Executive Summary:
Licit Schedule II Drug Use and Commercial Motor Vehicle Driver Safety

Presented to

Federal Motor Carrier Safety Administration

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Prepared for

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This report is comprised of research conducted to analyze the impact of Licit Schedule II Drug Use on Commercial Motor Vehicle Driver Safety. Federal Motor Carrier Safety Administration considers evidence, expert recommendations, and other data, however, all proposed changes to current standards and guidance (guidelines) will be subject to public-notice-and-comment and regulatory processes.

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Policy Statement

ECRI prepared this report under subcontract to MANILA Consulting Group, Inc., which holds prime Contract No. GS-10F-0177N/DTMC75-05-F-00062 with the Department of Transportation's Federal Motor Carrier Safety Administration. ECRI is an independent, nonprofit health services research agency and a Collaborating Center for Health Technology Assessment of the World Health Organization. ECRI has been designated an Evidence-based Practice Center (EPC) by the United States Agency for Healthcare Research and Quality. ECRI's mission is to provide information and technical assistance to the healthcare community worldwide to support safe and cost-effective patient care. The results of ECRI's research and experience are available through its publications, information systems, databases, technical assistance programs, laboratory services, seminars, and fellowships. The purpose of this evidence report is to provide information on the current state of knowledge on this topic. It is not intended as instruction for medical practice or for making decisions regarding individual patients.

Purpose of Evidence Report

Of all occupations in the United States, workers in the trucking industry experience the third-highest fatality rate, accounting for 12 percent of all worker deaths. About two-thirds of fatally injured truck workers were involved in highway crashes. According to statistics from the United States Department of Transportation for 2005, 137,144 crashes involved a large truck. Of these, 59,405 were crashes that resulted in an injury to at least one individual for a total of 89,681 injuries. In 2004,[1] 4,862 large trucks were involved in fatal crashes for a total of 5,190 fatalities. The purpose of this evidence report is to examine the relationship between the licit use of a Schedule II drug and the risk for a motor vehicle crash. To meet the aims of this evidence report, we addressed the following eight key questions:

Key Question 1: Does the licit use of a prescribed Schedule II drug increase the risk for a motor vehicle crash?

Key Question 2: Does the licit use of a prescribed Schedule II drug negatively impact indirect measures of driving ability?

Key Question 3: What is the correlation between the serum level of a Schedule II drug and the risk for a motor vehicle crash?

Key Question 4: What is the correlation between the serum level of a Schedule II drug and indirect measures of driving ability?

Key Question 5: Is there a relationship between the pharmacokinetics of a Schedule II drug and the risk for a motor vehicle crash?

Key Question 6: Is there a relationship between the pharmacokinetics of a Schedule II drug and indirect measures of driving ability?

Key Question 7: Are there common drug interactions that include a prescribed Schedule II drug that increase the risk for a motor vehicle crash?

Key Question 8: Are there common drug interactions that include a prescribed Schedule II drug that affect indirect measures of driving ability?

Identification of Evidence Bases

Separate evidence bases for each of the key questions addressed by this evidence report were constructed by performing a comprehensive search of the literature, examining the abstracts of identified studies to determine which articles would be retrieved, and selecting the actual articles that would be included in each evidence base.

A total of seven electronic databases (Medline, PubMed (pre-Medline), EMBASE, PsycINFO, CINAHL, TRIS, and the Cochrane library) were searched (through June 28, 2006). In addition, we examined the reference lists of all obtained articles with the aim of identifying relevant articles not identified by our electronic searches. Hand searches of the "gray literature" were also performed. Admission of an article into an evidence base was determined by formal retrieval and inclusion criteria determined a priori.

[1] Fatality data for 2005 were not available at the time of writing.

Grading the Strength of Evidence

Our assessment of the quality of the evidence took into account the quality of the individual studies that comprise the evidence base for each key question. We also considered the interplay between the quality, quantity, robustness, and generalizability (to the specific target population of interest) of the overall body of evidence.

Analytic Methods

Meta-analysis of the data extracted from the studies meeting the inclusion criteria for this evidence report was not appropriate. Consequently, the conclusions of this report are based on the findings of a series of qualitative assessments of the available evidence.

Presentation of Findings

The strength-of-evidence ratings assigned to the findings presented in this report are defined in Table 1.

Table 1. Strength-of-Evidence Ratings for Qualitative and Quantitative Conclusions

Strength of Evidence	Interpretation
High	The estimate of treatment effect in the conclusion is stable. The magnitude of this estimate is highly unlikely to change substantially as a result of the publication of new evidence.
Moderate	The estimate of treatment effect in the conclusion is somewhat stable. A small chance exists that the magnitude of this estimate will change substantially as a result of the publication of new evidence. ECRI recommends regular monitoring of the relevant literature.
Low	The estimate of treatment effect in the conclusion is likely to be unstable. A reasonable chance exists that the magnitude of this estimate will change substantially as a result of the publication of new evidence. ECRI recommends frequent monitoring of the relevant literature.
Unstable	Estimates of the treatment effect are too unstable to allow a quantitative conclusion to be drawn at this time. ECRI recommends frequent monitoring of the relevant literature.

Findings

Specific findings of our assessment of the evidence that pertains to the eight key questions addressed in this evidence report are presented below.

<u>Key Question #1:</u> Does the licit use of a prescribed Schedule II drug increase the risk for a motor vehicle crash?

Whether a relationship exists between the licit use of a Schedule II drug and motor vehicle (any category) crash risk cannot be determined at the present time.

Although our searches identified and retrieved 49 potentially relevant articles, none met the inclusion criteria for this key question. The primary reason for exclusion was that studies combined crash data from licit and illicit Schedule II drug users (32 studies). Because illicit drug users do not use drugs in a manner that is compatible with a therapeutic regimen (the aim of a drug abuser is to use the drug to deliberately initiate a change in mental state, whereas the aim of a licit user is to treat a disorder), crash data that include drug abusers cannot provide an answer to Key Question 1. The second reason for exclusion was that several studies were designed to examine the crash risk associated with a particular drug class that encompassed drugs spanning several drug schedules (eight studies). Not all opioids, stimulants, and

depressants are Schedule II drugs, and studies that evaluated crash risk by drug class did not stratify crash risk data by United States Drug Enforcement Agency drug schedule.

***Key Question #2:* Does the licit use of a prescribed Schedule II drug negatively impact indirect measures of driving ability?**

General Finding

1. **A paucity of data from studies that enrolled commercial motor vehicle (CMV) drivers precludes direct determination of whether the driving ability (as measured using a simulator or on a specific test circuit), cognitive and psychomotor function, or the mood and behavior of CMV drivers are adversely affected by the licit use of any Schedule II opioids.**

   Two included studies enrolled individuals who could potentially be considered CMV drivers. Both studies recruited individuals whom the study investigators termed "professional drivers". However, the articles describing these studies are unclear on how the study investigators defined a "professional driver". Consequently, the possibility remains that none, or only a small proportion, of the enrollees in these two studies actually drove large trucks or buses.

Findings Specific to Licit Schedule II Opioid Use

1. **A paucity of high-quality data makes it impossible to draw an evidence-based conclusion about whether first-time administration of a Schedule II opioid has a deleterious effect on driving ability.**

   A single, small, low-quality study evaluated the effects of a single 50 mg oral dose of codeine on driving ability as measured using a driving simulator in opioid-naïve healthy individuals. This study found that codeine had a significant deleterious effect on driving ability. Because this study is not of high quality, however, and its findings have not yet been replicated, an evidence-based conclusion cannot be drawn at the present time.

2. **A paucity of high-quality data makes it impossible to draw an evidence-based conclusion on whether licit Schedule II opioid use has a deleterious effect on driving ability among individuals who have used long-term stable doses of the drug for a legitimate medical reason.**

   A single, small, low-quality study evaluated the effects of stable doses of various opioids on the driving ability of individuals with chronic pain. No evidence of a driving ability deficit was observed in long-term opioid users on either a community driving course or an obstacle course. Because this study is not of high quality and its findings have not yet been replicated, an evidence-based conclusion cannot be drawn at the present time.

3. **First-time administration of a single therapeutic dose of a Schedule II opioid to opioid-naïve individuals has a deleterious effect on psychomotor and high-level (but not low-level) cognitive function (Strength of Evidence: Moderate).**

   Six small, but otherwise high-quality studies, assessed the effects of the administration of an opioid on some measures of cognitive (high-level) and psychomotor function among opioid-naïve healthy individuals. Four of the six studies found that psychomotor and high-level

cognitive function were adversely affected by a single dose of an opioid (morphine, alfentanil, meperidine, or fentanyl). The remaining two studies, both of which evaluated the effects of a single dose of codeine (30 to 100 mg), found no such drug effect. Whether the inconsistency in the findings of the six studies included in this assessment is a consequence of differences in the drugs themselves, dosage, measurement timing, the sensitivity of the psychometric instruments used to evaluate cognitive and psychomotor function, the size of the included studies, or the characteristics of the individuals enrolled in the studies cannot be determined at this time.

4. **Owing to a paucity of consistent data from high-quality trials, it is not possible at the present time to draw an evidence-based conclusion on whether chronic (>seven days) use of a Schedule II opioid has a deleterious impact on cognitive or psychomotor function.**

   Five low-quality studies assessed the effects of the long-term administration of an opioid on cognitive and psychomotor function among individuals with chronic pain. Three of the five included studies did not observe any detrimental effects of opioids on cognitive or psychomotor function. Two studies, however, provide limited evidence supporting the contention that the long-term use of a Schedule II opioid (transdermal fentanyl) may have a deleterious impact on cognitive and psychomotor function.

   None of the included studies in the evidence base considered here were designed as non-inferiority or equivalency studies. That is, they were not designed to test the hypothesis that the administration of therapeutic doses of an opioid does not have a deleterious impact on outcome. Rather, the included studies were designed to test the hypothesis that the administration of an opioid will have a deleterious impact on outcome. Failure to disprove the null hypothesis (not observing a treatment effect) by studies that use this design cannot be construed as providing evidence of no drug effect. Evidence from such studies, even when consistently observed by several independent studies can, at best, be considered suggestive of no treatment effect.

5. **A lack of data from studies in which a Schedule II opioid was administered to opioid-naïve individuals makes it impossible to determine whether first-time administration of an opioid has a detrimental effect on mood or behavior.**

   No included studies evaluated the effects of opioids on mood or behavior in opioid-naïve individuals.

6. **Currently available data do not provide evidence to support the contention that stable (no change in dose in the previous seven days) therapeutic doses of a Schedule II opioid (morphine) have a detrimental effect on mood or behavior (Strength of Evidence: Weak).**

   Two small, low-quality studies examined the effects of an opioid on mood or behavior among individuals with chronic pain. Neither study provided any evidence to support the contention that long-term use of morphine for a licit purpose has a negative impact on mood or behavior.

   As was the case above, neither included study was designed as a non-inferiority or equivalency study (designed to test the hypothesis that the administration of therapeutic

doses of an opioid does not have a deleterious impact on outcome). Consequently, the finding of no evidence of a deleterious effect cannot be interpreted as providing evidence of no effect.

Findings Specific to Licit Schedule II Stimulant Use

1. **A lack of data precludes determination of whether the licit long-term use of a Schedule II stimulant for the treatment of a legitimate medical condition has a detrimental effect on driving ability (as measured using a simulator or on a specific test circuit), cognitive and psychomotor function, or mood and behavior such that the risk for a motor vehicle crash is increased.**

   No included studies evaluated the effects of the long-term licit use of a stimulant on any of the outcomes relevant to Key Question 2.

2. **Owing to a paucity of consistent data, it is not possible to draw an evidence-based conclusion about whether administration of therapeutic doses of a Schedule II stimulant to stimulant-naïve individuals has a detrimental impact on driving ability.**

   Two high-quality studies assessed the effects of Schedule II stimulants (dextroamphetamine and methylphenidate) on simulated driving ability. The findings of these two studies were not consistent. One study found that a single dose of dextroamphetamine has a deleterious impact on daytime (but not nighttime) simulated driving in stimulant-naïve individuals. The other study did not observe any deleterious effects on simulated driving ability that could be associated with methylphenidate (10 or 20 mg) when given to individuals with attention deficit hyperactivity disorder. Whether these differences in findings are the consequence of differences in the drugs tested, dosage, measurement timing, sensitivity of the driving simulators used to evaluate driving ability, size of the included studies, or characteristics of the individuals enrolled in the studies cannot be determined at this time.

3. **Administration of a single therapeutic dose of a Schedule II stimulant (dextroamphetamine or methylphenidate) to stimulant-naïve individuals does not appear to have a deleterious impact on cognitive or psychomotor function (Strength of Evidence: Weak).**

   Five moderate- to high-quality studies presented data on the acute effects of stimulants on cognitive and psychomotor function. None of the studies found that the administration of a therapeutic dose of a Schedule II stimulant had a deleterious impact on cognitive or psychomotor function. Despite the fact that the overall quality of the evidence base underpinning this conclusion was high, and the data from all five studies are qualitatively consistent and robust, we refrain from assigning a strength-of-evidence rating of strong to this conclusion. This is because none of the included studies were non-inferiority or equivalency studies (see the discussion above: Conclusion 4 of the opioids section).

4. **Administration of a single therapeutic dose of a Schedule II stimulant (dextroamphetamine or methylphenidate) to stimulant-naïve individuals does not appear to have a deleterious impact on mood or behavior in a manner that would be considered detrimental to motor vehicle safety (Strength of Evidence: Weak).**

   Three high-quality studies presented data on the acute effects of a stimulant on mood and behavior. None of these studies found that stimulants had a deleterious effect on mood or behavior. In fact, data from the three studies suggest that some of the effects of the stimulants

on mood and behavior were positive (e.g., improved focus). Despite the fact that the studies from which these data originated were of high quality, the findings should be viewed with caution. This is because mood and behavior data from two of the three studies included were based on test subject self-perception. Individuals' internal perception of their own behavior while under the influence of a drug cannot be considered a good indicator of their actual demeanor. Data from the third study are equally suspect because they were based on a rather informal description of the behavior of the test subjects. To reflect our concern about the potential mischaracterizations of the true mood and behavior states of the individuals enrolled in the included studies, we have downgraded the strength-of-evidence rating from High to Weak.

Findings Specific to Licit Schedule II Depressant Use

1. **A lack of data makes it impossible to determine whether the licit long-term use of a Schedule II depressant for the treatment of a legitimate medical condition has a detrimental effect on driving ability (as measured using a simulator or on a specific test circuit), cognitive and psychomotor function, or mood and behavior such that the risk for a motor vehicle crash is increased.**

   No included studies evaluated the effects of the long-term licit use of a Schedule II depressant on any of the outcomes relevant to Key Question 2.

2. **A paucity of data makes it impossible to draw an evidence-based conclusion on whether the administration of therapeutic doses of a Schedule II depressant to a depressant-naïve individual has a detrimental impact on driving ability.**

   One included moderate-quality study evaluated the effects of repeated doses (five doses over 36 hours) of a Schedule II depressant (amylobarbitone) on driving ability as measured by a series of low-speed vehicle handling tests. Test subjects were all young, healthy individuals. The results of the study suggest that a therapeutic dose of amylobarbitone, when taken over the preceding 36-hour period by healthy individuals, has a detrimental impact on driving ability. Because this study is not of high quality, however, and its findings have not yet been replicated, an evidence-based conclusion cannot be drawn at the present time.

3. **Therapeutic doses of Schedule II depressants (secobarbital or pentobarbital) appear to have a deleterious impact on cognitive and psychomotor function (Strength of Evidence: Weak).**

   Two moderate-quality studies consistently found that cognitive and psychomotor functions were impaired following the administration of a single dose of a Schedule II depressant (secobarbital or pentobarbital). Whether the results of these two studies can be generalized to other depressants in the same class (barbiturates) cannot be determined.

4. **A paucity of consistent data from high-quality trials makes it impossible to draw an evidence-based conclusion about whether the deleterious effects of Schedule II depressants continue to affect performance the morning after administration of a therapeutic dose.**

   Because one of the primary medical indications for a Schedule II depressant is insomnia, determining whether the adverse effects the drug has on cognitive or psychomotor function can be observed the morning after administration of the drug is important.

Three studies evaluated the effects of a single dose of barbiturate the morning after its administration. The results of these studies were not consistent with one another. One moderate-quality study did not observe any reduction in cognitive or psychomotor function the morning after administration of a single 100 mg dose of amylobarbitone. However, the remaining two studies (one administered a single 200 mg dose of amylobarbitone and the other administered a single 200 mg dose of a mix of secobarbital and amobarbital) found that cognitive and psychomotor function were impaired the day after administration of the drug. Whether this inconsistency in the findings of the three included studies is a consequence of differences in drug dosage, the sensitivity of the psychometric instruments used to evaluate cognitive and psychomotor function, the size of the included studies, or in the characteristics of the individuals enrolled in the studies cannot be determined at this time.

5. **A paucity of data makes it impossible to draw an evidence-based conclusion about whether the chronic administration of therapeutic doses of a Schedule II depressant has a detrimental impact on cognitive or psychomotor function.**

   A single high-quality study evaluated the effects of seven days of administration of a Schedule II depressant (amylobarbitone) on cognitive or psychomotor function. This study enrolled individuals with a clinical diagnosis of anxiety neurosis who had been admitted to the hospital for crisis intervention. The study found that chronic therapeutic doses of amylobarbitone (463 mg/day) had a deleterious effect on cognitive and psychomotor function. Of the nine relevant outcomes measured, two were significantly impaired. Whether these findings are the consequence of chance or are representative of a true drug effect is not clear. Replication studies performed with different patient populations and Schedule II depressants are required before evidence-based conclusions about the effects of long-term Schedule II depressant treatment can be drawn.

6. **The best evidence currently available does not support the contention that therapeutic doses of a Schedule II depressant (amylobarbitone) have a deleterious impact on mood or behavior that would be detrimental to motor vehicle safety when administered to depressant-naïve individuals.**

   Two high-quality studies evaluated the effects of acute administration of a Schedule II depressant (amylobarbitone) on the mood and behavior of healthy, depressant-naïve individuals. Whether the results of these two studies can be generalized to other depressants in the same class (barbiturates) cannot be determined.

<u>Key Question #3:</u> What is the correlation between the serum level of a Schedule II drug and the risk for a motor vehicle crash?

1. **No conclusions from direct evidence on the relationship between the serum level of a Schedule II drug and motor vehicle (any category) crash risk can be drawn at the present time.**

   Although we retrieved 49 potentially relevant articles that described 49 unique studies, none was found to report on the relationship between the serum level of a Schedule II drug and motor vehicle crash risk. Consequently, no evidence base currently exists that can be used to answer this question.

<u>Key Question #4:</u> What is the correlation between the serum level of a Schedule II drug and indirect measures of driving ability?

1. **A lack of evidence makes it impossible to draw evidence-based conclusions about the relationship between serum levels of Schedule II stimulants and depressants and any of the outcomes of interest (driving ability, cognitive or psychomotor function, and mood or behavior).**

   No study meeting the inclusion criteria for Key Question 4 evaluated a Schedule II stimulant or depressant.

2. **A lack of evidence makes it impossible to draw evidence-based conclusions about the relationship between serum levels of Schedule II opioids and driving ability and mood or behavior.**

   No study meeting the inclusion criteria for Key Question 4 investigated the relationship between the serum level of a Schedule II opioid and driving ability and mood or behavior.

3. **The magnitude of the acute cognitive or psychomotor functional deficits observed among opioid-naïve individuals following administration of a Schedule II opioid is correlated with the serum level of the drug (Strength of Evidence: Strong).**

   Three moderate- to high-quality studies observed a relationship between serum levels of a Schedule II opioid (morphine) and some (but not all) measures of cognitive or psychomotor dysfunction. The measures that demonstrated the strongest relationship with drug serum level tended to be measures of higher order functioning.

4. **Measures of high-level cognitive or psychomotor function are inversely correlated with the serum level of Schedule II opioids (Strength of Evidence: Weak).**

   Two low-quality studies observed significant correlations between serum levels of a Schedule II opioid (fentanyl or morphine) and a number of high-level measures of cognitive or psychomotor function.

<u>Key Question #5:</u> Is there a relationship between the pharmacokinetics of a Schedule II drug and the risk for a motor vehicle crash?

1. **No conclusions from direct evidence on the relationship between Schedule II drug pharmacokinetics and motor vehicle (any category) crash risk can be drawn at the present time.**

   Although we retrieved 11 potentially relevant articles that described 11 unique studies, none provided direct evidence pertaining to the relationship between crash risk and the Schedule II drug pharmacokinetics. Consequently, no evidence base currently exists that can be used to answer this question.

<u>Key Question #6:</u> Is there a relationship between the pharmacokinetics of a Schedule II drug and indirect measures of driving ability?

1. **A lack of evidence makes it impossible to draw evidence-based conclusions about the relationship between the pharmacokinetics of Schedule II drugs and driving ability (as measured by a simulator or on a prespecified driving course).**

   No studies of Schedule II drugs meeting the inclusion criteria of Key Question 6 addressed this outcome.

2. **The pharmacokinetics of Schedule II opioids (morphine, fentanyl, and meperidine) are closely correlated with temporal changes in measures of cognitive and psychomotor function in healthy opioid-naïve individuals (Strength of Evidence: Strong).**

   Three included studies demonstrated the existence of the relationship between the pharmacokinetics of Schedule II opioids (morphine, fentanyl, and meperidine) and temporal changes in measures of cognitive or psychomotor function.

3. **A lack of data makes it impossible to draw evidence-based conclusions about the relationship between the pharmacokinetics of a Schedule II opioid and temporal changes in measures of cognitive and psychomotor function in chronic licit users of the drugs.**

   No studies of Schedule II drugs meeting the inclusion criteria for Key Question 6 addressed this question in a population of chronic licit users of opioids.

4. **A paucity of evidence makes it impossible to draw evidence-based conclusions about the relationship between the pharmacokinetics of Schedule II stimulants and temporal changes in measures of cognitive or psychomotor function in healthy stimulant-naïve individuals.**

   A single included study investigated the relationship between the pharmacokinetics of a Schedule II stimulant (dextroamphetamine) and temporal changes in cognitive or psychomotor function in healthy, stimulant-naïve individuals. This small, but otherwise high-quality study, demonstrated a temporal relationship between dextroamphetamine concentration and cognitive function. Because of the small size of the study, replication is required before evidence-based conclusions can be drawn.

5. **A lack of data makes it impossible to draw evidence-based conclusions about the relationship between the pharmacokinetics of Schedule II stimulants and temporal changes in measures of cognitive or psychomotor function in chronic licit users of the drugs.**

   No studies of Schedule II drugs meeting the inclusion criteria for Key Question 6 addressed this question in a population of chronic licit users of stimulants.

6. **A lack of evidence makes it impossible to draw evidence-based conclusions about the relationship between the pharmacokinetics of Schedule II depressants and temporal changes in measures of cognitive or psychomotor function.**

   No studies of Schedule II depressants met the inclusion criteria for Key Question 6.

7. **A lack of evidence makes it impossible to draw evidence-based conclusions about the relationship between the pharmacokinetics of Schedule II drugs and temporal changes in mood or behavior.**

   No studies of Schedule II drugs meeting the inclusion criteria for Key Question 6 addressed this outcome.

***Key Question #7:* Are there common drug interactions that include a prescribed Schedule II drug that increase the risk for a motor vehicle crash?**

1. **No conclusions from direct evidence concerning the relationship between the serum level of a Schedule II drug and motor vehicle (any category) crash risk can be drawn at the present time.**

   Although our searches identified 14 potentially relevant articles, none was found to meet the retrieval criteria. Consequently, no evidence base currently exists that can be used to answer this question.

***Key Question #8:* Are there common drug interactions that include a prescribed Schedule II drug that affect indirect measures of driving ability?**

1. **A paucity of data makes it impossible to draw evidence-based conclusions about the effect of combining a Schedule II drug with another drug on driving ability and cognitive or psychomotor function, mood or behavior.**

   Four relevant studies met the inclusion criteria for this report. Each study evaluated the effects of a different combination of one Schedule II drug with another drug. Because none of the studies was a high-quality mega-trial, replication is required before evidence-based conclusions about the effects of combining Schedule II drugs with other drugs can be drawn.

Conclusions

The fact that Schedule II controlled drugs are designed to interfere with neurochemical pathways in the brain leads to the expectation that these drugs may influence individuals' ability to perform complex tasks, such as driving. This expectation, combined with the wealth of incontrovertible evidence showing that individuals who abuse psychotropic drugs have a significantly increased risk for a motor vehicle crash, may lead to the hypothesis that individuals who take Schedule II controlled drugs for legitimate medical purposes will be at increased risk for a motor vehicle crash. The purpose of this evidence report is to determine whether currently available evidence supports that hypothesis.

On the Findings of this Evidence Report

The findings of the assessment, which are based on indirect measures of driving ability, suggest that use of Schedule II opioids or depressants may indeed pose a threat to road traffic safety when a driver first begins to use them. Evidence from several studies that administered the drugs to opioid- or depressant-naïve healthy individuals, though not providing strong evidence, has shown that simulated driving ability and high-level cognitive and psychomotor function are adversely affected by these drugs.

Studies of the effects of Schedule II stimulants do not provide evidence that the licit use of these drugs is likely to impair driver safety. However, evidence from several low-quality studies of

chronic Schedule II opioid users who use the drugs for the treatment of chronic pain suggests that after a week or two of administration of the opioids at stable therapeutic doses, the adverse effects of the drugs diminish to the point that cognitive and psychomotor performance of licit long-term opioid users is indistinguishable from drivers who do not use the drugs. Whether the findings of these studies can legitimately be interpreted as providing evidence that long-term users of stable, therapeutic doses of a Schedule II opioid are at no greater risk for a crash than comparable individuals who are not using the drugs, is not clear at this time.
Because no studies of the long-term effects of licit Schedule II barbiturate use met the inclusion criteria for this evidence report, whether the observed short-term detrimental effects of such drugs on driving ability and cognitive or psychomotor function diminish with long-term use is unknown.

On the Limitations of this Evidence Report

The findings of this evidence report cannot be viewed as definitive. As with all systematic reviews, the soundness of the answers they provide is entirely dependent on the quality, quantity, consistency, robustness, and generalizability (to the specific target population of interest) of the available evidence. In this report, most of our evidence-based conclusions were supported by weak or moderate evidence. Also, because only two studies were generalizable to CMV drivers, the generalizability of the findings of this evidence report to this specific population is unclear.