

## PRACTICE PARAMETER

## Practice Parameters for Clinical Use of the Multiple Sleep Latency Test and the Maintenance of Wakefulness Test

An American Academy of Sleep Medicine Report

Standards of Practice Committee of the American Academy of Sleep Medicine

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**Summary:** Characterization of excessive sleepiness is an important task for the sleep clinician, and assessment requires a thorough history and in many cases, objective assessment in the sleep laboratory. These practice parameters were developed to guide the sleep clinician on appropriate clinical use of the Multiple Sleep Latency Test (MSLT), and the Maintenance of Wakefulness Test (MWT). These recommendations replace those published in 1992 in a position paper produced by the American Sleep Disorders Association. A Task Force of content experts was appointed by the American Academy of Sleep Medicine to perform a comprehensive review of the scientific literature and grade the evidence regarding the clinical use of the MSLT and the MWT. Practice parameters were developed based on this review and in most cases evidence based methods were used to support recommendations. When data were insufficient or inconclusive, the collective opinion of experts was used to support recommendations. These recommendations were developed by the Standards of Practice Committee and reviewed and approved by the Board of Directors of the American Academy of Sleep Medicine.

The MSLT is indicated as part of the evaluation of patients with suspected narcolepsy and may be useful in the evaluation of patients with suspected idiopathic hypersomnia. The MSLT is not routinely indicated in the initial evaluation and diagnosis of obstructive sleep apnea syndrome, or in assessment of change following treatment with nasal continuous positive

airway pressure (CPAP). The MSLT is not routinely indicated for evaluation of sleepiness in medical and neurological disorders (other than narcolepsy), insomnia, or circadian rhythm disorders. The MWT may be indicated in assessment of individuals in whom the inability to remain awake constitutes a safety issue, or in patients with narcolepsy or idiopathic hypersomnia to assess response to treatment with medications. There is little evidence linking mean sleep latency on the MWT with risk of accidents in real world circumstances. For this reason, the sleep clinician should not rely solely on mean sleep latency as a single indicator of impairment or risk for accidents, but should also rely on clinical judgment. Assessment should involve integration of findings from the clinical history, compliance with treatment, and, in some cases, objective testing using the MWT. These practice parameters also include recommendations for the MSLT and MWT protocols, a discussion of the normative data available for both tests, and a description of issues that need further study.

**Key Words:** multiple sleep latency test; maintenance of wakefulness test; sleepiness; hypersomnia; daytime wakefulness.

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## 1.0 INTRODUCTION

**IDENTIFICATION AND CHARACTERIZATION OF EXCESSIVE SLEEPINESS IS ONE OF THE MOST IMPORTANT ROLES FOR THE SLEEP CLINICIAN.** Pathological sleepiness occurs in association with disorders and conditions such as narcolepsy, idiopathic hypersomnia, and sleep deprivation. It may occur due to the obstructive sleep apnea syndrome, periodic limb movement disorder, a variety of other medical and neurological disorders, or medication side effects. Excessive sleepiness is defined as sleepiness that occurs in a situation when an individual would usually be expected to be awake and alert. It affects approximately 5% of the general population<sup>1,2</sup> [1.0]. Excessive sleepiness is associated with significant morbidity and increased mortality risk to the individual and others. For example, sleepiness may adversely affect motor vehicle drivers and those in positions involving public transportation and safety<sup>3</sup>. In addition

to providing a diagnosis and treatment plan for patients with excessive sleepiness, the sleep clinician is responsible for assessing response to treatment, and making clinical decisions that affect individual and public safety.

In 1992 the American Academy of Sleep Medicine (formerly the American Sleep Disorders Association) published a position paper on the clinical use of the Multiple Sleep Latency Test (MSLT) <sup>4</sup>. The paper presented consensus opinion by the Standards of Practice committee (SPC) of the AASM. Clinical guidelines were accompanied by supporting evidence for the position paper. Since publication of the practice guidelines, the scientific literature regarding objective assessment of sleepiness has expanded significantly. More recent studies address the clinical usefulness of the MSLT, and a small but significant group of studies specifically address the operating characteristics of the MSLT as a diagnostic test. The Maintenance of Wakefulness Test (MWT), another laboratory-based objective measure of sleepiness/wakefulness, was not covered in the original paper. Since 1992 the MWT has gained wider clinical acceptance, results are cited more frequently in the literature, and normative data have been collected. Finally, methods used by the Standards of Practice committee have evolved since 1992, and practice parameters are now developed using primarily an evidence-based approach. For these reasons, the following new and updated recommendations were developed regarding the clinical use of the MSLT and MWT. These practice parameters replace the earlier recommendations.

The purpose of this practice parameter paper is to present recommendations for the clinical use of the MSLT and MWT. Recommendations are based on the accompanying review paper produced by a Task Force established by the Standards of Practice Committee <sup>5</sup>. The paper reviews the history of development of the MSLT and MWT, discusses issues related to the objective measurement of sleepiness, and grades the scientific evidence for use of the MSLT and MWT. The review paper and these practice parameters focus on the MSLT and MWT, the two most commonly used objective, laboratory-based methods for characterization of the ability to fall asleep and stay awake, respectively. Other techniques such as pupillometry, continuous EEG or EEG/video monitoring, actigraphy, and questionnaires fall outside the purview of this report, and were not considered. Recommendations involve clinical and not research uses for the MSLT and MWT. Recommendations are targeted to the practice of adult sleep medicine. Although the MSLT and MWT are being used in evaluation of children, special issues exist regarding performance, interpretation, and operating characteristics of these tests in children. The paucity of evidence regarding pediatric usage limits the scope of these recommendations to adolescents and adults.

## 2.0 METHODS

The Standards of Practice Committee of the AASM, in conjunction with specialists and other interested parties, developed these practice parameters based on the accompanying review paper <sup>5</sup>. A Task Force of content experts was appointed by the AASM to review and grade evidence in the scientific literature regarding the clinical use of the MSLT and MWT. In most cases recommendations are based on evidence from studies published in the peer-reviewed literature. When scientific data were absent, insufficient or inconclusive, the Rand/UCLA Appropriateness Method was used to develop recommendations by identifying the collective

opinion of experts in a subcommittee of the SPC and Task Force. The Rand/UCLA Appropriateness Method <sup>6</sup> combines the best available scientific evidence with the collective judgment of experts to yield statements regarding the appropriateness of performing procedures. Specifically, it involves development of a list of specific indications derived from the scientific evidence, and our expert panel rated the appropriateness of these indications in two rounds by individually completing rating sheets. Based on these ratings, our expert panel classified the indications as appropriate, uncertain, or inappropriate. Indications that were classified as appropriate were used to develop these recommendations; indications that were uncertain or inappropriate were rejected.

The Board of Directors of the AASM approved these recommendations. All members of the AASM Standards of Practice Committee and Board of Directors completed detailed conflict-of-interest statements and were found to have no conflicts of interest with regard to this subject.

These practice parameters define principles of practice that should meet the needs of most patients in most situations. These guidelines should not, however, be considered inclusive of all proper methods of care or exclusive of other methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding propriety of any specific care must be made by the physician, in light of the individual circumstances presented by the patient, available diagnostic tools, accessible treatment options, and resources.

The AASM expects these guidelines to have an impact on professional behavior, patient outcomes, and, possibly, health care costs. These practice parameters reflect the state of knowledge at the time of publication and will be reviewed, updated, and revised as new information becomes available. This parameter paper is referenced, where appropriate, using square-bracketed numbers to the relevant sections and tables in the accompanying review paper, or with additional references at the end of this paper. The Standards of Practice Committee's classification of evidence for evidentiary articles is listed in Table 1. Definitions of levels of recommendations used by the AASM appear in Table 2.

**Table 1**—AASM classification of evidence, with subscript:

Recommendation Grades	Evidence Levels	Study Design
A	I	Randomized well-designed trials with low alpha and beta error*
B	II	Randomized trials with high alpha and beta error*
C	III	Nonrandomized concurrently controlled studies
C	IV	Nonrandomized historically controlled studies
C	V	Case series

Adapted from Sackett <sup>7</sup>

\*Alpha error refers to the probability (generally set at 95% or greater) that a significant outcome (e.g.,  $p < 0.05$ ) is not a result of chance occurrence. Beta error refers to the probability (generally set at 80% to 90% or greater) that a nonsignificant result (e.g.,  $p > 0.05$ ) is the correct conclusion of the study or studies. The estimation of beta error is generally the result of a power analysis. The power analysis includes a sample size analysis to project the size of the study population necessary to ensure that significant differences will be observed if actually present.

The AASM appointed a Task Force in 2000 to perform a comprehensive review of the medical literature regarding clinical use of the MSLT and MWT, and to grade the strength of evidence for each citation. The initial literature search was performed on 1/7/00 using Medline. An updated search was performed using the same search strategy on 10/18/2000, and 8/28/2002. A final search was performed on 10/9/03. Details regarding search terms, exclusions, and methods for screening by Task Force members are provided in the review paper<sup>5</sup>. Three members of the Standards of Practice Committee (DGD, MSW, and TLC) served as liaisons between the Standards of Practice Committee and the Task Force.

### 3.0 RECOMMENDATIONS

The following are recommendations of the Standards of Practice Committee and the Board of Directors of the American Academy of Sleep Medicine. The classification of evidence was adapted from the suggestions of Sackett<sup>7</sup> (Table 1). Recommendations are given as standards, guidelines, and options, as defined in Table 2.

#### General Recommendations

1. The MSLT is a validated objective measure of the ability or tendency to fall asleep. [2.2; 2.5; 2.6; 2.7; 6.2.7] (Standard)

The MSLT is intended to measure physiological sleep tendency under standardized conditions in the absence of external alerting factors. The test is based on the premise that the degree of sleepiness is reflected by sleep latency [2.2]. The MSLT is considered the *de facto* standard for objective measurement of sleepiness. For this reason, evaluation of validity is challenging [2.6]. The MSLT has face validity as a measurement of sleepiness. Mean sleep latency values on the MSLT move in the expected direction following experimental sleep fragmentation and sleep restriction, in association with clinical sleep disorders known to produce excessive sleepiness such as narcolepsy and obstructive sleep apnea syndrome, and in subjects exposed to medications known to influence sleep and wakefulness [2.6; 6.2.7]. High test-retest reliability has been demonstrated with the four nap MSLT in normal healthy subjects (test-retest reliability

**Table 2**—AASM levels of recommendations

Term	Definition
Standard	This is a generally accepted patient-care strategy, which reflects a high degree of clinical certainty. The term standard generally implies the use of Level I Evidence, which directly addresses the clinical issue, or overwhelming Level II Evidence.
Guideline	This is a patient-care strategy, which reflects a moderate degree of clinical certainty. The term guideline implies the use of Level II Evidence or a consensus of Level III Evidence.
Option	This is a patient-care strategy, which reflects uncertain clinical use. The term option implies either inconclusive or conflicting evidence or conflicting expert opinion.

Adapted from Eddy<sup>8</sup>

0.97). Reliability is not affected significantly by retest interval or by degree of sleepiness [2.7]. The MSLT demonstrates excellent interrater and intrarater reliability for both sleep latency measurements and REM onset scores in a sleep-disordered population [2.7]. Mean sleep latency values are influenced by physiological, psychological, and test protocol variables [2.5]. Box 1 contains recommendations for the MSLT protocol, including technical aspects of performing the MSLT.

2. The MWT is a validated objective measure of the ability to stay awake for a defined time. [2.3; 2.4; 2.5; 6.2.1; 6.2.7] (Standard)

The MWT measures the ability to stay awake for a defined period of time [2.4]. Clinical relevance of the MWT is based on the premise that the volitional ability to remain awake provides important information regarding the ability to stay awake and response to intervention for a disorder associated with excessive sleepiness [2.4]. Studies demonstrate significant differences in mean sleep latency values between normal healthy subjects and patients with excessive sleepiness due to narcolepsy [6.2.1], and in subjects with narcolepsy studied before and after treatment [6.2.7]. As with the MSLT, mean sleep latency values are influenced by physiological, psychological, and test protocol variables [2.5]. Box 2 contains recommendations for the MWT protocol, including technical aspects of performing the MWT.

3. The MWT is used in association with the clinical history to assess the ability to maintain wakefulness. [2.3; 2.4; 2.5; 2.6] (Standard)

As in the case for the MSLT, findings from the MWT are most valuable when integrated with the clinical history, when the patient is compliant with treatment for his/her sleep disorder, and when the test is performed while the patient is on his/her usual sleep/wake schedule. This recommendation is based in part on data derived from peer-reviewed literature [2.3; 2.4; 2.5; 2.6] and based on consensus. The sleep clinician should inform the patient that a valid MWT can be obtained only after the patient has experienced an adequate quantity and quality of nocturnal sleep during the night prior to the MWT. The sleep clinician should inquire about the patient's sleep, and whether the patient feels normally awake and alert on the day of the test. If the patient reports suboptimal sleep the night before, or suboptimal alertness on the day of the test, or if reliable information is not available, the MWT should not be performed that day. Consideration should be given to rescheduling the MWT and possibly to performing polysomnography before the MWT.

4. The MWT 40 minute protocol is recommended when the sleep clinician requires objective data to assess an individual's ability to remain awake. [6.2.8; 7.0](Option)

A variety of MWT protocols have been used based on duration of trials, and rules for determining sleep latency and termination of trials. Standardization of the MWT offers obvious advantages to the sleep community. Use of the MWT 40 minute protocol is recommended, using the first epoch of sleep as the definition of sleep onset. A trial is terminated after 40 minutes (if no sleep occurs), or after unequivocal sleep onset (defined as 3 continuous epochs of stage 1 sleep or 1 epoch of any other stage of sleep) has occurred. Selection of the 40 minute version decreases the "ceiling effect"

which exists for the MWT, and provides guidance for clinical use of this test. The sleep clinician may elect to use other versions of the MWT in special circumstances, and to address specific research questions. This recommendation is based on limited normative and clinical data in the literature, and collective expert opinion using the Rand/UCLA Appropriateness Method.

5. To provide a valid assessment of sleepiness or wakefulness the MSLT and MWT must be performed under appropriate conditions using proper recording techniques and accepted protocols, with interpretation by a qualified and experienced clinician. [2.6; 6.2.6; 6.2.8; 7.0] (Standard)

Use of standard protocols for the MSLT and MWT improves the validity and reliability of results<sup>9</sup>. This recommendation is based on consensus and sound medical practice, and on limited data that indicate variation in results when protocol variations occur [6.2.8; 7.0]. Boxes 1 and 2 contain specific recommendations for the MSLT and MWT protocols, respectively, including technical details regarding performance of both tests.

Findings from the MSLT are most valuable when integrated with the clinical history, overnight polysomnography, and other information to reach a clinical diagnosis. Mean sleep latency is influenced by quantity of prior sleep, sleep fragmentation, clinical sleep disorders such as obstructive sleep apnea, and circadian phase [2.6; 6.2.6]. For these reasons polysomnography must be performed immediately before the MSLT during the patient's usual major sleep period as determined by the sleep clinician.<sup>9</sup>

Whenever possible, the MSLT should be performed before beginning treatment with stimulants, stimulant-like medications, wakefulness-promoting medications and substances, and REM suppressing medications. The MSLT and MWT should be performed by experienced technologists. The sleep clinician who interprets these tests should have a thorough understanding of standard protocols. He or she should be aware of technical, methodological, and patient-related issues that have the potential to affect validity and reliability of results.

Whereas formal guidelines are available for the performance of the MSLT,<sup>9</sup> no universally accepted guidelines exist for performance of the MWT. At least four different protocols have been used based on varied definitions for sleep onset and trial termination. In a report by Doghramji and colleagues<sup>10</sup> as well as other reports with control data by other investigators, normative data were collected following overnight polysomnography, yet there have been no published guidelines requiring prior polysomnography for MWT interpretation.

Factors which support performing comprehensive polysomnography (i.e., EEG, EOG, leg and chin EMG, EKG, snoring microphone, oronasal airflow, chest and abdominal wall movement, pulse oximetry) prior to the MWT include the following: 1) normative data for the MWT were collected using protocols that included nocturnal polysomnography, 2) total sleep time is important to know for interpretation, since mean sleep latency is influenced by total sleep time, 3) certain patients may wish to demonstrate inability to remain awake and this could be accomplished by appearing for the MWT in a sleep deprived state, and 4) the MSLT protocol requires polysomnography and therefore the MWT should be performed in the same way.

Factors which do not support routine performance of polysomnography prior to the MWT include the following: 1)

studies that report normative data or patient data rarely provide total sleep time results for analysis, 2) there is no information about whether the MWT is more or less useful from a clinical standpoint when prior sleep time is reported, 3) the primary purpose of the MWT is to document ability to remain awake following intervention and this issue can be addressed using mean sleep latency values without knowing the total sleep time, and 4) polysomnography is relatively expensive.

Thus, performance of polysomnography immediately prior to the MWT is optional, and the decision should be made by the sleep clinician based upon clinical circumstances. If the MWT is performed without polysomnography and results indicate inability to maintain wakefulness, the sleep clinician may have uncertainty about the cause of the subject's sleepiness. In this situation further evaluation, possibly including polysomnography, is necessary to determine the reason for inability to maintain wakefulness.

#### Specific Indications for Use of the MSLT

1. The MSLT is indicated as part of the evaluation of patients with suspected narcolepsy to confirm the diagnosis. [6.2.1; 6.2.2] (Standard)

The usefulness of the mean sleep latency value in the evaluation of patients with possible narcolepsy is supported by evidence reported in 13 papers that met inclusion criteria [6.2.1]. These articles were judged to be reasonably free of inclusion bias. Four papers included mean sleep latency values for a comparison group of normal control subjects. These papers report a total of 39 subjects with narcolepsy (weighted mean sleep latency = 3.0 +/- 3.1 minutes), compared with 40 control subjects (weighted mean sleep latency = 10.5 +/- 4.6 minutes). This difference is statistically significant ( $p < 0.001$ ). Nine papers reported a total of 255 patients with narcolepsy without a comparison group of normal control subjects. Results from this group revealed a mean sleep latency of 3.1 +/- 2.9 minutes [6.2.1]. These findings indicate that most patients with narcolepsy have objective evidence of hypersomnia as determined by mean sleep latency less than 5 minutes. However, these data suggest that approximately 16% of patients with narcolepsy would have a mean sleep latency above the 5 minute cutoff, and approximately 16% of normal controls would have a mean sleep latency below the 5 minute cutoff [6.2.1].

The usefulness of the MSLT for identification of sleep-onset REM periods (SOREMPs) is supported by nine studies that met inclusion criteria, and that were judged to be reasonably free of SOREMP requirements (inclusion bias) [6.2.2]. Results indicate that SOREMPs (defined as the first epoch of REM sleep at any time during the nap trial) are very common in individuals with narcolepsy. The presence of two or more SOREMPs was associated with a sensitivity of 0.78 and a specificity of 0.93 [6.2.2]. SOREMPs did not occur exclusively in patients with narcolepsy, and thus it is important to rule out or treat other sleep disorders before evaluating SOREMPs in the diagnosis of narcolepsy. Examples of other sleep disorders associated with SOREMPs include obstructive sleep apnea, or any condition associated with reduced nocturnal REM sleep leading to "REM rebound" during the day. The number of SOREMPs increased with decreasing mean sleep latency values on the MSLT [6.2.2].

The co-occurrence of obstructive sleep apnea syndrome and narcolepsy is well documented<sup>11-17</sup>.

- The MSLT may be indicated as part of the evaluation of patients with suspected idiopathic hypersomnia to help differentiate idiopathic hypersomnia from narcolepsy. [6.2.3] (Option)

This recommendation is based on data from four articles involving patients with idiopathic hypersomnia in which diagnostic criteria were not entirely dependent on mean sleep latency values [6.2.3]. These papers report a total of 92 patients with idiopathic hypersomnia with a weighted mean sleep latency of 6.2 +/-3.0 minutes. This value is intermediate between those reported for patients with narcolepsy and normal control subjects [6.2.3]. These values suggest that differentiation of sleepiness due to idiopathic hypersomnia from the sleepiness seen in normal controls may be difficult.

- The MSLT is not routinely indicated in the initial evaluation and diagnosis of obstructive sleep apnea syndrome or in assessment of change following treatment with nasal CPAP.

Individuals with a previously identified sleep disorder such as obstructive sleep apnea syndrome or other sleep-related breathing disorder, periodic limb movement disorder, or mood disorders who continue to experience excessive sleepiness despite optimal treatment may require evaluation for possible narcolepsy, including the MSLT. [6.2.4] (Guideline)

This recommendation represents a change from the initial guidelines published in 1992<sup>4</sup>. This recommendation is based on evidence presented in 16 papers that met inclusion criteria [6.2.4]. In two papers comparing subjects with obstructive sleep apnea with control subjects, there was significant overlap in mean sleep latency values on the MSLT. Among 10 papers assessing changes in mean sleep latency values pre-treatment and post-treatment for obstructive sleep apnea, nine studies showed statistically significant increases in mean sleep latency values. However, both pre-treatment and post-treatment mean values were within one standard deviation of normal control means, indicating that mean sleep latency values are poor discriminators of response to treatment. Four papers assessed changes in mean sleep latency values in subjects with obstructive sleep apnea treated with CPAP compared with placebo. Two studies showed increases in mean sleep latency values in treated obstructive sleep apnea subjects compared with placebo, and two studies showed no changes. Overnight polysomnography is the diagnostic procedure of choice for evaluation of individuals with possible sleep-related breathing disorders<sup>18</sup> and available evidence indicates that routine use of the MSLT does not contribute significantly to diagnosis or assessment of response to treatment for sleep-related breathing disorders.

- The MSLT is not routinely indicated for evaluation of sleepiness in medical and neurological disorders (other than narcolepsy), insomnia, or circadian rhythm disorders [6.2.5] (Option)

No studies were identified to provide support for the routine use of the MSLT for evaluation of sleepiness in medical and neurological disorders other than those specifically discussed in these guidelines, insomnia, or circadian rhythm disorders. This recommendation represents a change from the initial guidelines published in 1992, in that an MSLT is not routinely indicated in the evaluation of patients suspected of having periodic limb movement disorder, or other conditions except narcolepsy and idiopathic hypersomnia. This recommendation is based on collective expert opinion using the Rand/UCLA Appropriateness method.

- Repeat MSLT testing may be indicated in the following situations: (a) when the initial test is affected by extraneous circumstances or when appropriate study conditions were not present during initial testing, (b) when ambiguous or uninterpretable findings are present, (c) when the patient is suspected to have narcolepsy but earlier MSLT evaluation(s) did not provide polygraphic confirmation. [6.2.2] (Standard)

This recommendation is based on consensus and sound medical practice for situations (a) and (b). In situation (c), this recommendation is based on the observation that the sensitivity for identification of two or more SOREMPs in patients with narcolepsy is not 100% [6.2.2]. Thus, repeating the MSLT may increase the likelihood of recording two or more SOREMPs to provide polygraphic evidence to support the diagnosis of narcolepsy.

#### Specific Indications for Use of the MWT

- The MWT 40 minute protocol may be used to assess an individual's ability to remain awake when his or her inability to remain awake constitutes a public or personal safety issue. [6.2.6; 7.0] (Option)

Individuals with obstructive sleep apnea, narcolepsy, and possibly other sleep disorders, who are employed in occupations involving public transportation or safety may require assessment of their ability to remain awake. Data regarding usefulness of MSLT or MWT results to evaluate safety are limited [6.2.6;7.0]. Using the MWT to assess ability to remain awake has greater face validity than using the MSLT, which measures the ability or tendency to fall asleep. However, the predictive value of MSLT or MWT mean sleep latency for assessing accident risk and safety in real world circumstances is not established for either test [7.0]. Given this lack of supporting data, the Rand/UCLA Appropriateness Method was used to develop this parameter. In addition, the assessment of ability to remain awake and potential risk for accidents due to unintended sleepiness must involve integration of findings from the clinical history, compliance with therapy, and in some cases, objective testing with the MWT. The sleep clinician should not rely solely on the mean sleep latency as an indicator of risk for transportation, work or home-related accidents.

When the MWT is used, the minimum acceptable result should be based on the task requirements. A total of 97.5% of normal subjects had a mean sleep latency of  $\geq 8.0$  minutes. The data on the 40-min MWT from normal subjects using a definition for sleep onset of 3 epochs of stage 1 or the first epoch of any stage of sleep showed that 59% of normal subjects remained awake for the entire 40-min trial across each of four trials. Using a sleep onset definition of the first continuous 10 seconds of stage1 or the first epoch of any stage of sleep, which contributes to a more normal range of scores and less of a ceiling effect, 42% of subjects remained awake for the entire 40-min trial across each of four trials. Staying awake on all trials of a 40-min MWT provides the strongest objective data available supporting an individual's ability to stay awake and may provide an appropriate expectation for individuals requiring the highest level of safety. Based on these data, a mean sleep latency  $< 8.0$  minutes on the 40-min MWT is considered abnormal; values greater than this but less than 40 minutes are of uncertain significance. Documentation that an individual is able to fall into any of these categories for remaining awake in the MWT testing environ-

ment provides no guarantee that the subject will not experience sleepiness in the work environment. The ability to remain awake in the work environment on a daily basis is influenced by several variables. These may include the individual's compliance with treatment, quantity and quality of sleep, circadian variations, hours of prior work, and possibly medication side effects. In addition, clinical judgment should always prevail, since completely normal values do not necessarily ensure safety.

## 2. The MWT may be indicated in patients with excessive sleepiness to assess response to treatment. [6.2.7] (Guideline)

In some situations involving patients with disorders of excessive sleepiness, objective measures of ability to remain awake are necessary to help characterize response to treatment. Although there are no established levels to indicate what magnitude of change is considered significant, the direction of the change often can serve as an adjunct to clinical judgment in determining appropriate response to treatment. There are three studies demonstrating increases in mean sleep latency values on the MWT following administration of modafinil compared with placebo in subjects with narcolepsy [6.2.7]. Studies also document increases in mean sleep latency with stimulants and CPAP treatment, and decreases with benzodiazepines and barbiturates [2.5; 6.2.4].

## 4.0 DISCUSSION OF NORMATIVE VALUES FOR THE MSLT AND MWT

Establishing normative mean sleep latency values for the MSLT is complicated due to a variety of factors. Although it is a validated measure, there is no large systematically collected repository of normative data for the MSLT [2.8]. Most studies report findings regarding investigation of clinical sleep disorders and are not designed to establish normative values. The accompanying review paper identifies and discusses in detail the methodological factors and individual variables that influence mean sleep latency values, as well as challenges associated with establishing normative ranges [2.8; 6.2.8; 7.0].

Many papers cited in the scientific literature do not provide important data such as prior sleep time and sleep quality, definitions for establishing sleep onset and nap termination, whether four or five naps were used, and whether caffeine use was allowed. A review of 77 articles that used the clinical MSLT revealed that 43% did not specify any sleep onset definition or any methodology reference [6.2.8]. These observations indicate that unspecified methodological variations may be present in the data with the potential to alter mean sleep latency values and normative ranges.

Many studies did not provide information regarding how rigorously healthy control subjects were assessed, including whether the subject maintained a consistent sleep/wake schedule or kept a sleep diary prior to testing, whether urine drug screens were performed, and age of control subjects. Some studies relied upon questionnaires or clinical interview rather than polysomnography to screen for clinical sleep disorders. Significant age related changes were documented in one study as well as in the analysis in the review paper [6.2.8].

Identification of normative ranges is limited by the large standard deviation in mean sleep latency values on the MSLT, as well as floor and ceiling effects which suggests that values are not normally distributed. This results in significant overlap between

mean sleep latency values among healthy controls and populations with excessive sleepiness. Pooled data from normal subjects across all ages using the 4 or 5 nap MSLT with sleep onset defined as the latency to the first epoch of any sleep stage, give a mean sleep latency of 10.4 +/- 4.3 minutes and 11.6 +/- 5.2 minutes, respectively. This difference is statistically significant ( $p < 0.01$ ) [6.2.8]. Based on 2 SD from the mean, 95% of the values from control populations on the 4 nap MSLT would fall between 1.8 – 19 minutes while the values for the 5 nap MSLT would fall between 1.2 – 20 minutes [7.0]. The MSLT does not discriminate well between clinical and control populations, but in the clinical population the MSLT is useful for diagnostic purposes.

Based on evidence currently available, the mean sleep latency should not be the sole criterion for determining the presence or severity of excessive sleepiness, certifying a diagnosis or response to treatment [8.0]. Rather, assessment should involve integration of the clinical history, objective test results, and other medical information. Sleepiness should not be characterized solely on the basis of an isolated mean sleep latency value.

Table 3 summarizes MSLT mean sleep latency values from normal control subjects using the four and five nap protocols. For comparison, mean sleep latency values are also provided for a group of individuals with narcolepsy.

As with the MSLT, there is no large, multi-center, systematically collected repository of normative data for mean sleep latency values on the MWT [6.2.8]. Five articles reporting MWT results were identified with normative data [6.2.8], and in the accompanying review, data were used to generate estimates of normative data. In contrast to the clinical MSLT, there are at least four different MWT protocols based on differences in definition of sleep onset, and trial duration (20 minutes versus 40 minutes), and these variations affect normative values [6.2.8]. Whereas the MSLT demonstrates a “floor effect” in subjects with severe sleepiness, MWT results show evidence of a “ceiling effect” in subjects with normal levels of wakefulness, with many subjects remaining awake during each trial. This results in the data not being normally distributed among normal subjects. The ceiling effect is less pronounced in the 40-minute than the 20-minute protocol since the 40 minute test is more challenging and provides a greater distribution of values. Consequently, the 40-minute protocol may be better in identifying subjects with difficulty remaining awake [7.0]. Age related differences in mean sleep latency values exist for the MWT similar to those observed in the MSLT. Specifically, mean sleep latency values are lower for normal subjects 30-39 years of age compared with those of older normal subjects [6.2.8].

Table 4 summarizes findings regarding the MWT40 protocol based on the systematic control study performed by Doghramji

**Table 3**—Summary of control mean sleep latency values on MSLT (from pooled data as discussed in Sections 6.2.8 and 6.2.1)

Test protocol	Mean +/-SD (minutes)
MSLT 4 naps	10.4 +/- 4.3*
MSLT 5 naps	11.6 +/- 5.2*
MSLT in patients with Narcolepsy	3.1 +/-2.9

\*4 vs. 5 nap MSL  $p < 0.01$

Data for 4 and 5 nap MSLT are collapsed across age groups, however, there were significant differences for age so age appropriate comparisons are recommended.

**Table 4**—MWT 40 minute protocol control values

Mean sleep latency, using latency to first epoch of sleep	30.4 +/- 11.20 min
Upper limit of 95% confidence interval	40.0 min

and colleagues. The table provides the overall mean sleep latency value among normal control subjects, and the upper limit of the 95<sup>th</sup> percentile confidence interval.

## 5.0 FUTURE RESEARCH

A number of challenges exist with regard to improving the clinical usefulness of the MSLT and MWT. Despite an expand-

### Box 1

#### Recommendations for the MSLT Protocol

(Adapted from Carskadon and colleagues, Guidelines for the multiple sleep latency test (MSLT): a standard measure of sleepiness<sup>9</sup>. Modified by collective expert opinion using Rand/UCLA Appropriateness Method)

1. The MSLT consists of five nap opportunities performed at two hour intervals. The initial nap opportunity begins 1.5 to 3 hours after termination of the nocturnal recording. A shorter four-nap test may be performed but this test is not reliable for the diagnosis of narcolepsy unless at least two sleep onset REM periods have occurred.
2. The MSLT must be performed immediately following polysomnography recorded during the individual's major sleep period. The use of MSLT to support a diagnosis of narcolepsy is suspect if TST on the prior night sleep is less than 6 hours. The test should not be performed after a split-night sleep study (combination of diagnostic and therapeutic studies in a single night).
3. Sleep logs may be obtained for 1 week prior to the MSLT to assess sleep-wake schedules.
4. Standardization of test conditions is critical for obtaining valid results. Sleep rooms should be dark and quiet during testing. Room temperature should be set based on the patient's comfort level.
5. Stimulants, stimulant-like medications, and REM suppressing medications should ideally be stopped 2 weeks before MSLT. Use of the patient's other usual medications (e.g., antihypertensives, insulin, etc.) should be thoughtfully planned by the sleep clinician before MSLT testing so that undesired influences by the stimulating or sedating properties of the medications are minimized. Drug screening may be indicated to ensure that sleepiness on the MSLT is not pharmacologically induced. Drug screening is usually performed on the morning of the MSLT but its timing and the circumstances of the testing may be modified by the clinician. Smoking should be stopped at least 30 minutes prior to each nap opportunity. Vigorous physical activity should be avoided during the day and any stimulating activities by the patient should end at least 15 minutes prior to each nap opportunity. The patient must abstain from any caffeinated beverages and avoid unusual exposures to bright sunlight. A light breakfast is recommended at least 1 hour prior to the first trial, and a light lunch is recommended immediately after the termination of the second noon trial.
6. Sleep technologists who perform MSLTs should be experienced in conducting the test.
7. The conventional recording montage for the MSLT includes central EEG (C3-A2, C4-A1) and occipital (O1-A2, O2-A1) derivations, left and right eye electrooculograms (EOGs), mental/submental electromyogram (EMG), and electrocardiogram (EKG).
8. Prior to each nap opportunity, the patient should be asked if they need to go to the bathroom or need other adjustments for comfort. Standard instructions for bio-calibrations (i.e., patient calibrations) prior to each nap include: (1) lie quietly with your eyes open for 30 seconds, (2) close both eyes for 30 seconds, (3) without moving your head, look to the right, then left, then right, then left, right and then left, (4) blink eyes slowly for 5 times, and (5) clench or grit your teeth tightly together.
9. With each nap opportunity the subject should be instructed as follows: "Please lie quietly, assume a comfortable position, keep your eyes closed and try to fall asleep." The same instructions should be given prior to every test. Immediately after these instructions are given, bedroom lights are turned off, signaling the start of the test. Between naps, the patient should be out of bed and prevented from sleeping. This generally requires continuous observation by a laboratory staff member.
10. Sleep onset for the clinical MSLT is determined by the time from lights out to the first epoch of any stage of sleep, including stage 1 sleep. Sleep onset is defined as the first epoch of greater than 15 sec of cumulative sleep in a 30-sec epoch. The absence of sleep on a nap opportunity is recorded as a sleep latency of 20 minutes. This latency is included in the calculation of mean sleep latency (MSL). In order to assess for the occurrence of REM sleep, in the clinical MSLT the test continues for 15 minutes from after the first epoch of sleep. The duration of 15 minutes is determined by "clock time", and is not determined by a sleep time of 15 minutes. REM latency is taken as the time of the first epoch of sleep to the beginning of the first epoch of REM sleep regardless of the intervening stages of sleep or wakefulness.
11. A nap session is terminated after 20 minutes if sleep does not occur.
12. The MSLT report should include the start and end times of each nap or nap opportunity, latency from lights out to the first epoch of sleep, mean sleep latency (arithmetic mean of all naps or nap opportunities), and number of sleep-onset REM periods (defined as greater than 15 sec of REM sleep in a 30-sec epoch).
13. Events that represent deviation from standard protocol or conditions should be documented by the sleep technologist for review by the interpreting sleep clinician.

ing number of citations in the medical literature with regard to objective assessment of sleepiness, few studies were designed primarily to address the specific operating characteristics of the MSLT or MWT across different patient groups and ages. As a result there is a paucity of studies that provide well defined normative data, sensitivity and specificity data across patient groups, and determination of the impact of MSLT and MWT results on clinical decision-making or patient outcome. Future research is needed to define normative values using rigorous methods, to identify the impact of a standard clinical protocol for the MWT, and to correlate degree of sleepiness on objective testing with safety and occupational risk for the individual and for society in "real life" circumstances.

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### Box 2

#### Recommendations for the MWT protocol

(Developed from methods of Doghramji and colleagues, A normative study of the maintenance of wakefulness test (MWT), 1997.<sup>10</sup>  
Modified by collective expert opinion using Rand/UCLA Appropriateness Method)

1. The 4-trial MWT 40-minute protocol is recommended. The MWT consists of four trials performed at two hour intervals, with the first trial beginning about 1.5 to 3 hours after the patient's usual wake-up time. This usually equates to a first trial starting at 0900 or 1000 hours.
2. Performance of a PSG prior to MWT should be decided by the clinician based on clinical circumstances.
3. Based on the Rand/UCLA Appropriateness Method, no consensus was reached regarding the use of sleep logs prior to the MWT; there are instances, based on clinical judgment, when they may be indicated.
4. The room should be maximally insulated from external light. The light source should be positioned slightly behind the subject's head such that it is just out of his/her field of vision, and should deliver an illuminance of 0.10-0.13 lux at the corneal level (a 7.5 W night light can be used, placed 1 foot off the floor and 3 feet laterally removed from the subject's head). Room temperature should be set based on the patient's comfort level. The subject should be seated in bed, with the back and head supported by a bedrest (bolster pillow) such that the neck is not uncomfortably flexed or extended.
5. The use of tobacco, caffeine and other medications by the patient before and during MWT should be addressed and decided upon by the sleep clinician before MWT. Drug screening may be indicated to ensure that sleepiness/wakefulness on the MWT is not influenced by substances other than medically prescribed drugs. Drug screening is usually performed on the morning of the MWT but its timing and the circumstances of the testing may be modified by the clinician. A light breakfast is recommended at least 1 hour prior to the first trial, and a light lunch is recommended immediately after the termination of the secondnoon trial.
6. Sleep technologists who perform the MWT should be experienced in conducting the test.
7. The conventional recording montage for the MWT includes central EEG (C3-A2, C4-A1) and occipital (O1-A2, O2-A1) derivations, left and right eye electrooculograms (EOGs), mental/submental electromyogram (EMG), and electrocardiogram (EKG).
8. Prior to each trial, the patient should be asked if they need to go to the bathroom or need other adjustments for comfort. Standard instructions for bio-calibrations (i.e., patient calibrations) prior to each trial include: (1) sitlie quietly with your eyes open for 30 seconds, (2) close both eyes for 30 seconds, (3) without moving your head, look to the right, then left, then right, then left, right and then left, (4) blink eyes slowly for 5 times, and (5) clench or grit your teeth tightly together.
9. Instructions to the patient consist of the following: "Please sit still and remain awake for as long as possible. Look directly ahead of you, and do not look directly at the light." Patients are not allowed to use extraordinary measures to stay awake such as slapping the face or singing.
10. Sleep onset is defined as the first epoch of greater than 15 sec of cumulative sleep in a 30-sec epoch.
11. Trials are ended after 40 minutes if no sleep occurs, or after unequivocal sleep, defined as three consecutive epochs of stage 1 sleep, or one epoch of any other stage of sleep.
12. The following data should be recorded: start and stop times for each trial, sleep latency, total sleep time, stages of sleep achieved for each trial, and the mean sleep latency (the arithmetic mean of the four trials).
13. Events that represent deviation from standard protocol or conditions should be documented by the sleep technologist for review by the sleep specialist.

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