



**Federal Aviation
Administration**

DOT/FAA/AM-09/15
Office of Aerospace Medicine
Washington, DC 20591

Toxicological Findings of Pilots Involved in Aviation Accidents Operated Under Title 14 CFR Part 135

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August 2009

Final Report

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Technical Report Documentation Page

1. Report No. DOT/FAA/AM-09/15		2. Government Accession No.		3. Recipient's Catalog No.	
4. Title and Subtitle Toxicological Findings of Pilots Involved in Aviation Accidents Operated Under 14 CFR Part 135				5. Report Date August 2009	
				6. Performing Organization Code	
7. Author(s) Botch SR, Johnson RD				8. Performing Organization Report No.	
9. Performing Organization Name and Address FAA Civil Aerospace Medical Institute P.O. Box 25082 Oklahoma City, Oklahoma 73125				10. Work Unit No. (TRAIS)	
				11. Contract or Grant No.	
12. Sponsoring Agency Name and Address Office of Aerospace Medicine Federal Aviation Administration 800 Independence Ave., S.W. Washington, DC 20591				13. Type of Report and Period Covered	
				14. Sponsoring Agency Code	
15. Supplemental Notes This work was accomplished under the approved task AM-B-0-TOX-204.					
16. Abstract Introduction: Under the United States Code of Federal Regulations (CFR), aircraft flown under Title 14 (Aeronautics and Space) Part 135 are operated as either commuter or on-demand flights. The rules governing the operation of and the crewmembers on board such aircraft are detailed within these regulations. Aircraft operated under 14 CFR Part 135 include medical flights, on-demand cargo flights, on-demand air-taxis, and scheduled/non-scheduled domestic passenger flights with or without air cargo. Pilots operating under these regulations carry with them the added responsibility of passenger safety or, for those involved in emergency medical flights, the importance of their role for the survivability of patients in critical condition. The purpose of this study was to examine the toxicological findings of pilots involved in aircraft accidents operated under 14 CFR Part 135. Methods: Toxicological and aeromedical findings from Part 135 pilots that were involved in fatal accidents between the years 1997 and 2007 were collected. Toxicological information was obtained from the Civil Aerospace Medical Institute's (CAMI's) Bioaeronautical Sciences Research Laboratory. Accident information and the probable cause and/or factor(s) of these accidents were obtained from the National Transportation Safety Board (NTSB). Results: Between the years 1997 and 2007, CAMI received biological samples of 142 pilots operating under Part 135 who had been involved in aviation accidents. Of these 142 pilots, 139 had sustained fatal injuries. Of the 139 fatalities, 33 (23%) were found to have taken at least one drug and/or had consumed alcohol prior to the accident. The compounds detected in these pilots ranged from the benign (such as acetaminophen) to illicit compounds (such as cocaine and marijuana). The NTSB attributed either the cause and/or a factor in the accident to drugs and/or alcohol use in 6 of these 33 accidents. Conclusion: Over the examined time period, aviation accidents operated under these regulations accounted for ~4% of all fatal aviation accidents received at CAMI for toxicological analysis. Generally, these aircraft were operated without harm to crewmembers, passengers, or bystanders. When accidents did occur, the majority were not the result of drug or alcohol impairment but, instead, were due to mechanical malfunctions, pilot error, and/or operation of aircraft in adverse weather conditions.					
17. Key Words Emergency Medical Services, 14 CFR § 135, Toxicology, Aircraft Accident Investigation, Safety			18. Distribution Statement Document is available to the public through the Defense Technical Information Center, Ft. Belvoir, VA 22060; and the National Technical Information Service, Springfield, VA 22161		
19. Security Classif. (of this report) Unclassified		20. Security Classif. (of this page) Unclassified		21. No. of Pages 11	
				22. Price	

Form DOT F 1700.7 (8-72)

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CONTENTS

INTRODUCTION	1
METHODS	1
RESULTS	1
Pilots Involved in Fatal Accidents	1
Pilots Involved in Non-fatal Accidents	2
DISCUSSION.	3
CONCLUSIONS	6
REFERENCES.	6

TOXICOLOGICAL FINDINGS OF PILOTS INVOLVED IN AVIATION ACCIDENTS OPERATED UNDER TITLE 14 CFR PART 135

INTRODUCTION

Under the United States Code of Federal Regulations (CFR), aircraft flown under Title 14 (Aeronautics and Space), Part 135 are operated as such as either commuter or on-demand flights. The rules governing the operation of and the crewmembers on board such aircraft are detailed within these regulations. Aircraft operated under Part 135 include emergency medical service (EMS) flights, on-demand cargo flights, on-demand air taxis, and scheduled/unscheduled domestic passenger flights. Safe operation under these regulations is extremely important, as Part 135 pilots bear the added responsibility of passenger safety. Additionally, for those pilots involved in EMS flights, there is the added factor of the patients well being. Aviators operating under these regulations endure added stress due to these critical responsibilities.

Unfortunately, aviation accidents involving aircraft operated under Part 135 do occur. From an aviation safety perspective, it is important to determine why these accidents take place. The purpose of this study was to examine the toxicological findings obtained from pilots involved in aircraft accidents operated under these regulations. Toxicological results give the accident investigator information as to whether a substance consumed by the pilot prior to the flight could have diminished his or her capacity to operate the aircraft safely and if the substance may have been a factor in the accident. Toxicological results from the examined accidents have been summarized and combined with the National Transportation Safety Board's (NTSB's) finding(s) for these accidents. These data have shown that, although rare, pilots operating under Part 135 have taken medications or illicit substances that are currently not allowed and that some of these substances have been either the cause or a factor in fatal aviation accidents.

METHODS

The Civil Aerospace Medical Institute's (CAMI's) Bioaeronautical Sciences Research Laboratory analyzes specimens collected from pilots involved in civil aviation accidents.^{1,2} Toxicological and aeromedical findings from incidents involving pilots certified under Part 135 were collected for accidents that occurred between the years 1997 and 2007. Toxicological information was obtained from CAMI's ToxFlo™ toxicology database

(DiscoverSoft Development, LLC, Oklahoma City, OK). Accident-specific information and the probable cause(s) and/or factor(s) of these accidents were obtained from the NTSB database.¹⁵

RESULTS

From 1997 to 2007, 142 pilots operating under Part 135 certification were involved in aviation accidents (both fatal and non-fatal), and biological specimens from these pilots were received at CAMI for toxicological analysis. Over the examined time period, there were a total of 181 fatal aviation accidents operated as Part 135. Thirty-nine pilot fatalities were not received by CAMI due to various factors, including a limited amount or the lack of biological specimens available to conduct toxicological analysis. There were only 3 cases in which specimens were received and the pilots survived the accident. Of the remaining 139 pilot fatalities, specimens from 33 (23%) were found positive for ethanol, a pharmaceutical compound, and/or an illicit drug. The compounds found in these pilots ranged from benign substances such as acetaminophen to abused compounds such as cocaine and marijuana. Pilot fatalities from this certification category accounted for ~4% of the 3,354 fatal aviation accidents received by CAMI during this time period.

Pilots Involved in Fatal Accidents

Further analysis of these 33 drug-positive airmen demonstrated that more than half (19 of 33) had consumed either ethanol or an unapproved substance with potentially severe side effects prior to flight. A summary follows of the compounds that are not allowed prior to flight but were found in these 19 pilots. Of the 33 pilot fatalities that were positive for drugs, illicit compounds were detected in 5 cases. These illicit substances included tetrahydrocannabinol (THC), which is one of the pharmacologically active constituents of marijuana. THC was detected in 2 pilots. Also, cocaine and/or metabolites were found in 3 pilots. Ethanol was present in 5 of these 33 airmen. The FAA's legal limit for ethanol is 40 mg/dL (14CFR91.17); however, it must be stated that no pilot is allowed to fly until 8 hours has passed since the consumption of the last alcoholic drink.¹³ Three of these 5 pilots were found to have ethanol concentrations above 40 mg/dL in the blood. The NTSB deemed the consumption of ethanol to be a factor in 1 of these accidents. One or more opiates

were detected in 5 of the 33 pilots. Opioid compounds, including morphine, hydrocodone, codeine, dihydrocodeine, oxycodone, and oxymorphone, are commonly prescribed in the U.S. for pain management and other uses such as cough suppression.³ Due to the severe side-effects of opioid medications, including nausea, drowsiness, dizziness, and delirium, pilots are not allowed to use these medications prior to flight.^{3, 14}

Antidepressants are commonly prescribed in the U.S., with 10 to 15% of prescriptions written intended to affect mental processes and/or modify mood, thinking, or behavior.³ These compounds can have various undesirable side effects, including memory loss, confusion, drowsiness, and unsteadiness. Although controversial and primarily exhibited in young adults and children, clinical studies have shown that antidepressant use has been associated with an increase in suicidal thoughts.⁴ When considering all of these factors, the use of antidepressants by airmen was prohibited and remains prohibited per current FAA regulations.¹² Antidepressant medications, including paroxetine (Paxil®), sertraline (Zoloft®), fluoxetine (Prozac®), and citalopram (Celexa®) were present in 4 airmen examined in this study.

Over-the-counter medications are readily available to the general public without prescription. Unfortunately for pilots, however, some of these medications are performance-impairing and can be dangerous when taken prior to operating an aircraft. These side effects can be exasperated by concomitant use of more than one of these readily available compounds.⁵ Seven of the 33 certified pilots evaluated were found positive for an antihistamine medication. Each had taken an antihistamine medication belonging to the class of H₁-antagonists, including diphenhydramine (3 pilots), chlorpheniramine (3 pilots), and promethazine (1 pilot). Side effects of these compounds can be severe and include drowsiness and dizziness. Due to these adverse effects, the use of H₁-antihistamines by pilots is not allowed prior to flight.⁶ Allergy, respiratory, and over-the-counter cold medications were the most often detected drugs in this group of airmen. The frequency with which they were detected may be due to the accessibility of these compounds and the inability to control what airmen consume outside of consulting their aviation medical examiner (AME). Additional examples of drugs encountered from the over-the-counter class were pseudoephedrine (3 pilots), phenylpropanolamine (3 pilots), dextromethorphan (2 pilots), doxylamine (1 pilot), naphazoline (1 pilot), and theophylline (1 pilot).

Other medications found in these 33 airmen include amlodipine, a calcium channel blocker used alone or in combination with other medications to treat high blood

pressure and chest pain (angina); metoprolol, a beta blocker also used to treat high blood pressure; quinine, an anti-malarial drug; and phentermine, an anorectic drug which can be used to assist in weight loss. Azacyclonol, an active metabolite of terfenadine^{7,8} (Seldane®), was detected in 2 airmen. Terfenadine was found in rare cases to induce fatal arrhythmia when the metabolism of the compound was impaired by either liver disease or drugs that inhibit the Cytochrome P450 CYP3A family of enzymes. This severe side effect resulted in the drug's withdrawal from the U.S. market in 1998.³

Elevated glucose levels were detected in 5 airmen. Elevated glucose levels may indicate a diabetic condition or could be the result of stress. A diabetic condition, if undiagnosed and unknown to the pilot, would not have been properly controlled at the time of the accident, resulting in hyperglycemia, which can have significant side effects such as fatigue and blurred vision.⁹ One of the pilots had a reported history of diabetes that was, according to the pilot, controlled by diet. However, following analysis, this individual's urine glucose concentration was found to be an extraordinarily high at 1750 mg/dL. This elevated glucose concentration is evidence that the pilot's diabetic condition was not under control prior to the fatal flight.

Pilots Involved in Non-fatal Accidents

Of the 3 pilots who survived their accidents and whose specimens were received at CAMI, only 1 did not test positive for any pharmaceutical or illicit compounds. The NTSB's findings in this case attributed the cause of the accident to pilot error, improper training, and adverse weather conditions. The compound midazolam, a benzodiazepine derivative, was detected in 1 of the non-fatal airmen. Medical records documented that the pilot had been administered midazolam in the hospital post-accident, suggesting that the drug was not taken prior to the flight. The NTSB attributed the cause of this accident to a combination of pilot error and poor weather conditions. The compounds acetaminophen, lidocaine, morphine, and promethazine were detected in the third non-fatal accident victim. Promethazine has strong anticholinergic and sedative effects. Acetaminophen, lidocaine, and morphine are commonly given to patients who are hospitalized, and that may account for their presence in the airman. This pilot had a previously documented drug offense on his record; however, the NTSB report has not been finalized for this accident, so a determination has not been made deciding whether the compounds present were a cause or factor in the accident. These aircraft were operated as either scheduled or nonscheduled passenger and/or cargo flights.

DISCUSSION

After reviewing all aspects of an aviation accident the NTSB is responsible for the determination of cause and any factors that led to the event. CAMI provides the NTSB with toxicological information obtained after examination of biological specimens received from the pilots involved in both fatal and non-fatal accidents. After reviewing the toxicological findings obtained from CAMI, the NTSB attributed drug and/or alcohol use a cause, a factor, or a finding in 6 (18%) of the 33 fatal accidents in which the pilot had tested positive for some pharmaceutical compound or ethanol (Table 1). Of the non-fatal accidents in which a determination of the cause/factor had been made, the NTSB did not attribute the use of drug(s) and/or alcohol to any of the accidents in which the pilot survived and specimens were received at CAMI. Pilot error, weather, and/or mechanical issues were attributed to be a cause and/or factor in 21 of the fatal accidents and 2 of the non-fatal accidents. Physical impairment of the pilot was deemed a cause in 1 fatal accident, due to hemopericardium (blood in the pericardial sac) and blunt force trauma. The cause or factor in the remainder of these accidents (5 fatal and 1 non-fatal) had not been determined at the time of the publication of this report. Of the Part 135 accidents received by CAMI, 3 were operated as EMS flights. Pilot error and weather were cited as either a cause or a factor in 2 of these accidents, while pressure to complete the EMS mission was cited as an additional factor in 1. The cause/factor of the third accident is pending determination.

Federal law Title 49, United States Code sections 109(9), 40113(a), 44701-44703, and 44709 (1994), authorizes the FAA administrator to entrust AMEs to inspect, test, and examine so that they may issue, deny, or defer to the FAA a pilot's certificate.¹⁴ The Federal Air Surgeon may grant an Authorization for Special Issuance (SI) of a medical certificate to an airman whose specific medical conditions do not meet established medical standards. After the initial authorization for SI, the AME can re-issue an airman medical certificate under the provisions of an Authorization to an applicant who has a medical condition that is disqualifying under Part 67.¹⁴

Of the 35 drug-positive cases (fatal and non-fatal) evaluated by CAMI that were operating under Part 135, only one had been issued an SI. This pilot had a history of drug abuse and, following toxicological analysis, was found to have taken opiates (hydrocodone and dihydrocodeine) concomitantly with diphenhydramine. The pilot in question held an airline transport 2nd-class certificate and had self-disclosed the habitual use of dihydrocodeine 6 years prior to the accident. Subsequent drug screens

(pre-employment and randomly by his employer) had not revealed the use of opiates. However, the drug screen used was not comprehensive and could only reveal the use of codeine and/or morphine; therefore, the results would not have reflected the pilot's continued use of hydrocodone. This pilot had been issued a SI, and his history of drug abuse was noted in his airman medical file. Toxicological analysis performed by CAMI revealed hydrocodone and dihydrocodeine in each specimen examined, confirming the pilot's continued use of opioid medications.

In addition, there were 5 other airman that had reported previous drug and/or alcohol related offenses or substance-abuse problems. Of these 5, only 1 was found to be negative for all drugs. All were found to be negative for alcohol. Diphenhydramine, pseudoephedrine, cocaine, chlorpheniramine, amlodipine, acetaminophen, morphine, promethazine, and lidocaine were the various compounds detected in the other 4 pilots.

Of the 35 airmen involved in accidents where pharmaceutical compounds were found upon toxicological analysis, only 7 pilots had reported to their AME that they were taking medication(s). Of these 7, 3 had been issued a 2nd-class commercial certificate and had reported taking metoprolol (Lopressor® or Toprol XL®), pravastatin (Pravachol®), atorvastatin (Lipitor®), rosuvastatin (Crestor®), amlodipine (Norvasc®), benazepril (Lotensin®), lisinopril (Prinivil® or Tensopril®), metformin (Glucophage®), atenolol (Tenormin®), salicylic acid (aspirin), and hydrochlorothiazide (diuretic).

These medications are conditionally allowed for use by pilots prior to flight; indicated uses are as follows:

- Pravastatin, atorvastatin, and rosuvastatin are hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors used in the treatment of high blood cholesterol.
- Benazepril, a prodrug, is transformed following consumption into benazeprilat by hepatic esterases and acts as a potent angiotensin-converting enzyme (ACE) inhibitor.
- Lisinopril is also an ACE inhibitor; however, this compound has properties that prevent its accumulation in the body's tissues, as it is cleared from the body via the kidneys as the intact compound.
- Metformin, an antihyperglycemic, improves glycemic control and lipid concentrations.
- Atenolol is a β 1-receptor specific antagonist which cannot pass through the blood brain barrier and therefore does not cause as many central nervous system side effects.
- Aspirin is the most common analgesic and is readily available; its misuse and serious toxicity is often underappreciated.³

Table 1. Case Histories of Accidents Where Drugs or Alcohol Were Either a Cause or a Factor.

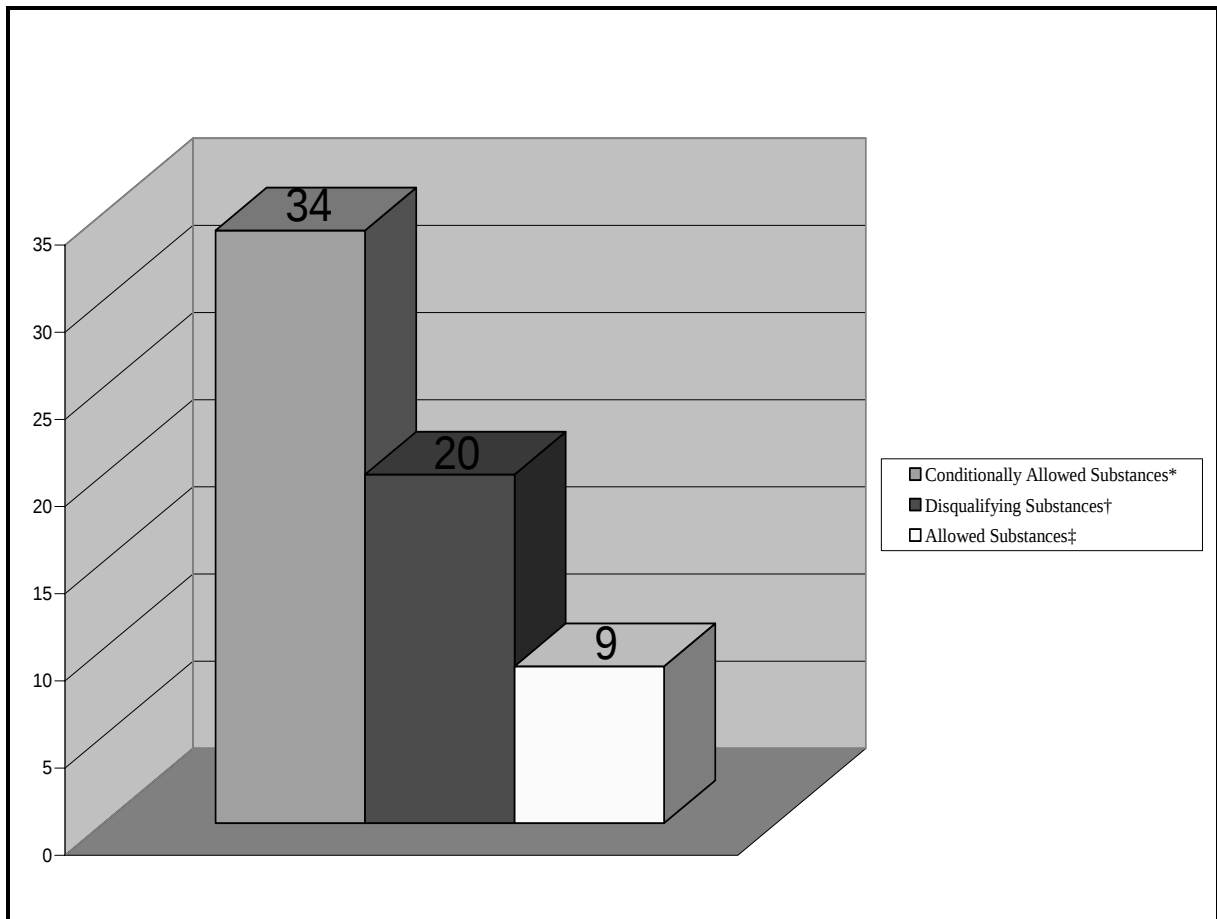
Case	Drugs Attributed to the Cause of an Accident (Concentration in blood if available)	Other Substances Detected	Drugs Reported to AME	Conditions Noted by AME	NTSB Findings (Cause/Factor/Finding)	Medical Certificate Category	Flying Certificate Category
1	Doxylamine (0.084 µg/mL), Dextromethorphan (0.045 µg/mL), Dextropropriamine, Pseudoephedrine, Ephedrine, Phenylpropanolamine	—	None	None	Factor related to the accident was the use of over-the-counter medications.	First Class	Airline Transport
2	Cocaine (0.062 µg/mL)	—	None	None	One of the causes of the accidents was the captain's impairment from drugs. A factor was the first officer's impairment from drugs.	First Class	Airline Transport
3	Codeine (0.049 µg/mL), Paroxetine	—	None	None	A finding was the pilot's use of FAA prohibited drug paroxetine.	First Class	Commercial
4	Ethanol (115 mg/dL)	—	None	Genitourinary-related condition(s)	Factor was the pilot's alcohol impaired condition.	Second Class	Commercial
5	Sertraline (0.027 µg/mL), Chlorpheniramine (0.007 µg/mL), Phenylpropanolamine, Pseudoephedrine	Acetaminophen (13.31 µg/mL, urine)	Antihistamine Medications	Allergic Rhinitis, Hernia	Cause of the accident was the pilot's failure to maintain aircraft control with the use of over-the-counter cold medications and the disqualifying compound sertraline noted.	Second Class	Airline Transport
6	Cocaine (0.985 µg/mL, urine), Chlorpheniramine	—	None	Multiple drug and alcohol related offenses, drug abuse not meeting the criteria for drug addiction, and use of contact lenses	Factors in the accident were the pilot's impairment from cocaine, alcohol, and over-the-counter cold medication, and the FAA's inadequate medical certification of the pilot and follow-up of his known substance abuse problems.	First Class	Airline Transport

- Hydrochlorothiazide is a diuretic drug of the thiazide class.

In these 35 pilots, 63 various compounds were detected. These compounds included those the FAA has deemed safe to consume prior to flight, which are allowed after waiting an appropriate period of time after consumption, and those which result in an airman being disqualified from duty. For the purpose of this study, the categories “allowed, conditionally allowed and disqualifying substances” (respectively) have been used to differentiate these compounds. The distribution of each type of compound can be seen in Figure 1. Sixteen of the 35 drug-positive airmen (~45%) were taking more than one compound. Some of the drug combinations seen are known to produce potentially severe drug interactions. The potentially dangerous drug combinations found included chlorpheniramine in combination with

ethanol. The use of these compounds has been shown to cause muscle tremors, convulsive seizures, and central stimulation.¹⁰ Naphazoline and phenylpropanolamine, which were detected together in one pilot, are both used as decongestants and have been shown to promote strokes in individuals with previous morbidities.¹¹

Additional drugs used in combination included dextromethorphan and azacyclonol, which is the active metabolite of terfenadine. Morphine, codeine, and the antidepressant paroxetine were detected in one pilot. The over-the-counter compounds chlorpheniramine, phenylpropanolamine, acetaminophen, pseudoephedrine, as well as the antidepressant sertraline, were detected in another pilot. The illicit compound, cocaine, and its metabolites were detected with chlorpheniramine in one airman and with quinine in another. Amlodipine and acetaminophen were used together. Another airman had consumed multiple cold medications with the compounds



*Conditionally allowed substances are those that are not immediately disqualifying and, when used appropriately, do not interfere with aviation safety.

†Disqualifying substances are those which result in denial of medical certification.

‡Allowed substances are those which are not likely to compromise aviation safety, unless in toxic levels.

Figure 1. Drug types detected in Part 135 pilots involved in fatal aviation accidents between 1997 and 2007.

pseudoephedrine, phenylpropanolamine, dextromethorphan, doxylamine, and dextrorphan. Finally, lidocaine, acetaminophen, morphine, and promethazine were all detected in one airman.

CONCLUSIONS

Accidents involving aircraft operating under Part 135 are not common events. Of the 3,354 fatal aviation cases received at CAMI over the examined time period (1997-2007), Part 135 accidents accounted for ~4% (139 of 3,354). Biological specimens were received for analysis from 139 fatal accidents, of which 33 pilots (23%) were found to have taken at least 1 compound and/or had consumed alcohol at some point prior to flight. In addition, 2 (66%) of the 3 non-fatal cases received were found positive for pharmaceutical compounds. The compounds detected and the concentrations of these compounds were not impairing in most cases, with the NTSB attributing a cause, factor, and/or finding to the use of drugs and/or alcohol in only 6 of the accidents received at the time of publication of this report. The vast majority of the Part 135 flights operated during this time period were performed safely and without injury to crewmembers, passengers, or in the event of an accident involving an EMS flight, to patients. The vast majority of all pilots that operated under Part 135 which resulted in an accident were found to be free of drugs and/or alcohol.

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