

ADHD LITIGATION WHITE PAPER



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Executive Summary

First it was Phen-Fen, then Baycol and Vioxx, now anti-psychotics and anti-depressants are on the trial lawyers' radar as the next wave of pharmaceutical litigation. What next? McGuireWoods predicts the next group of drugs to face lawsuits may be those aimed at Attention Deficit Hyperactivity Disorder (ADHD).

Owing to a variety of factors combining for the first time for ADHD prescription users, pharma faces what could be a serious wave of litigation. Plaintiffs will assert that the science is beginning to solidify on adverse reactions to the medication. Use by children and adults is skyrocketing. Young adults are illegally using the drugs in college and work. Adverse results for the Pharmaceutical Industry continue to fuel this type of products litigation. Lastly, novel theories of liability continue to create new avenues of exposure to manufacturers.

As many as 4 million Americans take ADHD medications. Of those, 2.5 million are children, and 1.5 million are adults.¹ ADHD is the most prevalent psychiatric disorder of childhood in the United States with 3-9% of youth affected.² Reported adult prevalence continues to grow. According to the FDA, adult use of ADHD medications grew 90% between March 2002 and June 2005. "Black Box" warnings may not be enough to protect companies from litigation, and may only add to the public's growing perception that ADHD drugs combined with other types of psychotropic medications can be a lethal combination for the patient ... and maybe the manufacturer.

Despite the long history of ADHD and the fact that millions of children are currently taking ADHD medications, data on the long-term effects that ADHD treatments have on children remain incomplete. FDA data from the Office of Drug Safety in 2004 could be read to suggest that ADHD drugs may be linked to as many as twenty-five deaths between January 1, 1999 and December 31, 2003. The FDA and the Pediatric Advisory Committee have concluded that it is not yet possible to determine whether cardiovascular adverse events, especially the more serious ones, are causally associated with ADHD treatments.

Plaintiffs' attorneys are already advertising heavily for cases involving injuries attributed to ADHD medications with headlines such as "Unsafe ADHD Drugs Put 2 Million Children at Risk" and "We believe that drug companies who place profit above people must be held accountable for their negligence and the damage they cause to innocent victims' lives." A cursory internet search finds multiple plaintiffs' attorneys soliciting ADHD clients and providing information on their websites pulled from media reports on the various perceived ADHD drug health hazards.

It is clearly time for manufacturers and health care providers to act in preparing for the potential wave of litigation. One verdict on the order of the Vioxx \$253 million jury award, and ADHD drugs will be dead in the bulls eye of the plaintiffs' lawyers.

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¹ Alonso-Zaldivar, Ricardo, "Warning Urged for ADHD Drugs; An FDA panel cites heart risks in its advisory on Ritalin and similar medications," *Los Angeles Times*, Feb. 10, 2006, p. A-1

² Wilens, Timothy E., MD, et al., "Effects of Once-Daily Osmotic-Release Methylphenidate on Blood Pressure and Heart Rate in Children with Attention-Deficit/Hyperactivity Disorder," *Journal of Clinical Psychopharmacology* 24, no. 1 (Feb. 2004): 36.

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Introduction

McGuireWoods has prepared this white paper to assist manufacturers, physicians, and those dispensing and overseeing the intake of Attention Deficit Hyperactivity Disorder (ADHD) medications in assessing their possible legal exposure resulting from claims related to potential adverse health effects from taking these medications. To assist in the assessment, this paper will provide:

- A brief history of the use of ADHD medications;
- A description of some of the most widely prescribed ADHD medications and their potential adverse health risks;
- Public perception of the issue; and
- Discussion of the direction that litigation may take in the future.

At present, studies of the long-term adverse health effects of ADHD medications are generally methodologically weak and lack precision. These limitations create uncertainty as to the risks associated with the medications and what the proper response should be. Media reports of adverse health effects of ADHD medications have intensified and plaintiffs' attorneys are taking notice. Novel legal theories put to successful use in tobacco, lead, and other mass tort product liability litigation may soon be applied to ADHD medications. Those involved in the manufacture and dispensation of these medications need to be prepared.

McGuireWoods has vast experience dealing with such novel legal claims and stands ready to help.

History

The history of ADHD medications dates back to 1956 when Ritalin was first introduced as a treatment for hyperactive children. Through the 1960s, stimulant medication became more widely used as the medical community's focus was on the treatment of hyperactivity itself. That emphasis changed in the 1970s when doctors and researchers began making the connection between patients' inward daydreaming and lack of focus and their outward impulsivity and hyperactivity. In 1980, "Attention Deficit Disorder with or without Hyperactivity" was officially identified by the American Psychiatric Association ("APA"). These separate disorders were known as ADD+ and ADD-, respectively. In 1987, the APA combined the separate diagnoses into one, Attention Deficit Hyperactivity Disorder ("ADHD"), in order to include the symptoms of hyperactivity-impulsivity as well as inattention. The APA classified ADHD as a medical condition that causes specific behavioral problems. They also noted that the behavioral problems caused by ADHD are different from behavioral problems that may be caused by an upsetting event such as divorce, changing schools, or moving to a new area. In 1996, a second medication, Adderall, was approved for the treatment of ADHD. Since 1999, several more ADHD medications, including Concerta and Strattera, have become FDA approved.

In October 2001, the American Academy of Pediatrics published recommendations for the treatment of children diagnosed with ADHD in the journal *Pediatrics*. The guidelines are intended for use by pediatricians working in primary care settings. Recommendations for doctors are as follows:

- Primary care doctors should establish a treatment program recognizing ADHD as a chronic condition.

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- The doctor, parents, and child—working together with school personnel—should specify appropriate goals to guide the daily management of ADHD.
- The doctor should recommend stimulant medication and/or behavior therapy as appropriate to improve target outcomes in children with ADHD.
- When the selected management of a child with ADHD has not met target outcomes, doctors should evaluate the original diagnosis, the use of all appropriate treatments, whether the treatment plan was followed properly, and the presence of coexisting conditions.
- The doctor should periodically provide follow-up for the child with ADHD. Monitoring should be directed to target outcomes and adverse effects (i.e., negative side effects), with information gathered from parents, teachers, and the child.

Prescriptions for stimulant medications to treat ADHD have increased substantially over the past decade, as have reports of their abuse. New medications continue to appear to meet the demand. Never in history have so many people taken stimulant medications for ADHD. The FDA's safety officials point out that reports of adverse side effects from ADHD drugs have grown in recent years as use of the medications has increased. Since 1969, nearly three-quarters of all reports of serious problems with amphetamines and half of all reports of serious side effects with drugs such as Ritalin occurred between 1999 and 2003.³

Despite the long history of coping with ADHD and the fact that millions of children are currently taking ADHD medications, there is still a lack of data on the long-term effects that ADHD treatments have on children.

ADHD Drugs and Adverse Reactions

All drugs, including those most valuable in health care, have side effects. Risks associated with use of ADHD drugs must be considered in light of the benefits they confer on those suffering from ADHD, with its attendant symptoms. Some of these, such as psychotic episodes, are quite serious.

Adverse reactions from ADHD medications range from mild to severe. Some of the milder reactions include upper abdominal pain, decreased appetite, headache, insomnia, and nausea.⁴ Some patients on ADHD medications have shown a higher incidence of anorexia as well.⁵ Some of the more severe reported reactions include increased risk of cardiovascular problems, stroke, liver damage, suicide, hallucinations, and psychotic episodes.

³ Vedantam, Shankar, "Cautions Issued on Use of Psychiatric Drugs; Antidepressants, ADHD Medications Cited," *Washington Post*, Feb. 9, 2006, p. A09.

⁴ Starr, H. Lynn, MD and Jason Kemner, MPH, "Multicenter, Randomized, Open-Label Study of OROS Methylphenidate versus Atomoxetine: Treatment Outcomes in African-American Children with ADHD," *Journal of the National Medical Association* 97, no. 10 (supp.) (Oct. 1995): 14S.

⁵ These reactions have been most frequently studied in those taking methylphenidate formulations. See Swanson, James M., et.al., "A Comparison of Once-Daily Extended-Release Methylphenidate Formulations in Children with Attention-Deficit/Hyperactivity Disorder in the Laboratory School (The Comacs Study)," *Pediatrics* 113, no. 3 (March 2004): 206-216.

New research is starting to raise questions about the long-term effects of MPH and how this drug may affect a child's developing brain.

Adverse reactions from ADHD medications appear to be different for children and adults. Patients, parents, and clinicians have struggled to balance serious but low-probability risks against known benefits, and researchers are trying to identify which patients might experience problems.⁶ Dr. David Graham, the FDA drug-safety investigator, undertook a preliminary study using information in the databases of large health insurers and government programs. Early findings suggested a higher-than-expected number of heart attacks and strokes among adults taking the medications. However, among children under 18, the number of strokes reported was higher than expected but the number of heart attacks was lower.⁷

The most popular ADHD medications are discussed below along with some of the various FDA and private studies on the effects of these drugs.

1. Methylphenidate

Methylphenidate (MPH) has been the most widely used stimulant in the treatment of ADHD for the past four decades.⁸ The most widely known brands of MPH are Ritalin, Concerta, Methylin and Metadate. The use of MPH in the United States has increased each year since 1971, with the exception of 1987-1990 when there was an active campaign to discourage stimulant medications for the treatment of children.⁹ From 1990 to 1995, there was a marked increase in the use of stimulant medications. This change is mostly accounted for by the increased use of MPH for the treatment of older children, adolescents, and adults with ADHD.¹⁰

While the short- and long-term effectiveness of MPH is well established, questions related to long-term adverse health effects of the drug linger.¹¹ New research is starting to raise questions about the long-term effects of MPH and how this drug may affect a child's developing brain. New studies in rats suggest that MPH may permanently alter the brain and may lead to depression in adulthood, especially in healthy children who have been wrongly diagnosed and thus wrongly prescribed ADHD medication.¹² Additionally, studies of vital signs in children and adolescents with ADHD receiving stimulants indicate a variable effect on blood pressure and heart rate.¹³ While some studies have reported no changes in vital signs, others have described a statistically significant increase in both heart rate and systolic and diastolic blood pressure that persisted in a small group of youth followed for one year.¹⁴

Studies have also stated that MPH can cause hallucinations at therapeutic doses. MPH is a phenylethylamine with structural and pharmacologic properties similar to those of amphetamine. Visual and auditory hallucinations are known to occur during amphetamine use.¹⁵ The prevalence of hallucinations in conjunction with MPH is rare, probably less than 0.2%.¹⁶

⁶ Vedantam, Shankar, A09.

⁷ Alonso-Zaldivar, Ricardo, A-1.

⁸ Connors, C.K., "Forty Years of Methylphenidate Treatment in Attention-Deficit/Hyperactivity Disorder," *Journal of Attention Disorders* 6, no. 1 (supp.) (2002): S-17.

⁹ Wolraich, Mark L. and Melissa A. Doffing, "Pharmacokinetic Considerations in the Treatment of Attention-Deficit Hyperactivity Disorder with Methylphenidate," *CNS Drugs* 18, no. 4: 243-250.

¹⁰ *Ibid.*, 244.

¹¹ Wilens, et al., 36.

¹² Parker-Pope, Tara, "Long-Term Ritalin Use in Kids May Lead to Adult Depression," *Pittsburgh Post-Gazette*, Feb. 1, 2005, p. C-1.

¹³ Wilens, et al., 36.

¹⁴ *Ibid.*

¹⁵ Gross-Tsur, Varda, MD, et al., "Hallucinations During Methylphenidate Therapy," *Neurology* 63, no. 4 (Aug. 24, 2004): 753.

¹⁶ *Ibid.*



MPH derivatives are Category II controlled substances. This is the designation used for substances that have a recognized medical value but which have a high potential for abuse.

a. Ritalin

Ritalin is manufactured by Novartis Pharmaceuticals and comes in regular and extended release formulations. It has been marketed in the United States since 1957 and was the first psycho-stimulant to be approved by the FDA for the treatment of hyperactivity, impulsivity, and inattention.¹⁷

Along with reports of cardiovascular and other serious side effects, Texas researchers wrote that after only three months, each of 12 children treated with Ritalin had a three-fold increase in chromosome abnormalities associated with increased risks of cancer.¹⁸ While the study cautions that more and larger studies are necessary, it adds another potential adverse side effect of ADHD medications to a growing list.

b. Concerta

Concerta is an extended release formulation of MPH marketed by McNeil. A twelve month study of the effects of Concerta on vital signs found that it produced statistically significant, but not clinically meaningful, changes in blood pressure or heart rate in children with ADHD.¹⁹ The paper noted that further study of the very long-term cardiovascular effects of stimulants as well as shorter-term effects on special groups of ADHD individuals with pre-existing cardiovascular conditions is warranted.²⁰ Separate studies involving Concerta and MPH formulations found little correlation between use of the drug and the occurrence of tics during treatment.^{21 22}

c. MTS

The methylphenidate transdermal system (MTS) has been developed by Shire Development Inc. and Noven Pharmaceuticals, Inc. to develop a transdermal, once-daily treatment for ADHD with MPH.²³ On April 6, 2006, the FDA approved the use of the MTS patch, called Daytrana, designed to be worn for nine hours.²⁴ The patch is offered as an alternative treatment for children 6 to 12, meaning doctors should prescribe it only if taking pills is too difficult for the child. The patch will carry the same warnings against use in children with heart problems that are carried by all MPH drugs.²⁵

¹⁷ Connors, C.K., S-18.

¹⁸ Wenske, Paul, "Small Study Links Ritalin, Cancer Risk," Kansas City Star, March 17, 2005, p. 1.

¹⁹ Wilens, et al., 38.

²⁰ Ibid., 40.

²¹ Palumbo, Donna, Ph.D., "Emergence of Tics in Children with ADHD: Impact of Once-Daily OROS Methylphenidate Therapy," Journal of Child and Adolescent Psychopharmacology 14, no. 2, (Summer 2004): 185-194.

²² Law, Samuel F. and Russell J. Schachar, "Do typical doses of methylphenidate cause tics in children treated for attention-deficit hyperactivity disorder?" Journal of the American Academy of Child and Adolescent Psychiatry 38, no. 8 (Aug. 1999): 944.

²³ Shire Development Inc. and Noven Pharmaceuticals, Inc., "Methylphenidate Transdermal System" [Briefing Document to FDA Psychopharmacologic Drugs Advisory Committee, NDA 21-514] Dec. 2, 2005.

²⁴ "FDA approves first skin patch to treat hyperactive children," Buffalo News (New York), April 7, 2006, p. A6.

²⁵ "Now, a Patch for ADHD," Washington Post, April 11, 2006, p. F04.

2. Amphetamine/Dextroamphetamine (Adderall/Dexedrine)

Adderall and Adderall XR are manufactured by Shire BioChem Inc. and are formulations of mixed amphetamine salts. Adderall is an immediate release capsule, and Adderall XR is an extended release capsule taken once a day.

Adderall XR was suspended from the Canadian market by Health Canada on February 9, 2005 because of concerns that use of Adderall and Adderall XR may be associated with an increased risk of sudden cardiac death and stroke in children and adults. After a reassessment of the decision by Health Canada, Adderall XR was returned to the market in August 2005 owing to insufficient evidence that such an increased risk of sudden cardiac death or stroke with Adderall exists compared to other ADHD treatments. Shire BioChem did revise its Canadian Product Monograph to add warnings regarding the threat of “serious cardiovascular adverse events,” including risk of sudden death with amphetamine treatment. The warning also advises against the use of Adderall XR in patients with pre-existing structural cardiac abnormalities owing to reported deaths of such patients.

Similarly, in the United States, based on FDA reviews of the potential health risks of Adderall, a paragraph was added to the “WARNINGS” section of the Adderall XR label discussing sudden death and pre-existing structural cardiac abnormalities.²⁶ Adderall and Adderall XR also contain a “black box” warning regarding the potential for “sudden death and serious cardiovascular adverse events” from the misuse of amphetamine.



3. Atomoxetine (Strattera)

Atomoxetine is a specific norepinephrine reuptake inhibitor used for ADHD in both children and adults. It has been marketed and labeled as a non-stimulant ADHD drug and is not scheduled as a controlled substance.²⁷ Cases of arrhythmia, syncope, cardiac arrest, myocardial infarction, and stroke in both children and adults have been reported with atomoxetine as with other ADHD medications.²⁸

Atomoxetine has been associated with other health risks in addition to those that are cardiovascular related. In 2004, Eli Lilly warned doctors to stop prescribing Strattera to patients with jaundice or who show signs of liver damage. This warning was recommended because of fear that Strattera could cause severe drug related liver injury that can progress to acute liver failure resulting in death or the need for a liver transplant

Some believe that there appears to be evidence that Strattera may contribute to suicide risk in children. Eli Lilly submitted results from a Strattera clinical trial of 1,357 children taking Strattera to the FDA. Lilly reported that five of the children had increased suicidal thoughts while none of the 851 children taking a placebo showed such changes. One additional minor attempted suicide during the trials, but researchers saw no signs of increased suicidal thoughts among adults.²⁹ On September 28, 2005, Eli Lilly announced that it was adding a “black box” warning to Strattera advising that the drug may increase suicidal thoughts in children and adolescents.

²⁶ FDA Safety Review Team, Follow up review of AERS search identifying cases of sudden death occurring with drugs used for the treatment of Attention Deficit Hyperactivity Disorder (ADHD), February 28, 2006.

²⁷ Ibid.

²⁸ Gelperin, Kate, M.D., M.P.H., “Studying Cardiovascular Risk with Drug Treatments of ADHD” [PowerPoint presentation of the FDA Drug Safety and Risk Management Advisory Committee], Feb. 9, 2006.

²⁹ Mosholder, Andrew, MD, MPH, “Psychiatric Adverse Events in Clinical Trials of Drugs for Attention Deficit Hyperactivity Disorder” [FDA Center for Drug Evaluation and Research Memorandum], PID D060163, March 3, 2006.

FDA Studies and Recommendations

Recent FDA focus has been on adverse health effects stemming from possible severe cardiovascular problems that could result in sudden death and psychiatric problems resulting from ADHD medications.

a. Sudden Death/Cardiovascular Problems

FDA data from the Office of Drug Safety in 2004 shows that ADHD drugs may be linked to as many as twenty-five deaths between January 1, 1999 and December 31, 2003.³⁰ Seventeen sudden death cases occurred in patients who had reportedly taken either Dexedrine (one case) or Adderall/Adderall XR (sixteen cases); eight were identified with methylphenidate (MPH) treatment. Of these deaths, nineteen involved children ages 7 to 16. These included eleven children treated with Adderall, one with Adderall XR, three with Ritalin, and four with Concerta. Six out of the twelve Adderall/Adderall XR and four out of the seven MPH (Ritalin and Concerta) pediatric sudden death cases occurred in patients with structural cardiovascular abnormalities or other potential risk factors for sudden death. What role, if any, the drugs played in the deaths is difficult to assess because the children had underlying heart conditions that could have contributed to their deaths. No cases of sudden death were found with methamphetamine and dexamethylphenidate.³¹

Furthermore, the FDA was advised of fifty-four cases involving serious cardiovascular problems such as heart attack, stroke, hypertension, heart palpitations, and arrhythmia in both adults and children said to have taken ADHD medications.³²

A 2006 follow-up to the 2004 FDA study addressed reports of sudden death for Adderall/Adderall XR and dextroamphetamine (A/DA), and MPH products before January 1999 and after December 2003.³³ Sudden deaths were also reviewed for two other drugs used in ADHD treatment—pomoline (Cylert) and atomoxetine (Strattera)—from their time of approval (January 1975 and November 2002, respectively) until February 2005. Cylert was withdrawn from the market in May 2005 and generic pomoline products were withdrawn in October 2005.

The FDA's updated search revealed three additional cases of sudden death among patients on A/DA (one case before 1999 and two after 2003), two in teenagers and one adult, and ten cases with MPH (all before 1999), making a total of twenty cases (fourteen pediatric and six adult) of sudden death among those on A/DA and eighteen cases among those on MPH.³⁴ Of the A/DA cases, seventeen were reported with Adderall/Adderall XR, one with Dexedrine, one with Adderall and Dexedrine, and one with Dexedrine and methylphenidate.

Of the eighteen cases of sudden death in patients on MP drugs, fourteen were pediatric and four were adult sudden death cases. These were reported from January 1992 through February 2005. Of the fourteen pediatric cases, six had a documented structural cardiovascular abnormality that may have increased the risk of death.³⁵ The



³⁰ Gelperin, Kate, M.D., M.P.H., et.al., "Review of AERS data for marketed safety experience during stimulant therapy: death, sudden death, cardiovascular SAEs (including strokes)" [FDA Center for Drug Evaluation and Research Memorandum], April 27, 2004.

³¹ Ibid.

³² Ibid.

³³ FDA Safety Review Team, "Follow up review of AERS search identifying cases of sudden death occurring with drugs used for the treatment of Attention Deficit Hyperactivity Disorder (ADHD)," Feb. 28, 2006.

³⁴ Ibid.

³⁵ Ibid.

The FDA and the Pediatric Advisory Committee have concluded that it is not yet possible to determine whether cardiovascular adverse events, especially the more serious ones, are causally associated with ADHD treatments.

FDA update notes that none of the eighteen MPH deaths appears to have been solely or directly related to methylphenidate.³⁶

The 2006 FDA update also reported a total of seven cases of sudden death associated with atomoxetine: three in children and four in adults taking atomoxetine at therapeutic doses, from November 2002 to February 2005.³⁷ The pediatric cases occurred six weeks to four months into atomoxetine treatment. None of the patients had a prior cardiovascular history or cardiovascular abnormalities; however, the report notes that none of the cases, adult or pediatric, appears solely or directly attributable to atomoxetine at therapeutic doses. Although none of the patients had structural cardiovascular abnormalities, the FDA notes that the extent of the role of atomoxetine in these deaths is difficult to establish.

The FDA paper notes that the reporting rate of sudden death with atomoxetine in the adult population appears to be greater than with Adderall/Adderall XR and methylphenidate; however, in the pediatric population it seems to be about the same or slightly greater than Adderall/Adderall XR. The apparently high reporting rate with atomoxetine in adults may be related to its more recent introduction to the market.³⁸

The FDA report concludes that the estimated rates of sudden death found in the FDA review of all drugs used to treat ADHD are actually below the background rates of sudden death reported in the literature, for both adults and children. Thus, causation is certainly not established and further research is necessary before any positive link can be postulated.

The FDA and the Pediatric Advisory Committee have concluded that it is not yet possible to determine whether cardiovascular adverse events, especially the more serious ones, are causally associated with ADHD treatments.³⁹ Nevertheless, in January 2006, an FDA advisory panel voted to recommend that the FDA order the inclusion of the most serious “black box” warning on all stimulant ADHD medications due to evidence of a potential risk of heart attacks, strokes, and sudden death. The advisory panel also voted to recommend that FDA require that the drugs include a medication guide for patients and parents. On March 22, 2006, the FDA’s Pediatric Advisory Committee rejected the recommendation for “black box” warnings on ADHD drugs but did recommend adding more information to the labels for the benefit of doctors, patients, and parents.⁴⁰

b. Psychiatric Problems

A summary of clinical trials of ADHD medications showing adverse psychiatric events put together by the product manufacturers for the FDA at its request showed that in studies lasting under one year:

- In double blind studies of 383 children taking Ritalin LA (the extended release formulation), there are reports of two psychosis/mania events, two aggression events, and no suicidal events. In open studies involving 125 children on Ritalin LA, one suicidal event was recorded, and no psychosis/mania events or aggression events were reported.⁴¹

³⁶ Ibid.

³⁷ Ibid

³⁸ Ibid

³⁹ Gelperin, “Studying Cardiovascular Risk.”

⁴⁰ “Dire Warning Not Urged for ADHD Drugs,” Washington Post, March 23, 2006, p. A10.

⁴¹ Mosholder, 22.

- Out of 2,824 children taking Concerta, eight were said to have experienced psychosis/mania events; six suicidal events, and fifty-two aggression events (five of which were deemed serious).⁴²
- In a double blind study of children taking Metadate CD, three aggression events were reported out of 493 participants. In the open label trials, six aggression events were reported out of 322 participants. All aggression events occurred in boys. One of them was deemed serious. No psychosis/mania events or suicidal events were reported in any of the clinical trials involving Metadate CD.⁴³
- MTS use by children suggested that out of 471 participants in a double blind trial, four experienced psychosis/mania events, six experienced aggression events, and none experienced suicidal events. Out of 617 participants in an open trial, there were six psychosis/mania events, one suicidal event, and seven aggression events (two of which were deemed serious).⁴⁴
- In a double blind study of 1,236 children and adults taking Adderall XR, there were no psychosis/mania events, one suicidal event, and twenty aggression events. In an open study involving 5,177 adults and children, fourteen had psychosis/mania events (nine children), eight had suicidal events (all children), and 166 had aggression events (150 children).⁴⁵

As a result of these findings, the FDA Pediatric Advisory Committee met in March 2006 and urged the use of new warnings about the possible risks of psychosis or mania associated with ADHD drugs.⁴⁶ The Committee noted that the most important finding of the review of psychiatric adverse events was that the signs and symptoms of psychosis or mania, particularly hallucinations, can occur in some patients with no identifiable risk factors, at usual doses of any of the drugs currently used to treat ADHD.⁴⁷ According to the FDA's Division of Drug Risk Evaluation (DDRE), a substantial portion of psychosis-related cases were reported in children age 10 or younger, a population in which such hallucinations are highly uncommon.⁴⁸ The DDRE went on to note that the predominance of patients reporting hallucinations, both visual and tactile, that involved insects, snakes, or worms is striking and deserves further evaluation. In many patients, reportedly, the events ceased after they stopped taking the drug. Dr. Kate Gelperin, one of the FDA reviewers noted, "[i]t was striking how often young children described various insects, bugs and worms, both visual

⁴² Ibid

⁴³ Ibid

⁴⁴ Ibid

⁴⁵ Ibid

⁴⁶ "FDA Rx Safety Officials Urge New Psychosis Warnings on ADHD Drugs," Drug Industry Daily 5, no. 53 (March 16, 2006).

⁴⁷ Gelperin, Kate, MD, MPH, et. al., "Psychiatric Adverse Events Associated with Drug Treatment of ADHD: Review of Postmarketing Safety Data" [FDA Center for Drug Evaluation and Research Memorandum], PID D050243, March 3, 2006.

⁴⁸ "FDA Rx Safety Officials Urge New Psychosis Warnings on ADHD Drugs."

and tactile—which we haven’t seen elsewhere.”⁴⁹ According to some physicians, it is no surprise that ADHD medications have these effects since they are “exactly the same chemicals” as popular street drugs known to trigger psychosis.⁵⁰

Public Perception

Media reports from as far away as Australia are sounding alarm bells over the reports of potential serious side effects of ADHD medications. One OP/ED piece from an Australian paper notes, “[h]eart attacks, strokes, convulsions, and hallucinations are not conditions usually associated with children. But these shocking symptoms could be the first ugly ramifications to surface from a society increasingly turning to ‘quick-fix’ drugs to solve behavioural problems.”⁵¹

The *New York Daily News* reports that “[m]ore than 500 children on medications for attention deficit hyperactivity disorder have reported bouts of psychosis” and “at least five kids on Adderall XR—one of the most prescribed ADHD drugs—have died from possible heart failure since it was approved for pediatric use in October 2004” according to the FDA. The article goes on to point out that in spite of this, “the FDA’s pediatric advisory panel last night decided the drugs did not need so-called ‘black box’ warnings about the medications’ risks.”⁵² The panel rejected a “black box” warning in part because of testimony by psychiatrists and other medical specialists that the drugs fill a critical need for treating mental health problems in children.⁵³

The media are also continuing to report that ADHD medications are being overprescribed. The *Los Angeles Times* notes that “Cleveland Clinic cardiologist Dr. Steven Nissen is urging the FDA to act “soon and decisively” to restrict the use of ADHD drugs. Nissen was among the first to raise concerns about the heart risks of the painkiller Vioxx, later withdrawn from the market...”⁵⁴

The media coverage of the potential health risks from exposure to ADHD medications is creating an atmosphere of suspicion around them before further testing can be done to confirm or deny the initial studies. These drugs are perceived to be causing serious health issues in both children and adults. In children, especially, this creates an emotionally charged issue that plaintiffs’ attorneys will take fullest possible advantage of to create viable legal claims.

Direction of Possible Litigation

Plaintiffs’ attorneys are already heavily advertising for cases involving injuries attributed to ADHD medications with headlines such as “Unsafe ADHD Drugs Put 2 Million Children at Risk” and “We believe that drug companies who place profit above people must be held accountable for their negligence and the damage they cause to innocent victims’ lives.” A cursory internet search finds multiple plaintiffs’ attorneys soliciting ADHD clients and providing information on their websites pulled from media reports on the various perceived ADHD drug health hazards.

⁴⁹ Alonso-Zaldivar, Ricardo, A-12.

⁵⁰ Rubin, Rita, “Re: Labeling ADHD drugs as psychosis/mania risk; advisory panel takes up question,” *USA Today*, March 21, 2006, p. 6D.

⁵¹ Cummings, Larissa, “When the cost of a well behaved child could be hallucinations or death,” *The Daily Telegraph* (Australia), March 28, 2006, Op/Ed., p. 17.

⁵² Shin, Paul H.B., “Feds Alarmed by Psychosis in Kids,” *New York Daily News*, March 23, 2006, p. 38.

⁵³ Alonso-Zaldivar, Ricardo, A-12.

⁵⁴ *Ibid.*

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Potentially the greatest litigation threat comes from nuisance claims that may be filed concerning ADHD medications.

Another angle is for plaintiffs' attorneys to target ADHD drugs being prescribed with atypical antipsychotics, which allegedly have their own array of side effects.⁵⁵ Drugs such as Seroquel, Risperdal, and Zyprexa are now being prescribed to more than 500,000 children in the United States.⁵⁶ Thus, the pool of potential plaintiffs is enormous.

At this point, smaller firms are relying on traditional product liability theories such as negligence, strict liability in tort, and breach of warranty. However, it is likely only a matter of time before the larger plaintiffs' firms begin to take notice of this issue and file lawsuits arguing increasingly expansive liability theories such as nuisance, deceptive trade practices, fraud, and conspiracy.

Larger firms will base their suits on more novel product liability theories that have begun to be successful for them over the past few years. The threat can come from suits brought by an individual, a class, or suits brought by a governmental body. If state attorneys general, Medicaid, school boards, or other large governmental plaintiffs get involved, the defenses to the claims become more limited owing to the limitations of legal defenses typically allowed against governmental entities bringing lawsuits.

Potentially the greatest litigation threat comes from nuisance claims that may be filed concerning ADHD medications. Historically, public nuisance claims have been separate causes of action which rarely have had any relation to product manufacturers or distributors, but rather were limited to owners' use of real property. However, in recent years, public nuisance claims have evolved from those involving an owner's use of property to a new theory of product liability to recover from product manufacturers. This transformation began to take shape during the tobacco litigation in the 1990s when, in the minds of some government plaintiffs and perhaps even some courts, the tobacco litigation as a whole was seen as successful expansion of the public nuisance theory to encompass a hazardous product. The expansion continued with the handgun litigation of the late 1990s and early 2000s in which government plaintiffs garnered their first modest successes in the court system when employing the public nuisance theory of liability against product manufacturers.

Building upon the foundation laid in the 1990s tobacco and gun litigation, in recent months and years, courts in several different jurisdictions have modified, or in some cases outright rejected, the traditional elements of public nuisance law. In the context of lead paint litigation, courts are beginning to reject any distinction between a products liability claim and public nuisance claim. Accordingly, plaintiffs have much more leeway in pleading public nuisance cases than they did a few years ago and have actively sought to expand this doctrine.

It is clearly time for manufacturers and health care providers to act in preparing for the potential wave of litigation. One verdict on the order of the Vioxx \$253 million jury award, and ADHD drugs will be dead in the bulls eye of the plaintiffs' lawyers.

Pharmaceutical litigation has become big business for the Plaintiffs' Bar. As manufacturers continue to turn out new drugs, trial lawyers continue to seek remedies for any perceived problem no matter how small. FDA preemption may be only a temporary cure to the litigation woes of pharmaceutical makers, but one can be sure the trial lawyers will do everything possible to overturn the roadblock.

⁵⁵ "Psychiatrists, Children and Drug Industry's Role," New York Times, May 10, 2007.

⁵⁶ Ibid.

For those manufacturers of ADHD drugs, now is the time to really prepare for the possible onslaught of litigation. Lawsuits over the use of such prescriptions and the side effects looks to be the proverbial “perfect storm.” Despite the undoubted benefits of these drugs, they are associated with side effects, as all drugs are: recent papers have brought new attention to these problems. The scientific community is poised to continue the investigation, and more bad news is possible. Then the pharmaceutical community must deal with the plaintiffs- children. Litigation involving the health of children is extremely difficult to defend, and now it seems like manufacturers are on notice of possible adverse effects. Finally, there is the factor that usage of these drugs is increasing in adults, both legal and illegal.

One of three factors could open the flood gates of litigation: a) a terrible scientific study demonstrating a direct causal link to adverse effects; b) a headline making death that gets the media truly involved on a national scale; and/or c) a current case getting to a jury with a huge “Vioxx” type verdict. If the tidal wave of litigation begins before companies are prepared, the cost of defending is much higher and the likelihood of adverse consequences is more probable.

What can your company do now? Getting a litigation team in place to begin the historical review of documents and to create the company’s story is vital to an early and successful defense. It is never too early to begin. In addition, the defense team can also begin to use the factual information to structure defenses to likely claims.

Start interviewing and preserving witness testimony. This information helps with development of the company’s story, and assists in witness development for presenting a defense. In addition, these witnesses can help in identifying likely experts.

Trial lawyers have a stable of experts. Potential defendants need to do the same- now. Waiting until the litigation begins can almost assure that many of the best experts are off the market. In high stakes “bet the company” litigation the experts can make or break your case. Many times it can take months to properly prepare an expert, so an early start is likely to increase the expert’s knowledge and testifying ability.

Proper defense counsel brought in early can develop a comprehensive strategy to have the defense in place before the litigation even begins.

Conclusion

In summary, industry executives and in-house counsel are wise to watch the development of novel legal theories being used by the Plaintiffs’ lawyers in bringing new product liability and toxic tort actions. These novel arguments, which appear to be gaining traction around the country, are being used to thwart statutory limitations limiting the old tried and true causes of action. As the science continues to evolve towards establishing a link between various ADHD drugs and medical problems it is certain to attract even more attention from trial lawyers around the country. No doubt this is an area where strategic planning and preparation are required right now in order to prepare for the possible and likely onslaught of litigation.

If the tidal wave of litigation begins before companies are prepared, the cost of defending is much higher and the likelihood of adverse consequences is more probable.

About McGuireWoods and the Author

At McGuireWoods, serving clients is our primary focus. Our commitment to providing top quality work and personalized service has allowed us to become one of the most client-centric law firms in the country. That commitment to service includes delivering exceptional value, using technology to provide effective and efficient legal solutions, and employing a diverse work force to bring real-world and innovative perspectives and solutions to our clients.

With approximately 750 lawyers in 15 strategically located offices worldwide, McGuireWoods uses client-focused teams to serve public, private, government and nonprofit clients from many industries including automotive, banking, consumer products, energy resources, health care, real estate, technology and transportation, thus meeting clients' needs from virtually any area of law.

Our lawyers defend pharmaceutical, medical device and biotechnology clients in complex product liability litigation which is national in both scope and subject matter. We regularly represent clients in the defense of cases involving prescription, over-the-counter supplements and medical devices. We have defended a variety of chemical compounds in the areas of cardiovascular, upper respiratory and oncology. Our experience runs the full range of representation from single-plaintiff high exposure drug or medical device cases to multi-district litigation involving multiple plaintiffs.



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Mr. Hite's practice involves representing corporations in complex litigation. His experience includes substantial first chair trial experience in both state and federal courts. As part of his practice, he handles cases involving class actions, business litigation, toxic torts, and products liability. Mr. Hite also possesses extensive experience in handling nuisance claims based on exposure to toxic substances. Most of the cases that he handles involve "parallel proceedings": competing actions that must be defended simultaneously in multiple jurisdictions.

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