared with Asymptomatic Control Subjects. *Sleep* 11(1): 54-60, 1988. PMID: 3363270
121. Young D, Zorick F, Wittig R, Roehrs T, Roth T: Narcolepsy in a Pediatric Population. *Am J Dis Children* 142: 210-213, 1988. PMID: 3341326
122. Wittig RM, Roth T, Keenum AJ, Sarnaik S: Snoring, Daytime Sleepiness, and Sickle Cell Anemia. *Am J Dis Children* 142: 589, 1988. PMID: 3369389
123. Stepanski EJ, Conway WA, Young DK, Zorick FJ, Wittig RM, Roth T: A Double-Blind Trial of Protriptyline in the Treatment of Sleep Apnea Syndrome. *Henry Ford Hosp Med J* 36(1): 5-8, 1988. PMID: 3294213
124. Ton D, Zorick FJ, Roehrs TA, Wittig RM, Sicklesteel JM, Roth T: Sleep-Wake Complaints and Their Relation to Sleep Disturbance. *Henry Ford Hosp Med J* 36(1): 9-12, 1988. PMID: 3397302
125. Wittig RM, Zorick FJ, Roehrs TA, Sicklesteel JM, Roth T: Familial Childhood Sleep Apnea. *Henry Ford Hosp Med J* 36(1): 13-15, 1988. PMID: 3397291
126. Hartse KM, Zorick FJ, Sicklesteel JM, Roth T: Isolated Cataplexy: A Familial Study. *Henry Ford Hosp Med J* 36(1): 24-27, 1988. PMID: 3397292
127. Zammit GK, Rosenbaum AH, Stokes P, Davis J, Zorick F, Roth T: Biological Differences in Endogenous Depressive Placebo Responders Versus Nonresponders: Dexamethasone Suppression Test and Sleep EEG Data. *Biol Psych* 24: 97-101, 1988. PMID: 3370281
128. He J, Kryger MH, Zorick FJ, Conway W, Roth T: Mortality and Apnea Index in Obstructive Sleep Apnea: Experience in 385 Male Patients. *Chest* 94(1): 9-14, 1988. PMID: 3289839
129. Roth T, Roehrs T: Sleepiness and Motor Vehicle Accidents. *Int Clin Psychopharm* 3(1): 111-116, 1988. PMID: 3042858
130. Roth T, Roehrs T, Conway W: Behavioral Morbidity of Apnea. *Seminars in Resp Med* 9(6): 554-559, 1988.
131. Zwyghuizen-Doorenbos A, Roehrs T, Schaefer M, Roth T: Test-Retest Reliability of the MSLT. *Sleep* 11(6): 562-565, 1988. PMID: 3238258
132. Zwyghuizen-Doorenbos A, Roehrs T, Lamphere J, Zorick F, Roth T: Increased Daytime Sleepiness Enhances Ethanol's Sedative Effects. *Neuropsychopharmacology* 1(4): 279-286, 1988. PMID: 3251507
133. Levine B, Lumley M, Roehrs T, Zorick F, Roth T: The Effects of Acute Sleep Restriction and Extension on Sleep Efficiency. *Intern J Neurosci* 43(3-4): 139-143, 1988. PMID: 3243670
134. Lamphere J, Young D, Roehrs T, Wittig RM, Zorick F, Roth T: Fragmented Sleep, Daytime Somnolence and Age in Narcolepsy. *Clinical Electroencephalography* 20(1): 49-54, 1989. PMID: 2924427

135. Merlotti L, Roehrs T, Koshorek G, Zorick F, Lamphere J, Roth T: The Dose Effects of Zolpidem on the Sleep of Healthy Normals. *J of Clin Psychopharm* 9(1): 9-14, 1989. PMID: 2651493
136. Lamphere JK, Roehrs TA, Zorick FJ, Koshorek G, Roth T: The Dose Effects of Zopiclone. *Human Psychopharmacology* 4: 41-46, 1989.
137. Roehrs T, Zorick F, Wittig R, Conway W, Roth T: Predictors of Objective Level of Daytime Sleepiness in Patients with Sleep-Related Breathing Disorders. *Chest* 95(6): 1202-1206, 1989. PMID: 2721252
138. Roehrs T, Timms V, Zwyghuizen-Doorenbos A, Roth T: Sleep Extension in Sleepy and Alert Normals. *Sleep* 12(5): 449-457, 1989. PMID: 2799218
139. Phillipson EA, Remmers JE, Cohn MA, Edelman N, Fletcher E, Goldstein R, Guilleminault C., Hugel D, Kryger MH, Martin RJ, McGinty D, Orr WC, Pack AI, Rapoport DM, Roth T, Shephard JW, Skatrud JB, Smith PL, Strohl K, Suratt PM, Weil J, Westbrook PR, Zwillich CW. American Thoracic Society, Medical Section of the American Lung Association, Indications and Standards for Cardiopulmonary Sleep Studies. *American Review of Respiratory Disease* 139(2): 559-568, 1989.
140. Stepanski E, Koshorek G, Zorick F, Glinn M, Roehrs T, Roth T: Characteristics of Individuals Who Do or Do Not Seek Treatment for Chronic Insomnia. *Psychosomatics* 30(4): 421-427, 1989. PMID: 2798735
141. Roehrs T, Zwyghuizen-Doorenbos A, Timms V, Zorick F, Roth T: Sleep Extension, Enhanced Alertness and the Sedating Effects of Ethanol. *Pharm Biochem and Behav* 34: 321-324, 1989. PMID: 2622988
142. Lamphere J, Roehrs T, Wittig R, Zorick F, Conway W, Roth T: Recovery of Alertness after CPAP in Apnea. *Chest* 96(6): 1364-1367, 1989. PMID: 2684554
143. Zwyghuizen-Doorenbos A, Roehrs TA, Lipschutz L, Timms V, Roth T: Effects of Caffeine on Alertness. *Psychopharmacology* 100: 36-39, 1990. PMID: 2296626
144. Rosenthal LD, Merlotti L, Young DK, Zorick FJ, Wittig RM, Roehrs TA, Roth T: Subjective and Polysomnographic Characteristics of Patients Diagnosed with Narcolepsy. *Gen Hosp Psych* 12: 191-197, 1990. PMID: 2335305
145. Rosenthal LD, Zorick FJ, Merlotti L, Wittig RM, Roehrs TA, Roth T: Signs and Symptoms Associated with Cataplexy in Narcolepsy Patients. *Biol Psychiat* 27: 1057-1060, 1990. PMID: 2334746
146. Lamphere J, Roehrs T, Vogel G, Koshorek G, Fortier J, Roth T: The Chronic Efficacy of Midazolam. *Intl Clin Psychopharm* 5: 31-39, 1990. PMID: 2332606
147. Roehrs T, Zwyghuizen-Doorenbos A, Zwyghuizen H, Roth T: Sedating Effects of Ethanol after a Nap. *Alcohol, Drugs & Driving* 5(4)/6(1): 351-356, 1989/90.
148. Roth T, Roehrs T, Merlotti L: Ethanol and Daytime Sleepiness. *Alcohol, Drugs & Driving* 5(4)/6(1): 357-362, 1989/90.
149. Zwyghuizen-Doorenbos A, Roehrs T, Timms V, Roth T: Individual Differences in the Sedating Effects of Ethanol. *Alcohol Clin Exp Res* 14(3): 400-404, 1990. PMID: 2378424
150. Roehrs T, Vogel G, Sterling W, Roth T: Dose Effects of Temazepam in Transient Insomnia. *Drug Research* 40(II)8: 859-862, 1990. PMID: 2242077

151. Roth T, Roehrs T, Linnoila M, Judd LL: Characteristics of Chronic Insomniacs Examined in a Multicenter 14-Day Study of Flurazepam and Midazolam. *J of Clin Psychopharm* 10(4): 24S-27S, 1990. PMID: 2229461
152. Kripke DF, Hauri P, Ancoli-Israel S, Roth T: Sleep Evaluation in Chronic Insomniacs during 14-Day Use of Flurazepam and Midazolam. *J Clin Psychopharm* 10(4): 32S-43S, 1990. PMID: 2229462
153. Zammit GK, Pollak C, Rosenbaum AH, Roth T: Early Onset and Accumulation of REM Sleep in Depression: A Study of the Phase-Advance Hypothesis. *Chronobiology International* 7(2): 165-169, 1990. PMID: 2242510
154. Roehrs TA, Timms V, Zwyghuizen-Doorenbos A, Buzenski R, Roth T: Polysomnographic, Performance, and Personality Differences of Sleepy and Alert Normals. *Sleep* 13(5): 395-402, 1990. PMID: 2287851
155. Stepanski EJ, Markey JJ, Zorick FJ, Roth T: Psychometric Profiles of Patient Populations with Excessive Daytime Sleepiness. *Henry Ford Hosp Med J* 38(4): 219-222, 1990. PMID: 2086547
156. Zorick FJ, Roehrs T, Conway W, Potts G, Roth T: Response to CPAP and UPPP in Apnea. *Henry Ford Hosp Med J* 38(4): 223-226, 1990. PMID: 2086548
157. Rosenthal L, Roehrs TA, Zwyghuizen-Doorenbos A, Plath D, Roth T: Alerting Effects of Caffeine After Normal and Restricted Sleep. *Neuropsychopharmacology* 4(2): 103-108, 1991. PMID: 2025377
158. Schweitzer PK, Koshorek G, Muehlbach MJ, Morris DD, Roehrs T, Walsh JK, Roth T: Effects of Estazolam and Triazolam on Transient Insomnia Associated with Phase-Shifted Sleep. *Human Psychopharm* 6: 99-107, 1991.
159. Roth T, Roehrs TA: A Review of the Safety Profiles of Benzodiazepine Hypnotics. *J Clin Psychiatry* 52(9,Suppl): 38-41, 1991. PMID: 1680124
160. Rosenthal L, Roehrs TA, Hayashi H, Zorick FJ, Wittig RM, Rosenthal J, Roth T: HLA DR2 in Narcolepsy with Sleep-Onset REM Periods but Not Cataplexy. *Biol Psych* 30: 830-836, 1991. PMID: 1751625
161. Rosenthal L, Merlotti L, Roehrs TA, Roth T: Enforced 24-Hour Recovery Following Sleep Deprivation. *Sleep* 14(5): 448-453, 1991. PMID: 1759097
162. Roehrs T, Yoon J, Roth T: Nocturnal and Next-day Effects of Ethanol and Basal Level of Sleepiness. *Human Psychopharm* 6: 307-311, 1991.
163. Merlotti L, Roehrs T, Zorick F, Roth T: Rebound Insomnia: Duration of Use and Individual Differences. *J of Clin Psychopharmacol* 11(6): 368-373, 1991. PMID: 1770156
164. Roehrs T, Roth T: Multiple Sleep Latency Test: Technical Aspects and Normal Values. *J of Clin Neurophysiology* 9(1): 63-67, 1992. PMID: 1552009
165. Roth T, Richardson GR, Sullivan JP, Lee RM, Merlotti L, Roehrs T: Comparative Effects of Pravastatin and Lovastatin on Nighttime Sleep and Daytime Performance. *Clin Cardiol* 15: 426-432, 1992. PMID: 1617822

166. Salin-Pascual RJ, Grandos-Fuentes D, Galicia-Polo L, Nieves E, Roehrs TA, Roth T: Biperiden Administration During REM Sleep Deprivation Diminished the Frequency of REM Sleep Attempts. *Sleep* 15(3): 252-256, 1992. PMID: 1621026
167. Roehrs T, Merlotti L, Zorick F, Roth T: Rebound Insomnia and Hypnotic Self-Administration. *Psychopharmacology* 107: 480-484, 1992. PMID: 1603890
168. Roth T, Roehrs TA: Issues in the Use of Benzodiazepine Therapy. *J Clin Psychiatry* 53(6 Suppl): 14-18, 1992. PMID: 1613014
169. Salin-Pascual RJ, Roehrs TA, Merlotti LA, Zorick F, Roth T: Long-Term Study of the Sleep of Insomnia Patients with Sleep State Misperception and Other Insomnia Patients. *Am J Psychiatry* 149(7): 904-908, 1992. PMID: 1609869
170. Roehrs T, Zwyghuizen-Doorenbos A, Knox M, Moskowitz H, Roth T: Sedating Effects of Ethanol and Time of Drinking. *Alcoholism: Clin & Exper Resch* 16(3): 553-557, 1992. PMID: 1626655
171. Roehrs T, Merlotti L, Zorick F, Roth T: Rebound Insomnia in Normals and Patients with Insomnia after Abrupt and Tapered Discontinuation. *Psychopharmacology* 108: 67-71, 1992. PMID: 1410148
172. Orenstein HB, Schumsky DA, Roth T, and Trinder J: The Reinforcing Signal as a Conditioned Stimulus in Human Operant Discrimination Training. *Bulletin of the Psychonomic Society* 30(5): 381-384, 1992.
173. Roth T, Roehrs TA, Moskowitz H: Issues in Drug-Related Performance Impairment. *Clinical Therapeutics* 14(5): 654-666, 1992. PMID: 1468085
174. Rosenthal L, Roehrs TA, Rosen A, Roth T: Level of Sleepiness and Total Sleep Time Following Various Time in Bed Conditions. *Sleep* 16(3): 226-232, 1993. PMID: 8506455
175. Roehrs T, Zwyghuizen-Doorenbos A, Roth T: Sedative Effects and Plasma Concentrations Following Single Doses of Triazolam, Diphenhydramine, Ethanol and Placebo. *Sleep* 16(4): 301-305, 1993. PMID: 8341890
176. Roehrs T, Claiborne D, Knox M, Roth T: Effects of Ethanol, Diphenhydramine, and Triazolam after a Nap. *Neuropsychopharm* 9(3): 239-245, 1993. PMID: 8280348
177. Rosenthal L, Roehrs TA, Roth T: The Sleep-Wake Activity Inventory: A Self-Report Measure of Daytime Sleepiness. *Biol Psychiatry* 34: 810-820, 1993. PMID: 8292685
178. Roehrs T, Merlotti L, Rosenthal L, Roth T: Benzodiazepine Associated Reversal of the Effects of Experimental Sleep Fragmentation. *Human Psychopharmacology* 8: 351-356, 1993.
179. Roehrs T, Beare D, Zorick F, Roth T: Sleepiness and Ethanol Effects on Simulated Driving. *Alcohol Clin Exp Res* 18(1): 154-158, 1994. PMID: 8198213
180. Scharf M, Roth T, Vogel G, Walsh J: A Multicenter, Placebo-Controlled Study Evaluating Zolpidem in the Treatment of Chronic Insomnia. *J Clin Psychiatry* 55:5: 192-199, 1994. PMID: 8071269
181. Roehrs T, Merlotti L, Petrucelli N, Stepanski E, Roth T: Experimental Sleep Fragmentation. *Sleep* 17(5): 438-443, 1994. PMID: 7991955

182. Roehrs T, Claiborne D, Knox M, Roth T: Residual Sedating Effects of Ethanol. *Alcohol Clin Exp Res* 18(4): 831-834, 1994. PMID: 7978092
183. Rosenthal L, Folkerts M, Roehrs T, Zorick F, Roth T: Sleepiness and Sleep Onset REM Periods in the Absence of Clinical Symptomatology. *Biological Psychiatry* 36: 341-343, 1994. PMID: 7993961
184. Stepanski E, Glinn M, Zorick F, Roehrs T, Roth T: Heart Rate Changes in Chronic Insomnia. *Stress Medicine* 10: 261-266, 1994.
185. Roehrs T, Merlotti L, Zorick F, Roth T: Sedative, Memory, and Performance Effects of Hypnotics. *Psychopharmacology* 116: 130-134, 1994. PMID: 7862941
186. Buysse DJ, Reynolds CF, Kupfer DJ, Thorpy MJ, Bixler E, Manfredi R, Kales A, Vgontzas A, Stepanski E, Roth T, Hauri P, Mesiano D: Clinical Diagnoses in 216 Insomnia Patients Using the International Classification of Sleep Disorders (ICSD), DSM-IV and ICD-10 Categories: A Report From the APA/NIMH DSM-IV Field Trial. *Sleep* 17(7): 630-637, 1994. PMID: 7846462
187. Buysse D, Reynolds C, Hauri P, Roth T, Stepanski E, Thorpy M, Bixler E, Kales A, Manfredi R, Vgontzas A, Mesiano D, Kupfer D: Interrater Agreement for Sleep Disorders Using Proposed DSM-IV and ICD-10 Diagnoses: A Report from the APA/NIMH DSM-IV Field Trial. *American Journal of Psychiatry* 151(9): 1351-1360, 1994. PMID: 8067492
188. Roehrs T, Merrion M, Pedrosi B, Stepanski E, Zorick F, Roth T: Neuropsychological Function in Obstructive Sleep Apnea Syndrome (OSAS) Compared to Chronic Obstructive Pulmonary Disease (COPD). *Sleep* 18(5): 382-388, 1995. PMID: 7676173
189. Roth T, Roehrs TA, Vogel G: Zolpidem in the Treatment of Transient Insomnia: A Double-Blind, Randomized Comparison With Placebo. *Sleep* 18(4): 246-251, 1995. PMID: 7618022
190. Roehrs T, Merlotti L, Halpin D, Rosenthal L, Roth T: Effects of Theophylline on Nocturnal Sleep and Daytime Sleepiness/Alertness. *Chest* 108(2): 382-387, 1995. PMID: 7634871
191. Stepanski E, Faber M, Zorick F, Basner R, Roth T: Sleep Disorders in Patients on Continuous Ambulatory Peritoneal Dialysis. *Journal of the American Society of Nephrology* 6(2): 192-197, 1995. PMID: 7579084
192. Roehrs T, Roth T: Alcohol-Induced Sleepiness and Memory Function. *Alcohol Health & Research World* 19(2): 130-135, 1995.
193. Breslau N, Roth T, Rosenthal L, Andreski P: Sleep Disturbance and Psychiatric Disorders: A Longitudinal Epidemiological Study of Young Adults. *Biological Psychiatry* 39: 411-418, 1996. PMID: 8679786
194. Rosenthal L, Bishop C, Helmus T, Krstevska S, Roehrs T, Roth T: Auditory Awakening Thresholds in Sleepy and Alert Individuals. *Sleep* 19(4): 290-5, 1996. PMID: 8776786
195. Folkerts M, Rosenthal L, Roehrs T, Krstevska S, Murlidhar A, Zorick F, Wittig F, Roth T: The Reliability of the Diagnostic Features in Patients with Narcolepsy. *Biological Psychiatry* 40: 208-214, 1996. PMID: 8830954
196. Roehrs T, Petrucelli N, Roth T: Sleep Restriction, Ethanol Effects and Time of Day. *Human Psychopharmacology* 11: 199-204, 1996.

197. Silva JACE, Chase M, Sartorius N, Roth T: Special Report from a Symposium Held by the World Health Organization and the World Federation of Sleep Research Societies: An Overview of Insomnias and Related Disorders - Recognition, Epidemiology, and Rational Management. *Sleep* 19(5): 412-416, 1996. PMID: 8843532
198. Roehrs T, Salin-Pascual, R, Merlotti L, Rosenthal L, Roth T: Phase Advance in Moderately Sleepy and Alert Normals. *Sleep* 19(5): 417-422, 1996. PMID: 8843533
199. Roth T, T Roehrs: Etiologies and Sequelae of Excessive Daytime Sleepiness. *Clinical Therapeutics* 18(4): 562-576, 1996. PMID: 8879887
200. Helmus T, Rosenthal L, Bishop C, Roehrs T, Krsevka S, Roth T: Nocturnal Sleep Latencies among Alert, Alert-Deprived and Sleepy Subjects. *Electroencephalography and Clinical Neurophysiology* 99: 10-15, 1996. PMID: 8758965
201. Bishop C, Rosenthal L, Helmus T, Roehrs T, Roth T: Sleep Onset—REM and NREM Sleep. The Frequency of Multiple Sleep Onset REM Periods among Subjects with No Excessive Daytime Sleepiness. *Sleep* 19(9): 727-730, 1996. PMID: 9122560
202. Roehrs T, Shore E, Papineau K, Rosenthal L, Roth T: A Two-Week Sleep Extension in Sleepy Normals. *Sleep* 19(7): 576-582, 1997. PMID: 8899937
203. Roehrs T, Pedrosi B, Rosenthal L, Roth T: Hypnotic Self-Administration and Dose Escalation. *Psychopharmacology* 127: 150-154, 1997. PMID: 8888381
204. Ware JC, Walsh JK, Scharf MB, Roehrs T, Roth T, Vogel GW: Minimal Rebound Insomnia After Treatment with 10-mg Zolpidem. *Clinical Neuropharmacology* 20(2): 116-125, 1997. PMID: 9099463
205. Helmus T, Rosenthal L, Bishop C, Roehrs T, Syron ML, Roth T: The Alerting Effects of Short and Long Naps in Narcoleptic, Sleep-Deprived, and Alert Individuals. *Sleep* 20(4): 251-257, 1997. PMID: 9231950
206. Buysse D, Reynolds C, Kupfer D, Thorpy M, Bixler E, Kales A, Manfredi R, Vgontzas A, Stepanski E, Roth T, Hauri P, Stapf D: Effects of Diagnosis on Treatment Recommendations in Chronic Insomnia - A Report from the APA/NIMH DSM-IV Field Trial. *Sleep* 20(7): 542-552, 1997. PMID: 9322270
207. Breslau N, Roth T, Rosenthal L, Andreski P: Daytime Sleepiness: An Epidemiological Study of Young Adults. *American Journal of Public Health* 87(10): 1649-1653, 1997. PMID: 9357347
208. Roth TG, Roehrs TA, Koshorek GL, Greenblatt DJ, Rosenthal LD: Hypnotic Effects of Low Doses of Quazepam in Older Insomniacs. *Journal of Clinical Psychopharmacology* 17(5): 401-406, 1997. PMID: 9315991
209. Bishop C, Roehrs T, Rosenthal L, Roth T: Alerting Effects of Methylphenidate under Basal and Sleep-Deprived Conditions. *Experimental and Clinical Psychopharmacology* 5(4): 344-352, 1997. PMID: 9386961
210. Roehrs T, Pedrosi B, Rosenthal L, Zorick F, Roth T: Hypnotic Self Administration: Forced-Choice Versus Single-Choice. *Psychopharmacology* 133: 121-126, 1997. PMID: 9342777
211. Roth T, Richardson G: Commentary: Is Melatonin Administration an Effective Hypnotic? *Journal of Biological Rhythms* 12(6): 666-669, 1997. PMID: 9406043

212. Rosenthal L, Bishop C, Helmus T, Roehrs T, Roth T: Letter to the Editor - Response to Rye and Bliwise. *Sleep* 20(9): 814, 1997.
213. Rosenthal L, Bishop C, Guido P, Syron ML, Helmus T, Rice FM, Roth T: The Sleep/Wake Habits of Patients Diagnosed as Having Obstructive Sleep Apnea. *Chest* 111: 1494-1499, 1997. PMID: 9187162
214. Nowell PD, Buysse DJ, Reynolds CF, Hauri PJ, Roth T, Stepanski EJ, Thorpy MJ, Bixler E, Kales A, Manfredi R, Vgontzas A, Stapf D, Houck P, Kupfer DJ: Clinical Factors Contributing to the Differential Diagnosis of Primary Insomnia and Insomnia Related to Mental Disorders. *American Journal of Psychiatry* 154(10): 1412-1416, 1997. PMID: 9326824
215. Johnson E, Roehrs T, Roth T, Breslau N: Epidemiology of Alcohol and Medication as Aids to Sleep in Early Adulthood. *Sleep* 21(2): 178-186, 1998. PMID: 9542801
216. Papineau K, Roehrs T, Petrucelli N, Rosenthal LD, Roth T: Electrophysiological Assessment (The Multiple Sleep Latency Test) of the Biphasic Effects of Ethanol in Humans. *Alcoholism: Clinical and Experimental Research* 22(1): 231-235, 1998. PMID: 9514312
217. Bishop C, Rosenthal L, Folkerts M, Nykamp K, Helmus T, Guido P, Syron ML, Roehrs T, Rice M, Roth T: The Perception of Sleep as a Function of the Level of Daytime Sleepiness among Patients with Obstructive Sleep Apnea. *Comprehensive Psychiatry* 39(5): 312-317, 1998. PMID: 9777285
218. Nykamp K, Rosenthal L, Folkerts M, Roehrs T, Guido P, Roth T: The Effects of REM Sleep Deprivation on the Level of Sleepiness/Alertness. *Sleep* 21(6): 609-614, 1998. PMID: 9779520
219. Rosenthal L, Nykamp K, Guido P, Syron ML, Day R, Rice FM, Roth T: Daytime CPAP Titration – a Viable Alternative for Patients with Severe Obstructive Sleep Apnea. *Chest* 114: 1056-1060, 1998. PMID: 9792577
220. Walsh J, Fry J, Erwin CW, Scharf M, Roth T, Vogel GW: Efficacy and Tolerability of 14-day Administration of Zaleplon 5mg and 10mg for the Treatment of Primary Insomnia. *Clin Drug Invest* 16(5): 347-354, 1998.
221. Roehrs T, Papineau K, Rosenthal L, Roth T: Ethanol as a Hypnotic in Insomniacs: Self Administration and Effects of Sleep and Mood. *Neuropsychopharmacology* 20(3): 279-286, 1999. PMID: 10063488
222. Johnson EO, Breslau N, Roth T, Roehrs T, Rosenthal L: Psychometric Evaluation of Daytime Sleepiness and Nocturnal Sleep Onset Scales in a Representative Community Sample. *Biol Psychiatry* 45: 764-770, 1999. PMID: 10188007
223. Ancoli-Israel A, Roth T: Characteristics of Insomnia in the United States: Results of the 1991 National Sleep Foundation Survey I. *Sleep* 22(2): S347-353, 1999. PMID: 10394606
224. Roth T, Ancoli-Israel: Daytime Consequences and Correlates of Insomnia in the United States: Results of the 1991 National Sleep Foundation Survey. II. *Sleep* 22(2): S354-358, 1999. PMID: 10394607
225. Johnson EO, Roehrs T, Roth T, Breslau N: Epidemiology of Medication as Aids to Alertness in Early Adulthood. *Sleep* 22(4): 485-488, 1999. PMID: 10389224

226. Roehrs T, Papineau K, Rosenthal L, Roth T: Sleepiness and the Reinforcing and Subjective Effects of Methylphenidate. *Experimental and Clinical Psychopharmacology* 7(2): 145-150, 1999. PMID: 10340154
227. Rosenthal L, Nykamp K, Day R, Syron ML, Roehrs T, Fortier J, Roth T: The Detection of Brief Daytime Sleep Episodes. *Sleep* 22(2): 211-214, 1999. PMID: 10201065
228. Roth T, Roehrs T, Costa e Silva JA, Chase MH: Public Health and Insomnia: Consensus Statement Regarding its Status and Needs for Future Actions. *Sleep* 22(3): S417-S420, 1999.
229. Nykamp K, Rosenthal L, Helmus T, Gerhardstein R, Day R, Roehrs T, Syron ML, Roth T: Repeated Nocturnal Sleep Latencies in Narcoleptic, Sleepy and Alert Subjects. *Clinical Neurophysiology* 110: 1531-1534, 1999. PMID: 10479019
230. Walsh JK, Vogel GW, Scharf M, Erman M, Erwin CW, Schweitzer PK, Mangano RM, Roth T: A Five Week, Polysomnographic Assessment of Zaleplon 10 mg for the Treatment of Primary Insomnia. *Sleep Medicine* 1(1): 41-49, 2000. PMID: 10733619
231. Stepanski E, Zorick F, Roehrs T, Roth T: Effects of Sleep Deprivation on Daytime Sleepiness in Primary Insomnia. *Sleep* 23(2): 215-219, 2000. PMID: 10737338
232. Roehrs T, Roth T: Sleep-Wake State and Memory Function. *Sleep* 23(3): S64-S68, 2000. PMID: 10809188
233. Roth T: Diagnosis and Treatment of Insomnia. *Clinical Cornerstone* 2(5): 28-38, 2000. PMID: 10875044
234. Rosenthal L, Gerhardstein R, Lumley A, Guido P, Day R, Syron ML, Roth T: Compliance with CPAP in Elderly Patients with OSA. *Sleep Medicine* 1(3): 215-220, 2000.
235. Roehrs T, Turner L, Roth T: Effects of Sleep Loss on Waking Actigraphy. *Sleep* 23(6): 793-797, 2000. PMID: 11007446
236. Walsh, Roth T, Randazzo A, Erman M, Jamieson A, Scharf M, Schweitzer P, Catesby Ware J: Eight Weeks of Non-Nightly use of Zolpidem for Primary Insomnia. *Sleep* 23(8): 1087-1096, 2000. PMID: 11145323
237. Roth T, Roehrs T: An Overview of Normal Sleep and Sleep Disorders. *European Journal of Neurology* 7(4): 3-8, 2000.
238. Drake CL, Rice MF, Roehrs TA, Rosenthal L, Guido P, Roth T: Scoring Reliability of the Multiple Sleep Latency Test in a Clinical Population. *Sleep* 23(7): 911-913, 2000. PMID: 11083600
239. Drake CL, Roehrs TA, Mangano RM, Roth T: Dose-Response Effects of Zaleplon as Compared with Triazolam (0.25mg) and Placebo in Chronic Primary Insomnia. *Human Psychopharmacology Clin. Exp.* 15: 595-604, 2000. PMID: 12404612
240. Drake CL, Roehrs TA, Royer H, Koshorek G, Turner RB, Roth T: Effects of an Experimentally Induced Rhinovirus Cold on Sleep, Performance, and Daytime Alertness. *Physiology and Behavior* 71: 75-81, 2000. PMID: 11134688
241. Roth T, Hajak G, Ustun TB: Consensus for the Pharmacological Management of Insomnia in the New Millennium. *International Journal of Clinical Practice* 55(1): 1-11, 2001. PMID: 11219318

242. Roth T, Roehrs T: Sleep- Wake Variations and Drug Self-Administration. *Archives Italiennes de Biologie* 139: 243-252, 2001. PMID: 11330204
243. Day R, Guido P, Helmus T, Fortier J, Roth T, Koshorek G, Rosenthal L: Self-Reported Levels of Sleepiness Among Subjects with Insomnia. *Sleep Medicine* 2: 153-157, 2001. PMID: 11226864
244. Roehrs T, Bonahoom A, Pedrosi B, Rosenthal L, Roth T: Treatment Regimen and Hypnotic Self-Administration. *Psychopharmacology* 155: 11-17, 2001. PMID: 11374329
245. Rosenthal L, Day R, Gerhardstein R, Meixner R, Roth T, Guido P, Fortier J: Sleepiness/Alertness Among Healthy Evening and Morning Type Individuals. *Sleep Medicine* 2: 243-248, 2001. PMID: 11311688
246. Roehrs T, Rosenthal L, Koshorek G, Mangano RM, Roth T: Effects of Zaleplon or Triazolam with or without Ethanol on Human Performance. *Sleep Medicine* 2: 323-332, 2001. PMID: 11438249
247. Roehrs T, Roth T: Sleep, Sleepiness, Sleep Disorders and Alcohol Use and Abuse. *Sleep Medicine Reviews* 5(4): 287-297, 2001. PMID: 12530993
248. Roehrs T, Roth T: Sleep, Sleepiness, and Alcohol Use. *Alcohol Research & Health* 25(2): 101-109, 2001. PMID: 11584549
249. Drake C, Roehrs T, Burduvali E, Bonahoom A, Rosekind M, Roth T: Effects of Rapid Versus Slow Accumulation of Eight Hours of Sleep Loss. *Psychophysiology* 38: 979-987, 2001. PMID: 12240674
250. Ohayon MM, Roth T: What are the Contributing Factors for Insomnia in the General Population? *Journal of Psychosomatic Research* 51: 745-755, 2001. PMID: 11750297
251. Erman MK, Erwin CW, Gengo FM, Jamieson AO, Lemmi H, Mahowald MW, Regestein QR, Roth T, Roth-Schechter B, Scharf MB, Vogel GW, Walsh JK, Ware JC: Comparative Efficacy of Zolpidem and Temazepam in Transient Insomnia. *Hum Psychopharmacol* 16: 169-176, 2001. PMID: 12404587
252. Roehrs T, Bonahoom A, Pedrosi B, Rosenthal L, Roth T: Disturbed Sleep Predicts Hypnotic Self-Administration. *Sleep Medicine* 3: 61-66, 2002. PMID: 14592256
253. Roth T, Zammit G, Kushida C, Doghramji K, Mathias SD, Wong JM, Buysse DJ: A New Questionnaire to Detect Sleep Disorders. *Sleep Medicine* 3: 99-108, 2002. PMID: 14592227
254. Roehrs T, Bonahoom A, Pedrosi B, Zorick F, Roth T: Nighttime Versus Daytime Hypnotic Self-Administration. *Psychopharmacology* 161: 137-142, 2002. PMID: 11981593
255. Richardson GS, Roehrs TA, Rosenthal L, Koshorek G, Roth T: Tolerance to Daytime Sedative Effects of H1 Antihistamines. *Journal of Clinical Psychopharmacology* 22(5): 511-515, 2002. PMID: 12352276
256. Richardson GS, Roth T, Kramer JA: Management of Insomnia: The Role of Zaleplon. *Gen Med* 4(9), 2002. PMID: 11965211
257. Ohayon MM, Roth T: Prevalence of Restless Legs Syndrome and Periodic Limb Movement Disorder in the General Population. *Journal of Psychosomatic Research* 53: 547-554, 2002. PMID: 12127170

258. Roehrs T, Hollebeek E, Drake C, Roth T: Substance Use for Insomnia in Metropolitan Detroit. *Journal of Psychosomatic Research* 53: 571-576, 2002. PMID: 12127173
259. Drake CL, Mason KM, Bowyer SM, Roth T, Barkley GL, Tepley N: Topographic Distribution of Sleep Spindles Using 2DII. In: *Biomag: Proceedings of the 13th International Conference on Biomagnetism*, (eds: H. Nowak, J. Haueisen, F. Giebler, R. Huonker) Verlag: Berlin: 152-154, 2002.
260. Drake CL, Mason KM, Bowyer SM, Roth T, Barkley GL, Tepley N: Vertex Sharp Waves during Sleep Localized by 2DII. In: *Biomag: Proceedings of the 13th International Conference on Biomagnetism*, (eds: H. Nowak, J. Haueisen, F. Giebler, R. Huonker) Verlag: Berlin: 164-166, 2002.
261. Ohayon MM, Roth T: Place of Chronic Insomnia in the Course of Depressive and Anxiety Disorders. *Journal of Psychiatric Research* 37: 9-15, 2003. PMID: 12482465
262. Drake CL, Roehrs T, Turner L, Scofield HM, Roth T: Caffeine Reversal of Ethanol Effects on the Multiple Sleep Latency Test, Memory, and Psychomotor Performance. *Neuropsychopharmacology* 28: 371-378, 2003. PMID: 12589390
263. Drake CL, Day R, Hudgel D, Stefadu Y, Parks M, Syron ML, Roth T: Sleep During Titration Predicts Continuous Positive Airway Pressure Compliance. *Sleep* May 1;26(3): 308-311, 2003. PMID: 12749550
264. Drake CL, Nickel C, Burduvali E, Roth T, Jefferson C, Badia P: The Pediatric Daytime Sleepiness Scale (PDSS): Sleep Habits and School Outcomes in Middle-School Children. *Sleep* 26(4): 1-4, 2003. PMID: 12841372
265. Roth T, Rye DB, Borchert LD, Bartlett C, Bliwise DL, Cantor C, Gorell JM, Hubble JP, Musch B, Olanow CW, Pollak C, Stern MB, Watts RL: Assessment of Sleepiness and Unintended Sleep in Parkinson's Disease Patients Taking Dopamine Agonists. *Sleep Medicine* 4: 275-280, 2003. PMID: 14592299
266. Brodsky MA, Godbold J, Roth T, Olanow CW: Sleepiness in Parkinson's Disease: A Controlled Study. *Movement Disorders* 18(6): 668-672, 2003. PMID: 12784270
267. Krystal AD, Walsh JK, Laska E, Caron J, Amato DA, Wessel TC, Roth T: Sustained Efficacy of Eszopiclone Over 6 Months of Nightly Treatment: Results of a Randomized, Double-Blind, Placebo-Controlled Study in Adults with Chronic Insomnia. *Sleep* 26(7): 793-799, 2003. PMID: 14655910
268. Drake CL, Roehrs T, Roth T: Insomnia Causes, Consequences, and Therapeutics: An Overview. *Depression and Anxiety* 18: 163-176, 2003. PMID: 14661186
269. Roehrs T, Burduvali E, Bonahoom A, Drake C, Roth T: Ethanol and Sleep Loss: A "Dose" Comparison of Impairing Effects. *Sleep* 26(8): 981-985, 2003. PMID: 14746378
270. Drake C, Richardson G, Roehrs T, Scofield H, Roth T: Vulnerability to Stress-related Sleep Disturbance and Hyperarousal. *Sleep* 27(2): 285-291, 2004. PMID: 15124724
271. Atkinson MJ, Allen RP, DuChane J, Murray C, Kushida C, Roth T: Validation of the Restless Legs Syndrome Quality of Life Instrument (RLS-QLI): Findings of a Consortium of National Experts and the RLS Foundation. *Quality of Life Research* 13: 679-693, 2004. PMID: 15130030
272. Breslau N, Roth T, Burduvali E, Kapke A, Schultz L, Roehrs T: Sleep Lifetime Posttraumatic Stress Disorder. A Community-Based Polysomnographic Study. *Arch Gen Psychiatry* 61: 508-516, 2004. PMID: 15123496

273. Mendelson WB, Roth T, Cassella J, Roehrs T, Walsh JK, Woods JH, Buysse DJ, Meyer RE: The Treatment of Chronic Insomnia: Drug Indications, Chronic Use and Abuse Liability. Summary of a 2001 New Clinical Drug Evaluation Unit Meeting Symposium. *Sleep Medicine Reviews* 8: 7-17, 2004. PMID: 15062207
274. Roehrs T, Johanson CE, Meixner R, Turner L, Roth T: Reinforcing and Subjective Effects of Methylphenidate: Dose and Time in Bed. *Experimental and Clinical Psychopharmacology* 12(3): 180-189, 2004. PMID: 15301635
275. Roehrs T, Greenwald M, Roth T: Risk-Taking Behavior: Effects of Ethanol, Caffeine, and Basal Sleepiness. *Sleep* 27(5): 887-893, 2004. PMID: 15453546
276. Roehrs T, Roth T: 'Hypnotic' Prescription Patterns in a Large Managed-Care Population: *Sleep Medicine* 5: 463-466, 2004. PMID: 15341891
277. Roth T, Drake C: Evolution of Insomnia: Current Status and Future Direction. *Sleep Medicine* 5(1): S23-S30, 2004. PMID: 15301994
278. Drake CL, Roehrs T, Richardson G, Walsh JK, Roth T: Shift Work Sleep Disorder: Prevalence and Consequences Beyond that of Symptomatic Day Workers. *Sleep* 27(8): 1453-1462, 2004. PMID: 15683134
279. Zammit GK, McNabb LJ, Caron J, Amato DA, Roth T: Efficacy and Safety of Eszopiclone Across 6-Weeks of Treatment for Primary Insomnia. *Current Medical Research and Opinion* 20(12): 1979-1991, 2004. PMID: 15701215
280. Rosenberg R, Caron J, Roth T, Amato D: An Assessment of the Efficacy and Safety of Eszopiclone in the Treatment of Transient Insomnia in Healthy Adults. *Sleep Medicine* 6: 15-22, 2005. PMID: 15680290
281. Roth T, Stubbs C, Walsh JK: Ramelteon (TAK-375), a Selective MT1/MT2-Receptor Agonist, Reduces Latency to Persistent Sleep in a Model of Transient Insomnia Related to a Novel Sleep Environment. *Sleep* 28(3): 303-307, 2005. PMID: 16173650
282. Roehrs T, Roth T: Sleep And Pain: Interaction of Two Vital Functions. *Seminars in Neurology* 25(1): 106-116, 2005. PMID: 15798943
283. Jefferson CD, Drake CL, Scofield HM, Myers E, McClure T, Roehrs TA, Roth T: Sleep Hygiene Practices in a Population-Based Sample of Insomniacs. *Sleep* 28(5): 611-615, 2005. PMID: 16171275
284. Walsh JK, Randazzo AC, Frankowski S, Shannon K, Schwietzer, PK, Roth T: Dose Response Effects of Tiagabine on the Sleep of Older Adults. *Sleep* 28(6): 673-676, 2005. PMID: 16477953
285. Johnson DA, Orr WC, Crawley JA, Traxler B, McCullough J, Brown KA, Roth T: Effect of Esomeprazole on Nighttime Heartburn and Sleep Quality in Patients with GERD: A Randomized, Placebo-Controlled Trial. *Am J Gastroenterol* 100(9): 1914-1922, 2005. PMID: 16128933
286. Czeisler CA, Walsh JK, Roth T, Hughes RJ, Wright KP, Kingsbury L, Arora A, Schwartz JRL, Neibler GE, Dinges DF: Modafinil for Excessive Sleepiness Associated with Shift-Work Sleep Disorder. *N Engl J Med* 353(5): 26-36, 2005. PMID: 16079371

287. Roth T, Walsh JK, Krystal A, Wessel T, Roehrs TA.: An Evaluation of the Efficacy and Safety of Eszopiclone Over 12 Months in Patients with Chronic Primary Insomnia. *Sleep Medicine* 6: 487-495, 2005. PMID: 16230048
288. Singh M, Drake CL, Roehrs T, Hudgel DW, Roth T: The Association Between Obesity and Short Sleep Duration: A Population-Based Study. *Journal of Clinical Sleep Medicine* 1(4): 357-363, 2005. PMID: 17564401
289. Shepard JJW, Buysse DJ, Chesson JAL, Dement WC, Goldberg R, Guilleminault C, Harris CD, Iber C, Mignot E, Mitler MM, Moore KE , Phillips BA, Quan SF, Rosenberg RS, Roth T, Schmidt HS, Silber MS, Walsh JK, White DP. History of the Development of Sleep Medicine in the United States. *Journal of Clinical Sleep Medicine* 1(1): 61-82, 2005. PMID: 17561617
290. Roehrs T, Kapke A, Roth T, Breslau N: Sex Differences in the Polysomnographic Sleep of Young Adults: A Community-Based Study. *Sleep Medicine* 7: 49-53, 2006. PMID: 16194623
291. Walsh JK, Perlis M, Rosenthal M, Krystal A, Jiang J, Roth T: Tiagabine Increases Slow-Wave Sleep in a Dose-Dependent Fashion Without Affecting Traditional Efficacy Measures in Adults with Primary Insomnia. *Journal of Clinical Sleep Medicine* 2(1): 35-41, 2006. PMID: 17557435
292. Johnson EO, Roth T, Schultz L, Breslau N: Epidemiology of DSM-IV Insomnia in Adolescence: Lifetime Prevalence, Chronicity, and an Emergent Gender Difference. *Pediatrics* 117: e247 - e256, 2006. PMID: 16452333
293. Roehrs TA, Hyde M, Blaisdell B, Greenwald M, Roth T: Sleep Loss and REM Sleep Loss are Hyperalgesic. *Sleep* 29(2): 145-151, 2006. PMID: 16494081
294. Roth T, Wright KP, Walsh J: Effect of Tiagabine on Sleep in Elderly Subjects with Primary Insomnia: A Randomized, Double-Blind, Placebo-Controlled Study. *Sleep* 29(3): 335-341, 2006. PMID: 16553019
295. Walsh JK, Zammit G, Schweitzer PK, Ondrasik J, Roth T. Tiagabine Enhances Slow Wave Sleep and Sleep Maintenance in Primary Insomnia. *Sleep Medicine* 6: 155-161, 2006. PMID: 16260179
296. Mindell JA, Emslie G, Blumer J, Genel M, Glaze D, Ivanenko A, Johnson K, Rosen C, Steinberg F, Roth T, Banas B. Pharmacologic Management of Insomnia in Children and Adolescents: Consensus Statement. *Pediatrics* 117: 1223-1232, 2006. PMID: 16740821
297. Walsh JK, Randazzo AC, Stone K, Eisenstein R, Feren SD, Kajy S, Dickey P, Roehrs T, Roth T, Schweitzer PK. Tiagabine is Associated with Sustained Attention During Sleep Restriction: Evidence for the Value of Slow Wave Sleep Enhancement? *Sleep* 29(4): 433-443, 2006. PMID: 16676776
298. Fava M, McCall WV, Krystal A, Wessel T, Rubens R, Caron J, Amato D, Roth T. Eszopiclone Co-Administered with Fluoxetine in Patients with Insomnia Coexisting with Major Depressive Disorder. *Biol Psychiatry* 59: 1052-1060, 2006. PMID: 16581036
299. Roth T, White D, Schmidt-Nowara W, Wesnes KA, Niebler G, Arora S, Black J. Effects of Armodafinil in the Treatment of Residual Excessive Sleepiness Associated with Obstructive Sleep Apnea/Hypopnea Syndrome: A 12-Week, Multicenter, Double-Blind, Randomized, Placebo-Controlled Study in nCPAP-Adherent Adults. *Clinical Therapeutics* 28(5): 689-706, 2006. PMID: 16861091

300. Roth T, Soubrane C, Titeux L, Walsh JK. Efficacy and Safety of Zolpidem-MR: A Double-Blind, Placebo-Controlled Study in Adults with Primary Insomnia. *Sleep Medicine* 7: 397-406, 2006. PMID: 16815744
301. Roth T, Seiden D, Sainati S, Wang-Weigand S, Zhang J, Zee P. Effects of Ramelteon on Patient-Reported Sleep Latency in Older Adults with Chronic Insomnia. *Sleep Medicine* 7: 312-318, 2006. PMID: 16709464
302. Johnson EO, Roth T. An Epidemiologic Study of Sleep-Disordered Breathing Symptoms Among Adolescents. *Sleep* 29(9): 1135-1142, 2006. PMID: 17040001
303. Harsh JR, Hayduk R, Rosenberg R, Wesnes KA, Walsh JK, Arora S, Niebler GE, Roth T. The Efficacy and Safety of Armodafinil as Treatment for Adults with Excessive Sleepiness Associated with Narcolepsy. *Curr Med Res Opin* 22(4): 761-774, 2006. PMID: 16684437
304. Roth T, Jaeger S, Jin R, Kalsekar A, Stang P, Kessler RC. Sleep Problems, Comorbid Mental Disorders, and Role Functioning in the National Comorbidity Survey Replication (NCS-R). *Biol Psychiatry* 60(12): 1364-1371, 2006. PMID: 16952333
305. Roehrs T, Roth T. Safety of Insomnia Pharmacotherapy. *Sleep Med Clinics* 1: 399-407, 2006.
306. Drake CL, Jefferson C, Roehrs T, Roth T. Stress-Related Sleep Disturbance and Polysomnographic Response to Caffeine. *Sleep Med* 7: 567-572, 2006. PMID: 16996309
307. Johnson EO, Roth T, Breslau N. The Association of Insomnia with Anxiety Disorders and Depression: Exploration of the Direction of Risk. *Journal of Psychiatric Research* 40: 700-708, 2006. PMID: 16978649
308. Soares CN, Joffe H, Rubens R, Caron J, Roth T, Cohen L: Eszopiclone in Patients with Insomnia During Perimenopause and Early Postmenopause. *Obstetrics & Gynecology* 108(6): 1402-1410, 2006. PMID: 17138773
309. Harsh JR, Hayduk R, Rosenberg R, Wesnes KA, Walsh JK, Arora S, Niebler GE, Roth T: The Efficacy and Safety of Armodafinil as Treatment for Adults with Excessive Sleepiness Associated with Narcolepsy. *Current Medical Research and Opinion* Vol. 22, No. 4: 761-774, 2006. PMID: 16684437
310. Singh M, Drake CL, Roth T: The Prevalence of Multiple Sleep-Onset REM Periods in a Population-Based Sample. *Sleep*, Vol. 29, No. 7, 890-895, 2006. PMID: 16895255
311. Hirshkowitz M, Black JE, Wesnes K, Niebler G, Arora S, Roth T. Adjunct Armodafinil Improves Wakefulness and Memory in Obstructive Sleep Apnea/Hypopnea Syndrome. *Respiratory Medicine* 101(3): 616-627, 2007. PMID: 16908126
312. Krystal A, Fava M, Rubens R, Wessel T, Caron J, Wilson P, Roth T, McCall WV: Evaluation of Eszopiclone Discontinuation after Cotherapy with Fluoxetine for Insomnia with Coexisting Depression. *Journal of Clinical Sleep Medicine* 3(1): 48-55, 2007. PMID: 17557453
313. Kryger M, Wang-Weigand S, Roth T: Safety of Ramelteon in Individuals with Mild to Moderate Obstructive Sleep Apnea. *Sleep Breath* 11: 159-164, 2007. PMID: 17294232
314. Budhiraja R, Parthasarathy S, Drake C, Roth T, Sharief I, Budhiraja P, Saunders V, Hudgel D: Early CPAP Use Identifies Subsequent Adherence to CPAP Therapy. *Sleep* 30(3): 320-324, 2007. PMID: 17425228

315. Roth T, Seiden D, Wang-Weigand S, Zhang J: A 2-Night, 3-Period, Crossover Study of Ramelteon's Efficacy and Safety in Older Adults with Chronic Insomnia. *Current Medical Research and Opinion* 23(5): 1005-1014, 2007. PMID: 17519067
316. Roth T, Krystal AD, Lieberman JA III. Long-Term Issues in the Treatment of Sleep Disorders. *CNS Spectr.* 2007;12(7 suppl 10):1-16.
317. Walsh JK, Krystal AD, Amato DA, Rubens R, Caron J, Wessel TC, Schaefer K, Roach J, Wallenstein G, Roth T: Nightly Treatment of Primary Insomnia with Eszopiclone for Six Months: Effect on Sleep, Quality of Life and Work Limitations. *Sleep* 30(8): 959-968, 2007. PMID: 17702264
318. Zammit G, Erman M, Wang-Weigand S, Sainati S, Zhang J, Roth T: Evaluation of the Efficacy and Safety Ramelteon in Subjects with Chronic Insomnia. *Journal of Clinical Sleep Medicine* 3(5): 495-504, 2007. PMID: 17803013
319. Roth T, Rippon GA, Arora S: Armodafinil Improves Wakefulness and Long-Term Episodic Memory in nCPAP-Adherent Patients with Excessive Sleepiness Associated with Obstructive Sleep Apnea. *Sleep Breath* 10, 2007.
320. Walsh JK, Moscovitch A, Burke J, Farber R, Roth T: Efficacy and Tolerability of Indiplon in Older Adults with Primary Insomnia. *Sleep Medicine* 8(7-8): 753-759, 2007. PMID: 17825616
321. Roth T, Schwartz JRL, Hirshkowitz M, Erman MK, Dayno JM, Arora S: Evaluation of the Safety of Modafinil for Treatment of Excessive Sleepiness. *Journal of Clinical Sleep Medicine* 3(6): 595-602, 2007. PMID: 17993041
322. Roth T, Rogowski R, Hull S, Schwartz H, Koshorek G, Corser B, Seiden D, Lankford A: Efficacy and Safety of Doxepin 1mg, 3mg and 6mg in Adults with Primary Insomnia. *Sleep* 30(11): 1555-1561, 2007. PMID: 18041488
323. Roth T, Zammit GK, Scharf MB, Farber R: Efficacy and Safety of As-Needed, Post Bedtime Dosing with Indiplon in Insomnia Patients with Chronic Difficulty Maintaining Sleep. *Sleep* 30(12): 1731-1738, 2007. PMID: 18246982
324. Kryger M, Wang-Weigand S, Zhang J, Roth T. Effect of Ramelteon, a Selective MT1/MT2-Receptor Agonist, on Respiration during Sleep in Mild to Moderate COPD. *Sleep Breath* 10, 2007.
325. Villareal A, Hudgel D, Roth T. Improvement of Obstructive Sleep Apnea after Radiation Therapy of Vocal Cord Carcinoma. *Sleep Medicine* Dec;9(1): 96-97, 2007. PMID: 17825614
326. Rosenberg R, Roth T, Scharf MB, Lankford DA, Farber R: Efficacy and Tolerability of Indiplon in Transient Insomnia. *Journal of Clinical Sleep Medicine*, Jun 15; Vol. 3 No. 4: 374-379, 2007. PMID: 17694726
327. Walsh JK, Soubrane C, Roth T. Efficacy and Safety of Zolpidem Extended Release in Elderly Primary Insomnia Patients. *Am J Geriatr Psychiatry* Jan;16(1): 44-57, 2008. PMID: 18165461
328. Roth T, Mayleben D, Corser BC, Singh NN. Daytime Pharmacodynamic and Pharmacokinetic Evaluation of Low-Dose Sublingual Transmucosal Zolpidem Hemitartrate. *Human Psychopharmacology Clinical and Experimental* Jan;23(1): 13-20, 2008. PMID: 17907263
329. Krystal AD, Erman M, Zammit G, Soubrane C, Roth T. Long-Term Efficacy and Safety of Zolpidem Extended-Release 12.5 mg, Administered 3 to 7 Nights Per Week for 24 Weeks, in Patients with

- Chronic Primary Insomnia: a 6-month, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study. *Sleep* Jan;31(1): 79-90, 2008. PMID: 18220081
330. Krystal AD, Thakur M, Roth T. Sleep Disturbance in Psychiatric Disorders: Effects on Function and Quality of Life in Mood Disorders, Alcoholism and Schizophrenia. *Annals of Clinical Psychiatry* Jan-Mar; 20(1): 39-46, 2008. PMID: 18297585
331. Roehrs T, Roth T: Caffeine: Sleep And Daytime Sleepiness. *Sleep Medicine Reviews* Apr; 12(2): 153-162, 2008. PMID: 17950009
332. Drake CL, Scofield H, Roth T: Vulnerability to Insomnia: The Role of Familial Aggregation. *Sleep Medicine* Mar; 9(3): 297-302, 2008. PMID: 17825612
333. Pollack M, Kinrys G, Krystal A, McCall V, Roth T, Schaefer K, Rubens R, Roach J, Huang H, Krishnan R: Eszopiclone Coadministered With Escitalopram in Patients With Insomnia and Corborbid Generalized Anxiety Disorder. *Arch Gen Psychiatry* Vol 65 (5): 551-562, 2008. Also available at www.archgenpsychiatry.com PMID: 18458207
334. Schwartz JRL, Hughes RJ, Roth T: Pharmacologic Therapy for Sleep-Related Breathing Disorders. *Expert Rev Clin Pharmacol* I(3): 441-455, 2008. Also available at www.expert-reviews.com
335. Valentina G, Robinson S, Jefferson C, Roth T, Tepley N, Drake C: Brain-changes During Transition from Awake to Sleep: (MEG) Study. *Biomagnetism-Transdisciplinary Research and Exploration*: 200-202, 2008.
336. Scofield H, Roth T, Drake C: Periodic Limb Movements During Sleep: Population Prevalence, Clinical Correlates, and Racial Differences. *Sleep*, Vol 31, No 9: 1221-1227, 2008. PMID: 18788647
337. Roth T, Hull SG, Lankford DA, Rosenberg R, Scharf MB, Intermezzo Study Group: Low-Dose Sublingual Zolpidem Tartrate is Associated with Dose-Related Improvement in Sleep Onset and Duration in Insomnia Characterized by Middle-of-the-Night (MOTN) Awakenings. *Sleep*, Vol 31, No 9: 1277-1284, 2008. PMID: 18788653
338. Scharf M, Rogowski R, Hull S, Cohn M, Mayleben D, Feldman N, Ereshefsky L, Lankford A, Roth T: Efficacy and Safety of Doxepin 1 mg, 3 mg, and 6 mg in Elderly Patients with Primary Insomnia: A Randomized Double-Blind, Placebo-Controlled Crossover Study. *J Clin Psychiatry* Oct; 69(10): 1557-1564, 2008. PMID: 19192438
339. Rajaratnam SMW, Polymeropoulos MH, Fisher DM, Roth T, Scott C, Birznieks G, Klerman EB: Melatonin Agonist Tasimelteon (VEC-162) for Transient Insomnia after Sleep-Time Shift: Two Randomised Controlled Multicentre Trials. *Lancet* 373(9662): 482-491. www.thelancet.com Published on line DOI:10.1016/S0140-6736(08)61812-7: 1-10, Dec 2, 2008. PMID: 19054552

340. Rosenberg R, Seiden DJ, Hull SG, Erman M, Schwartz H, Anderson C, Prosser W, Shanahan W, Sanchez M, Chuang E, Roth T: APD125, a Selective Serotonin 5-HT Receptor Inverse Agonist, Significantly Improves Sleep Maintenance in Primary Insomnia. *Sleep*, Vol 31, No 12: 1663-1671, 2008. PMID: 19090322
341. Roth T, Rippon GA, Arora S: Armodafinil Improves Wakefulness and Long-Term Episodic Memory in nCPAP-Adherent Patients with Excessive Sleepiness Associated with Obstructive Sleep Apnea. *Sleep Breath*, Mar; 12: 53-62, 2008. PMID: 17874255
342. Krystal AD, Goforth H, Roth T. Effects of antipsychotic medications on sleep in schizophrenia. *Int J Clinical Psychopharmacology*, 2008;65:551-62.
343. Kryger M, Roth T, Wang-Weigand S, Zhang J: The Effects of Remelteon on Respiration During Sleep in Subjects with Moderate to Severe Chronic Obstructive Pulmonary Disease. *Sleep Breath*, Mar; 13(1): 79-84, 2009. PMID: 18584227
344. Roth T: Hypnotic use for Insomnia Management in Chronic Obstructive Pulmonary Disease. *Sleep Medicine* 10: 19-25, 2009. PMID: 18693067
345. Staner L, Eriksson M, Cornette F, Santoro F, Muscat N, Luthinger R, Roth T: Sublingual Zolpidem is More Effective than Oral Zolpidem in Initiating Early Onset of Sleep in the Post-Nap Model of Transient Insomnia: A Polysomnographic Study. *Sleep Medicine* 10(6): 616-620, 2009. PMID: 18996742
346. Kushida CA, Walters AS, Becker P, Thein SG, Perkins AT, Roth T, Canafax D, Barrett RW: A Randomized, Double-Blind, Placebo-Controlled, Crossover Study of XP13512/GSK1838262 in the Treatment of Patients with Primary Restless Legs Syndrome. *Sleep* 32 (2): 159-168, 2009. PMID: 19238802
347. Zammit G, Schwartz H, Roth T, Wang-Weigand S, Sainati S, Zhang J: The Effects of Ramelteon in a First-Night Model of Transient Insomnia. *Sleep Medicine*, Jan;10(1): 55-59, 2009. PMID: 18691937
348. Gumenyuk V, Roth T, Moran JE, Jefferson C, Bowyer SM, Tepley N, Drake CL: Cortical Locations of Maximal Spindle Activity: Magnetoencephalography (MEG) Study. *Journal of Sleep Research* 18(2): 245-253, 2009. PMID: 19645968
349. Fava M, Asnis GM, Shrivastava R, Lydiard B, Bastani B, Sheehan D, Roth T: Zolpidem Extended-Release Improves Sleep and Next-Day Symptoms in Comorbid Insomnia and Generalized Anxiety Disorder. *Journal of Clinical Psychopharmacology*, Jun; Vol 29, Number (3): 222-230, 2009. PMID: 19440075
350. Chhangani BS, Roehrs TA, Harris EJ, Hyde M, Drake C, Hudgel DW, Roth T: Pain Sensitivity in Sleepy Pain-Free Normals. *Sleep*, Aug, 32, No. 8: 1011-1017, 2009. PMID: 19792573
351. Adler LA, Goodman D, Weisler R, Hamdani M, Roth T: Effect of Lisdexamfetamine Dimesylate on Sleep in Adults with Attention-Deficit/Hyperactivity Disorder. *Behavioral and Brain Functions*, Aug; 5:34, 2009. www.behavioralandbrainfunctions.com/content/5/1/34. PMID: 19650932
352. Czeisler CA, Walsh JK, Wesnes KA, Arora S, Roth T: Armodafinil for Treatment of Excessive Sleepiness Associated With Shift Work Disorder: A Randomized Controlled Study. *Mayo Clinic Proceedings* 84(11): 958-972, November 2009. PMID: 19880686

353. Palesh OG, Roscoe JA, Mustian KM, Roth T, Savard J, Ancoli-Israel S, Heckler C, Purnell JQ, Janelsins MC, Morrow, GR: Prevalence, Demographics and Psychological Associations of Sleep Disruption in Patients with Cancer: University of Rochester Cancer Center-Community Clinical Oncology Program. Journal of Clinical Oncology (27): 1-7, November, 2009.
354. Roth T, Price JM, Amato DA, Rubens RP, Roach JM, Schnitzer TJ: The Effect of Eszopiclone in Patients with Insomnia and Coexisting Rheumatoid Arthritis: A Pilot Study. Prim Care Companion J Clin Psychiatry, 11(6): 292-301, 2009. PMID: 20098520
355. Roth T, on Behalf of the Workshop Participants: Does Effective Management of Sleep Disorders Reduce Substance Dependence? Drugs, Vol. 69, Suppl. 2: 65-75, 2009. PMID: 20047351
356. Ancoli-Israel S, Krystal AD, McCall WV, Schaefer K, Wilson A, Claus R, Rubens R, Roth T: A 12-Week, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Effect of Eszopiclone 2 mg on Sleep/Wake Function in Older Adults with Primary and Comorbid Insomnia. Sleep, Vol 33, No. 2, pp 225-234, 2010. PMID: 20175406
357. Roth T, Lines C, Vandormael K, Ceesay P, Anderson D, Snavely D: Effect of Gaboxadol on Patient-reported Measures of Sleep and Waking Function in Patients with Primary Insomnia: Results from Two Randomized, Controlled, 3-month Studies. Journal of Clinical Sleep Medicine, Feb; 15, Vol. 6, No. 1, 30-39, 2010. PMID: 20191935
358. Ohayon MM, Krystal A, Roehrs TA, Roth T, Vitiello MV: Using Difficulty Resuming Sleep to Define Nocturnal Awakenings. Sleep Medicine, Mar; 11(3), 236-241, 2010. PMID: 20075004
359. Roth T, Zammit G, Lankford A, Mayleben D, Stern T, Pitman V, Clark D, Werth JL: Nonrestorative Sleep as a Distinct Component of Insomnia. Sleep, Apr; Vol. 33, No. 4, 449-458, 2010. PMID: 20394313
360. Gumenyuk V, Roth T, Korzyukov O, Jefferson C, Kick A, Spear L, Tepley N, Drake CL: Shift Work Sleep Disorder is Associated with an Attenuated Brain Response of Sensory Memory and an Increased Brain Response to Novelty: An ERP Study. Sleep, May; Vol. 33, No. 5, 703-713, 2010. PMID: 20469813
361. Drake C, Roehrs T, Breslau N, Johnson E, Jefferson C, Scofield H, Roth T: The 10-Year Risk of Verified Motor Vehicle Crashes in Relation to Physiologic Sleepiness. Sleep, Jun; Vol. 33, No. 6, 745-752, 2010. PMID: 20550014
362. Zee PC, Wang-Weigand S, Wright Jr KP, Peng X, Roth T: Effects of Ramelteon on Insomnia Symptoms Induced by Rapid, Eastward Travel. Sleep Medicine, Jun; 11, 525-533, 2010. PMID: 20483660
363. Steinmiller CL, Roehrs TA, Harris E, Hyde M, Greenwald MK, Roth T: Differential Effect of Codeine on Thermal Nociceptive Sensitivity in Sleepy Versus Nonsleepy Healthy Subjects. Experimental and Clinical Psychopharmacology, Jun; Vol. 18, No.3, 277-283, 2010.
364. Roth, T, Durrence HH, Jochelson P, Peterson G, Ludington E, Rogowski R, Scharf M, Lankford A: Efficacy and Safety of Doxepin 6 mg in a Model of Transient Insomnia. Sleep Medicine, 11, 843-847, 2010. PMID: 20817598
365. Stroe, AF, Roth T, Jefferson C, Hudgel DW, Roehrs T, Moss K, Drake CL: Comparative Levels of Excessive Daytime Sleepiness in Common Medical Disorders. Sleep Medicine, Oct; 11, 890-896, 2010. PMID: 20817600

366. Roth T, van Seventer R, Murphy TK: The Effect of Pregabalin on Pain-Related Sleep Interference in Diabetic Peripheral Neuropathy or Postherpetic Neuralgia: A Review of Nine Clinical Trials. Current Medical Research & Opinion, Vol. 26, No. 10, 2411-2419, 2010. PMID: 2081279
367. Krystal AD, Durrence HH, Scharf M, Jochelson P, Rogowski R, Ludington E, Roth T: Long-Term Safety and Efficacy of Doxepin for Elderly Insomnia. Efficacy and Safety of Doxepin 1mg and 3mg in a 12-week Sleep Laboratory and Outpatient Trial of Elderly Subjects with Chronic Primary Insomnia. Sleep, Vol. 33, No. 11, 1553-1561, 2010. PMID: 21102997
368. Kessler RC, Coulouvrat C, Hajak G, Lakoma MD, Roth T, Sampson N, Shahly V, Shillington A, Stephenson JJ, Walsh JK, Zammit GK: Reliability and Validity of the Brief Insomnia Questionnaire. Reliability and Validity of the Brief Insomnia Questionnaire in the America Insomnia Survey. Sleep, Nov; Vol. 33, No. 11, 1539-1549, 2010. PMID: 21102996
369. Ohayon MM, Smolensky MH, Roth T: Consequences of Shiftworking on Sleep Duration, Sleepiness and Sleep Attacks. Chronobiol Int. May; 27(3), 575-589. PMID: 20524802 (PubMed-indexed for MEDLINE) Related citations. 2010. PMID: 20524802
370. Hayes S, Cytryn K, Johnson M, Roth T, Murray S: Sleep-Wake Disorders: Can CME Panel Discussion Activity Improve Clinical Practice? CD Meas. Volume 4, Issue 4: 68-73, 2010.
371. Rosenberg RP, Bogan RK, Tiller JM, Yang R, Youakim JM, Earl CQ, Roth T: A Phase 3, Double-Blind, Randomized, Placebo-Controlled Study of Armodafinil for Excessive Sleepiness Associated With Jet Lag Disorder. Mayo Clin Proc., July; 85(7): 630-638. doi: 10.4065/mcp.2009.0778, 2010. PMID: 20530317
372. Roehrs TA, Randall S, Harris E, Maan S, Roth T: Twelve Months of Nightly Zolpidem Does Not Lead to Dose Escalation: A Prospective Placebo-Controlled Study. Sleep, Vol. 34, No. 2, 207-212, 2011. PMID: 21286241
373. Roth T, Coulouvrat C, Hajak G, Lakoma MD, Sampson NA, Shahly V, Shillington AC, Stephenson JJ, Walsh JK, Kessler RC: Prevalence and Perceived Health Associated with Insomnia Based on DSM-IV-TR; International Statistical Classification of Diseases and Related Health Problems, Tenth Revision; and Research Diagnostic Criteria/International Classification of Sleep Disorders, Second Edition Criteria: Results from the America Insomnia Survey. Biol Psychiatry, 69: 592-600, 2011.
374. Verster JC, Roth T: Standard Operation Procedures for Conducting the On-The-Road Driving Test, and Measurement of the Standard Deviation of Lateral Position (SDLP). International Journal of General Medicine, 4: 359-371, 2011. PMID: 21625472
375. Yaremchuk K, Tacia B, Peterson E, Roth T: Change in Epworth Sleepiness Scale after Surgical Treatment of Obstructive Sleep Apnea. The Laryngoscope, 121, July: 1590-1593, July, 2011. PMID: 21671233
376. Fava M, Asnis GM, Shrivastava RK, Lydiard B, Bastani B, Sheehan DV, Roth T: Improved Insomnia Symptoms and Sleep-Related Next-Day Functioning in Patients with Comorbid Major Depressive Disorder and Insomnia Following Concomitant Zolpidem Extended-Release 12.5 mg and Escitalopram Treatment: A Randomized Controlled Trial. J Clin Psychiatry, Jul; 72(7): 914-928. Epub Dec. 28, 2010, July, 2011. PMID: 21208597
377. Kessler RC, Berglund PA, Coulouvrat C, Hajak G, Roth T, Shahly V, Shillington AC, Stephenson JJ, Walsh JK: Insomnia and the Performance of US Workers: Results from the America Insomnia Survey. Sleep, Vol. 34, No. 9, 1161-1171, 2011. PMID: 21886353

378. Surman CBH, Roth T: Impact of Stimulant Pharmacotherapy on Sleep Quality: Post Hoc Analyses of 2 Large, Double-Blind, Randomized, Placebo-Controlled Trials. J Clin Psychiatry, 72:7, 903-908, July, 2011. PMID: 21824454
379. Budhiraja R, Roth T, Hudgele DW, Budhiraja P, Drake, CL: Prevalence and Polysomnographic Correlates of Insomnia Comorbid with Medical Disorders. Sleep, Jul 1; Vol. 34, No. 7, 859-867, 2011. PMID: 21731135
380. Drake CL, Friedman NP, Wright Jr KP, Roth T: Sleep Reactivity and Insomnia: Genetic and Environmental Influences. Sleep, Sep 1; Vol. 34, No. 9, 1179-1188, 2011. PMID: 21886355
381. Walsh JK, Coulouvrat C, Hajak G, Lakoma MD, Petukhova M, Roth T, Sampson NA, Shahly V, Shillington A, Stephenson JJ, Kessler RC: Nighttime Insomnia Symptoms and Perceived Health in the America Insomnia Survey (AIS). Sleep, Aug 1; Vol. 34, No. 8, 997-1011, 2011. PMID: 21804662
382. Krystal AD, Lankford A, Durrence HH, Ludington E, Jochelson P, Rogowski R, Roth T: Efficacy and Safety of Doxepin 3 and 6 mg in a 35-day Sleep Laboratory Trial in Adults with Chronic Primary Insomnia. Sleep, Vol. 34, No. 10, 1433-1442, 2011. PMID: 21966075
383. Wang-Weigand S, Watissee M, Roth T: Use of a Post-Sleep Questionnaire-Interactive Voice Response System (PSQ-IVRS) to Evaluate the Subjective Sleep Effects of Ramelteon in Adults with Chronic Insomnia. Sleep Medicine 12, 920-923, 2011. PMID: 21925941
384. Hajak G, Petukhova M, Lakoma MD, Coulouvrat C, Roth T, Sampson NA, Shahly V, Shillington AC, Stephenson JJ, Walsh JK, Kessler RC: Days-Out-of-Role Associated with Insomnia and Comorbid Conditions in the America Insomnia Survey. Biological Psychiatry 70 (11), 1063-1073, 2011. PMID: 21962491
385. Roehrs TA, Randall S, Harris E, Maan R, Roth T: MSLT in Primary Insomnia: Stability and Relation to Nocturnal Sleep. Sleep, Dec 1; Vol. 34, No. 12, 1647-1652, 2011. PMID: 22131601
386. Gumenyuk V, Roth T, Korzyukov O, Jefferson C, Bowyer S, Drake CL: Habitual Short Sleep Impacts Frontal Switch Mechanism in Attention to Novelty. Sleep, Vol. 34, No. 12, 1659-1670, 2011.
387. Khalid I, Roehrs TA, Hudgele DW, Roth T: Continuous Positive Airway Pressure in Severe Obstructive Sleep Apnea Reduces Pain Sensitivity. Sleep, Vol. 34, No. 12, 1687-1691, 2011.
388. Verster JC, Spence DW, Shahid A, Pandi-Perumal SR, Roth T: Zopiclone as Positive Control in Studies Examining the Residual Effects of Hypnotic Drugs on Driving Ability. Current Drug Safety, Vol. 6, No. 4, 209-218, 2011.
389. Kollins SH, Lopez FA, Vince BD, Turnbow JM, Farrand K, Lyne A, Wigal SB, Roth T: Psychomotor Functioning and Alertness with Guanfacine Extended Release in Subjects with Attention-Deficit/Hyperactivity Disorder. Journal of Child and Adolescent Psychopharmacology, Volume 21, Number 2, 111-120. DOI: 10.1089/cap.2010.0064, 2011. PMID: 21476931
390. Verster JC, Roth T: Thirty Years of Dutch Drugs and Driving Research: Strengths and Limitations of the On-The-Road Highway Driving Test and Future Challenges. Current Psychopharmacology, Vol. 1, No. 1, 97-102, 2012.
391. Verster JC, Roth T: Drivers Can Poorly Predict Their Own Driving Impairment: A Comparison Between Measurements of Subjective and Objective Driving Quality. Psychopharmacology, 219 (3), 775-781, 2012. PMID: 21750898

392. Verster JC, Roth T: The Prevalence and Nature of Stopped On-The-Road Driving Tests and the Relationship with Objective Performance Impairment. Accident Analysis & Prevention, 45: 498-506, 2012. PMID: 22269535
393. Verster JC, Roth T: Predicting Psychopharmacological Drug Effects on Actual Driving Performance (SDLP) from Psychometric Tests Measuring Driving-Related Skills. Psychopharmacology, Volume 220, Number 2, 293-301, 2012. PMID: 21922169
394. Lankford A, Rogowski R, Essink B, Ludington E, Durrence HH, Roth T: Efficacy and Safety of Doxepin 6mg in a Four-Week Outpatient Trial of Elderly Adults with Chronic Primary Insomnia. Sleep Medicine, Volume 13, Issue 2, 133-138, 2012. PMID: 22197474
395. Roth T, Lankford DA, Bhadra P, Whalen E, Resnick EM: Effect of Pregabalin on Sleep in Patients With Fibromyalgia and Sleep Maintenance Disturbance: A Randomized, Placebo-Controlled, 2-Way Crossover Polysomnography Study. Arthritis Care & Research, Vol. 64, No. 4, pp 597-606, April 2012. PMID: 22232085
396. Roth T: Appropriate Therapeutic Selection for Patients with Shift Work Disorder. Sleep Medicine, Volume 13, Issue 4, April, 335-341, 2012. PMID: 22353444
397. Verster JC, Roth T: Gender Differences in Highway Driving Performance After Administration of Sleep Medication: A Review of the Literature. Traffic Injury Prevention, 13(3), 286-292, May, 2012. PMID: 22607251
398. Kessler RC, Berglund PA, Coulouvrat C, Fitzgerald T, Hajak G, Roth T, Shahly V, Shillington AC, Stephenson JJ, Walsh JK: Insomnia, Comorbidity, and Risk of Injury Among Insured Americans: Results from the America Insomnia Survey. Sleep, Jun; (1), Vol. 35, No. 6, 825-834, 2012. PMID: 22654202
399. Roehrs TA, Randall S, Harris E, Maan R, Roth T: Twelve Months of Nightly Zolpidem Does Not Lead to Rebound Insomnia or Withdrawal Symptoms: A Prospective Placebo-Controlled Study. Journal of Psychopharmacology, 26(8), 1088-1095, 2012. PMID: 22004689
400. Gumenyuk V, Roth T, Drake CL: Circadian Phase, Sleepiness, and Light Exposure Assessment in Night Workers With and Without Shift Work Disorder. Chronobiology International, 29 (7), 928-936, 2012. PMID: 22823876
401. Greenblatt D, Roth T: Zolpidem for Insomnia. Expert Opinon on Pharmacotherapy, 13(6), 879-893, 2012. PMID: 22424586
402. Steinmiller CL, Diederichs C, Roehrs TA, Hyde-Nolan M, Roth T, Greenwald MK: Postsurgical Patient-Controlled Opioid Self-Administration is Greater in Hospitalized Abstinent Smokers than Nonsmokers. Journal of Opioid Management 8:4, July/August, 227-235, 2012. PMID: 22941850
403. Babajani-Feremi A, Gumenyuk V, Roth T, Drake CL, Soltanian-Zadeh H: Connectivity Analysis of Novelty Process in Habitual Short Sleepers. NeuroImage 63, 1001-1010, 2012. PMID: 22906789
404. Roehrs T, Roth T: Insomnia Pharmacotherapy. Neurotherapeutics, The Journal of the American Society for Experimental NeuroTherapeutics ISSN 1933-7233, Volume 9, Number 4, 728-738, 2012. PMID: 22976558
405. Randall S, Roehrs TA, Roth T: Efficacy of Eight Months of Nightly Zolpidem: A Prospective Placebo-Controlled Study. Sleep, Vol. 35, No. 11, 1551-1557, 2012. PMID: 23115404

406. Shahly V, Berglund PA, Coulouvrat C, Fitzgerald T, Hajak G, Roth T, Shillington AC, Stephenson JJ, Walsh JK, Kessler RC: The Associations of Insomnia with Costly Workplace Accidents and Errors: Results from the America Insomnia Survey. Arch Gen Psychiatry, Vol 69 (No. 10), 1054-1063, Oct 2012. PMID: 23026955
407. Roehrs TA, Harris E, Randall S, Roth T: Pain Sensitivity and Recovery from Mild Chronic Sleep Loss. Sleep, Vol. 35, No. 12, 1667-1672. PMID: 23204609
408. Herring WJ, Snyder E, Budd K, Hutzelmann J, Snavely D, Liu K, Lines C, Roth T, Michelson D: Orexin Receptor Antagonism for Treatment of Insomnia: A Randomized Clinical Trial of Suvorexant. Neurology, 2012. PMID: 23197752
409. Palesh OG, Mustian KM, Peppone LJ, Janelsins M, Sprod LK, Kesler S, Innominato PF, Roth T, Manber R, Heckler C, Fiscella K, Morrow GR: Impact of Paroxetine on Sleep Problems in 426 Cancer Patients Receiving Chemotherapy: A trial from the University of Rochester Cancer Center Community Clinical Oncology Program. Sleep Medicine, Oct;13 (9), 1184-1190, 2012. PMID: 22858235
410. Roehrs T, Diederichs C, Gillis M, Burger AJ, Stout RA, Lumley MA, Roth T: Nocturnal Sleep, Daytime Sleepiness and Fatigue in Fibromyalgia Patients Compared to Rheumatoid Arthritis Patients and Healthy Controls: A Preliminary Study. Sleep Medicine, Jan;14(1), 109-115, 2013. PMID: 23149217
411. Kleinman L, Buysse DJ, Harding G, Lichstein K, Kalsekar A, Roth T: Patient-Reported Outcomes in Insomnia: Development of a Conceptual Framework and Endpoint Model. Behavioral Sleep Medicine, Jan;11(1): 23-36, 2013. PMID: 23347114
412. Roth T, Krystal A, Steinberg FJ, Singh NN, Moline M: Novel Sublingual Low-Dose Zolpidem Tablet Reduces Latency to Sleep Onset Following Spontaneous Middle-of-the-Night Awakening in Insomnia in a Randomized, Double-Blind, Placebo-Controlled, Outpatient Study. Sleep, Vol. 36, No. 2: 189-196, 2013. PMID: 23372266
413. Verster JC, Roth T: Blood Drug Concentrations of Benzodiazepines Correlate Poorly with Actual Driving Impairment. Sleep Medicine Reviews: 17: 153-159, 2013. PMID: 22884949
414. Gumenyuk V, Korzyukov O, Roth T, Bowyer SM, Drake CL: Sleep Extension Normalizes ERP of Waking Auditory Sensory Gating in Healthy Habitually Short Sleeping Individuals. PLoS One, 8(3), e59007. 2013. PMID: 23520548
415. Jobert M, Wilson FJ, Roth T, Ruigt GeSF, Anderer P, Drinkenburg WHIM, The IPEG Pharmacology-EEG Guidelines Committee: Guidelines for the Recording and Evaluation of Pharmacology-Sleep Studies in Man: The International Pharmacology-EEG Society (IPEG). Neuropsychobiology; 67: 127-167, 2013. PMID: 23548759
416. Greenblatt DJ, Harmatz JS, Roth T, Singh NN, Moline ML, Harris SC, Kapil RP: Comparison of Pharmacokinetic Profiles of Zolpidem Buffered Sublingual Tablet and Zolpidem Oral Immediate-Release Tablet: Results from a Single-Center, Single-Dose, Randomized, Open-Label Crossover Study in Healthy Adults. Clinical Therapeutics. 35(5), 604-611, 2013. PMID: 23541711
417. Krystal AD, Richelson E, Roth T: Review of the histamine system and the clinical efforts of H1 antagonists: Basis for a new model for understanding the effects of insomnia medications. Sleep Medicine Reviews. 17, 263-272, 2013. PMID: 23357028

418. Roth T, Berglund P, Shahly Vi, Shillington AC, Stephenson JJ, Kessler RC: Middle-of-the-night use in a large national health plan. *Journal of Clinical Sleep Medicine*. 9(7), 661-668, 2013. PMID: 23853559
419. Andlauer O, Moore H, Jouhier L, Drake C, Peppard PE, Fang H, Hong SC, Poli F, Plazzi G, O'Hara R, Haffen E, Roth T, Young T, Mignot E. Nocturnal rapid eye movement sleep latency for identifying patients with narcolepsy/hypocretin deficiency. *JAMA Neurol*. 70(7): 891-902, 2013. PMID: 23649748
420. Verster JC, Roth T. Vigilance decrement during the on-the-road driving tests: the importance of time-on-task in psychopharmacological research. *Accident Analysis and Prevention* 58: 244-248, 2013. PMID: 23176755
421. Roth T, Dauvilliers Y, Mignot E, Montplaisir J, Paul J, Swick T, Zee P. Disrupted Nighttime Sleep in Narcolepsy. *Journal of Clinical Sleep Medicine* 9(9): 955-965, 2013. PMID: 23997709
422. Herring WJ, Liu K, Hutzelmann J, Snavely D, Snyder E, Ceesay P, Lines C, Michelson D, Roth T. Alertness and psychomotor performance effects of the histamine-3 inverse agonist MK-0249 in obstructive sleep apnea patients on continuous positive airway pressure therapy with excessive daytime sleepiness: a randomized adaptive crossover study. *Sleep Medicine* 14(10): 955-963, 2013. PMID: 23920422
423. Drake C, Roehrs T, Shambroom J, Roth T. Caffeine Effects on Sleep Taken 0, 3, or 6 hours before going to bed. *Journal of Clinical Sleep Medicine* 9(11): 1195-1200, 2013. PMID: 24235903
424. Greenblatt DJ, Harmatz JS, Singh NN, Roth T, Harris SC, Kapil RP. Influence of food on pharmacokinetics of zolpidem from fast dissolving sublingual zolpidem tartrate tablets. *The Journal of Clinical Pharmacology* 53(11): 1194-1198, 2013. PMID: 23939537.
425. Verster JC, Bervoets AC, de Klerk S. Lapses of attention as outcome measure of the on-the-road driving test. *Psychopharmacology* 231: 283-292, 2014. PMID: 23975036.
426. Nakajima S, Okajima I, Sasai T, Kobayashi M, Furudate N, Drake C, Roth T, Inoue Y. Validation of the Japanese version of the Ford Insomnia Response to Street Test and the association of sleep reactivity with trait anxiety and insomnia. *Sleep Medicine* 15: 196-202, 2014. PMID: 24380783.
427. Verster JC, Roth T. Effects of central nervous system drugs on driving: speed variability versus standard deviation of lateral position as outcome measure of the on-the-road driving test. *Human Psychopharmacology* 29: 19-24, 2014. PMID: 24375715.
428. Roth T, Steinberg F, Singh NN, Moline M. Gender influences on efficacy and safety of sublingual zolpidem tartrate for middle-of-the-night awakening in insomnia. *Human Psychopharmacology* 29: 25-30: 545-556, 2014. PMID: 24424704
429. Gumenyuk V, Howard R, Roth T, Korzyukov O, Drake C. Sleep loss, circadian mismatch, and abnormalities in reorienting of attention in night workers with shift work disorders. *Sleep* 37(3):489-496, 2014. PMID:
430. Vermeeren A, Vuurman E, Leufkens TRM, Van Leeuwen CJ, Van Oers ACM, Laska E, Rico S, Steinberg F, Roth T. Residual effects of low-dose sublingual zolpidem on highway driving performance the morning after middle-of-the-night use. *Sleep* 37(3), 2014.
431. Roth T, Arnold LM, Garcia-Borreguero D, Resnick M, Clair AG. A review of the effects of pregabalin on sleep disturbance across multiple clinical conditions. *Sleep Medicine Reviews* 18:241-251, 2014.

432. Roth T, Eklov SD, Drake CL, Verster JC. Meta-analysis of on-the-road experimental studies of hypnotics: effects of time after intake, dose and half-life. *Traffic Injury Prevention* 15:5, 439-445, 2014.
433. Miguel GS, Yaremchuck K, Roth T, Peterson E. The effect of insomnia on Tinnitus. *Annals of Otolaryngology, Rhinology & Laryngology*. May 9, 2014.
<http://aor.sagepub.com/content/early/2014/05/09/0003489414532779>: PMID: 24816421
434. Roth T, Steinberg F, Singh NN, Moline M. Gender influences on efficacy and safety of sublingual zolpidem tartrate for middle-of-the-night awakening in insomnia. *Human Psychopharmacology* 29(1):25-30, 2-14, 2014. PMID: 24424704
435. Howard R, Roth T, Drake CL. The effects of armodafinil on objective sleepiness and performance in a shift work disorder sample unselected for objective sleepiness. *Journal of Clinical Psychopharmacology* 34(3): 369-373, 2014. PMID: 24717254
436. Pillai V, Steenburg LA, Ciesla JA, Roth T, Drake CL. A seven day actigraphy-based study of rumination and sleep disturbance among young adults with depressive symptoms. *Journal of Psychosomatic Research* 77:70-75, 2014. PMID: 24913345
437. Michelson D, Paradis E, Chengan-Liu M, Snavely DB, Hutzelmann J, Walsh JK, Krystal AD, Benca RM, Cohn M, Lines C, Roth T, Herring WJ. Safety and efficacy of suvorexant during 1-year treatment of insomnia with subsequent abrupt treatment discontinuation: a phase 3 randomised, double-blind, placebo-controlled trial. *Lancet Neurol* 13:461-71. 2014. PMID: 24680372
438. Horoszok L, Baleeiro T, Aniello F, Gropper S, Santos B, Guglietta A, Roth T. A single-dose, randomized, double-blind, double dummy, placebo and positive-controlled, five-way cross-over study to assess the pharmacodynamics effects of lorediplon in a phase advance model of insomnia in healthy Cuacasian adult male subjects. *Human Psychopharmacology* 29: 266-273, 2014. PMID: 24911577
439. Pillai V, Roth T, Mullins H, Drake C. Moderators and mediators of the relationship between stress and insomnia: stressor chronicity, cognitive intrusion and coping. *Sleep* 37(7), 2014. PMID:
440. Verster JC, Roth T. Methylphenidate significantly reduces lapses of attention during on-road highway driving in patients with ADHD. *Journal of Clinical Psychopharmacology* 34(5), 2014, PMID: 24978156
441. Drake CL, Hays RD, Morlock R, Wang F, Shikiar R, Frank L, Downey R, Roth T. Development and evaluation of a measure to assess restorative sleep. *Journal of Clinical Sleep Medicine* 10(7), 2014. PMID: 25024650
442. Greenblatt DJ, Harmatz JS, Singh NN, Steinberg F, **Roth T**, Moline ML, Harris SC, and Kapil RP. Gender differences in pharmacokinetics and pharmacodynamics of zolpidem following sublingual administration. *J Clin Pharmacol* 54(3):282-290, 2014. PMID: 24203450
443. Drake CL, Pillai V, Roth T. Stress and sleep reactivity: a prospective investigation of the stress-diathesis model of insomnia. *Sleep* 37(8): 1295-1304, 2014. PMID: 25083009
444. Kalmbach D, Pillai V, Roth T, Drake C. The interplay between daily affect and sleep: a 2-week study of young women. *J Sleep Res*, 2014.
445. Verster JC, Bervoets AC, de Klerk S, Vreman RA, Olivier B, Roth T, Brookhuis KA. Effects of alcohol hangover on simulated highway driving performance. *Psychopharmacology* 231:2999-3008, 2014. PMID: 24563184

446. Verster JC, Roth T. Excursions out-of-lane versus standard deviation of lateral position as outcome measure of the on-the-road driving test. *Human Psychopharmacology* 29: 322-329, 2014. PMID: 24753058
447. Roth T, Freeman J, Zammit G, Donnelly P, Gao J, Ferreira-Cornwell C, Gasior M. A generalized estimating equation approach to analysis of maintenance of wakefulness testing in a study of Lisdexamfetamine dimesylate, armodafinil, and placebo in sleep-deprived adults. *Journal of Clinical Psychopharmacology* 34(5), 2014. PMID: 25180798
448. Greenblatt DJ, Harmatz JS, Singh NN, Steinberg F, Roth T, Harris SC, Kapil RP. Pharmacokinetics of zolpidem from sublingual zolpidem tartrate tablets in health elderly versus non-elderly subjects. *Drugs Aging* 31: 731-736, 2014. PMID: 25246162
449. Ma J, Svetnik V, Snyder E, Lines C, Roth T, Herring, J. Electroencephalographic power spectral density profile of the orexin receptor antagonist suvorexant in patients with primary insomnia and healthy subjects. *Sleep* 37(10): 1609-xxx, 2014. PMID: 25197807
450. Kleinman L, Mannix S, Arnold LM, Burbridge C, Howard K, McQuarrie K, Pitman V, Resnick M, Roth T, Symonds T. Assessment of sleep in patients with fibromyalgia: qualitative development of the fibromyalgia sleep diary. *Health and Quality of Life Outcomes* 12:1-11, 2014. PMID: 25017458
451. Drake CL, Vargas I, Roth T, Friedman NP. Quantitative measures of nocturnal insomnia symptoms predict greater deficits across multiple daytime impairment domains. *Behavioral Sleep Medicine* 12:1-15, 2014. PMID: 24617964
452. Furey SA, Hull SG, Leibowitz MT, Jayawardena S, Roth T. A randomized, double-blind, placebo-controlled, multicenter, 28-day, polysomnographic study of Gabapentin in transient insomnia induced by sleep phase advance. *Journal of Clinical Sleep Medicine* 10(10):1101-1100. PMID: 25317091
453. Rosenberg RP, Hull SG, Lankford DA, Mayleben DW, Seiden DJ, Furey SA, Jayawardena S, Roth T. A randomized, double-blind, single-dose, placebo-controlled, multicenter, polysomnographic study of Gabapentin in transient insomnia induced by sleep phase advance. *Journal of Clinical Sleep Medicine* 10(10):1093-1100, 2014. PMID: 25317090
454. Verster JC, van de Loo AJ, Moline ML, Roth T. Middle-of-the-night administration of sleep medication: a critical review of the effects of next morning ability. *Current Drug Safety* 9: 205-211, 2014. PMID: 24909576
455. Drake C, Gumenyuk V, Roth T, Howard R. Effects of Armodafinil on simulated driving and alertness in shift work disorder. *Sleep* 37(12):1987-1994, 2014. PMID: 25325498
456. Gumenyuk V, Belcher R, Drake CL, Roth T. Differential sleep, sleepiness, and neurophysiology in the insomnia phenotypes of shift work disorder. *Sleep* 38(1): 119-126, 2015, PMID: 25325466
457. Pillai V, Roth T, Drake CL. The nature of stable insomnia phenotypes. *Sleep* 38(1): 127-138, 2015. PMID: 25325468
458. Roth T, Nir T, Zisapel N. Prolonged release melatonin for improving sleep in totally blind subjects: a pilot placebo-controlled multicenter trial. *Nature and Science of Sleep* 7: 13-23, 2015. PMID: 25678831

459. Pillai V, Anderson JR, Cheng P, Bazan L, Bostock S, Espie CA, Roth T, Drake CL. The Anxiolytic Effects of Cognitive Behavior Therapy for Insomnia: Preliminary Results from a Web-delivered Protocol. *J Sleep Med Disord* 2(2): 1017.2015 PMID
460. Cheng P, Pillai V, Mengel H, Roth T, Drake CL. Sleep Maintenance Difficulties in Insomnia are Associated with Increased Incidence of Hypertension. *Sleep Health* 1:1 50-54, 2015. PMID:
461. Verster JC, Aurora JAE, van de Loo AJ, Roth T. Mirtazepine as a Positive Control Drug in Studies Examining the Effects of Antidepressants on Driving Ability. *European Journal of Pharmacology* 753, 252-256, 2015. PMID:
462. Belcher, R, Gumenyuk, V, Roth, T. Insomnia in Shift Work Disorder Relates to Occupational and Neurophysiological Impairment. *J ClinSleep Med* 11(4):457-465, 2015.
463. Bogan, R, Roth, T, Schwartz, J, Miloslavsky M. Time to Response with Sodium Oxybate for the Treatment of Excessive Daytime Sleepiness and Cataplexy in Patients with Narcolepsy. *J Clin Sleep Med* 2015; 11(4):427-432.
464. Drake, CL, Vargas, I, Roth, T, Friedman, NP. Quantitative Measures of Nocturnal Insomnia Symptoms Predict Greater Deficits Across Multiple Daytime Impairment Domains. *Behavioral Sleep Medicine*; 73-87, 2015.
465. Miller, Y, Roth, T, Roehrs, T, Yaremchuk, K. Correlation between Sleep Disruption on Postoperative Pain. *Otolaryngology-Head and Neck Surgery*; 152(5) 964-968, 2015.
466. Drake, CL Belcher, R. Howard, R Toth, T Levin, AM Gumenyuk, V. Length of Polymorphism in the Period 3 Gene is Associated with Sleepiness and Maladaptive Circadian Phase in Night-Shift Workers. *J.Sleep Res.* 24, 254-261 2015.
467. Roehrs T, Diederichs C, Gillis M, Burger AJ, Stout RA, Lumley MA, Roth T. Effects of Reduced Time in Bed on Daytime Sleepiness and Recovery Sleep in Fibromyalgia and Rheumatoid Arthritis. *J. of Psychosomatic Research.* 2015.
468. Cooper S, Laurora I, Wang Y, Venkartaraman An R, Roth T. Efficacy and Tolerability Studies Evaluating a Sleep Aid and Analgesic Combination of Naproxen Sodium, and Diphenhydramine in Dental Impaction Pain Model in Subjects with Induced Transient Insomnia. *Int. J Clin Pract.* 2015.
469. Ivgy-May N, Roth T, Ruwe F, Walsh F. Esmirtazepine in Non-Elderly Adult Patients with Primary Insomnia: Efficacy and Safety from a 2-Week Randomized Outpatient Trial. *Sleep Medicine* 16, 831-837, 2015.
470. Albert, S. M., Roth, T., Toscani, M., Vitiello, M. V., & Zee, P. Sleep Health and Appropriate Use of OTC Sleep Aids in Older Adults—Recommendations of a Gerontological Society of America Workgroup. *The Gerontologist*, Vol. 00, No. 00, 1-9, 2015.
471. Verster JC, Van DeLoo AJAE, Roth T. Mirtazepine as Positive Control Drug in Studies examining the Effects of Antidepressants on Driving Ability. *European Journal of Pharmacology* 753, 252-256 2015.
472. Ivgy-May N, Ruwe F, Krystal A, Roth T. Esmirtazepine in Non-Elderly Adult Patients with Primary Insomnia: Efficacy and Safety from a Randomized, 6-Week Sleep Laboratory Trial. *Sleep Medicine* 16, 838-844, 2015.

473. Donners, A M T D, Tromp M D P, Garssen J, Roth T, Verster JC. Perceived Immune Status and Sleep: A Survey among Dutch Students. *Sleep Disorders*, Vol 2015 Article ID 721607 5 pages. 2015.
474. Ondo W, Grieger F, Stat D, Moran K, Kohnen R, Roth T. Post Hoc Analysis of Data from Two Clinical Trials Evaluating the Minimal Clinically Important Change in International Restless Legs Syndrome Sum Score in Patients with Restless Legs Syndrome (Willis-Ekbom Disease). *Journal of Clinical Sleep Medicine*, 12 (1):63-70. 2016.
475. Herring, W. J., Connor, K. M., Ivgy-May, N., Snyder, E., Liu, K., Snavely, D. B.,.... & Roth, T. Suvorexant in patients with insomnia: results from two 3-month randomized controlled clinical trials. *Biological Psychiatry*, 79: 136-148. 2016.
476. Roth T, Rhadra-Brown P, Pitman VW, Roehrs TA, Resnick EM. Characteristics of Disturbed Sleep In Patients With Fibromyalgia Compared With Insomnia or With Healthy Volunteers. *Clinical Journal of Pain*, 32:302-307. 2016.
477. Roth T, Rhadra-Brown P, Pitman VW, Resnick EM. Pregabalin Improves Fibromyalgia-Related Sleep Disturbance. *Clinical Journal of Pain*, 32:308-312. 2016.
478. Roehrs T, Roth T. Gender Differences in the Efficacy and Safety of Chronic Nightly Zolpidem. *Journal of Clinical Sleep Medicine*, 12 (3):319-325. 2016.
479. Wickwire, E. M., Williams, S. G., Roth, T., Capaldi, V. F., Jaffe, M., Moline, M.,... Lettieri, C. J. Sleep, Sleep Disorders and Mild Traumatic Brain Injury. What We Know and What We Need to Know: Findings from a National Working Group. *Neurotherapeutics, The Journal of the American Society for Experimental NeuroTherapeutics*, 1-15. 2016.
480. Albert, S.M., Roth, T., Toscani, M., Vittielo, M., Zee, P. Need for Care in Use of Over-the-Counter Sleep Aids in Older Adults. *Today's Geriatric Medicine*, 9(2): 20-23. 2016.
481. Pillai, V., Cheng, P., Kalmbach, D.A., Roehrs, T., Roth, T., Drake, C.L. Prevalence and Predictors of Prescription Sleep Aid Use Among Individuals with DSM-5 Insomnia: The Role of Hyperarousal. *SLEEP*, 39(4):825–832. 2016.
482. Muzet, A., Werner, S., Fuchs, G., Roth, T., Saoud, J.B., Viola, A.U., .. Luthringer R. Assessing Sleep Architecture and Continuity Measures through the Analysis of Heart Rate and Wrist Movement Recordings in Healthy Subjects: Comparison with Results Based on Polysomnography. *Sleep Medicine*, 21: 47-56. 2016.
483. Herring, W. J., Connor, K. M., Snyder, E., Snavely, D. B., Zhang, Y., Hutzelmann, J., ... & Michelson, D. Suvorexant in Patients with Insomnia: Pooled Analyses of Three-Month Data from Phase-3 Randomized Controlled Clinical Trials. *Journal of Clinical Sleep Medicine*, 12(9): 1215-1225. 2016.
484. Roehrs, T. A., & Roth, T. Hyperarousal in insomnia and hypnotic dose escalation. *Sleep Medicine*, 23, 16-20. 2016.
485. Ruwe, F., IJzerman-Boon, P., Roth, T., Zammit, G., & Ivgy-May, N. (2016). A Phase 2 Randomized Dose-Finding Study With Esmirtzapine in Patients With Primary Insomnia. *Journal of Clinical Psychopharmacology*, 36(5), 457-464.

486. Connor, K. M., Mahoney, E., Jackson, S., Hutzelmann, J., Zhao, X., Jia, N., ... & Herring, W. J. A Phase II Dose-Ranging Study Evaluating the Efficacy and Safety of the Orexin Receptor Antagonist Filorexant (MK-6096) in Patients with Primary Insomnia. *International Journal of Neuropsychopharmacology*, 19(8). 2016.
487. Pillai, V., Roth, T., Roehrs, T., Moss, K., Peterson, E., Drake, C.L. Effectiveness of Benzodiazepine Receptor Agonists in the Treatment of Insomnia: An Examination of Response and Remission Rates. *Sleep*, 40 (2). 2017.
488. Roth, T., Black, J., Cluydts, R., Charef, P., Cavallaro, M., Kramer, F.... & Walsh, J. Dual Orexin Receptor Antagonist, Almorexant, in Elderly Patients with Primary Insomnia: A Randomized, Controlled Study. *Sleep*, 40 (2). 2017.
489. Roehrs, T A. & Roth, T. Increasing Presurgery Sleep Reduces Postsurgery Pain and Analgesic Use Following Joint Replacement: A Feasibility Study. *Sleep Medicine*, 33, 109-113. 2017.
490. Pillai, V., Roth, T., Drake, C.L. Towards Quantitative Cutoffs for Insomnia: How Current Diagnostic Criteria Mischaracterize Remission. *Sleep Medicine*. (In press).
491. Marques, D.R., Gomes, A.A., Drake, C.L., Roth, T., Pinto de Azevedo, M.L. Assessing Stress-Induced Sleep Reactivity in College Students: The European Portuguese Version of the Ford Insomnia Response to Stress Test (FIRST). *Behavioral Sleep Medicine*. (In press).
492. Roth, T., Dauvilliers, Y., Guinta, D., Alvarex-Horine, S., Dynin, E., Black, J. Effect of Sodium Oxybate on Disrupted Sleep in Patients with Narcolepsy. *Journal of Sleep Research*, 26, 407–414. 2017. doi: 10.1111/jsr.12468
493. van Schrojenstein Lantman, M., Roth, T., Roehrs, T., Verster, J. Alcohol Hangover, Sleep Quality, and Daytime Sleepiness. *Sleep Vigilance*. 2017. doi:10.1007/s41782-017-0008-7
494. Herring, W. J., Connor, K. M., Snyder, E., Snavely, D. B., Zhang, Y., Hutzelmann, J., ... & Lines, C. Suvorexant in Elderly Patients with Insomnia: Pooled Analyses of Data from Phase III Randomized Controlled Clinical Trials. *The American Journal of Geriatric Psychiatry*, 25(7), 791-802. 2017.
495. Herring, W. J., Connor, K. M., Snyder, E., Snavely, D. B., Zhang, Y., Hutzelmann, J., ... & Lines, C. Clinical profile of suvorexant for the treatment of insomnia over 3 months in women and men: subgroup analysis of pooled phase-3 data. *Psychopharmacology*, 234(11), 1703-1711. 2017.
496. van Schrojenstein Lantman, M., Mackus, M., Roth, T., Verster, J. Total sleep time, alcohol consumption, and the duration and severity of alcohol hangover. *Nature and Science of Sleep*, 9, 181-186. 2017.
497. Drake, C. L., Durrence, H., Cheng, P., Roth, T., Pillai, V., Peterson, E. L., ... & Tran, K. M. Arousability and fall risk during forced awakenings from nocturnal sleep among healthy males following administration of zolpidem 10 mg and doxepin 6 mg: A randomized, placebo-controlled, four-way crossover trial. *Sleep*, 40 (7). 2017.

EDITED VOLUMES

1. Hindmarch I, Ott H, Roth T (Eds). Sleep Benzodiazepines and Performance. Springer-Verlag, Heidelberg, 1984.
2. Kryger MH, Roth T, Dement WC (Eds). Principles and Practice of Sleep Medicine. W.B. Saunders Company, Philadelphia, PA, 1989.
3. Roth T, Roehrs T (Eds). Clinics in Geriatric Medicine Vol 5, No 2. W.B. Saunders Company, Philadelphia, PA, 1989.
4. Chase MH, Roth T (Eds). Slow Wave Sleep - Its Measurement and Functional Significance. Brain Information Service/Brain Research Institute, UCLA, Los Angeles, 1990.
5. Carskadon MA, Rechtschaffen A, Richardson G, Roth T, Siegel JM (Eds). Encyclopedia of Sleep and Dreaming. MacMillan, New York, 1993.
6. Morley JE, Roth T (Eds). Sleep Disorders and Insomnia in the Elderly. Facts and Research in Gerontology. Vol 7(S), Springer Publishing, New York, 1993.
7. Kryger MH, Roth T, Dement WC (Eds). Principles and Practice of Sleep Medicine, 2nd Edition. W.B. Saunders Company, Philadelphia, PA, 1994.
8. Chase MH, Roth T, O'Connor C (Eds). Sleep Research. Vol 24(A), Brain Information Service/Brain Research Institute, UCLA, Los Angeles, 1995.
9. Freeman H, Puech AJ, Roth T (Eds). Zolpidem: An Update of its Pharmacological Properties and Therapeutic Place in the Management of Insomnia. Elsevier, Paris, 1996.
10. Sonnenblick E, Lesch M, Roth T (Eds). Progress in Cardiovascular Diseases. W.B. Saunders Company, Philadelphia, PA, March/April 1999.
11. Roth T, Walsh J, Simon R, Zammit G. Family Practice Recertification. Dental Learning Systems Co., Jamesburg, NJ, September 1999.
12. Kryger MH, Roth T, Dement WC (Eds). Principles and Practice of Sleep Medicine, 3rd Edition. W.B. Saunders Company, Philadelphia, PA, 2000.
13. Kryger MH, Roth T, Dement WC (Eds). Principles and Practice of Sleep Medicine, 4th Edition. W.B. Saunders Company, Philadelphia, PA, 2005.
14. Roth T, Dijk DJ (Eds). Slow-wave Sleep: Beyond Insomnia. The Importance of Slow-Wave Sleep for your Patients. Wolters Kluwer Pharma Solutions, 250 Waterloo Road, London SE1 8RD, UK, 2010.
15. Kryger MH, Roth T, Dement WC (Eds). Principles and Practice of Sleep Medicine, 5th Edition. Elsevier Saunders, St. Louis, Missouri, 2011.
16. Kryger MH, Roth T, Dement WC (Eds). Principles and Practice of Sleep Medicine, 6th Edition. Elsevier Saunders, Philadelphia, PA, 2016.

CHAPTERS

1. Pradhan S, Beer B, Roth T: The Effects of Several Anti-Cholinergic Agents on a Multiple Schedule of Reinforcement in Rats. Proc 5th Intl Cong Neuropsychopharm, Exerpta Medica Foundation, 1967.
2. Kramer M, Roth T, Trinder J, Cohen A: Technical Report on Noise Disturbance and Sleep: The Relationship of Noise-Disturbed Sleep to Post-Sleep Behavior. Department of Transportation, Federal Aviation Administration, Office of Noise Abatement. Report No. FAA-No-70-16, January, 1971.
3. Kramer M, Roth T: The Mood-Regulating Function of Sleep. Proc 1st Europe Congr Sleep Res, Basel 1972, pp 563-571, (Karger, Basel 1973).
4. Kramer M, Winget C, Roth T: Problems in the Definition of the REM Dream. Proc 2nd Europe Congr Sleep Res. Rome 1974, pp 149-156, (Karger, Basel, 1975).
5. Kramer M, Roth T, Czaya J: Dream Development Within a REM Period. Proc 2nd Europe Congr Sleep Res. Rome 1974, pp 406-408, (Karger, Basel, 1975).
6. Roth T, Kramer M, Roehrs T: The Consistency of Sleep Measures. Proc 3rd Europe Congr Sleep Res. Montpellier, 1976, pp 286-288, (Karger, Basel, 1977).
7. Kramer M, Roth T, Cisco J: The Meaningfulness of Dreams. Proc 3rd Europe Congr Sleep Res. Montpellier, 1976, pp 314-316, (Karger, Basel, 1977).
8. Kramer M, Roth T: Responsibility and Accountability: A Look From Within. World J Psychosyn. 10(3): 29-34, 1978.
9. Kramer M, Roth T: Dreams in Psychopathologic Patient Groups: A Critical Review. In: Sleep Disorders: Diagnosis and Treatment. RL Williams and I Karacan (Eds), Wiley, New York, 323-349, 1978.
10. Kramer M, Roth T: Dreams in Psychopathology. In: Handbook of Dreams: Research, Theories and Applications. BB Wolman (Ed), Van Norstrand Reinhold Co, New York, 361-387, 1979.
11. Roth T, Kramer M, Salis PJ: Drugs, REM Sleep and Dreams. In: Handbook of Dreams: Research, Theories and Applications. BB Wolman (Ed), Van Norstrand Reinhold Co, New York, 203-225, 1979.
12. Kramer M, Roth T: The Relationship of Dream Content to Night-Morning Mood Change. Proc 4th Europe Congr Sleep Res. Tirgu-Mures, 1978, 621-624, (Karger, Basel, 1980).
13. Roth T: Fisiologia del sueno y tratamiento del insomnio. Revista Dpto Psiquiatria Facult Med Barna, 8(6): 513-516, 1981.
14. Roth T, Roehrs T, Zorick F, Stepanski E, Wittig R: Pharmacological and Clinical Considerations in Hypnotic Use. In: Benzodiazepine in der Behandlung von Schlafstorungen. H Hippus (Ed), Informed, Munich, 85-92, 1982.
15. Roth T, Zorick F, Kaffeman M, Stepanski E: Estudo Controlado, Duplo-Cego, do Estazolam No Tratamento de Insonia. A Folha Medica 85(2): 625-629, 1982.

16. Roth T, Zorick F: The Use of Hypnotics in Specific Disorders of Initiating and Maintaining Sleep (Insomnias). In: Sleep Disorders: Basic and Clinical Research. M Chase and E Weitzman (Eds), Spectrum Publications, New York, 255-264, 1983.
17. Breimer DD, Hyland M, Lader M, MacLeod N, Marks J, Nicholson AN, Oswald I, Roth T, Straw RN: Experience With Triazolobenzodiazepines as Hypnotics. Forum Series No 8, The Royal Society of Medicine, 1983.
18. Roth T: Hypnotic Use in Clinical Practice. In: Clinical Aspects of Sleep Disorders. (Eds) JK Walsh, AD Bertelson, and PK Schweitzer. Deaconess Hospital, St. Louis, Missouri, pp 51-71, 1983.
19. Zorick F, Kribbs N, Roehrs T, Roth T: Polysomnographic and MMPI Characteristics of Patients With Insomnia. In: Sleep Benzodiazepines and Performance. I Hindmarch, H Ott, and T Roth (Eds), Springer-Verlag, Berlin Heidelberg, pp 2-10, 1984.
20. Roehrs T, McLenaghan A, Koshorek G, Zorick F, Roth T: Amnesic Effects of Lormetazepam. In: Sleep Benzodiazepines and Performance. I Hindmarch, H Ott, and T Roth (Eds), Springer-Verlag, Berlin Heidelberg, pp 165-172, 1984.
21. Roth T, Roehrs T, Zorick F, Conway W: Pharmacological Effects of Sedative-Hypnotics, Narcotic Analgesics, and Alcohol During Sleep. *Med Clin North Amer* 69(6): 1281-1288, 1985.
22. Roth T, Roehrs T, Zorick F, Stepanski E, Wittig R: Pharmacological and Patient Considerations in Hypnotic Use. Presented at the World Psychiatric Association Symposium: Psychopathology Dreams and Sleeping. Helsinki, Finland. Psychiatria Fennica (Supplement): 222-230, 1985.
23. Roth T, Roehrs T, Zorick F: Determinants of Adverse Effects of Hypnotics. In: Proceedings of the 4th world Congress of Biological Psychiatry. C Shagass et al., (Ed), Philadelphia, PA, 1985.
24. Roth T, Roehrs T, Zorick F: Assessing Patient's Sleep-Wake Complaints. *Mental Health Adviser*, Vol. 1(1): 13-14, 1986.
25. Roth T, Roehrs T, Zorick F: Sleep Disorders. In: Encyclopedia of Neuroscience, Vol. II. G Adelman (Ed), Arcata Graphics/Halliday, West Hanover, MA, pp 1101-1103, 1987.
26. Roth T, Roehrs T, Rosenthal L, Zorick F: Sleep-Wake Function and Age. *Psychogeriatrics* 12: 1987.
27. Stepanski E, Koshorek G, Zorick F, Roehrs T, Roth T: Sleep and Personality Characteristics of Patients and Subjects With Chronic Complaints of Insomnia. In: Imidazopyridines in Sleep Disorders: A Novel Experimental and Therapeutic Approach. (Ed) JP Sauvanet et al, Raven Press, New York, NY: 211-217, 1988.
28. Roth T, Roehrs TA, Zorick FJ: Pharmacological Treatment of Sleep Disorders. In: Sleep Disorders: Diagnosis and Treatment, Second Edition. (Ed) RL Williams et al, John Wiley & Sons, NY, pp 373-395, 1988.
29. Roth T: Sleep Disorders Medicine (Editorial). *Henry Ford Hosp Med J* 36(1): 4, 1988.
30. Vogel GW, Roth T, Gillin JC, Mendelson WC, Buffenstein A: REM Sleep and Depression. In: Neurobiology of Sleep-Wakefulness Cycle. (Ed) T Oniani. Metsniereba, Tbilisi, USSR, pp 187-214, 1988.

31. Roehrs T, Zwyghuizen-Doorenbos A, Smith D, Zorick F, Roth T: Reversal by Caffeine of Triazolam-Induced Impairment of Waking Function. In: Benzodiazepine Receptor Ligands, Memory and Information Processing. (Eds) I Hindmarch and H Ott. Psychopharmacology Series, Vol 6: 194-202, Springer-Verlag, Berlin, Heidelberg, 1988. PMID: 3217412
32. Roth T, Roehrs T, Zwyghuizen-Doorenbos A, Stepanski E, Wittig R: Sleep and Memory. In: Benzodiazepine Receptor Ligands, Memory and Information Processing. (Eds) I Hindmarch and H Ott. Psychopharmacology Series, Vol 6: 140-145, Springer-Verlag, Berlin, Heidelberg, 1988.
33. Roth T, Roehrs TA, Carskadon MA, Dement WC: Daytime Sleepiness and Alertness. In: Principles and Practice of Sleep Medicine. (Eds) M Kryger, T Roth, and WC Dement. WB Saunders Co, Philadelphia, PA, pp 14-23, 1989.
34. Roehrs TA, Zorick F, Roth T: Transient Insomnias and Insomnias Associated with Circadian Rhythm Disorders: In: Principles and Practice of Sleep Medicine. (Eds) MH Kryger, T Roth, and WC Dement. WB Saunders Co, Philadelphia, PA, pp 433-441, 1989.
35. Dinner DS, Erman MK, Roth T: Help For Geriatric Sleep Problems. Patient Care (D Whieldon, ed) 23: 74-85, 1989.
36. Roehrs TA, Roth T: Drugs, Sleep Disorders, and Aging. In: Clinics in Geriatric Medicine, Vol 5, Number 2. (Eds) T Roth and T Roehrs. WB Saunders Company, Philadelphia, PA, pp 395-404, 1989.
37. Roth T, Roehrs TA: Sleep Disorders in the Elderly (Editorial). Clinics in Geriatric Medicine, Vol 5, Number 2. WB Saunders Company, Philadelphia, PA, 1989.
38. Kryger MH, He J, Roth T, Zorick F, Conway W: Mortality in Sleep Apnea. (Letter to the Editor). Chest 95(6): 1363, 1989.
39. Roth T, Merlotti L: Advances in the Diagnosis of Narcolepsy. (Eds) SA Burton, WC Dement, RK Ristanovic. In: Narcolepsy 3rd International Symposium: Selected Symposium Proceedings. Matrix Communications, Chicago IL: 3-6, 1989.
40. Roehrs T, Zwyghuizen-Doorenbos A, Roth T: Residual Sedating Effects of Ethanol. In: Alcohol, Drugs & Traffic Safety: Proceedings of the 11th International Conference on Alcohol, Drugs and Traffic Safety. Chicago, IL, October, 1989.
41. Roth T: Introduction: Critical Issues in the Management of Insomnia: Investigators Report on Estazolam. Proceedings of a Symposium held June 3, 1989, Dallas, TX. (Guest Editor). The American J of Medicine 88(3A): 3A-1S, 1990.
42. Roehrs T, Vogel G, Roth T: Rebound Insomnia: Its Determinants and Significance. In: Critical Issues in the Management of Insomnia: Investigators Report on Estazolam. The American J of Medicine 88(3A): 3A-39S—3A-42S, 1990.
43. Roth T, Roehrs TA, Stepanski EJ, Rosenthal LD: Hypnotics and Behavior. In: Critical Issues in the Management of Insomnia: Investigators Report on Estazolam. The American J of Medicine 88(3A): 3A-43S—3A-46S, 1990. PMID: 1968720
44. Roth T: Summary: Critical Issues in the Management of Insomnia: Investigators Report on Estazolam. Proceedings of a Symposium held June, 1989, Dallas, TX. (Guest Editor). The American J of Medicine 88(3A): 3A-47S—3A-48S, 1990.

45. Roth T, Roehrs T, Kryger M: Mortality in Obstructive Sleep Apnea. In: Sleep and Respiration: Proceedings of the First International Symposium on Sleep and Respiration. (Eds) FG Issa, PM Suratt, and JE Remmers. AJ Wiley & Sons, Inc, New York, NY, pp 347-352, 1990.
46. Stepanski EJ, Zorick F, Roth T: Insomnia: a 24-Hour Problem. Effects of Sleep Deprivation in Chronic Insomnia. In: Insomnie et Imidazopyridines. Symposium International, Paris, April 1989. (Ed) P Barthouil. Excerpta Medica, Amsterdam, pp 180-184, 1990.
47. Roehrs T, Roth T: Sedating Drugs and Breathing During Sleep. In: Sleep and Aging: Proceedings of the Second Milano International Symposium on Sleep. (Eds) S Smirne, M Franceschi, L Ferini-Strambi. Milano, pp 225-232, 1991.
48. Stepanski EJ, Zorick FJ, Roth T: Pharmacotherapy of Insomnia. In: Case Studies in Insomnia. (Ed) PJ Hauri. Plenum Publishing Corporation: 115-129, 1991.
49. Carskadon MA, Roth T: Sleep Restriction. In: Sleep, Sleepiness and Performance. (Ed) TH Monk. John Wiley & Sons, England, pp 155-168, 1991.
50. Mendelson WB, Roth T: New York Triplicate Prescription Program Misguided. (Editorial) In: The Psychiatric Times: Medicine & Behavior Vol. IX, No. 3, p16, March 1992.
51. Dinner DS, Erman MK, Roth T: Help For Geriatric Sleep Problems. Patient Care 26 (11): pp 166-189, 1992.
52. Roth T, Roehrs TA: Insomnia: Diagnostic Approaches. ASEAN J of Psychiatry 2(2): 22-27, 1992.
53. Roth T: Drugs for Medical Disorders. In: Carskadon MA, Rechtschaffen A, Richardson G, Roth T, Siegel JM (Eds). Encyclopedia of Sleep and Dreaming. MacMillan, New York, p 197, 1993.
54. Roth T: Early Morning Awakenings. In: Carskadon MA, Rechtschaffen A, Richardson G, Roth T, Siegel JM (Eds). Encyclopedia of Sleep and Dreaming. MacMillan, New York, pp 199-200, 1993.
55. Roth T: Hallucinations. In: Carskadon MA, Rechtschaffen A, Richardson G, Roth T, Siegel JM (Eds). Encyclopedia of Sleep and Dreaming. MacMillan, New York, p 268, 1993.
56. Roth T: Hypersomnia. In: Carskadon MA, Rechtschaffen A, Richardson G, Roth T, Siegel JM (Eds). Encyclopedia of Sleep and Dreaming. MacMillan, New York, pp 287-288, 1993.
57. Roth T: Sleep Extension. In: Carskadon MA, Rechtschaffen A, Richardson G, Roth T, Siegel JM (Eds). Encyclopedia of Sleep and Dreaming. MacMillan, New York, pp 549-550, 1993.
58. Roth T: Sleep in the Elderly. In: Morley JE, Roth T (Eds). Sleep Disorders and Insomnia in the Elderly. Facts and Research in Gerontology. Vol 7(S), p7-9, Springer Publishing, New York, 1993.
59. Roehrs T, Roth T: Polysomnographic Assessment of Hypnotic Efficacy in the Elderly. In: Morley JE, Roth T (Eds). Sleep Disorders and Insomnia in the Elderly. Facts and Research in Gerontology. Vol 7(S), pp 183-188, Springer Publishing, New York, 1993.
60. Mendelson WB, Roehrs TA, Roth T: Replacement of Benzodiazepines with "Old-Fashioned" Hypnotics: A Cause for Concern? (Guest Editorial) Drug Safety, Vol 9(3): pp 149-150, 1993.

61. Rosenthal L, Folkerts M, Roth T: Estudios Polisomnograficos En Pacientes Con Hipertiroidismo. In: Vigilia Sueño (Ed) E Estivill. Grinver, S.A., Barcelona, Spain, pp 8-10, 1993.
62. Roth T, Roehrs TA, Carskadon MA, Dement WC: Daytime Sleepiness and Alertness. In: Principles and Practice of Sleep Medicine, 2nd Edition. (Eds) MH Kryger, T Roth, and WC Dement. WB Saunders Co, Philadelphia, PA, pp 40-49, 1994.
63. Kryger MH, Roth T, Carskadon M: Circadian Rhythms in Humans: An Overview. In: Principles and Practice of Sleep Medicine, 2nd Edition. (Eds) MH Kryger, T Roth, and WC Dement. WB Saunders Co, Philadelphia, PA, pp 301-308, 1994.
64. Roehrs T, Roth T: Chronic Insomnias Associated with Circadian Rhythm Disorders. In: Principles and Practice of Sleep Medicine, 2nd Edition. (Eds) MH Kryger, T Roth, and WC Dement. WB Saunders Co, Philadelphia, PA, pp 477-481, 1994.
65. Roehrs T, Zorick F, Roth T: Transient and Short-Term Insomnia. In: Principles and Practice of Sleep Medicine, 2nd Edition. (Eds) MH Kryger, T Roth, and WC Dement. WB Saunders Co, Philadelphia, PA, pp 486-493, 1994.
66. Roth T, Roehrs T, Rosenthal L: Measurement of Sleepiness/Alertness: Multiple Sleep Latency Test. In: Sleep Disorders Medicine: Basic Science, Technical Considerations, and Clinical Aspects. (Ed) S Chokroverty. Butterworth-Heinemann, Stoneham, MA, pp 133-140, 1994.
67. Roth T, Roehrs TA, Rosenthal L: Normative and Pathological Aspects of Daytime Sleepiness. In: American Psychiatric Press Review of Psychiatry, Vol 13. (Eds) JM Oldham and MB Riba. American Psychiatric Press, Washington, DC, pp 707-728, 1994.
68. Strohl K, Roth T, Redline S: Cardiopulmonary and Neurological Consequences of Obstructive Sleep Apnea. In: Snoring and Obstructive Sleep Apnea. Second Edition, (Eds) D.N.F. Fairbanks, S Fujita. Raven Press, Ltd., New York, NY, pp 31-43, 1994.
69. Roth T, Shapiro C, Partinen M, Billiard M: Sleep and Psychiatric Disorders. In: Sleep Disorders in Anxiety and Depression, Vol 38. (Eds) R Mayou, C Shapiro. Elsevier Science Ltd, pp 1-3, 1994.
70. Roth T, Roehrs TA, Vogel GW, Dement WC: Evaluation of Hypnotic Medications. In: Clinical Evaluation of Psychotropic Drugs, Principles and Guidelines. (Eds) RF Prien, DS Robinson. Raven Press, New York, NY, pp 579-592, 1994.
71. Roth T: Panel 2 - Narcolepsy and Other Sleep Disturbances, Diagnosis and Treatment, Strategy and Treatment. Strategy Development Workshop on Sleep Education. National Center of Sleep Disorders Research, NIH Pub No 95-3800, June 1994.
72. Strohl KP, Bonnie RJ, Findley L, Fletcher EC, Getsy J, Kryger MH, Millman R, Novak R, Roth T, Walsleben J, Williams A: Sleep Apnea, Sleepiness, and Driving Risk. In: Am J Respir Crit Care Med. Vol 150, pp. 1463-1473, 1994.
73. Roth T: Introduction to Sleep Disorders. In: Sleep and Biological Rhythms in Health and Sickness, 1994.

74. Buysse D, Reynolds C, Hauri P, Roth T, Stepanski E, Thorpy M, Bixler E, Kales A, Manfredi R, Vgontzas A, Mesiano D, Houck P, Kupfer D: Diagnostic Concordance for Insomnia Patients Among Sleep Specialists Using DSM-IV, ICD-10, and ICSD Diagnostic Systems: A Report from the APA/NIMH DSM-IV Field Trial. In: DSM-IV Source Book (First Edition). T Widiger et al (Eds.), American Psychiatric Association, 1994.
75. Roehrs T, Roth T: The Effect of Drugs on Sleep Quality and Architecture: In: Medicine, Up-To-Date, p 603, 1994.
76. Pack AI, Remmers JE, Roth T, Phillipson EA, Westbrook PR: Guidelines for In-Home Testing: A Need for Reassessment. Sleep (Letter to Editor) 18(2): 136-137, 1995.
77. Roth T, Roehrs TA, and Rosenthal: Hypersomnolence and Neurocognitive Performance in Sleep Apnea. In: Pulmonary Medicine, Vol 1, Rapid Science Publishers, pp 488-490, 1995.
78. Roth T: An Overview of the Report of the National Commission on Sleep Disorders Research. In: European Psychiatry. Vol 10, Suppl 3. Elsevier, Paris, pp109s-113s, 1995.
79. Roth T: Normal Sleep Physiology. In: European Psychiatry, Vol 11, Suppl 4. Elsevier Publishers, pp 237s-238s, 1996.
80. Roth T: Developing Appropriate Strategies: Clinical Research in Practice Settings. In: Council on Scientific Affairs, American Medical Association, Washington DC. pp 103-106, March 1996.
81. Roth T: Social and Economic Consequences of Sleep Disorders. In: Sleep 19(8): S46-S47, 1996.
82. Roth T, Roehrs T: Clinical Development of Hypnotics. In: Sleep 19(8): S48-S49, 1996.
83. Roth T: Management of Insomniac Patients. In: Sleep 19(8): S52-S53, 1996.
84. Roth T: Insomnia, Recognition Diagnosis and Public Health Influence. Sleep Problems Among Psychological Problems in General Health Care: Form, Frequency, Comorbidity and Related Disability: WHO Collaborating Center for Research and Training in Mental Health, Tokyo, Japan, pp 19-22, 1996.
85. Freeman H, Roth T, Guelfi JD: Insomnia: Diagnosis, Consequences, and Management. In: Zolpidem: An update of its pharmacological properties and therapeutic place in the management of insomnia: (Eds) H Freeman, AJ Puech, T Roth. Elsevier, Paris: 7-19, 1996.
86. Roth T, Puech AJ, Paiva T: Zolpidem - place in therapy. In: Zolpidem: An update of its pharmacological properties and therapeutic place in the management of insomnia: (Eds) H Freeman, AJ Puech, T Roth. Elsevier, Paris: 215-230, 1996.
87. Roehrs T, Roth T: Hypnotics, Alcohol, and Caffeine: Relation to Insomnia. In: Understanding Sleep - The Evaluation and Treatment of Sleep Disorders, American Psychological Association, pp 339-355, 1997.
88. Roehrs T, Roth T: Assessing Pharmacotherapy in Insomnia. In: The Handbook of Psychopharmacology Trials An Overview of Scientific, Political, and Ethical Concerns. (Eds) Marc Hertzman, Douglas E. Feltner. New York University Press, pp 268-284, 1997.

89. Roth T, Roehrs T, Rosenthal L: Daytime Sleepiness in Normals: Individual Differences in Sleep Need Not Ability to Fall Asleep. In: Sleep and Sleep Disorders: From Molecule to Behavior. Academic Press, pp 163-175, 1997.
90. Roth T, Roehrs T: Assessing Sedating and Alerting Drug Effects: The Multiple Sleep Latency Test. In: Human Psychopharmacology 6: 57-66, 1997.
91. Roth T, Roehrs T, Rosenthal L: Measurement of Sleepiness and Alertness: Multiple Sleep Latency Test. In: Sleep Disorders Medicine. Butterworth-Heinemann, pp 223-229, 1998.
92. Roehrs T, Roth T: State-Alerting Actions of Ethanol, Caffeine, and Nicotine. In: Handbook of Behavioral State Control – Cellular and Molecular Mechanisms. CRC Press, pp 421-432, 1999.
93. Day R, Gerhardstein R, Lumley A, Roth T, Rosenthal L: The Behavioral Morbidity Of Obstructive Sleep Apnea. In: Progress in Cardiovascular Diseases. 41(5): 341-354, 1999.
94. Roth T: Treating Insomnia in the Depressed Patient: Practical Considerations. In: Hospital Medicine. 35(7): 23-28, July 1999.
95. Roth T, Walsh J, Simon R, Zammit G: Introduction. In: Family Practice Recertification. 21(10): 3, September 1999.
96. Walsh JK, Benca RM, Bonnet M, Buysse DJ, Ricca J, Hauri PJ, Morin C, Roth T, Simon Jr RD, Kiley J, Monjan A, Rogus S: Insomnia: Assessment and Management in Primary Care. In: American Family Physician. 59(11): 3029-3038, June 1999.
97. Gillette MU, Roth T, Kiley JP: NIH Funding of Sleep Research: A Prospective and Retrospective View. In Sleep. 22(7): 956-958, 1999.
98. Roth T: Introduction to Management of Sleep Disorders. In: Family Practice Recertification. 21(10), September 1999.
99. Roth T: New Trends in Insomnia Management. In: Journal of Psychopharmacology. 13(4), Suppl 1: S37-S40, 1999.
100. Roth T, Roehrs T: Disorders of Sleep and Wakefulness. In: Principles of Neural Science. McGraw-Hill, pp 948-958, 2000.
101. Olanow CW, Schapira AHV, Roth T: Falling Asleep at the Wheel: Motor Vehicle Mishaps in People Taking Pramipexole and Ropinirole. In: Neurology. 54: 274, January (1 of 2) 2000.
102. Roth T: Overview of Insomnia for the Primary Care Physician. In: Insomnia Treatment - A Postgraduate of Medicine Special Report. 5-13, April 2000.
103. Roehrs T, Carskadon M, Dement W, Roth T: Daytime Sleepiness and Alertness. In: Principles and Practice of Sleep Medicine, 3rd Edition, pp. 43-52, 2000.
104. Roehrs T, Roth T: Hypnotics: Efficacy and Adverse Effects. In: Principles and Practice of Sleep Medicine, 3rd Edition, pp. 414-418, 2000.
105. Roehrs T, Zorick F, Roth T: Transient and Short-Term Insomnia. In: Principles and Practice of Sleep Medicine, 3rd Edition, pp. 624-632, 2000.

106. Roth T: Practical management of insomnia in primary care: an overview for the busy practitioner. Sleep 23(1): S7-S8, 2000.
107. Olanow CV, Schapira HV, Roth T: Waking up to sleep episodes in Parkinson's disease. Mov Disord 15: 212-215, 2000.
108. Roth T: Zaleplon: Its Unique Role in Insomnia Therapeutics. The Canadian Journal of Diagnosis. November 2000 Suppl, 21-25, 2000.
109. Roth T, Roehrs T: Sleep Organization and Regulation. Neurology 54(1): S2-7, 2000.
110. Roth T: New Developments for Treating Sleep Disorders. The Journal of Clinical Psychiatry. 62(10), S3-S4, 2001.
111. Roth T: The relationship between psychiatric diseases and insomnia. International Journal of Clinical Practice 116: S3-S8, January 2001.
112. Richardson GS, Roth T: Future Directions in the Management of Insomnia. J Clin Psychiatry 62(10): 39-45, 2001.
113. Roth T, Costa e Silva JA, Chase MH: Sleep and cognitive (memory) function: research and clinical perspectives. Sleep Medicine. 2(5): 379-387, September 2001.
114. Roehrs T, Roth T: Sleep-Wakefulness and Drugs of Abuse. In: Sleep Medicine Chapter 60: 575-585, 2002.
115. Roehrs T, Roth T: Letter to the Editor – Response to Wessendorf and Teschler. Sleep Medicine Reviews: 6(1): 73, 2002.
116. Roehrs T, Roth T: Editorial – Chronic Insufficient Sleep and Its Recovery. Sleep Medicine 4: 5-6, 2003.
117. Roehrs T, Roth T: Hypnotics: An Update. Curr Neurol Neurosci Rep 3: 181-184, 2003.
118. Roehrs T, Roth T: Editorial. Sleep Medicine 4: 169-170, 2003.
119. Roth T, Roehrs T: Insomnia: Epidemiology, Characteristics, and Consequences. Clinical Cornerstone 5(3): 5-15, 2003.
120. Roth T, Buysse D, Hajak G, Levy P: The Art of Good Sleep. Sleep Medicine 5(1): S1, 2004.
121. Roth T, Drake C: Evolution of Insomnia: Current Status and Future Direction. Sleep Medicine 5(1): S23-30, 2004.
122. Krystal AD, Roth T: Definitions, Measurements and Management in Insomnia. J Clin Psychiatry 65(8): 5-7, 2004.
123. Ancoli-Israel S, Benca RM, Edinger JD, Krystal AD, Mendelson W, Moldofsky H, Petrie J, Roth T, Walsh JK, Winkelman J. Panel Discussion: Changing How We Think About Insomnia. J Clin Psychiatry. 2004;65(Supplement 8):44-46.
124. Krystal AD, Walsh JK, Laska E, Caron J, Amato DA, Wessel TC, Roth T. Sustained efficacy of eszopiclone over six months of nightly treatment: Response to Letter to the Editor. Sleep. 2004;27:346-7.

125. Roth T: Measuring Treatment Efficacy in Insomnia. J Clin Psychiatry 65(8): 8-12, 2004.
126. Roth T, Doghramji K, Doghramji P, Schwartz JR, Walsh JK: Sleepiness Versus Sleeplessness: Shift Work and Sleep Disorders. J Clin Psychiatry 65(7): 1007-1008, July 2004.
127. Roth T, Drake C: Understanding the Effects of Age on "Normal" Human Sleep (Editorial). Sleep 27(7): 1-2, 2004.
128. Roth T: Stress, Anxiety, and Insomnia: What Every PCP Should Know. Medscape Neurology/Neurosurgery. December 2004. Available at: <http://www.medscape.com/viewprogram/3686>.
129. Roth T: Characteristics and Determinants of Normal Sleep. J Clin Psychiatry 65(16): 8-11, 2004.
130. Roth T, Drake C: Introduction - Improving Function: Assessing and Managing Shift Work Sleep Disorder. Consultant: (Supplement): S3-S4, December 2004.
131. Roth T, Drake C: The Impact of Shift Work Sleep Disorder: Clinical and Public Health Consequences. Consultant: (Supplement): S5-S10, December 2004.
132. Roehrs T, Roth T: Behavioral and Environmental Countermeasures. Sleep Deprivation: Clinical Issues, Pharmacology, and Sleep Loss Effects 193: 447-454, 2005.
133. Walsh JK, Roth T: The Role of Pharmacological Interventions for Sleep Deprivation. Sleep Deprivation: Clinical Issues, Pharmacology, and Sleep Loss Effects 193: 539-550, 2005.
134. Roehrs T, Roth T: Sleep and Pain: Interaction of Two Vital Functions. Sleep in Neurology 25(1): 106-116, 2005.
135. Roehrs TA, Carskadon MA, Dement WC, Roth T: Daytime Sleep and Alertness. In: Principles and Practice of Sleep Medicine, 4th Edition. W.B. Saunders Company, Philadelphia, PA, 2005.
136. Walsh JK, Roehrs TA, Roth T: Pharmacologic Treatment of Primary Insomnia. In: Principles and Practice of Sleep Medicine, 4th Edition. W.B. Saunders Company, Philadelphia, PA, 2005.
137. Roth T: Sedative Hypnotics. In: SRS Guide Basics of Sleep. Chapter 15: 143-149, Sleep Research Society, Westchester, IL, 2005.
138. Roth T: Advances in Understanding the Nature of Insomnia. In: Medscape Neurology & Neurosurgery, July 28, 2005. Available at: <http://www.medscape.com/viewarticle/508955>
139. Buysse D, Hajak G, Levy P, Roth T: Forum Scientific Committee: The Art of Good Sleep, Paris, France, September 2004. Sleep Medicine 6(1): S1-S2, 2005.
140. Roth T: Prevalence, Associated Risks and Treatment Patterns of Insomnia. J Clin Psychiatry 66(9): 10-13, 2005.
141. Jefferson C, Roth T, Roehrs T, Drake C: Sleep Reactivity to Stress in Insomniacs. In: Proceedings of the World Association of Sleep Medicine, 1st Congress. Berlin (Germany) October 15-18. 79-82, 2005.

142. Roth T: Chapter 15, Sedative Hypnotics. Sleep Research Society, SRS Basics of Sleep Guide. Sleep Research Society, 143-149, 2005.
143. Hyde M, Roehrs T, Roth T: Drugs of Abuse and Sleep. Sleep: A Comprehensive Handbook. 114: 873-877, 2006.
144. Hyde M, Roehrs T, Roth T: Alcohol, Alcoholism and Sleep. Sleep: A Comprehensive Handbook. 113: 867-871, 2006.
145. Roth T. Expert Column - The Sleep-Wake Cycle and Its Clinical Implications in Understanding and Managing Insomnia. Medscape Current Perspectives in Insomnia 8: 2006. Available at: <http://www.medscape.com/viewarticle/525731>
146. Roth T: Introduction – Excessive Sleepiness: What it Means for us All. Research Review, Supplement to Consultant: 2-21, February 2006.
147. Roth T, Drake C. Defining Insomnia: The Role of Quantitative Criteria. Sleep 29(4): 2006.
148. Breslau N, Roth T, Burduvali E, Kapke A, Schultz L, Roehrs T. Distinguishing Current from Remitted Posttraumatic Stress Disorder - Reply. Archives of General Psychiatry 63: 940-941, 2006.
149. Roth T: Preface. Sleep Medicine Clinics 1(3): xiii-xiv, 2006.
150. Drake CL, Roth T. Predisposition in the Evolution of Insomnia: Evidence, Potential Mechanisms, and Future Decisions. Sleep Medicine Clinics 1(3): 333-349, 2006.
151. Schwartz JRL, Roth T. Shift Work Sleep Disorder: Burden of Illness and Approaches to Management. Drugs 66(18): 2357-2370, 2006.
152. Roth T: Editorial - Prospects for Insomnia Treatment. Sleep Medicine; 7(S1):S1-S2, 2006.
153. Roth T: Editorial – Conclusion: Challenges in Insomnia Treatment. Sleep Medicine; 7(S1);S32, 2006.
154. Roth T, Roehrs T. The Physiology of Sleep. Neurology and Clinical Neuroscience 14: 2007.
155. Roth T, Roehrs T, Pies R. Insomnia: Pathophysiology and Implications for Treatment. Sleep Medicine Reviews 11: 71-79, 2007.
156. Roth T: Introduction to Beyond Excessive Sleepiness - Implications for Cognitive Function and Management Strategies. Journal of Clinical Psychiatry Special Section: S8, 2007.
157. Roth T, Harrison N, Mendelson W, Mignot E: Navigating Neuronal Pathways: Novel Targets for the Management of Sleep Disorders. [Electronic version]. Medscape; SciMed: 2007. Available at: www.medscape.com
158. Roth T, Buysse DJ, Krystal A, Banas B: Overview of Insomnia: Recent Perspectives in the Management of Insomnia. SMEI Sleep Medicine Education Institute: 2007.
159. Roth T: Introduction: Understanding Neuronal Pathways: Novel Targets for the Management of Insomnia. The Journal of Clinical Psychiatry; 68(5): 4-5, 2007.

160. Roth T: A Physiologic Basis for the Evolution of Pharmacotherapy for Insomnia. The Journal of Clinical Psychiatry; 68(5): 13-17, 2007.
161. Roth T: The Nature of Insomnia. Long-Term Issues in the Treatment of Sleep Disorders. Clinical Information Supplement CNS Spectra; 12:7(Suppl 10): 3-5, 2007. PMID: 17603408
162. Roth T: Sleep Therapy: New Generation Pharmacologic Agents for Managing Insomnia. Journal of Clinical Sleep Medicine; 3(5): S5-S6, 2007.
163. Roth T: Insomnia: Definition, Prevalence, Etiology and Consequences. Journal of Clinical Sleep Medicine; 3(5): S7-S10, 2007.
164. Roth T: Introduction: The Sleepy Patient in the Primary Care Setting. Consultant Supplement: S4, 2007.
165. Roth T: Normal Sleep and Sleep-Wake Hygiene. Consultant Supplement: S5-S13, 2007.
166. Roth T: Narcolepsy: Treatment Issues. Journal of Clinical Psychiatry; 68(0): 16-20, 2007.
167. Roth T: Introduction: Narcolepsy and Excessive Daytime Sleepiness: From the Bench to the Bedside. Journal of Clinical Psychiatry; 68(0): 4, 2007.
168. Roth T: Editorial: Introduction – Advances in our Understanding of Insomnia and its Management. Sleep Medicine 8: S25-S26, 2007.
169. Roth T: Managing Excessive Sleepiness in a Patient with RLS (CME/CE). Medscape 2007. Available at: www.medscape.com/viewprogram/8278.
170. Thorpy MJ, Lieberman III JA, Roth T, Owens GS: Patient Identification. American Journal of Managed Care 13(6): S132-S139, 2007.
171. Thorpy MJ, Lieberman III JA, Roth T, Owens GS: Patient-Management Strategies. American Journal of Managed Care 13(6): S140-S147, 2007.
172. Roth T, Franklin M, Bramley TJ: The State of Insomnia and Emerging Trends. American Journal of Managed Care 13(6): S117-S120, 2007.
173. Thorpy MJ, Lieberman JA, Roth T, Owens GS: Managed Care Considerations. American Journal of Managed Care 13(6): S148-S153, 2007.
174. Roth T: Editorial – Challenges in the Comorbid Condition. Sleep Medicine 8 (Suppl 4): S1-S2, 2007.
175. Roth T, Culpepper L: Insomnia Management in Primary Care. Clinical Symposia 58(1): 1-32, 2008.
176. Roehrs T, Roth T: Sleep, Alcohol, and Quality of Life. Sleep and Quality of Life in Clinical Medicine: 333-339, 2008.
177. Culpepper L, Doghramji P, Kornstein S, Roth T: The Art of Sleep. Recognizing and Treating Insomnia in Primary Care Practice. Supplement to The Journal of Family Practice: S1-S12, 2008. Available at: www.jfponline.com

178. Roth T, Roehrs T: Efficacy and Safety of Sleep-Promoting Agents. Sleep Med Clin 3: 175-187, 2008.
179. Randall S, Roehrs T, Roth T: Over-the-Counter Sleep Aid Medications and Insomnia. Primary Psychiatry Vol 15 No 5: 52-58, 2008.
180. Roth T: Novel Outcome Measures of Sleep, Sleep Loss and Insomnia (Editorial). Sleep Medicine, 9 Suppl. 1: S1-S2, 2008.
181. Roth T: Conclusion: Directions for Future Research Into Optimizing Outcomes Measurement in Sleep Medicine (Editorial). Sleep Medicine, 9 Suppl. 1: S35, 2008.
182. Roth T: Insomnia and Sleep-related Disorders (Editorial). Psychiatric Annals, September, 575-577, 2008.
183. Weilburg JB, Stakes JW, Roth T: Section VIII, Sleep Disorders. Massachusetts General Hospital Comprehensive Clinical Psychiatry: Expert Consult. Mosby: 1 Har/Onl edition: 285, April, 2008.
184. Schwartz JRL, Roth T: Neurophysiology of Sleep and Wakefulness: Basic Science and Clinical Implications. Current Neuropharmacology, 6: 367-378, 2008.
185. Roehrs TA, Roth T: Alcohol, Sleep, Sleep Disorders and Consequent Daytime Impairment. Sleep Disorders Diagnosis and Therapeutics. Informa UK Ltd, Distributed by Taylor & Francis, 6000 Broken Sound Parkway, NW (Suite 300), Boca Raton, FL 33487, Chapter 41, pp 480-486, 2008.
186. Drake CL, Schwartz JRL, Roth T: The Evolution of Insomnia in Relation to Comorbidity. Psychiatric Annals, September, 621-626, 2008.
187. Roth, T: Comorbid Insomnia: Current Directions and Future Challenges. The American Journal of Managed Care 15 (1): S6-S13, 2009.
188. Roth T: Slow Wave Sleep: Does it Matter? Journal of Clinical Sleep Medicine, Supplement to Vol 5, No 2: S4-S5, 2009.
189. Roth T: Current and Emerging Pharmacotherapies for the Treatment of Insomnia: Efficacy and Safety. Psychiatric Times Reporter, Supplement, March: 6-10, 2009.
190. Roth T: Sleep Duration, Insomnia and Longevity. Sleep Medicine (Editorial), pp 1071-1072 2009
191. Roth T: Sleep and Society. Sleep Medicine (Editorial). 2009
192. Roth T, Roehrs TA: Measurement of Sleepiness and Alertness: Multiple Sleep Latency Test. Sleep Disorders Medicine, Third Edition. (Ed) S Chokroverty. Saunders Elsevier, Philadelphia, PA, pp 218-223, 2009.
193. Roth T: Forward. Atlas of Clinical Sleep Medicine. Saunders Elsevier, Philadelphia, PA, p. xi, 2009.
194. Kryger M, Roth T: Insomnia. Atlas of Clinical Sleep Medicine, Chapter 9. Saunders Elsevier, Philadelphia, PA, pp 98-106, 2009.

195. Schwartz JRL, Roth T, Hirshkowitz M, Wright KP Jr.: Recognition and Management of Excessive Sleepiness in the Primary Care Setting. Prim Care Companion J Clinical Psychiatry, 11(5), 197-204, 2009.
196. Culpepper L, Roth T: Recognizing and Managing Obstructive Sleep Apnea in Primary Care. Prim Care Companion J Clin Psychiatry, 11(6), 330-338, 2009. PMID: 20098525
197. Dement WC, Cartwright RD, Roth T, Ware JC: Ismet (John) Karacan, MD, DSc OBITUARY. Sleep 32(9): 1238-1239. PDF Full-Text, 2009.
198. Roth T: Editorial - Conclusion. Sleep Medicine, 10, S26, 2009.
199. Roth T, Zinsenheim J: Sleep in Adults with ADHD and the Effects of Stimulants. Primary Psychiatry, 16(12): 32-37, 2009
200. Doghramji K, Zee PC, Roth T: Sleep Disorders Across a Woman's Life Span: A Challenge to Obstetricians and Gynecologists. Monthly Prescribing Reference, www.PrescribingReference.com , 1-22, CME Activity Release Date: October, 2009.
201. Roth T, Benca RM, Erman M: An Introduction to the Clinical Correlates of Disrupted Slow-Wave Sleep. Journal of Clinical Psychiatry, 71(4):e09, 2010.
202. Schwartz JRL, Roth T, Drake C: Armodafinil in the Treatment of Sleep/Wake Disorders. Neuropsychiatric Disease and Treatment, (6), 417-427, 2010.
203. Roth T, Dijk DJ: Editorial. Slow-Wave Sleep: Beyond Insomnia. The Importance of Slow-Wave Sleep for your Patients. Publishing Manager: Matt Weitz. Editorial office and editorial inquiries: Wolters Kluwer Pharma Solutions, 250 Waterloo Road, London SE1 8RD, UK, p5, 2010.
204. Roth T, Walsh JK: Interventions to Enhance Slow-Wave Sleep. Slow-Wave Sleep: Beyond Insomnia. The Importance of Slow-Wave Sleep for your Patients. Publishing Manager: Matt Weitz. Editorial office and editorial inquiries: Wolters Kluwer Pharma Solutions, 250 Waterloo Road, London SE1 8RD, UK, Chapter 9, p132, 2010.
205. Roth T, Roehrs T: Pharmacotherapy for Insomnia. Medications and Sleep. Sleep Med Clin 5, 529-539, 2010.
206. Roehrs T, Roth T: Drug-Related Sleep Stage Changes: Functional Significance and Clinical Relevance. Sleep Med Clin 5, 559-570, 2010.
207. Roth T: What is the Nature of Nonrestorative Sleep? Editorial/Sleep Medicine 11, 963-964, 2010.
208. Roth T, Bogan RK, Culpepper L, Doghramji K, Doghramji P, Drake C, Grauke JH, Knoepflmacher P, Pagel JF, Sateia M, Silvershein D, Thorpy MJ: Excessive Sleepiness: Under-Recognized and Essential Marker for Sleep/Wake Disorder Management. Special supplement to: Current Medical Research & Opinion, Volume 26, Supplement 2, S3-S27, 2010. PMID: 21077746
209. Roehrs T, Roth T. Benzodiazepine Receptor Agonist Safety. In: Sateia MJ, Buysse DJ eds. Insomnia: Diagnosis and Treatment. London: Informa, 387-96, 2010.
210. Roehrs T, Carskadon MA, Dement WC, Roth T: Daytime Sleepiness and Alertness. Principles and Practice of Sleep Medicine 5th Edition. Part I, Section 1, 42-53. Elsevier Saunders, St. Louis, Missouri, 2011.

211. Walsh JK, Roth T: Pharmacologic Treatment of Insomnia: Benzodiazepine Receptor Agonists. Principles and Practice of Sleep Medicine 5th Edition. Part II, Section 10, 905-915. Elsevier Saunders, St. Louis, Missouri, 2011.
212. Roehrs T, Roth T: Medication and Substance Abuse. Principles and Practice of Sleep Medicine 5th Edition. Part II, Section 16, pp 1512-1523. Elsevier Saunders, St. Louis, Missouri, 2011.
213. Krystal AD, Roth T, Simon RD: Recognition and Assessment of Shift Work Disorder. Journal of Clinical Psychiatry. 72(2): 248-257, 2011.
214. Roth T: Commentary. The Effect of Pregabalin on Pain-Related Sleep Interference in Diabetic Peripheral Neuropathy or Postherpetic Neuralgia: A Review of Nine Clinical Trials. Lee-Chiong, Teofile. Best of Sleep Medicine 2011, 246-248. ISBN-13: 978-1460993859; ISBN-10: 1460993853, 2011.
215. Roth T: Commentary. The Challenges of Interpreting Residual Effects of Hypnotics. Sleep, Vol. 34, No. 10, 1285-1286, 2011. PMID: 21966057
216. Roehrs T, Roth T: The effects of medications on sleep quality and sleep architecture. Up To Date, Nov 18, 2011.
217. Roehrs TA, Diederichs C, Roth T: Pharmacology of Benzodiazepine Receptor Agonist Hypnotics. Therapy in Sleep Medicine, Section 3, Chapter 7, 99-108. ISBN978-1-4377-1703-7, Elsevier Saunders, Philadelphia, PA, 2012.
218. Gargaro CE, Roth T, Drake CL: Insomnia: Etiology, Clinical Manifestations, and Morbidity. Essentials of Sleep Medicine: An Approach for Clinical Pulmonology, Respiratory Medicine, DOI 10.1007/978-1-60761-735-8_13, Springer Science+Business Media, LLC, 233-248, 2012.
219. Bazan L, Roth T, Drake CL: Management of Insomnia. Essentials of Sleep Medicine: An Approach for Clinical Pulmonology, Respiratory Medicine, DOI 10.1007/978-1-60761-735-8_14, Springer Science+Business Media, LLC, 249-276, 2012.
220. Roth T: Shift Work Disorder: Overview and Diagnosis (Brief Report). J Clin Psychiatry, 73(3):e09. <http://www.psychiatrist.com/briefreports/series-1/BRS/index.asp?>, 2012.
221. Foulkes D, Rechtschaffen A, Roth T: Obituary for Gerald W. Vogel, MD. Sleep, Vol. 35, No. 6, 889, 2012.
222. Krystal AD, Roth T, Simon RD Jr. Shift work disorder case studies: applying management principles in clinical practice. J Clin Psychiatry. 2012;73(8):e25.
223. Roth T: Investigating Nonrestorative Sleep. Editorial, Sleep Medicine, 13, 557-558, 2012.
224. Roth T: Pharmacotherapy of Excessive Sleepiness. Sleep Med Clin, 7, 333-340, 2012.
225. Roehrs T, Roth T: Sleep and Sleep Disorders. Drug Abuse and Addiction in Medical Illness: Causes, Consequences and Treatment, Part III, Chapter 30, 375-384, DOI 10.1007/978-1-4614-3375-0_30, © Springer Science+Business Media, LLC, 2012.
226. Roth T, Ancoli-Israel S: Obituary for Peter Hauri. Sleep, Vol. 36, No. 4, 617-618, 2013.

227. Roth T, Drake C, Roehrs T: Behavioral Sleep Medicine. Journal of Clinical Sleep Medicine. Vol 9(9), 2013.
228. Thorpy MJ, Roth T. Toward a Classification of Medications for Sleep and Circadian Rhythm Disorders. *Nature of Science of Sleep*. 5, 143-145, 2013.
229. Roth T: Forward to the Second Edition. Atlas of Clinical Sleep Medicine, 2nd Edition, xi, 2014.
230. Edinger JD, Kryger M, Roth T. Insomnia. Atlas of Clinical Sleep Medicine, 2nd Edition, 10, 148-158, 2014.
231. Krystal AD, Doghramji K, Roth T, Scammell, TE. New Insights Into the Sleep-Wake System: The Neurobiology and Pathophysiology of Insomnia. Psychiatric News, May 16, 2014; 49 (10) (Suppl).
232. Roehrs T, Gumenyuk V, Drake C, Roth T. Physiological correlates of insomnia. *Curr Top Behav Neurosci* 2014; PMID: 24920447.
233. Verster JC, Roth T. Insomnia and driving ability. Sleep 37(9), 2014; PMID: 25142560.
234. Krystal AD, Doghramji K, Roth T, & Scammell TE. Targeting neurotransmitters in the management of insomnia. Psychiatric News. October 17, 2014; 49 (20) (Suppl).
235. Roth T, More on Insomnia Disorders in Older Patients Current Psychiatry Comments and Controversies . 6 February 2015
236. Roehrs T, Roth T. Pain and sleep. In: Babson KA, Feldner MT (eds). *Sleep and Affect*. New York: Elsevier 2015, pp 377-397
237. Roth T. Effects of Daytime Sleepiness and Fatigue On Overall Health and Cognitive Function. *J. Clin. Psychiatry* ; 76 (9); e1145, 2015
238. Roth T. The Effect of Comorbid Psychiatric and Medical Illnesses on Sleep Disorders Treatment *J. Clin. Psychiatry*; 76 (9); e 1146, 2015.
239. Roehrs T, Roth T. The Effects of Medications on Sleep Quality and Sleep Architecture Up To Date October 2015.
240. Roth T, Rosenberg RP , Managing Excessive Daytime Sleepiness. *J Clin. Psychiatry*;76:0, 2015.
241. Roehrs T, Roth T. Sleep Disturbance in Substance Use Disorders. *Psychiatr Clin N Am* 38: 793-803, 2015.
242. Roehrs T, Carskadon MA, Dement WC, Roth T: Daytime Sleepiness and Alertness. Principles and Practice of Sleep Medicine 6th Edition. Part I, Section 1, 39-48. Elsevier Saunders, Philadelphia, PA, 2016.
243. Roehrs T, Roth T. The Effects of Medications on Sleep Quality and Sleep Architecture Up To Date October 2016.
244. Verster JC, van de Loo AJ, Roth T: Effects of Hypnotic Drugs on Driving Performance. Principles and Practice of Sleep Medicine 6th Edition. Part I, Section 6, 499-505. Elsevier Saunders, Philadelphia, PA, 2016.

245. Walsh JK, Roth T: Pharmacologic Treatment of Insomnia: Benzodiazepine Receptor Agonists. Principles and Practice of Sleep Medicine 6th Edition. Part II, Section 11, 832-841. Elsevier Saunders, Philadelphia, PA, 2016.
246. Roehrs T, Roth T: Medication and Substance Abuse. Principles and Practice of Sleep Medicine 6th Edition. Part II, Section 17, 1380-1389. Elsevier Saunders, Philadelphia, PA, 2016.
247. Culpepper L, Wright WL, Roth T. Enhancing the Management of Insomnia in Older Patients. myCME Website. <http://www.mycme.com/enhacing-the-managemtn-of-insomnia-in-older-patients/activity/4552>. March, 2017.
248. Roth, T., Roehrs, T. Multiple Sleep Latency Test. Sleep Disorders Medicine. 391-398. Springer Publishing, New York. 2017.

ABSTRACTS

1. Pradhan S, Roth T: Effects of Ditrane (JB329) on a Multiple Schedule of Reinforcement in Rats. *The Pharmacologist* 8: 1966.
2. Pradhan S, Roth T: Some Behavioral Effects of Nicotine in Rats. *Federation Proc* 26: 1967.
3. Roth T, Pradhan S: Behavioral Effects of Some Cholinergic Agents in Rats. *The Pharmacologist* 9: 1967.
4. Roth T, Kramer M, Trinder J, Sandler L, Riechers M, Fishbein H: The Effect of Noise on Sleep and Post-Sleep Behavior. *Psychophysiol* 7: 357, 1970.
5. Trinder J, Kramer M, Riechers M, Fishbein H, Roth T: The Effect of Dream Length on Dream Content. *Psychophysiol* 7: 333, 1970.
6. Arand D, Trinder J, Kramer M, Roth T: Trace Decay, Retroactive Interference, and Repression as Determinants of the Recency Effect in Dream Recall. *Psychophysiol* 9: 116, 1972.
7. Kramer M, Roth T, Clark J, Trinder J: The Use of Dreams in Drawing Clinical Inferences. *Psychophysiol* 9: 117, 1972.
8. Kramer M, Curtis T, Trinder J, Roth T: A Comparison of Dream Content in Laboratory Dream Reports of Schizophrenic and Depressive Psychopathological Groups. *Psychophysiol* 9: 118, 1972.
9. Brunner R, Kramer M, Clark J, Day N, Trinder J, Roth T: Dream Recall in Chronic Brain Syndrome Patients. *Psychophysiol* 9: 138, 1972.
10. Trinder J, Kramer M, Roth T: Problems in the Scaling of Sleep Stage Change. *Psychophysiol* 9: 148, 1972.
11. Roth T, Kramer M, Trinder J: Volunteers Versus Non-Volunteers in Dream Research. *Psychophysiol* 9: 116, 1972.
12. Kramer M, Roehrs T, Roth T: The Relationship Between Sleep and Mood. *Sleep Research* 1: 92, 1972.
13. Clark J, Trinder J, Kramer M, Roth T, Day N: An Approach to the Content Analysis of Dream Content Scales. *Sleep Research* 1: 118, 1972.
14. Kramer M, Roth T, Arand D, Palmer T: A Psychoregulatory Function of the Dream: A Preliminary Report of a Pilot Study. *Sleep Research* 1: 123, 1972.
15. Arand D, Kramer M, Czaya J, Roth T: Attitudes Toward Sleep and Dreams in Good Versus Poor Sleepers. *Sleep Research* 1: 130, 1972.
16. Palmer T, Roehrs T, Kramer M, Roth T: A Comparison of the Manifest Content of Dream Reports and TAT Responses. *Sleep Research* 1: 144, 1972.
17. Roehrs T, Kramer M, Lefton W, Lutz T, Roth T: Mood Before and After Sleep. *Sleep Research* 2: 95, 1973.
18. Palmer T, Kramer M, Roth T: A Comparison of the Manifest Content of REM and TAT Reports. *Sleep Research* 2: 125, 1973.

19. Czaya J, Kramer M, Roth T: Changes in Dream Quality as a Function of Time into REM. *Sleep Research* 2: 122, 1973.
20. Roth T, Kramer M, Roehrs T: The Relationship Between Sleep Physiology and Mood. *Sleep Research* 2: 96, 1973.
21. Schwartz J, Kramer M, Palmer T, Roth T: The Relationship of Personality Factors to REM Interruption and Diary Recall of Dreams. *Sleep Research* 2: 113, 1973.
22. Roth T, Kramer M, Roehrs T: The Consistency of Sleep Measures. *Sleep Research* 2: 102, 1973.
23. Schwartz J, Roth T, Kramer M, Hlasny R: A New Benzodiazepine Hypnotic and Its Effect on Mood. *Sleep Research* 3: 65, 1974.
24. Roehrs T, Kramer M, Arand D, Roth T: The Relationship between REM Time and Depressive Affect. *Sleep Research* 3: 90, 1974.
25. Kramer M, Czaya J, Arand D, Roth T: The Development of Psychological Content Across the REM Period. *Sleep Research* 3: 121, 1974.
26. Roth T, Kramer M, Schwartz J: Some Preliminary Observations on the Nature of Insomniac Patients. *Sleep Research* 3: 145, 1974.
27. Roth T, Kramer M, Schwartz J: A Sleep Laboratory Evaluation of a New Benzodiazepine Hypnotic in Insomniac Patients. *Sleep Research* 3: 64, 1974.
28. Roth T, Kramer M, Lefton W, Lutz T: The Effects of Sleep Deprivation on Mood. *Sleep Research* 3: 154, 1974.
29. Roth T, Kramer M, Lutz T: The Nature of Insomnia: A Descriptive Summary of a Sleep Clinic Population. *Dig Neur Psychiat* 68, 1976.
30. Roth T, Kramer M, Lutz T: Intermediate Use of Triazolam: A Sleep Laboratory Study. *Sleep Research* 4: 117, 1975.
31. Roth T, Kramer M: The Nature of Insomnia: A Descriptive Summary of a Sleep Clinic Population. *Sleep Research* 4: 234, 1975.
32. Kramer M, Hlasny R, Jacobs G, Roth t: Do Dreams Have Meaning? An Empirical Inquiry. *Sleep Research* 4: 186, 1975.
33. Lutz T, Kramer M, Roth T: The Relationship Between Mood and Performance. *Sleep Research* 4: 152, 1975.
34. Roth T, Kramer M, Roehrs T, Lutz T: The Comparative Effects of Three Hypnotic Drugs. I. Sleep Parameters. *Sleep Research* 4: 114, 1975.
35. Roth T, Kramer M, Roehrs T, Lutz T: The Comparative Effects of Three Hypnotic Drugs. II. Subjective State. *Sleep Research* 4: 115, 1975.
36. Roth T, Kramer M, Roehrs T, Lutz T: The Comparative Effects of Three Hypnotic Drugs. III. Performance. *Sleep Research* 4: 116, 1975.

37. Piccione P, Thomas S, Roth T, Kramer M: Incorporation of the Laboratory Situation in Dreams. *Sleep Research* 5: 120, 1976.
38. Lutz T, Roth T, Kramer M, Grissom T: A Review of Methodologies for the Evaluation of Hypnotics. *Sleep Research* 5: 202, 1976.
39. Kramer M, Roth T, Cisco J: The Meaningfulness of Dreams. *Sleep Research* 5: 118, 1976.
40. Lysaght R, Roth T, Kramer M, Lutz T: Sleep in Insomniacs. *Sleep Research* 5: 179, 1976.
41. Roth T, Kramer M, Felson J, Grissom T, Lutz T: Evaluation of Hypnotics in Geriatric Patients. *Sleep Research* 5: 77, 1976.
42. Lutz T, Roth T, Kramer M, Felson J: The Relationship Between Sleepiness and Performance. *Sleep Research* 5: 104, 1976.
43. Johnson B, Roth T, Kramer M: Subjective and Electrophysiological Evaluation of Ketazolam. *Sleep Research* 5: 67, 1976.
44. Roth T, Kramer M, Arand D: Dreams as a Reflection of Immediate Psychological Concern. *Sleep Research* 5: 122, 1976.
45. Kramer M, Roehrs T, Roth T: Mood Change and the Physiology of Sleep. *Psychiat Jan*: 36, 1977.
46. Kramer M, Roth T: Responsibility and Accountability: A Look From Within. *Proc Amer Psychiat Assn Mtg*, May 1977, Toronto.
47. Lysaght R, Roth T, Kramer M, Lutz T: The Consistency of Subjective and Objective Aspects of Sleep on Drug and Placebo Nights. *Sleep Research* 6: 77, 1977.
48. Lundberg P, Roth T, Kramer M, Grissom T, Zorick F: A Hospital Survey of Prescription Versus Administration of Hypnotics Used. *Sleep Research* 6: 75, 1977.
49. Johnson B, Roth T, Jansen T, Kramer M: The Effects of Drugs on REM Density. *Sleep Research* 6: 40, 1977.
50. Zorick F, Roth T, Kramer M, Flessa H: Intensification of Excessive Daytime Sleepiness by Lymphoma. *Sleep Research* 6: 199, 1977.
51. Tietz E, Roth T, Kramer M, Bellus S: The Effect of a New Hypnotic (Sch-16134) on Chronic Insomniacs. *Sleep Research* 6: 86, 1977.
52. Piccione P, Jacobs G, Kramer M, Roth T: The Relationship Between Daily Activities, Emotions, and Dream Content. *Sleep Research* 6: 133, 1977.
53. Lutz T, Roth T, Kramer M, Arand D, Grissom T, Zorick F: An Overview of Methodologies Used in Research on Hypnotics. *Sleep Research* 6: 76, 1977.
54. Lysaght R, Roth T, Kramer M, Lutz T, Zorick F: A Dose-Response Study of The Acute Effects of Diazepam and Alprazolam on Human Sleep. *Sleep Research* 6: 78, 1977.
55. Roth T, Lutz T, Kramer M, Tietz E: The Relationship Between Objective and Subjective Evaluations of Sleep in Insomniacs. *Sleep Research* 6: 178, 1977.

56. Karacan I, Roth T, Orr WC, Kramer M, Shurley JT, Thornby JI, Bingham SF, Salis PJ, Ambuehl RA: VA Cooperative Study on Drugs and Sleep: Relative Potency Comparisons of Flurazepam and Phenobarbital. *Sleep Research* 6: 72, 1977.
57. Lundberg P, Roth T, Kramer M, Zorick F, Piccione P: The Effects of Terfenadine and Diphenhydramine on Sleep, Performance, and Subjective State. *Sleep Research* 7: 105, 1978.
58. Tietz E, Roth T, Kramer M, Saab P, Piccione P: The Effect of Quazepam (Sch-16134) 15 and 20mg on the Sleep of Chronic Insomniacs. *Sleep Research* 7: 116, 1978.
59. Karacan I, Orr WC, Roth T, Kramer M, Shurley JT, Thornby JI, Bingham SF, Ambuehl RA: Flurazepam 45mg and Phenobarbital 240mg in Controls and Insomniacs. *Sleep Research* 7: 104, 1978.
60. Lysaght R, Roth T, Kramer M, Salis P: Variations in Subjective State and Body Temperature across the day. *Sleep Research* 7: 308, 1978.
61. Kramer M, Mealey L, Roth T: The Relationship of Dream Content to Evening-To-Morning Mood Change. *Sleep Research* 7: 178, 1978.
62. Roth T, Kramer M, Tallerigo R, Salis P: Personality Differences Between Insomniacs and Non-Insomniacs in a Psychiatric Outpatient Counseling Clientele. *Sleep Research* 7: 203, 1978.
63. Zorick F, Roth T, Salis P, Kramer M, Lutz T: Insomnia and Excessive Daytime Sleepiness as Presenting Symptoms in Nocturnal Myoclonus. *Sleep Research* 7: 256, 1978.
64. Salis P, Roth T, Kramer M, Zorick F, Piccione P: Enlarged Tonsils in an Adult With Sleep-Apnea Syndrome: A Case Report. *Sleep Research* 7: 245, 1978.
65. Zorick F, Roth T, Kramer M, Grissom T, Saab P: Automatic Behavior and Narcolepsy: A Case Report. *Sleep Research* 7: 255, 1978.
66. Kaffeman M, Piccione P, Salis P, Kramer M, Roth T: A Comparison of Three Hypnotics on Sleep and Performance. *Sleep Research* 8: 100, 1979.
67. Saab P, Hartse KM, Piccione P, Kramer M, Roth T: The Effects of Flurazepam, Lorazepam, and Triazolam on Memory. *Sleep Research* 8: 105, 1979.
68. Tietz E, Piccione P, Zorick F, Salis P, Roth T, Kramer M: The Acute Effects of Quazepam on Sleep. *Sleep Research* 8: 111, 1979.
69. Lysaght R, Kramer M, Roth T: Dream Adaptation. *Sleep Research* 8: 155, 1979.
70. Kramer M, Roth T: Some Psychological and Physiologic Aspects of Insomnia. *Sleep Research* 8: 165, 1979.
71. Lineback W, Zorick F, Salis P, Kaffeman M, Roth T: Psychopathology in Geriatrics and Non-Geriatrics. *Sleep Research* 8: 167, 1979.
72. Lysaght R, Kramer M, Roth T: Mood Differences Before and After Sleep: A Test of its Generalizability. *Sleep Research* 8: 168, 1979.
73. Conway W, Victor L, Magilligan D, Fujita S, Zorick F, Roth T: Long-Term Experience with Tracheostomy For Sleep Apnea. *Sleep Research* 8: 176, 1979.

74. Conway W, Zorick F, Hartse KM, Piccione P, Roth T: Protriptyline in the Treatment of Sleep Apnea. *Sleep Research* 8: 177, 1979.
75. Hartse KM, Zorick F, Sicklesteel J, Piccione P, Roth T: Nap Recordings in the Diagnosis of Daytime Somnolence. *Sleep Research* 8: 190, 1979.
76. Karacan I, Orr WC, Kramer M, Shurley JT, Thornby JI, Bingham SF, Kay DC, Roth T: Characteristics of Insomniac Applicants in a Cooperative Study. *Sleep Research* 8: 197, 1979.
77. Piccione P, Zorick F, Hartse KM, Kaffeman M, Roth T: Use of ASDC Nosology With 100 Patients. *Sleep Research* 8: 209, 1979.
78. Zorick F, Piccione P, Hartse KM, Zammit G, Roth T: Disturbed Nocturnal Sleep in Narcolepsy. *Sleep Research* 8: 223, 1979.
79. Hartse KM, Roth T, Zorick FJ, Zammit G: The Effect of Instruction Upon Sleep Latency During Multiple Daytime Naps of Normal Subjects. *Sleep Research* 9: 123, 1980.
80. Piccione PM, Zorick FJ, Roth T, Stepanski E: Sleep and Personality in Subjective Insomniacs. *Sleep Research* 9: 176, 1980.
81. Stepanski EJ, Hartse KM, Roth T, Zorick FJ, Piccione PM: MMPI Evaluations in Different Insomniac Populations. *Sleep Research* 9: 182, 1980.
82. Fujita S, Zorick F, Conway W, Roth T, Hartse KM, Piccione PM: Uvulo-Palato-Pharyngoplasty: A New Surgical Treatment for Upper Airway Sleep Apnea. *Sleep Research* 9: 197, 1980.
83. Hartse KM, Roth T, Zorick FJ, Moyles TP: REM Sleep Episodes During Multiple Daytime Naps of Narcoleptic Subjects. *Sleep Research* 9: 203, 1980.
84. Hartse KM, Zorick FJ, Roth T, Kaffeman ME, Moyles TP: Daytime Sleep Tendency in Normal, Insomniac and Somnolent Populations. *Sleep Research* 204, 1980.
85. Hartse KM, Zorick FJ, Roth T, Sicklesteel JM: Isolated Cataplexy: A Familial Study. *Sleep Research* 9: 205, 1980.
86. Roth T, Fujita S, Hartse KM, Zorick FJ, Piccione PM: Upper Airway Sleep Apnea in Three Male Siblings. *Sleep Research* 9: 219, 1980.
87. Tietz EI, Zorick FJ, Roth T, Kaffeman ME: Objective and Subjective Sleep Parameters in Documented and Undocumented Insomniacs. *Sleep Research* 9: 227, 1980.
88. Zorick F, Hartse K, Roth T, Stepanski E: Polysomnographic Characteristics of Diagnosed Insomniacs. *Sleep Research* 9: 234, 1980.
89. Karacan I, Bonnet MH, Orr WC, Ware JC, Kramer M, Bingham SF, Thornby JI, Salis PJ, Roth T: VA Cooperative Study on Drugs Sleep: Reliability of Baseline Sleep Parameters in Insomniacs. *Sleep Research* 9: 292, 1980.
90. Kaffeman M, McLenaghan A, Koshorek GL, Koshorek GJ, Roth T: The Efficacy of Estazolam. *Sleep Research* 10: 87, 1981.

91. Stepanski E, Kaffeman M, Zorick F, Sicklesteel J, Roth T: The Effects of Chronic Administration of Triazolam 0.5mg on Insomniacs Sleep. *Sleep Research* 10: 101, 1981.
92. Tietz E, Zorick F, Sicklesteel J, Kaffeman M, Roth T: The Acute Efficacy of 15mg of Flurazepam in Insomniacs. *Sleep Research* 10: 102, 1981.
93. Saab P, Stepanski E, Roth T, Zorick F, Kaffeman M, Roehrs T: Readaptation to the Laboratory in Long-Term Sleep Studies. *Sleep Research* 10: 142, 1981.
94. Fujita S, Zorick F, Koshorek GJ, Wittig R, Conway W, Roth T: Treatment of Upper Airway Sleep Apnea With Uvulo-Palato-Pharyngoplasty (UPP): Recent Experience. *Sleep Research* 10: 197, 1981.
95. Sicklesteel J, Zorick F, Wittig R, Conway W, Roth T: Daytime Somnolence and Insufficient Sleep: A Case Series. *Sleep Research* 10: 233, 1981.
96. Wittig R, Zorick F, Roth T, Piccione P, Sicklesteel J: Narcolepsy and Disturbed Nocturnal Sleep. *Sleep Research* 10: 243, 1981.
97. Tietz EI, Berman R, Roth T: 3H Diazepam Binding Following Sleep Deprivation in Rats. *Sleep Research* 11: 49, 1982.
98. Koshorek GL, Roth T, Zorick F, Wittig R, Roehrs T: The Acute Efficacy of Brotizolam. *Sleep Research* 11: 61, 1982.
99. Koshorek GL, Roth T, Zorick F, Wittig R, Roehrs T: Dose Effects of Estazolam on Sleep. *Sleep Research* 11: 60, 1982.
100. Roehrs T, Zorick F, Wittig R, McLenaghan A, Roth T: Antidepressant and Hypnotic Effects of Doxepin. *Sleep Research* 11: 70, 1982.
101. Roth T, Roehrs T, Zorick F, Sicklesteel J, Wittig R, Hartse K: Benzodiazepines and Memory. *Sleep Research* 11: 72, 1982.
102. Barone N, Sicklesteel J, Zorick F, Roehrs T, Roth T: Persistent Insomnia Complaint and the MMPI. *Sleep Research* 11: 137, 1982.
103. Sicklesteel J, Zorick F, Conway W, Roth T, Wittig R: Obesity, Sleep & Respiration. *Sleep Research* 11: 173, 1982.
104. Silvestri R, Guilleminault C, Coleman R, Roth T, Dement WC: Nocturnal Sleep Versus Daytime Nap Findings in Patients With Breathing Abnormalities During Sleep. *Sleep Research* 11: 174, 1982.
105. Wittig R, Zorick F, Conway W, Fujita S, Roth T: Upper Airway Anatomic Abnormalities Associated With Sleep Apnea Syndrome. *Sleep Research* 11: 183, 1982.
106. Zorick F, Conway W, Sicklesteel J, Wittig R, Roth T: Protriptyline in the Treatment of Upper Airway Sleep Apnea Syndrome: A Controlled Trial. *Sleep Research* 11: 184, 1982.
107. Zorick F, Koshorek GJ, Conway W, Sicklesteel J, Roehrs T, Wittig R, Roth T: The Consistency of Apneas During Sleep. *Sleep Research* 11: 185, 1982.
108. Moyles TL, Czekaj J, Sicklesteel J, Zorick F, Roth T: An Oxygen Saturation Data Collection and Analysis System. *Sleep Research* 11: 206, 1982.

109. Wittig R, Roehrs T, Roth T, Zorick F, Perks S, McLenaghan A: Consistency of NPT Evaluations. *Sleep Research* 11: 209, 1982.
110. Karacan I, Dement WC, Roth T, Seidel W, Zorick F, Thornby J, Koshorek G, Moore C, Bowers P: The Long Term Efficacy of Brotizolam. *Sleep Research* 12: 103, 1983.
111. Lamphere J, Paxton C, Roehrs T, Zorick F, Wittig R, Roth T: Effects of Temazepam on Sleep Latency and Continuity. *Sleep Research* 12: 108, 1983.
112. Roehrs T, McLenaghan A, Koshorek GL, Zorick F, Roth T: Effects of Lormetazepam, Temazepam and Flurazepam on Anterograde Amnesia. *Sleep Research* 12: 123, 1983.
113. Stepanski E, Badia P, Lamphere J, Roth T: Sleep Fragmentation and Daytime Sleepiness. *Sleep Research* 12: 165, 1983.
114. Ton D, Sicklesteel J, Koshorek GJ, Zorick F, Wittig R, Roth T: Different Sleep-Wake Complaints in the Absence of Positive Findings. *Sleep Research* 12: 216, 1983.
115. Balkin T, Zorick F, Sicklesteel J, Wittig R, Roehrs T, Roth T: REM Parameters in Narcoleptic Patients. *Sleep Research* 12: 222, 1983.
116. Fujita S, Conway W, Zorick F, Sicklesteel J, Roehrs T, Wittig R, Roth T: Evaluation of the Effectiveness of Uvulopalatopharyngoplasty. *Sleep Research* 12: 248, 1983.
117. Kribbs N, Zorick F, Sicklesteel J, Wittig R, Roehrs T, Roth T: Patterns of Wakefulness in Patients Complaining of Insomnia. *Sleep Research* 12: 256, 1983.
118. Roehrs T, Zorick F, Sicklesteel J, Wittig R, Roth T: Age-Related Sleep-Wake Disorders at a Sleep Disorders Center. *Sleep Research* 12: 278, 1983.
119. Rosenthal L, Roehrs T, Sicklesteel J, Zorick F, Wittig R, Roth T: Periodic Leg Movements, Sleep Fragmentation and Sleep-Wake Complaints. *Sleep Research* 12: 279, 1983.
120. Wittig R, Wolford G, Conway W, Zorick F, Sicklesteel J, Roehrs T, Roth T: Mandibular Advancement as a Treatment of Sleep Apnea Syndrome. *Sleep Research* 12: 296, 1983.
121. Wittig R, Zorick F, Roehrs T, Sicklesteel J, Roth T: Chronically Insufficient Sleep Complicated by an Irregular Sleep-Wake Schedule: A Case Report. *Sleep Research* 12: 297, 1983.
122. Fortier J, Kribbs N, Thomas L, Koshorek G, Lamphere J, Roehrs T, Roth T: Efficacy of Chronic (6 weeks) Estazolam in Patients With Insomnia. *Sleep Research* 13: 47, 1984.
123. Karacan I, Dement WC, Roth T, Seidel W, Zorick F, Thornby J, Koshorek G, Moore C, Bowers P: Investigation of Early Morning and Rebound Insomnia Following Long-Term Use of Brotizolam. *Sleep Research* 13: 48, 1984.
124. Paxton C, Vogel G, Vogel F, Roehrs T, Lamphere J, Roth T: Dose Effects of Temazepam on Sleep. *Sleep Research* 13: 59, 1984.
125. Roehrs T, Koshorek G, Zorick F, Hauri P, Sateia M, Kipp J, Roth T: Middle-of-the-Night Administration of Midazolam and Temazepam. *Sleep Research* 13: 62, 1984.

126. Seidel WF, Roth T, Roehrs T, Zorick F, Dement WC: Treatment of Simulated Jet-Lag with Benzodiazepines. *Sleep Research* 13: 67, 1984.
127. Roehrs T, Zorick F, McLenaghan A, Sicklesteel J, Lamphere J, Wittig R, Roth T: Sleep and MSLT Norms for Middle Age Adults. *Sleep Research* 13: 87, 1984.
128. Nicholson A, Spencer MB, Stone B, Roehrs T, Roth T: Sustained Performance With Short Evening and Morning Sleeps. *Sleep Research* 13: 95, 1984.
129. Roehrs T, Zorick F, Paxton C, Wittig R, Sicklesteel J, Roth T: The Refreshing Quality of Naps in Patients With Excessive Daytime Sleepiness. *Sleep Research* 13: 160, 1984.
130. Wittig R, Fujita S, Conway W, Sicklesteel J, Roth T: Epiglottidectomy as Treatment of Refractory Sleep Apnea Syndrome: Report of Two Cases. *Sleep Research* 13: 174, 1984.
131. Wittig R, Roth T, Zorick F, Roehrs T: Sleep Related Ventricular Arrhythmia: A Case Report. *Sleep Research* 13: 175, 1984.
132. Zorick F, Fujita S, Conway W, Sicklesteel J, Roehrs T, Roth T: Uvulopalatopharyngoplasty: One Year Followup. *Sleep Research* 13: 176, 1984.
133. Stepanski E, Salava W, Lamphere J, Roehrs T, Zorick F, Badia P, Roth T: Experimental Sleep Fragmentation and Sleepiness in Normal Subjects: A Preliminary Report. *Sleep Research* 13: 193, 1984.
134. Lamphere J, Vogel G, Vogel F, Roehrs T, Zorick F, Roth T: Eligibility Requirements in Hypnotic Trials. *Sleep Research* 13: 209, 1984.
135. Kribbs N, Sicklesteel J, Roehrs T, Zorick F, Wittig R, Roth T: Performance and MSLT Measures of Hypnotic Residual Effects. *Sleep Research* 14: 38, 1985.
136. Roehrs T, Koshorek G, Lamphere J, Paxton C, Zorick F, Roth T: Dose Effects of Zopiclone on Sleep. *Sleep Research* 14: 53, 1985.
137. Roehrs T, Zorick F, Wittig R, Sicklesteel J, Fortier J, Roth T: Dose Determinants of Rebound Insomnia. *Sleep Research* 14: 54, 1985.
138. Sicklesteel J, Koshorek G, Paxton C, Zorick F, Lamphere J, Roehrs T, Roth T: Efficacy of Reduced Triazolam Dosage in Elderly Insomniacs. *Sleep Research* 14: 58, 1985.
139. Hernandez-Field A, Fortier J, Zorick F, Wittig R, Roehrs T, Roth T: Relation of Age and Abnormal NPT in Patients Complaining of Impotence. *Sleep Research* 14: 74, 1985.
140. Lumley M, Roehrs T, Zorick F, Lamphere J, Wittig R, Roth T: Alerting Effects of Naps in Normal Sleep Deprived Subjects. *Sleep Research* 14: 99, 1985.
141. Stepanski E, Lamphere J, Roehrs T, Zorick F, Salava W, Roth T: The Effect of Experimental Sleep Fragmentation on Daytime Sleepiness in Normal Subjects. *Sleep Research* 14: 105, 1985.
142. Roehrs T, Zorick F, Paxton C, Wittig R, Sicklesteel J, Roth T: The Refreshing Quality of Naps in Patients With Excessive Daytime Sleepiness. II. *Sleep Research* 14: 202, 1985.
143. Wittig R, Zorick F, Lamphere J, Roehrs T, Roth T: Sleep Related Ventricular Ectopy. *Sleep Research* 14: 249, 1985.

144. Seidel WF, Roth T, Cohen SA, Dement WC: Phase-Shift of REM Distribution with Triazolam. *Sleep Research* 14: 311, 1985.
145. Nicholson AN, Pascoe PA, Spencer MB, Stone BM, Roehrs T, Roth T: Adaptation to a New Time Zone After An Inter-Continental Flight: Use Of A Rapidly Eliminated Hypnotic (Brotizolam). *Sleep Research* 14: 50, 1985.
146. Nicholson A, Pascoe P, Spencer M, Stone B, Roehrs T, Roth T: Sleep After A Transmeridian Flight: Use of a Rapidly Eliminated Hypnotic (Brotizolam). *Proceedings of the British Pharmacological Society*: 95, April 1985.
147. Lamphere J, Roehrs T, Vogel G, Koshorek G, Fortier J, Roth T: Efficacy of Chronic Midazolam Administration In Insomnia Patients. *Sleep Research* 15: 34, 1986.
148. Roehrs T, Lumley M, Asker D, Zorick F, Roth T: Ethanol and Caffeine Effects on Daytime Sleepiness. *Sleep Research* 15: 41, 1986.
149. Roth T, Roehrs T, Koshorek G, Sicklesteel J, Zorick F: Central Effects of Antihistamines. *Sleep Research* 15: 43, 1986.
150. Lumley M, Roehrs T, Levine B, Zorick F, Roth T: Nocturnal Sleep in Normals After Sleep Restriction or Extension. *Sleep Research* 15: 74, 1986.
151. Roehrs T, Levine B, Stepanski E, Clark R, Wittig R, Roth T: The Recuperative Value of Fragmented and Non-Fragmented Naps. *Sleep Research* 15: 75, 1986.
152. Zammit G, Rosenbaum A, Stokes P, Davis J, Zorick F, Roth T: The DST and Sleep EEG in Two Types of Depressed Patients: Placebo Responders and Persistent Depressives. *Sleep Research* 15: 98, 1986.
153. Stepanski E, Zorick F, Sicklesteel J, Young D, Roth T: Daytime Alertness-Sleepiness in Patients With Chronic Insomnia. *Sleep Research* 15: 174, 1986.
154. Wittig R, Zorick F, Conway W, Ward J, Roth T: Normalization of the MSLT After Six Weeks of CPAP for Sleep Apnea Syndrome. *Sleep Research* 15: 185, 1986.
155. Young D, Zorick F, Lamphere J, Roehrs T, Wittig R, Roth T: Fragmented Sleep, Daytime Somnolence and Age in Narcolepsy. *Sleep Research* 15: 186, 1986.
156. Levine B, Moyles T, Roehrs T, Fortier J, Roth T: Actigraphic Monitoring and Polygraphic Recording in Determination of Sleep and Wake. *Sleep Research* 15: 247, 1986.
157. Kripke DF, Hauri P, Roth T: Sleep Evaluation in Chronic Insomniacs During Short- and Long-Term Use of Two Benzodiazepines, Flurazepam and Midazolam. *Sleep Research* 16: 99, 1987.
158. Roth T, Linnoila M, Judd LL: Characteristics of Chronic Insomniacs Examined in a Multicenter Study of Two Benzodiazepines, Flurazepam and Midazolam. *Sleep Research* 16: 122, 1987.
159. Roth T, Vogel G, Sterling W: Effects of Temazepam on Transient Insomnia. *Sleep Research* 16: 123, 1987.
160. Zwyghuizen-Doorenbos A, Roehrs T, Lamphere J, Wittig R, Roth T: Increased Daytime Sleepiness Exacerbates Ethanol's Sedative Effects. *Sleep Research* 16: 160, 1987.

161. Zwyghuizen-Doorenbos A, Roehrs T, Smith D, Tietz E, Roth T: Caffeine's Reversal of Triazolam-Induced Impairment of Waking Function. *Sleep Research* 16: 161, 1987.
162. Levine B, Roehrs T, Lamphere J, Zorick F, Stepanski E, Roth T: Daytime Sleepiness in Young Adults. *Sleep Research* 16: 207, 1987.
163. Addison RG, Thorpy MJ, Roth T: A Survey of the United States Public Concerning the Quality of Sleep. *Sleep Research* 16: 244, 1987.
164. Merlotti L, Roehrs T, Young D, Zorick F, Fortier J, Roth T: Symptom Patterns of Narcolepsy Patients: A Questionnaire Study. *Sleep Research* 16: 391, 1987.
165. Merlotti L, Young D, Roehrs T, Fortier J, Zwyghuizen-Doorenbos A, Roth T: Sleepiness Related Daytime Behaviors in Narcoleptics As A Function of Age. *Sleep Research* 16: 392, 1987.
166. Stepanski E, Koshorek G, Zorick F, Roehrs T, Roth T: Sleep and Personality Characteristics of Patients and Subjects With Chronic Complaints of Insomnia. *Sleep Research* 16: 439, 1987.
167. Stepanski E, Markey J, Young D, Zorick F, Sicklesteel J, Roth T: MMPI Profiles of Patient Populations With Excessive Daytime Sleepiness. *Sleep Research* 16: 440, 1987.
168. Wittig RM, Conway WA, Zorick F, Sicklesteel J, Roehrs T, Roth T: CPAP: Reduction in Daytime Sleepiness After One Night's Use. *Sleep Research* 16: 459, 1987.
169. Young D, Zorick F, Wittig R, Roehrs T, Stepanski E, Roth T: Narcolepsy in a Pediatric Population. *Sleep Research* 16: 461, 1987.
170. Zorick F, Henry K, Russo L, Stepanski E, Roehrs T, Conway WA, Roth T: Correlates of Daytime Sleepiness in Apnea Patients. *Sleep Research* 16: 462, 1987.
171. Wittig RM, Keenum AJ, Sarnaik S, Roth T: Snoring, Daytime Sleepiness and Sickle Cell Anemia. *Sleep Research* 16: 514, 1987.
172. Karacan I, Kay DC, Roth T, Orr WC, Kramer M, Williams RL, Salis PJ, Thornby JI, Howell JW, Hirshkowitz M: Subjective and Objective Rebound Insomnia Resulting From The Use of Flurazepam. *Sleep Research* 17: 45, 1988.
173. Koshorek G, Roehrs T, Sicklesteel J, Merlotti L, Russo L, and Roth T: Dose Effects of Zolpidem on Transient Insomnia. *Sleep Research* 17: 47, 1988.
174. Lipschutz L, Roehrs T, Spielman A, Zwyghuizen H, Lamphere J, Roth T: Caffeine's Alerting Effects in Sleepy Normals. *Sleep Research* 17: 49, 1988.
175. Merlotti L, Roehrs T, Koshorek G, Zorick F, Lamphere J, Roth T: The Dose Effects of Zolpidem on the Sleep of Healthy Normals. *Sleep Research* 17: 51, 1988.
176. Merlotti L, Roehrs T, Zorick F, Stepanski E, Russo L, Roth T: Rebound Insomnia, Duration of Administration, and Individual Differences. *Sleep Research* 17: 52, 1988.
177. Nicholson AN, Pascoe PA, Roehrs T, Roth T: Sleep After Transmeridian Flights: Use Of A Rapidly Eliminated Hypnotic (Brotizolam). *Sleep Research* 17: 54, 1988.

178. Zwyghuizen-Doorenbos A, Roehrs T, Timms V, Lamphere J, Russo L, Roth T: Level of Sleepiness and Ethanol's Sedating Effects. *Sleep Research* 17: 68, 1988.
179. Roehrs T, Timms V, Zwyghuizen-Doorenbos A, Fortier J, Stepanski E, and Roth T: Polysomnographic, Performance, and Personality Differences of Sleepy and Alert Subjects. *Sleep Research* 17: 87, 1988.
180. Timms V, Roehrs T, Zwyghuizen-Doorenbos A, Fortier J, Roth T: Sleep Extension in Sleepy and Alert Individuals. *Sleep Research* 17: 92, 1988.
181. Stepanski E, Glinn M, Zorick F, Markey J, Koshorek G, Roth T: The Relation Between Sleep on the First Night in the Laboratory and Personality. *Sleep Research* 17: 132, 1988.
182. Zammit G, Pollak C, Rosenbaum A, Roth T: Early REM Onset and Accumulation in Major Depression: A Test of the Phase-Advance Hypothesis. *Sleep Research* 17: 134, 1988.
183. Rosenthal L, Moyles T, Zorick F, Conway W, Sicklesteel J, Roth T: Hypoxemia and Sleep Fragmentation Is Sleep Apnea. *Sleep Research* 17: 241, 1988.
184. Wittig R, Fujita S, Fortier J, Zorick F, Potts G, Roth T: Results of Uvulopalatopharyngoplasty (UPPP) in Patients With Both Oropharyngeal and Hypopharyngeal Collapse on Mueller Maneuver. *Sleep Research* 17: 269, 1988.
185. Zorick F, Merlotti L, Conway W, Fujita S, Rosenthal L, Roth T: Patient Response to Various Treatments for Sleep Apnea. *Sleep Research* 17: 270, 1988.
186. Wittig R, Keenum A, Sarnaik S, Roth T: Obstructive Sleep Apnea And Sickle Cell Anemia: An Update. *Sleep Research* 17: 309, 1988.
187. Roehrs T, Zwyghuizen-Doorenbos A, Schaefer M, Sicklesteel J, Wittig R, Roth T: Test-Retest Reliability Of The MSLT. *Sleep Research* 17: 348, 1988.
188. Nicholson AN, Pascoe PA, Roehrs T, Roth T, Spencer MB: Sleep After Transmeridian Flights. *Sleep Research* 17: 390, 1988.
189. Roehrs T, Zwyghuizen A, Roth T: Increased Daytime Sleepiness Enhances Ethanol's Sedative Effects. *Alcohol Clin Exp Res* 12(2): 326, 1988.
190. Browman CP, Winslow DH, Starz KE, Roehrs TA, Harris AE, Rosenthal LD, Roth T: Effects of Triazolam, a New Formulation of Triazolam, and Placebo on the Sleep of Patients With Chronic Insomnia. *Sleep Research* 18: 48, 1989.
191. Karacan I, Roth T, Orr WC, Kramer M, Thornby J, Hirshkowitz M: Blood Levels of Flurazepam and Phenobarbital. *Sleep Research* 18: 57, 1989.
192. Koshorek GL, Roehrs TA, Lamphere JK, Harris AE, Nahirniak SR, Roth T: Sedative Effects of the Antihistamine Rocastine. *Sleep Research* 18: 58, 1989.
193. Roehrs TA, Merlotti L, Rosenthal LD, Zorick FJ, Fortier J, Roth T: Benzodiazepine Self Administration in Insomnia. *Sleep Research* 18: 70, 1989.
194. Roehrs TA, Zwyghuizen-Doorenbos A, Zwyghuizen H, Timms V, Fortier J, Roth T: Sedating Effects of Ethanol and Time of Drinking. *Sleep Research* 18: 71, 1989.

195. Vogel G, Scharf M, Walsh J, Roth T: Effects of Chronically Administered Zolpidem on the Sleep of Healthy Insomniacs. *Sleep Research* 18: 80, 1989.
196. Zwyghuizen-Doorenbos A, Roehrs TA, Russo L, Buzenski R, Wittig RM, Lamphere J, Roth T: Continued Sedation and Decline in Drug Concentrations. *Sleep Research* 18: 84, 1989.
197. Plath D, Roehrs TA, Zwyghuizen-Doorenbos A, Sicklesteel J, Wittig RM, Roth T: The Alerting Effects of Caffeine After Sleep Restriction. *Sleep Research* 18: 124, 1989.
198. Zwyghuizen H, Roehrs TA, Zwyghuizen-Doorenbos A, Zorick FJ, Koshorek GL, Roth T: Sedating Effects of Ethanol After A Nap. *Sleep Research* 18: 131, 1989.
199. Merlotti L, Roehrs TA, Clark R, Hilts T, Lamphere J, Roth T: Adaptation to Experimental Sleep Fragmentation. *Sleep Research* 18: 155, 1989.
200. Merlotti L, Roehrs TA, Stepanski EJ, Zorick FJ, Sicklesteel J, Roth T: Consistency of Insomnia With No Objective Findings. *Sleep Research* 18: 261, 1989.
201. Rosenthal LD, Zorick FJ, Merlotti L, Wittig RM, Roehrs TA, Roth T: Signs And Symptoms Associated With Cataplexy In Narcolepsy Patients. *Sleep Research* 18: 298, 1989.
202. Stepanski EJ, Glinn M, Fortier J, Sicklesteel J, Zorick FJ, Roth T: Physiological Reactivity In Chronic Insomnia. *Sleep Research* 18: 306, 1989.
203. Stepanski EJ, Glinn M, Zorick FJ, Lamphere JK, Roth T: Predisposition To and Reliability Of The First Night Effect. *Sleep Research* 18: 307, 1989.
204. Zorick FJ, Potts GE, Wittig RM, Roehrs TA, Rosenthal LD, Roth T: A Comparative Trial of CPAP and UPPP in Alleviating Daytime Sleepiness In Sleep Apnea Patients. *Sleep Research* 18: 325, 1989.
205. Moyles T, Erlandson R, Roth T: A Statistical Technique for Automatic Apnea Detection. *Sleep Research* 18: 396, 1989.
206. Roehrs TA, Wittig RM, Zorick FJ, Conway WA, Roth T: Recovery of Alertness After CPAP in Apnea. *Am Rev Respir Dis* 139 (4Pt2): A115, 1989.
207. Roehrs TA, Potts GE, Zorick FJ, Conway WA, Roth T: Response to CPAP and UPPP in Apnea. *Am Rev Respir Dis* 139 (4Pt2): A115, 1989.
208. Merlotti L, Roehrs TA, Hilts T, Stepanski EJ, Roth T: Reversal of the Effects of Experimental Sleep Fragmentation with Triazolam. *Sleep Research* 19: 78, 1990.
209. Merlotti L, Roehrs TA, Zorick FJ, Lamphere J, Roth T: Self-Administration of Hypnotics in Different Insomnia Populations and Conditions. *Sleep Research* 19: 79, 1990.
210. Roehrs TA, Koshorek G, Merlotti L, Zorick FJ, Wittig RM, Roth T: Dose Related Effects on Rebound Insomnia. *Sleep Research* 19: 84, 1990.
211. Schweitzer PK, Koshorek G, Muehlbach MJ, Morris DD, Groves L, Roehrs T, Walsh JK, Roth T: The Effects of Estazolam 2mg and Triazolam .25mg on Sleep, Performance and Alertness After 180 Degree Sleep/Wake Schedule Reversal. *Sleep Research* 19: 91, 1990.
212. Yoon JS, Roehrs TA, Fortier J, Sicklesteel J, Roth T: Basal Level of Sleepiness and Nocturnal Effects on Ethanol. *Sleep Research* 19: 99, 1990.

213. Roehrs TA, Vogel G, Claiborue D, Lamphere J, Bohannon M, Roth T: Sleepy Versus Alert Subjects in a Phase Advance. *Sleep Research* 19: 123, 1990.
214. Rosenthal LD, Roehrs TA, Hayashi H, Jasti R, Wittig RM, Zorick FJ, Roth T: HLA Typing in Narcolepsy Without Cataplexy. *Sleep Research* 19: 275, 1990.
215. Stepanski E, Zorick F, Peters M, Roth T: Effects of Sleep Deprivation on Alertness in Chronic Insomnia. *Sleep Research* 19: 297, 1990.
216. Zorick FJ, Roehrs TA, Rosenthal LD, Potts G, Conway WA, Wittig RM, Roth T: Natural Course of Sleep Apnea: A Preliminary Report. *Sleep Research* 19: 312, 1990.
217. Rosenthal LD, Roehrs TA, Merlotti L, Lamphere J, Roth T: Enforced 24-Hour Recovery Sleep Following Sleep Deprivation. *Sleep Research* 19: 355, 1990.
218. Carlson ML, Addison RG, Roth T, Thorpy MJ, Wagner R: Subjective Reports of Sleep Parameters and Actigraph Data Compared With Ratings of the Characteristics of Two Different Mattresses: A Pilot Study. *Sleep Research* 19: 363, 1990.
219. Chen D, Chernik DA, Ellinwood E, Hauri P, Johnson LC, Judd LL, Kripke DF, Linnoila M, Moskowitz H, Roth T, Roehrs T, Sateia MJ: A Multicenter Study of Sleep, Performance, and Plasma Levels in Chronic Insomniacs During 14-Day Use of Flurazepam and Midazolam: Executive Summary. *J of Clin Psychopharm* 10(4): 3S, 1990.
220. Knox M, Roehrs TA, Claiborue D, Stepanski EJ, Roth T: Duration of Residual Sedation After Ethanol. *Sleep Research* 20: 66, 1991.
221. Merlotti L, Roehrs TA, Halpin D, Zorick FJ, Roth T: Effects of Azelastine on Daytime Function. *Sleep Research* 20: 70, 1991.
222. Merlotti L, Roehrs TA, Wittig RM, Fortier J, Roth T: Subjective Effects and Benzodiazepine Hypnotic Self Administration. *Sleep Research* 20: 71, 1991.
223. Norman S, Livesey D, Knox M, Roehrs TA, Roth T: Conditioned Drug Effects and Daytime Sleepiness/Alertness. *Sleep Research* 20: 73, 1991.
224. Roehrs TA, Claiborue D, Knox M, Fortier J, Roth T: Napping and the Reversal of Drug-Induced Sedation. *Sleep Research* 20: 77, 1991.
225. Roehrs TA, Merlotti L, Beare D, Rosenthal LD, Stepanski EJ, Roth T: Benzodiazepine Hypnotic Self Administration and Dose Escalation. *Sleep Research* 20: 78, 1991.
226. Roehrs TA, Merlotti L, Zorick FJ, Sicklesteel J, Salin-Pascual RJ, Roth T: Rebound Insomnia After Abrupt or Tapered Discontinuation. *Sleep Research* 20: 79, 1991.
227. Salin-Pascual RJ, Granados-Fuentes D, Galicia-Polo L, Nieves E, Roehrs TA, Roth T: Biperiden Administration During REM Sleep Deprivation Diminished Frequency of REM Sleep Attempts. *Sleep Research*: 20: 82, 1991.
228. Addison RG, Thorpy MJ, Roehrs TA, Roth T: Sleep/Wake Complaints in the General Population. *Sleep Research* 20: 112, 1991.

229. Rosenthal LD, Rosen A, Wittig RM, Zorick FJ, Roehrs TA, Roth T: A Sleep-Wake Activity Inventory to Measure Daytime Sleepiness. *Sleep Research* 20: 130, 1991.
230. Stepanski EJ, Davis T, Sicklesteel J, Zorick FJ, Roth T: Arousal Threshold in Chronic Insomnia. *Sleep Research* 20: 339, 1991.
231. Zorick FJ, Wittig RM, Rosenthal LD, Potts GE, Roehrs TA, Roth T: Natural Course of Sleep Apnea: A 2 Year Follow-Up Study. *Sleep Research* 20: 354, 1991.
232. Rosenthal LD, Merlotti L, Rosen A, Jasti RB, Roehrs TA, Roth T: Total Sleep Time and Level of Sleepiness Following Partial and Total Sleep Deprivation. *Sleep Research* 20: 418, 1991.
233. Merlotti L, Halpin D, Maglio R, Roehrs TA, Rosenthal LD, Roth T: The Effect of Theophylline on Daytime Sleepiness/ Alertness. *Sleep Research* 20A: 158, 1991.
234. Roehrs TA, Roth T: Circadian Rhythm of Sleepiness/ Alertness and Drug Effects. *Sleep Research* 20A: 171, 1991.
235. Rosenthal L, Kozler C, Roehrs TA, Roth T: Nap Behaviors and Subjective Daytime Sleepiness Among College Students. *Sleep Research* 20A: 241, 1991.
236. Rosenthal L, Roehrs TA, Zorick FJ, Roth T, Orenstein HB: The Frequency of Various Sleep Disorders in Different Age Groups. *Sleep Research* 20A: 383, 1991.
237. Merlotti L, Halpin D, Maglio R, Roehrs TA, Rosenthal LD, Wittig R, Roth T: Dose Effects of Theophylline on Nocturnal Sleep and Daytime Alertness. *Sleep Research* 21: 63, 1992.
238. Merlotti L, Roehrs TA, Sicklesteel J, Kaffeman M, Ochs-Campbell R, Wittig RM, Roth T: Sedative, Memory and Performance Effects of Hypnotics. *Sleep Research* 21: 64, 1992.
239. Roehrs TA, Roth T, Scharf M, Vogel G, Walsh J, Ware J, Kaffeman M, Ochs-Campbell R. Rebound Insomnia Potential of Zolpidem 10mg as Evaluated by Three Different Methods. *Sleep Research* 21: 69, 1992.
240. Roth T, Wittek TJ Jr, Merlotti L, Roehrs TA, Fortier J, Riker DK. Dose Related Effect of Diphenhydramine on Daytime Sleepiness. *Sleep Research* 21: 71, 1992.
241. Beare DJ, Roehrs TA, Battle D, Waller P, Zorick FJ, Roth T: Sleepiness and Ethanol Effects on Simulated Driving Performance. *Sleep Research* 21: 99, 1992.
242. Marion J, Roehrs TA, Pedrosi B, Stepanski EJ, Zorick FJ, Roth T. Neuropsychological Test Performance in Obstructive Sleep Apnea, Chronic Insufficient Sleep and Chronic Obstructive Pulmonary Disease. *Sleep Research* 21: 106, 1992.
243. Rosenthal LD, Krstevska S, Roehrs TA, Kontich D, Fortier J, Roth T: Nocturnal Sleep Latencies and TST in Sleepy, Sleep Deprived Alert and Alert Subjects. *Sleep Research* 21: 110, 1992.
244. Rosenthal LD, Roehrs TA, Krstevska S, Rosen A, Sicklesteel J, Roth T: Auditory Awakening Thresholds in Sleepy, Alert, and Sleep Deprived Subjects. *Sleep Research* 21: 111, 1992.
245. Buysse D, Reynolds C, Kupfer D, Hauri P, Stepanski E, Roth T, Manfredi R, Bixler E, Kales A, Thorpy M: Inter-Rater Agreement in Insomnia Diagnoses: Preliminary Results From the DSM-IV Field Trial. *Sleep Research* 21: 184, 1992.

246. Rosenthal LD, Krstevska S, Murlidmar A, Wittig RM, Zorick FJ, Roth T: Reliability of Sleep Onset REM Periods in Narcolepsy. *Sleep Research* 21: 254, 1992.
247. Stepanski EJ, Livesey D, Zorick FJ, Davis T, Roth T: Partial and Total Sleep Deprivation in Insomnia: Preliminary Data. *Sleep Research* 21: 266, 1992.
248. Wittig RM, Mastis L, Zorick FJ, Fortier J, Sickelsteel J, Roth T: Nasal CPAP as a Cause of Central Sleep Apnea. *Sleep Research* 21: 279, 1992.
249. Stepanski EJ, Faber M, Ivey M, Livesey D, Zorick FJ, Wittig RM, Roth T: Sleep Disorders in Patients on Chronic Abdominal Peritoneal Dialysis (CAPD). *Sleep Research* 21: 314, 1992.
250. Roehrs TA, Roth T: The Recuperative Capacity of Fragmented Sleep. *J Sleep Research* 1(Suppl 1): 198, 1992.
251. Rosenthal LD, Roehrs TA, Zorick FJ, Wittig RM, Roth T: Sleep Habits Among Various Sleep Disorder Populations. *J Sleep Research* 1(Suppl 1): 200, 1992.
252. Pedrosi B, Roehrs TA, Stepanski E, Wittig RM, Roth T: Self-Administration of Hypnotics: Dose Escalation. *Sleep Research* 22: 43, 1993.
253. Pedrosi B, Roehrs TA, Stepanski E, Zorick F, Roth T: Hypnotic Self-Administration: Comparison of Methods. *Sleep Research* 22: 44, 1993.
254. Pedrosi B, Roehrs TA, Rosenthal L, Brouillard L, Roth T: Sedating Effects of Triazolam After Sleep Extension. *Sleep Research* 22: 95, 1993.
255. Roehrs TA, Beare DJ, Anderson TG, Koshorek G, Roth T: Ambulatory EEG During Simulated Driving: Effects of Sleep Restriction and Ethanol. *Sleep Research* 22: 98, 1993.
256. Rosenthal L, Kontich D, Folkerts M, Fortier J, Roehrs T, Roth T: Total Sleep Time During an Enforced Time in Bed Period in Sleepy and Alert Subjects. *Sleep Research* 22: 99, 1993.
257. Rosenthal L, Krstevska S, Murlidhar A, Sickelsteel J, Roehrs T, Zorick F, Wittig R, Roth T: The Speed and Nature of Repeated Nocturnal Sleep Onsets in Alert, Sleepy and Narcoleptic Subjects. *Sleep Research* 22: 100, 1993.
258. Roth T, Roehrs TA, Livesey D, Petrucelli N, Shore E: Nocturnal Sleep and Daytime Sleepiness in Normal Volunteers for Research Studies. *Sleep Research* 22: 101, 1993.
259. Pedrosi B, Roehrs TA, Zorick F, Stepanski E, Roth T: Treatment Regimen and Subsequent Self-Administration of Benzodiazepine-Hypnotics. *Sleep Research* 23: 73, 1994.
260. Petrucelli N, Roehrs TA, Rosenthal L, Brouillard L, Roth T: Time of Drinking, Sleep Restriction, and the Sedative Effects of Ethanol. *Sleep Research* 23: 74, 1994.
261. Petrucelli N, Roehrs TA, Wittig RM, Roth T: The Biphasic Effects of Ethanol on Sleep Latency. *Sleep Research* 23: 75, 1994.
262. Roehrs TA, Pedrosi B, Zorick F, Stepanski E, Roth T: Benzodiazepine-Hypnotic Preference: Daytime Versus Nighttime. *Sleep Research* 23: 76, 1994.
263. Roehrs TA, Petrucelli N, Brouillard L, Roth T: Effect of Ethanol on MSLT, Mood, and Performance as a Function of Ethanol Preference. *Sleep Research* 23: 77, 1994.

264. Roehrs TA, Petrucelli N, Wittig RM, Koshorek G, Roth T: Nocturnal Sleep, Daytime Sleepiness, and Ethanol Drinking History. *Sleep Research* 23: 78, 1994.
265. Roehrs TA, Shore E, Papineau K, Rosenthal L, Roth T: A Two-Week Sleep Extension in Sleepy Normals. *Sleep Research* 23: 142, 1994.
266. Rosenthal L, Estivill-Sancho E, Helmus T, Folkerts M, Wittig RM, Roth T: Exacerbating Factors of Behavioral Morbidity in Sleep Apnea Patients in Spain and the United States. *Sleep Research* 23: 144, 1994.
267. Stepanski E, Zorick F, Wittig RM, Brouillard L, Roth T: Modified MSLT Procedure. *Sleep Research* 23: 164, 1994.
268. Rosenthal L, Helmus T, Folkerts M, Krstevska S, Zorick F, Roth T: Auditory Awakening Thresholds in Sleepy and Narcoleptic Subjects. *Sleep Research* 23: 313, 1994.
269. Wittig RM, Zorick F, Fortier J, Kathawalla S, Brouillard L, Roth T: Extending Sleep in Mild to Moderate Sleep Apnea Syndrome. *Sleep Research* 23: 346, 1994.
270. Rosenthal L, Folkerts M, Fortier J, Sicklesteel J, Roehrs TA, Roth T: The Effects of Selective REM Deprivation on Daytime Sleepiness. *Sleep Research* 23: 422, 1994.
271. Roth T, Roehrs TA: Side Effects of Hypnotics—Role of Dose. *Neuropsychopharmacology*, Vol 10, No 3S/Part 1, p 422S, May 1994.
272. Roth T, Roehrs TA: Benzodiazepine Agonists in Insomnia: Efficacy and Safety. *Neuropsychopharmacology*, Vol 10, No 3S/Part 1, p 861S, May 1994.
273. Buysse DJ, Reynolds CF 3D, Hauri PJ, Roth T, Stepanski EJ, Thorpy MJ, Bixler EO, Kales A, Manfredi RL, Vgontzas AN, et al: Diagnostic Concordance for DAM-IV Sleep Disorders: A report from the APA/NIMH DSM-IV Field Trial. *American Journal of Psychiatry* 151(9): 1351-60, 1994.
274. Roehrs T, Claiborne D, Knox M, Roth T: Residual sedating effects of ethanol. *Alcohol Clin Exp Res* 18(4): 831-4, 1994.
275. Billiard M, Partinen M, Roth T, Shapiro C: Sleep and psychiatric disorders. *J Psychosom Res* 38 Suppl 1: 1-2, 1994.
276. Roehrs TA, Merlotti L, Zorick F, Roth T: Sedative, memory, and performance effects of hypnotics. *Psychopharmacology (Berl)* 116(2): 130-4, 1994.
277. Buysse DJ, Reynolds CF 3rd, Kupfer DJ, Thorpy MJ, Bixler E, Manfredi R, Kales A, Vgontzas A, Stepanski E, Roth T et al: Clinical diagnoses in 216 insomnia patients using the International Classification of Sleep Disorders (ICSD), DSM-IV and ICD-10 categories: A report from the APA/NIMH DSM-IV Field Trial. *Sleep* 17(7): 630-7, 1994.
278. Roehrs TA, Merlotti L, Petrucelli N, Stepanski E, Roth T: Experimental sleep fragmentation. *Sleep* 17(5): 438-43, 1994.
279. Koshorek G, Roehrs TA, Rosenthal L, Brouillard L, Roth T: Effects of Low Doses of Quazepam in Elderly Insomniacs. *Sleep Research* 24: 46, 1995.

280. Pedrosi B, Roehrs TA, Rosenthal L, Fortier J, Roth T: Daytime Function and Benzodiazepine Effects in Insomniacs Compared to Normals. *Sleep Research* 24: 48, 1995.
281. Pedrosi B, Roehrs TA, Rosenthal L, Shore E, Rice M, Roth T: Subjective Drug Effect and Treatment Regimen. *Sleep Research* 24: 49, 1995
282. Roehrs TA, Rosenthal L, Pedrosi B, Papineau K, Roth T: Predictors of Hypnotic Self Administration. *Sleep Research* 24: 51, 1995
283. Rosenthal L, Roehrs TA, Paxton J, Koshorek G, Roth T: Tolerance to the Sedative Effects of Antihistamines. *Sleep Research* 24: 52, 1995.
284. Roth T, Roehrs TA, Fortier J, Koshorek G, Fry J, Vogel G, Nino-Murcia J, Beer B: Dose Response Effects of a New Hypnotic in Insomniacs. *Sleep Research* 24: 53, 1995.
285. Rosenthal L, Folkerts M, Helmus T, Feldkamp C, Brouillard L, Roehrs TA, Roth T: Administration of Dexamethasone and its Effects on Sleep and Daytime Alertness. *Sleep Research* 24: 58, 1995.
286. Breslau N, Roth T, Roehrs TA, Rosenthal L, Andreski P: Sleep Disturbance and Psychiatric Disorders. *Sleep Research* 24: 205, 1995.
287. Erman M, Erwin C, Gengo F, Jamieson A, Lemmi H, Mahowald M, Regestein Q, Roth T, Scharf M, Vogel G, Walsh J, Ware JC: Efficacy of Zolpidem and Temazepam in Transient Insomnia. *Sleep Research* 24: 228, 1995.
288. Guido P, Rosenthal L, Bishop C, Roehrs TA, Michaelson S, Syron M, Roth T: The Measurement of Sleepiness in a Sleep Apnea Population. *Sleep Research* 24: 241, 1995.
289. Helmus T, Rosenthal L, Roehrs TA, Roth T: Subjective Level of Daytime Alertness Among Insomnia Patients. *Sleep Research* 24: 245, 1995.
290. Rosenthal L, Bishop C, Helmus T, Roehrs TA, Brouillard L, Roth T: The Frequency of Multiple Sleep Onset REM Periods Among Subjects With No EDS. *Sleep Research* 24: 331, 1995.
291. Walsh JK, Beer B, Erman M, Erwin CW, Fry J, Karacan I, Neubauer D, Rosenthal L, Vogel G, Zammit G, Nelson B, Baker S, Roth T: Treatment of Primary Insomnia Comparing Zaleplon, Triazolam and Placebo. *Sleep Research* 24: 363, 1995.
292. Roehrs TA, Papineau K, Koshorek G, Roth T: The Self Administration of Ethanol as a Hypnotic. *Sleep Research* 24A: 146, 1995.
293. Roehrs TA, Rosenthal L, Bishop C, Farchione T, Henderson T, Roth T: The Alerting Effects of Methylphenidate Under Normal and Deprived Sleep Conditions. *Sleep Research* 24A: 147, 1995.
294. Rosenthal L, Helmus T, Shore E, Mickelson, S, Roehrs TA, Roth T: Polysomnographic Characteristics of OSA as a Function of Differing MSLT Scores. *Sleep Research* 24A: 360, 1995.
295. Roth T: Recognition of insomnias, Their Diagnosis and Public Health Importance. *Sleep Research* 24A: 361. 1995.
296. Koshorek G, Paxton J, Roehrs TA, Rosenthal L, Roth T: Effects of Nighttime Cold Preparations on the Sleep of Healthy Normals. *Sleep Research* 25: 60, 1996.

297. Papineau K, Roehrs TA, Rosenthal L, Roth T: The Self-Administration of Methylphenidate as a Function of Time in Bed. *Sleep Research* 25: 66, 1996.
298. Papineau K, Roehrs TA, Winfuhr K, Tojek T, Rosenthal L, Roth T: Ethanol Effects on Sleep in Normals and Insomniacs. *Sleep Research* 25: 67, 1996.
299. Roehrs T, Papineau K, Fortier J, Rosenthal L, Roth T: The Reinforcing and Subjective Effects of Ethanol as a Hypnotic. *Sleep Research* 25: 70, 1996.
300. Roehrs T, Shore E, Papineau K, Rosenthal L, Roth T: Individual Differences in Response to Sleep Extension: Preliminary Results. *Sleep Research* 25: 110, 1996.
301. Bishop C, Rosenthal L, Guido P, Mickelson SA, Nasir IA, Roehrs TA, Roth T: The Sleep-Wake Habits of Patients with Obstructive Sleep Apnea. *Sleep Research* 25: 203, 1996.
302. Helmus T, Rosenthal L, Syron M, Roehrs TA, Roth T: The Effects of Short and Long Naps Among Narcoleptic, Sleep Deprived and Alert Subjects. *Sleep Research* 25: 254, 1996.
303. Rosenthal L, Folkerts M, Bishop C, Guido P, Syron M, Mickelson SA, Roehrs TA, Roth T: The Level of Daytime Sleepiness and the Perception of Sleep on the MSLT. *Sleep Research* 25: 348, 1996.
304. Rosenthal L, Helmus T, Syron M, Guido P, Roehrs TA, Roth T: The Effect of a Structured Environment on the Recovery of Alertness in OSA Patients Treated with CPAP. *Sleep Research* 25: 349, 1996.
305. Rice FM, Roehrs T, Tojek T, Winfuhr K, Rosenthal L, Guido P, Roth T: MSLT Scoring Reliability in a Patient Population. *Sleep Research* 25: 524, 1996.
306. Bonahoom A, Roehrs TA, Pedrosi B, Rosenthal L, Roth T: Treatment Regimen and Hypnotic Self Administration: Capsule Choice and Predictors. *Sleep Research* 26: 94, 1997.
307. Koshorek G, Roehrs TA, Rosenthal L, Roth T: Performance Effects of Zaleplon and Triazolam With and Without Ethanol. *Sleep Research* 26: 109, 1997.
308. Roehrs TA, Bonahoom A, Pedrosi B, Rosenthal L, Roth T: Treatment Regimen and Hypnotic Self Administration: Subjective Evaluations Of Sleep. *Sleep Research* 26: 124, 1997.
309. Rosenthal L, Day R, Helmus T, Guido P, Syron ML, Roehrs T, Nykamp K, Roth T: The Effects of 8 mg of Dexamethasone on Sleep and Daytime Sleepiness. *Sleep Research* 26: 125, 1997.
310. Breslau N, Rosenthal L, Roehrs TA, Roth T: Factors Associated With Daytime Sleepiness in the General Population. *Sleep Research* 26: 183, 1997.
311. Nykamp K, Rosenthal L, Guido P, Roehrs T, Rice FM, Syron ML, Helmus T, Roth T: The Effects of Sleepiness on Performance Among Patients With OSA. *Sleep Research* 26: 450, 1997.
312. Rosenthal L, Mickelson S, Day R, Guido P, Syron ML, Bishop C, Fortier J, Altman J, Roehrs T, Roth T: The Diagnosis of OSA Based on the Pattern of Snoring and Nocturnal Oximetry. *Sleep Research* 26: 487, 1997.
313. Rosenthal L, Nykamp K, Guido P, Day R, Syron ML, Fortier J, Furcron E, Rice FM, Roehrs T, Roth T: Daytime CPAP Titration Among Patients With Severe OSA. *Sleep Research* 26: 488, 1997.

314. Rosenthal L, Nykamp K, Guido P, Syron ML, Day R, Fortier J, Bishop C, Rice FM, Roehrs T, Roth T: Compliance With CPAP During The First Week of Treatment. *Sleep Research* 26: 489, 1997.
315. Day R, Guido P, Rosenthal L, Syron ML, Nykamp K, Senior B, Roehrs T, Roth T: Effects of Different CPAP Schedules on EDS. *Sleep 21 Suppl.*: 123, 15 Apr 1998.
316. Guido P, Rosenthal L, Nykamp K, Syron ML, Conway C, Roehrs T, Roth T: Sleep Inertia Following One and Twenty Minute Nap Opportunities. *Sleep 21 Suppl.*: 164, 15 Apr 1998.
317. Benham H, Roehrs T, Koshorek G, Fortier J, Rosenthal L, Roth T: Effects of Rhinovirus Type 23 on Sleep and Daytime Function. *Sleep 21 Suppl.*: 176, 15 Apr 1998.
318. Bonahoom A, Roehrs T, Breslau N, Fortier J, Rosenthal L, Roth T: Sleep and Daytime Function Trauma Patients With and Without PTSD. *Sleep 21 Suppl.*: 192, 15 Apr 1998.
319. Roth T, Roehrs T, Bonahoom A, Rosekind M, Koshorek G, Rosenthal L: Cumulative Effects on Sleep Loss. *Sleep 21 Suppl.*: 239, 15 Apr 1998.
320. Rosenthal L, Nykamp K, Day R, Syron ML, Roehrs T, Roth T: The Perception of Sleep During Brief Daytime Sleep Episodes. *Sleep 21 Suppl.*: 259, 15 Apr 1998.
321. Nykamp K, Rosenthal L, Day R, Furcron E, Lumley A, Roehrs T, Roth T: The Characteristics of Sleep and the Level of Sleepiness/Alertness Across the Menstrual Cycle. *Sleep 21 Suppl.*: 260, 15 Apr 1998
322. Rosenthal L, Nykamp K, Day R, Syron ML, Roehrs T, Roth T: The Level of Sleepiness/Alertness Among Evening Type Healthy Subjects. *Sleep 21 Suppl.*: 260, 15 Apr 1998.
323. Johnson EO, Roehrs T, Rosenthal L, Roth T, Breslau N: Epidemiology of Medication as Aids to Alertness in Early Adulthood. *Sleep 21 Suppl.*: 265, 15 Apr 1998.
324. Roehrs TA, Johanson CE, Schuh K, Warbasse L, Roth T: Effects of Cocaine and its Abstinence on Sleep and Daytime Sleepiness. *Sleep 21 Suppl.*: 265, 15 Apr 1998.
325. Turner L, Roehrs T, Rice FM, Guido P, Rosenthal L, Roth T: Effects of Sleep Loss on Waking Actigraphy. *Sleep 21 Suppl.*: 296, 15 Apr 1998.
326. Johnson E, Breslau N, Roehrs T, Roth T: Insomnia in Adolescence: Epidemiology and Associated Problems. *Sleep 22 Suppl.*: S22, 15 Apr 1999.
327. Lumley A, Gerhardstein R, Rosenthal L, Day R, Guido P, Syron ML, Roehrs T, Roth T: The Efficacy of CPAP Treatment in Patients With Mild OSA. *Sleep 22 Suppl.*: S27, 15 Apr 1999.
328. Roth T, Roehrs TA, Bonahoom A, Burduvali E, Rosenthal L: Comparative "Dose" Effects of Ethanol and Sleep Loss. *Sleep 22 Suppl.*: S87, 15 Apr 1999.
329. Greenwald MK, Roehrs T, Turner L, Furcron E, Roth T: "Living On The Edge": Effects of Ethanol, Caffeine, and Basal Sleepiness on Risk-Taking Behavior. *Sleep 22 Suppl.*: S88, 15 Apr 1999.
330. Day R, Rosenthal L, Guido P, Senior B, Syron ML, Walker N, Gerhardstein R, Roth T: Gender Differences Among Patients With Obstructive Sleep Apnea: *Sleep 22 Suppl.*: S198, 15 Apr 1999
331. Roehrs TA, Greenwald MK, Turner L, Koshorek G, Roth T: Effects of Sleep Loss on Risk Taking Behavior. *Sleep 22 Suppl.*: S244, 15 Apr 1999.

332. Roehrs T, Turner L, Rosenthal L, Roth T: Caffeine Reversal of Ethanol Effects on MSLT, Mood and Performance. *Sleep 22 Suppl.*: S338, 15 Apr 1999.
333. Turner L, Roehrs T, Rosenthal L, Roth T: Ethanol and Caffeine Effects on the Sleep of Insomniacs. *Sleep 23 Abstract Supplement: 2*: A48, 15 Apr 2000.
334. Drake CL, Burduvali E, Bonahoom A, Roehrs T, Roth T: Evidence for an Adaptive Process Associated With Cumulative Sleep Loss. *Sleep 23 Abstract Supplement: 2*: A72, 15 Apr 2000.
335. Rosenthal L, Day R, Guido P, Meixner R, Syron ML, Munro J, Roth T: The Prediction of Suitable Candidates for Split-Night Protocols In OSA Populations. *Sleep 23 Abstract Supplement: 2*: A77, 15 Apr 2000.
336. Walsh JK, Roth T, Jamieson A, Schweitzer PK, Scharf MB, Ware JC, Erman M: Intermittent Use of Zolpidem for the Treatment of Primary Insomnia. *Sleep 23 Abstract Supplement: 2*: A86, 15 Apr 2000.
337. Day R, Rosenthal L, Guido P, Koshorek G, Fortier J, Roehrs T, Roth T: Self-Reported Levels of Sleepiness Among Subjects With Insomnia. *Sleep 23 Abstract Supplement: 2*: A89, 15 Apr 2000.
338. Meixner R, Rosenthal L, Day R, Syron ML, Roehrs T, Fortier J, Roth T: The Alerting Effect of 4 mg of Dexamethasone on a Sleep Deprived Population. *Sleep 23 Abstract Supplement: 2*: A121, 15 Apr 2000.
339. Burduvali E, Roehrs TA, Bonahoom A, Rosenthal L, Roth T: Ethanol and Sleep Loss: A "Dose" Comparison of Their Impairing Effects. *Sleep 23 Abstract Supplement: 2*: A159, 15 Apr 2000.
340. Roehrs TA, Andrews M, Koshorek G, Roth T: Outpatient Prescription Patterns of Hypnotic, Anxiolytics and Antidepressants. *Sleep 23 Abstract Supplement: 2*: A168, 15 Apr 2000.
341. Roth T, Zammit G, Kushida C, Doghramji K, Mathias S, Buysse D: Use of the Global Sleep Assessment Questionnaire to Identify Patients With a Sleep Disorder. *Sleep 23 Abstract Supplement: 2*: A323, 15 Apr 2000.
342. Richardson GS, Kaplan RF, Loparo KA, Johnson SE, Roth T: Very High Frequency Energy (Kappa) in Human Surface EEG: Correlation With Behavioral State. *Sleep 23 Abstract Supplement: 2*: A378, 15 Apr 2000.
343. Roehrs TA, Bonahoom A, Pedrosi B, Fortier J, Rosenthal L, Roth T: Treatment Regimen and Self Administration of Hypnotics. *Sleep 24 Abstract Supplement: A65*, 15 Apr 2001.
344. Roehrs TA, Bonahoom A, Pedrosi B, Rossman B, Koshorek G, Rosenthal L, Roth T: Daytime Versus Nighttime Self-Administration of Hypnotics. *Sleep 24 Abstract Supplement: A80*, 15 Apr 2001
345. Johnson EO, Breslau N, Roehrs T, Chase G, Drake C, Roth T: Epworth and Daytime Sleepiness Scales: Psychometric Comparison in a Community-Based Sample. *Sleep 24 Abstract Supplement: A108*, 15 Apr 2001.
346. Richardson GS, Poe GR, Seymour A, Roth T: Objective and Subjective Sleep Disruption Following Dietary Salt Restriction in Normal Subjects. *Sleep 24 Abstract Supplement: A114*, 15 Apr 2001.
347. Meixner RM, Rosenthal L, Gerhardstein R, Day R, Stefadu Y, Syron M, Fortier T, Roehrs T, Roth T: The MSLT Across the Menstrual Cycle in Young Healthy Females. *Sleep 24 Abstract Supplement: A116*, 15 Apr 2001.

348. Hollebeek E, Drake C, Scofield H, Roehrs T, Johnson E, Breslau N, Roth T: Past-Year Opiate Use and Sleep Problems in the General Population. *Sleep 24 Abstract Supplement: A170*, 15 Apr 2001.
349. Burduvali E, Richardson G, Roehrs T, Roth T: Habitual Moderate Caffeine Use: MSLT and Vigilance Performance. *Sleep 24 Abstract Supplement: A173*, 15 Apr 2001.
350. Stefadu Y, Roth T, Roehrs T: Ten-Second Breath Holding in Wake and Overnight Oximetry as a Apnea Screen: A Preliminary Report. *Sleep 24 Abstract Supplement: A295*, 15 Apr 2001.
351. Stefadu Y, Roth T, Rosenthal L: Severe Obstructive Sleep Apnea During Pregnancy Treated With Cpap and Resolved After Delivery: A Case Study. *Sleep 24 Abstract Supplement: A295*, 15 Apr 2001.
352. Johnson EO, Breslau N, Roehrs T, Chase G, Drake C, Roth T: The Association of Insomnia and Alcohol Use: Is it Purely Pharmacological? *Sleep 24 Abstract Supplement: A342*, 15 Apr 2001.
353. Drake C, Johnson EO, Scofield H, Hollebeek E, Roehrs T, Breslau N, Roth T: Insomnia and its Relationship to Sleepiness in a Community-Based Sample. *Sleep 24 Abstract Supplement: A348*, 15 Apr 2001.
354. Day R, Drake CL, Roehrs TA, Hudgel D, Stefadu Y, Parks M, Syron ML, Fortier J, Roth T: Sleep Efficiency During CPAP Titration Predicts Subsequent Compliance. *Sleep 25 Abstract Supplement: A25*, 15 April 2002.
355. Roehrs TA, Johanson CE, Meixner R, Asti T, Fortier J, Roth T: Methylphenidate Preference and Subjective Effects: Time-In-Bed and Dose. *Sleep 25 Abstract Supplement: A44*, 15 April 2002.
356. Rosenberg RP, Jamieson A, Vaickus L, Roth T: Esopiclone, A Novel Non-Benzodiazepine Sedative-Hypnotic: Efficacy and Safety in a Model of Transient Insomnia. *Sleep 25 Abstract Supplement: A68*, 15 April 2002.
357. Drake CL, Roehrs TA, Richardson GS, Roth T: Epidemiology and Morbidity of Excessive Daytime Sleepiness. *Sleep 25 Abstract Supplement A91*, 15 April 2002.
358. Scofield H, Jefferson C, Roehrs T, Burduvali E, Roth T: Neuroticism Predicts Lifetime Prevalence of Insomnia. *Sleep 25 Abstract Supplement: A96*, 15 April 2002.
359. Richardson GS, Drake CL, Roehrs TA, Roth T: Habitual Sleep Time Predicts Accuracy of Self-Reported Alertness. *Sleep 25 Abstract Supplement: A145*, 15 April 2002.
360. Roehrs TA, Johanson CE, Meixner R, Koshorek G, Blaisdell B, Roth T: Methylphenidate's Alerting Effects: Time-In-Bed and Dose. *Sleep 25 Abstract Supplement: A178*, 15 April 2002.
361. Burduvali E, Roehrs TA, Drake C, Richardson GS, Roth T: Substance Use for Insomnia: Daytime Symptoms and Disability. *Sleep 25 Abstract Supplement: A298*, 15 April 2002.
362. Borchert LD, Roth T, Bliwise DL, Cantor C, Gorell JM, Hubbel JP, Pollack C, Rye DB, Stern MB, Watts RL: Unintended Sleep Episodes in Parkinson's Disease Patients Receiving Dopaminergic Agents. *Sleep 25 Abstract Supplement: A372*, 15 April 2002.
363. Drake CL, Roehrs TA, Scofield H, Myers E, Roth T: Polysomnographic and Health Outcomes in an Epidemiological Sample of Individuals with Restless Leg Symptoms. *Sleep 25 Abstract Supplement: A488*, 15 April 2002.

364. Jefferson C, Drake CL, Scofield HM, Roehrs TA, Roth T: The Effects of Obesity on Sleep and Daytime Sleepiness in the Absence of Sleep-Related Breathing Disorders. *Sleep 25 Abstract Supplement: A499*, 15 April 2002.
365. Roth T, Borchert LD, Bartlett C, Math M, Bliwise D, Cantor C, Gorell JM, Hubbel JP, Musch B, Olanow CW, Pollak C, Rye DB, Stern MB, Watts RL: Excessive Daytime Sleepiness in Parkinson's Disease Patients with Unintended Sleep Episodes when Treated with Dopaminergic Agonists. *Neurology 58 (Suppl 3): A433*, April 2002.
366. Brodsky MA, Godbold J, Roth T, Olanow W: Sleepiness in Parkinson's disease: a Controlled Study. *Neurology 58 (Suppl 3): A434*, April 2002.
367. Walsh JK, Lankford DD, Krystal A, Roth T, Jochelson P, Garber M, Alexander T, Burke P: Efficacy and Tolerability of Four Doses of Indiplon (NBI-34060) Modified-Release in Elderly Patients with Sleep Maintenance Insomnia. *Sleep 26 Abstract Supplement: A78*, May 15, 2003.
368. Blaisdell B, Roehrs TA, Greenwald MK, Roth T: Sedative Effects of Codeine. *Sleep 26 Abstract Supplement: A82*, May 15, 2003.
369. Burduvali E, Roehrs TA, Richardson GS, Roth T: Methylphenidate Self Administration and Sampling State of Sleepiness. *Sleep 26 Abstract Supplement: A83*, May 15, 2003.
370. Jochelson P, Bozigian H, Garber M, Baron C, Boyd M, Burke J, Roth T, Campbell B: The Activity of Modified Release Indiplon (NBI-34060) in a Transient Nighttime Venipuncture Model. *Sleep 26 Abstract Supplement: A84*, May 15, 2003
371. Roth T, Walsh JK, Rogowski R, Farber R, Burke J, Jochelson P: Efficacy and Tolerability of Indiplon (NBI-34060) Solution in Healthy Adults in a Model of Transient Insomnia. *Sleep 26 Abstract Supplement: A87*, May 15, 2003.
372. Walsh JK, Hughes R, Czeisler C, Dinges DF, Niebler G, Roth T: Sleepiness on the Night Shift in Shift Work Sleep Disorder. *Sleep 26 Abstract Supplement: A110*, May 15, 2003.
373. Czeisler CA, Dinges DF, Walsh JK, Roth T, Niebler G: Modafinil for the Treatment of Excessive Sleepiness in Chronic Shift Work Sleep Disorder. *Sleep 26 Abstract Supplement: A114*, May 15, 2003.
374. Czeisler CA, Dinges DF, Walsh JK, Neibler G, Roth T: Absence of Detectable Effect of Modafinil on Daytime Sleep After a Simulated Night Shift in SWSD Patients. *Sleep 26 Abstract Supplement: A115*, May 15, 2003.
375. Myers EJ, Drake CL, Roehrs TA, Breslau N, Johnson E, Roth T: Population-Based, Normative Data for the Epworth Sleepiness Scale. *Sleep 26 Abstract Supplement: A194*, May 15, 2003.
376. Roehrs TA, Blaisdell B, Greenwald MK, Roth T: Pain Threshold and Sleep Loss. *Sleep 26 Abstract Supplement: A196*, May 15, 2003.
377. Roth T, Walsh J: Phase II Study of the Selective ML-1 Receptor Agonist TAK-375 in a First Night Effect Model of Transient Insomnia. *Sleep 26 Abstract Supplement: A294*, May 15, 2003.
378. Zammit GK, Gillin JC, McNabb L, Caron J, Roth T: Eszopiclone, a Novel Non-Benzodiazepine Anti-Insomnia Agent: A Six-Week Efficacy and Safety Study in Adult Patients with Chronic Insomnia. *Sleep 26 Abstract Supplement: A297*, May 15, 2003.

379. Drake CL, Scofield HM, Jefferson CD, Roehrs TA, Richardson GS, Roth T: Trait Vulnerability to Stress-Related Sleep Disturbance and Hyperarousal. *Sleep 26 Abstract Supplement: A306*, May 15, 2003.
380. Gillis ME, Roehrs TA, Drake CL, Koshorek G, Roth T: Past-Year Opiate Use and its Correlates in an Age-and-Sex-Matched Sample From the General Population. *Sleep 26 Abstract Supplement: A307*, May 15, 2003.
381. Roehrs TA, Blaisdell B, Richardson GS, Roth T: Insomnia as a Path to Alcoholism: Dose Escalation. *Sleep 26 Abstract Supplement: A307*, May 15, 2003.
382. Krystal A, Walsh J, Roth T, Amato DA, Wessel T: The Sustained Efficacy and Safety of Eszopiclone Over Six Months of Nightly Treatment: A Placebo-Controlled Study in Patients with Chronic Insomnia. *Sleep 26 Abstract Supplement: A310*, May 15, 2003.
383. McClure TK, Drake CL, Roth T, Richardson GS: Sleep and Endocrine Responses to Psychological Stress in Primary Insomnia. *Sleep 26 Abstract Supplement: A311*, May 15, 2003.
384. Drake CL, Myers EJ, Roehrs TA, Miller J, Hudgel D, Roth T: Racial Differences in the Prevalence of Periodic Limb Movement Disorder. *Sleep 26 Abstract Supplement: A337*, May 15, 2003.
385. Mundel T, Martin S, LaMoreaux L, Hotary L, Roth T: Polysomnographic Evaluation of Sleep Disturbance in Neuropathic Pain. *Sleep 26 Abstract Supplement: A354*, May 15, 2003.
386. Roehrs TA, Blaisdell B, Cruz N, Roth T: Tolerance to Hypnotic Effects of Ethanol in Insomniacs. *Sleep 27 Abstract Supplement: A52*, June 2004.
387. Randazzo AC, Roth T, Frankowski S, Shannon K, Walsh JK: The Effects of Tiagabine on the Sleep of Older Adults. *Sleep 27 Abstract Supplement: A53*, June 2004.
388. Burduvali E, Roehrs TA, Blaisdell B, Fortier J, Roth T: Codeine, Pain Threshold, and Midday Sleepiness. *Sleep 27 Abstract Supplement: A53*, June 2004.
389. Erman MK, Dinges DF, Czeisler CA, Walsh JK, Roth T: Patient Functional Status and Tolerability of Long-term Modafinil in Shift Work Sleep Disorder. *Sleep 27 Abstract Supplement: A56*, June 2004.
390. Thorpy MJ, Black J, Erman MK, Roth T, Walsh JK, Czeisler CA, Dinges DF: Tolerability of Modafinil in Disorders of Sleep and Wakefulness. *Sleep 27 Abstract Supplement: A58*, June 2004.
391. Johnson EO, Roth T, Breslau N: Epidemiology of DSM-IV Insomnia among a Community-based Cohort of Adolescents. *Sleep 27 Abstract Supplement: A112*, June 2004.
392. Czeisler CA, Roth T, Walsh JK, Schwarz JR, Dinges DF: Effect of Modafinil During the Night Shift and on the Commute Home in Patients with Excessive Sleepiness Associated with Chronic Shift Work Sleep Disorder. *Sleep 27 Abstract Supplement: A169*, June 2004.
393. Sachdeva P, Budhiraja R, Hudgel DW, Drake CL, Sharief I, Dorazio L, Roth T: The Gender of Obstructive Sleep Apnea Patients does not determine their Adherence to CPAP Therapy. *Sleep 27 Abstract Supplement: A221*, June 2004.
394. Roehrs TA, Drake CL, Roth T: Alcohol Used for Sleep and Increased Social Drinking. *Sleep 27 Abstract Supplement: A255*, June 2004.

395. Walsh JK, Zammit G, Roth T: Sleep-Consolidating Effects of Tiagabine in Patients with Primary Insomnia. *Sleep 27 Abstract Supplement: A256*, June 2004.
396. Walsh JK, Rosenberg R, Roth T, Lankford DA, Jochelson P: Treatment of Primary Insomnia for Five Weeks with Indiplon-IR. *Sleep 27 Abstract Supplement: A259*, June 2004.
397. Roth T, Krystal A, Walsh J, Roehrs T, Wessel T, Caron J: Twelve Months of Nightly Eszopiclone Treatment in Patients with Chronic Insomnia: Assessment of Long-Term Efficacy and Safety. *Sleep 27 Abstract Supplement: A260*, June 2004.
398. Jochelson P, Scharf M, Roth T, Walsh JK, Garber M: Efficacy of Indiplon in Inducing and Maintaining Sleep in Patients with Chronic Sleep Maintenance Insomnia. *Sleep 27 Abstract Supplement: A262*, June 2004.
399. Meola GM, Roth T, Richardson GS: Differential Autonomic Response to Audio Stimulation During Sleep in Primary Insomnia. *Sleep 27 Abstract Supplement: A264*, June 2004.
400. Scharf M, Roth T, Rosenberg R, Lankford DA, Theresa A: Efficacy and Tolerability of Indiplon-IR in the Treatment of Transient Insomnia. *Sleep 27 Abstract Supplement: A267*, June 2004.
401. Drake C, Jefferson C, Roehrs T, Richardson G, Roth T: Vulnerability to Chronic Insomnia: A Longitudinal Population-based Prospective Study. *Sleep 27 Abstract Supplement: A270*, June 2004.
402. Jefferson C, Drake CL, Scofield HM, Myers EJ, Roehrs T, Koshorek G, Roth T: Sleep Hygiene Practices in Insomniacs and Matched Controls in the General Population. *Sleep 27 Abstract Supplement: A273*, June 2004.
403. Drake C, Richardson G, Roehrs T, Walsh JK, Roth T: Prevalence and Consequences of Disturbed Sleep Among Rotating Shift Workers. *Sleep 27 Abstract Supplement: A274*, June 2004.
404. Scofield H, Drake CL, Jefferson CD, Myers EJ, Roth T: Gender Differences in Insomnia are Mediated by Co-Morbid Conditions. *Sleep 27 Abstract Supplement: A275*, June 2004.
405. Budhiraja R, Drake CL, Hudgel DW, Sachdeva P, Sharief I, Roth T: Prevalence of Sleep Disruption is Increased in Subjects with Diverse Medical Disorders even in Absence of Significant Sleep Complaints. *Sleep 27 Abstract Supplement: A276*, June 2004.
406. Budhiraja R, Drake CL, Hudgel DW, Sachdeva P, Sharief I, Roth T: Presence of Underlying Medical Disorders is Associated with more Disrupted Sleep in Subjects with Insomnia. *Sleep 27 Abstract Supplement: A277*, June 2004.
407. McClure TK, Drake CL, Roth T, Richardson GS: Sustained Endocrine and Sleep Responses to a Psychological Stressor in Primary Insomnia. *Sleep 27 Abstract Supplement: A283*, June 2004.
408. Koch H, McClure TK, Meola GM, Drake CL, Roth T, Richardson GS: Prevalence and Correlates of Physiological Hyper-arousal in Patients with Primary Insomnia. *Sleep 27 Abstract Supplement: A284*, June 2004.
409. Hsu T, Roth T, LaMoreaux L, Martin S, Hotary L: Polysomnographic Profile of Patients with Neuropathic Pain and Self-Reported Sleep Disturbance. *Sleep 27 Abstract Supplement: A333*, June 2004.
410. Roth T, Hsu T, LaMoreaux L, Martin S, Hotary L: Disturbed Sleep, Insomnia, and Neuropathic Pain. *Sleep 27 Abstract Supplement: A333*, June 2004.

411. Gillis ME, Snyder-Manson A, Root L, Scholten S, Jones E, Roehrs T, Drake C, Roth T: Diagnosis and Treatment of RLS Among 737 Hemodialysis Patients. *Sleep 27 Abstract Supplement: A334*, June 2004.
412. Johnson D, Orr W, Traxler B, Cuccia A, Marple C, Brown K, Roth T: Effects of Esomeprazole and Placebo on Relief of Moderate to Severe Nighttime Heartburn, Sleep Disturbance and Sleep Quality in Patients with GERD: A Multicenter, Randomized, Controlled Trial. *Sleep 27 Abstract Supplement: A335*, June 2004.
413. Stamatakis KA, Roth T, Kaplan GA: Sleep in the Population: Socioeconomic and Demographic Predictors of Sleep over 34 Years. *Sleep 27 Abstract Supplement: A414*, June 2004.
414. Hsu T, Rogowski R, Roth T: Low-Dose Doxepin in the Treatment of Primary Insomnia. *Sleep 28 Abstract Supplement: A50*, June 2005.
415. Johnson EO, Breslau N, Roth T: Symptoms Of Sleep-Disordered Breathing And Attention Deficit/Hyperactivity Disorder In A Population-Based Sample Of Adolescents. *Sleep 28 Abstract Supplement: A98*, June 2005.
416. Seibold C, Roth T, Johnson EO: Parent and Child Reports of Children's Insomnia: An Assessment of Their Concurrence. *Sleep 28 Abstract Supplement: A99*, June 2005.
417. Budhiraja R, Drake CL, Koshorek G, Roth T: Objective Sleep Quality In Midlife In The General Population. *Sleep 28 Abstract Supplement: A112*, June 2005.
418. Hyde ME, Roehrs TA, Blaisdell B, Burduvali E, Roth T: REM Sleep Deprivation Produces Hyperalgesia. *Sleep 28 Abstract Supplement: A128*, June 2005.
419. Sainati S, Tsymbalov S, Demissie S, Roth T: Double-Blind, Placebo-Controlled, Two-Way Crossover Study of Ramelteon in Subjects With Mild to Moderate Chronic Obstructive Pulmonary Disease (COPD). *Sleep 28 Abstract Supplement: A162*, June 2005.
420. Sainati S, Tsymbalov S, Demissie S, Roth T: Double-Blind, Single-Dose, Two-Way Crossover Study of Ramelteon in Subjects With Mild to Moderate Obstructive Sleep Apnea. *Sleep 28 Abstract Supplement: A163*, June 2005.
421. Hirshkowitz M, Roth T, Black J, Wesnes K, Arora S, Niebler G, White D: Armodafinil as Adjunct Therapy Improves Wakefulness and Fatigue in Patients With Obstructive Sleep Apnea/Hypopnea Syndrome. *Sleep 28 Abstract Supplement: A180*, June 2005.
422. Black J, Wesnes K, Arora S, Niebler G, Roth T: Efficacy and Safety of Armodafinil 150 or 250 mg as Adjunct Therapy for Residual Excessive Sleepiness and Fatigue Associated With Obstructive Sleep Apnea/Hypopnea Syndrome. *Sleep 28 Abstract Supplement: A212*, June 2005.
423. Singh M, Drake C, Roehrs T, Koshorek G, Roth T: The Prevalence of SOREMPS in the General Population. *Sleep 28 Abstract Supplement: A221*, June 2005.
424. Seiden D, Zee P, Weigan S, Sainati S, Bayuk J, Zhang J, Roth T: Double-Blind Placebo-Controlled Outpatient Clinical Trial of Ramelteon for the Treatment of Chronic Insomnia in an Elderly Population. *Sleep 28 Abstract Supplement: A228*, June 2005.

425. Zammit G, Roth T, Erman M, Sainati S, Weigand S, Zhang J: Double-Blind, Placebo-Controlled Polysomnography and Outpatient Trial to Evaluate the Efficacy and Safety of Ramelteon in Adult Patients With Chronic Insomnia. *Sleep 28 Abstract Supplement: A228, June 2005.*
426. Walsh JK, Roth T, Moscovitch A, Farber R, Jochelson P: Efficacy and Tolerability of Indiplon-IR in Elderly Patients with Primary Insomnia. *Sleep 28 Abstract Supplement: A229, June 2005.*
427. Roth T, Zammit G, Scharf MB, Boyd M, Jochelson P: Efficacy And Safety of Indiplon-IR in Adults With Chronic Insomnia Characterized by Prolonged Nighttime Awakenings With Difficulty Returning to Sleep. *Sleep 28 Abstract Supplement: A229, June 2005.*
428. Jefferson C, Drake C, Roehrs T, Roth T, Parker S: Sleep Habits in Healthy Normal Sleepers. *Sleep 28 Abstract Supplement: A238, June 2005.*
429. Scofield H, Drake C, Myers E, Jefferson C, Roth T: Familial Vulnerability to Sleep Disturbance. *Sleep 28 Abstract Supplement: A239, June 2005.*
430. Drake CL, Coyle MA, Jefferson C, Myers E, Derchak P, Roth T: Evidence for Greater Night to Night Variability in Standard Sleep Parameters in Primary Insomniacs Versus Controls in the Naturalistic Setting. *Sleep 28 Abstract Supplement: A242, June 2005.*
431. Roehrs TA, Soubrane C, Roth T: Zolpidem Modified-Release Objectively and Subjectively Improves Sleep Maintenance and Retains the Characteristics of Standard Zolpidem on Sleep Initiation and Duration in Elderly Patients with Primary Insomnia. *Sleep 28 Abstract Supplement: A244, June 2005.*
432. Rosenberg R, Roth T: The Effect of Tiagabine on Sleep in Adult and Elderly Patients With Primary Insomnia: A 30-Day, Placebo-Controlled Study. *Sleep 28 Abstract Supplement: A244, June 2005.*
433. Soubrane C, Walsh J, Roth T: Zolpidem Modified-Release Improves Sleep Induction, Sleep Maintenance, Sleep Duration, and Quality of Sleep Without Next-Day Residual Effects in Adults With Primary Insomnia. *Sleep 28 Abstract Supplement: A244, June 2005.*
434. Johnson EO, Roth T, Breslau N: The Association Of Insomnia With Anxiety Disorders: Exploration of the Direction of Risk Among Adolescents. *Sleep 28 Abstract Supplement: A247, June 2005.*
435. Cruz N, Roehrs TA, Fortier J, Kay S, Roth T: Mood Effects of Pre-Sleep Ethanol in Insomniacs. *Sleep 28 Abstract Supplement: A249, June 2005.*
436. Wright KP, Roth T: The Effects Of Tiagabine In Elderly Patients With Primary Insomnia: A Double-Blind, Placebo-Controlled Study. *Sleep 28 Abstract Supplement: A250, June 2005.*
437. Hays RD, Morlock RJ, Spritzer K, Drake C, Roth T: Psychometric Properties of the Restorative Sleep Questionnaire and Daytime Consequences of Sleep Questionnaire. *Sleep 28 Abstract Supplement: A251, June 2005.*
438. McClure TK, Roth T, Richardson GS: Effects of Induced Sympathetic Arousal on Sleep of Normal Subjects. *Sleep 28 Abstract Supplement: A254, June 2005.*
439. Richardson GS, McClure TK, Meola G, Roth T: Dex-CRH Test in Primary Insomnia. *Sleep 28 Abstract Supplement: A256, June 2005.*
440. Gillis ME, Roehrs TA, Lumley MA, Roth T: Unique REM Rebound Following Sleep Restriction in Fibromyalgia Patients Compared to Rheumatoid Arthritis and Healthy Controls. *Sleep 28 Abstract Supplement: A295, June 2005.*

441. McCall V, Fava M, Wessell T, Rubens R, Caron J, Amato D, Roth T: Eszopiclone Co-Administered With Fluoxetine for Insomnia Associated With Major Depressive Disorder (MDD): An Analysis of the Effects on Depression. *Sleep 28 Abstract Supplement: A310*, June 2005.
442. Buysse D, McCall V, Roach J, Wessel T, Wilson P, Caron J, Roth T: Eszopiclone Co-Administered With Fluoxetine for Insomnia Associated With Major Depressive Disorder (MDD): Sleep Effects. *Sleep 28 Abstract Supplement: A310*, June 2005.
443. Krystal A, Rubens R, Fava M, McCall V, Wessel T, Amato D, Caron J, Roth T: Eszopiclone Co-Administered With Fluxetine for Insomnia Associated With Major Depressive Disorder (MDD): Effects Following Eszopiclone Discontinuation. *Sleep 28 Abstract Supplement: A311*, June 2005.
444. Corrigan M, McCall WV, Fava M, Rubens R, Wessel T, Caron J, Amato D, Roth T: Adjunctive Eszopiclone and Fluoxetine in Major Depressive Disorder and Insomnia: Effects on Sleep and Depression. *Neuropsychopharmacology 30 Abstract Supplement 1*, December 2005.
445. Roth T, Corser B, Singh N, Roth-Schechter B, Mayleben D, Roth A, Pather I: Daytime Pharmacokinetic (PK) And Pharmacodynamic (PD) Evaluation of Low-Dose Transmucosal Zolpidem (TMZ). *Sleep 29 Abstract Supplement: A46*, June 2006.
446. Drake C, Walsh J, Roth T: Armodafinil Improves Sleep Latency in Patients With Shift Work Sleep Disorder. *Sleep 29 Abstract Supplement: A64*, June 2006.
447. Hyde M, Roehrs T, Blaisdell B, Burduvali E, Roth T: REM Deprivation Effects on Physiologic Sleepiness, Performance and Mood. *Sleep 29 Abstract Supplement: A129*, June 2006.
448. Singh M, Drake C, Koshorek G, Roehrs T, Roth T: The Association Between Assays of Sleep Drive and Objective Versus Subjective Sleepiness. *Sleep 29 Abstract Supplement: A139*, June 2006
449. Hayduk R, Harsh J, Roth T: Armodafinil Improves Subjective Measures of Sleepiness in Patients With Excessive Sleepiness Associated With Obstructive Sleep Apnea/Hypopnea Syndrome, Narcolepsy, and Shift Work Sleep Disorder. *Sleep 29 Abstract Supplement: A227*, June 2006.
450. Hull S, Roth T, Roehrs T: Armodafinil Does Not Affect Intended Sleep as Determined by Polysomnography in Patients With Excessive Sleepiness. *Sleep 29 Abstract Supplement: A228*, June 2006.
451. Roth T, Jaeger S, Jin R, Krishnan A, Stang PE, Kessler RC: Sleep Problems, Comorbid Mental Disorders, and Role Functioning in the National Cormorbidity Survey Replication (NCS-R). *Sleep 29 Abstract Supplement: A234*, June 2006. PMID: 16952333
452. Zammit G, Schwartz H, Roth T, Wang-Weigand S, Zhang J: Effect of Ramelteon, a Selective MT1/MT2 Receptor Agonist, in a First-Night-Effect Model of Transient Insomnia. *Sleep 29 Abstract Supplement: A238*, June 2006.
453. Seiden D, Wang-Weigand S, Zhang J, Sainati S, Roth T: Sleep-Promoting Effects of Ramelteon, a Selective MT1/MT2 Receptor Agonist, in Older Adults With Chronic Insomnia. *Sleep 29 Abstract Supplement: A238*, June 2006.
454. Schnitzer T, Rubens R, Wessel T, Caron J, Amato D, Hayduk R, Roth T: The Effect of Eszopiclone 3 mg Compared With Placebo in Patients With Rheumatoid Arthritis and Co-Existing Insomnia. *Sleep 29 Abstract Supplement: A238*, June 2006.

455. Roth T, Rogowski R, Hull S, Cohn M, Lankford A, Mayleben D, Scharf M: Efficacy and Safety of Doxepin 1, 3, and 6 mg in Elderly Adults With Primary Insomnia. *Sleep 29 Abstract Supplement: A239*, June 2006.
456. Krystal A, Walsh J, Fava M, McCall V, Schaefer K, Rubens R, Wessel T, Caron J, Wilson P, Roth T: Analysis of Individual Items of the Hamilton Depression Scale in a Study of Eszopiclone/Fluoxetine Co-Therapy. *Sleep 29 Abstract Supplement: A240*, June 2006.
457. McCall V, Krystal A, Rubens R, Wessel T, Caron J, Huang H, Anderson A, Roth T: Two Double-Blind, Placebo-Controlled, 6-Month Trials of Eszopiclone for Insomnia: Pooled Analysis by Race/Ethnicity. *Sleep 29 Abstract Supplement: A249*, June 2006.
458. McCall V, Krystal A, Fava M, Rubens R, Schaefer K, Huang H, Amato D, Roth T: Eszopiclone Co-Administered With Fluoxetine for Insomnia Co-Existing With Major Depressive Disorder (MDD): Analysis by Severity of Insomnia. *Sleep 29 Abstract Supplement: A249*, June 2006.
459. Krystal A, Walsh J, Rubens R, Wilson P, Caron J, Wessel T, Roth T: Efficacy and Safety of Six-Months of Nightly Eszopiclone in Patients with Primary Insomnia: A Second Long Term Placebo-Controlled Study. *Sleep 29 Abstract Supplement: A249*, June 2006.
460. Doghramji P, Winkelman J, Rubens R, Schaefer K, Claus R, Roach J, Roth T: Evaluation of Patient Satisfaction: Regimen of Eszopiclone Sleep Satisfaction Trial (RESST). *Sleep 29 Abstract Supplement: A250*, June 2006.
461. Staner L, Muscat N, Cornette F, Santoro F, Pettersson A, Roth T, Luthringer R: Sublingual Zolpidem Compared to Oral Zolpidem in the Post-Nap Sleep Model of Insomnia. *Sleep 29 Abstract Supplement: A254*, June 2006.
462. Scharf M, Roth T, Walsh JK, Landin R, Farber R: Efficacy of Indiplon During the First Treatment Night in Studies of Primary Insomnia. *Sleep 29 Abstract Supplement: A255*, June 2006.
463. Jefferson C, Roth T, Roehrs T, Drake C: Correlates of Sleep Estimates in Insomniacs and Controls. *Sleep 29 Abstract Supplement: A259*, June 2006.
464. Watson KS, Koch H, Roth T, Richardson GS: Dexamethasone Attenuates Effects of Sleep Deprivation on Alertness in Primary Insomnia. *Sleep 29 Abstract Supplement: A266*, June 2006.
465. McClure TK, Linn S, Watson KS, Roth T, Richardson GS: Primary Insomnia With Hyperarousal is Associated With a History of Childhood Stress. *Sleep 29 Abstract Supplement: A267*, June 2006.
466. Scofield H, Roth T, Drake C: Presence of Sleep/Wake Symptoms in Periodic Leg Movement Disorders. *Sleep 29 Abstract Supplement: A290*, June 2006.
467. Walsh JK, Randazzo AC, Stone K, Dickey P, Feren S, Eisenstein RD, Kay S, Roth T, Schweitzer PK: Slow Wave Sleep Enhancement Promotes Sustained Attention Independently From Alertness. *Sleep 29 Abstract Supplement: A364*, June 2006.
468. Schweitzer P, Czeisler C, Dinges D, Roth T, Walsh J: Individual Differences in Alertness and Performance at Night in Patients With Shift-Work Sleep Disorder. *Sleep 30 Abstract Supplement: A50*, June 2007.
469. Schweitzer P, Griffin K, Roth T, Walsh J: Intraindividual Decrements in Sleepiness and Performance Following Sleep Restriction are Unrelated. *Sleep 30 Abstract Supplement: A122*, June 2007.

470. Drake C, Scofield H, Jefferson C, Roehrs T, Breslau N, Johnson E, Myers E, Roth T: MSLT Defined Sleepiness Predicts Verified Automotive Crashes in the General Population. *Sleep 30 Abstract Supplement: A131*, June 2007.
471. Harsh J, Bogan R, Roth T: Modafinil Improves Patients' Ability to Sustain Wakefulness in Everyday Situations: An Analysis of Responses to the Individual Questions of the Epworth Sleepiness Scale. *Sleep 30 Abstract Supplement: A171*, June 2007.
472. Kleinman L, Roth T, Buysse D, Kalsekar A, Harding G, Lichstein K, Revicki D: Patient-Reported Outcomes (PROS) in Insomnia: An Endpoint Model. *Sleep 30 Abstract Supplement: A231*, June 2007.
473. Anderson D, Roth T, Zheng Y, Vandormael K, Smith A, Li M, Digraivo D: Efficacy and tolerability of Gaboxadol in Adults With Primary Insomnia: A 3-Month, Randomized, Double-Blind, Placebo-Controlled Trial. *Sleep 30 Abstract Supplement: A234*, June 2007.
474. Hull S, Roth T, Scharf M, Lankford A, Rosenberg R, Rosenthal M, Singh N, Maguire Y: Dose-Response Effects of Sublingual Transmucosal Zolpidem 3.5mg And 1.75mg in Middle-Of-The-Night (MOTN) Insomnia. *Sleep 30 Abstract Supplement: A240*, June 2007.
475. Erman M, Krystal A, Zammit G, Soubrane C, Roth T: Long-Term Efficacy of Zolpidem Extended-Release in the Treatment of Sleep Maintenance and Sleep Onset Insomnia with Improvements in Next-Day Functioning. *Sleep 30 Abstract Supplement: A241*, June 2007.
476. Roth T, Scharf M, Hull S, Lankford A, Rosenberg R, Rosenthal M, Maguire Y, Singh N: Efficacy And Safety of Sublingual Transmucosal Zolpidem 3.5mg And 1.75mg In The Middle-Of-The-Night (MOTN) Insomnia. *Sleep 30 Abstract Supplement: A241*, June 2007.
477. Erman M, Krystal A, Zammit G, Soubrane C, Roth T: No Evidence of Rebound Insomnia in Patients With Chronic Insomnia Treated With Zolpidem Extended-Release 12.5mg Administered "As Needed" 3-7 Nights/Week for 6 Months. *Sleep 30 Abstract Supplement: A241*, June 2007.
478. Schaefer K, McCall W, Krystal A, Rubens R, Wilson P, Pflieger K, Roth T: Relative Effect Sizes of Eszopiclone Treatment for Insomnia in Patients With Primary Insomnia and Insomnia Co-Morbid With Major Depressive Disorder, Generalized Anxiety Disorder, Perimenopausal Transition or Rheumatoid Arthritis. *Sleep 30 Abstract Supplement: A243*, June 2007.
479. Krystal A, Fava M, Pollack M, Rubens R, Schaefer K, Amato D, Roth T: Sleep Outcomes Following Eszopiclone Discontinuation in Patients With Primary Insomnia and Insomnia Co-Existing With Major Depressive Disorder or Generalized Anxiety Disorder. *Sleep 30 Abstract Supplement: A245*, June 2007.
480. Morin C, Schaefer K, Roach J, Pflieger K, McCall W, Roth T: Baseline Sleep Impairment As Assessed by the Insomnia Severity Index in Patients With Primary Insomnia and Insomnia Co-Morbid With Psychiatric or Other Physical Disorders. *Sleep 30 Abstract Supplement: A245*, June 2007.
481. Roth T, Wilson P, Schaefer K, Rubens R, Walsh J, Krystal A: Baseline Insomnia Severity in Patients With Primary Insomnia and Insomnia Co-Morbid With Major Depressive Disorder, Generalized Anxiety Disorder, Perimenopausal Transition Or Rheumatoid Arthritis. *Sleep 30 Abstract Supplement: A247*, June 2007.
482. Rubens R, Wilson P, Schaefer K, McCall W, Roth T: Changes in Sleep Outcomes With Placebo Treatment in Patients With Primary Insomnia and Insomnia Co-Morbid With Peri-Menopausal Transition or Rheumatoid Arthritis. *Sleep 30 Abstract Supplement: A247*, June 2007.

483. McClure T, Drake C, Roth T: Work Productivity in Insomnia. *Sleep 30 Abstract Supplement: A251*, June 2007.
484. Lankford A, Hull S, Scharf M, Schwartz H, Seiden D, Jochelson P, Rogowski R, Roth T, Group S: Efficacy and Safety of Doxepin 3 and 6mg in Adults With Primary Insomnia. *Sleep 30 Abstract Supplement: A256*, June 2007.
485. Drake C, Roehrs T, Schwartz J, Scofield H, Roth T: Degree and Associations of Sleepiness in Insomniacs and Controls. *Sleep 30 Abstract Supplement: A263*, June 2007.
486. Birznieks G, Scott C, Baroldi P, Polymeropoulos M, Roth T: Melatonin Agonist VEC-162 Improves Sleep Onset and Maintenance in a Model of Transient Insomnia. *Sleep 30 Abstract Supplement: A264*, June 2007.
487. Schwartz H, Hull S, Seiden D, Rogowski R, Jochelson P, Peterson G, Ludington E, Durrence H, Roth T: Efficacy and Safety of Doxepin 6mg in a Model of Transient Insomnia. *Sleep 30 Abstract Supplement: A266*, June 2007.
488. Watson K, McClure T, Linn S, Roth T, Richardson G: ACTH and Cortisol Responses to DEX/CRH in Primary Insomnia. *Sleep 30 Abstract Supplement: A273*, June 2007.
489. Burger A, Stout R, Gillis M, Burduvali E, Lumley M, Roehrs T, Roth T: Unique REM Rebound Following Sleep Restriction in Fibromyalgia Patients is Not Related To a Prior History of Depression. *Sleep 30 Abstract Supplement: A322*, June 2007.
490. Stout R, Burger A, Villareal A, Gillis M, Lumley M, Roehrs T, Roth T: Objective Sleepiness Following Sleep Restriction in Rheumatoid Arthritis and Fibromyalgia. *Sleep 30 Abstract Supplement: A323*, June 2007.
491. Hyde M, Roehrs T, Greenwald M, Roth T: Post-Surgical Analgesia Predicted by Pre-Surgical Self Reported Sleep. *Sleep 30 Abstract Supplement: A327*, June 2007.
492. Pollack M, Rubens R, Amato D, Schaefer K, Pfleeger K, Hayduck R, Roth T: Effects of Eszopiclone Co-Therapy With Escitalopram on Measures of Anxiety and Mood Outcomes in Patients With Insomnia and Comorbid Generalized Anxiety Disorder. *Sleep 30 Abstract Supplement: A330*, June 2007.
493. McCall W, Schaefer K, Rubens R, Huang H, Pfleeger K, Hayduk R, Roth T: Effects Of Eszopiclone Co-Therapy With Escitalopram On Sleep Outcomes In Patients With Insomnia And Comorbid Generalized Anxiety Disorder. *Sleep 30 Abstract Supplement: A330*, June 2007.
494. Amato D, McCall W, Roth T, Schaefer K, Rubens R, Wilson P, Walsh J: A Comparison of Nightly and Weekly Patient Reports of Sleep by Insomniacs Using Integrated Voice Response System (IVRS). *Sleep 30 Abstract Supplement: A344*, June 2007.
495. Linn S, McClure T, Monaghan K, Bluhm D, Watson K, Roth T, Richardson G: Association of Serotonin Transporter (5HTT) Gene Polymorphism With Amount of Slow-Wave Sleep in Human Subjects. *Sleep 30 Abstract Supplement: A365*, June 2007.
496. Gumenyuk V, Robinson S, Jefferson C, Roth T, Barkley GL, Tepley N, Drake C: Brain Micro-Changes during the Transition to Sleep: Evidence from Magnetoencephalographic (MEG) Localization of Differences between 8-11Hz and 12-15Hz Frequency. *Sleep 31 Abstract Supplement: A12*, 2008.

497. Roehrs T, Harris E, Hyde M, Roth T: Codeine Effects in Sleepy Versus Alert Healthy Normals. Sleep 31 Abstract Supplement: A33, 2008.
498. Randall S, Maan R, Roehrs T, Roth T: Pre-Sleep Salivary Cortisol Levels in Insomniacs Using Zolpidem Long-Term. Sleep 31 Abstract Supplement: A37, 2008.
499. Roth T, Lankford A, Accomando WP, Sprenger KJ, Aneiro L: Sleep Onset and Maintenance in Patients with Chronic Insomnia Treated with Adipiplon in a Cross-Over Study. Sleep 31 Abstract Supplement: A40, 2008.
500. Rosenberg R, Seiden DJ, Hull SG, Erman M, Schwartz H, Anderson C, Prosser W, Sanchez M, Chuang E, Roth T: APD125, a Selective Serotonin 5-HT_{2A} Receptor Inverse Agonist, Significantly Improves the Key Parameters of Sleep Maintenance in Patients with Primary Insomnia. Sleep 31 Abstract Supplement: A224, 2008.
501. Mayleben D, Lankford A, Pitman V, Clark DJ, Werth J, Stern T, Roth T: A Non-Interventional Study to Objectively Validate Non-Restorative Sleep as a Component of Insomnia Distinct from Difficulty Initiating or Maintaining Sleep. Sleep 31 Abstract Supplement: A230, 2008.
502. Roth T, Durrence H, Gotfried M, Hull S, Corser B, Scharf M, Orr W, Buddharaju V, Schwartz H, Jochelson P: Efficacy and Safety of Doxepin 1 and 3 mg in a 3-Month Trial of Elderly Adults with Chronic Primary Insomnia. Sleep 31 Abstract Supplement: A230, 2008.
503. Friedman NP, Roth T, Wright KP, Drake CL: Sleep Reactivity to Stress and Insomnia: Genetic and Environmental Contributions. Sleep 31 Abstract Supplement: A231, 2008.
504. Linn S, McClure TK, Monaghan K, Bluhm D, Roth T, Richardson G: Serotonin Transporter (5HTT) Gene Polymorphisms and Risk of Primary Insomnia. Sleep 31 Abstract Supplement: A233, 2008.
505. Roth T, Krystal AD, Maguire Y, Singh N, Maytom M: Pharmacokinetics of the Sublingual Zolpidem Tartrate 3.5 mg Lozenge Compared to the Oral Zolpidem Tartrate 10 mg Tablet. Sleep 31 Abstract Supplement: A235, 2008.
506. Chhangani B, Roehrs T, Cruz N, Roth T: Effects of Ethanol on Sleep in Insomniacs: An Analysis by Halves of the Night. Sleep 31 Abstract Supplement: A246, 2008.
507. Lankford A, Segal S, Borders J, Anderson D, Durrence H, Rogowski R, Ludington E, Roth T: Efficacy and Safety of Doxepin 6 mg in a 4-Week Outpatient Trial of Elderly Adults With Primary Insomnia. Sleep 31 Abstract Supplement: A256, 2008.
508. Lankford A, Krystal A, Durrence H, Jochelson P, Rogowski R, Kittrelle J, Roth T: Doxepin 3 and 6 mg in a 35-Day Trial of Adults with Primary Insomnia: Effects Following Discontinuation. Sleep 31 Abstract Supplement: A256, 2008.
509. Krystal A, Lankford A, Durrence H, Jochelson P, Rogowski R, Kittrelle J, Roth T: Efficacy of Doxepin 3 and 6 mg on Early Morning Awakenings in Adults with Primary Insomnia. Sleep 31 Abstract Supplement: A257, 2008.
510. Ancoli-Israel S, Krystal A, Durrence H, Jochelson P, Rogowski R, Roth T: Consistency of Symptom Improvement in Elderly Adults with Chronic Insomnia Treated with Doxepin 1,3, and 6 mg. Sleep 31 Abstract Supplement: A257, 2008.

511. Stroe AF, Roth T, Jefferson C, Gajos K, Hudgel DW, Drake C: Excessive Sleepiness Predicted by Specific Medical Disorders and Depression: A Population-Based Study. *Sleep 31 Abstract Supplement: A298, 2008.*
512. Harris E, Roehrs T, Hyde M, Roth T: Pain Sensitivity in Sleepy Versus Alert Healthy Normals. *Sleep 31 Abstract Supplement: A300, 2008.*
513. Vernon MK, O'Quinn S, McQuarrie K, Norquist JM, Dinges D, Roth T, Herring W, Brodovicz K: Development of a Excessive Sleepiness Diary. *Sleep 31 Abstract Supplement: A308, 2008.*
514. Fava M, Asnis G, Shrivastava R, Lydiard RB, Bastani B, Sheehan D, Roth T: Improved Insomnia Symptoms and Daily Functioning in Patients with Comorbid Major Depressive Disorder and Insomnia Following Zolpidem Extended-Release 12.5 mg and Escitalopram Co-Treatment. *Sleep 31 Abstract Supplement: A324, 2008.*
515. Sheehan D, Asnis G, Shrivastava R, Lydiard RB, Bastani B, Roth T, Fava M: Zolpidem Extended-Release 12.5 mg Co-Administered with Escitalopram Improves Insomnia Symptoms and Next-Day Functioning in Generalized Anxiety Disorder Comorbid with Chronic Insomnia. *Sleep 31 Abstract Supplement: A325, 2008.*
516. Gumenyuk V, Spear L, Jefferson C, La-Rose C, Roth T, Korzyukov O, Drake C: Armodafinil Improves Brain Activity Related to Sensory Memory and Pre-Attentive Novelty Detection in Patients with Shift Work Disorder. *Sleep 32 Abstract Supplement: A5, 2009.*
517. Drake C, Gumenyuk V, Jefferson C, La-Rose C, Spear L, Kick A, Roth T: Armodafinil in Shift Work Disorder: Normalization of the MSLT. *Sleep 32 Abstract Supplement: A34, 2009.*
518. Randall S, Roehrs T, Maan R, Roth T: Chronic Hypnotic Use: Risk of Rebound Insomnia. *Sleep 32 Abstract Supplement: A34, 2009.*
519. Randall S, Roehrs T, Maan R, Roth T: Chronic Hypnotic Use: Its Abuse Liability. *Sleep 32 Abstract Supplement: A34-A35, 2009.*
520. Diederichs C, Roehrs T, Hyde M, Greenwald M, Roth T: Post Surgery Patient Controlled Analgesia in Smokers and Non Smokers. *Sleep 32 Abstract Supplement: A41-A42, 2009.*
521. Wright KP, Dinges DF, Roth T, Walsh JK, Czeisler CA: Circadian Phase in Patients with Shift-Work Disorder (SWD): Influence on Nighttime Sleepiness, Performance and Daytime Sleep. *Sleep 32 Abstract Supplement: A46, 2009.*
522. Zee P, Wang-Weigand S, Ogrinc F, Roth T: The Use of Ramelteon to Advance Sleep Timing and Melatonin Phase in Delayed Sleep Phase Disorder. *Sleep 32 Abstract Supplement: A48-A49, 2009.*
523. Rosenberg R, Bogan RK, Yang R, Tiller J, Youakim JM, Roth T: Sleep Characteristics in Subjects Recruited for a Jet Lag Study. *Sleep 32 Abstract Supplement: A51, 2009.*
524. Bogan R, Tiller J, Yang R, Youakim J, Roth T: Armodafinil for Excessive Sleepiness Associated with Jet Lag Disorder. *Sleep 32 Abstract Supplement: A52, 2009.*
525. Hirshkowitz M, Lankford A, Roth T, Yang R, Rippon GA: Adjunctive Armodafinil Improves Wakefulness Throughout the Day in CPAP-Treated Patients With Excessive Sleepiness Associated with Obstructive Sleep Apnea. *Sleep 32 Abstract Supplement: A194-A195, 2009.*

526. Roth T, Harsh J, Walsh J, Rosenberg R, Yang R, Rippon G: Armodafinil Improves Wakefulness Throughout the Day in Patients with Excessive Sleepiness Associated with Narcolepsy. *Sleep 32 Abstract Supplement: A245, 2009.*
527. Richardson GS, Renier K, Kristin M, Shapiro L, Roth T: CRH Type 1 Receptor (CRHR1) Polymorphisms and Risk for Primary Insomnia. *Sleep 32 Abstract Supplement: A253, 2009.*
528. Friedman NP, Roth T, Wright KP, Drake CL: Genetic and Environmental Relations Between Insomnia and Intrusive Thinking: The Contribution of Sleep Reactivity to Stress. *Sleep 32 Abstract Supplement: A255, 2009.*
529. Kessler RC, Coulouvrat C, Hajak G, Roth T, Shillington AC, Walsh JK, Vita AJ: American Insomnia Survey: Methodology. *Sleep 32 Abstract Supplement: A265-A266, 2009.*
530. Morin C, Krystal A, McCall V, Schaefer K, Claus R, Wilson A, Friedman M, Roth T, Ancoli-Israel S: A Responder Analysis Using the Insomnia Severity Index in Older Adults Treated for 12 Weeks with Eszopiclone 2 MG or Placebo. *Sleep 32 Abstract Supplement: A-266-A267, 2009.*
531. Krystal A, Cooper J, Schaefer K, Friedman M, Roth T: Weight Changes in Patients with Primary Insomnia Following Long-Term Eszopiclone Treatment. *Sleep 32 Abstract Supplement: A280-A281, 2009.*
532. Roth T, Rosenberg R, Seiden D, Singh N, Steinberg F, Sakai S, Krystal A: As-Needed Treatment of Insomnia Following MOTN Awakening: Clinical Efficacy of Low-Dose Zolpidem Tartrate Sublingual Lozenge. *Sleep 32 Abstract Supplement: A282, 2009.*
533. Rosenberg R, Roehrs T, Singh N, Steinberg F, Roth T: Absence of Rebound Effects with Low-Dose Zolpidem Tartrate Sublingual Lozenge 3.5 MG (ZSL) PRN Use: Preliminary Analysis. *Sleep 32 Abstract Supplement: A282-A283, 2009.*
534. Randall S, Maan R, Drake C, Roehrs T, Roth T: Elevated MSLTs in Insomniacs Compared to Population Controls. *Sleep 32 Abstract Supplement: A283, 2009.*
535. Diederichs C, Roehrs T, Stout R, Burger A, Lumley M, Roth T: Sleepiness and Fatigue in Fibromyalgia and Rheumatoid Arthritis Patients. *Sleep 32 Abstract Supplement: A336, 2009.*
536. Kleinman L, Harding G, Van Brunt DL, Sarsour K, Kalsekar A, Lichstein KL, Buysse DJ, Roth T: Psychometric Validation of the Assessment of Sleep Questionnaire. *Sleep 32 Abstract Supplement: A369-A370, 2009.*
537. Kleinman L, Harding G, Van Brunt DL, Sarsour K, Kalsekar A, Lichstein KL, Buysse DJ, Roth T: Psychometric Validation of the Daytime Consequences of Insomnia Questionnaire. *Sleep 32 Abstract Supplement: A371, 2009.*
538. Harris E, Roehrs T, Hyde M, Roth T: Extended Sleep in Sleepy Normals is Analgesic. *Sleep 32 Abstract Supplement: A410, 2009.*
539. Harris E, Roehrs T, Hyde M, Roth T: A Four-Night Sleep Extension Normalizes MSLT in Sleepy Normals. *Sleep 32 Abstract Supplement: A410-A411, 2009.*
540. Drake C, Jefferson C, Kick A, Roth T: The Effects of Caffeine Given 0, 3, or 6 Hours Before Bed on Objective Sleep Parameters Measured in the Home. *Sleep 33 Abstract Supplement: A107, 2010.*

541. Drake C, Gumenyuk V, Jefferson C, Kick A, Coaker M, Roth T: Extending Time in Bed in Short Sleepers: Effects on Objective Sleep Parameters Measured in the Home. *Sleep 33 Abstract Supplement: A113*, 2010.
542. Khalid I, Roehrs T, Li SM, Cruz N, Hudgel D, Roth T: CPAP in Severe Obstructive Sleep Apnea Reduces Pain Sensitivity. *Sleep 33 Abstract Supplement: A170-A171*, 2010.
543. Gumenyuk V, Roth T, Spear L, Jefferson C, Kick A, Drake C: Impairment of Neurophysiological Markers of Attention Captured in Shift Work Disorder Patients: Effects of Armodafinil. *Sleep 33 Abstract Supplement: A184*, 2010.
544. Walsh JK, Coulouvrat C, Kessler RC, Sampson N, Hajak G, Roth T: Impairment and Disability Associated with Insomnia Diagnosed by DSM-IV, RDC and ICD Criteria and Associated with Insomnia Symptoms: Results from the American Insomnia Survey. *Sleep 33 Abstract Supplement: A192*, 2010.
545. Richardson GS, Cassidy-Bushrow A, Roth T: Correlation Between Urine Norepinephrine and Cortisol in Insomnia: Evidence for Central Dysregulation. *Sleep 33 Abstract Supplement: A195-A196*, 2010.
546. Herring WJ, Budd KS, Hutzelmann J, Snyder E, Snavely D, Liu K, Lines C, Michelson D, Roth T: Efficacy and Tolerability of the Dual Orexin Receptor Antagonist MK-4305 in Patients with Primary Insomnia: Randomized, Controlled, Adaptive Crossover Polysomnography Study. *Sleep 33 Abstract Supplement: A199*, 2010.
547. Randall S, Roehrs T, Harris E, Maan R, Roth T: Twelve Months of Nightly Zolpidem Does Not Enhance the Likelihood of Rebound Insomnia: A Prospective Placebo Controlled Study. *Sleep 33 Abstract Supplement: A199-A200*, 2010.
548. Roehrs T, Randall S, Harris E, Maan R, Roth T: Twelve Months of Nightly Zolpidem Does Not Lead to Dose Escalation: A Prospective Placebo Controlled Study. *Sleep 33 Abstract Supplement: A200*, 2010.
549. Roth T, Kessler RC, Hajak G, Coulouvrat C, Walsh JK: Prevalence and Risk Factors for Insomnia Symptoms and Diagnoses. *Sleep 33 Abstract Supplement: A202*, 2010.
550. Randall S, Roehrs T, Harris E, Maan R, Roth T: Chronic Use of Zolpidem is not Associated with Loss of Efficacy. *Sleep 33 Abstract Supplement: A221*, 2010.
551. Herring WJ, Hutzelmann J, Liu K, Ceesay P, Snavely D, Snyder E, Michelson D, Dinges DF, Roth T: Alerting and Performance Effects of the Histamine Inverse Agonist MK-0249 in Obstructive Sleep Apnea Patients on CPAP With Excessive Daytime Sleepiness: A Randomized, Controlled, Adaptive Crossover Study. *Sleep 33 Abstract Supplement: A272*, 2010.
552. Gumenyuk V, Roth T, Jefferson C, Drake C: Electrophysiological Evidence of Impact on Auditory Pre-Attentive Brain Mechanism in Habitual Short Sleepers: Study I. *Sleep, 34, Abstract Supplement: A82-A83*, 2011.
553. Gumenyuk V, Roth T, Jefferson C, Drake C: Electrophysiological Evidence of Improvement of the Brain Mechanism of Auditory Pre-Attentive Processing in Habitual Short Sleepers After Sleep Extension: Study II. *Sleep, 34, Abstract Supplement: A99*, 2011.
554. Drake C., Gumenyuk V, Jefferson C, Roth T: Circadian Phase Differences in Patients with Shift Work Disorder Relative to Asymptomatic Shift Workers. *Sleep, 34, Abstract Supplement: A164*, 2011.

555. Mamedov O, Roth T, Jefferson C, Drake C: Cortisol Responsivity to a Cold Pressor Challenge in Insomniacs. *Sleep*, 34, Abstract Supplement: A170, 2011.
556. Roehrs T, Randall S, Harris E, Maan R, Roth T: MSLT and Total Sleep Time in Primary Insomniacs. *Sleep*, 34, Abstract Supplement: A170, 2011.
557. Dasgupta R, Randall S, Roehrs, Harris E, Maan R, Roth T: Greater Total Sleep Time is Associated with Lower Pre-Sleep Salivary Cortisol During Chronic Zolpidem Use. *Sleep*, 34, Abstract Supplement: A174, 2011.
558. Lankford A, Krystal AD, Dorsey B, Rogowski R, Ludington E, Durrence H, Davis CS, Roth T: Patient-Reported Symptom Improvement in Sleep Maintenance Endpoints in Adult and Elderly Patients with Insomnia Treated with Doxepin 3 and 6 MG. *Sleep*, 34, Abstract Supplement: A175, 2011.
559. Roehrs T, Randall S, Harris E, Maan R, Roth T: Twelve Months of Nightly Zolpidem does not Produce Withdrawal Symptoms on Drug Discontinuation: A Prospective Placebo Controlled Study. *Sleep*, 34, Abstract Supplement: A178, 2011.
560. Krystal AD, Lankford A, Dorsey B, Rogowski R, Ludington E, Durrence H, Roth T: Improvement in Sleep Maintenance and Early Morning Awakenings in Adult and Elderly Patients with Insomnia Treated with Doxepin 3 and 6 MG. *Sleep*, 34, Abstract Supplement: A182, 2011.
561. Randall S, Roehrs T, Harris E, Maan R, Roth T: Individual Differences in the Likelihood of Rebound Insomnia. *Sleep*, 34, Abstract Supplement: A182, 2011.
562. Davuluri S, Drake C, Roth T: Identification of Natural Short Sleepers Based on Bout Length Data Obtained from Polysomnography. *Sleep*, 34, Abstract Supplement: A264, 2011.
563. Norquist J, Liao J, Dinges DF, Roth T, Herring WJ, Brodovicz K: Validation of an Excessive Sleepiness Diary (ESD). *Sleep*, 34, Abstract Supplement: A328, 2011.
564. Ontiveros CS, Kappler JA, Clark DF, Thorpy MJ, Roth T: Sleep/Wake Medicine Among Self-Identified Sleep Specialists and Primary Care Providers: Gaps in Knowledge and the Effectiveness of Continuing Education. *Sleep*, 34, Abstract Supplement: A336, 2011.
565. Roth T: New Directions in Insomnia Therapeutics. *International Journal of Psychiatry in Clinical Practice*, 15, 11-11, 2011.
566. Roth T, Berglund P, Shahly V, Shillington AC, Stephenson JJ, Cooke D, Singh N, Kessler R: The Nature and Prevalence of Middle-of-the-Night use of Prescription Hypnotics. *Sleep Medicine* 12, Suppl. 1, S6, 2011.
567. Vermeeren A, Leufkens TRM, VanLeeuwen C, VanOers A, Vuurman E, Singh NN, Steinberg F, Rico S, Laska E, Roth T: Effect of Middle-of-the-Night Doses of Zolpidem Sublingual Tablet 3.5 MG on Next-Morning Driving Performance. *Sleep Medicine* 12, Suppl. 1, S7, 2011.
568. Wilson FJ, Resnick EM, Freeman J, Pitman V, Bhadra P, Roth T: Effect of Pregabalin on Quantitative Electroencephalography (QEEG) During Non-REM Sleep in Patients with Fibromyalgia and Sleep Maintenance Difficulties. *Sleep Medicine* 12, Suppl. 1, S22, 2011.
569. Roth T, Singh NN, Steinbert FJ, Rosenberg R, Krystal A: Absence of Tolerance, Dependence Potential, and Rebound during PRN Treatment of Middle-of-the-Night Awakening with Zolpidem Tartrate Sublingual Tablet 3.5 MG. *Sleep Medicine* 12, Suppl. 1, S58, 2011.

570. Roth T, Cooke D, Singh NN: Treatment of Middle-Of-The-Night Insomnia: Current Medical Practice. *Sleep Medicine* 12, Suppl.1, S66, 2011.
571. Resnick EM, Lankford DA, Bhadra P, Whalen E, Roth T: Objective and Subjective Benefits of Pregabalin on Measures of Sleep and Pain in Patients with Fibromyalgia and Sleep Maintenance Disturbance. *Sleep Medicine* 12, Suppl. 1, S92, 2011.
572. Gumenyuk V, Roth T, Korzyukov O, Drake C: Sleep Extension Normalizes Waking Auditory Sensory Gating in Short Sleepers. *Sleep*, Volume 35, Abstract Supplement: A99, 2012.
573. Babajani-Feremi A, Gumenyuk V, Roth T, Drake C, Soltanian-Zadeh H: Brain Connectivity Analysis to Study Chronic Short Sleep. *Sleep*, Volume 35, Abstract Supplement: A114, 2012.
574. Koshorek J, Roth T, Eklov S, Kluck S, Drake C: Dose-Related Effects of Caffeine: Sensitivity of a Portable Sleep Monitoring Device. *Sleep*, Volume 35, Abstract Supplement: A129, 2012.
575. Roehrs T, Randall S, Roth T: Daytime Urinary Norepinephrine Levels in Hyperaroused Insomniacs. *Sleep*, Volume 35, Abstract Supplement: A213, 2012.
576. Kessler RC, Berglund P, Shahly V, Shillington AC, Stephenson JJ, Roth T: A Population-Based Study of the Nature and Prevalence of Off-Label MOTN Use of Prescription Hypnotics. *Sleep*, Volume 35, Abstract Supplement: A216-A217, 2012.
577. Herring WJ, Snyder E, Paradis E, Liu M, Snively D, Roth T, Michelson D: Long Term Safety and Efficacy of Suvorexant in Patients with Primary Insomnia. *Sleep*, Volume 35, Abstract Supplement: A217, 2012.
578. Friedman H, Navon N, Koshorek G, Reinberg R, Roth T: Double Blind, Polysomnographic, Two-Way Crossover Study with a Gastric Retentive Accordion-Pill Zaleplon, in Subjects with Insomnia. *Sleep*, Volume 35, Abstract Supplement: A218, 2012.
579. Roehrs T, Randall S, Roth T: Chronic Hypnotic Self-Administration and Hyperarousal in Insomnia. *Sleep*, Volume 35, Abstract Supplement: A219, 2012.
580. Randall S, Roehrs T, Roth T: Chronic Zolpidem: Correlation of Subjective and Objective Efficacy Measures and Daytime Function. *Sleep*, Volume 35, Abstract Supplement: A219, 2012.
581. Randall S, Roehrs T, Roth T: Age Effects on Zolpidem Efficacy. *Sleep*, Volume 35, Abstract Supplement: A220, 2012.
582. Herring WJ, Ma J, Snyder E, Svetnik V, Hutzelmann J, Liu K, Lines C, Roth T, Michelson D: EEG Power Spectral Profile of the Orexin Receptor Antagonist Suvorexant (MK-4305) in Patients with Primary Insomnia and in Healthy Subjects. *Sleep*, Volume 35, Abstract Supplement: A222, 2012.
583. Krystal AD, Roth T, Pong A, Stet L, Ivgy-May N: Efficacy and Safety of Esmirtzapine in Elderly Patients with Primary Insomnia in a 2-Week Sleep Laboratory Trial. *Sleep*, Volume 35, Abstract Supplement: A222, 2012.
584. Ivgy-May N, Roth T, Amari N, Pathiraja K, Walsh JK: Efficacy and Safety of Esmirtzapine in Non-Elderly Adult Patients with Primary Insomnia: A 2-Week Outpatient Trial. *Sleep*, Volume 35, Abstract Supplement: A222-A223, 2012.

585. Ivgy-May N, Amari N, Pathiraja K, Rowe E, Roth T: Efficacy and Safety of Esmirtazapine in a Six-Week Sleep Laboratory in Patients with Primary Insomnia. *Sleep*, Volume 35, Abstract Supplement: A224, 2012.
586. Ruwe F, Ivgy-May N, IJzerman-Boon P, Roth T, Zammit G: A Phase II Randomized, 4-Way Cross-Over, Double-Blind, Placebo-Controlled, Multicenter Dose-Finding Trial with Esmirtazapine in Patients with Primary Insomnia. *Sleep*, Volume 35, Abstract Supplement: A224, 2012.
587. Roth T, Hull SG, Singh NN, Steinberg F, Krystal AD: Gender Effects of 1.75 mg and 3.5 mg Zolpidem Tartrate Sublingual Tablets Formulated with a Carbonate-Bicarbonate Buffer on Sleep Onset Following Middle-Of-The-Night Awakening and On Next-Day Residual Effects. *Sleep*, Volume 35, Abstract Supplement: A225-A226, 2012.
588. Baleeiro T, Horoszok L, D'Aniello F, Staner L, Lindauer A, Santos B, Gropper S, Roth T, Guglietta A: Objective and Subjective Dose Effects of Lorediplon and Zolpidem in a Phase Advance Model of Insomnia. *Sleep*, Volume 35, Abstract Supplement: A227, 2012.
589. Drake C, Koshorek J, Gable M, Rojas A, Roth T: Cortisol Responsivity in Individuals Vulnerable to Insomnia. *Sleep*, Volume 35, Abstract Supplement: A239, 2012.
590. Mansoor E, Koshorek J, Roth T, Seto J, Drake C: Hypertension Prevalence and Severity in Relation to Insomnia Symptom Pattern. *Sleep*, Volume 35, Abstract Supplement: A241-A242, 2012.
591. Andlauer O, Moore HE, Han F, Hong S, Plazzi G, Haffen E, Roth T, Young T, Mignot E: Short REM Latency as a Screening Tool for Narcolepsy. *Sleep*, Volume 35, Abstract Supplement: A269, 2012.
592. Roth T, Bhadra P, Pitman V, Roehrs T, Resnick M: Disturbed Sleep in Patients with Fibromyalgia Compared with Insomnia or with Healthy Normal Subjects. *Sleep*, Volume 35, Abstract Supplement: A301, 2012.
593. Johnson M, Roth T: CME on Excessive Sleepiness and Sleep-Wake Disorders can Address Gaps in Clinical Knowledge and Competence. *Sleep*, Volume 35, Abstract Supplement: A443, 2012.
594. Cheung CW, van Seyen M, Olivier B, Roth T, Verster JC: Methylphenidate Significantly Reduces Lapses of Attention During On-Road Highway Driving and Improves Vehicle Control (SDLP). Supplement to *Journal of Psychopharmacology*, Volume 26, Supplement to Issue 8, A73, 2012.
595. Herring WJ, Ma JS, Snyder E, Svetnik V, Hutzelmann J, Liu K, Lines C, Roth T, Michelson D: Power Spectral Profile of the Orexin Receptor Antagonist Suvorexant (MK-4305) in Primary Insomnia Patients and Healthy-Subjects. *Biological Psychiatry* 71(8): 297S-298S, 2012.
596. Ivgy-May N, Leibensperger H, Froman S, Hutzelmann J, Snavely D, Snyder E, Liu K, Walsh J, Roth T, Michelson D, Herring WJ: Efficacy and Safety of Suvorexant, an Orexin Receptor Antagonist, in Patients with Primary Insomnia: a 3-month Phase 3 Trial (Trial #2). *Journal of Sleep Research*, 21: 351-352, 2012.
597. Nejad-Davarani SP, Gumenyuk V, Drake C, Bagher-Ebadian H, Budaj J, Peltier S, Noll D, Roth T, Chopp M, Jiang Q: Circuits in the Resting State fMRI Brain Connectivity Network Correlated with MSLT Score, a Study in Night Shift Workers. *Sleep*, Volume 36, Abstract Supplement: A103, 2013.
598. Popat C, Parikh N, Bazan L, Roth T: Differences in Automated Computerized Scoring Versus Manual Scoring of Portable Ambulatory Sleep Studies. *Sleep*, Volume 36, Abstract Supplement: A126, 2013.

599. Popat C, Bazan L, Drake C, Roth T: Clinical and Demographic Characteristics of Patients with REM-Specific and REM-Dominant Obstructive Sleep Apnea. *Sleep*, Volume 36, Abstract Supplement: A171, 2013.
600. Drake C, Howard R, Levin A, Roth T, Gumenyuk V: Period 3 Polymorphism Predicts Sleepiness and Circadian Phase in Night Workers. *Sleep*, Volume 36, Abstract Supplement: A181, 2013.
601. Howard R, Gumenyuk V, Roth T, Gable M, Drake C: Armodafinil Improves Creativity Performance on the Remote Associates Test in Night Workers with Shift Work Disorder. *Sleep*, Volume 36, Abstract Supplement: A182, 2013.
602. Parikh N, Howard R, Spear L, Popat C, Moss K, Roth T, Drake C: Armodafinil Improves Driving Simulator Performance in Night Workers with Shift Work Disorder (SWD). *Sleep*, Volume 36, Abstract Supplement: A185, 2013.
603. Howard R, Drake C, Roth T, Gumenyuk V: Sensitivity of a Brief Questionnaire to Circadian Phase in Night Workers. *Sleep*, Volume 36, Abstract Supplement: A188, 2013.
604. Ivgy-May N, Snavely D, Minigh J, Wu M, Hutzelmann J, Snyder E, Connor KM, Walsh JK, Roth T, Herring WJ: Efficacy of Suvorexant, An Orexin Receptor Antagonist, in Patients with Primary Insomnia: Integrated Results from 2 Similarly Designed Phase 3 Trials. *Sleep*, Volume 36, Abstract Supplement: A192, 2013.
605. Gumenyuk V, Howard R, Roth T, Roehrs T, Drake C: Cortical Excitability in Night Workers with Insomnia is Attenuated Following a Night Shift: An ERP Study. *Sleep*, Volume 36, Abstract Supplement: A194, 2013.
606. Mullins H, Mengel H, Roth T, Drake C: Specific Life Events as Risk Factors for the Development of Chronic Insomnia: A Prospective Population-Based Study. *Sleep*, Volume 36, Abstract Supplement: A196-197, 2013.
607. Drake C, Mullins H, Roth T, Alexander G, Mengel H: Sleep Reactivity as a Risk Factor for the Development of Chronic Insomnia and Depression in a Large Community-Based Sample. *Sleep*, Volume 36, Abstract Supplement: A197, 2013.
608. Gumenyuk V, Howard R, Roth T, Roehrs T, Drake C: Insomnia in Shift Work Disorder (SWD) Associated with Cortical Excitability: An ERP Study Prior to a Night Shift. *Sleep*, Volume 36, Abstract Supplement: A199, 2013.
609. Singh NN, Steinberg F, Roth T, Moline M: Factors Determining Ratings of Sleep Quality and Daytime Sleepiness/Alertness Following Treatment of Insomnia Characterized by Middle-of-the-Night Awakening. *Sleep*, Volume 36, Abstract Supplement: A206, 2013.
610. Mengel H, Roth T, Roehrs T, Singh M, Drake C: Familial Risk of Insomnia is Associated with a Blunted Cortisol Response to Stress. *Sleep*, Volume 36, Abstract Supplement: A216, 2013.
611. Verster J, Eklov S, Drake C, Roth T: The Effects of Benzodiazepine Receptor Agonists on Driving Performance as Assessed by Standard Deviation of Lateral Position. *Sleep*, Volume 36, Abstract Supplement: A221, 2013.
612. Hull SG, Leibowitz MT, Furey SA, Jayawardena S, Roth T: A Randomized, Double-Blind, Placebo-Controlled, Multicenter, 28-Day, Polysomnographic Study of Gabapentin in Transient Insomnia Induced by Sleep Phase Advance. *Sleep*, Volume 36, Abstract Supplement: A221, 2013.

613. Rosenberg R, Hull SG, Lankford A, Mayleben D, Seiden D, Furey SA, Jayawardena S, Roth T: A Randomized, Double-Blind, Single-Dose, Placebo-Controlled, Multicenter, Polysomnographic Study of Gabapentin in Transient Insomnia Induced by Sleep Phase Advance. *Sleep*, Volume 36, Abstract Supplement: A222, 2013.
614. Conner KM, Matzura-Wolfe D, Zhang Y, Ivgy-May N, Snively D, Snyder E, Benca R, Roth T, Herring WJ: Safety of Suvorexant, an Orexin Receptor Antagonist, in Patients with Primary Insomnia: Integrated Phase 3 Results. *Sleep*, Volume 36, Abstract Supplement: A223, 2013.
615. Herring WJ, Ivgy-May N, Conner KM, Wu M, Liu K, Snyder E, Snively D, Walsh JK, Krystal AD, Roth T: Effect of Suvorexant, an Orexin Receptor Antagonist, on Patient-Reported Outcomes in Patients with Primary Insomnia: Integrated Results from Two Phase-3 Trials. *Sleep*, Volume 36, Abstract Supplement: A223, 2013.
616. Kohnen R, Roth T, Grieger F, Moran K, Ondo W, Trenkwalder C: Minimal Clinically Important Improvement in IRLS Total Score in Patients with Restless Legs Syndrome Treated with the Rotigotine Transdermal System. *Sleep*, Volume 36, Abstract Supplement: A244-245, 2013.
617. Roth T, Black J, Dauvilliers Y, Skowronski R, Steininger T: Effect on Sodium Oxybate on Sleep Stage Shifts and Sleep Quality in Patients with Narcolepsy. *Sleep*, Volume 36, Abstract Supplement: A255, 2013.
618. Roehrs T, Randall S, Roth T: Increasing Preoperative Sleep Reduces Postoperative Pain and Analgesic Use. *Sleep*, Volume 36, Abstract Supplement: A294, 2013.
619. Roehrs T, Lundahl L, Steinmiller C, Roth T: Marijuana Normalizes Sleep Efficiency in Marijuana Dependent Volunteers. *Sleep*, Volume 36, Abstract Supplement: A308, 2013.
620. Roth T, Mengel H, Koshorek G: Hypnotics and the Risk of Falls: A Review. *Sleep*, Volume 36, Abstract Supplement: A429, 2013.
621. Eklov S, Drake C, Verster J, Roth T: Risk of Automobile Accidents Associated with the Use of Benzodiazepine Receptor Agonists Hypnotics. *Sleep*, Volume 36, Abstract Supplement: A429, 2013.
622. Parikh N, Roth T: Sleep Related Eating Disorder and Situational Stress. *Sleep*, Volume 36, Abstract Supplement: A441, 2013.
623. Kohnen R, Roth T, Grieger F, Moran K, Ondo W. Determination of the minimal clinically important improvement in irls total score in patients with moderate to severe restless legs syndrome treated with rotigotine transdermal system: A post HOC analysis from a 6-month placebo-controlled european study. *Neurology*. 2013;80(1).
624. Ondo W, Roth T, Grieger F, Moran K, Kohnen R. Minimal clinically important improvement in irls total score in patients with restless legs syndrome: A post HOC analysis from a 6-month placebo-controlled us-based study with rotigotine transdermal system. *Neurology*. 2013;80(1).
625. Abboud R, Mengel HJ, Roth T, Bazan L. Differential prevalence of OSA comorbidities as a function of age and gender. *Sleep*, Volume 37, Abstract Supplement: A446, 2014.
626. Roth T, Belcher R, Drake CL, Mengel HJ, Koshorek GL, Gable M, Gumenyuk V. Differential sleep disturbances in two phenotypes of shift work disorder. *Sleep*, Volume 37, Abstract Supplement: A468, 2014.

627. Belcher R, Roth T, Gumenyuk V, Mengel HJ, Philport J, Drake CL. Occupational and neurophysiological deficits in shift work disorder relate to insomnia, not sleepiness. *Sleep*, Volume 37, Abstract Supplement: A486, 2014.
628. Gumenyuk V, Belcher R, Roth T, Bazan L, Larose C, Drake CL. Attentional brain responses in night shift workers are sensitive to occupational impairment. *Sleep*, Volume 37, Abstract Supplement: A487, 2014.
629. Roehrs T, Roth T. Effects of gender on zolpidem efficacy and safety. *Sleep*, Volume 37, Abstract Supplement: A492, 2014.
630. Pillai V, Roth T, Mengel HJ, Drake CL. The interaction between stress and sleep-reactivity: a prospective investigation of the stress-diathesis model of insomnia. *Sleep*, Volume 37, Abstract Supplement: A505, 2014.
631. Gumenyuk V, Belcher R, Drake CL, Spear L, Roth T. Cortical arousal is present in alert insomnias but absent in sleep insomniacs within shift work disorder; an ERP study. *Sleep*, Volume 37, Abstract Supplement: A508, 2014.
632. Mengel HJ, Pillai V, Roth T, Belcher R, Drake CL. Moderators and mediators of the relationship between stress and insomnia: stressor chronicity, cognitive intrusion and coping behaviors. *Sleep*, Volume 37, Abstract Supplement: A511, 2014.
633. Drake CL, Mengel HJ, Roth T, Belcher R, Pillai V. The differential contribution of insomnia symptoms to hypertension. *Sleep*, Volume 37, Abstract Supplement: A515, 2014.
634. Roehrs T, Roth T. Ethnicity and zolpidem sleep effects in insomnia. *Sleep*, Volume 37, Abstract Supplement: A523, 2014.
635. Roth T, Singh N, Waldron A, Moline M. Sex influence on sleep architecture following treatment of patients with middle-of-the-night insomnia with buffered sublingual zolpidem or placebo. *Sleep*, Volume 37, Abstract Supplement: A524, 2014.
636. Vargas I, Drake CL, Roth T, Friedman NP. Vulnerability to stress-related sleep disturbance and insomnia: investigating the link with comorbid depressive symptoms. *Sleep*, Volume 37, Abstract Supplement: A528, 2014.
637. Mengel HJ, Drake CL, Pillai V, Belcher R, Roth T. Distribution and stability of insomnia phenotypes. *Sleep*, Volume 37, Abstract Supplement: A557, 2014.
638. Verster JC, van de Loo AJ, Moline M, Roth T. Next-morning driving performance after middle-of-the-night administration of hypnotic drugs: evidence from dutch on-road driving studies. *Sleep*, Volume 37, Abstract Supplement: A558, 2014.
639. Levin AM, Howard R, Derringer JL, Mengel HJ, Datta I, Friedman NP, Roth T, Drake CL. A multi-phenotype genome-wide association study of insomnia-related sleep traits. *Sleep*, Volume 37, Abstract Supplement: A568, 2014.
640. Belcher R, Roth T, Drake CL, Mengel HJ, Bazan L, Gumenyuk V. Belcher R, Roth T, Drake CL, Mengel HJ, Gumenyuk V. Separated insomnia severity index (ISI) distinguishes two phenotypes of shift work disorder. *Sleep*, Volume 37, Abstract Supplement: A586, 2014.

641. Bogan RK, Roth T, Schwartz J, Miloslavsky M, Scharf M. Time to response with sodium oxybate for the treatment of excessive daytime sleepiness (EDS) and cataplexy in patients with narcolepsy. *Sleep*, Volume 37, Abstract Supplement: A667, 2014.
642. Pillai V, Kalmbach D, Roth T, Drake CL. A seven-day actigraphy based study of sleep disturbance in high trait ruminators. *Sleep*, Volume 37, Abstract Supplement: A771, 2014.
643. Kalmbach DA, Roth T, Drake CL, Pillai V. Different affect states target distinct actigraphy-based sleep parameters. *Sleep*, Volume 37, Abstract Supplement: A815, 2014.
644. Verster JC, Bervoets AC, de Klerk S, Vreman RA, Brookhuis KA, Roth T. The impact of alcohol hangover and total sleep time on simulated highway driving. *Sleep*, Volume 37, Abstract Supplement: A818, 2014.
645. Drake CL, Belcher R, Roehrs TA, Koshorek GL, Roth T. Nocturnal wakebout during predicts daytime sleepiness. *Sleep*, Volume 37, Abstract Supplement: A1028, 2014.
646. Mamelak M, Swick T, Emsellem H, Montplaisir J, Lai C, Black J. A 12-week, open-label study evaluating sodium oxybate (SXB) in patients with narcolepsy. *Ann Neurol*. 2014;76(Suppl S18):in press. Abstract 350121.
647. Verster JC, Roth T. Total sleep time, alcohol consumption, and the duration and severity of alcohol hangover. *Journal of Psychopharmacology* 2014, 28 (supplement to #8): A19.
648. Gordon V C, Bradley P, Bazan L, Mordis C, Roth T, Roehrs TA. Pre Operative Stop Bang Screening Predicts Post Operative Pain and Opioid Use. *Sleep* Volume 38, Abstract Supplement A172, 2015.
649. Anderson JR, Fellman-Couture C, Koshorek G, Roehrs TA, Roth T, Arnedt JT, Drake CL. Efficacy of Cognitive Behavioral Therapy For Insomnia and Sleep Restriction Therapy for Post-Menopausal Insomnia and Comorbid Vasomotor Symptoms. *Sleep* Volume 38, Abstract Supplement A230, 2015.
650. Donners AAMT, Cheng P, Verster JC, Roth T, Drake CL, Pillai V, Ciesla JA. Nocturnal rumination as a mediator between sleep disturbance and negative affect. *Sleep Medicine* 2015, 16 (supplement 1): S247.
651. Donners AAMT, Bury D, Fernstrand AM, Garssen J, Roth T, Verster JC. The association between insomnia and perceived health status. *Sleep Medicine* 2015, 16 (supplement 1): S191.
652. Fernstrand, AM, Bury D, Garssen J, Roth T, Verster JC. Insomnia and the dietary intake of tryptophan and niacin. *Pharma Nutrition*, 2015.
653. Van de Loo AJAE, Bervoets AC, Mooren L, Garssen J, Roth T, Verster JC. The impact of having a 15-minute break with and without consuming an energy drink on prolonged simulated highway driving. *Sleep Medicine*, 16 (supplement 1): S201, 2015
654. Verster JC, Fernstrand AM, Bury D, Roth T, Garssen J. The association of sleep quality and insomnia with dietary intake of tryptophan and niacin. *Sleep Medicine*, 16 (supplement 1): S191, 2015.
655. Van de Loo AJAE, Roth T, Verster JC. Lapses during on road driving: determining a cut-off value for clinically relevant driving impairment. *European Neuropsychopharmacology*, 25 (Supplement 2): S616-S617, 2015.
656. Roehrs T, Koshorek G, Withrow D, Tancer M, Roth T. How representative are insomnia clinical trials? *Sleep*, Volume 39, Abstract Supplement: A198, 2016.

657. Pillai V, Tran KM, Roth T, Drake CL. Limitations of current diagnostic criteria for insomnia: a case for quantitative cut-offs. *Sleep*, Volume 39, Abstract Supplement: A198, 2016.
658. Fellman-Couture C, Pillai V, Arnedt J, Anderson J, Moss K, Roth T, Drake C. Long term efficacy of cognitive behavior therapy for menopausal insomnia. *Sleep*, Volume 39, Abstract Supplement: A198, 2016.
659. Roehrs T, Koshorek G, Withrow D, Roth T. Cortisol and hyperarousal in insomnia. *Sleep*, Volume 39, Abstract Supplement: A201, 2016.
660. Durrence H, Roth T, Tran KM, Singh M, Cheng P, Pillai V, Drake C. Arousability of insomnia patients and healthy volunteers is not impacted by the sleep-specific doses of doxepin (3mg and 6mg), but is impacted in healthy volunteers using zolpidem 10mg. *Sleep*, Volume 39, Abstract Supplement: A201, 2016.
661. Durrence H, Drake CL, Tran KM, Bazan L, Cheng P, Pillai V, Roth T. Double-blind, placebo-controlled, 4-way crossover study comparing the effects of doxepin 6mg and zolpidem 10mg on gait, balance, and cognitive performance in healthy volunteers. *Sleep*, Volume 39, Abstract Supplement: A206, 2016.
662. Verster JC, Bouwmeester NH, van de Loo AJ, Peters LV, Tiplady B, Alford C, Roth T. Meta-analysis on the next-morning effects of hypnotic drugs on psychomotor speed and motor control in healthy subjects. *Sleep*, Volume 39, Abstract Supplement: A210, 2016.
663. Verster JC, Peters LV, van de Loo AJ, Bouwmeester NH, Tiplady B, Alford C, Roth T. Meta-analysis on the next-morning effects of hypnotic drugs on short- and long-term memory functioning in healthy adults and elderly. *Sleep*, Volume 39, Abstract Supplement: A210, 2016.
664. Carr AN, Ramsey DL, Brum JM, Thomas P, Kappler G, Chan K, Koshorek G, Roth T. Diphenhydramine hcl improves both objective and subjective sleep parameters in an occasional sleeplessness population. *Sleep*, Volume 39, Abstract Supplement: A212, 2016.
665. Withrow D, Koshorek G, Roth T, Roehrs T. At-home actigraphy vs. in-laboratory PSG in insomnia. *Sleep*, Volume 40, Abstract Supplement: A122, 2017.
666. Koshorek G, Withrow D, Roth T, Roehrs T. Actigraphy in insomnia with and without event-marking. *Sleep*, Volume 40, Abstract Supplement: A122, 2017.
667. Drake C, Cheng P, Luik A, Peterson E, Joseph C, Tallent G, Tran K, Ahmedani B, Roehrs T, Roth T. Preliminary data for the sleep to prevent evolving affective disorders (SPREAD) trial. *Sleep*, Volume 40, Abstract Supplement: A131, 2017.
668. Hyde-Nolan ME, Arnedt JT, Cheng P, Fellman-Couture C, Tallent G, Kalmbach D, Singh M, Roth T, Drake CL. Efficacy of behavioral insomnia treatment on post-menopausal quality of life. *Sleep*, Volume 40, Abstract Supplement: A133, 2017.
669. Roth T, Mayleben D, Feldman N, Lankford A, Grant T, Nofzinger E. A novel forehead temperature regulating device for insomnia: A randomized clinical trial. Volume 40, Abstract Supplement: A142, 2017.
670. Verster J, van de Loo AJ, Roehrs T, Roth T. Are clinical trial participants representative for patients with insomnia? Volume 40, Abstract Supplement: A148, 2017.

671. Van de Loo AJ, Mackus M, Knipping K, Kraneveld AD, Garssen J, Roth T, Verster JC. Cytokines, sleep and daytime sleepiness. Volume 40, Abstract Supplement: A291, 2017.
672. Cheng P, Fellman-Couture C, Ahmedani B, Tallent G, Arnedt J, Roehrs T, Roth T, Drake C. CBT-I for menopause related insomnia also reduces depression severity. Volume 40, Abstract Supplement: A405, 2017.

CURRICULUM VITAE

January 11, 2016

NAME: Todd J. Swick, M.D.

OFFICE ADDRESS: 7500 San Felipe, Suite 525, Houston, Texas 77063
21216 Northwest Frwy, #510, Cypress, Texas 77429

OFFICE PHONE: (713) 465-9282 (Houston Office)
(713) 465-7066 (Research Number)
(832) 678-2971 (Cypress Office)

OFFICE FAX: (713) 465-9248
(713) 467-2954 (Research)

E-mail: tswick@houstonssleepcenter.com
URL Site: www.sleepandneurology.com

(b) (6)

(b) (6)

BOARD STATUS: Board Certified - Neurology - American Board of Psychiatry and Neurology, April 1982.
Certified MRI/CT Neuroimaging – American Society of Neuroimaging
February 1998.
Board Certified - American Board of Sleep Medicine, April 2002.
Board Certified - American Board of Psychiatry and Neurology- Subspeciality of Sleep
Medicine, November 2007.

TYPE OF PRACTICE:

7/78 -11/79 Private Practice - Neurology;
New Hyde Park, New York

11/79 - 5/80 Staff Physician; Ambulatory Care Division -
University Hospital; SUNY at Stony Brook,
Stony Brook, New York

7/80 – 1/02 Private Practice; Diagnostic Neurology Clinic
of Houston, P.A., Houston, Texas

2/02- Present Private Practice; Todd J. Swick, P.A.
Houston, Texas

8/05- Present Neurology and Sleep Medicine Consultants of Houston,
Houston, Texas

1/83 – 5/00 Medical Director; Sleep Disorders Center,
Spring Branch Medical Center, Houston, Texas

1/87 - 12/87 Vice Chief of Staff, Sam Houston Memorial Hospital
Houston, Texas

1/88 - 12/88 Chief of Staff, Sam Houston Memorial Hospital
Houston, Texas

7/94 - 6/96 Chief of Staff Elect, Spring Branch Medical Center
Houston, Texas 77055

7/96 – 6/98 Chief of Staff, Spring Branch Medical Center
Houston, Texas 77055

1/94-6/2000 Member of Board of Trustees, Spring Branch Medical Center
Houston, Texas 77055

8/99-11/2011 The Houston Sleep Center,
The Institute of Sleep Medicine, Inc. Houston, Texas 77063

1/06-7/06 Medical Director, The Sleep Disorders Laboratory,
College Station Medical Center, College Station, Texas 77845

4/06-1/07 Section Chief, Division of Sleep Medicine, Department of Neurology,
Methodist Neurological Institute, Houston, Texas 77030

4/06-1/07 Co-Director, Sleep Disorders Center, Sleep Medicine Section,
The Methodist Neurological Institute, Houston, Texas 77030

1/07-Present Medical Director, The Sleep Center at North Cypress Medical Center,
North Cypress Medical Center, Cypress, Texas 77429

12/11-Present Medical Director, Apnix Sleep Diagnostics, Memorial and Katy Sleep
Centers, Houston, TX

5/14- 6/2015 Medical Director, American Sleep and Breathing Academy
Ogden, Utah

LICENSURE:

10/75 New York #125775
3/80 Arizona # 11801
6/80 Texas #F7939

ACADEMIC POSITIONS:

7/77-6/78 Assistant Clinical Professor in the Institute of Advanced
Psychological Studies, Adelphi University, Garden City, NY

12/77-9/79 Assistant Instructor in Medicine, School of Medicine,
State University of New York at Stony Brook, Stony Brook, NY

10/79-5/80 Instructor in Medicine, School of Medicine,
State University of New York at Stony Brook, Stony Brook, NY

12/84-Present Clinical Assistant Professor of Neurology, University of Texas
Medical School, Health Sciences Center at Houston,
Houston, Texas

PROFESSIONAL SOCIETIES:

Fellow - American Academy of Neurology
Fellow - American Academy of Sleep Medicine
American Academy of Sleep and Breathing
American Medical Association
Texas Neurologic Society
Houston Neurological Society
Harris County Medical Society
Sleep Research Society
Southern Sleep Society
American Society of Neuroimaging
American Clinical Neurophysiology Society

PROFESSIONAL COMMITTEES/ACTIVITIES and AWARDS:

American Academy of Sleep Medicine- National Standards of Practice Committee;
June 2005-June 2007.

National Medical Advisory Board, Narcolepsy Network 129 Waterwheel Lane, North
Kingston, RI 02852; June 2013-Present

Vanda Pharmaceuticals, FDA New Drug Application Advisory Committee
Washington, D.C.; November 2013.

National Medical Director, Member of the Medical Advisory Board and Member of
Executive Committee, American Sleep and Breathing Academy, Ogden, UT; May
2014-2015

Reviewer, Sleep Medicine, Elsevier Publishers, Editor-In-Chief: S. Chokroverty,
January 2013-Present.

2014 Robert Clark, MD, Clinician of The Year Award, National Narcolepsy Network,
Denver, CO, October 2014.

ADVISORY BOARD MEMBERSHIP:

Jazz Pharmaceuticals, Palo Alto, CA.
Merck Pharmaceuticals, North Wales, PA
Vanda Pharmaceuticals, Washington, DC
XenoPort Pharmaceuticals, Santa Clara, CA
UCB, Inc., Smyrna, GA
Sunovion Pharmaceuticals, Marlborough, MA
Narcolepsy Network, National Medical Advisory Board, North Kingston, RI

PUBLICATIONS:

Nathanson M, Swick TJ: Persistent Brainstem Reflexes During
Prolonged Electro-Cerebral Silence. XI World Congress of Neurology 1977,
Excerpta Medica

Swick, TJ, Chisholm, R.: Bilateral Rhythmic Synchronous Movements of the Lower Extremities in Sleep - A Form of Epilepsy? International Conference on Sleep in the Diseased Brain - Current Opinion in Neurology. 1994

Swick, TJ. The Neurology of Sleep. In Neurologic Clinics, Vol 23, ed. Fayle, RW. Saunders, Philadelphia, 967-989, 2005

Xyrem International Study Group. Further evidence supporting the use of sodium oxybate for the treatment of cataplexy: a double-blind, placebo-controlled study in 28 patients. Sleep Medicine, 2005; 6 (5): 415-421

Xyrem International Study Group. A double-blind, placebo-controlled study demonstrates sodium oxybate is effective for the treatment of excessive daytime sleepiness in narcolepsy. J Clin Sleep Med 2005; 1(4): 391-397

Kushida CA, Littner MR, Hirshkowitz M, Morgenthaler TI, Alessi CA, Bailey D, Boehlecke B, Brown TM, Coleman J, Friedman L, Kapen S, Kapur VK, Kramer M, Lee-Chiong T, Owens J, Pancer JP, Swick TJ, Wise MS. Practice Parameters for the Use of Continuous and Bilevel Positive Airway Pressure Devices to Treat Adult Patients With Sleep-Related Breathing Disorders. Sleep. 2006; 29(3): 375-380

Morgenthaler TI, Kapen S, Lee-Chiong t, Alessi C, Boehlecke B, Brown T, Coleman J, Friedman L, Kapur V, Owens J, Pancer J, Swick T. Practice Parameters for the Medical Therapy of Obstructive Sleep Apnea. Sleep. 2006; 29(8): 1031-1035

Swick T. The Nightly Administration of Sodium Oxybate Is Associated with Significant Improvements in Nocturnal Sleep Quality, Pain and Fatigue in Patients with Fibromyalgia. Abstract/Poster presentation, 58th American Academy of Neurology Meeting, April 2006, San Diego, CA

Morgenthaler TI, Kapur VK, Brown T, Swick TJ, Alessi C, Aurora N, Boehlecke B, Chesson AL, Friedman L, Maganti R, Owens J, Pancer J, Zak R. Practice Parameters for the Treatment of Narcolepsy and Other Hypersomnias of Central Origin. Sleep. 2007; 30(12): 1705-1711

Morgenthaler TI, Aurora N, Brown T, Zak R, Alessi C, Boehlecke B, Chesson AL, Friedman L, Kapur V, Maganti R, Owens J, Pancer J, Swick TJ. Practice Parameters for the Use of Autotitrating Continuous Positive Airway Pressure Devices for Titrating Pressures and Treating Adult Patients with Obstructive Sleep Apnea Syndrome: An Update for 2007. Sleep. 2008; 31 (1): 141-147

Ondo WG, Perkins T, Swick T, Hull KL, Jimenez JE, Garris TS, Pardi D. Sodium Oxybate for Excessive Daytime Sleepiness in Parkinson Disease. Arch Neur. 2008; 65(10); 1337-1340

Swick TJ, Alvarez-Horine S, Zheng Y, Guinta D, Inhaber N, Holman, A, Smith TR, Russell IJ. Impaired Sleep and Daytime Functioning at Baseline in Subjects with Fibromyalgia: A 14-Week Randomized, Double-Blind, Placebo Controlled Trial of Sodium Oxybate (Abstract). Sleep. 2009; 32; A330

Swick TJ, Alvarez-Horine S, Zheng Y, Rothman J., Inhaber N, Holman A, Smith TR, Russell IJ. Sodium Oxybate Improves Pain, Fatigue, and Sleep in Fibromyalgia: Results from a 14-week Randomized, Double-Blind, Placebo Controlled Trial (Abstract). Sleep. 2009; 32; A321

Wang YG, Swick TJ, Carter LP, Thorpy MJ, Benowitz NL. Safety overview of postmarketing and clinical experience of sodium oxybate (Xyrem®): abuse, misuse, dependence, and diversion. *J Clin Sleep Med* 2009; 5(4): 365-371

Russell JI, Holman AJ, Swick TJ, Alvarez-Horine S, Wang YG, Guinta; Sodium Oxybate reduces pain, fatigue, and sleep disturbance and improves functionality in fibromyalgia: results from a 14-week, randomized, double-blind, placebo-controlled study. *Pain*. 2011; 152(5): 1007-1017

Swick TJ. The Neurology of Sleep. In *Sleep Medicine Clinics*, Vol 6, No. 1, ed. Strickgold, R. Saunders, Philadelphia, 1-14, 2011

Swick TJ. Sodium Oxybate: a potential new pharmacological option for the treatment of fibromyalgia syndrome. *Ther Adv Musculoskel Dis*. 2011; 3(4): 167-178

Swick TJ. The Neurology of Sleep-2012. In *Sleep Medicine Clinics*, Vol 7, No. 3, ed. Strickgold, R. Saunders, Philadelphia, 399-415, 2012

Swick TJ. Parkinson's disease and sleep/wake disturbances. *Parkinson's Dis* 2012:205471

Roth, T, Dauvilliers, Y, Mignot, M, Montplaisir, J, Paul, J, Swick, T, Zee, P. *Disrupted nighttime sleep in narcolepsy*. *J Clin Slp Med* 2013; 9(9): 955-965

Swick TJ, Friedman JH, Chaudhuri KR, Surmann E, Boroojerdi B, Moran K, Ghys L, Trenkwalder, C. Associations between Severity of Motor Function and Nonmotor Symptoms in Parkinson's disease: A Post Hoc Analysis of the RECOVER study. *Eur Neuro*. 2014; 71:140-147.

Swick TJ, Sliman JA, Dressman MA, Xiao C, Licamele L, Baroldi P, Polymeropoulos MH. *Tasimelteon, a dual melatonin agonist for the treatment of Non-24 Hour Disorder: Pooled safety analysis in placebo controlled randomized trials*. (Abstract) American Psychiatric Association, New York, New York 2014.

Black J, Swick T, Feldman N, Doekel Jr. R, Khayrallah M, Bream G, Ruoff, C. *Efficacy and Safety of Oral ADX-N05 for the Treatment of Excessive Daytime Sleepiness in Adults with Narcolepsy: Results of a Randomized, Double-Blind, Placebo-Controlled Trial*. (Abstract) APSS [Sleep] (2014) Minneapolis, MN.

Lee DO, Swick T, Poxceta S, Jaros M, Kim R, Shang G. *Sleep Pain, and International Restless Legs Scale Outcomes as Predictors of Response on the Patient-Rated Clinical Global Impression-Improvement Scale In Patients with Moderate-to-Severe Primary RLS Treated with Gabapentin Enacarbil: Pooled Analyses from 2 Randomized Trials*. (Abstract) APSS [Sleep] (2014) Minneapolis, MN.

Mamelak M, Swick T, Emsellem H, Montplaisir J, Lai C, Black J. *A 12-week open label, multicenter study evaluating the safety of sodium oxybate (SXB) in patients with narcolepsy*. (Abstract) APSS [Sleep] (2014) Minneapolis, MN.

Bogan R, Swick T, Mamelak M, Ristanovic R, Lai C, Black J, Villa K, Montplaisir J. *Evaluation of Quality-of-Life in Patients with Narcolepsy Treated with Sodium Oxybate: Use of the 36-Item Short-Form Health Survey in a Clinical Trial*. (Abstract) APSS [Sleep], Seattle, WA, 2015.

Black J, Bassetti C, Bogan R, Lai C, Swick T. Sodium Oxybate Treatment in Patients with Narcolepsy Stratified by the Presence of Cataplexy: Retrospective Subgroup Analysis of a Randomized Clinical Trial. (Abstract) APSS, [Sleep] Seattle, WA, 2015.

Black J, Swick T, Feldman NT, Doekel R, Khayrallah M, Bream G, Ruoff R. Efficacy and Safety of Oral JZP-110 for the treatment of Excessive Daytime Sleepiness in Adults with Narcolepsy: Results of a Phase 2b, Randomized, Double-Blind, Placebo-Controlled Trial. (Abstract) Canadian Sleep Society Conference, Toronto, Canada, September 2015.

Swick, TJ. *Treatment paradigms for cataplexy in narcolepsy: past, present and future.* Nature and Sci of Sleep. 2015, 7:159-169.

Scrima L and Swick T. Narcolepsy. In: *Synopsis of Sleep Medicine.* Pandi-Perumal SR Editor, CRC Informa Press, London, Chapter 7, 2016 (In Press).

Swick TJ and Ondo, WG. Sleep in Parkinson's Disease. In: *Dopamine and Sleep: Molecular, Functional and Clinical Aspects.* Monti JM, Pandi-Perumal SR and Chokroverty S; Editors; Elsevier, Philadelphia, 2016 (In Press).

INVITED LECTURES:

Introduction to Sleep Disorders
Sam Houston Memorial Hospital
General Staff Meeting, February 1983

Sleep Apnea Syndrome
Department of Anesthesia Grand Rounds
Baylor College of Medicine, January 1984

Clinical Sleep Disorders
Memorial Northwest Hospital
CME Luncheon Lecture Series, August 1985

Pain Mechanisms and Management
Spring Branch Memorial Hospital
Medical Education Lecture, May 1986

Magnetic Resonance Imaging - Principles and Applications
Western Branch - Harris County Medical Society
Program director, October 1986

Sleep Disorders Medicine
La Universidad Autonoma de Guadalajara School of Medicine,
Continuing Medical Education. Jalisco, Mexico, August 1987

Osler Institute
Neurology - Neurosurgery Board Review Course
Faculty - Neurological Aspects of Sleep Disorders
Houston Texas, March 1991

Mind Matters Seminars
Sleep Disorders
Houston, San Antonio, Galveston, Texas May 1992

Bilateral Rhythmic Synchronous Movements of the Lower Extremities in Sleep - A Form of Epilepsy?
International Conference on Sleep in the Diseased Brain
Jerusalem, Israel, March 13-18, 1994

Sleep Disorders in Critical Care Settings
Houston Critical Care Conference
Houston, Texas, November 2000

Narcolepsy – Into the New Millenium
Grand Rounds, Department of Neurology UT School of Medicine,
Houston, Texas, November 2000

Sleep Disorder for Neurologists
Department of Neurology, University of Texas School of Medicine-
Houston, Texas, Spring 2001

Movement Disorders in Sleep
The Southern Sleep Society Annual Meeting, March 2001

Degenerative Neurologic Diseases and Sleep
The Southern Sleep Society, March 2003

The Physiologic Consequences of Snoring and Sleep Apnea
Houston Critical Care Conference, November 2003

New Advancements in Narcolepsy
Grand Rounds, Scott and White Clinic, Temple, Texas
Texas A&M University School of Medicine, November 2003

A Problem Based Sleep Medicine Course for the Primary Care Practitioner,
Co-Director: The Houston Sleep Consortium, September 2004

Efficacy of Sodium Oxybate for the Treatment of Excessive Sleepiness in Patients with Narcolepsy. Investigator Meeting, Jazz Pharmaceuticals, January 2006

The Neurology of Sleep: Advances in Neurology
Methodist Neurological Institute, January 2006

A Problem Based Sleep Medicine Course for the Primary Care Practitioner, Second Annual Course,
Co-Director: The Houston Sleep Consortium, February 2006.

Sleep and the Law: "But Officer I Was Asleep!"
Association of Professional Sleep Societies, Annual Meeting, June 2007

Advances in Understanding and Treatment of Narcolepsy
Methodist Neurological Institute 3rd Annual Advances in Neurology, September 2007

A Problem Based Sleep Medicine Course for the Primary Care Practitioner,
Pain and Sleep: A Bi-Directional Relationship
The Houston Sleep Education Consortium, February 2008

Clinical Experience with Sodium Oxybate in Narcolepsy and Fibromyalgia: Clinical Trials and Clinical Practice Perspectives.
Investigator Meeting, Jazz Pharmaceuticals, March 2008

Problem based Sleep Medicine Course to Enhance Your Clinical Practice: Establishing a Differential Diagnosis and Treatment Plan, Chronic Pain and Sleep Disorders.
The Houston Sleep Education Consortium, March 2009

Problem Based Sleep Medicine Course to Enhance Your Clinical Practice: Establishing a Differential Diagnosis and Treatment Plan
The Houston Sleep Education Consortium, February 2010

Problem Based Sleep Medicine Course to Enhance Your Clinical Practice: Establishing a Differential Diagnosis and Treatment Plan
The Houston Sleep Education Consortium, February 2011

Parasomnias: Things that Go Bump In The Night. Texas Medical Association Annual Meeting; Section on Psychiatry, June 2011.

National Experts Panel on Narcolepsy. Disturbed Nocturnal Sleep; Jazz Pharmaceuticals, Minneapolis, MN, June 2011.

Excessive Somnolence and Excessive Quantity of Sleep: Prevalence, Comorbidity and Mortality. Patients with Hypersomnia in a Dedicated Sleep Practice. Stanford Sleep Epidemiology Research Center. April 2012.

Problem Based Sleep Medicine Course to Enhance Your Clinical Practice: Establishing a Differential Diagnosis and Treatment Plan
The Houston Sleep Education Consortium, February 2012

Physician Fatigue. Physician Health and Rehabilitation Training Session and Retreat, Texas Medical Association Committee on Physician Health and Rehabilitation Annual Retreat 2012, Moody Gardens, Galveston, Texas Feb 2012.

Basics of Narcolepsy. National Narcolepsy Network Annual Conference, October 2012, Cleveland, OH.

Comorbidity of Sleep Disorders and Mortality: Excessive Sleepiness & Hypersomnolence Issues. Comorbidities of Hypersomnolence: Chicken or Egg? Stanford Sleep Epidemiology Research Center. August 2013.

Advancements in Narcolepsy: Pathophysiology and Etiology. National Narcolepsy Network Annual Conference, October 2013, Atlanta, GA.

Problem Based Sleep Medicine Course to Enhance Your Clinical Practice: Establishing a Differential Diagnosis and Treatment Plan.
The Houston Sleep Education Consortium, 10th Annual Course, January 2014

Sleep Medicine Lecture Series-Introduction to clinical sleep medicine, neuroanatomy, physiology, pathophysiology and treatment. Houston Methodist Hospital, Department of Neurology, Houston, TX 2014-2015.

Sleep and Pain: A Bi-Directional Relationship. American Sleep and Breathing Academy, Annual Meeting, Scottsdale, AZ, May 2014.

Review of Request for Orphan Drug Designation

1	For Original Requests *Date of Request: *Date Received by FDA:	Click here to enter a date. Click here to enter a date.
2	For Amendments: *Date Original Request Received: *Date of Amendment: *Date Amendment Received:	4/20/2016 10/13/2017 12/13/2017
3	Date Review Completed:	12/21/2017
4	*Designation Number:	16-5302
5	*Prior or Related Designation Number: (e.g., if the 1-year deficiency response period to prior similar submission was exceeded)	
6	*Chemical Name:	
7	*Generic Name:	FT218 (sodium oxybate for extended-release oral suspension)
8	Other (Code) Name:	
9	*Sponsor:	Flamel Ireland Limited Block 10-1 Blanchardstown Corporate Park Ballycoolin Dublin 15 Ireland
10	*Proposed Orphan Disease or Condition:	For the treatment of cataplexy and excessive daytime sleepiness in narcolepsy
11	*Sponsor Resident Agent or Contact:	U.S. Agent for Flamel Marla Scarola Phone: 202.730.4129 E-mail: marla.scarola@weinberggroup.com
12	*Manufacturer:	The drug substance, sodium oxybate is manufactured in accordance with Good Manufacturing Practice at the following facilities:

		(b) (4) Manufacture of FT218 drug product is conducted in accordance with Good Manufacturing Practice at the following facility: (b) (4)
13	*Regulatory Status:	FT218 is currently being tested under IND 126,321 for the treatment of cataplexy and excessive daytime sleepiness in narcolepsy. It is not approved or marketed in any country including the US for any indication. No adverse regulatory actions have been taken against FT218 in any country.
14	* Sponsor Provided Self-Certification? <i>If no, request from sponsor.</i>	Yes <input type="checkbox"/> No <input type="checkbox"/>
15	Orphan Drug Designation History:	Six drugs currently hold orphan drug designation for the treatment of narcolepsy: DRU-2016-5268, DRU-2012-3751, DRU-2010-3072, DRU-1994-858, DRU-1993-737 and DRU-1987-263. Two have been approved: DRU-1994-858 (oxybate) and DRU-1993-737 (modafinil).

*Filled out by Program Support Team

16	Disease Proposed by Sponsor: <i>(Provide several line descriptors not to exceed two paragraphs; cite page numbers in the request for more details.)</i>	Narcolepsy is a neurological disorder characterized by excessive daytime sleepiness, cataplexy, hypnagogic hallucination and sleep paralysis. The prevalence of narcolepsy in the US is 0.02-0.18%. Narcolepsy preferentially affects males with a male to female ratio of 2 to 1. Narcolepsy is thought to have genetic predispositions. Certain human leukocyte antigen (HLA) subtypes and abnormal hypocretin (orexin) neurotransmission have been associated with narcolepsy. An autoimmune etiology is also suggested. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) defines narcolepsy as recurrent episodes of irrepressible need to sleep, lapsing into sleep, or napping occurring within the same day. These sudden sleep attacks may occur during any type of activity at any time of the day.
----	---	--

		<p>Although narcolepsy has traditionally been a disease of adulthood, most cases have their onset in childhood or adolescence. Sleep attacks must have been occurring at least three times per week over the past 3 months for the diagnosis of narcolepsy. There also must be the presence of at least one of the following:</p> <ul style="list-style-type: none"> • Episodes of cataplexy occurring at least a few times per month • Hypocretin deficiency • REM sleep latency ≤ 15 minutes, or a mean sleep latency ≤ 8 minutes and two or more sleep-onset REM periods (SOREMPs) <p>Two tests that are considered essential in confirming a diagnosis of narcolepsy are the polysomnogram (PSG) and the Multiple Sleep Latency Test (MSLT). Three forms of narcolepsy are recognized: narcolepsy with cataplexy, narcolepsy without cataplexy, and narcolepsy due to a medical condition. Treatments of narcolepsy include both pharmacologic and nonpharmacologic approaches. Pharmacologic treatment of narcolepsy involves the use of central nervous system (CNS) stimulants such as methylphenidate, modafinil, dextroamphetamine sulfate, methamphetamine, and amphetamine. Modafinil (Provigil, Modasomil, Modiodal, Vigil) is the first-line pharmacological treatment of excessive daytime sleepiness and irresistible episodes of sleep in association with behavioral measures. Sodium Oxybate (XYREM[®]) is currently the first-line treatment for cataplexy in patients with narcolepsy. Antidepressants, either tricyclics or newer antidepressants, are used treatments. Clinical trials on intravenous immunoglobulin (IVIg) have shown some promising results.</p>
17	"Same Drug(s)" already approved for the same indication?	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
18	If YES, list the drug(s)	Xyrem [®] , sodium oxybate oral solution (500 mg/ml), is currently approved by the FDA under NDA 21196 for the treatment of cataplexy and excessive daytime in narcolepsy.
19	If YES, has the sponsor provided a plausible hypothesis for clinical superiority over all previously approved same drugs?	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> <i>A sleepiness</i>
20	List all hypotheses presented by the sponsor.	The sponsor claims that FT218 provides a major contribution to patient care (MC to PC) over the approved marketed product Xyrem [®] (NDA 021196) by reducing the twice nightly dosing to once before bedtime. The sponsor did not make

		claims on superior clinical safety and efficacy.
21	<p>If YES, provide an analysis of, at a minimum, the plausible hypothesis for clinical superiority that will be the basis of the designation. If NO, provide an analysis why all hypotheses presented by the sponsor are not plausible.</p>	<p>Upon review of the original request, OOPD issued the following deficiency on August 23, 2016: The OOPD acknowledges that the proposed dosing regimen of FT218 is more convenient to the patient and/or caregivers than that of Xyrem®. However, based on your current submission, this reduction in dosing frequency is not considered as providing a major contribution to patient care. You have also not submitted a plausible hypothesis for superior efficacy or safety for your product over the approved product used per marketing label.</p> <p>This amendment (submitted on 10/13/2017) contains the sponsor's response to OOPD's deficiency letter dated 08/23/2016. The sponsor provided letters from four Key Opinion Leaders (Dr. Krahn, Dr. Kryger, Dr. Roth and Dr. Swick) in the field of narcolepsy describing their experiences with narcolepsy patients and how they expect a reduction in dosing frequency to impact their patients to support the sponsor's claim of major contribution to patient care (MCTPC).</p> <p>Sponsor rationale for MCTPC (as described in the original submission and in this amendment by the four narcolepsy experts):</p> <ol style="list-style-type: none"> 1. The sponsor cited a statement distributed at the September 24, 2013 FDA meeting on Drug Development for Narcolepsy: "...an ideal therapy included, a drug that would provide consistent and adequate control of the daytime sleepiness without the hard crash and one that would require dose taken at bedtime resulting in 8 hours of restorative sleep". 2. Eliminate the obvious disadvantage of needing to disrupt sleep in order to take a drug that promotes sleep. 3. Reduce the potential for decreased efficacy if the second of dose of Xyrem® is missed. 4. Eliminate the need to disrupt the sleep of roommates and partners or parents/caregivers of affected children. 5. Reduce safety risks of a second nightly dose of Xyrem® which include: 6. Potential for consumption of the product left on a bedside table by a child

		<ol style="list-style-type: none"> 7. Risk of falls or other accidental injuries if the second dose is not consumed in bed because of the rapid onset of effects 8. The risk of accidental measurement errors in nightly dose preparations 9. Potential impact on diversion: FT218 will be provided as white granules as opposed to Xyrem® which is a clear to slightly opalescent oral solution. Since sodium oxybate has a history of being the “date-rape drug”, the appearance and mouth feel of the white granules could alert the target of the misuse that a substance has been added to his/her drink. <p>After initial review of this amendment, OOPD sent a formal consult request to Division of Neurology Products (DNP) in the Center for Drug Evaluation and Research (CDER) on November 2, 2017, in which OOPD asked DNP’s opinion on whether the once nightly dosing would constitute as MCTPC.</p> <p>CDER/DNP consult (attached with this review) was received by OOPD on December 20, 2017. DNP agrees that the once nightly dosing would be considered as major contribution to patient care. Dr. Mani provided the following statement in his consult review: “Assuming that it is determined by the Agency that any sodium oxybate product (such as FT218) can be administered once each night, at bedtime, rather than twice in a night as is the case for the currently approved marketed sodium oxybate product, Xyrem (for the same indications as Xyrem), that would be a major contribution to patient care. The reasons for the view summarized in the previous paragraph are readily apparent, and have already been outlined in Section 5. Most notably, a once-before-bedtime dosing regime for sodium oxybate would be more convenient (and less disruptive of patient sleep), and more safe, than the administration of two separate doses each night as is the case with Xyrem.”. Dr. Mani also stated in Section 5 of his review: “A once-nightly dosing regimen may present less risk to a patient than a twice-nightly regimen. The twice nightly dosing regimen for Xyrem has, for example, resulted in several patients getting out of bed to take the second dose (contrary to what is recommended in the Prescribing Information), while under the sedating effects of the first dose, and falling and sustaining serious injuries as a result.”</p> <p>Taken into consideration of information provided in the sponsor’s original submission and amendment, as well as</p>
--	--	--

		<p>CDER/DNP consult, OOPD determines that the sponsor has provided a plausible hypothesis for clinical superiority based on major contribution to patient care.</p> <p>In addition, as stated by Dr. Mani, cases have been reported that patients fell and sustained serious injuries when getting out of bed to take the second dose of Xyrem® while under the sedating effects of the first dose. A once before bedtime dosing regimen enabled by FT218 would reduce the risk of falling and subsequent injuries in these patients, therefore, provides a plausible hypothesis of better safety.</p>
22	<p>If YES, select one type of clinical superiority and describe in one sentence the plausible hypothesis that will be the basis for designation. If NO, leave blank.</p>	<p>Safety <input checked="" type="checkbox"/> Effectiveness <input type="checkbox"/> MC to PC <input checked="" type="checkbox"/></p> <p>Plausible Hypothesis:</p> <ol style="list-style-type: none"> 1. FT218 would provide major contribution to patient care compared to Xyrem® by eliminating the need to disrupt sleep. 2. FT218 would provide better safety compared Xyrem® by reducing the risk of falls and subsequent injuries during nighttime.
23	<p>Is subject of request for Orphan Drug Designation a subset of a disease or condition?</p>	<p>Yes <input type="checkbox"/> No <input checked="" type="checkbox"/></p>
24	<p>If YES, is the sponsor seeking a designation for a pediatric subpopulation of a common disease?</p>	<p>Yes <input type="checkbox"/> No <input type="checkbox"/></p>
25	<p>If YES, has the sponsor submitted a property of the product that would limit the product's use to the subset of the disease or condition?</p>	<p>Yes <input type="checkbox"/> No <input type="checkbox"/></p>
26	<p>If YES, describe property that limits use of product to targeted subset. If NO describe if the sponsor has made any attempt at explaining why use of the product is limited to the subset of interest.</p>	
27	<p>Sponsor's Population Estimate and Estimating Methodology : (cite page number in the request)</p>	<p><i>Prevalence of narcolepsy in the US is estimated to be 182,412.</i></p> <p><i>For more information, please see my previous review on the original submission.</i></p>

28	Reviewer agrees with sponsor's assessment that the population is less than 200,000.	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
29	If the reviewer has concerns with population provided by the sponsor, list concerns and include any calculations performed by the reviewer.	
30	Scientific Rationale: Describe the drug and provide a brief description of the mechanism of action if known.	Please see my previous review on the original submission. Scientific rationale is adequate.
31	Is the disease treated by the product the disease that is the subject of the request for orphan drug designation?	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
32	If the disease or condition treated by the product is not the subject of the request for orphan drug designation, describe the disease or condition for the purposes of orphan drug designation and why you believe that to be the case.	
33	If YES, does the sponsor rely on human data?	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
34	If YES, provide a brief description of the human data with page reference to the designation request. No need to describe all human studies. Briefly describe best study and note that others exist. If NO, go to Animal Data.	
35	Animal Data: are the data from an appropriate animal model of the disease?	Yes <input type="checkbox"/> No <input type="checkbox"/>
36	Provide a brief description of the animal data (if any) and make comment upon adequacy of the data (appropriate animal model, appropriate timing of drug delivery, etc.)	

37	If no animal or human data are provided, is there an appropriate animal model of the disease or condition?	Yes <input type="checkbox"/> No <input type="checkbox"/>
38	If NO, are there in vitro data and other supportive data to provide an adequate scientific rationale?	Yes <input type="checkbox"/> No <input type="checkbox"/>
39	Describe the in vitro or other supportive data used to provide an adequate scientific rationale.	

40	Recommendation:	Designate: <input checked="" type="checkbox"/> Abeyance: <input type="checkbox"/> Denial: <input type="checkbox"/>
41	Summarize the Recommendation:	This amendment contains the sponsor's response to OOPD's deficiency letter dated August 23, 2016. Taken into consideration of information submitted by the sponsor and CDER/DNP consult, OOPD has determined that the sponsor has established plausible hypotheses of clinical superiority of FT218 over Xyrem [®] by providing major contribution to patient care and better safety. Scientific rationale is adequate. The estimated population of narcolepsy is 182,412 in the US. Therefore, I recommend this orphan drug designation request be granted.

[Redacted Signature]

Date: 12/21/2017

Gumei Liu, MD, PhD, Staff Fellow

Concur: [Redacted Signature]

Date: 12/26/2017

Henry H. Startzman III, M.D.
Director, Orphan Drug Designation Program

Secondary Reviewer Comments (optional): for example, is a meeting with the sponsor recommended?
Safety also due to possible dosing errors with formation of a second dose. Urginate for Treatment of Narcolepsy.
NHS

Orphan Drug (OD) and Rare Pediatric Disease (RPD) Designation Checklist

- Completed by Designation Reviewer and placed behind a completed orphan designation review when the review results in a recommendation for Orphan Drug or RPD designation status being awarded.
- Completed review and checklist are submitted to the Director, Orphan Drug Designation Program.
- Checklist will aid the Designation Administrator to correctly populate the Designation Database at the time the designation letter is issued to Sponsor.

Designation Application # 16-5302		
Generic, Chemical or Meaningful Descriptive Name: FT218 (sodium oxybate for extended-release oral suspension)		
Orphan or RPD Designation: For the treatment of cataplexy and excessive daytime sleepiness in narcolepsy Disease is Narcolepsy. Treatment of Narcolepsy.		
Patient Population Estimate: 182,412		
IND # 126321		
Circle whether the product is a DRUG or BIOLOGIC (if combination product, circle primary mode of action)		
Check if any of the following apply for Orphan Drug (OD) or Rare Pediatric Disease (RPD) Designation Letters:		
	OD and RPD OPTION 1	Please note that the designation granted is broader than the indication proposed in your designation request.
	OD OPTION 2	Please note that the designation granted is based on the information you submitted and reliance upon additional supportive information.
X	OD OPTION 3	Our decision to grant designation is based on the <i>plausible hypothesis</i> that your drug may be clinically superior to the <u>same drug(s)</u> already approved for the same indication because your drug may <u>(be more safe)</u> provide a major contribution to patient care] due to [that the once before bedtime dosing regimen of FT218 eliminates the need to disrupt sleep and reduces risks of falls and subsequent injuries during nighttime]
	RPD OPTION 2	We determined that [disease name] meets the definition of a rare pediatric disease based on the information you submitted and reliance upon additional supportive information.
	RPD OPTION 3	<i>USE IF WE CANNOT DESIGNATE THE MARKETING APPLICATION</i>
	RPD OPTION 4	<i>USE IF WE CONDITIONALLY DESIGNATE THE APPLICATION</i>
For Database:		
	Combination Product	<i>potential for product to be classified as a drug-biologic, drug-device, biologic-device or biologic-drug-device</i>
	Personalized Medicine	<i>uses genetic or other biomarker information to make treatment decisions about patients</i>
	Bioterrorism	<i>designated for counter-terrorism use</i>
x	Serious	<i>designated for a serious and life threatening disease or condition</i>
x	Same drug designated for same use	<i>If checked, specify other orphan drug designation file number(s): DRU-1994-858</i>
x	MCTPC	<i>designated on a hypothesis that the product is clinically superior in that it will provide a major contribution to patient care [21 CFR 316.3(a)(3)(iii)]</i>
x	Safety	<i>designated on a hypothesis that the product is clinically superior in that it will provide greater safety in a substantial portion of the target population [21 CFR 316.3(a)(3)(ii)]</i>
	Efficacy	<i>designated on a hypothesis that the product is clinically superior in that it will provide greater effectiveness [21 CFR 316.3(a)(3)(i)]</i>
	Orphan Subset	<i>designated for a subset of a non-orphan disease or condition</i>
	Policy Issue	<i>contains issue(s) that could be used to set precedence and/or is controversial. If checked, briefly describe issue below so that Designation Administrator can note in Designation Database comment field:</i>
	Economic	<i>designated based on nonrecovery of costs</i>
	EMA submission	<i>application for same product/disease has been submitted to EMA</i>
	EMA designation	<i>same product/disease holds EMA designation</i>

Specialty (Select up to 3 pertinent specialties from the Groups below and number 1 to 3 from greatest to least importance. Specialty 1 must be from Group A but specialties 2 and 3 can be any listed in Group A or B).

Group A		Group B
	Analgesics/Anesthesiology	Orthopedics
	Cardiology	Otolaryngology/Head & Neck
	Dental	Pharmacology/Toxicology/Poisoning/Chelators
	Dermatology	Physical Medicine and Rehabilitation
	Endocrinology	Psychiatry
	Gastroenterology/Liver	Pulmonary
	Genetics	Radiopharmaceutical/Nuclear Medicine/Radiology
	Hematology	Rheumatology
	Immunology	Substance Abuse
	Infectious Diseases	Transplant
	Metabolism	Urology
	Nephrology	Vascular
x	Neurology	
	Obstetrics and Gynecology	
	Oncology	
	Ophthalmology	
		<i>Bone Marrow Transplant</i>
		<i>Burn</i>
		<i>Devices</i>
		<i>Gene Therapy</i>
		<i>Geriatrics</i>
		<i>HIV/AIDS</i>
		<i>Laser/Photodynamic Therapy</i>
		<i>Medical Foods</i>
		<i>Neonatology</i>
		<i>Neurosurgery</i>
		<i>Nutrition</i>
		<i>Pain</i>
		<i>Pediatrics</i>
		<i>Sickle Cell Disease</i>
		<i>Supplement</i>

Version 10/4/2017



**U.S. FOOD & DRUG
ADMINISTRATION**

Office of Orphan Products Development
Food and Drug Administration
WO32- 5295
10903 New Hampshire Avenue
Silver Spring, MD 20993

JAN 08 2018

The Weinberg Group Inc.
1129 Twentieth St., NW, Suite 600
Washington, DC 20036

Attention: Marla Scarola, MS
Senior Consultant
marla.scarola@weinberggroup.com

Re: Designation request # DRU-2016-5302
Amendment dated: October 13, 2017
Amendment received: October 13, 2017

Dear Ms. Scarola:

This letter responds to your amended request submitted on behalf of Flamel Ireland Limited for orphan-drug designation of sodium oxybate for extended-release oral suspension for “treatment of cataplexy and excessive daytime sleepiness in narcolepsy.”

Pursuant to section 526 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bb), your orphan-drug designation request of sodium oxybate extended-release oral suspension is granted for *treatment of narcolepsy*. Please note that the designation granted is broader than the indication proposed in your designation request

Our decision to grant designation is based on the *plausible hypothesis* that your drug may be clinically superior to the same drug(s) already approved for the same indication because your drug may be more safe due to the ramifications associated with the dosing regimen for the previously approved sodium oxybate in treating patients with narcolepsy. See section 527 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360cc) and 21 CFR 316.3(b)(3) (defining “clinically superior”); and see 21 CFR 316.3(b)(14) (defining “same drug” in this context). Our determination that this hypothesis is plausible does not suggest that this is the only plausible hypothesis for your drug to be clinically superior to any same drug(s) already approved for the same indication.

In order to obtain orphan-drug exclusivity upon approval, you will need to demonstrate that your drug is clinically superior to any already approved version of the same drug for the same indication. Failure to demonstrate clinical superiority over the already approved same drug(s) will result in your drug not receiving orphan-drug exclusivity. *See* 21 CFR 316.34(c). The demonstration of clinical superiority does not need to substantiate the precise hypothesis upon which we based this designation, but instead may demonstrate clinical superiority any way that meets the statutory definition.

If your drug receives marketing approval for an indication broader than what is designated, it may not be entitled to exclusive marketing rights under section 527 (21 U.S.C. 360cc). Therefore, prior to submission of your marketing application, we request that you compare the drug's orphan designation with the proposed marketing indication and submit additional information to amend the orphan-drug designation if warranted. 21 CFR 316.26.

You must submit to the Office of Orphan Products Development a brief progress report of drug development within 14 months after this date and annually thereafter until marketing approval. 21 CFR 316.30.

Please notify this Office within 30 days of submitting a marketing application for the drug's designated use. Once your marketing application is approved, please contact Jeffrey Fritsch, RPh at 301-796-8682 or alternatively at 301-796-8660 to assess eligibility for orphan-drug exclusivity.

If you have questions regarding the development of your designated product, please feel free to contact Gumei Liu, MD, PhD, at 301-796-0495 or alternatively at 301-796-8660. Congratulations on obtaining your orphan-drug designation.

Sincerely,



Debra Y. Lewis, OD, MBA
Acting Director
Office of Orphan Products Development