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INTRODUCTION

The diet pills fenfluramine (Pondimin) and dexfenfluramine (Redux) were pulled from the market voluntarily by American Home Products (through its subsidiaries A.H. Robins and Wyeth-Ayerst) on September 15, 1997.¹ Those two pills made up the “fen” portion of the extraordinarily popular fen-phen diet drug combination. Redux and Pondimin allegedly caused valvular heart disease, primary pulmonary hypertension, and in some cases neurotoxic brain injury. The U.S. Department of Health and Human Services, the American College of Cardiology, and the American Heart Association all made recommendations for persons who had ingested Redux and Pondimin. Following the widespread publication of the heart valve and primary pulmonary hypertension (“PPH”) problems associated with fen-phen use, many Redux/Pondimin users filed lawsuits against American Home Products. While some of these plaintiffs had actually been diagnosed with valvular heart disease and PPH, many were suing for the right to medical monitoring paid for by American Home Products. American Home Products has settled several cases out of court and jury verdicts were returned in two important trials, the Lovett trial in Texas and the Washington trial in Mississippi. All the federal cases were consolidated in 1997 in MDL 1203 before Judge Louis Bechtle in the U.S. District Court for the Eastern District of Pennsylvania in Philadelphia. Several state cases were consolidated as well, including cases in New York and California. In October of 1999 American Home Products reached a Settlement Agreement with plaintiffs’ lawyers for all valvular heart disease claims. Judge Bechtle has given preliminary approval to that Settlement Agreement, and he will make a decision on whether to grant Final Judicial Approval after a Fairness Hearing scheduled for May 1 – 5, 2000. The litigation has raised issues concerning off-label drug prescriptions, drug manufacturer liability, class actions, and medical monitoring

¹See U.S. Food and Drug Administration Center for Drug Evaluation and Research (CDER), *FDA Announces Withdrawal Fenfluramine and Dexfenfluramine*, CDER WEBSITE P97-32, Sept. 15, 1997, online at www.fda.gov/cder/news/fenphenpr81597.htm

claims.

This paper is divided into three sections. The first section discusses the diet drugs used in the fen-phen combination and the health problems associated with those drugs.²It also considers the matter of off-label drug prescriptions and the role of obesity/cosmetic-weight loss in fen-phen prescriptions.

The second section addresses issues raised in the fen-phen litigation. It begins with a discussion of drug manufacturer liability and of the main fen-phen defendant, American Home Products. It follows with a discussion of medical monitoring, the multi-district litigation, the fen-phen class actions, and a comprehensive description of the proposed Settlement Agreement. Key state trials and settlements, particularly in Texas, Mississippi, and Massachusetts, are also examined in this section.

The third part of the paper identifies some of the lessons learned by the entire fen-phen experience, and specifically a major lesson related to the widespread use of the diet drugs for cosmetic weight loss and the dangers of off-label diet drug prescriptions. The paper argues that in light of the context of societal pressure for weight loss and the insatiable thirst of the American population for weight loss drugs, the FDA should have more stringent approval standards for diet drugs than for other pharmaceuticals, and off-label prescriptions of diet drugs should be prohibited. This is because of the propensity for misuse of diet drugs for cosmetic weight loss, where their original risk-benefit analysis goes astray because often the ‘disease’ they are being used to combat is actually nonexistent. Off-label prescribing for diet drugs should be prohibited (it is otherwise legal).

The paper concludes with an assessment of the likely outcome of the fen-phen litigation situation. It is important to note that this is an ongoing situation and the paper cannot address the final outcome of the fen-phen litigation. While the opt-out deadline for the Settlement was a March 30, 2000 postmark, the results of opt-out numbers will not be posted until the paper is completed. In addition, the Fairness Hearing for the

²**It is important to note that American Home Products maintains that there is no clear causal link between Pondimin and/or Redux and valvular heart disease.**

Settlement is not scheduled until May 1 – 5, 2000, and the outcome of that hearing will play an extremely critical role on the eventual results of the fen-phen experience. This paper asserts that the Settlement will be approved and assesses who wins and loses in that situation.

The fen-phen affair has spawned thousands of lawsuits and a multitude of scientific studies concerning valvular heart disease. It has also led to a lively debate over off-label prescriptions, medical monitoring, and class actions. The proposed Settlement Agreement, while an attempt to put an end to the valvular litigation, will not be the end of the fen-phen affair. The Settlement Agreement has been widely criticized and plaintiffs' lawyers have indicated that there will be a large number of opt-outs, which could lead to a termination of the Agreement by American Home Products. In addition, PPH claims are generally not settled by the Agreement and plaintiffs are free to pursue those claims in court. American Home Products may be facing liability for fen-phen for years to come, and there is still much to be learned about the valvular heart disease associated with Redux and Pondimin use. In addition, there are new diet drug concerns related to an attempt to recreate fen-phen by the use of Prozac in place of Redux and/or Pondimin, and the new diet drug Meridia works in a very similar way to Redux and Pondimin. The lessons learned from fen-phen will be invaluable in other mass-tort pharmaceutical drug liability situations, and also with other diet drugs that are currently or soon to be on the market.

PART I

THE WIDESPREAD USE OF FEN-PHEN, THE WITHDRAWAL OF FENFLURAMINE AND DEXFEN

FEN-PHEN – THE DIET DRUGS

FENFLURAMINE, DEXFENFLURAMINE, AND PHENTERMINE

The Fen-Phen Cocktail

The combination of drugs popularly referred to as “fen-phen” actually consists of a cocktail of two drugs, fenfluramine (Pondimin) or dexfenfluramine (Redux) (the “fenfluramines”) and phentermine. The fenfluramine or dexfenfluramine is the “fen” part of the drug combination, and the phentermine makes up the “phen” portion.³ It is the “fen” part of the fen-phen cocktail which is the alleged cause of the medical problems at issue in the fen-phen litigation. Dexfenfluramine and fenfluramine are the drugs that are associated with the problems and they have been removed from the market. Phentermine is still on the market and is not generally considered to have caused the health problems associated with the fen-phen combination.

The Food and Drug Administration (“FDA”) approved fenfluramine in 1973 and phentermine in 1959 as “INDIVIDUAL agents for short-term use [a few weeks] in the medical management of obesity. The use of the products concomitantly has never been approved in the United States, although recently, the combination of the two products has been used ‘off-label’ by many American health care practitioners for the management of obesity.”⁴ An article written by Michael Weintraub⁵ in 1992 indicated that the use of fenfluramine and

³See U.S. Food and Drug Administration Center for Drug Evaluation and Research (CDER), *FDA Announces Withdrawal Fenfluramine and Dexfenfluramine*, CDER WEBSITE P97-32, Sept. 15, 1997, online at www.fda.gov/cder/news/fenphenpr81597.htm

⁴U.S. Food and Drug Administration/U.S. Department of Health and Human Services Public Health Service, *Reports of Valvular Heart Disease in Patients Receiving Concomitant Fenfluramine and Phentermine*, FDA PUBLIC HEALTH ADVISORY, DEAR HEALTH PROFESSIONAL LETTER, July 8, 1997.

⁵Michael Weintraub, the researcher who began the fen-phen craze, was a University of Rochester obesity researcher when he wrote about the off-label long-term combination use of fenfluramine and phentermine. His actions and behavior from the 1992 study forward have raised serious ethical and moral concerns. Weintraub joined the FDA in 1993 as a top official, and he served as division director for over the counter drugs and head of an office that managed three divisions. While at the FDA he served on a fen-phen task force formed in 1997 to review reports of valvular heart disease in fen-phen patients. Weintraub was at the FDA for five years, and he left in 1998 to become a pharmaceutical industry consultant. While at the FDA, Weintraub agreed to advise John Trevena, a Florida lawyer, about starting a diet-center business. Trevena was to use fen-phen at his centers. Trevena was a fen-phen user himself who later developed valvular regurgitation, as did his wife, also a fen-phen user. His diet centers failed and he went into business and personal bankruptcy. Trevena is now practicing law in the private sector and has

phentermine together could produce dramatic weight loss effects.⁶ The article indicated that “the anorexi-
genic effects of fenfluramine could be duplicated and its side effects minimized by the use of smaller doses of
the drug in combination with phentermine”⁷ The authors reported that the fen-phen combination was safe
and effective.⁸ After the publication of this article, which studied 121 obese patients who lost an average of
30 pounds while using fenfluramine and phentermine, the popularity of fen-phen spread quickly.⁹ By 1996
total U.S. prescriptions for fenfluramine and phentermine together reached a number over 18 million.¹⁰ Most
of the use of fen-phen was in women and in people under 60 years of age. Overall, “[b]ased on an assumed
treatment course of 3-12 months and an average prescription length of 1 month, an estimated 1.2-4.7 million

filed a lawsuit against Wyeth-Ayerst that he has attempted to get the government to join and prosecute, to no avail. Trevena
had offered to pay Weintraub for his diet center advice, but Weintraub refused to accept money because of governmental ethics
policies. However, Weintraub made staff recommendations for Trevena’s medical centers, spoke favorably about the centers to
the media, allowed his name to be used in advertising for the centers, talked with and wrote to prospective Trevena clients who
were considering the use of fen-phen, and flew to Florida to recommend that the State Medical Board not ban fen-phen. One
Trevena center client who spoke with Weintraub about fen-phen asked for a physician referral and Weintraub sent back a reply
on FDA stationery that recommended Trevena’s marketing consultant. Weintraub said that he saw himself offering Trevena
the same help that he gave others, and he did not consider himself as helping Trevena start his diet business. He said he may
have spoken to some potential Trevena clients, but he did not recall for sure. He said that he always used a checklist that
included all potential side effects when anyone asked about fen-phen and he stressed the need for a full physical. Weintraub
said that he could not reject talking to people who called him regarding fen-phen because he believed that the drugs could be
of great benefit to people. Weintraub claims his FDA superiors knew of his work but did not object because he informed them
that he was not being paid by outside interests.

See Donna Shaw, *Tarnish on FDA’s Vaunted Image: The Researcher Responsible For the Fen-Phen Drug Used
His Expertise To Promote A Florida Diet Center*, PHILADELPHIA INQUIRER, Sept. 26, 1999, available online at
www.phillynews.com/inquirer/99/Sep/26/front-page/DIE126.htm; See also Kris Huntley, *Fen-Phen King Turns Tables On
Drug Maker: Once a Promoter and User of the Weight-Loss Drug Combination, John Trevena Has Filed a Civil Suit Against
Drugmaker Wyeth-Ayerst Laboratories, Inc., Accusing It of Fraud*, ST. PETERSBURG TIMES, Oct. 10, 1999, Business Section.

⁶See M. Weintraub et al., Long-term weight control study: I-VII, 51 *Clinical Pharmacology and Therapeutics* 581-646 (1992)
See also Jaime A. Wilsker, *One Half-Phen In the Morning/One Fen Before Dinner: A Proposal For FDA Regulation of Off-
Label Uses of Drugs*, 6 J.L. & POL’Y 795, 823 (1998) for a discussion of Dr. Weintraub’s fen-phen study. In the study, he
administered the combination of 60 mg fenfluramine and 15 mg phentermine in addition to behavior modification to 121 obese
women for 190 weeks. He found this combination drug therapy to lead to significant weight loss over 210 weeks. 26 out of the
121 patients lost more than 10% of their body weight. Id.

⁷Alfred P. Fishman, M.D., *Current Perspective - Aminorex to Fen/Phen: An Epidemic Foretold*, CIRCULATION – THE
JOURNAL OF THE AMERICAN HEART ASSOCIATION 1999:99 156-161, 158 (1999).

See also: U.S. Food and Drug Administration Center for Drug Evaluation and Research (CDER), *Questions and
Answers about Withdrawal of Fenfluramine (Pondimin) and Dexfenfluramine (Redux)*, CDER WEBSITE, online at
www.fda.gov/cder/news/phen/fenphenqa2.htm. On the Q+A website, the FDA says that “the results of these studies were not
reviewed by FDA, and the conclusion about long term use of the combination of drugs has not received FDA approval.” Id.

⁸See Weintraub, M., Sundaresan, R.P., Schuster, B., Averbuch, M., Stein, E.C., and Byrne, L. *Long-Term Weight Control
Study V (Weeks 190-210); Follow-Up of Participants After Cessation of Medication*, CLINICAL PHARMACOLOGICAL THERAPY
51, 651-618 (1992).

⁹See Paul D. Rheingold, *Fen-Phen and Redux: A Tale of Two Drugs - The Story of How Fen-Phen and Redux Came to Be
Used By 6 Million Americans is Chilling*, 34 TRIAL 78 (1998).

¹⁰See CNN Interactive, *Valvular Heart Disease Associated With Fenfluramine-Phentermine – Dr. Heidi M. Connolly –
Manuscript Of Study Submitted To New England Journal of Medicine*, CNN WEBSITE, July 8, 1997, available online at
www.cnn.com/Heath/0/07/08/fenphen.report/.

persons in the United States have been exposed to these drugs.”¹¹ From 1992 to 1997, new prescriptions for fen-phen (phentermine and fenfluramine) increased by 442% for phentermine and 6390% for fenfluramine.¹² Many of these prescriptions had been given by doctors who had only a cursory relationship with the patient. Patients were able to get fen-phen prescriptions over the internet, and Nutri-System and Jenny Craig set up “medical weight loss” programs where doctors prescribed large numbers of fen-phen to patients with whom they did not have long term relationships.¹³

Dexfenfluramine was made by Wyeth-Ayerst Laboratories in Philadelphia, Pennsylvania, under a license from Interneuron Pharmaceuticals, Inc. of Lexington, Massachusetts. Wyeth-Ayerst is a subsidiary of American Home Products, Inc. Fenfluramine was made by A.H. Robins Co., Inc. of Richmond, Virginia. A.H. Robins Co. was also a subsidiary of American Home Products (see later discussion of American Home Products). American Home Products is the corporation at issue in the fen-phen litigation. American Home Products Corporation has proposed to settle the legal claims surrounding the fenfluramines in the proposed Settlement Agreement discussed at length later in this paper.¹⁴ Phentermine, the other half of fen-phen, is not implicated in the proposed Settlement Agreement, has been dismissed from most lawsuits, and has not been taken off the market.

¹¹Centers for Disease Control, U.S. Department of Health and Human Services Interim Public Health Recommendations, *Cardiac Valvulopathy Associated with Exposure to Fenfluramine or Dexfenfluramine*, CDC MORBIDITY AND MORTALITY WEEKLY REPORT 1061 Vol. 46, No. 45, Nov. 14, 1997.

¹²See ARCHIVES OF INTERNAL MEDICINE Vol. 157 502-604, March 24, 1997.

¹³One Illinois plaintiff said that she obtained fen-phen from a weight-loss clinic and never saw a doctor. She regularly saw a nurse who gave her the fen-phen prescriptions. Nutri-System centers highlighted the fact that a doctor would provide a fast check-up and then a fen-phen prescription. Fen-phen could easily also be obtained over the Internet. One doctor, Peter Hitzig, advertised that he would prescribe fen-phen by other means if you could not make it physically to his office. Most of these doctors had little or no training in obesity. See Jaime A. Wilsker, *One Half-Phen In the Morning/One Fen Before Dinner: A Proposal For FDA Regulation of Off-Label Uses of Drugs*, 6 J.L. & POL'Y 795, 827-828, (1998). This common practice broke down the alleged careful risk-benefit calculation a doctor was supposed to engage in with his or her patient to determine if the risks of obesity were greater or lesser than the risks associated with fen-phen. The fen-phen risk at issue before the valvular disease problem became known was the increased PPH risk. See Martha Neil, *Lawyer Seeks Plaintiff Group to Bolster Diet-Drug Litigation*, CHICAGO DAILY LAW BULLETIN Vol. 143 No. 184, Sept. 19, 1997.

¹⁴See *Two Weight-Loss Drugs Disrupt Certain Brain Functions in Animals*, DOCTOR'S GUIDE & OTHER MEDICAL NEWS, Aug 26, 1997.

Fenfluramine and Dexfenfluramine

Dexfenfluramine and fenfluramine (the “fenfluramines”) are “cogeners of amphetamines” and are anorectic agents.¹⁵ Both fenfluramine and dexfenfluramine work by “affecting the metabolism of the neurotransmitter serotonin in the brain”.¹⁶ Fenfluramine and dexfenfluramine promote the rapid release of serotonin and inhibit its reuptake.¹⁷ By getting into the brain and changing serotonin levels, the fenfluramines make their users experience positive feelings and believe they are full. The drugs “trick” the brain into believing that the user does not desire any more food. The fenfluramines are pharmacologically similar to anti-depressants such as Prozac, and several patients on fen-phen indicated that they felt less depressed while taking the drugs, although much more so with dexfenfluramine than fenfluramine.¹⁸ Fenfluramine (Pondimin) did not have the same anti-depressant effect to the degree of dexfenfluramine (Redux) and therefore dexfenfluramine became a popular “fen” part of the fen-phen combination.¹⁹

Fenfluramine was approved by the FDA in 1973 as a short term single use appetite suppressant. It was to be used in combination with a diet and exercise weight-loss plan.²⁰ It was not approved as a combination drug. It is a Class IV controlled substance, which means that there is a low potential for abuse of the drug. Fenfluramine was sold under the trade names Pondimin and Ponderol, and it was produced by A.H. Robins, a subsidiary of American Home Products. Fenfluramine is a sympathomimetic amine, which is a drug that

¹⁵See Alfred P. Fishman, M.D., *Current Perspective - Aminorex to Fen/Phen: An Epidemic Foretold*, CIRCULATION, at 157. Anorectic agents are appetite suppressants. Anorectic means “characterized by lack of appetite” THE NEW SHORTER OXFORD ENGLISH DICTIONARY 83 (1993).

¹⁶NAPOLI, KAISER & BERN LLP, THE FEN-PHEN E-RESOURCE, *Cardiac Valvulopathy Associated with Exposure to Fenfluramine or Dexfenfluramine; U.S. Department of Health and Human Services Interim Public Health Recommendations*, available online at www.dietdrugsettlement.com.

¹⁷See John T. Evans and Robert L. Kerner, Jr., *A Primer on Fen-Phen Litigation: Allegations and Defenses*, 65 DEF. COUNS. J. 353, 355 (1998).

¹⁸See Telephone Interview with Tori Marnell, M.D., University of Texas - Southwestern Medical School in Dallas, Physician in Tulia, Texas (March 18, 2000).

¹⁹See Fenfluramine seemed to produce more depression than stimulation in patients, unlike most other similar drugs. Several patients on fenfluramine complained of depression, and many were switched to dexfenfluramine as a result of their complaints. See Interview with Dr. Tori Marnell (March 18, 2000). See also Evans and Kerner, *A Primer on Fen-Phen Litigation: Allegations and Defenses*, 65 DEF. COUNS. J. at 354.

²⁰See Evans and Kerner, *A Primer on Fen-Phen Litigation: Allegations and Defenses*, 65 DEF. COUNS. J. at 354.

“mimic[s] sympathetic nervous system stimulation”, although fenfluramine produced more depression than stimulation, unlike other sympathomimetic amines. The usual fenfluramine dose is 20 milligrams three times per day, which may be increased by one tablet after each week of use. The maximum dose is 120 milligrams per day. Fenfluramine is:

contraindicated in patients with glaucoma, hypersensitivity to sympathomimetic amines, history of drug abuse, history of psychosis and/or symptomatic cardiovascular disease. Fenfluramine has been shown to cause paranoia, depression and psychosis in alcoholics. It has been associated with numerous cases of pulmonary hypertension and there is one report of fatal cardiac arrest following induction of anesthesia. Fenfluramine is not recommended for use in children under 12 years of age. It is embryonic in rats, but there have been no adequate studies involving pregnant women.²¹

Dexfenfluramine,²² the dex isomer of fenfluramine, was approved on April 29, 1996, also as an appetite suppressant.²³ It is a purified form of fenfluramine, and it was thought to have less side effects and toxicity than fenfluramine. It acts in basically the same way as fenfluramine, as a serotonin reuptake inhibitor and releaser.²⁴ Dexfenfluramine can be pharmacologically distinguished from fenfluramine in that “fenfluramine contains dexfenfluramine and levofenfluramine. Levofenfluramine may have some activities not directly related to appetite suppression. Dexfenfluramine contains only dexfenfluramine.”²⁵

²²The corporate history of Redux’s approval and marketing is as follows “Les Laboratoires Servier, S.A., a French pharmaceutical company, held the intellectual property rights to dexfenfluramine and entered into a licensing agreement with Interneuron for the development of dexfenfluramine in the United States market. Interneuron is in the business of testing pharmaceuticals and obtaining FDA approval for their sale in the United States. Following FDA approval of dexfenfluramine, Interneuron sublicensed the United States distribution rights for dexfenfluramine to an entity which is now American Home Products Corporation. American Home Products marketed dexfenfluramine under the brand name ‘Redux’ and began selling the drug in June 1996. Under the sublicensing agreement, Interneuron received royalties from American Home Products’ sales of Redux.... An estimated 2 million individuals ingested Redux during the course of its almost sixteen-month market life.” In re Diet Drugs Products Liability Litigation (Phentermine, Fenfluramine, Dexfenfluramine), MDL Docket No. 1203 Civil Action No. 98-20594, Memorandum and Pretrial Order, U.S. District Court for the Eastern District of Pennsylvania.

²³Note: the Redux labeling indicated that safety had not been shown for over one year of use of Redux. This one year limit reflects the length of the study upon which the FDA approved dexfenfluramine. The study took place in Europe, it had 1,000 subjects, and 500 of those subjects were given dexfenfluramine. 80% of the subjects were women and the average age was 41. There was no note of heart disease, and no follow up study to determine the presence of heart disease was undertaken. Dexfenfluramine had been on the market in Europe for over 10 years without any indication of a link between dexfenfluramine and heart disease. See U.S. Food and Drug Administration Center for Drug Evaluation and Research (CDER), *Questions and Answers about Withdrawal of Fenfluramine (Pondimin) and Dexfenfluramine (Redux)*, CDER WEBSITE, online at www.fda.gov/cder/news/phen/fenphenqa2.htm.

²⁴See Alfred P. Fishman, M.D., *Current Perspective - Aminorex to Fen/Phen: An Epidemic Foretold*, CIRCULATION, at 158.

²⁵U.S. Food and Drug Administration Center for Drug Evaluation and Research (CDER), *Questions and Answers about Withdrawal of Fenfluramine (Pondimin) and Dexfenfluramine (Redux)*, CDER WEBSITE, online at www.fda.gov/cder/news/phen/fenphenqa2.htm.

Dexfenfluramine (Redux) was the first anti-obesity drug approved in the U.S. in over 20 years, and sales of Redux were expected to reach \$1 billion within the first five years of use.²⁶ Dexfenfluramine was approved as a “single-drug, prescription appetite suppressant for longer term use in markedly obese persons, noting that safety beyond 1 year of use had not been established in clinical trials.”²⁷ Literature from Redux manufacturers stated of the drug, “Redux, combined with a reduced-calorie diet, is indicated for the management of obesity, including weight loss and maintenance of that weight loss. In clinical trials, Redux helped produce a significant reduction in weight during the first 4 to 6 months, and that loss was maintained during the year-long therapy. The safety and effectiveness of Redux beyond one year have not been determined.”²⁸ Redux’s popularity came about partly because of its anti-depressant affects, and it quickly became popular as a part of the fen-phen cocktail.

Dexfenfluramine’s “[a]pproval did not have an easy passage: the vote for approval was close, 6:5. After approval, a unanimous vote insisted on postmarketing studies and careful labeling concerning patient selection.”²⁹ Initially, the FDA Advisory Committee declined to approve Redux by a five to three vote. They cited inadequate evidence of the drug’s safety. After Redux’s approval, “many neuroscientists sent a letter to the FDA, criticizing the agency for ignoring animal tests that suggested that prolonged use of Redux damaged brain tissue.”³⁰

The difficult approval of dexfenfluramine also came amidst concerns about PPH. Reports of PPH linked to the fenfluramines had appeared throughout the European literature in the 1980’s and 1990’s.³¹ Two months

²⁶See ARCHIVES OF INTERNAL MEDICINE Vol. 157 502-604, March 24, 1997.

²⁷See NAPOLI, KAISER & BERN LLP, THE FEN-PHEN E-RESOURCE, *Cardiac Valvulopathy Associated with Exposure to Fenfluramine or Dexfenfluramine*; U.S. Department of Health and Human Services Interim Public Health Recommendations, available online at www.dietdrugsettlement.com.

²⁸Letter from Marc W. Deitch, M.D., Senior Vice President, Medical Affairs and Medical Director, Wyeth-Ayerst Laboratories Division of American Home Products Corporation, to Redux Prescribing Physicians (Aug. 22, 1997).

²⁹Alfred P. Fishman, M.D., *Current Perspective - Aminorex to Fen/Phen: An Epidemic Foretold*, CIRCULATION, at 158.

³⁰Apryl A. Ference, *Rushing to Judgment on Fen-Phen and Redux: Were the FDA, Drug Manufacturers, and Doctors Too Quick To Respond To Americans’ Infatuation With A Cure-All Diet Pill For Weight Loss?*, 9 ALB. L.J. SCI. & TECH. 77, 84 (1998).

³¹See Roche, N., Labrune, S., Braun, J.M., and Huchon, G. *Letter on Pulmonary Hypertension and Dexfenfluramine*, LANCET 339, 436-437, (1992).

after dexfenfluramine’s approval, the International Primary Pulmonary Hypertension Study (“IPPHS”) indicated that anorectic agents increased PPH to a level of between 23 and 46 per million, rather than the normal 1-2 per million background risk. However, concern over the increased PPH risk from the IPPHS was considered by many to be outweighed by the potential for the fenfluramines to contribute to weight loss for the seriously obese. One editorial in the *New England Journal of Medicine* stated, “the possible risk of pulmonary hypertension associated with the use of dexfenfluramine is small and appears to be outweighed by the benefit (from treating obesity) when the drug is used appropriately.”³² The FDA did approve Redux “only on the condition that it be prescribed for obesity, defined as a body mass index of 30 kilograms/m² or greater.”³³ The brochure Wyeth-Ayerst provided to doctors for Redux patients said of the PPH risk:

There is a small risk of a serious, potentially life-threatening cardiovascular condition called pulmonary primary hypertension associated with the use of prescription weight-loss drugs. In a review of PPH cases where any weight-loss drug was used (excluding 10 cases where the specific drug or date of use were unknown), the risk was estimated to be about 18 cases per 1 million patients per year. In the general population, the yearly incidence of PPH is one to two cases per million persons. Warning signals of PPH are shortness of breath, chest pain, fainting, and swelling of the legs, ankles, or feet. *If you have had any of these symptoms before starting Redux therapy, or if they occur during therapy, please discuss them with your health care provider*³⁴

After its approval, dexfenfluramine, marketed as Redux, appeared in stores in June of 1996.³⁵ Much advertising surrounded its release, and 1.2 million Redux prescriptions were filled. Amid the excitement over Redux and the massive advertising program, “little heed was paid to the manufacturer’s cautions about duration of use or to drug interactions with other serotonin releasers. No information was provided – because none was available – about the effectiveness and consequences of taking the drug for > one year. Lost in the hyperbole of advertising was the limited efficacy of the drug, i.e., that continued usage leads only to small

³²Manson, J.E. and Faich, G.A. *Editorial - Pharmacotherapy For Obesity: Do The Benefits Outweigh The Risks?*, N. ENGL. J. MED. 335, 659-660, (1996).

³³Evans and Kerner, *A Primer on Fen-Phen Litigation: Allegations and Defenses*, 65 DEF. COUNS. J. at 355.

³⁵See Interneuron Pharmaceuticals licensed Redux to Wyeth-Ayerst (American Home Products subsidiary) for marketing. See Michael D. Lemonick et al., *The New Miracle Drug? There’s Great Excitement About Redux, The First Diet Pill Approved By The FDA In 23 Years. But It’s Hardly The Ideal Way To Lose Weight*, TIME, Sept. 23, 1996, at 61, 63.

sustained weight loss averaging 10% compared with the 6% weight loss of control subjects.”³⁶ For both the obese and the non-obese, dexfenfluramine was widely prescribed in combination with phentermine, until the report by the Mayo Clinic in 1997 set off the alarm over valvular heart disease.

Dexfenfluramine and fenfluramine were both pulled from the market after the 1997 Mayo Clinic discovery of a high incidence of valvular heart disease among fen-phen users. The 1998 Physician’s Desk Reference “contains an introductory warning that fenfluramine has been reported to be associated with serious regurgitant cardiac valvular disease.”³⁷

Phentermine

The FDA approved phentermine in 1959 as an appetite suppressant, marketed under the trade names “Fastin”, “Adipex”, and “Ionamin”. It is marketed primarily by SmithKline Beecham. Phentermine, like fenfluramine, is a Class IV controlled substance.³⁸ The usual phentermine dose is 30 milligrams per day, taken in the morning. Phentermine is to be used “only for a few weeks as an adjunct to a diet,”³⁹ and under strict doctor’s supervision. Phentermine acts as a stimulant, and it was approved for single drug use for a few weeks for obesity treatment. Phentermine increases the metabolism and affects dopamine levels in the brain. It is a nonamphetamine appetite suppressant, although it can produce the same adverse effects as amphetamine appetite suppressants. Phentermine produces “central nervous system stimulation, elevation of blood pressure, tolerance and tachyphylaxis. Tachyphylaxis is the rapid immunization of the body to a toxic dose of a drug.”⁴⁰ Phentermine was thought to reduce undesirable side effects of fenfluramine, like

³⁶Alfred P. Fishman, M.D., *Current Perspective - Aminorex to Fen/Phen: An Epidemic Foretold*, CIRCULATION, at 158.

³⁷Evans and Kerner, *A Primer on Fen-Phen Litigation: Allegations and Defenses*, 65 DEF. COUNS. J. at 355.

³⁸See Evans and Kerner, *A Primer on Fen-Phen Litigation: Allegations and Defenses*, 65 DEF. COUNS. J. at 354.

³⁹BERT STERN AND LAWRENCE D. CHILNICK, *THE PILL BOOK* 5th EDITION 708 (1992).

⁴⁰Evans and Kerner, *A Primer on Fen-Phen Litigation: Allegations and Defenses*, 65 DEF. COUNS. J. at 354.

drowsiness.⁴¹ Common side effects of phentermine include “a false sense of well-being, nervousness, overstimulation, restlessness, and trouble sleeping.”⁴² Less common side effects include palpitations, high blood pressure, weakness, dizziness, and headache.⁴³

Phentermine is generally not implicated in the fen-phen litigation⁴⁴, and it has not been pulled from the market by the FDA. Dr. Heidi Connolly, the Mayo Clinic doctor who first discovered the valvular heart disease problem associated with fen-phen use, said “initially we thought it may be the combination of medications (fenfluramine and phentermine) that caused the valve problems, but it appears to be the fenfluramine medication alone.”⁴⁵ Phentermine appears safe when used alone, and by itself has not proven to be a cause of valvular regurgitation.⁴⁶ In the FDA’s Question and Answer section on its Fen-Phen Website, the question “[w]hy isn’t phentermine being withdrawn from the market” is answered with, “[a]t the present time, no cases of heart valve disease meeting FDA’s case definition have been reported with phentermine alone. Analysis

⁴¹See Paul D. Rheingold, *Fen-Phen and Redux: A Tale of Two Drugs - The Story of How Fen-Phen and Redux Came to Be Used By 6 Million Americans is Chilling*, 34 TRIAL at 78.

⁴²BERT STERN AND LAWRENCE D. CHILNICK, THE PILL BOOK 5th EDITION 706 - 707 (1992).

⁴³See *id.*

⁴⁴On January 11, 2000 Judge Bechtel in the multi-district litigation in Philadelphia ruled on several plaintiffs’ motions to amend their complaints to add phentermine defendants. The phentermine defendants objected to being added at the late stage in the case where discovery was almost complete. The phentermine defendants claimed that they would be unduly prejudiced by having to begin discovery after numerous deadlines in the multi-district litigation had passed. The plaintiffs argued that the phentermine defendants were aware of the issues involved in the multi-district litigation and therefore would not be prejudiced by being added at the later date. The plaintiffs also stated that the phentermine defendants could participate in discovery that had not yet gone forward. Judge Bechtel denied the motions of the plaintiffs since they sought to add the phentermine defendants at such a late stage, and because the plaintiffs did not timely serve their amended complaints upon the phentermine defendants pursuant to Pretrial Order No. 19 of the multi-district litigation. Pretrial Order No. 19 required the plaintiffs to serve their complaint and a summons on each defendant not served previously no later than 30 days after the date on which their action was docketed in the Eastern District of Pennsylvania.

See: *In re Diet Drugs (Phentermine, Fenfluramine, Dexfenfluramine) Products Liability Litigation*, *Davoust v. Wyeth-Ayerst v. American Home and Howard v. A.H. Robins Co. v. American Home Products Corporation*, Memorandum and Pretrial Order No. 1056, U.S. District Court for the Eastern District of Pennsylvania, Jan. 11, 2000, WL 62307. (E.D. Pa.).

⁴⁵*Fen-Phen Valvulopathy Presented by Heidi M. Connolly, M.D., F.A.C.C.*, CASES IN ECHOCARDIOGRAPHY, Directed by Rick A. Nishimura, M.D., F.A.C.C. and Fletcher A. Miller, Jr., M.D., F.A.C.C., Edited Transcript of a Talk Presented by Dr. Connolly at the Heart House Learning Center, (1999).

⁴⁶See Edward G. Lance, IV and Philip Tortorich, *Popular Diet Drugs Pulled From Market*, 9 LOY. CONSUMER L. REP. 296 (1997).

One article discussing the fen-phen litigation summed up the situation of phentermine with the statement: “Phentermine, the other half of the fen-phen mix, hasn’t been linked to problems when taken alone. It is made by another company [than American Home Products] and is still on the market.” Amy Westfeldt, *Many Decline Diet Drug Settlement*, ASSOCIATED PRESS, Oct. 15, 1999.

of the data points to an association of heart valve disease with fenfluramine and dexfenfluramine.”⁴⁷ The data so far indicates that the valvular heart disease and PPH increase is associated with serotonin levels and serotonin absorption. The fenfluramines are the drugs that affect brain serotonin metabolism, while phentermine acts primarily only as a stimulant. The problem that comes in with phentermine use in combination with fenfluramine and dexfenfluramine use is that phentermine “interferes with the pulmonary clearance of serotonin, which may explain its association with primary pulmonary hypertension.”⁴⁸ Since fenfluramine and dexfenfluramine cause an increase in the amount of serotonin released by the body and a decrease in the amount the body reabsorbs, when phentermine interferes with the pulmonary clearance of that serotonin, it magnifies the serotonin related effects of the fenfluramines in the lungs. Phentermine alone is not the problem, but it can compound the problems caused by fenfluramine and dexfenfluramine. Independent of serotonin problems, phentermine can also cause cardiac arrhythmias and increased blood pressure (a danger with all stimulants).⁴⁹

While phentermine alone appears not to cause the valvular problems and PPH associated with combined use with phentermine and dexfenfluramine or fenfluramine, the FDA stated that phentermine “has only mixed [weight loss] results when used alone.”⁵⁰ However, some patients who had weight loss success with fen-phen are now having continued weight loss success with phentermine alone.⁵¹

In one of the first major fen-phen cases, Linnen, which eventually settled in January of 2000, Judge Raymond Brassard of the Massachusetts Superior Court dismissed a former phentermine manufacturer on the grounds that the plaintiffs failed to present sufficient evidence that phentermine contributes to or causes PPH. Judge Brassard ruled to exclude the testimony of Texas A&M University scientist Paul Wellman, stating that

⁴⁷U.S. Food and Drug Administration Center for Drug Evaluation and Research (CDER), *Questions and Answers about Withdrawal of Fenfluramine (Pondimin) and Dexfenfluramine (Redux)*, CDER WEBSITE, online at www.fda.gov/cder/news/phen/fenphenqa2.htm

⁴⁸Evans and Kerner, *A Primer on Fen-Phen Litigation: Allegations and Defenses*, 65 DEF. COUNS. J. at 354.

⁴⁹See ARCHIVES OF INTERNAL MEDICINE Vol. 157 502-604, March 24, 1997.

⁵⁰Lance and Tortorich, *Popular Diet Drugs Pulled From Market*, 9 LOY. CONSUMER L. REP. at 296.

⁵¹See website of Ben Krentzman, M.D., available online at www.loop.com/~bkrentzman.

there was “no evidence that Wellman ‘utilized sound scientific methodology in arriving at his opinions in this case.’”⁵² The conclusions of Paul Wellman were cited in over 400 fen-phen suits in the United States, so Judge Brassard’s decision is likely to have wide-ranging effects on phentermine manufacturer liability in all fen-phen litigation. Judge Brassard reached his decision on expert testimony admissibility pursuant to the standards set forth in Daubert v. Merrell Dow Pharmaceuticals, Inc. and Commonwealth v. Lannigan. Judge Brassard found that there was “no testing of the [plaintiffs’] experts hypotheses, no known error rate, lack of acceptance among the scientific community for the hypotheses proposed by the experts, and an insufficient degree of scientific certainty by the experts themselves regarding their key theories.”⁵³ The lawyers for the phentermine manufacturers expressed the hope that “this decision will mark a turning point in all of the fen-phen litigation... [and stated that] Judge Brassard’s thorough and thoughtful decision is likely to influence the court’s approach to this issue nationwide.”⁵⁴ Phentermine is also not included in the proposed Settlement Agreement with American Home Products. The proposed settlement agreement for the diet drug litigation only addresses fenfluramine (Pondimin) and dexfenfluramine (Redux), not phentermine.

NEW DIET DRUGS REPLACING FENFLURAMINE AND DEXFENFLURAMINE

Meridia

While both fenfluramine and dexfenfluramine have been pulled from the market in light of the valvular problems and PPH risk increase, the current diet drug Meridia (sibutramine) also works by affecting serotonin

⁵²Bloomberg, *Judge Balks at Testimony in AHP Fen-Phen Lawsuit, Paper Says*, MADISON, NEW JERSEY BLOOMBERG REPORT, Jan. 6, 1999.

⁵³Business Wire – Boston, *Phentermine Dismissed From Massachusetts ‘Fen-Phen Case*, BUSINESS/LEGAL EDITORS, Jan. 7, 2000.

⁵⁴id.

levels in the brain, making the user believe he or she is full.⁵⁵ The FDA approved sibutramine on November 24, 1997. It is also an appetite suppressant and works by inhibiting the re-uptake of serotonin and norepinephrine (neurotransmitters that send messages in the brain).⁵⁶ Fenfluramine and dexfenfluramine worked by affecting the release of brain neurotransmitters. The difference between Meridia and the fenfluramines is that Meridia does not cause an increase in the release of serotonin from nerve cells, rather it only slows the body's reabsorption of serotonin that was naturally produced.⁵⁷ Several experts claim that it was the release of serotonin from nerve cells that caused the PPH and valvular heart damage associated with the fenfluramines.⁵⁸ However, the FDA stated that clinical studies on Meridia did not show any increased PPH risk or any higher rates of valvular heart disease in Meridia users.⁵⁹ However, in light of the problems with fen-phen, Meridia does not remain an extremely popular anti-obesity drug today, and it is target marketed at the clinically obese, with more care taken to avoid the fen-phen type of rampant use for cosmetic weight loss.⁶⁰ Meridia's manufacturer, Knoll Pharmaceuticals, has been "conservative and cautious in its recommendations and advertisements. The company's market launch, described by one journalist as 'low-key', is replete with warnings and caveats that confine the administration of Meridia to a highly restricted class of obese patients.... Knoll cautions cosmetic dieters against using the product, and it intends to chastise doctors who prescribe the drug for patients the company does not consider appropriate for treatment with Meridia".⁶¹ Both Meridia's manufacturer and the FDA want to prevent the type of rampant cosmetic weight loss use with Meridia that plagued fen-phen. "Dr. James Bilstad, FDA's metabolic drug chief, told USA

⁵⁵See Interview with Dr. Tori Marnell (March 18, 2000).

⁵⁶See Heart Information Network, *Anti-Obesity Drug Sibutramine Approved by FDA – Not Recommended for Heart Patients*, HEART INFORMATION NETWORK WEBSITE, Nov. 1997, available online at www.heartinfo.org.

⁵⁷See *id.*

⁵⁸See Mayo Clinic Health Oasis, *Heart Valve Disease and Fen-Phen: An Interview With Mayo Cardiologist Heidi Connolly, M.D.*, MAYO CLINIC WEBSITE, July 8, 1997, available online at www.mayohealth.org/mayo/9707/htm/fen.1sb.htm.

⁵⁹See Heart Information Network, *Anti-Obesity Drug Sibutramine Approved by FDA – Not Recommended for Heart Patients*, HEART INFORMATION NETWORK WEBSITE, Nov. 1997, available online at www.heartinfo.org.

⁶⁰Many doctors do not want to put their patients on Meridia in light of its similarities with fenfluramine and dexfenfluramine. Xenical is the more popular drug to prescribe to patients to lose weight, since it does not affect serotonin levels and works completely differently than the fenfluramines. See Interview with Dr. Tori Marnell (March 18, 2000).

⁶¹Steven R. Salbu, *The FDA And Public Access To New Drugs: Appropriate Levels Of Scrutiny In The Wake of HIV, AIDS, and the Diet Drug Debacle*, 79 B.U. L. REV. 93, 128 (1999).

Today that sibutramine is not intended to be used by people who simply want to lose a few pounds – it is for people who are obese. Specifically, the FDA reports that sibutramine is indicated for people with a body mass index (BMI) of 30 or more (e.g. a person 5’6 weighing 185 pounds or more).⁶² People with other risk factors such as diabetes are also candidates for the drug if their BMI is at least 27 (e.g. a person 5’6 weighing at least 167 pounds). The drug is indicated for use with a reduced calorie diet.”⁶³

FDA clinical trials with over 6,000 people showed that Meridia combined with a reduced calorie diet and exercise could lead to a weight loss in 6 months of between 10 to 15 pounds (depending on dose) that could be maintained for one year. Meridia’s common side effects include headache, dry mouth, and insomnia. Meridia can also lead to an increase in blood pressure and is not recommended for patients with heart disease, congestive heart failure, or patients with a stroke history.⁶⁴ The American Heart Association urges caution when considering Meridia because in some individuals it elevated blood pressure or led to increased pulse rates or irregular heartbeats (atrial fibrillation).⁶⁵

Xenical

The more popular diet drug today, Xenical, does not work by affecting serotonin levels like the fenfluramines.⁶⁶ Xenical works by preventing absorption of fat by the body, and uncomfortable stomach pains caused by eating fatty foods while on Xenical can work to ‘train’ patients to cut their fat intake. Because

⁶²The literature that accompanied fen-phen also included this guideline of above 30 BMI. See Interview with Dr. Tori Marnell (March 18, 2000).

⁶³Heart Information Network, *Anti-Obesity Drug Sibutramine Approved by FDA – Not Recommended for Heart Patients*, HEART INFORMATION NETWORK WEBSITE, Nov. 1997, available online at www.heartinfo.org. See also *FDA Talk Paper, FDA Approves Sibutramine to Treat Obesity*, USA TODAY, Nov. 24, 1997; Damaris Christensen, *FDA Approves New Obesity Alternative*, MEDICAL TRIBUNE NEWS SERVICE, Nov. 25, 1997; and *FDA Approves New Diet Drug*, REUTERS HEALTH INFORMATION SERVICES, INC., Nov. 25, 1997.

⁶⁴See Heart Information Network, *Anti-Obesity Drug Sibutramine Approved by FDA – Not Recommended for Heart Patients*, HEART INFORMATION NETWORK WEBSITE, Nov. 1997, available online at www.heartinfo.org.

⁶⁵See American Heart Association, *AHA Urges Caution on New Diet Drug (NR 97-4832 Statement/Meridia)*, AMERICAN HEART ASSOCIATION MEDIA ADVISORY, Dallas, Texas, Nov. 1998.

⁶⁶See Interview with Dr. Tori Marnell (March 18, 2000).

Xenical does not work like the fenfluramines, it is significantly more popular than Meridia as a weight loss drug today in light of the PPH and valvular heart disease scares associated with the fenfluramines. Some patients are not as enthusiastic about Xenical as they were about fen-phen because of its unpleasant effects on the stomach when patients eat fatty foods. However, in light of Meridia's similarities to Redux and Pondimin in terms of affecting serotonin, Xenical is currently the more popular diet drug. Doctors have had good results with Xenical and it has not produced any seriously harmful side effects at the present time.⁶⁷

“Phen-Pro” – Prozac and Phentermine

Although there have been no studies on the use of Prozac and other anti-depressants in conjunction with phentermine in an attempt to recreate the fen-phen weight loss phenomenon, some doctors have been prescribing this combination using Prozac and its close relatives to mimic the use of the fenfluramines in a “new” fen-phen cocktail.⁶⁸ After the FDA had already warned of the dangers of long-term use of the fen-phen combination but before Redux and Pondimin were pulled from the market, “a spokesperson for the Nutri-System Weight Loss Centers announced that the company would discontinue its use of the appetite suppressant drugs [fenfluramine and dexfenfluramine] in the treatment of obesity. Instead, phentermine and the anti-depressant Prozac will be prescribed at the weight loss centers. This combination is known as phen-pro.”⁶⁹ Despite use of this combination, the FDA has not established that the phen-pro combination is safe and effective. On the FDA website appears the question “[c]an selective serotonin reuptake inhibitor (SSRI) antidepressants such as Prozac, Zoloft, Luvox and Paxil be substituted for fenfluramine in

⁶⁷See *id.*

⁶⁸Eli Lilly has come out against the use of Prozac in combination with phentermine. The manufacturers of Ionamin (phentermine) have also sent letters to physicians stating that their product should not be combined. See Ben Krentzman, M.D., *What About Phen-Pro?*, available online at <http://www.loop.com/~bkrentzman/editorials/morefaqs.htm>.

⁶⁹Heart Information Network, *Weight Loss Center Responds to New Warnings About Fen-Phen*, HEART INFORMATION NETWORK WEBSITE, available online at www.heartinfo.org. See also *Nutri-System is Dropping Fen-Phen Drug*, THE NEW YORK TIMES, Sept. 4, 1997.

the fen-phen combination?”, and the FDA responded, “FDA has not reviewed the safety or efficacy of such combinations and has not approved their use.”⁷⁰ And while the SSRI drugs are similar to the fenfluramines in that they affect “serotonin metabolism,... [they] have somewhat different activity than fenfluramine and dexfenfluramine. No currently available weight-loss drugs have been studied adequately in combinations to permit a recommendation by FDA for combined use.”⁷¹

HEALTH PROBLEMS ASSOCIATED WITH THE FEN-PHEN COMBINATION

There are two major health problems currently allegedly associated with use of the fenfluramines. The first is vascular heart disease, which is at issue in the proposed class action Settlement Agreement with American Home Products. The Settlement Agreement covers all valvular heart disease claims by fen-phen plaintiffs. The fenfluramines-vascular heart disease connection was unknown at the time fen-phen began to be used on a widespread basis, and it was discovered by Mayo Clinic doctors in 1997.⁷²

⁷⁰Note: The FDA did not per se approve the use of fenfluramine/dexfenfluramine and phentermine together either. The use of fen-phen for extended periods of time was an off-label use of drugs that were approved for single use for short periods. Off-label use is not illegal and is a common practice. Thus forth, absence of FDA approval of use of SSRI antidepressants with phentermine would not make it an illegal drug, rather it would be an off-label use akin to the use of aspirin for blood thinning as opposed to pain relief. Many oncology and AIDS drugs are prescribed for off-label use. See Steven R. Salbu, *Off-Label Use, Prescription, and Marketing of FDA-Approved Drugs: An Assessment of Legislative and Regulatory Policy*, 51 FLA L. REV 181 (1999).

⁷¹U.S. Food and Drug Administration Center for Drug Evaluation and Research (CDER), *Questions and Answers about Withdrawal of Fenfluramine (Pondimin) and Dexfenfluramine (Redux)*, CDER WEBSITE, available online at www.fda.gov/cder/news/phen/fenphenqa2.htm.

⁷²Note: In response to a question on why the valve disease problem was not discovered earlier, the FDA responded by stating: “The type of valve disease that FDA believes may be associated with fenfluramine and dexfenfluramine is an extremely unusual type of drug reaction. Because valve disease is not usually associated with drug use, it is not normally screened for in human clinical testing of drugs. Since valvular heart disease is not screened for in clinical trials, it would usually not be detected unless patients developed symptoms. No cases were detected in 500 patients followed for one year in a clinical trial of dexfenfluramine. Furthermore, asymptomatic heart valve disease (heart valve disease without symptoms) would not likely be detected in patients taking the drugs as part of a weight loss program. The number of patients who have been reported to have symptoms of heart valve disease associated with recent exposure to the [diet] drugs has been very small, compared to the number of recent prescriptions, although there may be a delay in the development of symptoms. And even in symptomatic patients, the link between the symptoms and drug use may not be obvious because such a reaction is not common. These factors may explain why this problem was not discovered earlier.” U.S. Food and Drug Administration Center for Drug Evaluation and Research (CDER), *Questions and Answers about Withdrawal of Fenfluramine (Pondimin) and Dexfenfluramine (Redux)*,

The second major health problem, which is extremely severe, is PPH. The increased risk of PPH with drugs like the fenfluramines was known at the time fen-phen became extremely popular. An increased risk of PPH had been identified in European studies and the level was increased by the multinational IPPHS done in 1996, shortly after dexfenfluramine's FDA approval. PPH claims are not included in the proposed class action Settlement Agreement, and plaintiffs with PPH claims can pursue them in court even if they do not opt out of the Settlement Agreement.⁷³ The existence of an increased PPH risk was known and identified during the entire fen-phen craze, and the increased risk found with the IPPHS was eventually reflected in new FDA mandated labeling on the fenfluramines. Thus forth, patients were aware of the PPH risk when they took the diet drugs and presumably patients and doctors assessed that risk in making the decision whether or not to take fen-phen.⁷⁴ On the other hand, valvular heart disease was not a known risk and did not figure per-se into the risk benefit calculus of fen-phen patients and their prescribing doctors.⁷⁵

There is also a third medical problem that may or may not be linked to fen-phen use, which is serotonin neurotoxicity that may affect brain functions. Because the fenfluramines affect brain serotonin levels, several animal studies have found adverse neurotoxic affects resulting from long-term fenfluramines use. No human studies are available, and the proposed class action Settlement Agreement clearly precludes all present and future neurotoxicity claims for any plaintiffs who do not opt-out.

CDER WEBSITE, available online at www.fda.gov/cder/news/phen/fenphenqa2.htm

⁷³Pursuant to certain limited restrictions set forth in the Settlement Agreement. Certain PPH claims may be classified as "Settled Claims".

⁷⁴However, in many cases that risk was not fully processed by the patients and many doctors did not have careful consultations with patients to assess the PPH risk. See Interview with Dr. Tori Marnell (March 18, 2000).

⁷⁵There have been allegations that the valvular heart damage link with anorectic drugs was known throughout most of the fen-phen craze. In 1994, Dr. Marianne Wealenko, a cardiologist in Belgium, reported finding valvular regurgitation in 7 of her patients, all of whom had taken anorectic diet pills. She informed the manufacturer and spoke about the unusual link between leaky valves and anorectic drugs at several obesity conferences. See Vivi Vanderslice, *Viability of a Nationwide Fen-Phen/Redux Class Action Lawsuit in Light of Amchem v. Windsor*, 35 CAL. W. L. REV. 199, 201, (1998).

Valvular Problems

Discovery of Valvular Problems in Fen-Phen Users and FDA Action

Valvular heart disease occurs when the heart valve is damaged and cannot open properly or does not close properly, which causes blood to leak backwards.⁷⁶ Mayo Clinic doctors discovered the link between fen-phen and valvular heart disease in 1997.⁷⁷

Dr. Heidi Connolly was the primary author of the clinical observation of valvular heart disease that was publicly reported in the *New England Journal of Medicine* on July 8, 1997. It included 24 cases of valvular heart disease in women who had been treated with fenfluramine and phentermine. The report prompted an FDA Public Health Advisory and the eventual removal of fenfluramine and dexfenfluramine from the U.S. market.⁷⁸ By September 30, 1997 the “FDA had received 144 individual, provider initiated reports involving fenfluramine or dexfenfluramine, with or without phentermine, in association with valvulopathy (this total included the 24 publicly reported cases).”⁷⁹

The initial problem was identified through Mayo Clinic doctors coming into contact with a series of patients [24 in total] who had valvular disease and who had also been taking fen-phen. The first patient they saw had valve surgery at the Mayo Clinic and developed a second valve problem following the surgery. Dr. Connolly and her colleagues noted that he did not have an underlying cause for valvular disease such as

⁷⁶See American Heart Association, *AHA Urges Caution on New Diet Drug (NR 97-4832 Statement/Meridia)*, AMERICAN HEART ASSOCIATION MEDIA ADVISORY, Dallas, Texas, Nov. 1998.

⁷⁷See Centers for Disease Control, U.S. Department of Health and Human Services Interim Public Health Recommendations, *Cardiac Valvulopathy Associated with Exposure to Fenfluramine or Dexfenfluramine*, CDC MORBIDITY AND MORTALITY WEEKLY REPORT 1061 Vol. 46, No. 45, Nov. 14, 1997.

⁷⁸See *id.*

⁷⁹*Id.*

Note: According to the CDC Report, out of those 132 spontaneous reports, 113 met the case definition of fenfluramine or dexfenfluramine associated cardiac valvulopathy, which is defined as “documented aortic regurgitation of mild or greater severity and/or mitral regurgitation of moderate or greater severity after exposure to these drugs”. *Id.* Of the 113 cases, 111 occurred among women, the median patient age was 44, 2% used fenfluramine alone, 14% used dexfenfluramine alone, 79% used fenfluramine/dexfenfluramine and phentermine, and 5% used a combination of dexfenfluramine, fenfluramine, and phentermine. The median duration of drug use was 9 months, 77% of the cases were symptomatic, 24% of patients required valve replacement surgery, and 3 of those patients died after the surgery. See *id.*

carcinoid⁸⁰ cancer or having taken the migraine medications ergotamine or methysergide. In January of 1997 Mayo Clinic doctors saw another patient with valvular disease, and additional patients were then referred to the Mayo Clinic by Dr. Jack Crary, a cardiologist from Fargo, North Dakota. The 24 patients had been taking fen-phen for an average of 12 months and their average age was 43. Dr. Connolly noted that it was unusual for patients of that age to have such a high incidence of valvular disease, and none of the 24 patients had any previously known cardiac or pulmonary disease, aside from high blood pressure. Eight of the women also had newly documented PPH. Dr. Connolly noted that the pulmonary valve was the least commonly affected, and that the damaged valves were identical to the valves seen in patients with carcinoid heart disease (cancer) and in patients with valve damage resulting from use of the migraine medications methysergide and ergotamine. The damaged valves in the fen-phen users were different from valvular damage resulting from rheumatic heart disease and infection. The damaged valves were thickened and did not function normally. Fibrous material was layered on the valve leaflet and created a glistening white appearance like that of patients with ergotamine induced or carcinoid induced valvular damage.⁸¹ Dr. Connolly noted that “in carcinoid syndrome, patients with high circulating levels of serotonin are more likely to have valve disease than those with lower levels. In ergotamine-induced valve disease, it is suggested that valve injury is due to the fact that ergotamine and serotonin have a similar chemical structure.”⁸² Dr. Connolly followed up on the connection between serotonin and fen-phen associated valvular heart disease in stating, “[w]e know that fenfluramine – the ‘fen’ in fen-phen – alters serotonin metabolism by promoting its release and decreasing its reuptake in the brain. And we know that phentermine – the ‘phen’ in fen-phen – may have some effect on serotonin metabolism in the lung. We postulate that there may be valve injury by the alteration of serotonin

⁸⁰Carcinoid tumors secrete a large amount of serotonin. “It is the effects of serotonin that are believed to cause severe regurgitant cardiac valvular disease and pulmonary hypertension. Serotonin is secreted by nuclei that originate in the brain stem. It acts as an inhibitor of pain pathways in the spinal cord and is believed to control the mood of the person and induce normal sleep.” Evans and Kerner, *A Primer on Fen-Phen Litigation: Allegations and Defenses*, 65 DEF. COUNS. J. at 353.

⁸¹See Mayo Clinic Health Oasis, *Heart Valve Disease and Fen-Phen: An Interview With Mayo Cardiologist Heidi Connolly, M.D.*, MAYO CLINIC WEBSITE, July 8, 1997, available online at www.mayohealth.org/mayo/9707/htm/fen.1sb.htm.

⁸²Id.

metabolism in the body. We do know from our experience with other patient groups – the carcinoid patients and the patients with ergotamine-induced valve disease – that serotonin or serotonin-like structures appear to be related to valve disease. Pathologically, the carcinoid and ergotamine-induced valve disease is identical to the findings in the 24 women reported.”⁸³

Dr. Connolly stated that the Mayo Clinic observation suggests that:

there appears to be an association between this combination of medications [fen-phen] and heart disease, but we can't prove it based on current information... we suspect there is an association between fen-phen and valve disease, but we don't know who taking this combination of medications is at risk. We don't know how long the medications need to be taken before patients might develop this problem. And we don't know whether the valve disorder is reversible. Of the 24 women we've identified who had valve disease, eight also had moderate or severe pulmonary hypertension, which had not been previously identified. The cluster of unusual cases of valve disease in fen-phen users suggested that there might be an association between fen-phen use and valve disease.⁸⁴

The Mayo Clinic doctors reported their findings in the *New England Journal of Medicine*, which began the series of events that led to the removal of fenfluramine and dexfenfluramine from the market. The *New England Journal of Medicine* report concluded by stating:

significant de-novo left-sided regurgitant valvular heart disease in a population less than 50 years old is rare. Thus, the association of valvular regurgitation with fenfluramine-phentermine is not likely due to chance. Moreover, the unusual echocardiographic morphology of the lesions further diminishes the likelihood of a coincidental observation. These cases should raise concern that this combination of appetite suppressants has important implications regarding valvular heart disease. Prospective studies of this association will be required to validate the possibility that this combination of medications may cause valvular heart disease. The mechanism of valve injury and the frequency of the association have yet to be determined. Candidates for fenfluramine-phentermine therapy should be informed about serious potential adverse effects, including pulmonary hypertension and valvular heart disease.⁸⁵

In 1997, after the Mayo Clinic report was published, the FDA conducted a study in five U.S. areas (Florida, Minnesota, Wisconsin, Indiana, and Pennsylvania) and found a 32.8% (95% Confidence-Interval) presence of lesions causing FDA Positive valvular regurgitation, significantly higher than is to be expected amongst

⁸³Id.

the general population.⁸⁶ This study contributed to the FDA's series of actions leading to the fenfluramine and dexfenfluramine withdrawal from the U.S. market.

FDA Actions

On July 8, 1997, the FDA issued a Health Advisory warning over 700,000 health care professionals and institutions of the valvular heart disease concern associated with fen-phen. The FDA stated that “[p]resently there is no conclusive evidence establishing a causal relationship between these two products and valvular heart disease. However, given the seriousness of the reported valvular disease and its rare occurrence in otherwise healthy obese women in this age range, we believe that patients and health care professionals should be notified of this information.”⁸⁷ The advisory summarized the reports of valvular heart disease as of July 8, 1997, at which time there were 33 reports of unusual significant valvular regurgitation of the mitral and aortal valves. The 33 patients were all U.S. women between 35 and 72, with a mean age of 43.4, who had taken fen-phen for an average of 10 months, with a range from 1 to 16 months. Approximately half of those 33 patients also had pulmonary hypertension. Surgery was required in six of the patients as of July 8, 1997, and the surgery showed valves similar to patients who had carcinoid syndrome or who had taken the migraine drug ergotamine. The FDA indicated that the course of the valvular heart disease after the

⁸⁶See Centers for Disease Control, U.S. Department of Health and Human Services Interim Public Health Recommendations, *Cardiac Valvulopathy Associated with Exposure to Fenfluramine or Dexfenfluramine*, CDC MORBIDITY AND MORTALITY WEEKLY REPORT 1061 Vol. 46, No. 45, Nov. 14, 1997.

See also *Questions and Answers Concerning the Department of Health and Human Services (DHHS) Interim Recommendations For Patients Who Have Taken Either Fenfluramine or Dexfenfluramine*, available online at www.fda.gov/cder/news/phenqa1111397.htm (noting the following: In addition to the FDA data supporting the link between the fenfluramines and FDA Positive regurgitation, Dr. Mehmood Kahn performed a control study in Minneapolis shortly after the July 1997 announcement about the fen-phen associated valvular heart disease. Dr. Kahn's data found that approximately 25% of the 226 fenfluramine/dexfenfluramine users in his study had aortal regurgitation of mild or greater severity, compared with 1% mild or greater aortal regurgitation in the 81 control patients who did not take fenfluramine or dexfenfluramine).

⁸⁷U.S. Department of Health and Human Services, *Reports of Valvular Heart Disease In Patients Receiving Concomitant Fenfluramine and Phentermine*, FDA PUBLIC HEALTH ADVISORY DEAR HEALTH PROFESSIONAL LETTER, July 8, 1997.

patients stopped taking fen-phen was unknown at the time.⁸⁸ In the advisory the FDA told all health care professionals that “the safety and effectiveness of the use of fenfluramine and phentermine in combination have not been established and that serious concerns about the safety of such combined use have been raised. Until further information is available, the FDA recommends that, if practitioners choose to use these products in a manner different from the approved labeling (i.e., in combination with each other, or for durations or at dosages different than those approved), they should follow patients closely with thorough cardiac evaluations, and if signs and symptoms of cardiopulmonary disease develop, further cardiac evaluation should be pursued.”⁸⁹ The health advisory also asked all health care professionals to report any abnormalities in fen-phen patients to FDA’s MedWatch Program⁹⁰ or to the drug manufacturers.⁹¹ The FDA indicated a special interest in the dosage and duration of therapy, other medications taken by the patient, a history of pre-existent cardiac disease, and the degree of obesity of the patient when they began taking fen-phen⁹² By August 22, 1997, the FDA had received reports of 82 cases of valvular heart disease in patients who ingested fen-phen. Sixteen of those 82 patients required surgery to repair their heart valves, and at least one patient died following surgery.⁹³

⁸⁸See *id.*

⁸⁹U.S. Department of Health and Human Services, *Reports of Valvular Heart Disease In Patients Receiving Concomitant Fenfluramine and Phentermine*, FDA PUBLIC HEALTH ADVISORY DEAR HEALTH PROFESSIONAL LETTER, July 8, 1997.

⁹⁰The MedWatch System run by the FDA conducts ‘passive surveillance’, relying on health care professionals to report details of serious adverse reactions to the FDA. In the wake of the fen-phen situation it has been criticized for not identifying the problem before 18 million fen-phen prescriptions had been written. Raymond Woosley, a professor of pharmacology at Georgetown University, said that MedWatch is the “best voluntary system in the world, but... it’s not enough. In France, they have 30 centers around the country with people trained to look for adverse drug effects. They go into hospitals, look at charts, talk to patients, talk to doctors, fill out forms and enter them into a database. We don’t have one site like that”. Steve Sternberg, *Lawsuits: Drug Development’s Side Effects*, USA TODAY, Jan 12, 2000, Health Section. In response to Woosley’s criticisms of MedWatch and the French comparison, “FDA Deputy director Peter Honig says the agency plans to graft a similar program onto MedWatch. In the new program, trained staff members would actively seek out unexpected drug reactions. Honig says a mandatory reporting system would generate too much information for the agency to handle efficiently.” *Id.*

⁹¹See U.S. Department of Health and Human Services, *Reports of Valvular Heart Disease In Patients Receiving Concomitant Fenfluramine and Phentermine*, FDA PUBLIC HEALTH ADVISORY DEAR HEALTH PROFESSIONAL LETTER, July 8, 1997.

⁹²After the July warnings went out, reduced sales of fenfluramine and phentermine suggested a 40% decline in their combination use in the United States. After the FDA warned of the dangers, the Jenny Craig diet center recommended that its doctors no longer prescribe fen-phen until further studies determined whether long-term use of the drug combination is safe. The Nutri-System Weight Loss Centers also ceased prescribing fen-phen following the FDA notice. See Heart Information Network, *FDA Warns of Potential Danger of Fen-Phen Diet Drugs*, HEART INFORMATION NETWORK WEBSITE, available online at www.heartinfo.org; See also Heart Information Network, *Weight Loss Center Responds to New Warnings about Fen-Phen*, HEART INFORMATION NETWORK WEBSITE, available online at www.heartinfo.org.

⁹³See Fen-Phen Update, available online at www.fda.gov/cder/fenphenupdate.htm/.

On August 28, 1997, the FDA requested all manufacturers of phentermine, fenfluramine, and dexfenfluramine to stress the potential risk of cardiac valvular disease in a black box warning in the drugs' labeling and in patient package inserts. The FDA required these black box warnings to ensure that the potential serious valvular heart disease risks associated with combination fen-phen long-term use would be known to prescribers and patients. The new safety information was to be displayed prominently in a black box located at the beginning of the label. The warning was to state that the safety had not been established for combined fen-phen use or for the use of phentermine, fenfluramine, or dexfenfluramine for longer than the short-term use approved by the FDA. The FDA also reiterated that the drugs should only be given to people with serious obesity problems, not for cosmetic weight loss purposes.⁹⁴

On September 8, 1997, Florida temporarily banned prescriptions of combination fen-phen. The Board of Medicine in Florida voted to suspend fen-phen use pending the establishment of strict rules regulating the drug combination. Following the Board of Medicine decision, Florida doctors were prohibited from prescribing the combination fen-phen to new patients and patients taking fen-phen at the time of the decision had to be weaned off the drug combination within 30 days.⁹⁵

On September 15, 1997, the FDA asked manufacturers to voluntarily withdraw dexfenfluramine and fenfluramine from the market. The manufacturers agreed to voluntarily withdraw the drugs.⁹⁶ The FDA did not request phentermine's withdrawal. The FDA recommended that anyone using fenfluramine or dexfenfluramine either alone or with phentermine cease taking the drugs either immediately or by quickly tapering off their use.⁹⁷ The FDA took this action in response to "new findings from doctors who have evaluated

⁹⁴See Fen-Phen Update, available online at www.fda.gov/cder/fenphenupdate.htm/.

⁹⁵See *Florida Temporarily Bans Prescriptions on Fen-Phen*, THE WALL STREET JOURNAL INTERACTIVE EDITION, Sept 8, 1997.

⁹⁶In response to the U.S. withdrawal, the French company Servier, which sold fenfluramine and dexfenfluramine globally, withdrew dexfenfluramine and fenfluramine abroad. It was estimated that 60 million people had taken the drugs throughout the world. See Lance and Tortorich, *Popular Diet Drugs Pulled From Market*, 9 LOY. CONSUMER L. REP. at 296.

⁹⁷Dr. Heidi Connolly of the Mayo Clinic stated that "Depression has been reported in some patients stopping the medications suddenly. So particularly for patients on a high dose, we would encourage physician consultation and tapering therapy if the medications are to be discontinued." Mayo Clinic Health Oasis, *Heart Valve Disease and Fen-Phen: An Interview With Mayo Cardiologist Heidi Connolly, M.D.*, MAYO CLINIC WEBSITE, July 8, 1997, available online at

patients taking these two drugs with echocardiograms... These findings indicate that approximately 30% of patients who were evaluated had abnormal echocardiograms, even though they had no symptoms. This is a much higher than expected percentage of abnormal test results... [t]hese new findings suggest fenfluramine and dexfenfluramine are the likely cause of heart valve problems of the type that prompted FDA's two earlier warnings concerning fen-phen."⁹⁸ Michael A. Friednam, M.D., Lead Deputy Commissioner of the FDA, stated that "[t]hese findings call for prompt action... fenfluramine and the chemically closely related dexfenfluramine present an unacceptable risk at this time to patients who take them."⁹⁹

At that time the FDA also requested all health care professionals to report any valvular heart disease or PPH cases to the FDA's MedWatch Program or to the fenfluramine/dexfenfluramine manufacturers. The information the FDA requested included (1) The patients' age, sex, weight, height, and blood pressure; (2) The daily dosage of fenfluramine, dexfenfluramine, phentermine; (3) The duration of use of appetite suppressant drugs; (4) The interval of time since stopping the use of the appetite suppressant drugs and the time of echocardiography; (5) Clinical history of the patient, including the presence or absence of an audible cardiac heart murmur; (6) Echocardiogram results, including the presence of regurgitation at each valve, the severity grading of regurgitation, and the presence or absence of pulmonary hypertension and estimated pulmonary artery pressure; and (7) The use by the patient of any medications other than fenfluramine, dexfenfluramine, or phentermine.¹⁰⁰ The FDA continues to receive reports of valvular heart disease in fen-phen patients.¹⁰¹

www.mayohealth.org/mayo/9707/htm/fen.lsb.htm.

⁹⁸U.S. Food and Drug Administration, *For Immediate Release - FDA Announces Withdrawal of Fenfluramine and Dexfenfluramine (Fen-Phen) P97-32*, FDA WEBSITE, Sept. 15, 1997, available online at www.fda.gov/cder/news/fenphenpr81597.htm.

⁹⁹*Id.*

¹⁰⁰*See* U.S. Food and Drug Administration, *Information Requested for MedWatch Reports of Valvular Dysfunction with Use of Appetite Suppressant Drugs*, FDA CDER WEBSITE, Nov. 13, 1997, available online at www.fda.gov/cder/inforeqvalv.htm.

¹⁰¹*See* U.S. Food and Drug Administration, *For Immediate Release - FDA Announces Withdrawal of Fenfluramine and Dexfenfluramine (Fen-Phen) P97-32*, FDA WEBSITE, Sept. 15, 1997, available online at www.fda.gov/cder/news/fenphenpr81597.htm.

Discussion of the Medical Aspects of the Vascular Heart Disease

Heart valve abnormalities have appeared in diet drug users primarily in the valves on the left side of the heart. Lesions have developed in both the aortic valves and the mitral valves. The aortic valve allows blood to flow out of the heart, and the mitral valve is the valve between the upper and lower chambers of the heart. The upper chamber of the heart takes in blood from the lungs and the lower chamber pumps the blood to the rest of the body. The lesions that have formed on the valves of the diet drug users cause blood to flow backwards instead of forwards, which is called “regurgitation”.¹⁰² Regurgitation can be either (1) trace or physiologic; (2) mild; (3) moderate; or (4) severe. Mitral valve and aortic valve regurgitation that is trace or physiologic is extremely common among the general population and is not considered abnormal by the FDA. The FDA also considers mild mitral valve regurgitation to be common in the general population and not abnormal. However, aortic valve regurgitation that is mild, moderate, or severe is considered abnormal and may be ‘medically significant’. Mitral valve regurgitation that is moderate or severe is also considered abnormal and may also be ‘medically significant’. Mild, moderate or severe aortic regurgitation and moderate or severe mitral regurgitation are considered “FDA Positive Regurgitation”, and the valvular lesions that cause FDA Positive Regurgitation are classified as “valvular heart disease”.¹⁰³ The FDA reported that less than 5% of the general U.S. adult population has significant valvular regurgitation that would be classified as FDA Positive, but in September of 1997 the FDA found that out of 291 people who used fen-phen, approximately 30% had FDA Positive regurgitation as identified by echocardiogram.¹⁰⁴ Dr. Connolly of the Mayo Clinic

¹⁰²Janet Woodcock, Director of the FDA’s Center for Drug Evaluation and Research, said that “[heart] valves are a lot like valves in a pump or a car. The flow is supposed to go forward and not backward. If your valves are affected there can be backward leakage... it means the heart has to pump harder because it is less efficient”. Maggie Fox, *Fen-Phen Pulled!*, WASHINGTON (REUTERS), Sept. 15, 1997, Health and Science.

¹⁰³*Important Notice on the Proposed Class Action Settlement/A Class Member’s Guide to the Diet Drug Litigation Settlement*, p. 5

¹⁰⁴See Heart Information Network, *Government Recommends Exams for Former Users of Diet Drugs*, HEART INFORMATION NETWORK WEBSITE, Nov. 1997, available online at www.heartinfo.org.

stated that “when severe regurgitation is present, the patient may have a lack of energy, shortness of breath, and eventually, congestive heart failure.”¹⁰⁵

Valvular heart disease may have no visible symptoms. It is possible that the patient’s doctor may hear a new heart murmur, or the physician may detect the valvular disease with an echocardiogram. It is often difficult for doctors to hear heart murmurs, especially on obese people who may make up a significant portion of fen-phen users.¹⁰⁶ An echocardiogram is a painless test that uses ultrasound technology to take a ‘moving picture’ of the heart, and it allows the doctor to see any valvular lesions and determine if the patient suffers from mitral or aortal regurgitation. If the patient has serious valvular heart disease, the patient may experience some outward symptoms like shortness of breath, edema (swelling of the legs), chest pains, fainting, and excessive tiredness.¹⁰⁷

Researchers are not certain of the health implications of valvular heart disease. At a lecture on fen-phen valvulopathy, Dr. Connolly concluded by stating “there is actually probably more that we don’t know about this entity... than that we do know. We don’t really know the natural history. We don’t know who is at risk for developing valve disease, the mechanism of valve injury, nor the public health impact. We do know that up to 30% of patients who have taken diet drugs may develop valve disease and it is estimated that millions of people have developed valve disease from diet drugs. From personal communication with the FDA, they believe this is one of the largest adverse drug reactions they have ever dealt with.”¹⁰⁸

What is known at the present time is that valvular heart disease causes increased vulnerability to an infection

¹⁰⁵Mayo Clinic Health Oasis, *Heart Valve Disease and Fen-Phen: An Interview With Mayo Cardiologist Heidi Connolly, M.D.*, MAYO CLINIC WEBSITE, July 8, 1997, available online at www.mayohealth.org/mayo/9707/htm/fen.lsb.htm.

¹⁰⁶See *Important Notice on the Proposed Class Action Settlement/A Class Member’s Guide to the Diet Drug Litigation Settlement*, p. 6

¹⁰⁷See Food and Drug Administration Center for Drug Evaluation and Research (CDER), *Questions and Answers about Withdrawal of Fenfluramine (Pondimin) and Dexfenfluramine (Redux)*, CDER WEBSITE, online at www.fda.gov/cder/news/phen/fenphenqa2.htm.

¹⁰⁸*Fen-Phen Valvulopathy Presented by Heidi M. Connolly, M.D., F.A.C.C.*, CASES IN ECHOCARDIOGRAPHY, Directed by Rick A. Nishimura, M.D., F.A.C.C. and Fletcher A. Miller, Jr., M.D., F.A.C.C., Edited Transcript of a Talk Presented by Dr. Connolly at the Heart House Learning Center, (1999).

of the heart when patients undergo certain types of medical or dental procedures.¹⁰⁹ “Many doctors believe that individuals who have FDA Positive valvular regurgitation may be at risk for developing an infection in their hearts if bacteria enter the bloodstream during routine dental hygiene or surgery. Therefore, current medical practice is to recommend that individuals with VHD receive antibiotics when they have their teeth cleaned or undergo some kinds of surgery.”¹¹⁰

If the valvular regurgitation is severe, it will need to be treated so that it does not cause heart damage.

Treatment options may include medication or valve replacement through open heart surgery.¹¹¹

¹⁰⁹Some reports have also identified other problems associated with fen-phen use. One woman asserted that her son suffered heart damage as a result of her ingestion of fen-phen during pregnancy. Dawn Serina’s son Nicholas suffers from blue baby syndrome, which caused her to sue Nutri-System, American Home Products, and several drug stores. Nutri-System said that clients sign a health release and are pre-informed about all medications they receive from Nutri-System centers. Serina’s attorney claims that Nutri-System downplayed fen-phen’s side effects. Two other women also have complained that their babies were born with health problems after they took Redux and/or Pondimin while pregnant. A spokesperson for the FDA says that the connection between Redux and/or Pondimin and birth defects has not been proven, although the damage to the babies could have been caused by the drugs. In response to Serina’s complaint the FDA asked all parents who think that their children may have fen-phen related health problems to have their doctors contact the FDA.

See CNN News Network Fen-Phen Article, October 10, 1997, available online at www.cnn.com/HEALTH/9710/10/fen-phen.babies/.

Also, there have been some reports of fen-phen related problems during surgery. Anesthesiologists believe that fenfluramine may reduce the body’s amount of norepinephrine, which lowers blood pressure. A patient can have a heart or a stroke if blood pressure becomes too low for too long a period of time. Some fen-phen patients had experienced extremely low blood pressure during surgery, which can be a life-threatening situation. In Tyler, Texas, in two surgeries on fen-phen patients, anesthesiologists had to inject norepinephrine to increase the patients’ blood pressure, which is a rare occurrence. Tyler hospitals thereafter instituted a rule that in all non-emergency situations, patients had to be off fen-phen for two weeks before surgery. Numerous other hospitals followed suit, including Cedars-Sinai in Los Angeles. There were been problems with patients failing to admit that they were taking fen-phen. Wyeth-Ayerst and the FDA identified one case of a 19-year-old fen-phen patient who went into cardiac arrest during anesthesia. In addition, the American Society of Anesthesiologists issued a statement saying its members were concerned about reports that some patients taking fen-phen were experiencing ‘adverse and potentially deadly reactions while under general anesthesia.’ However, there is no definitive proof that fen-phen caused dramatic blood pressure decreases, and most fen-phen patients have not had problems during surgery. And many anesthesiologists did not see any reason to delay operations, although others were more cautious and preferred not to take any chances.

See Elizabeth Cohen, CNN News Network Article, *Diet Drug Combo May Cause Problems During Surgery*, Nov. 4, 1996, available online at www.cnn.com/HEALTH/9611/04/fen-phen.surgery/

¹¹⁰*Important Notice on the Proposed Class Action Settlement/A Class Member’s Guide to the Diet Drug Litigation Settlement*, p. 6.

Note: The CDC Morbidity and Mortality Weekly Report stated that the FDA was aware of at least one person with FDA Positive regurgitation who “presented with fever and signs and symptoms of cardiac failure and, on echocardiogram, had both aortic regurgitation, mitral regurgitation, and a large endocarditic vegetation; blood cultures from this patient were positive for streptococci.” Centers for Disease Control, U.S. Department of Health and Human Services Interim Public Health Recommendations, *Cardiac Valvulopathy Associated with Exposure to Fenfluramine or Dexfenfluramine*, CDC MORBIDITY AND MORTALITY WEEKLY REPORT 1061 Vol. 46, No. 45, Nov. 14, 1997.

¹¹¹See *Important Notice on the Proposed Class Action Settlement/A Class Member’s Guide to the Diet Drug Litigation Settlement*, p. 6.

At the present time, it is not known for certain whether the valvular heart problems will improve as time elapses since the patients ingested the diet drugs. (See section below on Recent Studies). Dr. Connolly stated that there have been anecdotal reports of regression of valvular heart disease after patients stopped taking Redux or Pondimin.¹¹² In response to the question on reversibility of damage, the FDA responded that “One report has been submitted to FDA in which the valve disease appeared to improve. However, we encourage those people who have taken fenfluramine or dexfenfluramine to contact their physician and discuss the appropriate follow up, even after stopping their medicine. The full medical implications of these findings are not known at this time, especially as they relate to the asymptomatic valvular changes. The FDA and other governmental agencies, the manufacturers, and medical researchers will aggressively follow this concern and keep patients and health care providers informed of what is learned about the natural history of the valvular disease caused by these medications.”¹¹³ The Official Court Notice of the Settlement Agreement states that “[p]resently, there is little scientific evidence on whether the type of Valvular Heart Disease that has been linked to diet drug use is progressive in nature. However, many respected doctors and researchers have concluded that certain other types of Valvular Heart Disease (unrelated to diet drug use) are progressive in nature – that is, that mild to moderate regurgitation can progress to more severe levels of regurgitation over time. The American Heart Association and the American College of Cardiology recommend that individuals with FDA Positive regurgitation see their doctors at least once a year for evaluation.”¹¹⁴

¹¹²See *Fen-Phen Valvulopathy Presented by Heidi M. Connolly, M.D., F.A.C.C.*, CASES IN ECHOCARDIOGRAPHY, Directed by Rick A. Nishimura, M.D., F.A.C.C. and Fletcher A. Miller, Jr., M.D., F.A.C.C., Edited Transcript of a Talk Presented by Dr. Connolly at the Heart House Learning Center, (1999).

¹¹³See U.S. Food and Drug Administration Center for Drug Evaluation and Research (CDER), *Questions and Answers about Withdrawal of Fenfluramine (Pondimin) and Dexfenfluramine (Redux)*, CDER WEBSITE, online at www.fda.gov/cder/news/phen/fenphenqa2.htm

¹¹⁴*Important Notice on the Proposed Class Action Settlement/A Class Member's Guide to the Diet Drug Litigation Settlement*, p. 6.

Recommendations And Guidelines For Valvular Heart Disease Patients

U.S. Department of Health and Human Services Recommendations

The U.S. Department of Health and Human Services (“DHHS”) issued recommendations on November 14, 1997, for those people who were exposed to dexfenfluramine or fenfluramine. The recommendations were developed in a joint effort by the Centers for Disease Control, FDA, the National Institutes of Health, and in consultation with the American Heart Association, the American College of Cardiology, and the American Heart Association. The recommendations are based on data that associates fenfluramine and dexfenfluramine (alone or together with phentermine) with valvular heart disease. DHHS may change the recommendations as more data becomes available.¹¹⁵

DHHS made three recommendations for people exposed to fenfluramine or dexfenfluramine for any length of time, taken alone or with phentermine. These recommendations are: (1) Every one of these people should see a physician to have a complete medical history taken and physical examination performed with particular emphasis on the heart and lungs. This examination is to determine primarily if there are any signs or symptoms of possible heart or lung disease; (2) If the physician finds that heart or lung disease may be present, then these patients should have an echocardiogram to determine if there is any evidence of significant disease of the heart valves.; (3) Even if there is no evidence of heart or lung disease by history or on the physical examination, in one special situation, these patients’ physicians should nonetheless strongly consider having an echocardiogram performed on the patient to determine if there is any evidence or significant disease of the heart valves.¹¹⁶ That situation is IF the patient needs to undergo a medical or dental procedure

¹¹⁵See Centers for Disease Control, U.S. Department of Health and Human Services Interim Public Health Recommendations, *Cardiac Valvulopathy Associated with Exposure to Fenfluramine or Dexfenfluramine*, CDC MORBIDITY AND MORTALITY WEEKLY REPORT 1061, 1065 Vol. 46, No. 45, Nov. 14, 1997.

¹¹⁶See *Questions and Answers Concerning the Department of Health and Human Services (DHHS) Interim Recommendations For Patients Who Have Taken Either Fenfluramine or Dexfenfluramine*, available online at www.fda.gov/cder/news/phenqa1111397.htm.

before which the American Heart Association recommends giving patients with certain valvular disease an antibiotic¹¹⁷ to help prevent an infection of the heart called bacterial endocarditis.¹¹⁸ The reason for the echocardiogram in this situation is to “determine if a person without symptoms nonetheless has disease of the heart valves. If they do have heart valvular disease that needs antibiotic coverage, they need the antibiotic before undergoing a medical or dental procedure that could possibly lead to a heart infection.”¹¹⁹ It is important to note that the proposed Settlement Agreement with American Home Products provides for every patient who ingested fen-phen for 61 or more days to have an echocardiogram, which goes beyond the DHHS recommendations.¹²⁰

¹¹⁷Antibiotics are recommended for the following procedures: Dental – Dental extraction, other peridental procedures including surgery, scaling, root planing, probing, recall maintenance, dental implants, and reimplantation of teeth. Surgical – Surgical procedures that involve the mouth and oral cavity, upper respiratory tract and the gastrointestinal and genitourinary system (including tonsillectomy, biliary tract surgery, and operations involving the intestinal mucosa). Antibiotics are not recommended for the following procedures: Dental – Local anesthetic injection, placement of rubber dams, suture removal, taking of oral impressions, fluoride treatment, and orthodontic appliance adjustment. Surgical – Vaginal hysterectomy, vaginal delivery, cesarean section, cardiac catheterization, balloon angioplasty, implanted pacemakers or defibrillators, and coronary stents. The recommended dosage for antibiotics given to prevent bacterial endocarditis is a 2 gram single dose of amoxicillin with no follow up. Patients who are allergic to amoxicillin should take clarithromycin. See American Heart Association, *Recommendations*, THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION 277:1794-1801; June 11, 1997.

¹¹⁸DHHS defines bacterial endocarditis as “an infection of the tissues that line the heart chambers and cover the heart valves. Endocarditis can be caused by bacteria getting into the blood stream and infecting the heart lining and valve covering as the bacteria-laden blood is circulated through the heart. The body’s own defense systems do not work as well in the heart as they do in other parts of the body. As this type of endocarditis is caused by bacteria, it is called bacterial endocarditis.” *Questions and Answers Concerning the Department of Health and Human Services (DHHS) Interim Recommendations For Patients Who Have Taken Either Fenfluramine or Dexfenfluramine*, available online at www.fda.gov/cder/news/phenqa1111397.htm People with heart valve abnormalities are at an increased risk of endocarditis, which is why they should have antibiotic coverage before certain medical or dental procedures that can cause large amounts of bacteria to enter the bloodstream. The antibiotic is usually given as a single dose by mouth. In an emergency situation where a person who has taken fenfluramine or dexfenfluramine has not had an echocardiogram and they must have a medical or dental procedure that would require antibiotic coverage, the person should take the antibiotics before the procedure and later undergo an echocardiogram to determine if antibiotic coverage will be necessary for future procedures See id.

It should be noted that bacterial endocarditis is a serious infection that has the potential to be fatal. See Heart Information Network, *Government Recommends Exams for Former Users of Diet Drugs*, HEART INFORMATION NETWORK WEBSITE, available online at www.heartinfo.org.

¹¹⁹*Questions and Answers Concerning the Department of Health and Human Services (DHHS) Interim Recommendations For Patients Who Have Taken Either Fenfluramine or Dexfenfluramine*, available online at www.fda.gov/cder/news/phenqa1111397.htm.

¹²⁰See *Important Notice on the Proposed Class Action Settlement/A Class Member’s Guide to the Diet Drug Litigation Settlement*, p. 6.

Note: In the March 18, 2000 interview with Dr. Tori Marnell, I asked her if she thought an echocardiogram was necessary for every patient who had ingested fen-phen for 61 or more days, or if she agreed with the DHHS recommendations only indicating an echocardiogram if the physician finds signs of heart or lung disease. Dr. Marnell said that she agreed with the DHHS recommendations and felt that the medical monitoring provision of the Settlement Agreement was excessive. She said that if she had taken fen-phen she would most likely only get an echocardiogram in accordance with the DHHS recommendations, and that she will do an echocardiogram if the patient wishes to have one done, but otherwise she is working within the DHHS guidelines. See Interview with Dr. Tori Marnell (March 18, 2000).

In its recommendations for people who have been diagnosed with FDA Positive regurgitation, DHHS stressed that “we don’t know yet what happens over time to people with this kind of heart valve problem. Based on data known at present, many of those patients affected don’t have any symptoms of heart disease at present and don’t require any treatment other than careful follow-up by their doctor and pre-treatment with antibiotics before certain medical or dental procedures... The significance of mild heart valve leakage in patients without symptoms is currently unknown.”¹²¹ DHHS recommends that if patients do develop heart disease symptoms, including shortness of breath, heart palpitations, leg swelling, and chest pain, that they go to a cardiologist.¹²²

American Heart Association and American College of Cardiology Guidelines

The DHHS Guidelines were published on November 14, 1997.¹²³ In November of 1998 the American Heart Association (“AHA”) issued new guidelines for diagnosing and treating heart valve disease. The “Guidelines for the Management of Patients with Valvular Heart Disease” were developed by the American College of Cardiology (“ACC”) and the American Heart Association. They cover all heart-valve disorders, not just those associated with fen-phen use. The AHA reported that “heart-valve disease contributed to more than 34,000 deaths and 82,000 hospitalizations in the U.S. in 1995”, and noted that serious valve problems may require surgery for repair or valve replacement. The AHA also noted that the risk of valve problems increases with age, as constant opening and closing throughout a lifetime may lead to eventual problems.¹²⁴

¹²¹*Questions and Answers Concerning the Department of Health and Human Services (DHHS) Interim Recommendations For Patients Who Have Taken Either Fenfluramine or Dexfenfluramine*, available online at www.fda.gov/cder/news/phenqa1111397.htm.

¹²²See *id.*

¹²³See *id.*

¹²⁴Robert O. Bonow et. al., *ACC/AHA Guidelines for the Management of Patients with Valvular Heart Disease*, *ACC/AHA Task Force Report*, CIRCULATION – THE JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY Vol. 32, No. 5 1486 – 1582 (1998).

Robert O. Bonow, M.D., director of the division of cardiology at Northwestern University Medical School in Chicago and chairman of the joint American College of Cardiology/American Heart Association Committee on Management of Patients with Valvular Heart Disease, indicated that as the U.S. population ages, doctors are seeing an increase in valvular heart disease problems. He also noted the variety of possible valvular diseases, including both leaky valves and valves that are too tight. The fen-phen associated valvular disease involves leaky valves and resulting regurgitation. Dr. Bonow stated that too tight or leaky valves, “when severe, increase the work of the heart and ultimately may impair the heart’s ability to pump blood.”¹²⁵ The guidelines include: (1) Extensive recommendations on evaluating heart murmurs and distinguishing those that pose serious health threats; (2) Recommendations on treating adolescents and young adults who have valvular heart disease; (3) Recommendations on the use of diagnostic tests including echocardiograms; (4) Information on which valvular disorders may pose serious threats during pregnancy; and (5) Information on therapy to be used to prevent blood clots in patients with artificial heart valves.¹²⁶ The guidelines recommend an examination for all people who took either fenfluramine or dexfenfluramine, alone or in combination with phentermine. They state:

The committee recommends a stethoscope examination for people without symptoms and a follow-up exam six to eight months later if no problems are found. Those with symptoms or heart murmurs should be examined by echocardiography. Individuals in whom a heart murmur is difficult to detect – because of body size – should undergo an ultrasound exam prior to dental procedures to determine whether they should take precautions against bacterial endocarditis. Bonow says physicians should use clinical judgment to determine which patients without symptoms should have precautionary echocardiograms. Some individuals without symptoms who have aortic regurgitation or mitral regurgitation, in which blood leaks backward through the valve because it does not close properly, should have surgery to correct the defect.¹²⁷

The guidelines include extensive detail on which patients should have surgery and which patients should receive vasodilators to try to reduce the regurgitation level. These guidelines are primarily the same as the earlier DHHS guidelines with respect to echocardiography, but they go further in identification of patients

¹²⁵Id.

¹²⁶See id.

who may need surgery or other invasive procedures to reduce the backflow of blood resulting from valvular heart disease.¹²⁸

Recent Studies Presenting Conflicting Information on Valvular Heart Disease

The only real conclusion that can be reached on fen-phen and valvular heart disease to date is that studies have produced “contradictory data on the extent of heart valve disease caused by the diet drug combination phentermine/fenfluramine”.¹²⁹ The FDA/Mayo-Clinic studies suggest a strong association between fen-phen use and valvular heart disease, and also suggest that the incidence and severity¹³⁰ of disease increases with the length of use of the drugs. However, several other studies have presented data that directly conflicts with the FDA and Mayo Clinic data, and those studies are noteworthy in the context of a discussion of fen-phen litigation.¹³¹ A brief summary of these studies follows below.

¹²⁸See *id.*

¹²⁹American College of Cardiology, *Study Finds Low Rate of Heart Valve Disease Among Fen-Phen Users*, AMERICAN COLLEGE OF CARDIOLOGY WEBSITE, Oct. 1, 1999, available online at <http://acc.org/media/highlights/oct99/phenfen.html>.

¹³⁰See *id.* American Home Products claims that “problems detected to date have been mostly a mild form of valve malfunction common in the general population and considered relatively harmless.” L. Stuart Ditzen, *In Mass Litigation, The Serious Cases can Get Lost*, PHILADELPHIA INQUIRER, Nov 22, 1999 at A1. American Home Products also maintains that no cause-and-effect link has been established between Redux and/or Pondimin and serious valvular heart disease. See *id.*

¹³¹An AHP press release concerning the proposed Settlement Agreement stated that “More recent well-controlled clinical trials – many of which have already been published in peer-reviewed journals and presented at major medical meetings – indicate that serious heart valve disease among former diet drug users is rare and the actual prevalence of heart valve regurgitation is far lower than was suggested at the time of the products’ [Redux and Pondimin] withdrawal. These findings are consistent with the clinical experience of cardiologists.” American Home Products Corporation, *American Home Products Announces Diet Drug Settlement Plan*, AMERICAN HOME PRODUCTS PRESS RELEASES, Madison, N.J., Oct. 7, 1999, available online at www.ahp.com/releases/ahp.100799.htm.

AHP has issued numerous press releases on various studies that have not found a causal connection between valvular heart disease and Redux or Pondimin. See American Home Products Corporation, *Cardiovascular Results of New Redux/Fen-Phen Study Presented at AHA*, AMERICAN HOME PRODUCTS PRESS RELEASES, Dallas, Texas, Nov. 11, 1998, available online at www.ahp.com/releases/ahp.111198.htm; See also American Home Products Corporation, *New Study Examining Cardiovascular Status And Duration Of Fen-Phen Treatment Presented At ACC*, AMERICAN HOME PRODUCTS PRESS RELEASES, New Orleans, Louisiana, March 9, 1999, available online at www.ahp.com/releases/ahp.030999.htm; See also American Home Products Corporation, *Cardiovascular Results of New Fenfluramine Study Presented at The European Echocardiography Meeting*, AMERICAN HOME PRODUCTS PRESS RELEASES, Trieste, Italy Dec. 10, 1998, available online at www.ahp.com/releases/ahp.121098.htm; See also American Home Products Corporation, *Study Shows No Significant Increase In Valve Abnormalities In Patients Taking Redux*, AMERICAN HOME PRODUCTS PRESS RELEASES, Atlanta, Georgia, March 31, 1998, available online at www.ahp.com/releases/ahp.033198.htm.

Recent studies reported in late 1999 indicate that the valvular heart disease associated with fen-phen use may not be as serious as previously believed, and that the disease may improve as time elapses since the patients took the diet drugs.¹³² One recent study conducted by Dr. Andrew J. Burger at the Beth Israel Deaconess Medical Center in Boston looked at the echocardiograms of 226 patients who took fen-phen as part of a large clinical trial. The study found FDA positive aortic regurgitation in 6.6% of the subjects and FDA Positive mitral regurgitation in 1.3 percent of their subjects. None of the subjects had symptomatic valvular heart disease (an audible heart murmur, shortness of breath, fainting, edema). In addition, they did not find an association between valvular disease and the length of time the subjects ingested fen-phen.¹³³ The study found that “[t]he rate of heart valve disease was similar to a comparable group of patients who had been studied previously in the Framingham Heart Study and who had never taken fen-phen. Dr. Burger and his colleagues observed that a significant portion of healthy people may have abnormal echocardiograms without clinical disease, whether or not they took fen-phen.”¹³⁴ The study appeared in the October issue of the Journal of the American College of Cardiology (JACC). A related editorial by Nelson B. Schiller, M.D. of the University of California at San Francisco stated that “as studies have become more scientifically rigorous, the role of fen-phen in valve disease appears to be approaching the vanishing point.”¹³⁵ Dr. Schiller’s editorial also stated that “[t]his was the biggest drug recall the FDA has ever dealt with and has probably cost billions of dollars if you consider the cost of withdrawal, echocardiograms, and litigation.’...

¹³²A recent article in SELF MAGAZINE questioned the connection of fen-phen to the valve problems and their severity. SELF MAGAZINE is a fitness/health magazine aimed at young women who want to maintain a trim and healthy body. The fact that such a statement appeared in SELF MAGAZINE is significant because many of SELF’s readers are those who may have taken or would take diet drugs for cosmetic weight loss purposes. By downplaying the fen-phen incident to these readers, they may be less likely to stay away from anorectic diet drugs in the future. The article stated, “although research has shown that 5 percent to 38 percent of users experienced heart damage, none of the studies could isolate fen-phen as the cause. Even more reassuring, the damage that did occur was mild and reversible, according to a recent study”. *Health-Hazard Hype – Deflated: Sometimes, Scary Medical News Needs a Second Look*, SELF MAGAZINE, March 2000, at 80.

¹³³See American College of Cardiology, Study Finds Low Rate of Heart Valve Disease Among Fen-Phen Users, American College of Cardiology, www.acc.org/pressroom/pressreleases/1999/10/01/100199a.htm.

¹³⁴*Id.*
Note: These studies do not represent the official position of the American College of Cardiology

¹³⁵ACC MediaInfo, *Heart Problems Disappear Once Patients Stop Using Diet Pills*, AMERICAN COLLEGE OF CARDIOLOGY WEBSITE, Dec. 1, 1999, available online at www.acc.org/media/highlights/dec99/heart.html.

but instead of turning to the experts from the start... the FDA put out a call for cases from weightloss centers that lacked expertise in cardiology.”¹³⁶

Another study reported in the December issue of the Journal of the American College of Cardiology focused on what happens to valvular heart disease after patients ceased taking fen-phen for a significant period of time. The study found that the leaky valve problem disappeared after patients ceased ingesting fen-phen.¹³⁷ The lead author of the study, Dr. Neil J. Weissman of the Cardiovascular Research Foundation at Washington Hospital Center in Washington, D.C., stated, “[w]e didn’t know if the leakiness we saw at first was just the tip of the iceberg... [n]ow we know that instead of progressing, the leakiness probably goes away once patients stop using the drug.”¹³⁸ Dr. Weissman had patients who had taken Redux as part of an earlier randomized double blind placebo-controlled trial return for echocardiograms three to five months after they ceased taking Redux. Doctors examined 941 echocardiograms including both former Redux users and those who had taken placebos. “What they found was reassuring: nothing.”¹³⁹ In the previous study where the patients had taken Redux, researchers found a small increase in valvular abnormalities. However, after three to five months they did not find anything at all.¹⁴⁰ While this study is noteworthy and may shed some light on long term effects of dexfenfluramine use, this study is *not* the definitive statement on whether valvular heart disease goes away after users stop taking the diet drugs. The general consensus is that there is *no conclusive evidence* on whether valvular heart disease associated with fen-phen is progressive or regressive in nature.¹⁴¹

Another recent study of importance in the fen-phen debate was also reported in 1999. This study conflicts with the Burger study above. The study addressed the connection between the length of time a patient took

¹³⁶Id.

¹³⁷See ACC MediaInfo, *Heart Problems Disappear Once Patients Stop Using Diet Pills*, AMERICAN COLLEGE OF CARDIOLOGY WEBSITE, Dec. 1, 1999, available online at www.acc.org/media/highlights/dec99/heart.html.

¹³⁸Id.

¹³⁹Id.

¹⁴⁰See id.

¹⁴¹See *Important Notice on the Proposed Class Action Settlement/A Class Member’s Guide to the Diet Drug Litigation Settlement*, p. 6.

fen-phen and any resulting valvular problems. This multicenter study included 1,200 patients who took fen-phen for more than 90 days and 670 control patients who never took fen-phen at all. Echocardiography was used to determine whether any of those patients suffered from valvular heart disease. Dr. Thomas Ryan of Duke University presented the fen-phen study on March 9, 1999 at the American College of Cardiology 48th Annual Scientific Session, moderated by Dr. Robert Bonow, who chaired the writing group that published the ACC/AHA Guidelines for Vascular Heart Disease.¹⁴² The study found “no signs of valve leakage for those who took the drug for less than six months. However, [the study found] there was a statistically significant increase in the signs and symptoms of leakage in patients treated for more than six months.”¹⁴³

Primary Pulmonary Hypertension

Primary Pulmonary Hypertension Symptoms and Prognosis

Primary Pulmonary Hypertension is a very serious disease with a high mortality rate. PPH occurs when the blood pressure in the arteries supplying the lungs is extremely abnormally high. PPH is “caused by a constriction of blood vessels that lead into the lungs. As a result, first, that part of the heart has to pump harder to get blood into the lungs and second, the lungs receive less blood and the blood it does receive is not as well oxygenated.”¹⁴⁴ The most common PPH symptom is shortness of breath with exercise, and eventually shortness of breath while at rest. Other symptoms include becoming tired easily, fainting,

¹⁴²See ACC MediaInfo, *Study Explores Duration of Fen-Phen Treatment and Heart Valve Disease*, ACC 48th Annual Scientific Session News Conference Highlights, AMERICAN COLLEGE OF CARDIOLOGY WEBSITE, March 9, 1999, available online at www.acc.org/session/conf99/media/confnews/tuephen.html.

¹⁴³ACC MediaInfo, *Highlights of Studies Released at Five News Conferences*, ACC 48th Annual Scientific Session News Conference Highlights, AMERICAN COLLEGE OF CARDIOLOGY WEBSITE, March 9, 1999, available online at www.acc.org/conf99/media/confnews/fivenewsconf.html.

¹⁴⁴Lori Litchman, *Philadelphia Jury Returns \$8M in Fen-Phen Case*, THE LEGAL INTELLIGENCER, Feb 24, 2000.

coughing, chest pain, swelling of the legs and/or feet, and coughing up blood.¹⁴⁵ The median length of survival after a PPH diagnosis is 2.5 years, according to the National Institute of Health. Overall, “[n]o one in the diet-drug litigation – including American Home Products Corporation, which marketed Pondimin and Redux – disputes that PPH is a terrible disease. It causes the veins in the lungs to constrict and close, restricting the flow of oxygen in the blood. It makes breathing laborious. It saps strength and energy. And it reduces life expectancy to a few years.”¹⁴⁶

Connection Between Fenfluramine/Dexfenfluramine and PPH

It has long been known that anorectic diet drugs like the fenfluramines can lead to an increased risk of PPH. The PPH-anorectic drug connection was first discovered in Europe and associated with an appetite suppressant drug called aminorex, marketed under the trade name Menocil. A PPH outbreak in Western Europe from 1967 to 1972, which increased PPH by a factor of 10 was traced to Menocil.¹⁴⁷ “Pulmonary hypertension has been reported to occur in association with fenfluramine... given alone. In addition, the d-isomer of fenfluramine, dexfenfluramine, increases the risk of pulmonary hypertension, particularly when patients receive high doses for more than three months. These drugs may cause pulmonary hypertension through the vasoconstrictor action of serotonin or by alteration of pulmonary vascular smooth muscle membrane depolarization.”¹⁴⁸ However, that known risk level was increased two months after dexfenfluramine

¹⁴⁵See NAPOLI, KAISER & BERN LLP, THE FEN-PHEN E-RESOURCE, *Primary Pulmonary Hypertension*, available online at www.dietdrugsettlement.com.

¹⁴⁶L. Stuart Ditzen, *In Mass Litigation, The Serious Cases can Get Lost*, PHILADELPHIA INQUIRER, Nov. 22, 1999, at A1 (describing a woman with PPH who is almost entirely housebound and on a waiting list for a double lung transplant. The woman is connected to oxygen tubes 24 hours a day and an IV line delivers medicine directly into her heart from a pump she must have with her at all times. She said that as soon as she starts to move she gets very weak and can not concentrate. She likened living with PPH to living on Mount Everest without oxygen).

¹⁴⁷See Alfred P. Fishman, M.D., *Current Perspective - Aminorex to Fen/Phen: An Epidemic Foretold*, CIRCULATION, at 156.

¹⁴⁸CNN Interactive, *Valvular Heart Disease Associated With Fenfluramine-Phentermine – Dr. Heidi M. Connolly – Manuscript Of Study Submitted To New England Journal of Medicine*, CNN WEBSITE, July 8, 1997, available online at www.cnn.com/Heath/0/07/08/fenphen.report/.

was approved by the FDA when the International Primary Pulmonary Hypertension Study (“IPPHS”) was released. The IPPHS of 1996 set that increased risk at 23-46 cases per million. The background risk for the general population is 1-2 cases per million.¹⁴⁹ Doctors prescribing fenfluramines or dexfenfluramines, either alone or in combination with phentermine, even before the IPPHS was released, were told to be extremely vigilant for symptoms or signs of PPH.¹⁵⁰ The IPPHS found that “the use of any anorexigen (appetite suppressant) within the previous year was associated with a ten-fold risk of developing PPH, and the risk increased to more than 20-fold with use for longer than three months.”¹⁵¹ Dexfenfluramine and fenfluramine made up 90% of the anorexigens in the IPPHS.¹⁵²

Use of anorectics even for short periods of time can lead to PPH in certain cases. In one case “progressive, fatal pulmonary hypertension developed after she [a 29-year-old-woman] had taken fenfluramine and phentermine for only 23 days. A postmortem examination disclosed striking obstructive lesions in the muscular pulmonary arteries that were reminiscent of those induced by aminorex and indistinguishable from those of primary pulmonary hypertension.”¹⁵³

PPH Labeling on Pondimin and Redux

Labeling on Pondimin and Redux did reflect an increased PPH risk. However, on August 22, 1996, in response to the IPPHS, Wyeth-Ayerst Laboratories and Interneuron Pharmaceuticals, Inc. sent a “Dear Health Care Professional” Letter about Redux and the IPPHS. The letter imparted the fact that the final IPPHS report found that the incidence of PPH for patients taking anorexigens, including dexfenfluramine, was between

¹⁴⁹See Alfred P. Fishman, M.D., *Current Perspective - Aminorex to Fen/Phen: An Epidemic Foretold*, CIRCULATION, at 156.

¹⁵⁰See Interview with Dr. Tori Marnell (March 18, 2000).

¹⁵¹*Two Weight-Loss Drugs Disrupt Certain Brain Functions in Animals*, DOCTOR’S GUIDE & OTHER MEDICAL NEWS, Aug 26, 1997.

¹⁵²See *id.*

¹⁵³Alfred P. Fishman, M.D., *Current Perspective - Aminorex to Fen/Phen: An Epidemic Foretold*, CIRCULATION, at 156.

23 and 46 cases per million patients per year, as opposed to the background risk of 1 to 2 cases per million adults per year.¹⁵⁴ The letter states that “Although the incidence of PPH for patients taking anorexigens remains small, PPH is a serious disorder with an estimated 4-year mortality rate of 45%. Therefore, it is very important that Redux not be prescribed for cosmetic weight loss. Redux is indicated for use only in those patients with a Body Mass Index (“BMI”) of at least 30 kg/m squared (which is approximately 30 percent over desirable weight) or a BMI of at least 27 kg/m squared (which is approximately 20 percent over desirable weight) in the presence of other risk factors (e.g., hypertension, diabetes or hyperlipidemia).”¹⁵⁵ The purpose of the letter was to inform health care professionals that the drug companies and the FDA were working on new labeling for Redux that would reflect the IPPHS, and to provide data to health care professionals until that new labeling was complete.¹⁵⁶

PPH Legal Claims

PPH cases are not included in the proposed Settlement Agreement, and it is expected that American Home Products may have to spend an additional \$1 billion to resolve the PPH cases. American Home Products has already settled several PPH cases at a cost ranging from \$1.5 million to \$4.5 million¹⁵⁷ In PPH lawsuits, several plaintiffs have claimed that American Home Products and its subsidiary Wyeth-Ayerst “downplayed the dangers and understated the number of known cases of PPH to cash in on the profits from soaring sales of Pondimin and Redux during the mid-1990s.”¹⁵⁸ In 1995 only four reports of PPH were cited to have occurred among Pondimin users, while internal Wyeth-Ayerst documents indicate that that the company

¹⁵⁴See Letter - *Important Update on Redux (Dexfenfluramine Hydrochloride Capsules) C-IV*, from Wyeth-Ayerst Laboratories and Interneuron Pharmaceuticals, Inc. to Health Professionals (Aug. 22, 1996).

¹⁵⁵Id.

¹⁵⁶See id. Note: The new labeling was complete in 1997.

¹⁵⁷See L. Stuart Ditzen, *In Mass Litigation, The Serious Cases can Get Lost*, PHILADELPHIA INQUIRER, Nov. 22, 1999, at A1.

¹⁵⁸Id.

knew of 37 such occurrences. A high level Wyeth-Ayerst employee suggested changing the Pondimin label to reflect the higher incidences of PPH, but no changes were made until 1997.¹⁵⁹

Arnold Levin of Levin, Fishbein, Sedran & Berman in Philadelphia, co-chair of the diet drug MDL Plaintiffs' Management Committee and MDL plaintiffs' liaison, stated that "PPH cases were excluded from the Settlement 'because there is a definitive number of those cases.' He estimated the number to be between 120 and 130 'so far' [and also stated] '[t]hey are very, very severe cases and they are being dealt with on an individual basis, and they are a finite group'."¹⁶⁰ Mr. Levin opined that PPH liability for American Home Products is likely to be "well in excess of \$1 billion."¹⁶¹ American Home Product's V.P. for finance, John Considine, stated of the PPH cases that they "are relatively few and quite individual in nature."¹⁶² Judge Bechtel in Philadelphia has set up an expedited hearing "fast track" process that has been set up for PPH cases that were involved in the multi-district litigation. This move reflects the more serious nature of these cases and the fact that the plaintiffs may die or become very seriously incapacitated before their trials begin if they remain bunched with the other thousands of cases in the multi-district litigation.¹⁶³

Neurotoxicity

Since the fenfluramines work by impacting the serotonin metabolism in the brain, there has been speculation that long-term fen-phen use may have had an adverse impact on the brain functions of patients who used fen-phen for extended periods of time. Literature on Redux from its manufacturers sent to health care professionals states, "[I]n animals receiving high doses of Redux for short periods of time resulting in brain

¹⁵⁹See *id.*

¹⁶⁰*Id.*

¹⁶¹*Id.*

¹⁶²*AHP Agrees to Settle Heart Valve Cases For Up to \$3.75 Billion; Meetings Under Way As Some Attorneys Question Coverage, Adequacy*, MEALEY'S LITIGATION REPORT FEN-PHEN/REDUX, Oct. 12, 1999, available online at <http://mealeys.com/dietdrugsettlement.htm>.

¹⁶³See L. Stuart Ditzen, *In Mass Litigation, The Serious Cases can Get Lost*, PHILADELPHIA INQUIRER, Nov. 22, 1999, at A1

concentrations approximately 10 times those seen in humans, neurochemical changes were observed. The dose and brain serotonin concentration of dexfenfluramine may affect reversibility. The relevance of these findings to humans is not known.”¹⁶⁴ In addition, “a study reported in the September [1997] issue of the American Medical Association indicated that dexfenfluramine and fenfluramine can reduce the production of a key brain-signaling chemical and adversely affect memory, cognition and moods.”¹⁶⁵

Critics of the FDA’s approval of Redux pointed to the concerns over neurotoxicity as a reason to be suspect about Redux’s safety. They looked to a body of research linking dexfenfluramine to brain damage in animals to support their claims. “‘This has been observed in every animal species tested to date, from mice to baboons,’ said George Ricaurte, MD, Ph.D., assistant professor of neurology at Johns Hopkins University School of Medicine. He was among 22 neurology specialists and researchers who in December [1995] asked the FDA to delay its approval.”¹⁶⁶ In advising physicians who had prescribed or were considering prescribing Redux to their patients, Dr. Ricaurte said that “[i]t’s important to emphasize to patients and physicians that as yet, we don’t know if dexfenfluramine produces brain damage in humans. However, they ought to be apprised of the animal studies and the potential risk that should be weighed against any potential benefits the drug may offer.”¹⁶⁷ The FDA responded to those concerns surrounding the approval of Redux by saying that “the relevance of the [animal] findings to humans is not known and will require further study”.¹⁶⁸

While plaintiffs may be concerned about potential neurological damage resulting from ingestion of fenfluramines, the Official Court Notice which addresses the proposed Settlement states of the neurotoxicity issue: “Some people believe that a very subtle kind of brain damage- neuropsychiatric or neurotoxic injury – may be caused by the use of Pondimin and/or Redux. However, the question of whether such brain injury can

¹⁶⁴Letter from Marc W. Deitch, M.D., Senior Vice President, Medical Affairs and Medical Director, Wyeth-Ayerst Laboratories Division of American Home Products Corporation, to Redux Prescribing Physicians (Aug. 22, 1997).

¹⁶⁵See Lance and Tortorich, *Popular Diet Drugs Pulled From Market*, 9 LOY. CONSUMER L. REP. at 296.

¹⁶⁶Wayne Hearn, *There’s A Weight Loss Drug, But It’s No Magic Bullet*, American Medical News, June 3, 1996, Media Rounds Page.

¹⁶⁷Id.

¹⁶⁸Id.

occur as a result of diet drug use is controversial. Also, there are presently no published clinical studies that show that people who took Pondimin or Redux have any brain injury as a result. The Settlement provides no benefits for neuropsychiatric or neurotoxic injuries.”¹⁶⁹ Plaintiffs who accept the benefits of the proposed Settlement Agreement will not be able to pursue any neurotoxicity claims in any courts as a condition of the proposed Settlement Agreement.¹⁷⁰

While, as the Official Court Notice indicates, studies have not been done on humans and no conclusive human data is available, animal studies have shown fen-phen extended use to have negative impacts on the brain functions in mice and monkeys. One such study which assessed the neurotoxic effects of fenfluramine and phentermine alone and together on the mouse brain, found that its results “suggest that phentermine has the potential to exacerbate fenfluramine-induced serotonin neurotoxicity, if utilized in certain doses. Further, the present results indicate that phentermine possesses dopamine (DA) neurotoxic potential.”¹⁷¹ Una D. McCann, M.D. and colleagues from the National Institute of Mental Health conducted the study. The study’s basic lesson that the fenfluramines “result in a reduction in brain serotonin when administered to animals” is significant because “[s]erotonin is thought to be important in a variety of brain functions, including cognition and memory and the regulation of mood, anxiety, impulsivity, aggression, sleep and neuroendocrine function. However, the researchers admit not much is known about the effects of brain serotonin loss. Nor is it known if the effects on animals are the same in humans.”¹⁷² The researchers also attempted to determine whether ceasing use of the fenfluramines reversed the neurological changes observed in the animals. They found that “loss of serotonin axonal markers after fenfluramines is evident weeks, months, and in one primate study, as long as one year after drug discontinuation’... [t]hey found that some later nerve repair appeared to

¹⁶⁹ *Important Notice on the Proposed Class Action Settlement/A Class Member’s Guide to the Diet Drug Litigation Settlement*, p. 14

¹⁷⁰ *See id.*

¹⁷¹ McCann, U.D., Juan, U., and Ricaurte, G.A. - Unit on Anxiety and Affective Disorders, Biological Psychiatry Branch, National Institute on Mental Health, *Neurotoxic Effects of +/-Fenfluramine and Phentermine, Alone and In Combination, on Monoamine Neurons in the Mouse Brain*, SYNAPSE (3) 239-246, Nov. 30, 1998.

¹⁷² *Two Weight-Loss Drugs Disrupt Certain Brain Functions in Animals*, DOCTOR’S GUIDE & OTHER MEDICAL NEWS, Aug 26, 1997.

take place, but in one study in which rats were given higher doses of fenfluramine, the repairs were short-lived.”¹⁷³ The authors of the study urged that doctors of patients who took fen-phen should be aware of possible serotonin neurotoxicity, which the researchers stated could result in “things such as loss of memory, irregular moods, anxiety, impulsivity, aggression, and changes in sleep patterns”.¹⁷⁴ The researchers did also state that such symptoms may come from a variety of causes, not necessarily use of fenfluramines. The researchers concluded their work with an urging of doctors who see neurotoxicity symptoms to notify either the fenfluramines manufacturer or the FDA’s MedWatch program. In addition, they stated that “before initiating treatment with fenfluramines, patients should be apprised not only of the drugs’ benefits, but also of their potential adverse effects and, together with a physician, make an informed decision whether use of fenfluramines is indicated”.¹⁷⁵ The study on neurotoxicity was concluded before the fenfluramines were pulled from the market.

The study, while clearly not providing human data showing a connection between serotonin neurotoxicity and fenfluramines¹⁷⁶, does warn doctors of the possibility of serotonin neurotoxicity among diet drug users, as evidenced by the results of several animal studies.¹⁷⁷ Since the animal studies do not appear to indicate that ceasing use of the fenfluramines will cause the neurological effects to abate, this warning should be heeded for years to come. The neurotoxicity animal studies and various human complaints of neurological problems should also be taken into account when plaintiffs are deciding whether to opt out of the proposed

¹⁷³Id.

¹⁷⁴Id.

¹⁷⁵Id.

¹⁷⁶While the neurotoxicity studies have been confined to animals at this point, several people who took fenfluramine and dexfenfluramine have complained of various neuropsychological problems. “One woman said she took a butcher knife to her husband. Some people said they had to be hospitalized. Lesser complaints include mood or behavior changes, and cognitive and memory loss.... many former fen-phen and Redux users also complain of dizziness, headache, and flushing. These symptoms are also reported by some people taking antidepressant drugs that increase serotonin levels, like Prozac and Zoloft. The symptoms, when severe, are sometimes called ‘serotonin syndrome’.” Paul D. Rheingold, *Fen-Phen and Redux: A Tale of Two Drugs - The Story of How Fen-Phen and Redux Came to Be Used By 6 Million Americans is Chilling*, 34 TRIAL at 82.

¹⁷⁷See McCann, U.D., Juan, U., and Ricaurte, G.A. - Unit on Anxiety and Affective Disorders, Biological Psychiatry Branch, National Institute on Mental Health, *Neurotoxic Effects of +/-Fenfluramine and Phentermine, Alone and In Combination, on Monoamine Neurons in the Mouse Brain*, SYNAPSE (3) 239-246, Nov. 30, 1998.

Settlement Agreement, which allows no recovery for neurotoxicity claims, even if serious neurotoxicity health problems arise in the future.

OBESITY AS THE DISEASE FEN-PHEN WAS MEANT TO COMBAT

Risk-Benefit Calculations of Prescription Obesity Drugs

The debate on the safety of fen-phen necessitates a discussion on obesity. Obesity is a serious health problem¹⁷⁸, and fen-phen was initially hailed as a breakthrough tool in the fight against obesity in the United States. When the drug companies marketed fen-phen, they indicated to doctors that fen-phen was to be used for the clinically obese. The literature that came with the drugs to physicians stated that fen-phen was to be given to persons with 30 or over Body Mass Index, which would be a seriously overweight person.¹⁷⁹ When people are so overweight, they subject themselves to a whole host of other serious medical problems and the decision to take fen-phen became a risk-weighting calculation of the known heightened risk of PPH as opposed to the known heightened risk at remaining at an obese weight. Even once the valvular problems were discovered, fen-phen was not pulled immediately, and physicians were told to factor in the valvular disease risk into the calculation of whether a morbidly obese person was to be put on fen-phen.

In the manuscript of the Mayo Clinic study that first identified the alleged fen-phen valvular heart disease

¹⁷⁸The Third National Health and Nutrition Examination Survey (NHANES III) (1988-1991) estimates that 33% of the U.S. population is obese, compared with 25% in NHANES II (1976-1980). Obesity is associated with numerous health problems, including many forms of heart disease. In the U.S., a reduction in consumption of fat from 40% of calories in 1965 to 34% of calories in 1991 has not led to a decrease in U.S. obesity, most likely due to an increase in overall caloric intake and reduction in physical activity. Maintaining a BMI below 25 throughout adult life is recommended. For patients with a BMI between 25 and 30, lifestyle modifications like a decrease in caloric intake and increase in exercise are appropriate. Pharmaceuticals should be considered only with a BMI over 30 or a lesser BMI with other complications such as diabetes or high cholesterol. For people with a BMI over 35, gastrointestinal surgery may become an option. However, above all, diet and regular physical exercise are the most healthy ways to maintain good health in obesity management. See Robert H. Eckel, M.D., for the Nutrition Committee, American Heart Association, *Obesity In Heart Disease: A Statement for Healthcare Professionals From the Nutrition Committee*, AHA MEDICAL/SCIENTIFIC STATEMENT, CIRCULATION: THE JOURNAL OF THE AMERICAN HEART ASSOCIATION 96: 3248-3250 (1997).

¹⁷⁹See Interview with Dr. Tori Marnell (March 18, 2000)

link, the report closed with the statement that “[c]andidates for fenfluramine-phentermine therapy should be informed about serious potential adverse effects, including pulmonary hypertension and heart disease.”¹⁸⁰

One doctor put the trade-off in numbers. He claimed that every year 300,000 people in the U.S. die from obesity related complications. His numbers indicated that 8 million adults in the U.S. took fen-phen from 1992 to 1997. Using the IPPHS number of 23 PPH cases per one million adults using fenfluramine-type drugs, he found that would be 124 people per year in the U.S. getting PPH as a result of fen-phen. He said that 300,000 deaths from obesity per year translates to 833 deaths per day from obesity, while 184 deaths per year from PPH (assuming all PPH patients die) would be 15 deaths per month or one death every other day as a result of fen-phen. He concluded that the ratio was 833/0.5, or 1,666/1.¹⁸¹ He stated that “[w]ith 200 million adults, and a death total of 300,000 per year from obesity, that means that the death rate from obesity is 1,500 per million adults each year. Obesity is clearly an epidemic in this country. Why is the media focusing on the unsubstantiated deaths of under 400 per year, or 23 per million, and ignoring the obesity death rate?... More people die from aspirin every year than fen-phen.”¹⁸² However, in the counterargument

to Dr. Krentzman, Dr. Gregory D. Curfman, M.D. stated in a *New England Journal of Medicine* editorial,

¹⁸⁰CNN Interactive, *Valvular Heart Disease Associated With Fenfluramine-Phentermine – Dr. Heidi M. Connolly – Manuscript Of Study Submitted To New England Journal of Medicine*, CNN WEBSITE, July 8, 1997, available online at www.cnn.com/Heath/0/07/08/fenphen.report/.

¹⁸¹See Ben Z. Krentzman, M.D., *Scared by the Media Hammering Away on How Dangerous Fen-Phen Is? I Do Not Blame You!*, available online at www.loop.com/~bkrentzman/.

¹⁸²Id.

[g]iven the serious health hazards associated with anorectic drugs, can their continued, widespread use be justified? It has been argued previously that the potential health benefits of anorectic drugs outweigh their risks when considered against the health hazards of obesity. In fact, it was this argument that last year led the FDA to approve dexfenfluramine. I believe that there are serious problems with this argument. Weight reduction extends health benefits to overweight people only if it is maintained for a long period. It has never been shown, and it is highly implausible, that appetite-suppressant drugs can maintain weight loss indefinitely. To date, studies of these drugs have demonstrated efficacy only for short-term weight loss. Their safety if taken over a period of many years is doubtful, since the risk of serious toxicity appears to increase with the duration of use. Drug holidays would result in weight cycling (i.e. fluctuations in body weight), which in epidemiologic studies is associated with adverse outcomes such as coronary heart disease and death. Furthermore, clinical studies have never shown that appetite-suppressant drugs can prevent obesity-related illnesses or prolong life. Until we have a better understanding of the relative health risks and benefits of anorectic drugs, physicians need to distinguish between patients who have a legitimate health indication for the use of the drugs and those who seek them principally for cosmetic reasons. The only justifiable medical use of anorectic drugs is in seriously obese patients who have obesity-related illnesses such as coronary heart disease, diabetes, hypertension, and hyperlipidemia.¹⁸³

Dr. Curfman seems to indicate that it is not a clear tradeoff, that the use of fen-phen does not necessarily correlate with the benefits associated with a weight reduction. Dr. Curfman's editorial was written shortly before Redux and Pondimin were pulled from the market, as was Dr. Krentzman's piece on the obesity/fen-phen numbers tradeoff. Dr. Curfman's idea won out, it appears that the FDA agreed with his idea of the tradeoff in that the risks outweighed the benefits of fen-phen.

In a telephone interview with Tori Marnell, M.D., a physician in Tulia, Texas who had several of her patients on fen-phen before it was withdrawn, Dr. Marnell addressed the risk benefit idea of drug prescribing.¹⁸⁴ Her view of the fen-phen risk/benefit analysis was more akin with Dr. Krentzman, since she felt that it was imperative that obese patients lose weight to improve their health. She said she had significant success with weight loss with patients who were on fen-phen, although several of them have gained back a significant amount of the weight they lost without the diet drugs. Many of her patients are now on Xenical and are losing weight again, and Xenical has the added benefit of 'training' the patients not to eat the fatty foods since they

¹⁸⁴See Interview with Dr. Tori Marnell (March 18, 2000).

produce an upset stomach for Xenical users. As for the risk-benefit calculation for obesity and fen-phen, Dr. Marnell indicated that all drugs have risks, and she stressed that the decision to take a drug is a risk-benefit calculation in *every* situation. Dr. Marnell expressed the view that the media played a significant role in the “hype” surrounding fen-phen. She used penicillin as an example. She stated that one out of every 1500 people is allergic to penicillin and may go into anaphylactic shock if given a penicillin shot. Still, the benefits of penicillin outweigh their risks, and U.S. doctors continue to give penicillin shots to children and adults despite the risk of an allergic reaction. If someone is allergic, after the fact people may criticize the doctor for giving a shot instead of a pill, but on the whole, penicillin’s positive attributes outweigh the negatives of a possible allergy problem. The media has not focused on penicillin’s adverse reactions and created a state of quasi-hysteria as occurred with fen-phen. The same situation happens with childhood vaccinations. Some children may get the disease being vaccinated against and either die or become very sick and disabled. However, on the whole, in order to combat a serious societal medical problem in the form of an outbreak of a disease like polio or smallpox, we continue to give childhood vaccines.¹⁸⁵ If we consider obesity to be a serious enough problem in the U.S. then the calculation regarding fen-phen changes. The PPH problems were known all along (although the severity of the risk was increased in 1996 with the IPPHS) and were factored into the calculation of which was the more serious risk – the increased chance of developing PPH or the risk of death or serious complications resulting from obesity. The valvular problems could be figured into the same calculus, allowing for the fact that it is more difficult to operate on seriously overweight people if valvular replacement is needed, since they have wider chest walls, are more difficult to intubate, and may develop more complications during and after surgery.¹⁸⁶ The problem is that “because the diet pills were so readily available, it is doubtful that the original physical examination necessary to determine suitability of the drugs was ever done.”¹⁸⁷ While Dr. Marnell did discuss the risks and benefits with her patients, with

¹⁸⁵See *id.*

¹⁸⁶See *id.*

¹⁸⁷Vivi Vanderslice, *Viability of a Nationwide Fen-Phen/Redux Class Action Lawsuit in Light of Amchem v. Windsor*, 35

fen-phen on the whole this was not always the case. This leads into the topic of fen-phen use for cosmetic weight loss and its distortion of the risk benefit calculation of the problems associated with obesity versus the problems associated with Redux and Pondimin.

The Important Issue of the Widespread Use of Fen-Phen for Cosmetic Weight Loss

The risk benefit calculus associated with obesity broke down with fen-phen because of its widespread use for cosmetic weight loss.¹⁸⁸ After the Weintraub article appeared in 1992, “some doctors began to prescribe fen-phen for people who were not substantially overweight and therefore not at risk of the diseases associated with morbid obesity. Many doctors, including some associated with weight-loss clinics, prescribed fen-phen to people who simply wanted to shed a few pounds, a so-called cosmetic use. Worse yet, some doctors prescribed the drugs without first doing thorough patient examinations, or any examinations at all. In many cases, patients were not told of the risks associated with use of the drugs. In fact, the “drugs often were offered as an inducement to join weight-loss clinics and were promoted as free of side effects.”¹⁸⁹ A clear cut risk-benefit analysis cannot be completed with fen-phen like it could with penicillin, because fen-phen was being given out to those who were not obese. For people who wanted to lose weight for cosmetic reasons, the increased PPH risk and the later found valvular heart disease risk did outweigh the benefits of cosmetic weight loss in all cases. One editorial summed up the cosmetic weight loss issue as follows:

CAL. W. L. REV. 199, 203 (1998).

¹⁸⁸Note: In addition to the breakdown of the risk/benefit analysis due to cosmetic weight loss use of fen-phen, the fen-phen risk/benefit analysis also broke down because fen-phen may not be a long-lasting effective treatment of obesity. Appetite suppressant weight loss often leads to the weight coming back on in a short period of time. See Interview with Dr. Tori Marnell (March 18, 2000).

¹⁸⁹Paul D. Rheingold, *Fen-Phen and Redux: A Tale of Two Drugs - The Story of How Fen-Phen and Redux Came to Be Used By 6 Million Americans is Chilling*, 34 TRIAL at 79.

The use of appetite suppressants is associated with a rare but potentially fatal risk. On the other hand, these drugs can help someone with or at high risk for serious medical conditions like heart disease to substantially reduce that risk. In this way, they are not that different from many other medical interventions, which invariably have both risks and benefits. The difference here is that many persons are prescribed appetite suppressants not for medical but for cosmetic reasons. It is difficult to justify even a rare but potentially fatal risk when the goal is purely cosmetic. A simple rule of thumb: if you really need one of these drugs [fenfluramine or dexfenfluramine] because your weight is literally killing you, consider it but only under a doctor's care and in conjunction with an honest diet and exercise behavioral modification program. However, if you just want to fit into a smaller bathing suit or look better in an evening gown, you should think again.¹⁹⁰

The manufacturers' literature indicated that the drugs should only be given to people with a BMI equal to or over 30.¹⁹¹ The American Medical News, a publication read by physicians across America, said in June of 1996 that Redux "is recommended for patients who are at least 30% over their desirable weights. Patients with other risk factors, such as hypertension or diabetes, may benefit if they are 20% over their recommended weights."¹⁹² However, Americans were clamoring for an easy weight loss fix, and the American Medical News warned that "physicians may have to resist pressure from their patients".¹⁹³ There was much money to be made all around from America's desire for an easier effective way to lose weight, so the admonition not to prescribe fen-phen for cosmetic weight loss was often ignored. In an article discussing previous PPH problems associated with anorectic drugs like fenfluramine and dexfenfluramine, Dr. Alfred P. Fishman states,

One major weakness in the war against obesity is the blurred outlines of the targets. Although any degree of overweight is undesirable, not all degrees of obesity call for the same type of vigor or attack. For example, the goal of a 10% reduction in weight in an individual who is mildly obese and at risk for systemic hypertension and diabetes warrants more aggressive measures than does achieving the same weight loss by an individual determined to fit into last year's bathing suit. In turn, both of these indications are much less compelling than weight loss in a morbidly obese individual in whom quick weight loss may be lifesaving. Moreover, no matter what the goal in treating overweight and obesity, lasting success in losing weight calls for recognition that obesity is a chronic disorder that requires a long-term strategy for sustained success.¹⁹⁴

¹⁹¹See Interview with Dr. Tori Marnell (March 18, 2000).

¹⁹²Wayne Hearn, *There's A Weight Loss Drug, But It's No Magic Bullet*, American Medical News, June 3, 1996, Media Rounds Page.

¹⁹³Id. Dr. Marnell indicated that several patients on fen-phen said they would go to another doctor if she stopped prescribing it for them, and that they were outraged when she stopped prescribing it after the FDA warnings came out in 1997. See Interview with Dr. Tori Marnell (March 18, 2000).

Fen-phen was prescribed over the internet and by doctors who only saw patients for a few moments at a place like Jenny Craig or Nutri-System.¹⁹⁵ These doctors were not engaging in a careful risk benefit analysis in determining whether the risks of obesity were outweighed by the risks associated with an anorectic drug that increased the risk of PPH and also later caused valvular heart disease. People were taking the drugs for purely cosmetic reasons, where the risks clearly were not outweighed by the benefits. This is a pervasive problem in obesity management, as much of society fights to be thin without the more disciplined approach of calorie intake reduction and increased exercise. People will be looking for the diet pills and will go to great lengths to get them, regardless of the risks to their health.¹⁹⁶ Dr. Curfman, in his editorial in the *New England Journal of Medicine*, states of cosmetic weight loss: “People seeking to lose weight should consult with their own physicians and not try to obtain these drugs from doctors they do not know. For generally healthy people who want to lose a few pounds, there are safer alternatives. Although the traditional methods of calorie restriction and regular exercise require personal discipline, the reports [on PPH and valvular heart disease]... are chilling reminders that succumbing to the allure of diet pills as a quick fix for excess weight may be courting disaster.”¹⁹⁷

In the interview with Dr. Marnell, she stated that patients were devastated when they learned that she would no longer be prescribing fen-phen because of the FDA warnings that came out after the Mayo Clinic study. Before the Mayo Clinic study came out and during the fen-phen craze, Dr. Marnell said that she kept people on fen-phen for only six months, but that they would attempt to go to other physicians without the six-month time limit in order to continue taking fen-phen.¹⁹⁸ She said that before she put patients on

¹⁹⁵See Gregory D. Curfman, M.D., *Editorial*, NEW ENG. J. MED. Vol. 337, No. 9, Aug. 28, 1997.

¹⁹⁶See Wayne Hearn, *There's A Weight Loss Drug, But It's No Magic Bullet*, American Medical News, June 3, 1996, Media Rounds Page. The Hearn article in AMERICAN MEDICAL NEWS was meant for physicians. It states of fen-phen's popularity, “millions of overweight Americans, discouraged by failed attempts to shed pounds through dieting and exercise, are pinching themselves at the notion that the road to success may be just a pill pop away.” *Id.*

¹⁹⁷Gregory D. Curfman, M.D., *Editorial*, NEW ENG. J. MED. Vol. 337, No. 9, Aug. 28, 1997.

¹⁹⁸When a patient enrolled in Nutri-System's “NutriRx” fen-phen program was asked what she would do if her Nutri-System

fen-phen, she would carefully go over the known increased PPH risk with them and engage in a risk-benefit analysis with the patient. However, she said that most patients seemed to be unfocused on the risks as opposed to the benefits of the diet pills. Dr. Marnell maintained that she would only prescribe fen-phen to obese patients, but she said that many patients would initially inquire about fen-phen for purely cosmetic weight loss reasons. Dr. Marnell reiterated many times the need for the morbidly obese to lose weight, and stressed that a comprehensive risk calculation would be needed for each patient to assess if fen-phen was right for them. She says that even today, for some morbidly obese patients, the weight that came off with fen-phen outweighed the risks of the valvular lesions associated with fen-phen use. She has not seen any patients develop valvular problems who took fen-phen as of the present time, and she is following the U.S. Department of Health and Human Services guidelines on when to give an echocardiogram to patients who took fen-phen. Her experience with overweight patients illustrated the deep desire of Americans to take diet pills and often ignore the risks associated with the medications in the quest to lose weight, as well as the importance of a risk benefit calculation in the decision to take diet pills and to only prescribe the medications for the seriously obese.

THE OFF-LABEL USE OF PONDIMIN, PHENTERMINE, AND REDUX

IN THE FEN-PHEN COMBINATION

Off-Label Use of Prescription Drugs

Congress has delegated to the FDA the power to protect individuals by regulating which drugs are safe and

doctor ceased prescribing fen-phen for her, the patient responded that she would just find another Nutri-System center and another doctor. See Laura Fraser, *The New Diet Drugs, They Really Do Help Some People Lose Weight: But Are They Worth The Risk?*, 10 HEALTH 52 (1996).

effective. The Food, Drug, and Cosmetic Act was passed in 1938 and allowed for federal regulation of new drugs. New drugs must be approved by the FDA in accordance with a process that includes a pre-marketing investigation involving animal testing, as well as three phases of human clinical investigation. Following the required human and animal testing, the manufacturer must submit a New Drug Application to the FDA. The New Drug Application contains all of the studies performed on the drug, including all adverse affects and benefits of the products.¹⁹⁹ “Upon a showing that the drug is safe and effective for its proposed use or uses, the New Drug Application is approved by the FDA. However, such approval does not extend to other uses”²⁰⁰ When the FDA approves a drug, it approves it “for specific purposes associated with the clinical trial findings that supported the drug’s application... [and] pharmaceutical companies are required to convey, in the drug’s formal labeling, information regarding only those uses for which the drug was approved.”²⁰¹ The drug’s label will include information necessary for safe and effective use, warnings, precautions, clinical pharmacology, indications, contraindications, and adverse reactions. FDA approved labeling is included as a product insert and also as an entry in the Physician’s Desk Reference. The manufacturer must report adverse reactions associated with the drug to the FDA in the form of an FDA-1639 Drug Experience Report. Off-label use is the use of drugs in manners other than those described in the FDA approved label – all uses other than the use(s) for which the drug was approved.²⁰² “After the FDA approves a prescription drug for one ailment, doctors and researchers often find other ways to use it, and physicians are allowed to prescribe a drug for any use if it has been approved by the FDA for some purpose.”²⁰³

Off-Label Use of Fenfluramine, Dexfenfluramine, and Phentermine

¹⁹⁹See Steven R. Salbu, *Off-Label Use, Prescription, and Marketing of FDA-Approved Drugs: An Assessment of Legislative and Regulatory Policy*, 51 FLA L. REV 181 (1999).

²⁰⁰*Id.*

²⁰¹*Id.*

²⁰²See *id.*

²⁰³Rebecca Porter, *Manufacturers May Promote Off-Label Uses For Drugs*, 35-OCT TRIAL 92 (1999).

Fenfluramine, dexfenfluramine, and phentermine were all approved by the FDA. However, they were approved as single agent drugs and not for long term use. Specifically, fenfluramine and phentermine were only approved for short-term use for a few weeks. The longest study done on dexfenfluramine was for one year. There were three common off-label uses of fenfluramine during the fen-phen craze: (1) Extended long term use beyond brief approved periods; (2) Combination use with phentermine; and (3) Use by people who were not obese.²⁰⁴ No studies were ever submitted to the FDA to show either the effectiveness or safety of the combination of dexfenfluramine-phentermine or fenfluramine-phentermine, nor were any studies presented that addressed the safety of their long-term use.²⁰⁵

At the time of widespread fen-phen use promotion of off-label uses/prescriptions was impermissible.²⁰⁶ In Washington Legal Foundation v. Friedman, 13 F. Supp. 2d 51, 51-69 (D.D.C. 1998), Judge Royce Lamberth issued a permanent injunction against the FDA for restricting dissemination on off-label drug use. The FDA

²⁰⁴ Redux was approved by the FDA only on the condition that it be prescribed exclusively for obesity. Obesity was defined as a BMI (kilograms divided by square meter) of 30 or above. In addition, Redux was to be prescribed only together with an overall weight loss regimen that included dieting and increased physical activity. The FDA saw it as a drug with a risk that was to be used for a serious health condition (obesity) under controlled circumstances. This was not the reality at all. Redux was prescribed widely for people to lose a ‘few’ pounds for cosmetic purposes. Redux sales representatives visited all types of doctors. It was reported that fen-phen was given away free when people signed up at weight loss centers like Nutri-System, and that some doctors would give ‘lectures’ to fifty to seventy-five “patients” at a time and then hand out prescriptions where the physical exam consisted only of a questionnaire. Sometimes the doctor only appeared on videotape. See Vivi Vanderslice, *Viability of a Nationwide Fen-Phen/Redux Class Action Lawsuit in Light of Amchem v. Windsor*, 35 CAL. W. L. REV. 199, 203 (1998); See also Caren A. Crisanti, *Product Liability and the Prescription Diet Drug Cocktail, Fen-Phen: A Hard Combination to Swallow*, 15 J. CONTEMP. HEALTH L. & POL’Y 207, 225 (1998).

²⁰⁵ In the interview with Dr. Marnell, she expressed the view that doctors had much to do with creating the fen-phen problem because they widely prescribed the drugs off-label— in combination and for longer periods of time than approved by the FDA — and they discounted the PPH risks. See Interview with Dr. Tori Marnell (March 18, 2000). A USA Today article from 1999 also expressed that sentiment, stating “Doctors also must share the blame for the fen-phen mess, experts say, because they prescribed the diet-drug combination even though the drugs weren’t tested together or recommended for tandem use. As many as 6 million people are believed to have obtained prescriptions for the drug combination.” Steve Sternberg, *Lawsuits: Drug Development’s Side Effects*, USA TODAY, Jan 12, 2000, Health Section. The same thing occurred with American Home Products’ recall of the pain reliever Duract, because it led to cases of kidney failure. The USA Today article follows that “the Duract tragedy also occurred because the drug was misprescribed. Many doctors offered it for long-term relief of chronic pain, although AHP warned against using the drug for longer than 20 days. ‘The doctors structured those treatments,’ says George Sasic, an industry analyst who tracks AHP for Dominick & Dominick in New York.” *Id.* Raymond Woosley, Professor of Pharmacology at Georgetown, says that these problems should not come as a surprise. He claims that few doctors have sufficient training in pharmacology and doctors are inundated with information from drug companies, journals, and trade publications, which they must evaluate to the best of their abilities. He says this is difficult for today’s doctors, since their average age is 45 and three-fourths of the medicines they prescribe today were not in existence when they were in medical school. See *id.*

²⁰⁶ Note: In January of 1997 Wyeth-Ayerst sent letters to 470,000 medical professionals to advise them that it did not recommend the concomitant use of fenfluramine and phentermine in the fen-phen combination. See Jaime A. Wilsker, *One Half-Phen In the Morning/One Fen Before Dinner: A Proposal For FDA Regulation of Off-Label Uses of Drugs*, 6 J.L. & POL’Y at 828.

changed its policy on the matter with the Food and Drug Administration Modernization Act that President Clinton signed on November 21, 1997 (the “Modernization Act”). The Modernization Act changed the law on off-label promotion and made it a permissible practice in certain circumstances.²⁰⁷ The change in permitting certain off-label promotions did not come about until Pondimin and Redux had been pulled from the market, so there is no way to tell what changes the Modernization Act may have had on the level of use of the drugs.²⁰⁸ However, products liability attorney Robert Habush of Milwaukee’s Habush, Davis & Rottier claimed that “had it not been for the [off-label promotion] ban, drug companies undoubtedly would have disseminated two articles that appeared in peer-reviewed journals touting the drug combination fen-phen as a diet aid. And that, he said, would have dramatically increased the number of people taking fen-phen”²⁰⁹

Arguments For and Against Off-Label Use

²⁰⁷The Modernization Act permits drug manufacturers to disseminate qualified forms of written information concerning the safety, effectiveness, or benefits of off-label uses to certain groups, including health care practitioners, pharmacy benefit managers, health insurance issuers, group health plans, and federal or state governmental agencies. To qualify to disseminate the information the drug manufacturer must have filed an application or received a biologics license for the drug under the Public Health Service Act. Only authorized information is permitted, which includes unabridged peer reviewed articles (indexed in the Index Medicus of the National Library of Medicine of the National Institutes of Health) or qualified reference publications. The information cannot be derived from research conducted by another manufacturer unless the manufacturer received permission from the first manufacturer to disseminate the information. The information must be provided to the Secretary of Health and Human Services sixty days before dissemination. The manufacturer must also forward to the DHHS Secretary any clinical trial information or reports it has on the off-label use’s safety and effectiveness. The statute also requires the manufacturer to submit a supplemental application for off-label use. The DHHS Secretary can exempt the manufacturer from that provision if it would be economically prohibitive for the manufacturer to incur the costs necessary for such an application. This exception addresses very small manufacturers and follow-up studies that would be extremely expensive. In its off label promotion, the manufacturer must disclose that the information concerns a drug that has not been approved or cleared by the FDA, must enclose official labeling and labeling updates, and must identify sources of funding for research. The presentation of information must be complete and not tilted in favor of the manufacturer’s promotion for off-label drug use. See Steven R. Salbu, *Off-Label Use, Prescription, and Marketing of FDA-Approved Drugs: An Assessment of Legislative and Regulatory Policy*, 51 FLA L. REV at 209 – 216.

The fen-phen phenomenon predated the Modernization Act, and American Home Products was therefore not authorized to promote off-label fenfluramine/dexfenfluramine use. American Home Products maintained that Redux and Pondimin were to be used only in obese patients, it did not recommend their combined use with phentermine, and it reiterated that Redux had only been tested for up to one year and Pondimin was only approved for short term use. See id.

²⁰⁸In discussing Redux promotion, one article indicated that Wyeth-Ayerst sent salespeople to visit all types of doctors, not just obesity specialists, after Redux was approved. See Paul D. Rheingold, *Fen-Phen and Redux: A Tale of Two Drugs - The Story of How Fen-Phen and Redux Came to Be Used By 6 Million Americans is Chilling*, 34 TRIAL at 79. Since Redux was approved only for the treatment of obesity as defined as a BMI greater to or equal to 30, promoting Redux to non-obesity specialists may have been an off-label promotion. However, many doctors who are not obesity specialists may treat patients with a BMI over 30 and obese patients may not necessarily only seek treatment from an obesity specialist. In the interview with Dr. Marnell she indicated that she had several patients with a BMI over 30 who took fen-phen, and she was not an obesity specialist who limited her practice to overweight patients. See Interview with Dr. Tori Marnell (March 18, 2000).

²⁰⁹Paul D. Rheingold, *Fen-Phen and Redux: A Tale of Two Drugs - The Story of How Fen-Phen and Redux Came to Be Used By 6 Million Americans is Chilling*, 34 TRIAL at 79

While it arguably led to serious problems in the fen-phen situation, off-label use is a common and legal practice.²¹⁰ The American Medical Association estimates that 40 to 60 percent of all U.S. prescriptions today are off-label uses, including many AIDS and cancer medications.²¹¹ “Today, off-label use has become an important part of mainstream, legitimate medical practice. Many off-label uses are recommended by medical textbooks, research institutes, and professional organizations, as well as standard pharmaceutical reference works. According to some estimates, almost half the United States population may be taking a medication prescribed for an unapproved reason.”²¹² Off-label treatments are considered amongst the most effective treatments for cancer patients and have been called “the hallmark state of the art treatment”.²¹³ In addition, the majority of drugs prescribed for wound healing are off-label, and experts suggest that 90 to 100% of AIDS treatments are off-label, including the new antiretroviral combination therapies.²¹⁴ Off-label prescribing is common in obstetrics, infectious disease, and pediatrics.²¹⁵ Most pediatric prescriptions are off-label because many drugs are not tested in children. Proponents of the practice argue that off-label prescription and use allows expedition of the use of effective new treatments, since it would be prohibitively

²¹⁰See *Cheyenne v. Heckler*, 718 F. 2d 1174, 1191 (D.C. Cir. 1983) (holding that a doctor may, as part of the practice of medicine, prescribe a different dosage or use for the drug as long as the use is not contraindicated); See also Krauss, *Loosening the FDA's Drug Certification Monopoly: Implications for Tort Law and Consumer Welfare*, 4 GEO. MASON L. REV. 470 (1996) (stating that writing an off-label prescription is not per se negligent, and the standard of care is usually established by evidence of community medical standards).

The American Medical Association's policy is that the doctor may prescribe a drug off-label when the off-label use is based on sound scientific evidence and sound scientific opinion. Substantial evidence has been defined as two or more adequate and well-controlled studies performed by experts qualified by scientific training and experience. See Rayburn & Farmer, *Off-Label Prescribing During Pregnancy*, 24 OBSTET. & GYNECOL. CLIN. N. AM. 471 (1997).

A doctor could be subject to malpractice if he denied a patient what could have been the best possible treatment because that treatment was not included in the drug's official labeling. See *Policy Statement – Unapproved Uses of Approved Drugs: The Physician, the Package Insert, and the Food and Drug Administration: Subject Review*, 98 PED. 143 (1996).

²¹¹See Marlene Cimon, *Public Policy: FDA's Approval Process Faces Challenge in New Senate Bill Finding the Proper Balance Between Protecting and Overburdening Americans is at the Heart of Renewed Debate Over the Agency's Mission*, LOS ANGELES TIMES, July 22, 1997, at A5.

²¹²Veronica Henry, *Off-Label Prescribing: Legal Implications*, 20 J. LEGAL MED. 365 (1999).

²¹³*Id.*

²¹⁴See Steven R. Salbu, *The FDA And Public Access To New Drugs: Appropriate Levels Of Scrutiny In The Wake of HIV, AIDS, and the Diet Drug Debacle*, 79 B.U. L. REV. at 189.

²¹⁵Veronica Henry, *Off-Label Prescribing: Legal Implications*, 20 J. LEGAL MED. at 365.

expensive and time-consuming for drug-makers to have to file a new drug application with the FDA each time they discovered a new use for their drug.²¹⁶ Drug makers would not have an incentive to go through the timely and costly process, since “if an off-label use is already well known among physicians, then adding it to the label would have little effect on sales. Furthermore, because less than the full life of the patent is remaining, it is more difficult for a drug manufacturer to recover the monetary investment in seeking approval.”²¹⁷ Proponents cite the vast portion of today’s drug use that is off-label as support for the practice, claiming that off-label use has become an entrenched, important, and indispensable part of modern medical therapy.²¹⁸

While off-label use is common and legal, the diet drug experience demonstrates that it can lead to problems when “safe” drugs are used in different combinations and for different time periods than the FDA has approved. “The FDA agrees that there are safe off-label uses for drugs, but some uses are hazardous. For example, Duract, an effective short-term painkiller, proved dangerous when prescribed beyond ten days, which doctors routinely did. Heart drugs used to treat severe heart irregularities prescribed off-label for slight arrhythmia have caused an estimated 50,000 deaths.”²¹⁹ Doctors are not regulated in their off-label prescriptions, even when these prescriptions in effect create a new drug different from the one that received FDA approval. Doctors who prescribed fen-phen and those who prescribe other off-label drugs are, “in effect, creating a new drug that has not been proved generally safe and effective for human consumption”²²⁰ Opponents of off-label use argue that “the lack of regulatory control over off-label applications endangers human health and human life.”²²¹ They claim that any benefits from off-label use come at a high price,

²¹⁶See *id.*

²¹⁷*Id.* at 369.

²¹⁸See *id.*

²¹⁹Rebecca Porter, *Manufacturers May Promote Off-Label Uses For Drugs*, 35-OCT TRIAL 92 (1999).

²²⁰Jaime A. Wilsker, *One Half-Phen In the Morning/One Fen Before Dinner: A Proposal For FDA Regulation of Off-Label Uses of Drugs*, 6 J.L. & POL’Y at 798.

²²¹Steven R. Salbu, *Off-Label Use, Prescription, and Marketing of FDA-Approved Drugs: An Assessment of Legislative and*

since off-label drug uses/prescriptions “lack the FDA imprimatur, and therefore also lack the consumer safeguarding we usually associate with prescription drugs. The law requires that manufacturers submit rigorously developed evidence of safety and efficacy to receive approval to market a drug for purposes noted in the labeling. No such requirement is imposed in regard to subsequent, off-label uses. Accordingly, information regarding proper dosage, as well as drug safety and efficacy for the off-label application, need not be collected or recorded.”²²² Opponents of off-label drug use characterize it as ‘experimenting on the public’ and often cite the fen-phen fiasco as evidence for their claim that off-label drug use can be harmful as well as beneficial.²²³

Off-Label Use and Physician Liability in Fen-Phen Cases

Off-label use can be an issue in attempting to hold the prescribing doctor liable for giving a patient the fen-phen combination for longer periods than originally approved by the FDA.²²⁴ “As the FDA interprets the law, after the FDA approves a drug with its labeling, the physician ‘is then responsible for making the

Regulatory Policy, 51 FLA L. REV at 202.

²²²*Id.*

²²³See *id.* at 203.

²²⁴Although individual doctor liability is of importance when discussing off-label drug use, physician liability is not the focus of this paper. However, physician liability is clearly a key issue in fen-phen litigation. In addition to liability for off-label prescriptions, plaintiffs will “allege that physicians prescribed the drugs for cosmetic weight loss, notwithstanding the fact that the drugs were designed to treat obesity, as defined by a high body mass index. They will also assert that physicians exceeded the daily dosage recommendations and failed to monitor the patients for adverse side effects.” Evans and Kerner, *A Primer on Fen-Phen Litigation: Allegations and Defenses*, 65 DEF. COUNS. J. at 359.

However, whether or not a physician was negligent in a particular fen-phen case is fact specific and depends on the patient’s weight/health problems and the individual doctor-patient relationship and interaction concerning the fen-phen prescription. While clearly in many cases there was no real doctor-patient relationship to speak of, where patients got fen-phen off the internet or from “pill mills”, in other cases doctors did discuss the risks they were aware of (PPH) with their patients and conduct a reasoned analysis of whether the patient’s obesity problem warranted the use of fen-phen. “The feasibility of a negligence claim depends on each patient’s experience with their doctor.” Caren A. Crisanti, *Product Liability and the Prescription Diet Drug Cocktail, Fen-Phen: A Hard Combination to Swallow*, 15 J. CONTEMP. HEALTH L. & POL’Y at 226. See also Interview with Dr. Tori Marnell (March 18, 2000).

Whether or not doctors are liable will depend on the particular situation of the doctor and the patient, and “physicians who saw their patients on a regular basis and performed routine physical examinations before prescribing these drugs will probably fare better than those who casually prescribed the drugs without adequate follow-up.” Evans and Kerner, *A Primer on Fen-Phen Litigation: Allegations and Defenses*, 65 DEF. COUNS. J. at 359.

The liability issues in this paper concentrate on American Home Products. The issue of risk-benefit analysis and doctor patient relationships is discussed in the section on cosmetic weight loss and obesity, which are important issues in the fen-phen experience.

final judgment as to which, if any, of the available drugs the patient will receive in light of the information available in the labeling and other adequate scientific information available to him”²²⁵ In a Philadelphia fen-phen PPH trial, the prescribing doctor was held liable for half of the \$8 Million verdict. The doctor prescribed fen-phen for the plaintiff between 1995 and 1997.²²⁶ The plaintiff’s lawyer stated that “the claim against [the prescribing doctor] was that he not only prescribed the drug beyond the two weeks recommended by the manufacturer, but he prescribed it for years... and he prescribed it until she [the plaintiff] called him and said that she had heard on CNN when she was in Italy touring that there were side effects”²²⁷ The plaintiff’s expert at trial testified that “having prescribed the medication for a longer period than the manufacturer recommended, Guinta [the prescribing doctor] should have monitored Scott [the plaintiff] more closely than he had.”²²⁸ The lawyer for the defendant doctor “countered with evidence that ‘off-label’ usage of the drug was legal and ethical and appropriate in [this] case.”²²⁹ The plaintiff won a verdict of \$8 million, which the jury decided was to be equally split between American Home Products and the prescribing doctor (the doctor filed a cross claim against American Home Products after the plaintiff filed suit against him.) The \$8 million verdict was compensation for pain and suffering, lost wages (the plaintiff was a well-known jazz musician) and medical expenses.²³⁰

Argument Off-Label Use Should Be Illegal For Diet Drugs

Overall, off-label use has benefits and drawbacks. It has led to numerous innovations in medicine and is especially critical in the context of AIDS and oncology. However, in the fen-phen situation it was not a great

²²⁵Margaret Gilhooley, *When Drugs are Safe For Some But Not Others: The FDA Experience and Alternatives for Products Liability*, 36 HOUS. L. REV. 927, 939 (1999).

²²⁶See Lori Litchman, *Philadelphia Jury Returns \$8M in Fen-Phen Case*, THE LEGAL INTELLIGENCER, Feb 24, 2000.

²²⁷*Id.*

²²⁸*Id.*

²²⁹*Id.*

²³⁰See *id.*

success. Diet drugs present a special situation because of the danger of use in cases where the patient is not suffering from any disease (obesity) but rather wishes to improve his or her appearance. In the context of diet drugs, where the only real potential to reign in cosmetic weight loss use lies with the label, the FDA should not allow off-label use. This would still allow for off-label use in cases where it leads to new drug innovations, but it would address the problem of allowing off-label use in the diet drug context where the label is the prime tool in preventing non-obese persons from taking the drugs. Such a rule could be enforced by imposing physician liability in cases where diet drugs cause health problems and they were not prescribed to a clinically obese person. This would provide an incentive to keep diet drugs for the obese. Where the person is clinically obese and the FDA approved the drug for the treatment of obesity, presumably the FDA had already considered the risks-benefit analysis and decided that the drugs' risks were outweighed by its benefits in treating obesity and its attendant health harms. Where the use was off-label and the patient was not obese, the doctor would be liable. This would go a long way towards preventing use of diet drugs where the risks do outweigh the benefits of the drugs when the patient does not suffer from the disease the drugs were meant to treat. Off-label use is generally beneficial and should be permissible, but in the diet drug context, with the rampant cosmetic weight loss use problem, off-label use should not be permitted.

PART IIFEN-PHEN LITIGATION AGAINST AMERICAN HOME PRODUCTS

LIABILITY OF DRUG MANUFACTURERS FOR PRESCRIPTION DRUGS

The main defendant in the fen-phen products liability cases has been American Home Products and its A.H.

Robins and Wyeth-Ayerst subsidiaries, who marketed Pondimin and Redux.²³¹ Plaintiffs are currently claiming that American Home Products misled doctors, consumers, and regulators about the dangers of Redux and Pondimin.²³² In the opening statements in the Vadino New Jersey medical monitoring class action trial²³³, lead plaintiffs' attorney Esther Berezofsky, said that American Home Products should be held liable because it "enjoyed healthy sales while withholding information from consumers about its potentially deadly side effects" and that it was "not being honest with the FDA, not telling the doctors, and not telling you [the jury]" about the health risks associated with Pondimin.²³⁴ One plaintiff's lawyer, Paul Rheingold, wrote that "there is blame enough to go around. The doctors who set up store-front fen-phen clinics and prescribed the drugs are obvious culprits. So are drug companies that profited financially from the fad and may have neglected to pass on information about deadly side effects."²³⁵ There are several claims plaintiffs can bring against American Home Products, and the most likely success plaintiffs would have is with a failure to warn claim regarding the increased PPH risk. Since the drugs were all FDA approved, a strict

²³¹There are other fen-phen defendants, namely Interneuron Pharmaceuticals, Laboratories Servier, and the phentermine defendants (including Eon Laboratories and SmithKline Beecham). However, due to the dominance of American Home Products as the most prominent defendant, this paper only discusses litigation against American Home Products. American Home Products is also the defendant involved in the proposed Settlement Agreement dealt with at length in this paper.

²³²See Bob Van Voris, *Diet Drug Class Action Set For August Trial: Plaintiffs Are Seeking Medical Monitoring*, NAT'L L.J., Aug. 9, 1999, at A6.

Judge Bechtel described the variety of claims brought by fen-phen plaintiffs as follows: "The claims in individual Diet Drug Litigation actions vary, but they principally allege state law claims including product liability, negligence, misrepresentation and breach of warranty. Some of the cases request punitive damages. The plaintiffs in these actions allege that their ingestion of the Diet Drugs caused various illnesses, including, but not limited to PPH and valvular heart disease. In addition, many actions brought by plaintiffs without present injury request legal or equitable relief in the form of medical monitoring or refunds of purchase prices." In re Diet Drugs (Phentermine, Fenfluramine, Dexfenfluramine) Products Liability Litigation, *Jeffers v. American Home Products Corporation*, No. CIV. A. 98-20626 1999, Memorandum and Pretrial Order No. 865, U.S. District Court for the Eastern District of Pennsylvania, Aug. 26, 1999, WL 673066 (E.D. Pa.).

²³³Judge Marina Corodemus dismissed the jury in the Vadino trial on October 4, 1999 as American Home Products and plaintiffs' lawyers neared completion of the Settlement Agreement. The Vadino class was seeking echocardiograms for a 10 year period. The cost of such a medical monitoring program could be up to \$1 billion for American Home Products. Judge Corodemus said the case was not dismissed, and that if a Settlement was not reached she would conduct a bench trial. The Settlement was announced shortly thereafter, and it encompasses all of the plaintiffs in the Vadino class action. See Edward R. Silverman, *Diet Pill Jury is Dismissed as Settlement Grows Near*, NEW JERSEY STAR LEDGER, Oct. 5, 1999, available online at www.nj.com/business/ledger/d28061.html; See also Matt Ackermann, *Fen-Phen Lawyers Stick to Texas Formula: As New Jersey Trial Continues, A Similar Class-Action Suit is Dismissed in California*, NEW JERSEY LAW JOURNAL, Aug. 23, 1999.

²³⁴Matt Ackermann, *In Fen-Phen Trial, the Uninjured Sue for Preventative Maintenance*, NEW JERSEY LAW JOURNAL, Aug. 16, 1999.

²³⁵Paul D. Rheingold, *Fen-Phen and Redux: A Tale of Two Drugs - The Story of How Fen-Phen and Redux Came to Be Used By 6 Million Americans is Chilling*, 34 TRIAL at 82.

liability claim is not likely to succeed. In addition, if the valvular heart disease risk was not uncovered until shortly before the withdrawal of Redux and Pondimin from the market, a failure to warn claim for the valve problems will not likely be successful. A discussion of the alleged wrongdoing of American Home Products with respect to Redux and Pondimin follows in the section below on American Home Products. Plaintiffs' lawyers have alleged a host of irresponsible actions and failures to warn on the part of American Home Products, while the company has steadfastly maintained no wrongdoing in relation to the diet drugs.

Failure to Warn Claims

If American Home Products supplied an adequate warning about fenfluramine and dexfenfluramine, AHP will not be held strictly liable for adverse effects resulting from ingestion of these drugs.²³⁶ Comment k to § 402A of the Restatement (Second) of Torts provides that strict liability is not applicable to a sale of a product that is incapable of being made safe for its intended use, so long as its utility outweighs its apparent risks²³⁷ and a warning is supplied. Comment k contains a list of examples of “unavoidably unsafe” products and all refer to prescription drugs.²³⁸ “Many jurisdictions have applied comment k to cases involving the liability of drug manufacturers [and] [e]ven if a new drug proves less valuable than initially perceived, the manufacturer may still be exempt from strict liability under comment k provided it was unaware of the drug’s risks. Therefore, an manufacturer that acts reasonably in manufacturing and distributing an unavoidably unsafe product will not be subject to strict liability for harm caused by this product.”²³⁹ The law states that “a manufacturer is not strictly liable for injuries caused by a prescription drug so long as the drug was properly prepared and accompanied by warnings of its dangerous propensities that were either known or

²³⁶See Caren A. Crisanti, *Product Liability and the Prescription Diet Drug Cocktail, Fen-Phen: A Hard Combination to Swallow*, 15 J. CONTEMP. HEALTH L. & POL’Y at 220.

²³⁷See RESTATEMENT (SECOND) OF TORTS § 402A cmt. k (1965).

Courts generally assume that the health benefits of drugs outweigh risks that result from their use.

²³⁸See *id.*

²³⁹Jaime A. Wilsker, *One Half-Phen In the Morning/One Fen Before Dinner: A Proposal For FDA Regulation of Off-Label Uses of Drugs*, 6 J.L. & POL’Y at 815 – 816.

reasonably scientifically knowable at the time of distribution.”²⁴⁰ As a matter of law, if a drug is properly prepared and has received FDA approval, the product cannot be “defective”.²⁴¹ The policy rationale for this is that drug companies would be discouraged from undertaking research and development of new beneficial pharmaceuticals if they were held strictly liable for prescription drug adverse effects.²⁴²

The manufacturer still has a duty to warn of drug dangers. The duty to warn applies to the medical profession rather than the individual patient.²⁴³ The manufacturer must warn the attending physician of the risks associated with the drug’s use. The manufacturer also has a continuous duty to remain informed of scientific developments relating to the manufacturer’s drug and to inform the medical profession of any additional adverse effects associated with the drug’s use. If the manufacturer has given proper warnings of potential dangers associated with the drug and the warnings were read by the prescribing physician, the manufacturer

²⁴⁰Id.

²⁴¹See Grundberg v. Upjohn Co., 813 P.2d 89, 97 (Utah 1991).

²⁴²See Brown v. Superior Court, 751 P.2d 470, 482-83 (Cal. 1988).

²⁴³This is the “learned intermediary” doctrine. In some circumstances the learned intermediary doctrine has been eroding, and some of these contexts are relevant in the fen-phen situation. See Perez v. Wyeth Laboratories, Inc., 1999 WL 606729 (N.J.) In Perez, on Aug. 9, 1999 the New Jersey Supreme Court limited the learned intermediary doctrine with respect to drugs where the manufacturer engaged in extensive direct to consumer advertising. The court reasoned that the medical profession had changed with the advent of direct to consumer drug advertising, along with the prevalence of HMO’s and third party payers of drugs. The court held that drug manufacturers could not engage in direct to consumer advertising while maintaining that they did not have to inform the consumer of the drug’s risks. Direct to consumer advertising attempts to reach out to patients rather than their doctors, making patients the ones who required/would be receptive to the manufacturer’s warnings. See id. Fen-phen was not per se direct marketed to consumers as was the Norplant contraceptive at issue in Perez. However, weight loss centers like Jenny Craig ran ads that touted “Medical Weight Loss” programs, arguably reaching patients/consumers directly without requiring the consumer to go through a doctor to first get the idea of taking diet drugs. See Interview with Dr. Tori Marnell (March 18, 2000).

In several states there is a narrow exception to the learned intermediary doctrine for contraceptives. This is because the physician plays a passive role in prescribing contraceptives to women. Often after an initial consultation with a doctor a woman will get a contraceptive prescription for up to a year, with limited requirements for continued physician contact. In such a situation, several courts have held that there is a duty to warn the patient directly rather than the medical profession. In the Linnen PPH wrongful death trial, the plaintiffs tried to argue that that exception to the learned intermediary doctrine applied with fen-phen. The plaintiffs claimed that the fen-phen prescription situation was very similar to the birth control prescriptions. They said that most fen-phen users were healthy young women and often there was very limited contact with doctors, since the drugs were often handed out at “pill mills” run by nurses and were easily available over the phone and internet. The Linnen court held that such a characterization was inaccurate in the Linnen case and did not hold that the birth control exception to the learned intermediary doctrine generally applied in fen-phen cases. Mary Linnen had gone to her doctor to inquire if there was a medical reason that she was having difficulty losing weight. Her doctor conducted numerous tests to determine if she had a medical problem that was preventing her from losing weight. Only when medical tests came back negative did her doctor suggest fen-phen. In addition, Mary Linnen’s doctor only gave her a six-week prescription as opposed to the typical six month to one year prescription for contraceptives. Based on these facts, Judge Brassard in Linnen distinguished the fen-phen situation from the birth control context and held that the learned intermediary doctrine did apply. See Linnen v. A.H. Robins Company, Inc., 2000 WL 89379 (Mass. Supp. 1999).

has fulfilled its duty and is not liable.²⁴⁴ However, “when the warning to the intermediary is inadequate or misleading, the manufacturer remains liable for injuries sustained by the ultimate user.”²⁴⁵ The company is also not liable if the prescribing doctor relies solely on his own knowledge when deciding to prescribe a drug, although “even in a situation where a doctor is negligent in prescribing a drug, the manufacturer’s liability will not be vitiated when it has failed to warn the ‘learned intermediary.’”²⁴⁶

In the case where a manufacturer fails to provide a warning, that manufacturer is not strictly liable for failure to warn without a showing of proximate causation that an adequate warning would have prevented the injury. “If such an injury has never occurred before and with the exercise of due care, the manufacturer could not have foreseen such an injury, there can be no duty to warn.”²⁴⁷

Plaintiffs can also bring a negligent failure to warn claim against American Home Products. A drug manufacturer has a duty to warn for risks it reasonably should have been aware of. The reason for this negligence cause of action is so manufacturers do not put their heads in the sand in an attempt to avoid learning about new risks associated with the drugs they market. This may be a strong claim for fen-phen plaintiffs, if they can prove that American Home Products knew or should have known about the valvular heart disease problems. “Manufacturers are required to continually investigate and update the information and labeling of their products on the market; this includes conducting appropriate tests as new questions arise.”²⁴⁸ Plaintiffs can also allege that the warnings that American Home Products did provide were diluted by the mass media promotion and hype concerning the fen-phen combination, which gave rise to a duty for American Home Products to change its warnings to be effective in light of the background dilution. Plaintiffs could argue that American Home Products was fully aware of the widespread use of the drug combination and

²⁴⁴In the interview with Dr. Marnell, she indicated that American Home Products had warned of the dangers of PPH associated with fenfluramine and dexfenfluramine. She said that she went over that increased PPH risk with each patient who took fen-phen. See Interview with Dr. Tori Marnell (March 18, 2000).

²⁴⁵In re Norplant Contraceptive Prods. Liab. Litig., 955 F. Supp. 700, 703 (E.D. Tex. 1997).

²⁴⁶Caren A. Crisanti, *Product Liability and the Prescription Diet Drug Cocktail, Fen-Phen: A Hard Combination to Swallow*, 15 J. CONTEMP. HEALTH L. & POL’Y at 220.

²⁴⁷*Id.*

²⁴⁸*Id.* at 230.

should have done additional testing to ensure the safety of the combined use of Redux and Pondimin with phentermine for longer periods of time. Plaintiffs can claim that manufacturers are “in the best situation to assess the pharmacodynamics of their products, and for this reason plaintiffs will allege that the manufacturers knew of the risks associated with the diet drugs but chose to conceal or downplay them... just what the manufacturers knew and when they knew it will be a question for the trier of fact.”²⁴⁹ It appears that American Home Products may have had information about PPH cases that it did not report to the FDA, but the valvular heart disease problem basically appears to have been discovered by the Mayo Clinic in 1997. Perhaps some evidence may emerge that shows AHP knew of the valvular heart disease problem all along, but as of the present time this is not the case.²⁵⁰ Overall, “when evaluating the strength of a fen-phen plaintiff’s case, counsel should consider whether the warning could be deemed to have been diluted by over-promotion, statements by salesmen, and/or language in the warning. Attorneys will also need to review reported scientific studies, reports submitted to the FDA, and any reports submitted to the manufacturer to determine if the manufacturer should have known of the risk.”²⁵¹

Where the drug manufacturer has provided a label, issues of federal preemption come up with state law tort claims, since the FDA mandates what information must appear on the drug’s label. With the fen-phen case such preemption issues may be overcome because fenfluramine and dexfenfluramine were not being used in the manner indicated on their labels.²⁵² The test in a negligent failure to warn case is:

²⁴⁹Evans and Kerner, *A Primer on Fen-Phen Litigation: Allegations and Defenses*, 65 DEF. COUNS. J. at 358.

²⁵⁰There have been claims that the valvular problems were known about to a degree as early as 1994, but the general consensus is that they were found by Dr. Connolly and her colleagues at the Mayo Clinic in 1997.

²⁵¹Caren A. Crisanti, *Product Liability and the Prescription Diet Drug Cocktail, Fen-Phen: A Hard Combination to Swallow*, 15 J. CONTEMP. HEALTH L. & POL’Y at 231.

²⁵²The law is unclear on federal pre-emption of state law tort claims by the FDCA. The Fifth Circuit has held in *Hurley* that FDA warning regulations may implicitly pre-empt failure to warn claims. The court in *Hurley* did place a limit on such pre-emption, stating that a manufacturer may still be liable for failure to warn if it did not provide the FDA with information relevant to approval of the drug or relevant information after the drug’s approval. Other courts have disagreed with *Hurley* and held that FDA labeling requirements do not pre-empt state failure to warn claims. Such cases include *In re Tetracycline Cases*, *Mazur v. Merck & Co.*, and *Feldman v. Lederle Lab.* See Darrell M. Grams and Sean M. Higgins, *Food, Drug and Cosmetic Act Regulations May Trump State Failure-To-Warn Liability*, NATL. L.J., March 15, 1999, at B8. Overall, the law is unsettled and fen-phen “counsel should be cognizant of arguments for and against conflict pre-emption. In rejecting implied conflict pre-emption, courts have characterized FDA regulations as ‘minimum requirements.’ Courts have found strong support for this in the FDA’s reliance on manufacturers to provide clinical and other data to formulate and evaluate warnings. A close reading

whether the physician, and therefore, the patient, was provided with the detail needed to make an informed decision regarding the drug therapy. A plaintiff must prove three elements in a negligent breach of duty to warn claim: (1) the plaintiff must show the manufacturer knew or should have known the danger of the drug; (2) the manufacturer must not have had any reason to believe that those taking the drug would realize the drug's danger; and (3) the plaintiff must prove the manufacturer did not take reasonable steps to inform those taking the drug of its dangerous condition. If the plaintiff proves all three elements, the manufacturer may be held liable for damages.²⁵³

One issue that may come up in some jurisdictions regarding the negligence of American Home Products or the negligence of the prescribing doctor is contributory negligence. Statements by some fen-phen patients that they would take the drugs again even after suffering from heart valve damage and efforts by many former fen-phen users to obtain fen-phen from Mexico and Thailand indicate that patients may have ignored warnings in their quests to obtain the diet drugs. One man who lost eighty pounds on fen-phen and gained it back after Redux/Pondimin were withdrawn from the market said "I'm not so certain I many not risk fen-phen again to lose weight. But that's a fat person talking."²⁵⁴ Such behavior indicates that in some situations a stronger warning by American Home Products would not have led to a different outcome in terms of fen-phen usage. "In the fen-phen situation, there may even be evidence to show that the patient, given adequate warning, would still have decided to take the drug, despite the drug's inherent risk in an effort to lose weight. This will play an important role in pure contributory negligence jurisdictions."²⁵⁵

The issue with American Home Products is whether they adequately warned the medical profession about the true level of increased PPH risk (or the true level they should have reasonably been aware of), and also whether they informed the medical profession about the risk American Home Products knew or reasonably

of FDA labeling regulations, however, suggests potential conflicts with state common law failure to warn liability. For example, a judgment against a manufacturer for failing to warn of a condition the FDA does not deem severe or supported by reasonable evidence potentially conflicts with the FDA warning regulation." *Id.*

²⁵⁴Kris Huntley, *Fen-Phen King Turns Tables On Drug Maker: Once a Promoter and User of the Weight-Loss Drug Combination, John Trevena Has Filed a Civil Suit Against Drugmaker Wyeth-Ayerst Laboratories, Inc., Accusing It of Fraud*, ST. PETERSBURG TIMES, Oct. 10, 1999, Business Section.

²⁵⁵Caren A. Crisanti, *Product Liability and the Prescription Diet Drug Cocktail, Fen-Phen: A Hard Combination to Swallow*, 15 J. CONTEMP. HEALTH L. & POL'Y at 231.

should have been aware of regarding valvular heart disease. American Home Products had a duty to warn the health care profession about risks it knew about that were associated with Redux and Pondimin and also about risks it reasonably should have known about regarding the use of Redux and Pondimin. Whether it did this is an issue to be resolved in litigation.

The ultimate liability of American Home on the failure to warn claim is uncertain.²⁵⁶ It can be summed up as follows:

In the fen-phen situation, there were warnings regarding the danger of the possibility of brain damage and pulmonary hypertension. The heart-valve defects were only discovered shortly before the ban. The manufacturers followed FDA guidelines to warn doctors of the known dangers, and there appears to be no evidence to show that the manufacturers of fenfluramine and phentermine should have known of potential heart valve disfigurement caused by the use of the combined drugs. Here, it must also be noted that the drugs were not manufactured jointly, the doctor was solely responsible for prescribing their use in combination. Still, a plaintiff's case against the manufacturer may have some merit when arguments are posed that more thorough testing should have been conducted. Possible justifications for better testing are that the manufacturer had reason to believe the diet drug would be misused, or that there was widespread use of the drug cocktail and therefore, testing the combination of the drugs was necessary.²⁵⁷

Strict Liability/Design Defect Claims

A manufacturer can be held strictly liable for the side effects of a drug if the drug is unreasonably dangerous to the consumer. To sustain a strict liability claim, the plaintiff must prove that the drug was inherently

²⁵⁶There may also be causation problems in valvular heart disease fen-phen litigation. "As the facts stand, there is no definite causal connection between the drugs and the heart problems. Cardiovascular tests were never run for this pool of patients before treatment to determine if they had heart problems prior to drug therapy. Furthermore, when dealing with an overweight population, there is always a tendency toward heart problems due to the strain on the heart caused by excess weight" Caren A. Crisanti, *Product Liability and the Prescription Diet Drug Cocktail, Fen-Phen: A Hard Combination to Swallow*, 15 J. CONTEMP. HEALTH L. & POL'Y at 223. While the Mayo clinic studies found approximately 30% of fen-phen users suffered from valvular heart disease as opposed to less than 5% for the background population, some later studies have found no causal connection between valvular heart disease and fen-phen ingestion. The Mayo clinic also only had a pre-fen-phen use echocardiogram for one patient who had valvular heart disease after taking fen-phen. The pre-diet drug echocardiogram for that patient was normal. Several doctors have claimed that further studies need to be completed on overweight people who recently lost weight with before and after echocardiograms in order to determine if there is a causal connection between fen-phen and valvular heart disease. For PPH claims the IPPHS provides a solid basis for a causal connection between PPH and anorectic drugs, so causation will not likely be a heavily contested issue in PPH claims as opposed to valvular heart disease. See CNN Interactive, *Valvular Heart Disease Associated With Fenfluramine-Phentermine - Dr. Heidi M. Connolly - Manuscript Of Study Submitted To New England Journal of Medicine*, CNN WEBSITE, July 8, 1997, available online at www.cnn.com/Heath/0/07/08/fenphen.report/.

defective.

In defect litigation, prescription drugs are treated differently than non-drug items such as planes and automobiles. Prescription drugs are inherently different from these other items, as they are inherently unsafe to a certain degree and prone to cause side effects.²⁵⁸ The Restatement (Third) of Torts does not consider a prescription drug with adequate warnings to the physician to be defective if the drug is safe and effective for some patients but not for others. The Restatement (Third) of Torts holds a prescription product defective “if the foreseeable risks of harm... are sufficiently great in relation to its foreseeable therapeutic benefits that reasonable health care providers, knowing of such foreseeable risks and therapeutic benefits, would not prescribe the drug... for any class of patients.”²⁵⁹ This contrasts with the general test for non medical products, which asks whether “the foreseeable risks of harm posed by the product could have been reduced or avoided by the adoption of a reasonable alternative design” The test for prescription drugs is more difficult to meet so as to give pharmaceutical companies enough discretion to develop useful drugs. The Restatement assumes that doctors informed by adequate labeling will be able to ensure that the right drugs go to the right patients, and also that the regulatory system is the best way to set drug design standards.²⁶⁰ The Restatement (Third) defect test “looks not at the existence of reasonable alternatives, but at whether, in the judgment of reasonable and informed health care providers, the risks of the product outweigh its benefits for all classes of patients.”²⁶¹ FDA approval is extremely significant in defect litigation, since “[i]n most cases, the particular use of any drug approved by the FDA is likely to be considered a reasonable use... In the typical case, when the FDA-approved use is a reasonable use, the Restatement test will preclude any finding of a design defect with respect to risks from off-label and other misuses of approved drugs, even if these risks are unreasonably high. The Restatement test for defective drugs, in effect, leaves the decision on the use of

²⁵⁸*Id.* at 232.

²⁵⁹RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIABILITY § 6(c) & cmt. b (1998).

²⁶⁰See Margaret Gilhooley, *When Drugs are Safe For Some But Not Others: The FDA Experience and Alternatives for Products Liability*, 36 HOUS. L. REV. 927 (1999).

²⁶¹*Id.* at 936.

an approved drug for other uses, even unreasonable ones, to the judgment of a reasonable physician guided by adequate warnings.”²⁶² The test to determine if a product has a design defect “for prescription drugs narrowly focuses only on the risks and benefits of the particular product, and, unlike the test for non-drug products, this test does not expressly provide for a comparison with other products or designs... A drug that has usefulness to any class of patients is not defective in design even if it is harmful to other patients.”²⁶³ However, there can be liability for failure to warn even if the drug is not “defective”.

American Home Products will likely prevail if plaintiffs attempt to bring a strict liability claim. Fenfluramine and dexfenfluramine were approved by the FDA. They were used in an off-label manner for longer time periods and in combination with phentermine, but American Home Products was not directly promoting such uses in accordance with the law at that time. The off-label prescribing doctor legally was able to make the choice to use Redux and Pondimin in the fen-phen combination. The drugs were approved by the FDA through the normal approval process, and the FDA presumably considered that their risks were outweighed by their benefits. As to whether the problem was foreseeable, the valvular heart damage problem was not known at the time the drugs were being widely prescribed to the U.S. population. The increased PPH risk was known, and arguably American Home Products kept the information from the FDA.

American Home Products can also take advantage of two strong affirmative defenses for strict liability claims against it. First, a manufacturer cannot be held strictly liable if the benefit of the drug outweighs its risks. In cases of severely obese plaintiffs, American Home Products will have a strong argument that the risks of obesity outweighed the risks of valvular heart damage or an increased risk of PPH. This defense may not be as strong for plaintiffs who took fen-phen for cosmetic reasons, but American Home Products never per se promoted the use of fen-phen for people with a BMI below 30 or for any type of cosmetic weight loss use. Another affirmative defense available to American Home Products is the “comment k” defense,

²⁶²Id.

²⁶³Id. at 930.

which asserts that the drug was unavoidably unsafe but that its benefits outweighed its risks. AHP has to prove that Redux and Pondimin could not be made safe at the present time due to the current limitations of human knowledge, but that there was such a high degree of social need for the two drugs that their use was warranted by their benefits.²⁶⁴ American Home Products could assert the high social need for Redux and Pondimin given the high percentage of Americans who suffer from a serious weight problem and the overwhelming desire of those people to lose weight with the assistance of diet drugs.²⁶⁵

AHP also has an advantage on a strict liability claim in that “[h]istorically, courts have avoided deciding cases on strict liability theory. In light of the fact that diet products are put on the market for the purpose of alleviating a health problem, there is a general belief that manufacturers should not be held strictly liable if the risk is reasonable. In addition, there is no flexibility for fact-specific circumstances under strict liability. The resultant risk of a lawsuit poses a serious threat that could deter health research.”²⁶⁶

There is a strict liability failure to warn claim that plaintiffs could bring in the fen-phen cases. The duty to warn under a strict liability claim requires the manufacturer to “warn or give directions to prevent the drug from being unreasonably dangerous. The test for strict liability for duty to warn... is whether the doctor was properly apprised of all the information concerning the drug.”²⁶⁷ American Home Products was not aware of the heart valve dangers associated with combined use of fenfluramine/dexfenfluramine and phentermine. Comment j to § 402A of the Restatement (Second) of Torts suggests that the law does not impose a duty to warn when the danger is not generally known. Fen-phen users were warned of an increased PPH risk but not the valvular heart damage risk, which was not known until the Mayo Clinic identified the problem in 1997.²⁶⁸

²⁶⁴See 63 AM. JUR. 2D PRODUCTS LIABILITY § 591 (1996).

²⁶⁵See Caren A. Crisanti, *Product Liability and the Prescription Diet Drug Cocktail, Fen-Phen: A Hard Combination to Swallow*, 15 J. CONTEMP. HEALTH L. & POL’Y at 233.

²⁶⁶*Id.*

²⁶⁷*Id.* at 235 – 236.

²⁶⁸See *id.* at 237.

The above discussion presents the claims that plaintiffs could bring against American Home Products and assesses their viability based on the facts of the fen-phen situation. The valvular heart disease claims will likely be settled by the proposed Settlement Agreement, but these issues will come out with the opt-out plaintiffs. In addition, the PPH cases will be tried or settled individually, so liability in PPH cases will continue to be a viable concern. Overall, there are two sides to the American Home Products liability story and the cases are often fact specific. In essence, “[a] successful claim in a fen-phen case will depend largely on subjective circumstances unique to the case, including who is the complainant. Examples of issues that will have a bearing on the success of a case are: whether the plaintiff followed a doctor’s instructions, whether the instructions were adequate, and whether the plaintiff read, and understood the warnings, if there were any.”²⁶⁹ The liability for PPH will be determined case by case, and the fate of the Settlement will basically cover the liability in the valvular heart disease arena.

THE DEFENDANT - AMERICAN HOME PRODUCTS

Basic Overview of American Home Products

American Home Products is one of the world’s largest pharmaceutical companies. It was founded in 1926, has annual sales of \$13.6 billion, and operates in over 100 countries. American Home Products spent over \$1.7 billion in research and development in 1999. American Home Products is a leader in the prescription drug market, over the counter drugs, vaccines, biotechnology, agricultural products, and animal health care.²⁷⁰ American Home Products’ principal products include several popular prescription medications and

²⁶⁹*Id.* at 240

²⁷⁰*See* “*American Home Products Corporation*” *Corporate Overview*, AMERICAN HOME PRODUCTS WEBSITE, available online at www.ahp.com/overview.htm.

over the counter products, including Premarin (hormone replacement therapy), Lo/Ovral (a birth control pill), Advil, Anacin, Dimetapp, Dristan, Robitussin, Centrum, and Chapstick.²⁷¹ American Home Products' present operating units include Wyeth-Ayerst, Whitehall-Robins (formerly A.H. Robins Company), Cyanamid, and Fort Dodge Animal Health. American Home Products acquired A.H. Robins Company, with its well known products – Chapstick and Robitussin – in 1989. AHP focuses its R&D on women's health, oncology, vaccines, neuroscience, infectious disease, and hemophilia. The Chairman, President, and Chief Executive Officer of American Home Products is John R. Stafford. American Home Products' corporate headquarters are located in Madison, New Jersey.²⁷²

American Home Products marketed fenfluramine and Redux through its subsidiary Wyeth-Ayerst. Wyeth-Ayerst is the pharmaceutical unit of American Home Products, and the Wyeth-Ayerst organization includes Wyeth-Ayerst Laboratories, Wyeth-Ayerst International, Inc., and Wyeth-Ayerst Research.²⁷³ Wyeth-Ayerst is headquartered in suburban Philadelphia and employs over 40,000 people throughout the world.²⁷⁴ It provides more prescription products to Americans than any other pharmaceutical company.²⁷⁵

While American Home Products is a well-known pharmaceutical and consumer products leader, the fen-phen situation has led to serious problems for the company. "For generations, American Home Products of Madison, N.J. has stocked family medicine chests with remedies that inspire trust, including Robitussin, Preparation H, and Advil. Lately, though, some of American Home Products' most promising products have inspired something else: lawsuits, by the thousands."²⁷⁶ American Home Products' stock price has fallen significantly as a result of the liability it faces in fen-phen suits, and when it took Pondimin and Redux of

²⁷¹See *Ethical Pharmaceuticals, Vaccines and Nutritionals*, AMERICAN HOME PRODUCTS WEBSITE, available online at www.ahp.com/ahp/products.pharm.htm; See also *Consumer Health Care*, AMERICAN HOME PRODUCTS WEBSITE, available online at www.ahp.com/ahp/products/consumer.htm.

²⁷²See *Frequently Asked Questions*, AMERICAN HOME PRODUCTS WEBSITE, available online at www.ahp.com/faq.htm.

²⁷³See *Pharmaceutical R&D*, AMERICAN HOME PRODUCTS WEBSITE, available online at www.ahp.com/r&d.pharm.htm.

²⁷⁴See *Wyeth-Ayerst*, AMERICAN HOME PRODUCTS WEBSITE, available online at www.ahp.com/wyeth.htm.

²⁷⁵See *Wyeth-Ayerst Laboratories*, AMERICAN HOME PRODUCTS WEBSITE, available online at www.ahp.com/wyeth_labs.htm.

²⁷⁶Steve Sternberg, *Lawsuits: Drug Development's Side Effects*, USA TODAY, Jan 12, 2000, Health Section.

the market it lost between \$200 and \$300 million as a one-time cost of the product withdrawal.²⁷⁷ American Home Products has attempted to improve its financial position by settling the valvular heart disease fen-phen suits and ending the uncertainty surrounding its level of exposure resulting from Redux and Pondimin liability.

Recent Problems of American Home Products

In addition to the problems associated with Pondimin and Redux, American Home Products

has had a run of high-profile problems: AHP recently recalled a new rotavirus vaccine after doctors reported a link to serious bowel conditions in dozens of babies; AHP in August settled lawsuits filed by thousands of women who allegedly suffered side effects from its Norplant implantable contraceptive; and AHP in 1998 recalled the short term pain reliever Duract after 12 people suffered kidney failure. Sidney Wolfe of the non-profit watchdog organization Public Citizen Health Research Group says the cascade of calamities – and how each was handled – raises serious questions about AHP and its pharmaceutical subsidiary, Wyeth-Ayerst, and how they do business. ‘Why did they have such an unprecedented number of drugs go wrong?’²⁷⁸

Critics suggest that American Home Products’ problems demonstrate (1) The conflict pharmaceutical companies face when they must choose between loyalty to a possible new blockbuster drug and its responsibility to report any side effects when they occur; (2) The weakness of the U.S. government’s voluntary system for side effect tracking²⁷⁹ after the FDA has approved drugs for sale; and (3) The problem of doctors writing popular prescriptions to provide personal profit²⁸⁰, even when there is no medical justification for the

²⁷⁷See American Home Products Corporation, *Voluntary Recall Of Pondimin And Redux To Impact Earnings For 1997 And 1998*, AMERICAN HOME PRODUCTS PRESS RELEASES, Madison, N.J., Sept. 15, 1997, available online at www.ahp.com/releases/ahp_091597.htm.

²⁷⁹It is common for side effects to emerge after drugs are approved for sale. Often sales to the public are called “Phase IV” clinical trials, since much new information is gleaned during the initial period when the drug becomes available on a widespread basis. The FDA says it would take more than the 5,000 people who take part in most large scale drug studies to discover subtle side effects. The FDA’s adverse event reporting system is not mandatory, and the FDA depends on drug companies to voluntarily report adverse events. This was seen in the advisories sent out regarding fen-phen, which all included a request for health professionals to notify the FDA’s MedWatch Program or the manufacturers of Pondimin or Redux regarding valvular heart disease or PPH. All the notices included the MedWatch phone and fax numbers. See Steve Sternberg, *Lawsuits: Drug Development’s Side Effects*, USA TODAY, Jan 12, 2000, Health Section.

²⁸⁰This refers to the vast amounts of doctors who were prescribing fen-phen for cosmetic weight loss. Although the literature on Redux and Pondimin stated that it was only indicated for use in people with a BMI over 30, a great deal of Redux and Pondimin prescriptions were written for people who did not meet this qualification. People of all weights were requesting fen-phen in response to the national media craze surrounding the weight loss drugs. In the interview with Dr. Marnell, she indicated that she received calls from several friends and acquaintances asking her about fen-phen. She reiterated to them that Pondimin and Redux were only for those with a BMI over 30, but many other doctors did not adhere to this BMI limitation. Doctors were prescribing fen-phen over the internet and Jenny Craig and Nutri-System doctors were giving out fen-phen to

medication.²⁸¹

Alleged American Home Products Wrongdoing

Failure to Report PPH/Valvular Heart Disease Risks to FDA

Much of the fen-phen litigation has brought to light alleged wrongdoing by American Home Products, although it maintains it did not commit any such wrongdoing in its handling of Pondimin and Redux. Both in a trial in New Brunswick, N.J. (Vadino) and in the Lovett trial in Texas, jurors heard testimony that American Home Products had received many reports of valvular heart disease and PPH without informing the FDA. In those trials, plaintiffs' lawyers "argued that American Home [Products] concealed information from regulators, doctors and consumers about links to valvular heart disease and [PPH]".²⁸² In the Vadino trial, plaintiffs' lawyers presented evidence that American Home Products knew of over 30 cases where serious side effects occurred in Pondimin and Redux users but never reported those incidents to the FDA.²⁸³

patients who they barely knew and who did not meet the BMI requirement. In one high profile case, the wife of the Mayor of North Miami Beach, Patricia Ann Mishcon, suffered a fatal heart attack after she had been taking fen-phen for six months in an effort to lose ten pounds. Her prescribing doctor was an ophthalmologist who was operating a weight loss clinic. See Caren A. Crisanti, *Product Liability and the Prescription Diet Drug Cocktail, Fen-Phen: A Hard Combination to Swallow*, 15 J. CONTEMP. HEALTH L. & POL'Y at 243.

Note: This problem of cosmetic weight loss use was not a problem unique to fen-phen per se, it is a common problem with 'popular' drugs that Americans want even though they do not suffer from the medical problem that led to the drug's development. Viagra today is another example of this phenomenon, with doctors prescribing it over the internet and widespread use of the drug by people who do not suffer from clinical erectile dysfunction.

²⁸¹See Steve Sternberg, *Lawsuits: Drug Development's Side Effects*, USA TODAY, Jan 12, 2000, Health Section.

²⁸²Edward R. Silverman, *Diet Pill Jury is Dismissed as Settlement Grows Near*, NEW JERSEY STAR LEDGER, Oct. 5, 1999, available online at www.nj.com/business/ledger/d28061.html

²⁸³See id.

Frederick Wilson, one of AHP's medical monitors for Pondimin, testified that by 1994 the company had received reports of 41 Pondimin users with potentially fatal PPH – and that AHP did not update the drug's package insert with a warning about the problem for two years. AHP officials countered that the company was awaiting data from a large study on the lung disorder. In 1995, Wilson testified, the company received reports of heart-valve problems from Belgium. AHP experts responded that the European reports weren't alarming because the leaks were mild and typical of those commonly found in the general population. An FDA investigative report that emerged in the Lovett case found numerous deficiencies in AHP's adverse-event reporting in the USA.²⁸⁴

U.S. pharmaceutical companies are required to notify the FDA quickly of serious and unexpected adverse effects that occur in users of drugs they market. The companies “must notify the FDA regardless of whether the effects occur in the U.S. or abroad, and whether or not they appear to be related to the drug. American Home Products stated that after the Mayo study was released that they had known of the... Belgian cases and six others elsewhere in Europe. AHP said it told the FDA of ten of the cases and the FDA confirms receiving eight. AHP decided not to report all of the patients that had developed heart valve damage because they felt the unreported cases did not fit within the reporting requirements of the FDA.”²⁸⁵ In the Vadino trial, plaintiffs' attorney Sol Weiss said that “the valvular problems were evident from the beginning. Their [AHP's] French subsidiary knew about it, and American Home Products chose to ignore it.”²⁸⁶ American Home Products spokespersons “confirmed reports that they were aware of the heart valve problems for months before the FDA's warnings, stating, ‘we were being very cautious and working with the FDA to determine if these [heart valve problems] were isolated incidents or whether this required a higher level of warning.’”²⁸⁷ Peter Bleakley, an American Home Products attorney, said that “the overwhelming majority of people that reported problems had some kind of congenital heart disorder to begin with and the secondary pulmonary hypertension could have been a result of their obesity, or any of the other diet cures they had tried. There is no basis by which anyone reviewing these case reports would have seen a connection between

²⁸⁵Vivi Vanderslice, *Viability of a Nationwide Fen-Phen/Redux Class Action Lawsuit in Light of Amchem v. Windsor*, 35 CAL. W. L. REV. at 202.

²⁸⁶Matt Ackermann, *Fen-Phen Trial Testimony: Risks Stop One Year After Use*, NEW JERSEY LAW JOURNAL, Sept. 13, 1999, available online at www.lawnewsnetwork.com/stories.

²⁸⁷See Lance and Tortorich, *Popular Diet Drugs Pulled From Market*, 9 LOY. CONSUMER L. REP. at 297.

the drug and a valvular problem.”²⁸⁸

Kip Petroff, the attorney for the plaintiff Debbie Lovett in the first fen-phen case to result in a jury verdict, said that company memos introduced into evidence in the Lovett case “showed that American Home [Products] allegedly knew of people who took the drug and developed heart damage, but resisted putting warning labels on the product”²⁸⁹. In addition, in the Lovett trial evidence revealed American Home Products “had essentially paid for ghostwritten scientific papers and helped edit them to remove medical information before publication. The drug manufacturer contracted with medical publisher Excerpta Medica, which hired ghostwriters to cull the existing medical literature, develop a favorable spin, and assemble positive findings into a compendium of advantageous conclusions regarding the drug. The company then paid the original authors for permission to list their names as authors of the new articles.”²⁹⁰ In response to Petroff’s allegations and the evidence concerning the medical research, American Home Products has claimed repeatedly that it acted responsibly.²⁹¹

The PPH Label Numbers Issue

A major issue in all PPH cases concerns the numbers of PPH cases listed on the labels of Redux and Pondimin and whether American Home Products withheld information about new cases and failed to put the information on the label. (See discussion below of the Washington trial in Mississippi). The 1983 Pondimin Package Insert reported two PPH cases in female patients who took Pondimin for eight months. Internal Wyeth-Ayerst memos indicate that in 1994 Wyeth had received reports of 37 more PPH cases in Pondimin users. In June of 1994 a high level Wyeth-Ayerst official recommended updating the Pondimin

²⁸⁸Matt Ackermann, *Fen-Phen Trial Testimony: Risks Stop One Year After Use*, NEW JERSEY LAW JOURNAL, Sept. 13, 1999, available online at www.lawnewsnetwork.com/stories.

²⁸⁹John Council, *Fen-Phen Fight Has Just Begun, Plaintiffs Lawyers Say Verdict Sets the Market Rate*, TEXAS LAWYER, Aug. 16, 1999 at 1.

²⁹⁰Richard H. Middleton, Jr., *Our Quest For Corporate Honesty*, 35-OCT TRIAL 9 (1999).

²⁹¹See id.

label to reflect the higher PPH numbers. However, nothing was done at that time.²⁹² The label was revised on June 20, 1996 to report the IPPHS findings. The new label stated that a two-year international study found that 20 out of 95 patients diagnosed with PPH had taken fenfluramine and other anorexigens. The insert also stated that the PPH risk increased when patients took anorexigens for over three months. The insert also stated that in the majority of PPH cases patients had used fenfluramine for over 12 months.²⁹³ The insert advised doctors that “treatment should be discontinued in patients who develop new unexplained symptoms of dyspnea, angina pectoris, syncope or lower extremity edema. These patients should be evaluated for the etiology of these symptoms and the possible prevalence of pulmonary hypertension.”²⁹⁴ The Redux Physician Package Insert was also changed in 1996 to report the same findings from the IPPHS. The same updated PPH warnings were reported in the Redux insert as in the Pondimin insert. Plaintiffs in various fen-phen suits have claimed that the Pondimin and Redux warnings up until the 1996 changes only listed a handful of reported PPH cases at a time when AHP was aware of dozens more. The numbers issue was brought up in the New Jersey Vadino medical monitoring class action trial. Plaintiffs’ lawyers said that American Home Products had received 54 adverse reports and that Redux and Pondimin had caused nine deaths.²⁹⁵ The plaintiffs’ attorney said that American Home Products “should have hired an expert to pick up on these signals. They should have hired someone in 1995 instead of 1997 to prove there was something wrong with this drug.”²⁹⁶ American Home Products defense lawyer Peter Bleakley of Arnold & Porter said of this issue, “it’s true that Wyeth-Ayerst considered changing the numbers. I wish that there was a satisfactory reason for why it wasn’t done in a timely fashion.”²⁹⁷ In his testimony at the Vadino trial, Dr.

²⁹²See L. Stuart Ditzen, *In Mass Litigation, The Serious Cases can Get Lost*, PHILADELPHIA INQUIRER, Nov. 22, 1999, at A1.

²⁹³See In re: PA Diet Drugs (Phentermine, Fenfluramine, Dexfenfluramine) Products Liability Litigation No. 9709-3162 (Pa. C.1st 1999) American Home Products Exhibits 13, 14, and 16.

²⁹⁴Id.

²⁹⁵See Matt Ackermann, *Fen-Phen Lawyers Stick to Texas Formula, : As New Jersey Trial Continues, A Similar Class-Action Suit is Dismissed in California*, NEW JERSEY LAW JOURNAL, Aug. 23, 1999.

²⁹⁶Id.

²⁹⁷Bob Van Voris, *A Drug Maker’s Legal Migraine*, NATL. L.J., Aug. 23, 1999, at B20.

Marc Deitch, former senior Vice President of Medical Affairs at Wyeth Laboratories, said “I’m not saying we shouldn’t have changed the number. We should have. It was a mistake, and I am taking responsibility for it.”²⁹⁸

Black Box Warning in Physician’s Desk Reference Issue

There was also discussion over whether there should have been a “black box” warning in the Physician’s Desk Reference (“PDR”) for Pondimin and/or Redux. In Vadino, plaintiffs’ counsel presented a July 1996 report from Sophia Bayawakeh, a Wyeth marketing analyst, that said that a black box warning in the PDR could cut Pondimin and Redux sales by up to 50%. That marketing report was given to Carrie Smith Cox, vice president of women’s health care at Wyeth. Carrie Smith Cox was the head of marketing for Pondimin and Redux from 1995 until 1997. When plaintiffs’ counsel called Smith Cox as a witness in the Vadino trial, she said that she did not read the report from Bayawakeh and that she generally only read half of the material that came to her attention.²⁹⁹ However, Smith Cox wrote a memo to her supervisors in November of 1995 that said that a black box warning for Pondimin and/or Redux would be an “extremely strong negative that needed to be defused from day one... as you know this is probably the biggest single factor remaining to determine the future sales performance of the product[s].”³⁰⁰ These memos were presented in the Vadino trial. Vadino plaintiffs’ counsel said that a black box warning in the PDR would have alerted doctors to the risk of heart and lung problems and deterred prescriptions.³⁰¹

FBI Investigation

American Home Products also became involved in a federal investigation surrounding the approval of Redux.

²⁹⁸Matt Ackermann, *Fen-Phen Lawyers Stick to Texas Formula: As New Jersey Trial Continues, A Similar Class-Action Suit is Dismissed in California*, NEW JERSEY LAW JOURNAL, Aug. 23, 1999.

²⁹⁹See id.

³⁰⁰Id.

³⁰¹See id.

The FBI interviewed FDA employees about Redux's approval, according to Wall Street Journal reports.³⁰² The FBI was attempting to determine if American Home Products informed the FDA of all the information it had regarding adverse Redux reactions.³⁰³ In 1999, The New Jersey Star-Ledger reported that "the FBI and the FDA's own Office of Criminal Investigation are examining the handling of the two drugs".³⁰⁴ The FDA/FBI investigations were related to the Michael Weintraub/Trevena weight loss clinic affair in Florida.³⁰⁵ A lawyer with a firm that represents AHP downplayed the investigation, stating that "I can tell you, as a former prosecutor, agents can look into anything they want, it doesn't have to be substantial. Agents can take phone calls, respond to letters, and follow up on leads that don't lead to any action."³⁰⁶

Spoilation Sanctions For E-Mail Tapes in Linnen Trial

In the Linnen wrongful death trial in Massachusetts, which later settled, American Home Products faced sanctions for destroying e-mail evidence. Judge Raymond Brassard agreed to give a spoilation instruction when the case was tried. He was to charge the jury that it may infer that e-mails destroyed by American Home Products contained unfavorable evidence for the defense. American Home Products made backup tapes of employee e-mails each day, and it periodically re-used those tapes after retaining them for a period of time. After plaintiffs' lawyers requested the tapes, American Home Products failed to cease re-using the old tapes, and some e-mail tapes were lost. American Home Products did find over 1000 backup tapes when depositions were nearly complete, over one and a half years after plaintiffs' lawyers had requested them.

³⁰²See *Business-Watch Corporate Brief*, NATL. L.J., Sept. 20, 1999 at B4.

³⁰³See Matt Ackermann, *Fen-Phen Trial Testimony: Risks Stop One Year After Use*, NEW JERSEY LAW JOURNAL, Sept. 13, 1999, available online at www.lawnewsnetwork.com/stories.

³⁰⁴Edward R. Silverman, *Diet Pill Jury is Dismissed as Settlement Grows Near*, NEW JERSEY STAR LEDGER, Oct. 5, 1999, available online at www.nj.com/business/ledger/d28061.html

³⁰⁵See Kris Huntley, *Fen-Phen King Turns Tables On Drug Maker: Once a Promoter and User of the Weight-Loss Drug Combination, John Trevena Has Filed a Civil Suit Against Drugmaker Wyeth-Ayerst Laboratories, Inc., Accusing It of Fraud*, ST. PETERSBURG TIMES, Oct. 10, 1999, Business Section.

³⁰⁶Matt Ackermann, *Fen-Phen Trial Testimony: Risks Stop One Year After Use*, NEW JERSEY LAW JOURNAL, Sept. 13, 1999, available online at www.lawnewsnetwork.com/stories.

Statement of Mark Farley, a partner with Gibbons, Del Deo, Dolan, Griffinger & Vecchione. Farley was a former U.S. Attorney in Newark who worked on health fraud cases for eight years. See *id.*

Judge Brassard also ordered American Home Products to pay the plaintiffs' legal costs concerning the e-mail problem and for the restoration costs for some of the backup e-mail tapes. American Home Products issued a statement concerning Judge Brassard's ruling claiming that it had already provided over 50,000 pages of emails to plaintiff's lawyers. Plaintiffs' lawyers in the Linnen case expressed their "delight" with Judge Brassard's ruling. The spoliation instruction never came to bear since the Linnen case settled without ever going to the jury, but it will likely be an issue in future PPH trials.³⁰⁷

American Home Products Financial Situation

Failed Merger With Warner-Lambert

On November 4, 1999, AHP announced that it had entered into a merger agreement with Warner-Lambert in what was to be a friendly merger of equals. The merger would create the world's largest pharmaceutical and consumer health products company with pro forma sales of \$26 billion and one of the industry's largest R&D budgets of almost \$3 million. The new company was to be called AmericanWarner Inc. The new company would have the blockbuster drugs Lipitor, a \$3.6 billion anti-cholesterol drug, and Premarin, a \$1.8 billion hormone replacement therapy. It would also have several well known consumer health brands, including Advil, Listerine, Sudafed, Lubridern, Neosporin, and Preparation H. The merger of equals transaction was unanimously approved by both American Home Products' and Warner-Lambert's Boards of

³⁰⁷See Bob Van Voris, *Spoilation Sanctions for Fen-Phen Maker: American Home Products Destroyed E-Mail Backup Tapes*, NATL. L.J., July 5, 1999 at A4.

Note: The proposed Settlement Agreement does not cover PPH claims, so barring settlements, PPH trials will still occur and the destroyed AHP e-mails will continue to pose a problem. AHP concedes the emails were destroyed but asserts that the plaintiffs suffered no real harm as a result of the destruction, while Judge Brassard's ruling indicates that the court would allow the jury to infer that the destruction did cause harm to the Linnen family. Michael R. Overly, an electronic discovery expert at Foley & Lardner in Los Angeles, said that e-mails are often extremely valuable to plaintiffs, since people tend to express thoughts and emotions in e-mails that they would not write down in a formal memorandum. See Bob Van Voris, *Plaintiffs Say Firm Hid Data on Fen-Phen: E-Mails, Tapes Are at Issue in Mass. Suit Over Woman's Death*, NATL. L.J., May 31, 1999 at B1.

Directors. Shareholders of American Home Products and Warner-Lambert would each own approximately 50% of AmericanWarner. AmericanWarner was expected to achieve higher earnings growth than either company could expect by itself. The merger was expected to close in the second quarter of 2000. It would be subject to antitrust clearance, American Home Products and Warner-Lambert shareholder approval, and certain other conditions.³⁰⁸ Amid rumors that AHP was in discussions with Pharmacia & Upjohn and that the Warner-Lambert merger would not proceed, AHP issued a press release on December 10, 1999 stating that AHP was fully committed to the completion of that merger and that it would “create enormous near and long-term value for our shareholders.”³⁰⁹

However, the merger never occurred and American Home Products became embroiled in litigation with Pfizer and Warner-Lambert over the merger situation. The Warner-Lambert merger agreement was eventually terminated and at the present time American Home Products remains an independent company. On February 7, 2000 an American Home Products press release confirmed that the merger agreement with Warner-Lambert Company was terminated in accordance with its terms. The merger agreement provided for American Home Products to receive \$1.8 billion in connection with the termination, all litigation among American Home Products, Warner-Lambert, and Pfizer Inc. was discontinued, and American Home Products’ option to purchase Warner-Lambert shares was rescinded. American Home Products CEO John Stafford stated,

³⁰⁸See American Home Products Corporation, *Warner-Lambert and American Home Products to Merge, Creating World’s No. 1 Pharmaceutical and Consumer Health Products Company*, AMERICAN HOME PRODUCTS PRESS RELEASES, Madison, N.J. and Morris Plains, N.J., Nov. 4, 1999, available online at www.ahp.com/releases/ahp_110499.htm.

³⁰⁹American Home Products Corporation, *AHP Remains Committed to Completion of Announced Warner-Lambert Company Merger-of-Equals Agreement*, AMERICAN HOME PRODUCTS PRESS RELEASES, Madison, N.J., Dec. 10 1999, available online at www.ahp.com/releases/ahp_121099.htm.

While we regret that we were not able to complete the transaction, we understand the decision of the Warner-Lambert board to support the alternative transaction... the termination of our agreement brings to an immediate close the distracting and acrimonious litigation among the companies and allows us to focus on our growing health care business. AHP has one of the best pipelines in the pharmaceutical industry and we look forward to continuing to develop and market our outstanding new products and moving forward in what promises to be an excellent year for growth for our Company in 2000.³¹⁰

Securities Litigation against American Home Products Resulting From the Fen-Phen Affair

In Oran v. Stafford, investors in 1999 brought a Rule 10(b)(5) securities fraud claim against American Home Products and several American Home Products executives. Judge Politan of the U.S District Court in New Jersey dismissed the case with prejudice. Investors claimed that American Home Products and several of its insiders misrepresented and omitted facts concerning Redux and valvular heart disease in patients using the drug. The plaintiffs alleged that the defendants misled the investing public to believe that Redux was safe and would continue to generate large profits for American Home Products.³¹¹

In order to sustain a 10(b)(5) claim, any undisclosed information must be material. Material means that there must be a substantial likelihood that, under all the circumstances, the omitted fact would have assumed actual significance in the deliberations of the reasonable shareholder in whether to invest in that particular corporation.³¹² Based on the idea of an efficient market, any information that alters the corporation's share price is considered material.³¹³ If a company's eventual disclosure of the information at issue had no effect on the company's stock price, that information is immaterial as a matter of law.³¹⁴ And, if the information is not material, it is not actionable in a 10(b)(5) claim.³¹⁵

The Oran plaintiffs alleged that American Home Products knew of the valvular heart disease associated with Redux long before it publicly disclosed that information on July 8, 1997. However, during the four days

³¹¹See Oran v. Stafford, 915 F.Supp. 2d 906 (D. New Jersey 1999).

³¹²See In re Westinghouse Securities Litigation, 90 F.3d 696, 714 (3d Cir. 1996).

³¹³See In re Burlington Coat Factory Securities Litigation, 114 F.3d 1410, 1425 (3d Cir. 1997).

³¹⁴See id.

³¹⁵See id.

following the announcement of Redux's problems, American Home Products' share price rose by \$3.00. The share price did not begin to experience a downturn until September 15, 1997, when American Home Products announced it was withdrawing Redux from the market. Therefore, the Oran court found the medical data disclosed by American Home Products on July 8, 1997 to be immaterial as a matter of law.³¹⁶ The court refused to hold that "a pharmaceutical company owes a greater duty to disclose adverse medical data to the investing public than it owes to the FDA during a drug's approval process" and found that American Home Products' failure to disclose the adverse reaction reports to investors until July 8 was not actionable.³¹⁷

The plaintiffs also made claims that AHP continued to mislead the investing public after it made the July 8 disclosure by making the statement that the medical data was "limited and therefore inconclusive". The court held that this statement was too vague to be actionable, that a reasonable investor would not rely on such a vague statement, and that it was not false at the time it was made since there was no systematic study of Redux and valvular heart disease and no conclusive finding that the drug definitely caused the valve problems. The plaintiffs also claimed that American Home Products continued to mislead the investing public after the July 8 statement by failing to reveal additional European findings and adverse reaction reports. The court held that those facts would not have added anything to the July 8 disclosure and would not have significantly altered the total mix of information in a way that a reasonable investor would find to be relevant. The plaintiffs also alleged that American Home Products misled the investing public about the FDA approval process, because American Home Products suggested that it had disclosed to FDA all information it had regarding the safety of Redux.³¹⁸ The court found that American Home Products' statements to the investing public about Redux's FDA approval did not suggest that FDA approval "was based upon a review of every existing piece of relevant medical data. At best, the statements recited in the Complaint imply only that the FDA conducted a systematic and thorough review and concluded that Redux was safe

³¹⁶See Oran v. Stafford, 915 F.Supp. 2d 906 (D. New Jersey 1999).

³¹⁷Id.

³¹⁸See id.

and effective when used as a weight loss drug.”³¹⁹ The court also noted that the plaintiffs did not claim that American Home Products breached any of its obligations to report to the FDA, and they did not claim that the additional information/studies at issue would have changed the FDA’s decision on whether or not to approve Redux. The court found it most important that the plaintiffs did not state why a reasonable investor in making the decision whether to buy or sell American Home Products shares would be concerned about these particular aspects of the FDA’s Redux approval.³²⁰ The court concluded that “AHP did not materially mislead the investing public by failing to come forward with the reports of valvular heart disease prior to July 8, 1997; nor did AHP mislead the public by failing to disclose the specific medical data that formed the basis of its July 8 announcement; nor did the July 8 disclosure become materially misleading as a result of AHP’s failure to make any additional or subsequent disclosures.”³²¹

The Relationship of Pondimin and Redux and the Proposed Settlement to the American Home Products Stock Price

American Home Products stock suffered from the fen-phen situation and the uncertainty surrounding the thousands of suits filed against American Home Products and its subsidiaries. On August 6, 1999, when the Lovett verdict of \$23 million came down against the defense, American Home Products’ stock price dropped by 12%.³²² “In the past six months [from October, 1999], diet-drug suits have contributed to a steep decline in AHP’s value. From a 52-week high of \$70.25 a share on April 13, the stock hit a low of \$38.50 on Sept. 9, a 45% drop.”³²³

The impact of fen-phen liability on its stock price was a driving force in American Home Products’ desire to reach a settlement with plaintiffs’ lawyers. “American Home has been pressing for a quick settlement

³¹⁹Id.

³²⁰See id.

³²¹Id.

³²²See ob Van Voris, *A Drug Maker’s Legal Migraine*, NATL. L.J., Aug. 23, 1999, at B20.

³²³Donna Shaw, *Settlement Reached in Diet Drug Lawsuits*, PHILADELPHIA INQUIRER, Oct. 8, 1999, at A1.

because the diet-pill litigation, as well as setbacks involving other products and different business units, have sent its stock plunging nearly 40% since April.”³²⁴ When American Home Products was certain that a settlement would be announced in the very near future, it invited securities analysts and money managers to a presentation in New York on “the New American Home Products.”³²⁵

Between January and May of 1999 several American Home Products insiders cashed in many of their stock options and sold large number of shares for profits that ranged from \$1.4 million to \$7.3 million per person. American Home Products claimed that they were routine transactions and that executives and other high level officials had made similar transactions in years past. American Home Products also noted that the amount of shares traded were a small fraction of total shares held by top executives.³²⁶ “Alex Zisson, an analyst with investment firm Hambrecht & Quist, agreed that the insider stock sales appeared routine, and he noted that executives of firms cash in options and sell stock regularly. Any time there is disappointment afterward, people go back and point their finger.”³²⁷ In contrast, one plaintiffs’ attorney in Florida characterized the insider selling in the following manner: “I’ve seen it time and again. In an effort to instill confidence in investors and stabilize stock prices, corporations facing potentially massive litigation repeatedly downplay the seriousness of the threat posed by the litigation; then, when the threat becomes too big to ignore, the corporate big-wigs sell off large chunks of their stock before the corporations are forced to fess up.”³²⁸

Whatever the true reason for the insider selling, American Home Products has made great strides towards stemming the tide of fen-phen liability with the Settlement Agreement. While it still will face PPH suits even if the Settlement is given Final Judicial Approval and American Home Products decides not to terminate the agreement, American Home Products will dispose of the over 4,000 valvular heart disease suits that

³²⁴Edward R. Silverman, *Diet Pill Jury is Dismissed as Settlement Grows Near*, NEW JERSEY STAR LEDGER, Oct. 5, 1999, available online at www.nj.com/business/ledger/d28061.html.

³²⁵*Id.*

³²⁶*See* Susan Spielberg, *Executives Cashed In American Home Stock*, PHILADELPHIA INQUIRER, Sept. 11, 1999, Business Section.

³²⁷*Id.*

³²⁸*Insider Selling Reflects on True Scope of American Home Products’ Diet Drug Liability*, PR NEWswire, Sept. 7, 1999, Pensacola, Florida, available online at <http://leflaw.net/fenphen/insider9/99.htm>.

were negatively influencing its share price. At one point American Home Products was denying analysts information on the amount of liability insurance it had to cover potential verdicts, and there were reports from analysts that AHP may face resistance from their insurers over fen-phen liability.³²⁹ The Settlement has dramatically changed that negative situation and things are looking more positive for American Home Products at the present time.

In fact, many analysts see American Home Products' stock price today as undervalued and see the company as a prime takeover target. After the Settlement was announced, Business Week ran a story called "The Cloud Over American Home Products Dissipates", which stated that:

[t]hanks to its proposed \$4.8 billion settlement over fen-phen, investors are looking at the company again. It's rare that Wall Street is delighted to discover that a company's gross earnings will be reduced by nearly \$5 billion over the next few years. But more champagne than tears flowed among analysts and money managers who follow American Home Products when it announced just such a development on Oct. 7 [1999]. The reason for their joy was that \$4.8 billion is going to pay off plaintiffs who claimed that a cocktail of AHP drugs... had caused heart problems. It isn't unusual for such class actions to take years, if not decades, to settle. But AHP has reached an agreement less than two years after the first reports of the problem.³³⁰

Analysts have noted that the Settlement was for significantly less than American Home Products could have had to pay, as well as the presence of many promising drugs in American Home Products' pipeline. However, they have also noted that the Settlement has not yet received Final Judicial Approval and that American Home Products still has the right to walk away if there are too many opt-outs. However, at this time "AHP has the upper hand. If it comes to lots of individual lawsuits, most of the plaintiffs will be treading on legal thin ice, since few of them have actually suffered significant medical problems. Now that the specter of litigation is less ominous, analysts are enthusiastic about the stock."³³¹ While at one point the fen-phen problem was very damaging to American Home Products' share price and adversely impacted the proposed merger of equals with Warner-Lambert, that picture appears to have changed at the present time. AHP is

³²⁹See id.

³³¹Id.

doing well in terms of its current drug sales and has been doing well in the vaccine business as well.³³² “Now that the legal situation is clearing, many companies would love to own AHP. To make sure they ask nicely, the company’s board passed a poison-pill provision on Oct. 8 [1999] that will make a hostile takeover more difficult. Whether AHP is acquired or goes it alone, no one is disputing that the stock looks better now than it has in months. Although the company’s third-quarter earnings, which will be announced on Oct. 18, will sink to high heaven because of the settlement write-off, by next year AHP could be smelling like a rose.”³³³

Litigation with Interneuron

On Jan 24, 2000, Interneuron Pharmaceuticals, Inc. filed a complaint seeking damages against American Home Products in Superior Court of the Commonwealth of Massachusetts, Middlesex County. The complaint alleges that American Home Products and Wyeth-Ayerst (American Home Products’ subsidiary) withheld and concealed information from Interneuron on possible health risks associated with Redux. Interneuron claimed that that safety information was essential for Interneuron to determine the safety of dexfenfluramine (Redux), which was developed by Interneuron and marketed by American Home Products. While Pondimin (fenfluramine) was marketed only by American Home Products, Redux was marketed by American Home Products and co-promoted by Interneuron. Interneuron’s complaint seeks treble damages and attorney’s fees. Such damages are permissible under the Massachusetts law for knowing and willful deceptive acts and practices, fraud and misrepresentations. Interneuron attorneys stated that following Redux’s withdrawal from the market, over 2,000 lawsuits were filed against Interneuron. An Interneuron representative said that Interneuron would vigorously defend against each lawsuit and file a cross-claim against American Home Products seeking indemnification for each one.³³⁴

³³²See *id.*

³³³*Id.*

³³⁴See *Interneuron Pharmaceuticals Sues AHP for Fraud; Marketing Partner Withheld Critical Data Regarding Anti-Obesity Drugs*, BW HEALTHWIRE, Business Editors and Health/Medical Writers, Lexington, Mass., Jan. 24, 2000.

THE MEDICAL MONITORING ISSUE IN THE FEN-PHEN LITIGATION

Judicial Recognition of the Claim of Medical Monitoring

Medical monitoring was first recognized in the federal court system in Friends For All Children, Inc. v. Lockheed Aircraft Corp., 587 F. Supp. 180, 184-188 (D.D.C. 1984). In Friends For All Children, the plaintiffs were Vietnamese orphans who had survived a plane crash that occurred during a refugee evacuation mission. They sought diagnostic medical exams that were necessary to determine if brain injury had occurred when the plane's cabin suddenly depressurized. In Friends for All Children, the D.C. Circuit "affirmed the imposition of medical monitoring liability on the defendant tortfeasor, in a decision widely cited by subsequent medical monitoring cases around the country."³³⁵ Friends For All Children established the precedent for medical monitoring claims even in the absence of physical injury.³³⁶ In Ayers v. Jackson, 525 A.2d 287 (N.J. 1987), the New Jersey Supreme Court held that "compensation for reasonable and necessary medical expenses is consistent with well-accepted legal principles."³³⁷ The Ayers Court stated that "[i]t is inequitable for an individual, wrongfully exposed to dangerous toxic chemicals but unable to prove that disease is likely, to have to pay his own expenses when medical intervention is clearly reasonable and necessary."³³⁸ In medical monitoring cases, there is a fundamental distinction between proving that the defendant's wrongdoing caused the injury versus proving that the defendant's conduct caused the need to monitor for the presence of an injury.³³⁹ The U.S.

Court of Appeals for the Third Circuit clarified the distinction in In re Paoli R.R. Yard PCB Litigation, 916

³³⁵Elizabeth J. Cabraser and Fabrice N. Vincent, *Class Certification of Medical Monitoring Claims in Mass Tort Product Liability Litigation*, AMERICAN LAW INSTITUTE – AMERICAN BAR ASSOCIATION CONTINUING LEGAL EDUCATION COURSE OF STUDY, July 22, 1999, at 18.

³³⁶See id.

³³⁷Ayers v. Jackson, 525 A.2d 287, 309 - 312 (N.J. 1987).

³³⁸Id. at 312.

³³⁹See Cabraser and Vincent, *Class Certification of Medical Monitoring Claims in Mass Tort Product Liability Litigation*, AMERICAN LAW INSTITUTE – AMERICAN BAR ASSOCIATION CONTINUING LEGAL EDUCATION COURSE OF STUDY, July 22, 1999, at 18.

F.2d 829,850 (3d Cir. 1990), stating, “thus, the appropriate inquiry is not whether it is reasonably probable that plaintiffs will suffer harm in the future, but rather whether medical monitoring is, to a reasonable degree of medical certainty, necessary in order to diagnose properly the warning signs of disease”.³⁴⁰ The court in Friends For All Children held that an injunction compelling defendants to pay for medical monitoring is a proper use of a court’s equitable powers. Additionally, medical monitoring awards can be set up in the form of a court supervised fund in place of giving money directly to plaintiffs to pay for their medical expenses.³⁴¹ The California and Pennsylvania Supreme Courts have expressed a preference for a judicially supervised fund for medical screening as opposed to lump sum damages to the plaintiffs.³⁴²

Medical Monitoring Claims of Fen-Phen Plaintiffs

The medical monitoring fen-phen plaintiffs are currently claiming that leading public health organizations have urged fen-phen users to get medical examinations, including echocardiograms in certain cases (see above discussion on fen-phen health problems). The plaintiffs have moved for medical monitoring class certifications, asserting that “AHP should pay the quantifiable costs of periodic medical examinations necessary to detect the onset of heart and lung disease, because it is through their wrongful actions that plaintiffs have been made susceptible to such disease.”³⁴³ Medical monitoring has the potential to dramatically increase the tortfeasor’s costs, since the tortfeasor is no longer solely liable for only the exposed person who becomes sick but also to some degree to all exposed individuals. More sick plaintiffs will become aware of their conditions and the drug company or other tortfeasor will be liable for those problems, which it in fact paid

³⁴⁰In re Paoli R.R. Yard PCB Litigation, 916 F.2d 829,835 (3d Cir. 1990).

³⁴¹See Cabraser and Vincent, *Class Certification of Medical Monitoring Claims in Mass Tort Product Liability Litigation*, AMERICAN LAW INSTITUTE – AMERICAN BAR ASSOCIATION CONTINUING LEGAL EDUCATION COURSE OF STUDY, July 22, 1999, at 18.

³⁴²See *id.* at 22.

³⁴³Cabraser and Vincent, *Class Certification of Medical Monitoring Claims in Mass Tort Product Liability Litigation*, AMERICAN LAW INSTITUTE – AMERICAN BAR ASSOCIATION CONTINUING LEGAL EDUCATION ALI-ABA COURSE OF STUDY, July 22, 1999, at 18.

to discover.³⁴⁴

Elements of a Medical Monitoring Claim

The following are the substantive elements required for a medical monitoring claim: “(1) significant exposure to a proven hazardous substance; (2) significant resulting risk of contracting a serious latent disease; (3) significantly increased risk of disease as compared to the general population; (4) the existence of effective monitoring procedures; (5) reasonable necessity for monitoring, including endorsement by a qualified physician; (6) proof that the monitoring is different from regularly expected care; and (7) demonstrated clinical value in the early detection and diagnosis of the disease.”³⁴⁵

Fen-Phen Plaintiffs and the Medical Monitoring Claim Elements

Most of those substantive elements have been satisfied by the fen-phen plaintiffs. The first element, significant exposure to a proven hazardous substance, brings up the causation problem. Causation is not certain, but the data from the FDA and the Mayo Clinic give plaintiffs a strong foundation for the claim that Redux and Pondimin are proven hazardous substances in terms of valvular heart disease causation. AHP will argue that valvular heart disease is not a serious problem and that even if Redux and Pondimin caused the higher incidence of valvular heart disease, that does not make Redux and Pondimin proven hazardous substances. As for the second element, significant resulting risk of contracting a serious latent disease, plaintiffs can use data from the Mayo Clinic of a 30% chance of getting valvular heart disease after taking fen-phen as opposed to less than 5% in the general population. This data also supports the third element, a significantly increased risk of disease as compared to the general population. For the fourth element, existence of effective monitoring

³⁴⁴See Matt Ackermann, *In Fen-Phen Trial, the Uninjured Sue for Preventative Maintenance*, THE NEW JERSEY LAW JOURNAL, Aug. 16, 1999.

³⁴⁵*Id.* at 12.; See also *Potter v. Firestone Tire and Rubber Co.*, 863 P.2d 795 (Cal. 1993).

procedures, plaintiffs can point to modern echocardiography. For the fifth element, reasonable necessity for monitoring, plaintiffs can point to DHHS and American College of Cardiology Recommendations. However, plaintiffs will have to face the fact that those recommendations do not provide that every fen-phen user should have an echocardiogram, only those with symptoms or who may be at risk for bacterial endocarditis.³⁴⁶ For the sixth element, proof that monitoring is different from regularly expected care, plaintiffs can again look to DHHS and ACC recommendations, which go above what is recommended for the general population. Plaintiffs may have trouble with the seventh element, requiring demonstrated clinical value in the early detection and diagnosis of the disease. The fact is that it is unclear at the present time exactly what health problems valvular heart disease causes and how it impacts a person's ability to live a long and normal life. In some cases valvular replacement is needed, but in other cases valvular regurgitation does not seem to pose any day to day health problems aside from the threat of bacterial endocarditis during certain medical procedures. For PPH claims this would be an easy element to satisfy since early detection of PPH can be very beneficial to PPH patients. However, the facts are not so clear with valvular regurgitation, and the medical monitoring classes are all seeking medical monitoring for valvular heart disease problems. Overall, on the substantive elements for medical monitoring claims, the plaintiffs have strong arguments in their favor. The proposed Settlement Agreement reflects this, as it allows for a large sum for medical monitoring and echocardiograms for each patient who was exposed to Redux or Pondimin for over 61 or more days, which goes beyond what was recommended by DHHS and the ACC.

States That Have Recognized Medical Monitoring Claims and Certified Medical Monitoring Classes in Fen-Phen Litigation

While the fen-phen plaintiffs have strong claims on each of the elements of a medical monitoring claim as

³⁴⁶American Home Products Attorney Peter Bleakley focused on this fact, stating that no major health organization called for a monitoring program like the one envisioned by the asymptomatic medical monitoring plaintiffs. See Bob Van Voris, *A Drug Maker's Legal Migraine*, NAT'L. L.J., Aug. 23, 1999, at B20.

listed above, not all states recognize medical monitoring as a cause of action independent of a physical injury, and not all states will certify medical monitoring classes in fen-phen litigation.³⁴⁷ Judge Bechtel certified a federal medical monitoring class in the multi-district litigation on August 29, 1999.³⁴⁸ Texas, Illinois, Kentucky, New Jersey, Pennsylvania, Washington, West Virginia, Florida, and New York, and Montana have also certified medical monitoring classes as well.³⁴⁹ The issue is being litigated in other states as well, and some have refused to certify medical monitoring classes.

Manhattan Supreme Court Justice Helen E. Freedman certified a class of plaintiffs seeking medical monitoring because of their Redux/Pondimin exposure. Justice Freedman certified the class of asymptomatic plaintiffs in Cunningham v. American Home Products, and the class consisted of approximately 1 million NY consumers who took fen-phen and ingested either Pondimin or Redux. The plaintiffs claimed that exposure to Pondimin and Redux put them at increased risk for valvular heart disease and PPH. They further claimed that the sellers and manufacturers of fen-phen defectively designed Pondimin and Redux and marketed them while they knew or should have known about the health risks they posed. None of the plaintiff class members had valvular heart disease at the time of class certification. American Home Products denies that Redux and Pondimin increase risks of heart problems. Justice Freedman was the eighth state judge to certify a medical monitoring class in fen-phen litigation. She held that New York case law stated or implied that under proper circumstances New York would recognize a medical monitoring claim. Justice Freedman stayed the New York action because all of the New York plaintiffs are included in the national multi-district

³⁴⁷While not all states recognize medical monitoring as a claim independent of a physical injury, Judge Arthur Spiegel of the Southern District of Ohio wrote a series of influential opinions in the Telectronics defective pacemaker lead wire litigation where he “conducted a comprehensive evaluation of the laws of all fifty states and concluded that all states would recognize the monitoring remedy because the sound policy arguments in favor of medical monitoring, as well as the legal doctrines of avoidable consequences and recovery of future medical expenses, would persuade the states which have not yet addressed the issue to arrive at the same conclusion as those states that have, i.e., that medical monitoring is a permissible cause of action or element of damages.” Cabraser and Vincent, *Class Certification of Medical Monitoring Claims in Mass Tort Product Liability Litigation*, AMERICAN LAW INSTITUTE – AMERICAN BAR ASSOCIATION CONTINUING LEGAL EDUCATION ALI-ABA COURSE OF STUDY, July 22, 1999, at 12.

³⁴⁸See In re Diet Drugs (Phentermine, Fenfluramine, Dexfenfluramine) Products Liability Litigation, Jeffers v. American Home Products Corporation, No. CIV. A. 98-20626 1999, Memorandum and Pretrial Order No. 865, U.S. District Court for the Eastern District of Pennsylvania, Aug. 26, 1999, WL 673066 (E.D. Pa.).

³⁴⁹See id.

case in the Eastern District of Pennsylvania before Judge Bechtle. However, the Justice Freedman's decision was significant because until her ruling it was not clear whether New York recognized a pre-injury claim for medical monitoring.³⁵⁰

Texas was the first state to certify a medical monitoring class of fen-phen plaintiffs on October 14, 1998. Judge Fred Edwards of the 9th District of Texas certified a class seeking medical screening for all Texans who took Pondimin or Redux for 60 days or more.³⁵¹ The class excludes those who already filed personal injury suits for injuries they allegedly suffered as a result of taking fen-phen. Approximately 600,000 Texans are in that medical monitoring class.³⁵² In New Jersey, class certification for a medical monitoring class was initially denied. However, it was later certified by Judge Marina Corodemus in Vadino et al v. American Home Products Corporation et al. on January 25, 1999.³⁵³ The class action trial in New Jersey was suspended by Judge Corodemus because of the proposed Settlement Agreement. In Pennsylvania, Judge Stephen Levin certified a medical monitoring class of asymptomatic Redux and Pondimin exposed state residents on March 12, 1999. In West Virginia, a state circuit court certified a class of approximately 40,000 asymptomatic plaintiffs who were exposed to Pondimin or Re-

³⁵⁰See Michael Riccardi, *Class Status Granted in Fen-Phen Suit*, NEW YORK LAW JOURNAL, Sept. 17, 1999, available online at www.lawnewsnetwork.com/stories/A5881-1999Sep16.html.

³⁵¹See *Texas Fen-Phen Class is Certified*, NATL. L.J., Oct. 26, 1998 at A8.

³⁵²See *Fen-Phen's Test Case*, TEXAS LAWYER, Oct. 19, 1998 at 3.

³⁵³Judge Corodemus's opinion lists several equitable reasons justifying medical monitoring class treatment for diet drug users. American Home Products claimed that it would be inequitable to hold them responsible for medical monitoring because then they would be liable for determining if the class member suffered any harm. However, there are strong policy reasons in favor of holding American Home Products liable for medical monitoring costs. American Home Products would only have to pay medical monitoring if the plaintiffs actually established the liability of American Home Products, i.e. if they proved that American Home Products wrongfully concealed the risks of valvular heart disease associated with Redux and Pondimin. Once liability is established, a strong policy argument can be made that American Home Products should assume the responsibility for these costs, which American Home Products may be better able to absorb than the tort victim. See Cabraser and Vincent, *Class Certification of Medical Monitoring Claims in Mass Tort Product Liability Litigation*, AMERICAN LAW INSTITUTE – AMERICAN BAR ASSOCIATION CONTINUING LEGAL EDUCATION ALI-ABA COURSE OF STUDY, July 22, 1999, at 12. The Ayers court in New Jersey, which was influential in first recognizing pre-symptomatic medical monitoring, stated that “Allowing recovery for such [medical screening] expenses avoids the potential injustice of forcing an economically disadvantaged person to pay for expensive diagnostic examinations necessitated by another's negligence.” *Ayers v. Township of Jackson*, 525 A.2d 287, 311 (N.J. 1987). The policy reasons may be particularly strong in pharmaceutical drug liability cases like the fen-phen litigation, where exposure to dangerous drugs makes “prompt protection... and treatment essential to prevent or ameliorate injury.” Cabraser and Vincent, *Class Certification of Medical Monitoring Claims in Mass Tort Product Liability Litigation*, AMERICAN LAW INSTITUTE – AMERICAN BAR ASSOCIATION CONTINUING LEGAL EDUCATION ALI-ABA COURSE OF STUDY, July 22, 1999, at 27.

dux in Birch v. American Home Products. In Washington state, Judge Richard J. Shroeder certified a medical monitoring class on October 16, 1998 in St. John v. American Home Products. In Illinois, Circuit Judge Ellis E. Reid certified a class defined as Illinois residents who purchased and took Pondimin or Redux in Illinois and who had or would undergo the medical screening procedures recommended by DHHS and the Illinois Department of Public Health. The Illinois medical monitoring class specifically excluded any plaintiffs who were diagnosed with PPH, valvular regurgitation, or any other illness [allegedly] caused by Pondimin or Redux ingestion. In Kentucky, Judge Joseph Bamberger certified a medical monitoring class for certain exposed Kentucky residents in Guard, et. al. v. A.H. Robins Co., Inc.³⁵⁴ Florida certified a medical monitoring class in Petito v. A.H. Robins Co. on December 22, 1999. The trial court had held that Florida did not recognize a pre-injury medical monitoring claim, but the appellate court reversed that decision.³⁵⁵ Montana certified a statewide medical monitoring class on February 2, 2000 in Lamping, et al. v. American Home Products Inc., et. al. Missoula County District Court Judge Ed McLean found that the use of Redux and/or Pondimin carried a statistically high risk of heart damage and that the risk warranted medical monitoring class certification. At the time the plaintiffs in Montana filed their complaint, Montana did not recognize pre-injury medical monitoring.³⁵⁶

All of the above decisions follow Friends for All Children “in analyzing medical monitoring as a discrete equitable claim, best implemented in multiple exposure cases through the pragmatic and inherently equitable remedy of judicially supervised relief, rather than piecemeal or lump sum damages.”³⁵⁷

³⁵⁴See id. at 10-11.

³⁵⁵See Legal News: Medical Monitoring, 18 PRODUCTS LIABILITY LAW & STRATEGY 8 (1999).

³⁵⁶See Montana Judge Certifies Medical Monitoring Class, Citing High Risk of Injury, MEALEY’S LITIGATION REPORT FEN-PHEN/REDUX, available online at www.mealeys.com/fen.html.

Note: On January 10, 2000, Judge Richard G. Blane II in held in Luce, et. al v. Gate Pharmaceuticals, et. al that although Iowa does recognize medical monitoring under proper circumstances, Pondimin and Redux do not cause the latent effects that require certification of a medical monitoring class. See No Latent Injury Found, MEALEY’S LITIGATION REPORT FEN-PHEN/REDUX, available online at www.mealeys.com/fen.html.

³⁵⁷Cabraser and Vincent, Class Certification of Medical Monitoring Claims in Mass Tort Product Liability Litigation, AMERICAN LAW INSTITUTE – AMERICAN BAR ASSOCIATION CONTINUING LEGAL EDUCATION ALI-ABA COURSE OF STUDY, July 22, 1999, at 11 - 12.

Whether or not state courts certify medical monitoring classes and whether state law supports medical monitoring claims is critical in the multi-district litigation. Judge Bechtel, the MDL judge in Philadelphia, has “dropped from the case the claims of residents of states where medical monitoring relief is barred.”³⁵⁸ Significantly, California courts have rejected certification of medical monitoring classes.³⁵⁹

THE MULTI-DISTRICT LITIGATION – MDL 1203

Mass Tort Case Consolidation – History and Justifications

Mass tort cases are often consolidated for pretrial proceedings. This has been the case with asbestos cases, which are before Judge Charles Weiner of the Eastern District of Pennsylvania, silicone gel breast implant cases before Judge Sam Pointer of Alabama, and Norplant cases before Judge Richard Schell of the Eastern District of Texas.³⁶⁰ Traditionally, mass disasters such as plane crashes, explosions, site contaminations, or oil spills were confined to one area, where a single judge in a court near the area of the mass disaster would

³⁵⁸Michael Ricardi, *Class Status Granted in Fen-Phen Suit*, NEW YORK LAW JOURNAL, Sept. 17, 1999, available online at www.lawnewsnetwork.com/stories/A5881-1999Sep16.html.

³⁵⁹See id.
In *Tiffith, et al. v. Manhattan Weight Control, et al.*, Judge Daniel Solis Pratt of the California Superior Court, who is presiding over the California state court diet drug litigation, denied a plaintiffs’ motion to certify a California medical monitoring class. Judge Pratt found class certification improper because of the large number of factors unique to each plaintiff, like how long they took the drugs. He said the presence of these factors presented disparate issues concerning risk and damages. Judge Pratt found that common issues did not predominate among the proposed class of medical monitoring plaintiffs, which is a requirement of California law. See American Home Products Corporation, *American Home Products Media Statement On Diet Drug Decision in California State Court Denying Class Certification*, AMERICAN HOME PRODUCTS PRESS RELEASES, Madison, N.J., Aug. 20, 1999, available online at www.ahp.com/releases.082099.htm.

³⁶⁰Many state courts also consolidate cases for pretrial management. All fen-phen cases in New York have been consolidated and assigned to the Honorable Helen A. Freedman for pretrial management. See Helen E. Freedman, *Product Liability Issues in Mass Torts – View From the Bench*, 15 *TOURO L. REV.* 685, 687 (1999). New Jersey cases have also been consolidated before Judge Marina Corodemus. See Paul Rheingold, Michael Coren, and Sol Weiss, *NATL. L.J.*, Feb. 22, 1999, at C2. Texas did not consolidate its fen-phen cases before a single judge for pretrial management, although Rule 11 of the Texas Rules of Judicial Administration allow statewide consolidation for pretrial management in cases that have common issues of fact or law. American Home Products was in favor of the Texas consolidation, while plaintiffs attorneys were not, claiming that it was a tactic to delay discovery going on in various areas of the state. A judge was appointed for pretrial management in each of the nine administrative regions of Texas, but there is no statewide consolidation. See *No Fragmenting Fen-Phen*, TEXAS LAWYER, July 13, 1998 at 3.

manage the cases.³⁶¹ However, “[d]uring the last twenty-five years, a new type of mass tort, often national in scope, has emerged. In these cases, plaintiffs have claimed that toxic substances, toxic pharmaceuticals or defective devices have been put into the stream of commerce causing harm either in the short or long run to individuals to either ingest the drug, are exposed to the substance, or are implanted with the device.”³⁶² In such cases, “aggregation of mass tort cases have become the norm in many jurisdictions.”³⁶³ Advantages to consolidation include: (1) The judge handling the case develops expertise on the matter; (2) Rulings are more likely to be consistent; (3) Management is more efficient – usually parties develop a case management order allowing for uniform pleadings, interrogatories, and approaches to discovery; (4) Consolidation facilitates exploration of alternative dispute resolution, special masters, and settlement negotiations; and (5) Consolidation allows the judge to coordinate with other federal judges and state judges in other jurisdictions with similar cases for efficient disposition of cases. One disadvantage of consolidation is that the increased efficiency may encourage additional filings and therefore provide a welcoming environment for weak cases.³⁶⁴ Another aspect of consolidation is that “a mass tort judge’s perspective may differ from a judge viewing cases individually. A judge who has many cases is more likely to consider the ramifications of particular ruling on the entire litigation. This may even include the potential for bankruptcy and or the likelihood of increased insurance coverage. On the other hand, appellate courts, faced with appeals on individual cases, tend to look at the individual case without considering the impact of a particular ruling on the litigation as a whole.”³⁶⁵

Consolidation of the Diet Drug Litigation Into MDL 1203 Before Judge Louis Bechtle

The fen-phen litigation has been consolidated like the Norplant, asbestos, and silicon gel breast implant

³⁶¹See Helen E. Freedman, *Product Liability Issues in Mass Torts – View From the Bench*, 15 *TOURO L. REV.* 685 (1999).

³⁶²*Id.* at 685 – 686.

³⁶³*Id.* at 686.

³⁶⁴See *id.* at 687 – 689.

³⁶⁵*Id.* at 689.

cases. “On December 10, 1997, the Judicial Panel on Multidistrict Litigation named Senior U.S. District Judge Louis Bechtel of the U.S. District Court for the Eastern District of Pennsylvania to oversee a newly created MDL for fenfluramine, phentermine, and dexfenfluramine litigation. Judge Bechtel has extensive experience overseeing consolidated litigation”³⁶⁶

This decision came about after fen-phen plaintiffs lawyers in September of 1997 filed an with the Judicial Panel on Multi-District Litigation seeking to consolidate all of the fen-phen suits for pretrial proceedings. The Judicial Panel on Multidistrict Litigation ordered that consolidation on December 10, 1997, pursuant to 28 U.S.C. § 1407. All suits currently filed and any future lawsuits were to be handled by U.S. District Judge Louis Bechtel in the Eastern District of Pennsylvania. Since the consolidation, the MDL court has received over 1000 actions as part of MDL 1203.³⁶⁷

In February of 1998 Judge Bechtel selected nine well known litigators to form a committee to coordinate all pretrial stages of the litigation, and in May of 1998 he appointed defense liaison counsel for retailers, diet centers, and physicians in the MDL. He had the responsibility for class certification. Once the cases have finished pretrial proceedings, they will be returned to the federal courts where they were originally filed.³⁶⁸

Disadvantages of MDL Consolidation and the Fen-Phen Fast Track

While consolidation has led to increased efficiency and facilitated settlement negotiations, there are also some serious downsides to putting all the cases in an MDL. “There are two large inequities that can occur in mass litigation, in view of many lawyers and judges. One is that people who are not seriously injured can

³⁶⁶Evans and Kerner, *A Primer on Fen-Phen Litigation: Allegations and Defenses*, 65 DEF. COUNS. J. at 357. Judge Bechtel has over 15 years experience handling complex multiparty litigation. He was the MDL judge for the 1,357 cases that stemmed from the 1980 fire at the MGM Grand Hotel and Casino in Las Vegas. See Nation’s Fen-Phen Cases Consolidated in Philly, NATL. L.J., Dec. 29, 1997, at B2.

³⁶⁷See In re Diet Drugs (Phentermine, Fenfluramine, Dexfenfluramine) Products Liability Litigation, Jeffers v. American Home Products Corporation, No. CIV. A. 98-20626 1999, Memorandum and Pretrial Order No. 865, U.S. District Court for the Eastern District of Pennsylvania, Aug. 26, 1999, WL 673066 (E.D. Pa.).

³⁶⁸See Vivi Vanderslice, *Viability of a Nationwide Fen-Phen/Redux Class Action Lawsuit in Light of Amchem v. Windsor*, 35 CAL. W. L. REV. at 214 – 215.

clog the system for years. The other is that people with serious injuries can be overlooked in the clamor and the throng and be shortchanged on court attention and, ultimately, on compensation.”³⁶⁹ There has been a fear in the fen-phen litigation that more serious cases may get lost amidst the sheer volume of claims before Judge Bechtle. Many plaintiffs’ lawyers fear the MDL will slow the progress of their cases. The MDL can also affect the progress of state cases. “[A]lthough Judge Bechtle has no formal power over the conduct or scheduling of state court cases, state judges typically coordinate their cases with an ongoing MDL to avoid duplication of efforts. In effect, the MDL can act as something like a pace car, slowing or speeding the progress of state court cases, depending on how the MDL has handled.”³⁷⁰ In addition, “a handful of plaintiffs with life-threatening conditions worry the MDL means they may not live long enough to get their day in court.”³⁷¹ While having plaintiffs die before their trials occur is a personal tragedy for the plaintiff who never got their day in court, “[h]umanitarian concerns aside, there are cold strategic reasons plaintiffs’ lawyers prefer to try a case before the plaintiff dies. For one, jurors are likely to award more money to a sympathetic live plaintiff than to the memory of a dead one.”³⁷²

The problem of extremely sick plaintiffs trapped in the MDL was exemplified in the case of Carol Aserinsky, who developed PPH after she took fen-phen. Ms. Aserinsky is in very serious condition and her prognosis is very poor.³⁷³ Her case was originally assigned to federal Judge Marvin Katz in Philadelphia. If the case had stayed with Judge Katz it would have been ready for trial in June, 1998. However, the case was consolidated into MDL-1203 in December of 1997. Her attorney, Daniel Thistle, filed a motion for remand to state court, which Judge Bechtle denied on June 29, 1999.³⁷⁴ Thistle also made several requests to get Aserinsky’s case

³⁶⁹L. Stuart Ditzen, *In Mass Litigation, The Serious Cases can Get Lost*, PHILADELPHIA INQUIRER, Nov. 22, 1999, at A1.

³⁷⁰Bob Van Voris, *Fen-Phen Victims May Die Before MDL Ends: Federal Judge is Considering Creating a Fast Track For Most Seriously Ill Plaintiffs*, NATL. L.J., Feb. 23, 1998 at A7.

³⁷¹*Id.*

³⁷²*Id.*

³⁷³Aserinsky is housebound, she is on a waiting list for a double lung transplant, she is connected to oxygen at all times, and an IV implanted in her chest delivers medicine directly to her heart 24 hours a day. *See* L. Stuart Ditzen, *In Mass Litigation, The Serious Cases can Get Lost*, PHILADELPHIA INQUIRER, Nov. 22, 1999, at A1.

³⁷⁴*See* In re: Diet Drugs (Phentermine, Fenfluramine, Dexfenfluramine) Products Liability Litigation, Carol and Armand Aserinsky v. Wyeth & I, WL 554608 (E.D. Pa. 1999).

sent back to Judge Katz. His requests were all denied, as was an appeal to the Third Circuit. However, Judge Bechtle expressed concern about this problem and took action to separate the most serious cases from the mass of other cases comprising MDL 1203.³⁷⁵ In February of 1999 Judge Bechtle asked the lead plaintiffs' lawyers how many plaintiffs were claiming serious diagnosed injuries. The answer was eleven cases, less than one percent of all federal cases. Judge Bechtle wanted to ensure that those serious cases were not lost amidst all the other cases in MDL 1203. Judge Bechtle set up a fast track to expedite the serious cases and send them back to the districts where they were filed for trial. Aserinsky's case was at the top of that list of serious cases and it went back to Judge Katz.³⁷⁶

People with serious medical problems like Carol Aserinsky are at one end of the spectrum of diet drug plaintiffs, and people without any present medical problems in the medical monitoring suit are at the other. This will necessarily create tension when all those cases are put together in front of a single judge in an MDL consolidation. However, Judge Bechtle has shown that he is aware of the problem and has acted to solve it with the creation of the fast track for seriously ill patients. Therefore, MDL 1203 is taking advantage of the benefits of consolidation while attempting to eliminate its most major downside, making it an overall plus in the diet drug litigation as a whole.

CLASS ACTION LAWSUITS AND THE ISSUE OF CLASS CERTIFICATION

Class Action Description and the Requirements of Federal Rule of Civil Procedure 23.

³⁷⁵As of November 22, 1999, over 800 lawsuits had been consolidated in MDL 1203. If those cases were stacked on top of one another, they would rise 60 feet up, as tall as a six-story building. If all the state lawsuits were added to that stack, it would be double to triple that height. "In mass litigation, the serious cases can get lost." L. Stuart Ditzen, *In Mass Litigation, The Serious Cases can Get Lost*, PHILADELPHIA INQUIRER, Nov. 22, 1999, at A1.

³⁷⁶See id.

A class action is a lawsuit where “claims and rights of many people are decided in a single court proceeding brought by representative plaintiffs. Class actions avoid the necessity for hundreds, or even thousands, of people to file similar individual lawsuits, enable the court system to resolve these claims in a more efficient and economical way, and seek to assure that people with similar claims are similarly treated. In a class action, the court has a responsibility to assure that prosecution of the class claims by the Class Representatives and Class counsel is fair.”³⁷⁷

To be certified as a class, an action must first satisfy the requirements of Federal Rule of Civil Procedure (“FRCP”) 23(a). The four requirements of FRCP 23(a) are: “(1) the class is so numerous that joinder of all members is impracticable, (2) there are questions of law or fact common to the class, (3) the claims or defenses of the representative parties are typical of the claims or defenses of the class, and (4) the representative parties will fairly and adequately protect the interests of the class. Thus, Rule 23(a) requires numerosity, commonality, typicality and adequacy of representation.”³⁷⁸ An action for class certification must also satisfy the requirements of FRCP Rule 23(b)(2). Rule 23(b)(2) requires “first, that the defendant is alleged to have acted in some uniform way toward the class that would make relief appropriate, and second, that the injunctive relief requested is applicable to the entire class.”³⁷⁹ Finally, an action for class certification must satisfy the requirements of FRCP 23(b)(3), which requires that “questions of law or fact common to the members of the class predominate over any questions affecting only individual members, and that a class action is superior to other available methods for the fair and efficient adjudication of the controversy”³⁸⁰ When he certified the nationwide Jeffers medical monitoring class, Judge Bechtel found that

³⁷⁷Official Court Notice of Nationwide Diet Drug Class Action Settlement: In re Diet Drugs (Phentermine/Fenfluramine/Dexfenfluramine) Products Civil Action NO. 99-20593.

³⁷⁸In re Diet Drugs (Phentermine, Fenfluramine, Dexfenfluramine) Products Liability Litigation, Jeffers v. American Home Products Corporation No. CIV. A. 98-20626 1999, Memorandum and Pretrial Order No. 865, U.S. District Court for the Eastern District of Pennsylvania, Aug. 26, 1999, WL 673066 (E.D. Pa.).

³⁷⁹Id.

³⁸⁰FED. R. CIV. P. 23(b)(3).

the medical monitoring claims of asymptomatic fen-phen plaintiffs were proper for class treatment under the requirements of FRCP 23(a), FRCP 23(b)(2), and FRCP 23(b)(3). Judge Bechtel also found that all of those requirements were met when he granted provisional certification to the Brown nationwide settlement Class.³⁸¹

Class Action Lawsuits in the Fen-Phen Litigation

Individual and class action lawsuits were filed against American Home Products concerning fen-phen use, alleging injury as a result of ingestion of Pondimin and/or Redux or potential injury requiring medical monitoring. All federal diet drug cases were transferred to MDL 1203 before Judge Bechtel, and one of those cases, Brown v. American Home Products Corporation, was provisionally certified in a nationwide class action. The plaintiff in Brown seeks injunctive relief and compensatory damages. American Home Products has asserted that it is not liable to the plaintiff's class in any manner. Judge Bechtel also certified a nationwide medical monitoring class in In re Diet Drug Products Liability Litigation (Jeffers v. AHP), MDL Docket No. 1203.³⁸²

There are five subclasses within the larger Brown settlement class. These subclasses include: (1) Subclass 1(A) – Diet drug recipients who took Pondimin and/or Redux for 60 days or less and have not been diagnosed with FDA Positive regurgitation by an echocardiogram performed between the start of the diet drug use and September 30, 1999; Subclass 1(B) – Diet drug recipients who took Pondimin and/or Redux for 61 or more days and have not been diagnosed with FDA Positive regurgitation by an echocardiogram performed between the start of the diet drug use and September 30, 1999; (3) Subclass 2(A) – Diet drug recipients who took Pondimin and/or Redux for 60 days or less and have been diagnosed with FDA Positive regurgitation

³⁸¹See Official Court Notice of Nationwide Diet Drug Class Action Settlement: In re Diet Drugs (Phentermine/Fenfluramine/Dexfenfluramine) Products Liability Litigation, Sheila Brown, et al. v. American Home Products Corporation, Civil Action NO. 99-20593.

³⁸²See id.

by an echocardiogram performed between the start of the diet drug use and September 30, 1999; (4) Subclass 2(B) – Diet drug recipients who took Pondimin and/or Redux for 61 or more days and have been diagnosed with FDA Positive regurgitation by an echocardiogram performed between the start of the diet drug use and September 30, 1999; and (5) Subclass 3 – Diet Drug recipients who have been diagnosed with mild mitral regurgitation by an echocardiogram performed between the start of the diet drug use and the end of the screening period but who have not been diagnosed with FDA Positive regurgitation between the start of the diet drug use and the end of the Screening Program. Each subclass also includes all representative and derivative claimants whose claims are based on their personal or legal relationship with the diet drug user identified in each subclass.³⁸³

Class Certification in the Fen-Phen Litigation and the Supreme Court Amchem Decision

The class certification for settlement purposes in the fen-phen MDL was impacted by the Supreme Court case of Amchem Products, Inc. v. Windsor, which tightened up the requirements for class certification. The proposed settlement class in Amchem consisted of persons who had manifested physical injuries due to asbestos exposure and also those who had not yet manifested any injuries but who had been exposed to asbestos. The Supreme Court held that the proposed settlement class had to meet FRCP Rule 23 requirements and that the court would also have to consider the adequacy of the settlement. The court found that the Amchem proposed class did not meet Rule 23's requirements for certification, since it did not meet the commonality requirement or the adequacy of representation requirement.³⁸⁴ The court found that “the goal of class members who were currently injured and needed immediate payment conflicted with the interests of exposure only plaintiffs in ensuring an ample, inflation protected fund for the future.”³⁸⁵

³⁸³See id.

³⁸⁴See Vivi Vanderslice, *Viability of a Nationwide Fen-Phen/Redux Class Action Lawsuit in Light of Amchem v. Windsor*, 35 CAL. W. L. REV. at 199 – 204.

³⁸⁵Id. at 209.

Amchem presented the issue of maintaining present and future injuries in the same case.

Judge Bechtel did provisionally certify the Brown settlement class in the fen-phen litigation, so the Amchem concern did not come to bear. He still has to give Final Judicial Approval³⁸⁶ to the Settlement, and there the Amchem concerns may become important. However, the fen-phen Settlement addresses many of Amchem's concerns in its structure. It is critical to note that the Supreme Court acknowledged the fact that in Amchem there was no subclass division. In Amchem, “the Supreme Court indirectly encouraged the use of subclasses... to ameliorate the potential intra-class conflicts of interest between present and future claimants.”³⁸⁷ The court in Amchem stated: “where differences among members of a class are such that subclasses must be established, we know of no authority that permits a court to approve a settlement without creating subclasses.”³⁸⁸ The class in the fen-phen litigation is divided into 5 subclasses with separate counsel for each. (See detailed discussion of the Settlement below).

In Amchem the court also noted the issue of conflicts of interest among class members, particularly presently injured plaintiffs who desire payments as soon as possible versus plaintiffs facing future injury who want to preserve money for possible later payments. This is also less of a problem with the fen-phen Settlement, since its provisions for future and present injuries are divided clearly into Fund A and Fund B. Also, while American Home Products will have to pay out a large sum in the Settlement, it is not an amount that threatens to bankrupt American Home Products and prevent any future payments to injured diet drug users. In addition, the Settlement prevents conflict because plaintiffs who receive Fund A medical monitoring benefits will have the chance to qualify for Fund B payments if they later become sick. The money has been set aside for both types of plaintiffs today, so that the future injured are not in conflict with the presently injured. All can be

³⁸⁶Judge Bechtel's decision on whether to grant Final Judicial Approval to the Settlement will be reviewed by the U.S. Court of Appeals for the Third Circuit. See NAPOLI, KAISER & BERN LLP, THE FEN-PHEN E-RESOURCE, *Frequently Asked Questions*, available online at www.dietdrugsettlement.com.

³⁸⁷Ryan Kathleen Roth, *Mass Tort Malignancy: In The Search For A Cure, Courts Should Continue To Certify Mandatory, Settlement Only Class Actions*, 79 B.U. L. REV. 577 (1999).

³⁸⁸Amchem Products, Inc. v. Windsor, 521 U.S. 591, 627 (1997).

sure they will receive compensation.³⁸⁹

Judge Bechtle did provisionally certify the settlement class in Brown, and one of the issues to be determined in the Fairness Hearing to be held on May 1 – 5, 2000 will be whether that class shall remain certified.³⁹⁰

In all likelihood, the class will remain certified. This is because of the clear division of the class into five subclasses, the provision of separate counsel for each subclass, the flexibility for class members to change to a different subclass if their position changes, the separation of money into Fund A and Fund B, and the construction of safeguards to ensure a minimum of intra-class conflicts of interests.

THE PROPOSED SETTLEMENT AGREEMENT

Plaintiffs and [American Home Products] defense lawyers³⁹¹ negotiated a Settlement Agreement in October of 1999. Judge Bechtle gave preliminary approval to the Settlement on November 24, 1999.³⁹² The proposed settlement is subject to a Fairness Hearing and Final Judicial Approval.³⁹³

Members of the Brown Settlement Class

The Settlement includes all individuals who are members of the class that was provisionally certified in

³⁸⁹See Official Court Notice of Nationwide Diet Drug Class Action Settlement: In re Diet Drugs (Phentermine/Fenfluramine/Dexfenfluramine) Products Liability Litigation, Sheila Brown, et al. v. American Home Products Co., Civil Action NO. 99-20593.

³⁹⁰See id.

³⁹¹The team of plaintiffs' lawyers who negotiated the [settlement] deal will have the right to petition the court for up to \$429 million in attorney fees. See *Fen-Phen Settlement Gets Court Approval*, NAT'L. L.J., Dec. 6, 1999 at B4.

³⁹²See id.

³⁹³Judge Bechtle denied certification of a \$100 million Interneuron limited fund mandatory settlement on Sept. 30, 1999. Judge Bechtle said that elements of the Interneuron settlement "went astray" from the original intent of the Advisory Committee that wrote FRCP 23. The proposed Interneuron settlement was overall extremely different from the American Home Products proposed Settlement Agreement. See *Recent News*, MEALEY'S LITIGATION REPORT FEN-PHEN/REDUX, available online at www.mealeys.com/fen.html.

Brown v. American Home Products. The Settlement is also intended to resolve the claims of members of other diet drug class action lawsuits against American Home Products that have been certified or conditionally certified. These class actions include, but are not limited to: the Jeffers nationwide federal medical monitoring class, the West Virginia statewide personal injury and medical monitoring class, the Illinois statewide refund and monitoring reimbursement class, the New Jersey statewide Unfair and Deceptive Acts and Practices and medical monitoring class, the New York statewide medical monitoring class, the Pennsylvania statewide medical monitoring class, the Texas statewide medical monitoring class, and the Washington statewide medical monitoring class.³⁹⁴

Class members are defined as all individuals who used Pondimin and/or Redux and live in the United States or its possessions and territories. If a person meets that definition, he or she is a member of the nationwide class that was provisionally certified in the diet drug litigation for settlement purposes only, regardless of whether that person already has a lawsuit pending. Such persons are also class members even if they are class members in other diet drug class actions. Persons are also class members who are derivative or representative claimants of persons who used Pondimin and/or Redux and live in the U.S. or its possessions or territories. Such persons include family members or “significant others” of Pondimin/Redux users and persons with certain legal relationships with Pondimin/Redux users such as heir, beneficiary, or executor of an estate. Persons in the above listed categories are not class members if their claims against American Home Products or American Home Products Released parties arising out of Pondimin and/or Redux use have been finally resolved either by judgment or by a release.³⁹⁵

Settled Claims and Released Parties

³⁹⁴See Official Court Notice of Nationwide Diet Drug Class Action Settlement: In re Diet Drugs (Phentermine/Fenfluramine/Dexfenfluramine) Products Liability Litigation, Sheila Brown, et al. v. American Home Products Civil Action NO. 99-20593.

³⁹⁵See id.

Under the Settlement Agreement, in exchange for settlement benefits, class members are “agreeing to release any and all claims, including assigned claims, whether known or unknown, asserted or unasserted, regardless of the legal theory, existing now or arising in the future by any or all members of the Settlement Class arising out of or relating to the purchase, use, manufacture, sale, dispensing, distribution, promotion, marketing, clinical investigation, administration, regulatory approval, prescription, ingestion, and labeling of Pondimin and/or Redux, alone or in combination with any other substance, including, without limitation, any other drug, dietary supplement, herb, or botanical.”³⁹⁶ These settled claims include but are not limited to: all personal or bodily injury claims, claims for compensatory, punitive, and multiple damages, loss of wages, loss of support, consumer fraud claims, wrongful death and survival actions, medical screening or monitoring, economic or business losses, and prejudgment or post-judgment interest. The “Released Parties” include American Home Products and each of its subsidiaries, affiliates, and divisions (including A.H. Robins and Wyeth-Ayerst), American Home Products shareholders, any and all suppliers of materials, components, or services used in the manufacture of Redux and/or Pondimin, all Pondimin/Redux distributors, and all Redux/Pondimin prescribing physicians and dispensing pharmacies (only for certain claims). Released parties do not include prescribing physicians and dispensing pharmacies when the claims are based on their independent negligence or culpable conduct. Les Laboratoires Servier S.A. and all its affiliates and subsidiaries are not Released parties, nor are any phentermine manufacturers, sellers, or distributors. Interneuron Pharmaceuticals is also not a Released Party. Non-Settling Defendants are barred from bringing claims for contribution and/or non-contractual indemnity against American Home Products and other Released Parties to recover payments made to class members in fen-phen litigation.³⁹⁷

The Settlement does not include PPH claims. Pondimin/Redux users can pursue PPH claims outside of the Settlement, even if they did not opt-out. However, Pondimin/Redux users who do not opt out of the Settle-

³⁹⁶Id.

³⁹⁷See id.

ment cannot pursue PPH claims in court if they received Fund B (see below) matrix compensation benefits, unless the class member was diagnosed with PPH before they had left-sided heart valve abnormalities or endocardial fibrosis.³⁹⁸ The Settlement agreement contains a clear medical definition of PPH. The PPH definition in the Settlement agreement is broader than the definition in the IPPHS study. The Settlement does not provide any benefits for neurotoxic injuries and all Pondimin/Redux users who do not opt-out of the Settlement will not be able to pursue any neurotoxicity claims in court.³⁹⁹

Terms of the Settlement Agreement

Summary of Benefits

The following is a summary of the benefits provided in the Settlement agreement. The Settlement provides for a free echocardiogram and an appointment with a doctor to discuss the echocardiogram for all people who took Redux and/or Pondimin for 61 or more days. For people who took Redux and/or Pondimin for 60 days or less, they do not qualify for a free echocardiogram and doctor's visit but the Settlement allows exceptions in certain cases with humanitarian or compassionate reasons or true financial hardship. All people who have FDA positive regurgitation will receive a cash or medical services benefit for heart valve disease. People who took Pondimin and/or Redux for 61 or more days will receive \$6,000 in cash or \$10,000 in heart valve related medical services, and those who took the drugs for 60 days or less will receive \$3,000 in cash

³⁹⁸A plaintiffs' firm mass e-mail designed to answer fen-phen users' questions about the Settlement says "if you decide to opt-in to the Settlement and receive Fund B compensation for your valve-related heart injuries, you generally are precluded from bringing a separate lawsuit against American Home Products for PPH. In the event that you decide to opt-out of the Settlement, you may pursue any and all claims against American Home Products, including a PPH claim." *Answers to Frequently Asked Questions, Web Bulletin # 3*, FEN-PHEN MULTISTATE LITIGATION WEBSITE, Feb. 10, 2000, available online at <http://leflaw.net/fenphen>.

³⁹⁹See Official Court Notice of Nationwide Diet Drug Class Action Settlement: In re Diet Drugs (Phentermine/Fenfluramine/Dexfenfluramine) Products Liability Litigation, Sheila Brown, et al. v. American Home Products Co., Civil Action NO. 99-20593 at p.9

or \$5,000 in heart valve related medical services. For those patients with serious valvular heart disease as described in the Settlement Matrix Compensation Benefits Guide, they will receive benefits ranging from \$7,389 to \$1,485,000, depending on their age, severity of their disease, how long they took the drugs, and various other factors. American Home Products will also establish a fund for research and education on valvular heart disease and establish a medical registry to track Pondimin and Redux users for research and educational purposes

Detailed Description of Benefits Under The Settlement Agreement

In more detail, the Settlement provides for the following benefits:

1)

People who took Pondimin and/or Redux for 61 or more days and had not been diagnosed with FDA Positive regurgitation as of September 30, 1999 have a right to receive a screening echocardiogram. This purpose of the echocardiogram is to determine whether the patient has FDA Positive Regurgitation. The patient will have a chance to see a qualified doctor to discuss and evaluate the echocardiogram. People who took Pondimin or Redux for 60 days or less are not entitled to a screening echocardiogram. However, they may apply to receive an echocardiogram and accompanying doctor's visit to evaluate the echocardiogram if they can demonstrate compassionate and humanitarian reasons and/or true financial hardship.

2)

3)

People who took Pondimin and/or Redux for any period of time who have FDA Positive regurgitation or mild mitral regurgitation by the end of the echocardiogram screening period have the right to recover monetary compensation if they later develop serious valvular heart disease within approximately the next 15 years.⁴⁰¹ Patients with serious valvular heart disease can recover immediately under the Accelerated Implementation Option (see below). For patients without serious valvular heart disease at the present time, they can recover financial compensation if and when their disease gets worse. FIVE levels of Valvular Heart Disease are serious enough to qualify for compensation benefits under the Settlement. They are:

(1)

(2)

(3)

(4)

(5)

The amount of compensation that will be paid to patients who qualify for these compensation benefits depends on several factors listed in a compensation matrix. These factors include the severity of the patient's condition, the patient's age, whether or not the patient took Pondimin or Redux for over 60 days, whether the patient has any other causes for valvular regurgitation other than ingestion of Pondimin and/or Redux, and whether the class member is a derivative or representative claimant. The minimum compensation a patient can receive is \$7,389 (for a 70 – 79 year old patient with a severity level of I) and the maximum compensation a patient can receive is \$1,485,000 (for a patient 24 or younger with a severity level of V). The severity levels from I to IV are defined medically in the "Settlement Matrix Compensation Benefits Guide for Physicians, Attorneys, and Class Members"⁴⁰². There are four payment schedules (matrices) which set forth the compensation amounts for each particular patient according to their age at diagnosis, level of severity of valvular heart disease, and various other criteria such as the existence of alternative reasons for the valve problems. The compensation amounts are increased annually for inflation by 2% and are subject to certain court-approved deductions like attorneys' fees and costs. The spouses, children, "significant others" and certain legal representatives of persons who ingested Pondimin and/or Redux may also receive compensation payments under the Settlement. If a patient's medical condition worsens to a more serious level of valvular heart disease that would qualify them for a higher compensation benefit, the patient has the right to "step up" to a higher compensation level.

4)

All patients who took Pondimin and/or Redux have a right to receive a refund of \$30 per month for Pondimin and \$60 per month for Redux. If the patient took Redux and/or Pondimin for 61 or more days, there is a \$500 refund limit per person. In addition, if the patient took Redux and/or Pondimin for 61 days or more, the availability of refunds depends on whether Settlement funds remain after providing other benefits.

5)

If the patient had an echocardiogram after they started taking Pondimin and/or Redux, the patient may qualify for repayment of the cost of that echocardiogram. This benefit will only be available if sufficient Settlement funds remain after providing benefits to other class members, except for refund benefits for class members who used Pondimin and/or Redux for 61 or more days.

6)

The Settlement provides for American Home Products to sponsor medical research relating to cardiovascular disease. The Settlement establishes a fund, not to exceed \$25 million, for medical research and education for the benefit of all class members. A registry will be maintained to track people who took Pondimin and/or Redux and to perform medical research. Provisions in the Settlement Agreement assure that each class member's identity in the registry is kept in confidence.⁴⁰³

Opting-Out, Registration, and the Accelerated Implementation Option

As discussed above, Judge Bechtle provisionally certified the nationwide Settlement Class under FRCP 23(a), 23(b)(2), and 23(b)(3) for settlement purposes only. Therefore, all persons who took Pondimin and/or Redux are automatically members of the Settlement class if they do not opt out of the Settlement by sending in the "orange opt-out form" by March 30, 2000. Pondimin/Redux users could also opt out by writing a letter to the court. If Pondimin/Redux users do not opt out, their rights will be determined by the Settlement and they will be bound by its terms if it is approved. Diet drug users who do not opt out will be bound by the Settlement and will not be able to pursue any settled claims against American Home Products and other released parties, except in cases where the patient can exercise an intermediate or back end opt out. An intermediate opt out opportunity exists if the patient did not know they had an FDA Positive condition by September 30, 1999 and found out that they did have FDA positive regurgitation by the end of the Settlement's screening program. A back end opt out opportunity exists when patients did not know that they had a condition that would allow them to receive Matrix compensation benefits before the opt-out deadline but developed one at a later date. If the Pondimin/Redux user decides to opt out of the Settlement through a back end or intermediate opt out, their claims will not be barred by the statute of limitations. In back end or intermediate opt out cases, Pondimin/Redux users will not be able to recover punitive

or multiple damages against American Home Products.⁴⁰⁴ In order to collect compensation or receive medical monitoring, Pondimin/Redux users who do not opt out and want to participate in the Settlement must register for Settlement benefits. Pondimin/Redux users who are participating in the Settlement can choose to proceed by registering for benefits under the “blue form” registration or they can choose to receive benefits immediately by filling out the “pink form” and taking advantage of the “Accelerated Implementation Option”.

Pondimin/Redux users who do not want to presently opt-out but who may want to opt-out later through a back-end opt out or intermediate opt-out should proceed through the blue form registration. By registering for Settlement benefits by filling out the blue form sent to Pondimin/Redux users, the patient will receive Settlement benefits only if the Settlement receives final judicial approval. Pondimin/Redux users who know at the time of registration that they have serious valvular heart disease and are entitled to Matrix compensation payments do not have the option of a later intermediate or back end opt out.

Pondimin/Redux users who wish to participate in the Settlement can also proceed by taking part in the Accelerated Implementation Option. The Accelerated Implementation Option sets the Fen-phen Settlement apart from most other settlement agreements. In most other class action settlements class members must wait until final judicial approval of the settlement to receive benefits. If final judicial approval is not granted, then class members will not receive settlement benefits. The fen-phen Settlement is very different because Pondimin/Redux users may accept the Accelerated Implementation Option (“AIO”) and receive Settlement benefits quickly, irrespective of whether the Settlement receives final judicial approval. AIO participants do not have to wait until the completion of the court approval process in order to receive benefits, nor do they risk not receiving any Settlement benefits if the Settlement never receives final judicial approval. In order

⁴⁰⁴The fact that those who opt out at future points are barred from seeking punitive damages is a source of contention among many plaintiffs’ lawyers. See Arian Campo-Flores, *A Fen-Phen Fix – Big Suits: Top of the Docket* Vadino et. al. v. AHP, THE AMERICAN LAWYER, Nov. 1999.

to participate in the AIO, Redux/Pondimin users must give up their right to opt-out of the Settlement and also give up their rights to object to the Settlement. Any persons who want to join the AIO must fill out the pink AIO form by April 29, 2000.

The Fairness Hearing and Objecting to the Settlement Agreement

While he did give preliminary approval, Judge Bechtel has not given final approval to the Settlement, and a fairness hearing is scheduled for May 1-5, 2000 in the Courthouse in Philadelphia. The fairness hearing will be held to assist Judge Bechtel in deciding whether to approve the Settlement and to make it effective for all those Pondimin/Redux users who did not opt out or accept the AIO. Pondimin/Redux users can appear through an attorney or in person as long as they did not opt out or accept the AIO. The purpose of the Fairness Hearing is to determine if the Settlement class should remain certified, if the proposed settlement is fair, reasonable, and adequate, and to consider any other matters that the court determines are appropriate. The court can continue the Fairness Hearing on additional dates, without giving further notice to class members. Persons who wish to speak at the hearing should request time to do so in writing and that request must be postmarked by March 30, 2000. An attorney may appear on behalf of a class member at the hearing. Those class members who do not wish to object do not need to appear or file any papers. Class members can also submit written comments in support of or in objection to the Settlement. Such written comments must have been postmarked by March 30, 2000, or the objection will not be considered by the court in deciding whether to grant approval to the Settlement. If a settlement class member does not mail an intention to appear or a written comment by the set deadline, that class member shall have waived his or her right to object and will be permanently barred from objecting to the proposed Settlement.⁴⁰⁵

⁴⁰⁵All of the information in the sections on “Opting-Out, Registration, and the Accelerated Implementation Option” and “The Fairness Hearing and Objecting to the Settlement Agreement” come from the Official Court Notice of Nationwide Diet Drug Class Action Settlement: *In re Diet Drugs (Phentermine/Fenfluramine/Dexfenfluramine) Products Liability Litigation*, Sheila Brown, et al. v. American Home Products Co., Civil Action NO. 99-20593 (in its entirety).

Payment of Settlement Benefits by American Home Products

The Settlement Agreement provides for American Home Products to put money in a Settlement Trust. The Trust will put money into two separate funds, Fund A and Fund B. Fund A and Fund B will be used to pay for Settlement benefits for class members as well as for administrative costs and certain attorneys' fees. American Home Products has already started putting money into Fund A and Fund B and it will continue to put money into the Funds for 16 years, as is necessary. American Home Products must pay into the Funds \$1.85 billion within the next three years, and it may pay into the Funds as much as \$4.83 billion, which is \$3.75 billion in present value. Any payments into the Funds over the initial \$1.85 billion will be paid in only as necessary as determined by the amount of class members who register to receive benefits. The payments above the initial \$1.85 billion are subject to annual maximum amounts and these maximums will be adjusted to account for individuals who opt-out and for individuals who subsequently receive payments from American Home Products as a result of judgments or settlements. Fund A will be used for Pondimin/Redux refunds, medical monitoring costs, reimbursement for certain privately-obtained echocardiograms, additional medical services and cash payments made to class members, medical research and education costs, costs of the tracking registry, administrative costs (including mailing/publication of the Class Notice), and attorneys fees relating to the benefits provided by Fund A (paid by American Home Products into a separate escrow account). Fund B will be used for matrix compensation benefits to class members with serious heart disease as described in the Settlement Agreement, certain attorneys' fees related to the matrix compensation payments, and administrative costs (including mailing and publication of the Class Notice).⁴⁰⁶ American Home Products will record a charge of \$4.75 billion pretax (aftertax \$3.29 billion), which comes to \$2.51 per share, to provide for expected payments to Fund A and Fund B, for other

⁴⁰⁶See id.

fen-phen related judgments and settlements, and legal costs.⁴⁰⁷

Termination of Settlement Agreement

American Home Products has the option to terminate and withdraw from the Settlement Agreement within 30 days from March 30, 2000. The decision to terminate and withdraw is to be made at the discretion of American Home Products, if it determines that too many Redux/Pondimin users have opted out of the Settlement Agreement. If American Home Products decides to withdraw, it is still bound by all individual agreements entered into when Redux/Pondimin users accepted the AIO.⁴⁰⁸

The Settlement will also be terminated if it does not receive Final Judicial Approval.⁴⁰⁹ If Final Judicial Approval is denied, American Home Products will still be bound by individual agreements entered into by diet drug users who accepted the AIO.⁴¹⁰

Settlement Criticisms

The fact that American Home Products can terminate and withdraw from the Settlement if it determines there have been too many opt-outs leads to a discussion of the extensive criticism of the Settlement by

⁴⁰⁷See American Home Products Corporation, *American Home Products Announces Diet Drug Settlement Plan*, AMERICAN HOME PRODUCTS PRESS RELEASES, Madison, N.J., Oct. 7, 1999, available online at www.ahp.com/releases/ahp_100799.htm.

⁴⁰⁸See Official Court Notice of Nationwide Diet Drug Class Action Settlement: In re Diet Drugs (Phentermine/Fenfluramine/Dexfenfluramine) Products Liability Litigation, Sheila Brown, et al. v. American Home Products C, Civil Action NO. 99-20593.

⁴⁰⁹Law Professor John Coffee, Jr. said Judge Bechtel is likely to approve the Settlement, although his decision will be reviewed by the Third Circuit and may be reversed on appeal. Professor Coffee said that the Third Circuit has “in the past taken a very close look at class action settlements.” See Arian Campo-Flores, *A Fen-Phen Fix – Big Suits: Top of the Docket Vadino et. al. v. AHP*, THE AMERICAN LAWYER, Nov. 1999.

AHP lawyers expressed the view that Judge Bechtel would approve the Settlement and that his decision would be upheld by the Third Circuit. They also said they thought that most class members, especially those who were well-informed, would accept the Settlement. One AHP attorney characterized the Settlement as “fair, flexible, and generous” and said that “once claimants and their counsel have a chance to consider the benefits of the settlement, I believe that many will prefer those benefits to a lengthy and uncertain course of litigation.” *Id.*

⁴¹⁰See *Important Notice on the Proposed Class Action Settlement/A Class Member’s Guide to the Diet Drug Litigation Settlement*.

plaintiffs' lawyers around the country. Many plaintiffs' lawyers have praised the medical monitoring benefits of the Settlement and the Fund A provisions, but have sharply criticized the matrix compensation benefits. Many claim that it is too difficult to qualify for matrix compensation benefits and that the sums for qualifying class members are far too small.⁴¹¹ Marc Bern, a New York plaintiffs' lawyer whose firm represents over 5,000 fen-phen plaintiffs, said that the Settlement is great "for healthy people who just want future medical checkups. [however], '[f]or those people who are injured, it stinks'".⁴¹² While Settlement payments range from \$30-\$60 monthly prescription refunds to a maximum of \$1.5 million for people with very serious heart problems, attorney Bern says he does not know if there is anyone in the U.S. who would qualify for that maximum sum.⁴¹³ "To qualify for the maximum \$1.5 million... a plaintiff would have to have taken the diet drugs, had valve surgery and suffered even more dire consequences – dying, falling into a coma or undergoing a heart transplant".⁴¹⁴ In addition, the \$1.5 million could also only be paid to people who were 24 or younger when they got sick.⁴¹⁵ Attorney Bern stated that most fen-phen plaintiffs are middle aged women who fail to meet that age requirement, and that medical expenses alone for most of those women exceed the amount to which they would be entitled under the Settlement Agreement. In sum, he called it a "lousy settlement" and said that virtually everybody I speak to says they'll opt out".⁴¹⁶

⁴¹¹See Amy Westfeldt, *Many Decline Diet Drug Settlement*, ASSOCIATED PRESS, Oct. 15, 1999.

⁴¹²Id.

American Home Products has claimed that the website of Marc Bern's firm, Napoli, Kaiser & Bern, is endangering the Settlement. Napoli, Kaiser & Bern's website, www.dietdrugsettlement.com, reflects the firm's critical view of the Settlement. The firm calls the site educational, while American Home Products claims the site is misleading. American Home Products has gone to court to force the Napoli, Kaiser & Bern to make certain changes, including a change in website address. The official site of the MDL is www.settlementdietdrugs.com, and American Home Products asserts that the similarities in the web addresses is diverting visitors from the court-sanctioned site to the Napoli, Kaiser & Bern site. Marc Bern said that the firm's site has fine print that says it is not the official Settlement site. He says that the firm's site's purpose was not to solicit clients, and that it is protected by the First Amendment. The site includes an opt-out form prospective plaintiffs can mail to Judge Bechtel and includes an analysis of the proposed Settlement, which the firm website labels as "totally inadequate and unfair." Napoli Kaiser & Bern represents approximately 7,000 former Redux and Pondimin users. See *Practitioner's Newswire: AHP Goes To Court Over Law Firm Web Site*, 18 PRODUCT LIABILITY LAW & STRATEGY 10 (2000). After a hearing on January 14, 2000, Judge Bechtel issued a pretrial order temporarily restraining Napoli, Kaiser & Bern from using www.dietdrugsettlement.com with respect to the orange opt-out form. See *TRO continues against Law Firm's Settlement Site*, MEALEY'S LITIGATION REPORT FEN-PHEN/REDUX, available online at www.mealeys.com/fen.html.

⁴¹³See Amy Westfeldt, *Many Decline Diet Drug Settlement*, ASSOCIATED PRESS, Oct. 15, 1999.

⁴¹⁴Id.

⁴¹⁵See id.

⁴¹⁶Id.

Bern's law firm, Napoli, Kaiser & Bern, has a website with a "fen-phen frequently asked questions" section. In response to the question, "Do I qualify for any settlement benefits", the response includes the statement that "even when a claimant can qualify for benefits, the payments being offered in some cases may not even cover the amount of lost earnings and/or medical expenses incurred as a result of being injured. For example, in a recent Texas case, Debbie Lovett, the jury awarded 23.5 million dollars; yet under the settlement plan she would only receive \$6000."⁴¹⁷ The website also mentions the \$150 million verdict for five Mississippi plaintiffs in Washington.⁴¹⁸ The website says that "it is our firm's opinion that the payout leaves much to be desired."⁴¹⁹

Tom Pirtle, a Houston lawyer representing 3,200 fen-phen plaintiffs, used an example of a client who has \$2 million in medical expenses related to her valvular heart disease problem, yet would only qualify for \$1 million under the Settlement terms. Pirtle said that the agreement is "a whole lot better settlement for Wall Street than for Main Street ... [and the criteria for compensation payments] completely exclude a number of people injured from the drug".⁴²⁰

Other fen-phen plaintiffs' lawyers in Texas joined Pirtle in his criticism of the Settlement and indicated that they would have their clients opt out. Robert Kisselburgh, one of the lead plaintiffs' lawyers in the Lovett trial, stated "I think they're absolutely kidding themselves... I mean, I don't know if it's a ploy to bring the stock up, since it was down after our verdict, but I think they're kidding themselves if they think the majority of people in Texas are going to take this settlement".⁴²¹

⁴¹⁷See NAPOLI, KAISER & BERN LLP, THE FEN-PHEN E-RESOURCE, *Frequently Asked Questions*, available online at www.dietdrugsettlement.com.

⁴¹⁸Both of those cases later settled for significantly smaller amounts (see sections below on Lovett trial and Mississippi Washington trial). See Reuters, Dallas, TX, *Jury Awards \$23.3 Million in Texas Fen-Phen Case*, Aug. 6, 1998, available online at www.heartinfo.org; See also Kerry Whipple, *Settlement Reached in Fen-Phen Trial*, THE NATCHEZ DEMOCRAT, Dec. 21, 1999, available online at www.dietdrugsettlement.com.

⁴¹⁹NAPOLI, KAISER & BERN LLP, THE FEN-PHEN E-RESOURCE, *Frequently Asked Questions*, available online at www.dietdrugsettlement.com.

⁴²⁰Arian Campo-Flores, *A Fen-Phen Fix - Big Suits: Top of the Docket* Vadino et. al. v. AHP, THE AMERICAN LAWYER, Nov. 1999.

⁴²¹Susan Borreson, *Fen-Phen Plan Doesn't Thrill Texans: Most Plaintiff's Lawyers To Opt Out Of Settlement*, TEXAS LAWYER, Oct. 18, 1999, at 1. Statement of Dallas lawyer Robert Kisselburgh.

On its website, Rheingold, Valet, Rheingold & Shkolnik, a New York plaintiffs firm that represents thousands of fen-phen plaintiffs, says to fen-phen users:

[y]ou have probably read about a proposed class action settlement of these cases. Almost all of our present clients are planning to take the legal step of opting out of it. The plan does not provide any significant payment for the great number of persons injured by fen-phen. It does not cover PPH cases, nor does it cover many valve regurgitation cases. It has no payment for mild leaks nor for more serious mitral and aortic leaks unless there are serious complications. If these complications exist then payment is made pursuant to a grid. The amounts on the grid are much lower than the sums that our law firm and others have been able to obtain by starting suit and bringing the cases up to trial, at which time they are settled. However, until we represent you, we are not offering advice about whether a person should opt out or not.⁴²²

A Wyeth-Ayerst spokesman countered these criticisms with the statement that “the settlement offers a refund program for the drugs and a rich package of medical monitoring and treatment – with significant compensation for those with serious valve problems. ‘It’s a settlement for the patients... not the lawyers’”⁴²³

American Home Products General Counsel Louis L. Hoynes, Jr. said,

In designing the agreement with the plaintiffs’ attorneys, we wanted to ensure that the benefits are attractive to the claimants and provide a strong incentive for participation. We are confident that well-informed claimants will conclude that the range of benefits of this settlement is preferable to lengthy and uncertain litigation. The scientific studies conducted to date and clinical experience indicate that the health of the overwhelming majority of people who took Redux or Pondimin has not been adversely affected. The studies also show no increased risk of valvular heart disease among persons who took the drugs for three months or less – more than 75% of those who took the drugs. Yet this settlement provides a quality package of benefits for all individuals who used the drugs and financial protection in the event a person should develop serious heart valve disease.⁴²⁴

Settlement negotiators have responded to the barrage of plaintiffs’ lawyers criticism by praising the settlement’s flexibility and extensive medical monitoring benefits. Christopher Placitella of New Jersey, one of the seven plaintiffs’ negotiators, said that “It’s the most comprehensive consumer protection settlement ever from a public health perspective”.⁴²⁵ He said that the Settlement is unique because of its flexibility, since

⁴²³Steve Sternberg, *More Pain Promised In Court For AHP*, USA TODAY, Jan 12, 2000.

⁴²⁵Arian Campo-Flores, *A Fen-Phen Fix – Big Suits: Top of the Docket* Vadino et. al. v. AHP, THE AMERICAN LAWYER, Nov. 1999

“class members can initially choose to participate in the settlement – obtaining medical tests and free visits to the doctor – and later, if they discover a health problem or their condition worsens, withdraw from the agreement and pursue their cases in court.”⁴²⁶ However, those who opt out later are barred from seeking punitive damages.⁴²⁷

General Consensus and Observations on the Settlement Agreement

Overall, the general consensus seems to be that plaintiffs attorneys are satisfied with the medical monitoring provisions, which go beyond DHHS and ACC recommendations⁴²⁸, but are not satisfied with the matrix compensation benefits. Attorney Bern said that this is a result of the fact that the lawyers who negotiated the Settlement primarily represented the clients who were not ill or who were not suffering from serious medical complications.⁴²⁹ While clearly not a scientific percentage, Bern estimated that approximately 25% of plaintiffs’ lawyers in the U.S. supported the Settlement.⁴³⁰ The sentiment that the Settlement is unacceptable to plaintiffs has been voiced around the country⁴³¹ and this may have an impact on the amount of opt-outs. If the opt-out number is too high, then American Home Products’ whole purpose in entering

⁴²⁶Id.

⁴²⁷See id.

⁴²⁸DHHS recommended Redux/Pondimin users should be examined by their doctors and only in certain circumstances should they have echocardiograms. “In seeking a massive echocardiogram testing program, plaintiffs’ lawyers have gone beyond the recommendations of the federal government and of the medical profession. The American College of Cardiology and the American Heart Association recently issued guidelines recommending against echocardiograms for diet-drug users who showed no symptoms of heart damage. The groups urged instead that doctors perform physical and stethoscope exams on patients and that echocardiograms be done only for patients too obese to be diagnosed by stethoscope.” In fact, doctors for the two named plaintiffs in the nationwide medical monitoring class did not recommend echocardiograms for their patients. L. Stuart Ditzen, *In Mass Litigation, The Serious Cases can Get Lost*, PHILADELPHIA INQUIRER, Nov. 22, 1999, at A1.

⁴²⁹See Amy Westfeldt, *Many Decline Diet Drug Settlement*, ASSOCIATED PRESS, Oct. 15, 1999

⁴³⁰See id.

⁴³¹See Susan R. Miller, *3.75 Billion Diet Drug Settlement Threatened By Feuding Attorneys*, MIAMI DAILY BUSINESS REVIEW, Jan 13, 2000 (noting that several Miami plaintiffs attorneys are not satisfied with the terms of the settlement. The article also states that one New York plaintiffs’ lawyer is claiming that he is getting 300 or 400 opt outs per day. The article notes that AHP has the right to terminate the settlements if there are too many opt outs after the opt-out expiration date comes around on March 30, 2000).

One Houston lawyer stated, “In my view, American Home Products’ global settlement is now dead... a lot of people won’t go into the national settlement. If you look at that \$150 million award [in Mississippi], it just shows you how angry ordinary citizens get when they hear about these charges.” David Morrow, *American Home To Settle Some 1,400 Fen-Phen Suits*, Dec. 23, 1999, MEALEY’S LITIGATION REPORT FEN-PHEN/REDUX, available online at www.mealeys.com/fen.html.

into the Settlement and ending the huge threat of fen-phen litigation will be thwarted. American Home Products may then elect to withdraw from the Settlement and only then have to pay the benefits to those class members who accepted the AIO.⁴³²

On the whole, such an outcome will be “good” or “bad” depending on where the particular plaintiff stands with respect to his or her medical condition. For healthy plaintiffs who receive medical monitoring, the termination of the Settlement would be a negative occurrence. However, for plaintiffs with valvular heart disease, especially older plaintiffs, the termination of the Settlement may allow them to receive much higher amounts of compensation than would be forthcoming according to the Settlement Agreement. For American Home Products, a large number of opt-outs and a termination of the Settlement would be an overall negative outcome, since it would fail to ‘put to bed’ the threat of thousands of lawsuits that have plagued the stock price since the fen-phen safety problems became apparent in 1997. American Home Products would be forced to settle on a case by case basis or to try cases before juries in various state and federal courts, which would be a costly and uncertain undertaking. John R. Stafford, American Home Products CEO, said that

This Settlement provides fair and equitable terms for both diet drug claimants and American Home Products. Settling this matter was in the best interest of those who used Pondimin or Redux as well as of the company. We believe that this agreement is a sound way to resolve the claims raised by diet drug users and represents a prudent course for our company. It offers peace of mind to those who used the drugs and permits the company to move beyond the uncertainty and distractions of litigation. We agreed to this settlement so that we can focus on the business of making innovative pharmaceutical products. Today, we have in our research pipeline products to help solve some of the world’s most pressing health problems and this settlement allows us to pursue and expand that effort.⁴³³

Even if American Home Products does not terminate the Settlement Agreement and it obtains Final Judicial Approval, it still has to deal with the PPH claims that are not settled pursuant to the Agreement. Some estimates have put liability for those claims at approximately \$1 billion, and American Home Products has

⁴³²While the deadline has recently passed for opt-outs, it was a postmark deadline and the numbers are not yet available.

already settled several PPH cases for amounts reported to range from \$1.5 to \$4.5 million.⁴³⁴ American Home Products would have to put forth significantly more money and effort towards individually disposing of all the valvular heart damage cases as well. In addition, if Redux and Pondimin are later shown to cause neurotoxicity problems in humans as well as in animals, American Home Products may also have to settle or try a multitude of neurotoxicity claims that would be precluded by the Settlement Agreement. American Home Products will benefit immensely from a low number of opt-outs and having the Settlement gain Final Judicial Approval. It encouraged plaintiffs to give up their right to object or opt-out by accepting the AIO, and it has actively promoted and defended the Settlement Agreement. While it is yet too early to determine the number of opt-outs, their number will have a significant impact on the outcome of the fen-phen debacle for American Home Products and will also have a wide-ranging effect on American diet drug users with varying degrees of medical problems.

KEY PRIOR FEN-PHEN CASES AND SETTLEMENTS – TEXAS, MISSISSIPPI, AND THE LINNEN T

While the settlement is the most prominent focal point of the current fen-phen legal situation, there have been several key fen-phen cases and settlements that set the stage for the Settlement Agreement and that may set the state for post-settlement litigation, both for PPH claims and for opt-out valvular heart disease plaintiffs. If the Settlement Agreement does not receive Final Judicial Approval or if American Home Products terminates the Agreement because of a high number of opt-outs, these cases may be of central concern to litigators representing plaintiffs who ingested Pondimin or Redux. They are also critical for PPH cases not included in the Settlement. This paper discusses the first fen-phen case that resulted in a jury verdict, the Lovett case in Texas, along with certain important Texas settlements. The Texas cases are

⁴³⁴See L. Stuart Ditzen, *In Mass Litigation, The Serious Cases can Get Lost*, PHILADELPHIA INQUIRER, Nov. 22, 1999, at A1.

followed by a discussion of the Washington case in Mississippi and the settlement covering all Mississippi fen-phen users. Also included is a discussion of the Linnen wrongful death PPH trial in Massachusetts

Texas Cases/Settlements

The Lovett Trial, Verdict, and Settlement

The Lovett case was the first fen-phen case to end in a jury verdict. American Home Products had settled 20 cases before the Lovett case went to trial, and the company had been predicting that it would win.⁴³⁵ The case was tried before a jury of eight men and four women in the courtroom of Judge Tommy W. Wallace of Van Zandt County, Texas and the verdict was returned on August 6, 1999.⁴³⁶

Debbie Lovett was a 36 year old manicurist from Grand Saline, Texas. Lovett was a smoker who took fenfluramine and phentermine in combination for six months, beginning in October, 1995. Lovett sued Wyeth-Ayerst and American Home Products, claiming that she developed leaky heart valves as a result of her fen-phen use. Lovett had not had valve replacement surgery, although she did suffer from valvular regurgitation. Cases like Lovett's were those that American Home Products thought it would be most likely to win, since it is hard for plaintiffs to prove causation and also difficult for plaintiffs to show that they have suffered life-altering damage as a result of fen-phen use. As one defense lawyer stated, "if you have mild regurgitation, you can fly to the moon, you can play football... it's a lab finding. It's something, but it's

⁴³⁵See Bob Van Voris, *A Drug Maker's Legal Migraine*, NATL. L.J., Aug. 23, 1999, at B20.

⁴³⁶See id.

not life adjusting. That's why I think we'll be trying lots of regurgitation cases."⁴³⁷ Defense lawyers also focused on the fact that Lovett had smoked for eight years, claiming that her smoking history caused her heart problems.⁴³⁸ They claimed that Lovett's heart problems existed before she ever used fen-phen.⁴³⁹

Lovett was represented by Kip Petroff and Robert Kisselburgh, two plaintiffs lawyers at the forefront of the fen-phen litigation. Lovett claimed that "the manufacturer knew that fen-phen could cause damage to the heart and did not reveal that knowledge to the public in order to maximize profits"⁴⁴⁰

The jury found that the "negligence of the defendants was the proximate cause of the plaintiff's injury. It... found that the harm done to the plaintiff resulted from the malice of American Home Products, and awarded a total of \$23,362,000, including \$20,000,000 in punitives."⁴⁴¹ American Home Products lawyer Bob Schick of Vinson & Elkins said "we are disappointed by today's ruling. There simply is no scientific study that has established a causal link between the use of Pondimin and the heart problems claimed by Mrs. Lovett."⁴⁴²

The jury verdict was later drastically reduced in a settlement. American Home Products settled with Debbie Lovett on September 16, 1999 for 'less than 10%' of the jury award, rumored at around \$2 million. Kip Petroff, an attorney for Lovett, said that the settlement "represented 'more than 90%' of what he thought

⁴³⁷Id.

⁴³⁸See John Council, *Fen-Phen Fight Has Just Begun, Plaintiffs Lawyers Say Verdict Sets the Market Rate*, TEXAS LAWYER, Aug. 16, 1999 at 1.

⁴³⁹AHP issued a press release on the Lovett trial which said that "Deborah Lovett's long-standing history of heart problems began in 1980 when she was 17 years old. In 1990, prior to her use of the diet drugs, she was diagnosed with mitral valve prolapse syndrome with recurrent symptomatic palpitations, a condition caused by myxomatous degeneration of the mitral valve. In fact, her treating cardiologist, the only physician who actually examined Ms. Lovett as a patient, testified that her heart valve problems were caused by myxomatous degeneration and not by use of fen-phen. She had this condition prior to treatment with fen-phen, has evidence of it today and will not require surgery in the future." American Home Products Corporation, *American Home Products to Appeal Court's Ruling in Deborah Lovett v. American Home Products*, AMERICAN HOME PRODUCTS PRESS RELEASES, Madison, N.J., Aug. 6, 1999, available online at www.ahp.com/releases/ahp_080699.htm.

⁴⁴⁰Bob Van Voris, *A Drug Maker's Legal Migraine*, NAT'L. L.J., Aug. 23, 1999, at B20.

⁴⁴¹*Lovett v. Wyeth-Ayerst Laboratories, et al*, TEXLAW VERDICTS: PRODUCT LIABILITY

⁴⁴²Reuters, Dallas, TX, *Jury Awards \$23.3 Million in Texas Fen-Phen Case*, Aug. 6, 1998, available online at www.heartinfo.org.

the ultimate award would be given Texas law capping punitive damages.”⁴⁴³ Lovett’s lawyers claimed that they entered into the settlement with American Home Products after considering Texas laws on punitive damage caps. The settlement was reached before a judgment on the verdict was entered.⁴⁴⁴

In addition to being the first jury verdict in fen-phen litigation, the Lovett case was also noteworthy because of a particular defense strategy of American Home Products, namely the use of an internal FDA Memo. Leo Lutwak, a physician and medical officer for the FDA, wanted to testify to set the record straight about the FDA memo, which he claimed was being mischaracterized and used in American Home Products’ defense. The December 1997 memo from Lutwak to an FDA colleague stated that Lutwak had been considering the valvular heart disease reports from fen-phen users and that he concluded that there was no way anyone could have foreseen the adverse valvular effects of the drugs. American Home Products lawyers read the memo out loud to the Lovett jurors, attempting to characterize the ‘anyone’ as anyone at all, including anyone at American Home Products. In contrast, Lutwak states that he meant the ‘anyone’ to mean anyone at the FDA. Lutwak has been subpoenaed by plaintiffs to testify as to the true meaning of his memo, but FDA attorneys informed Lutwak he could not do so, since agency regulations prohibit testimony by agency employees except when authorized by the commissioner or the commissioner’s representative. The FDA has this policy in order to ‘stay above the legal fray’ and to prevent FDA employees from spending all of their time providing testimony in court about FDA regulated products. David Kessler, FDA Commissioner from 1991 to 1997, said that he agreed with this policy up to a certain point, but that Lutwak should be permitted to clarify his statement to prevent the continued mischaracterization of his words. American Home Products claimed that they did not misrepresent the comments and that Lutwak did not communicate with them to inform them of any mischaracterization. However, as discussed above, the jury found for Lovett regardless

⁴⁴³Richard B. Schmitt and Robert Langreth, *AHP Offer to Settle Diet-Pill Litigation May not Be Rich Enough For Lawyers*, WALL STREET JOURNAL, FEN-PHEN MULTISTATE LITIGATION WEBSITE, available online at <http://leflaw.net/fenphen>.

⁴⁴⁴See *Suit Settled*, TEXAS LAWYER, Sept. 27, 1999 at 3.

of the use of the memo and awarded her \$23.3 million. American Home Products lawyers also showed the Lutwak memo to jurors in the Vadino class action in New Jersey, but the case never went to the jury because of the proposed Settlement Agreement.⁴⁴⁵

Texas Fen-Phen Settlements/Other Litigation

American Home Products agreed to pay up to \$6 million to settle two Texas claims with women who claimed that fen-phen caused valvular heart damage. American Home Products agreed to pay between \$2-3 million to Freda Gilmore of Dallas and Esmerelda Rocha of Alice, Texas. Some analysts claimed that the settlement move was an attempt to increase share price and limit diet drug liability in American Home Products' quest to complete the now-defunct merger with Warner-Lambert. The settlement with Esmerelda Rocha was reached during a trial that had lasted three weeks. Jurors were hearing evidence about Rocha's medical problems when the settlement was reached. Rocha, 47, took Pondimin for over a year and allegedly developed PPH.⁴⁴⁶ "Rocha's lawyers argued her heart deteriorated to a point that she couldn't walk more than a few feet without gasping for breath. But American Home countered that a panel of doctors couldn't find anything wrong with Rocha's heart."⁴⁴⁷ Gilmore also took Pondimin and claimed that doctors had to do valve replacement surgery as a result of valvular heart damage caused by the drug. American Home Products claimed that Gilmore's problems resulted from her history of smoking and high-blood pressure. Her trial was set for October 20, 1999 but it was pushed ahead as plaintiff and defense lawyers engaged in settlement negotiations.⁴⁴⁸

In other diet drug litigation in Texas, in April of 1999 American Home Products settled the first fen-phen case to go to trial one week into the plaintiff's presentation. The trial was occurring in the Johnson County

⁴⁴⁵See *FDA Official Says AHP Misled Jurors about Memo*, PHILADELPHIA INQUIRER, Jan 9, 2000.

⁴⁴⁶See Bloomberg, *American Home To Pay Up To \$6 Million In Fen-Phen Cases, People Say*, MADISON, NEW JERSEY BLOOMBERG REPORT, Nov. 16, 1999.

⁴⁴⁷Id.

⁴⁴⁸See id.

District Court. While the exact number was not made public, the number was reported to be approximately \$500,000.⁴⁴⁹

In May of 1999, in Canton, Texas, a judge declared a mistrial after lawyers claimed they were unable to seat an impartial jury. Lawyers said that too many of the prospective jurors had been influenced by the media and already concluded that the fen-phen combination was dangerous.⁴⁵⁰

Mississippi – Washington Trial and All-Mississippi Settlement

The first fen-phen case in Mississippi to go to trial was brought by five plaintiffs who claimed that Pondimin and Redux damaged their hearts and lungs, and they claimed that American Home Products did not properly warn them of the health risks associated with Redux and Pondimin. The trial took place in Fayette, Mississippi, a town of less than 2,000 people. The plaintiffs in the Fayette trial were: Claude Pickett of Natchez, MS, Kenya Tenner Gaines of Fayette, MS, Vinester Williams of Itta Bena, MS, Ruth Bishop of Greenville, MS, and Brenda Hamm of Bay Springs, MS. The plaintiffs' lawyers claimed that all five were suffering from either valvular heart disease or PPH, a claim which American Home Products lawyers disputed. The five plaintiffs were seeking \$2 billion in damages. American Home Products attorneys claimed throughout the entire three week trial that doctors had warned the plaintiffs of the health risks associated with Pondimin and Redux, particularly the PPH risk. Plaintiffs claimed that American Home Products hid knowledge about Redux's health risks when they were trying to get the FDA to approve dexfenfluramine.⁴⁵¹

Plaintiffs' attorney Michael Gallagher stated in his opening statement that "American Home knew Pondimin

⁴⁴⁹See Charles Ornstein, *Fen-Phen Maker Settles Suit for \$500,000*, DALLAS MORNING NEWS, Apr. 9, 1999 at A1.

⁴⁵⁰See *Mistrial Declared In Fen-Phen Trial*, NY TIMES ON THE WEB, available online at www.nytimes.com/aponline/f/AP-Diet-Drug-Trial.html.

⁴⁵¹See Kerry Whipple, *Drug Trial Opens in Fayette*, THE NATCHEZ DEMOCRAT, Dec. 1, 1999, available online at www.dietdrugsettlement.com.

carried the risk of heart valve disease and pulmonary hypertension. He said the company listed only four cases of pulmonary hypertension on its warning label for the drug, although it knew about more and was required by the FDA to include those known cases.”⁴⁵² To counter this claim, Dr. Marc Deitch, retired Director of Medical Affairs for Wyeth-Ayerst, testified

that the company told the FDA as early as 1994 about more than 50 cases of pulmonary hypertension that could have been associated with Pondimin. At the time, the warning label on the drug showed only four cases of pulmonary hypertension associated with the drug. Deitch said the FDA never requested a label change for the drug. ‘What was in the label was sufficient information,’ Deitch said. ‘Whether it was four cases or 10 cases or 15 cases. ‘It made no sense to put a number in’ because not enough research had been done as to the association of the drug to the disease... [t]he label was eventually changed, Deitch said, because ‘we changed it on our own’.⁴⁵³

To support their claims, the plaintiffs brought in expert witness Dr. Lemuel Moye, a general causation expert, who testified that Redux and Pondimin did cause valvular heart disease and PPH. Dr. Moye said during the trial that American Home Products knew of the dangers of Redux and Pondimin and that they failed to inform the public, the FDA, or the medical community. The defense brought in expert witness Dr. Marcus Stoddard, a cardiologist who claimed that the plaintiffs were not sick and that even if they were he could not link any valvular heart disease to the plaintiffs’ use of Pondimin and Redux. Dr. Stoddard suggested that a secondary cause may be at fault in the valvular heart disease occurrences among fenfluramine and dexfenfluramine users.⁴⁵⁴

The jury in Fayette deliberated for two hours and returned with a verdict of compensatory damages of \$30 million for each plaintiff. Plaintiff and defense lawyers then gave their arguments for punitive damages. However, following those arguments, plaintiff and defense lawyers worked out a settlement agreement. Judge Lamar Pickard then dismissed the \$150 million verdict. The settlement was stated to be approximately \$350

⁴⁵²Id.

⁴⁵⁴See id.

million, which would cover virtually all of the fen-phen cases in Mississippi.⁴⁵⁵ American Home Products did not admit any wrongdoing and it maintained that the majority of people who took Redux and Pondimin have not experienced any adverse health effects – including the Mississippi plaintiffs.⁴⁵⁶ One plaintiff, Vinester Williams of Itta Bena, called the trial “stressful” and “depressing” and said that “it’s very hurtful to know you’ve been harmed and someone’s telling you there’s nothing wrong with you”.⁴⁵⁷ The Fayette trial was considered extremely important because at the time, analysts considered that the Warner-Lambert merger may have been jeopardized by a large verdict.⁴⁵⁸

American Home Products told stock analysts concerned about the verdict and its impact on American Home Products’ stock price and Warner-Lambert merger that the Mississippi legal environment was ‘anything but ordinary’. American Home Products also noted that many of the cases filed in Mississippi were from plaintiffs who resided in other far-away states.⁴⁵⁹

Massachusetts Linnen Wrongful Death Trial/Settlement

Mary Linnen, a computer designer in Boston, died in 1997 at the age of 30 from PPH. Mary Linnen had taken fenfluramine and phentermine in order to lose weight for her upcoming wedding. She took Pondimin for 24 days in April of 1996. Eleven days after she began treatment, Mary Linnen complained that she

⁴⁵⁵See Kerry Whipple, *Settlement Reached in Fen-Phen Trial*, THE NATCHEZ DEMOCRAT, Dec. 21, 1999, available online at www.dietdrugsettlement.com.

⁴⁵⁶AHP issued a press release on the Mississippi Settlement that read as follows: “American Home Products Corporation confirmed today that it has reached a resolution of substantially all of the diet drug cases pending in the state of Mississippi. The resolution was reached this evening [Dec. 21, 1999] following discussions with counsel for the plaintiffs in the case of *Washington et al v. American Home Products Corporation* and with the assistance of Judge Lamar Pickard, who presided over the trial. Judge Pickard has vacated the judgment for compensatory damages awarded earlier today in the *Washington* case and has entered a directed verdict dismissing plaintiffs’ claims for punitive damages. The terms of the settlement of the Mississippi litigation are confidential.” American Home Products Corporation, *American Home Products Corporation Confirms Resolution of Substantially All Mississippi Diet Drug Cases*, AMERICAN HOME PRODUCTS PRESS RELEASES, Madison, N.J., Dec. 21, 1999, available online at www.ahp.com/releases/ahp_122199a.htm.

⁴⁵⁷Kerry Whipple, *Settlement Reached in Fen-Phen Trial*, THE NATCHEZ DEMOCRAT, Dec. 21, 1999, available online at www.dietdrugsettlement.com.

⁴⁵⁸See Kerry Whipple, *Drug Trial May Affect More Than Plaintiffs*, THE NATCHEZ DEMOCRAT, Dec. 11, 1999, available online at www.dietdrugsettlement.com.

⁴⁵⁹See David Morrow, *American Home To Settle Some 1,400 Fen-Phen Suits*, Dec. 23, 1999, MEALEY’S LITIGATION REPORT FEN-PHEN/REDUX, available online at www.mealeys.com/fen.html.

was experiencing shortness of breath. She died 10 months later from PPH. Her parents brought suit against American Home Products, claiming that the company knew that fenfluramine caused PPH in other Pondimin users.⁴⁶⁰ In opening arguments in the trial, one of the lawyers representing Mary Linnen's family stated that "American Home officials 'knew the drugs were killing people in the U.S. and Europe and stayed silent... the motive for this was profit, pure and simple. That money is the reason Mary Linnen is dead today.'"⁴⁶¹ The Linnen suit was the first wrongful death suit to be tried before a jury (although it eventually settled).⁴⁶² American Home Products lawyers claimed that there was no concrete evidence linking Linnen's PPH to her use of Pondimin. Linnen's family claimed that by April 1996, when Mary Linnen was prescribed fen-phen in Massachusetts, American Home Products already had reports of over 60 Pondimin users who developed PPH, yet the company resisted updating Pondimin's warning label for fear it would decrease sales.⁴⁶³ One of the Linnen family lawyers said that "American Home was marketing Pondimin to the public at a time when it knew it had a deadly side effect."⁴⁶⁴ American Home Products countered by stating that it did not ever market fen-phen or promote the diet drugs together, but rather sales of Pondimin increased as doctors read favorable studies about the fen-phen combination. An American Home Products attorney stated that "Because Linnen's PPH progressed so quickly, its likely she already had the disease when she started taking Pondimin... the 5 foot 3 inch, 190 pound woman was worried that her inability to lose weight signaled she had other medical problems... this was not a cosmetic issue."⁴⁶⁵

⁴⁶⁰See *News This Week, Ticker*, NATL. L.J., Feb. 7, 2000, at A4.

⁴⁶¹*Id.*

⁴⁶²The case was also noteworthy because of a particular "jury innovation" used by Judge Brassard. Judge Brassard allowed the lawyers to address the jurors directly at different stages in the trial, a technique called "interim commentary" or "interim summation". It was the first time the technique was used by any Massachusetts judge. Judge Brassard also provided pictures of the witnesses to the jurors to help them connect the testimony in their notes to their memory of that testimony. Judge Brassard used these techniques because he thought the case was going to last six to eight weeks. The case settled after seven days. See Elizabeth Amon, *Shaking Up Juries, State By State - In Vogue: Juror Notes, Chats by Panel, Interim Summations*, NATL. L.J., Feb. 14, 2000, at A14.

⁴⁶³See Bloomberg, *Fen-Phen Drug Maker Files Last Minute Attempt to Avoid Court-Ordered Deposition of CEO*, BOSTON, MASSACHUSETTS BLOOMBERG REPORT, Jan. 18, 1997.

⁴⁶⁴*Id.*

⁴⁶⁵*Id.*

American Home Products and Mary Linnen's family announced a settlement on January 27, 2000. The details were not made public, but the Wall Street Journal reported the amount to be approximately \$10 million.⁴⁶⁶ "The Boston Herald quoted led plaintiff attorney Alex MacDonald... as saying the settlement was the largest wrongful death recovery in state history. The Herald said that would make the settlement higher than \$7 million."⁴⁶⁷ American Home Products indicated that much of the settlement sum would be used to fund a research foundation for PPH treatment and research. The fund will bear the name of Mary Linnen. The statement American Home Products issued in connection with the settlement did not admit any wrongdoing on the part of American Home Products that played a role in Mary Linnen's death.⁴⁶⁸ The joint press statement said that "the parties are pleased to settle this matter and are especially pleased to be able to commemorate the name of Mary J. Linnen [in the research foundation]."⁴⁶⁹

While the Linnen case settled and American Home Products did not admit any wrongdoing, "one news report quoted juror Bill Reed as saying that a majority of the jurors were leaning towards a plaintiff verdict as a 'wake-up-call' to AHP. The report said the juror said, 'a billion dollars for them would have been nothing.'"⁴⁷⁰ Other PPH cases have also resulted in verdicts for the plaintiffs. PPH claims are not covered in the proposed Settlement and other Linnen-type cases may result in large plaintiffs' verdicts against American Home Products. In addition, the Linnen case produced the noteworthy rulings excluding Linnen's phentermine experts and sanctioning Wyeth-Ayerst for the e-mail backup tape destruction.⁴⁷¹

⁴⁶⁶See MEALEY'S LITIGATION REPORT FEN-PHEN/REDUX, Vol. 3, Issue #4, Feb. 2000, available online at www.mealeys.com/fen.html

⁴⁶⁷*Id.*

⁴⁶⁸See *News This Week, Ticker*, NATL. L.J., Feb. 7, 2000, at A4.

⁴⁶⁹American Home Products Corporation, *AHP Joint Press Statement*, AMERICAN HOME PRODUCTS PRESS RELEASES, Cambridge, Mass., Jan. 27, 2000, available online at www.ahp.com/releases.ahp_012700.htm.

⁴⁷⁰MEALEY'S LITIGATION REPORT FEN-PHEN/REDUX, Vol. 3, Issue #4, Feb. 2000, available online at www.mealeys.com/fen.html

⁴⁷¹See *id.*

PART IIIA MAJOR LESSON WE CAN TAKE AWAY FROM THE FEN-PHEN EXPERIENCE AND AN

The above discussion sets forth a description of the medical and legal aspects of the fen-phen diet drug experience. It has provided numerous lessons in terms of medical knowledge and in products liability litigation.⁴⁷² However, its one of its most critical lessons has to do with the special situation of obesity drugs in modern American society. Due to background circumstances, the FDA should take a simple step that would prevent another widespread experience of the use of weight-loss drugs for cosmetic purposes. Obesity drugs have a purpose and a place, and fen-phen's most major lesson is that we have to limit that place in a way that was not done with Redux and Pondimin. Off-label use for prescription diet drugs should not be permitted, although off-label use should be permitted for non-obesity drugs because of its inherent benefits in medical innovation.

A MAJOR FEN-PHEN LESSON

The Need For Diet Drugs in Certain Situations to Treat Clinically Obese Individuals

Obesity is a serious concern in America and it leads to numerous associated medical problems. Obesity

⁴⁷²The fen-phen experience also arguably raised concerns about the way adverse drug reactions are reported to the FDA. However, whether or not the way the structure of U.S. adverse reaction reporting is at fault for the fen-phen problem depends on whether or not American Home Products acted responsibly in reporting adverse reactions. As this paper has discussed several times, there is a dispute between plaintiff and defense lawyers over whether American Home Products acted irresponsibly and failed to report or warn of Redux and Pondimin adverse reactions. If American Home Products failed to follow the procedures in place, then the lesson is that drug companies should face harsher sanctions for disregarding those procedures. American Home Products has faced serious repercussions in the form of thousands of lawsuits, monetary liability, and legal fees. Because the alleged wrongdoing of American Home Products is an issue that has yet to be definitively resolved (and this paper has presented both sides) it is difficult to concretely determine how the FDA reporting structure would need to be changed to prevent another fen-phen. Preventing another fen-phen where widespread use of risky drugs for a nonexistent disease would be better addressed by prohibiting off-label use for diet drugs.

affects 33% of American adults. Obesity in America needs to be treated, and a proven way of losing weight is reducing caloric intake while engaging in a daily program of physical activity. The U.S. Department of Health and Human Services recommends that:

A person who is less than 20% overweight should begin a life-long program of moderate physical exercise, such as brisk walking for 30 to 45 minutes, on most days of the week. Regular moderate physical activity is likely to improve weight control and will also strengthen the heart. Overweight persons should also begin to make moderate and life long changes in their food choices and eating practices, including reducing the total amount of calories they eat and ensuring that their diet is low in saturated fat and rich in fruits and vegetables. Persons who have a significant weight problem are advised to consult their physician to develop a strategy that is individualized for them. There are a number of options available that a physician can discuss with the patient.⁴⁷³

While a caloric reduction and exercise program would be the logical road to travel, it is not the road most Americans wish to follow. Americans are looking for a pill to take that will allow them to lose weight without summoning the discipline required for a serious diet and increased exercise. In the interview with Dr. Marnell, she indicated that patients would come to her and say that “nothing works” and that they had “tried everything”. Reducing caloric intake and engaging in a regular exercise program does work, but often people do not have the discipline to maintain such a regimen. People are willing to try any number of “easy fixes” for weight loss, hence the vast popularity of fen-phen. When overweight people are certain that “nothing works” but a pharmacological intervention, they will turn to diet drugs instead of attempting to maintain a healthy lifestyle. “Pick your poison as the cycle continues: if it’s not one drug it’s another. All of them promise to make one’s dream a reality, yet one must realize that the answer to trimming down is not found in a bottle. Despite the widespread use of pharmacologic therapies, the prevalence of obesity continues to increase, and the results of treatment remain unsatisfactory. In general, maintaining a reduced weight requires exercise and a diet, not necessarily medical supervision or drugs.”⁴⁷⁴ However, many Americans are unable or unwilling to exercise and diet their weight away. For many people diet pills provide a psychological

⁴⁷⁴Jaime A. Wilsker, *One Half-Phen In the Morning/One Fen Before Dinner: A Proposal For FDA Regulation of Off-Label Uses of Drugs*, 6 J.L. & POL’Y at 843.

benefit that allows them to lose weight, with the pill serving as a crutch or impetus to a diet/exercise program. And while Americans are willing to spend large amounts of money and risk serious side effects by taking diet pills, that effort is “often for naught because the weight is usually gained back.” immediately after people stop taking the pills.⁴⁷⁵ In addition, one study showed the total weight lost from fen-phen use to be only 5 and a half pounds.⁴⁷⁶

In light of the fact that Americans wish to solve their weight problems with pills instead of calorie reductions and exercising, diet drugs will generally be “blockbuster drugs” with enormous money making potential. Fen-phen became a national obsession, evidenced by the huge number of prescriptions written during its heyday. The discovery of the heart problems associated with fen-phen did cause people to think twice about diet drug use, but people are still trying to obtain fen-phen abroad and they have turned to the new “herbal fen-phen” (no pharmacological relation to fenfluramine or dexfenfluramine). The fact that herbal fen-phen is even advertised under that name belies the fact that the fen-phen fiasco did not scare Americans off of diet drugs for good. Metabolife is wildly popular and is now the new quick weight loss alternative. While Meridia has not been most doctors’ drug of choice for obese patients because of its similarity to Redux and Pondimin, Xenical has gained widespread popularity today for obesity treatment.⁴⁷⁷ Whatever happened with fen-phen, diet drugs will be developed and will be widely used to treat obesity, which has become an American epidemic. The issue will be how to harness the potential of those drugs for the fight against obesity while not allowing them to be used for the non-obese. Where the benefits outweigh the risks, America needs diet drugs. But where the disease is an attempt to shed a few pounds to look better, the use of diet drugs should be prohibited.

Cosmetic Diet Drug Use and The Resulting Recommendation that Off-Label Use Should Be Illegal For Diet Drugs

⁴⁷⁵Id at 820 – 821.

⁴⁷⁶See Jane E. Brody, *Hard Evidence Building Against Fen-Phen Safety*, PORTLAND OREGONIAN, Sept. 3, 1997 at E12.

⁴⁷⁷See Interview with Dr. Tori Marnell (March 18, 2000).

The fen-phen experience provided a valuable lesson about the inevitability of a diet drug being used by non-obese people for cosmetic weight loss. Obesity is a special ‘disease’ that warrants unique treatment by the FDA. With other pharmaceuticals the disease that the drugs are aimed at curing or preventing is generally more clear and easy to target than obesity. Since so many Americans are desperate to lose a few pounds without putting forth the discipline necessary to lower their caloric intake and engage in physical activity, diet drugs have a high propensity to be misused by those who are not clinically obese. Once word spread about fen-phen’s effectiveness in shedding pounds, the weight loss centers quickly established programs to capitalize on the fen-phen craze and the cocktail became widely available to millions of Americans who were not clinically obese. Our society places enormous pressure on women to maintain a slim physique, which for many is an unattainable dream. That pressure is pervasive and overwhelming to many American women, and it has bred a sense of desperation that led to the intense desire of these women to use fen-phen, no matter what the risks. The PPH risk was known, and while there are debates over whether American Home Products provided adequate warning of that risk, to many women that risk was simply disregarded in the quest to be thin. In addition, the FDA assesses a drug’s riskiness in the context of the benefits it provides against the disease it is meant to treat. The FDA acknowledged the risks presented by Redux during its troubled approval process, and the FDA approved Redux *because of the benefits it was to provide in obesity treatment*. However, if off-label use is legal, the desire to be thin by taking a pill, combined with the desire to make money, will thwart any attempt to limit diet drugs to use by the clinically obese. In the diet drug situation, taken in the context of modern American society and looking at the fen-phen pill-mill debacle, the FDA should make special rules for diet medications.⁴⁷⁸ The simple step of making off-label use illegal for drugs only approved for the clinically obese would ensure that the proper risk-benefit calculation is observed

⁴⁷⁸In the New Jersey Vadino trial opening statements, plaintiffs’ lawyer Esther Berezofsky held up a barbie doll and said that American Home Products preyed on overweight women by “promoting a distorted image of thinness and health, then selling them drugs that were ineffective in fostering long-term weight loss.” She claimed, “They created a market for something that didn’t work and wasn’t a cure.” Bob Van Voris, *A Drug Maker’s Legal Migraine*, NATL. L.J., Aug. 23, 1999, at B20.

with regard to diet drugs. If doctors were liable for off-label prescribing to the non-obese, this would curb cosmetic diet drug use. For the truly obese, even fen-phen may have been worth the risks, considering the havoc that obesity can wreak on the human body. Yet when fen-phen was made available in today's legal and societal context, it went to those for whom the risks far outweighed the benefits. Diet drugs need to be available to treat the clinically obese and off-label use should be legal to provide for innovative drug therapies, especially in the oncology and AIDS contexts. The way to allow this while ending cosmetic diet drug use is to only prevent off-label use in the diet drug context, and the way to enforce it is through physician liability. The reality of today's world is such that this step should be taken to prevent another fen-phen situation. In conclusion, a key fen-phen lesson learned is that in diet drug cases where cosmetic appearance is at issue, the FDA needs to take action to ensure that drugs are safe and effective for those who use them. Namely, the FDA needs to ensure that the proper risk-benefit calculation does not break down. An admonition to doctors that pills must only be taken by obese individuals is insufficient to quell the insatiable desire of the American population for a quick pill fix to lose a few pounds. For obesity drugs where the societal context makes it likely that the drugs will be used on a widespread basis for uses far beyond what is listed on their labels, the FDA needs to prohibit off-label use. This will go a long way towards ensuring that the drugs really will only go to people who suffer from obesity. We can then fight obesity and also avoid another costly and harmful fen-phen debacle.

CONCLUSION

Summary of Fen-Phen Situation and Eventual Outcome

The fen-phen situation was an overall detrimental experience for the diet drug users and for the diet drug

makers/marketers. It has broken much legal ground in terms of medical monitoring⁴⁷⁹ for asymptomatic plaintiffs and has been instrumental in detailing what characteristics are necessary for settlement class certification after the Supreme Court's Amchem decision. The fen-phen users and their associated medical problems have shed light on valvular heart disease and brought it to the forefront of the minds of many American medical professionals and much of the U.S. population. Fen-phen illustrated the problem of pill-mills for popular drugs where doctors never see patients to explain and assess the risks of medication. The litigation also has provided a model for multi-district litigation involving injured and asymptomatic plaintiffs, and Judge Bechtel set a good example with the fast-track process for the seriously ill. There are conflicting stories of who is to blame and who should pay who for what, and the eventual completion of the fen-phen story will produce some who have lost more than others. The most likely outcome of the entire situation is for the Settlement to be accepted, despite various threats of plaintiffs' lawyers for massive opt-outs. Many plaintiffs will probably want the certainty of the Settlement as opposed to taking their chances in court, and for the vast number of medical monitoring class members the Settlement provides generous benefits. The Settlement has been carefully structured in a way that is designed to secure Final Judicial Approval by Judge Bechtel, and it would be very much in American Home Products' best interests not to walk away. Thus forth, the Settlement will probably determine who has won and lost the most from the fen-phen experience.

Outlook for PPH Sufferers

For those people with PPH, the diet drug fiasco is the most tragic. The PPH context is where the issue of who is to blame becomes the most pointed. There are two sides to the story of whether American Home Products acted responsibly with respect to Redux and Pondimin. American Home Products maintains that

⁴⁷⁹The fen-phen litigation has led to several states having to examine whether or not their law recognizes medical monitoring claims and whether or not to certify a fen-phen medical monitoring class. See Cabraser and Vincent, *Class Certification of Medical Monitoring Claims in Mass Tort Product Liability Litigation*, AMERICAN LAW INSTITUTE – AMERICAN BAR ASSOCIATION CONTINUING LEGAL EDUCATION COURSE OF STUDY, July 22, 1999.

it committed no wrongdoing with respect to warning consumers about the risks associated with Redux and Pondimin, and that it kept the FDA informed according to the law. Plaintiffs' lawyers claim that American Home Products knew of the valvular heart problems and did not inform the FDA, physicians, or consumers, and that American Home Products failed to adequately reflect the true PPH risk associated with the diet drugs.

Based on PPH settlements so far, PPH sufferers will likely receive fairly high individual settlements from American Home Products in the neighborhood of \$2 million per patient.⁴⁸⁰ Some PPH sufferers may not be able to sue in court if they knew of their PPH before the opt-out date and received Fund B Settlement benefits, and those people would be the true losers in the outcome of the fen-phen litigation if the Settlement is accepted.

Assessment of Outcome For Valvular Heart Disease Plaintiffs (Symptomatic and Asymptomatic)

As for the valvular heart disease claims, those are encompassed in the Settlement Agreement, and in all likelihood it will close the chapter on valvular heart disease liability for American Home Products. The Settlement is good for the company since it eliminates the uncertainty of going jury by jury or settlement by settlement, and it also lets American Home Products off at a fairly low price estimated at about \$2.50 per share. The Settlement is also good for asymptomatic class members because they receive benefits over and above what the ACC, AHA, and DHHS recommends for Redux/Pondimin users. However, for those who suffer from serious valvular heart disease, the Settlement provides for low levels of matrix compensation benefits and makes it difficult for class members to qualify for those somewhat paltry sums. However, those plaintiffs would benefit from the Settlement in that they too, like American Home Products, eliminate the

⁴⁸⁰See Arian Campo-Flores, *A Fen-Phen Fix – Big Suits: Top of the Docket* Vadino et. al. v. AHP, THE AMERICAN LAWYER, Nov. 1999.

uncertainty of going to trial in favor of a getting a certain amount, albeit a smaller amount than they would likely obtain if they won in court.

Overall Conclusion – Final Predictions and Hopes for the Future

The Settlement outcome, which is probably inevitable, has winners and losers, and hopefully the media attention will have made people more cautious in the future about limiting their medications to those they really need to combat serious health problems. The final chapter of the fen-phen story has not been written and will remain unknown until the fate of the Settlement is determined and all the PPH claims and claims of opt-out plaintiffs have been resolved. However, it appears likely that the Settlement will be approved, that American Home Products will have less liability than it could have had, and that the medical monitoring plaintiffs will be those class members who gained the most out of the total outcome.

In sum, American Home Products can now turn to developing new drugs and perhaps finding a new merger partner, asymptomatic diet drug users can take advantage of the medical monitoring, valvular heart disease sufferers who did not opt-out can accept their benefits, those that did opt-out can sue, and PPH sufferers can also sue for damages. The FDA can consider making off-label use of diet drugs illegal and making doctors liable for adverse effects resulting from off-label diet drug prescriptions. And hopefully the U.S. population will have learned to exercise caution when faced with the prospect of a quick weight loss fix. The best outcome will be if a fen-phen litigation situation never again presents itself in the U.S. judicial system.