ENHANCING PATIENT DRUG SAFETY: MORE EDUCATION, SOME REGULATION

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"Prescription-only" drugs[1] are used to treat a variety of illnesses[2]. These drug are used to treat life-threatening diseases such as cancer and heart diseases and, other less serious diseases such allergy and male impotence[3]. However, in general, these drugs are very potent and have the potential to cause serious side effects[4]. In principle, regulations that limit patient access to prescription-only drugs aim to safeguard the patient's health. Therefore, till recently, the widely accepted practice, to ensure the safety and efficacy of the drug regimen, was for a patient to first visit his/her state-licensed physician, for an in-person evaluation and diagnosis of the patient's condition; then the physician, as appropriate, would write a prescription which the patient got "filled" at the "corner drug store" from a state-licensed pharmacist [5]. Recent developments have provided patients with two additional modes of access to prescription-only drugs. The first is the availability of such drugs from Internet[6] pharmacies[7], which in many cases do not require a prescription[8]. The second is the reclassification of prescription-only drugs to "over-the counter" (OTC) status[9]. This reclassification would make available prescription-only drugs to patients without a prescription from the patient's physician[10]. The net effect of the two developments is the same: patients have unsupervised access to highly potent drugs with potential for serious, even fatal, side effects.

The proponents of regulating Internet access of prescription-only drugs support the hypothesis that such unsupervised access poses a public health hazard in view of the serious side effects of such drugs. In contrast, proponents of the switch of prescription-only status to OTC status support the opposite hypotheses that patients have the ability to use such drugs in safe and effective manner. This paper evaluates the validity of these hypotheses based on clinical experiences relating to safety and efficacy of prescription-only drugs and proposes alternative regulatory solutions to optimize efficacy of drugs, both prescription-only and OTC drugs.

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[1] See Part I
[2] See generally, Physician's Desk Reference 56th Edn., Medical Economics Co. Oradell, NJ (2002).
[3] Id
[4] Id
[5] See Rebecca Porter, *Internet Pharmacies: Who's Minding the Store,* 36-May Trial 12
[6] Joanna M. Carlini, *Liability on the Internet: Prescription Drugs and the Virtual Pharmacy.* 22 Whittier L. Rev. 157, 161 ("Internet is a collection of interconnected computers"); also see ACLU v. Reno 929 F. Supp 824, 830 (E.D. Pa, 1997)"([I]nternet is a giant worldwide network, which connects innumerable smaller groups of linked computer networks and is a "network of networks")
[7] See Part I
[8] Id.
[9] Id.
[10] From a regulatory standpoint, reclassification of prescription-only drugs to OTC would no longer make them prescription drugs.

Drug therapy is the most common approach to disease management. In 1998, 2.8 billion prescriptions were written to combat disease.[11] This number is projected to increase to 4 billion by 2005[12]. In principle, the availability of prescription-only drugs over the Internet has raised two major issues: First, such availability has minimized or eliminated supervision of a patient's drug therapy by a physician or another qualified health care provider. Second, uncertainties exist regarding the quality of drug products obtained from Internet sources, particularly from overseas sources, which are outside US jurisdiction. These concerns grow as Internet access and commerce, including on-line drug purchases, are on the increase. For example, it is estimated that about 48 million people accessed the Internet in 1998; this number has been predicted to increase to 320 million by 2005[13]. Money spent on on-line purchases is also expected to show a corresponding rise from $11.4 billion to $49.5 billion by the end of 2002[14].

Internet pharmacies are also increasing at a rapid rate[15]. The number of such pharmacies has increased from 30 to more than 400 in a six-month period (January to July 1999). It has also been estimated by the American Medical Association (AMA)[16] that there are at least 400 "instant prescription" web sites where a patient can obtain prescription-only[17] drugs after a consultation ("cyber-consolation")" with an on-line physician ("cyber doctor'). Cyber-consultation usually involves the filling of a short questionnaire by the patient and a waiver of liability. It has been stated that "online drug stores are one of the hottest categories of e-commerce"[18]. Another prediction is that by 2004 the Internet "prescription drug market will grow from almost nothing in 1998 to $15 billion by 2004"[19].

Proponents of regulating Internet drug prescribing[20] are concerned about patient welfare with respect to drug efficacy and drug safety[21]. Such regulation is aimed to protect patients from "unsafe use of drugs, including the requirement that drugs be dispensed only after valid prescriptions and that new prescriptions be issued only after a physical examination" and from "adverse effects from inappropriately prescribed medications,

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[11] See Michael Menduno, *Apothecary Now; Online Pharmacies,* Hosp & Health Networks (1999) (July 1, at 34) (citing 55 Food & Drug Law L.J., 619, 621)

[12] Id

[13] See Michael Casey, *The Internet Writes Its Own Prescription,* Med. Industry Today, (1999) (Mar. 24) (citing 55 Food & Drug Law L.J., 619, 621)

[14] Id.

[15] See Kerry T. Rost, *Policing the "Wild West" World of Internet Pharmacies. 55 Food & Drug L.J. 619, 620.*

[16] See Douglass Carnall, *American Medical Association Moves to regulate Prescribing on the Internet*, 319 Brit. Med. J. 213, 213 (1999)

[17] See Part I

[18] See James Ledbetter*, No prescription? No Problem: Online Drug Stores Don't Always Work the Way You'd Expect.* (June 30, 1999) http://www.pcworld.com/resource/printable/article/0,aid,11633,00.asp (last visited April 28, 2002)

[19] See FN 5

[20] Id

[21] See Anon. *The Clinton Administration Unveils New Initiative To Protect Consumers Buying Prescription Drug Products Over the Internet,* The White House, Office of the Press Secretary (http://clintyon3.nara.gov/WH/New/html/19991229.html (last visited, April 26, 2002) (A budget of $10 million was proposed for the FY 20001 budget to fund such activities)

dangerous drug interactions, or contaminated drugs"[22]. These concerns are legitimate in that while drugs have the potential for great "good" when used properly, they also have the potential for great "harm", when used improperly. However, there is no evidence to support that such prescribing has resulted in any harm to public safety with respect to drug use. The calls for regulation of internet prescribing of prescription-only drugs appears to have been based mostly on sensational stories in the media[23] relating to tragic experiences with one drug - sildenafil (Viagra®). Viagra®), popularly known as "blue pill was (and still is) the first prescription-only [24] drug to be available in pill form to treat erectile dysfunction (male impotency). The drug has also generated much interest in and demand by men[25]. Therefore, this "life-style"[26] drug has attracted much attention in the news media more than any other single drug. One case in the news media relates to how a 16-year old boy, was sold Viagra® by an online pharmacy[27]. This was a "sting" operation and the state of Kansas brought action against the nonresident doctor under the state's Consumer Protection Act[28]. While the court "enjoin[ed] the doctor from dispensing medication or practicing medicine in Kansas", it also noted "no actual harm was done to anyone"[29]. Another is the story where an online pharmacy sold Viagra® to a cat[30], as part of a prank. However, articles continue to appear in the press that fuels the suspicion that Internet prescribing of prescription-only drugs is a serious public health problem[31]. Knowledge gaps with respect to proper use and side-effects of prescription-only drugs are the major cause of serious side effects encountered with these drugs in clinical practice.[32] The tragic experiences with Viagra®) further show that patients, in spite of receiving this prescription-only drug dispensed on a valid prescription from his physician, can suffer fatal adverse drug reactions (ADRs) [33].

One major concern of the opponents of Internet dispensing is the perceived lack of ability of a patient to safely and effectively self-medicate with prescription-only drugs. However, ongoing regulatory changes are reclassifying prescription-only drugs as OTC drugs[34]. In essence, such reclassification would provide patient access to prescription–

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[22] Id

[23] See Shannon Brownlee and Stacey Schultz, Dying for Sex, http://www.usnews.com/usnews/nycu/helath/articles/99011/nucu/11viag.htm (visited April 1, 2002)

[24] see Part I

[25] FN 12 (shannon/ us news)

[26] See Chester Chuang; *Is There a Doctor in the House? Using Failure-to-Warn Liability to Enhance the Safety of Online Prescribing*. 75 N.Y.U.L. Rev. 1542 (2000) (These are drugs used to enhanced quality of life than to treat diseases; well known examples include drugs for hair growth (Propecia®), weight loss (Xenical®) and male impotency (Viagra®)

[27] See 38 P.3d 707

[28] Id

[29] Id at 710

[30] See Michael F. Conlan, *NET WACHERS; Congress Weighs New Laws as it Probes the Practices of On-Line Pharmacies* 143 Drug Topics (August 16, 1999) (available at 1999 WL 100218900

[31] See Frank J. Murray, *Web Prescriptions Thrive Despite Sting*, The Washington Times (2002) (Mar. 5) (http:///www.washtimes.com/national/20020305-661542.htm (last visited Mar. 6, 2002)

[32] See Karen E. Lasser, *Timing of New Black Box Warnings and Withdrawals for Prescription Medications.* 287 JAMA 2215 (2002)

[33] See Part II

[34] See David G. Adams et al., *Fundamentals of Law and Regulations Vol. II.* Food and Drug Law Institute (1997), at 197

only drugs without a prescription from his/her physician. Therefore, this situation is similar in many respects to the situation where patients obtain prescription-only drugs from an Internet source. This reclassification is based on the assumption that patients have the ability to self diagnose and medicate themselves. This reclassification is gaining momentum pressured by "forces of economics, government and a health-conscious public"[35]. The criteria for this reclassification effort will be discussed later in detail in this article[36]. Therefore, any discussion to regulate Internet drug prescribing has to include issues relating to reclassification of prescriptions-only drugs to OTC status[37]. In principle, proponents of this reclassification would speak against regulating Internet prescribing of drugs, since a prescription-only drug by regulatory fiat is available to the patient without a prescription from a physician or other health professional permitted to prescribe drugs.

The central and common question that needs to be addressed in discussing regulation of internet prescribing and the reclassification of prescription-only drugs to OTC status is: What is the most efficient way from a therapeutic standpoint to promote patient therapy and safety with respect to drug treatment? This paper will focus only on drug safety and efficacy issues[38]. In order to promote a full understanding of complex issues involved in drug therapy, this article is divided into 3 parts. Part I will provide a definition of terms as used in this paper, a comprehensive background of the drug classification system and the process by which a prescription-only drug is approved for sale in the US. Part II will present arguments in support of the hypothesis that fatalities encountered with prescription-only drugs is more dependent on lack of complete information about their toxicities, especially when first marketed and inadequate training of physicians in drug therapy, than on their Internet availability. Part III will propose, in light of discussions presented in Parts II, clinical science based regulatory alternatives, than Internet Regulation, to protect patients from the potential health hazards of Internet-prescribing of prescription-only drugs. Proponents of Internet-regulation have been silent on the issue of similar drug-related hazards from the reclassification of prescription-only drugs to OTC status. This issue is also addressed in Part II.

Part I: Regulation of Drug Access to Patients

Classification of Internet Pharmacies: An Internet pharmacy is one that "sells medications through its website"[39]. There are three[40] types of such pharmacies: (1) pharmacies that dispense prescriptions written by a licensed medical practitioner, who is often the patient's physician; such prescriptions are usually written after an initial office visit, though refills can be obtained subsequently after the initial visit without additional

[35] Id.
[36] See Part II.
[37] See Thomas A. Gossel, *Implications of the Reclassification of Drugs from Prescription-Only to Over-the Counter Status. 13 Clin. Ther. 200 (1991).*
[38] Related issues such as patient convenience and privacy, cost/benefit analysis of unsupervised access to prescription-only drugs is not included.
[39] See FN 15
[40] Id

in-person visits (2) pharmacies that dispense a prescription, written by a 'cyber-doctor" after a "cyber-consultation" which usually involves the patients filling a questionnaire and (3) pharmacies that dispense without a prescription of any sort.

Internet Drug Prescribing: This refers to the situation where an Internet pharmacy dispenses a prescription-only drug to a patient without the benefit of a "valid" prescription from the patient's physician. In this context, a valid prescription is defined as one written by a physician after an in-person examination and evaluation and diagnosis of the patient's condition. When an Internet pharmacy dispenses a prescription-only drug to a patient based on a valid prescription, then such as act is called Internet dispensing distinguished from Internet prescribing. Internet drug dispensing has gained acceptance[41] The accreditation program overseen by the National Boards of Pharmacy provides adequate safeguard of patients who use Internet pharmacies to get their prescriptions "filled".[42]
The first type of Internet Pharmacy is almost identical to the situation where patient, after an in-person physician visit for diagnosis of illness and treatment, stops at the "corner" drug store to get his/her prescription filled. If a patient gets his prescription filled in a drug store, the pharmacist is required in many states by law[43] to provide, upon request, additional information on potential side effects and "how to use" information. It is not clear if a pharmacist is available to the patient to discuss these issues when the prescription is filled by a pharmacist on-line.

Dangers of Internet Access to Drugs: It is the second and third, especially the latter, types of pharmacy that has caused many to voice concerns of patient safety and product quality (especially products obtained from foreign pharmacies). The American Medical Association has acknowledged that "cyber consultation" can result in a "legitimate clinical decision"[44], even when the physician had not seen the patient when "the physician and patient have an ongoing relationship, the patient routinely uses this physician, and history and physical examination are already in the medical world".[45]

Prescription-only drugs: The Food and Drugs Administration, authorized by the Federal Drug and Cosmetic Act (FDCA)[46], is the major Federal Agency that regulates all types of drugs. Under this act:
A prescription-only drug is defined as:[47]

> A drug intended for use by man, which –
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> a. is a habit forming drug to which section 352(d) of this title applies; or

[41] A description of the VIPPS (The Verified Internet Pharmacy Practice Site) program can be found at http://www.nabp.net/vipps/intro.asp (last visited April 26, 2002)
[42] Id
[43] In Missouri, the practice of pharmacy is defined as ". . . consultation with patients . . . abut the safe and effective use of drugs . . ." (RSMo338.0100
[44] See FN 15
[45] Id.
[46] Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301-907
[47] See David W. Opderbeck, *How Should FDA Regulate Prescription Drug Promotion on the Internet? 53 Food & Drug L. J. 47, 54.*

b. because of its toxicity or other potentiality for harmful effect, or the collateral measures necessary to its use, is not safe for use except under the supervision of a practitioner licensed by law to administer such drug; or

c. is limited by an approved application under section 355 of this title to use under the professional supervision of a practitioner licensed by law to administer such drug

shall be dispensed only by the prescription or authorized prescription refill.

Approval of a Prescription-only Drug: A manufacturer of a prescription-only drug must provide "substantial evidence" that it is "safe and effective" before it can be marketed[48]. This proof is sought by submission of a New Drug Application (NDA) to the FDA[49]. In brief, the first step involves laboratory and animal testing[50]. The second step involves human testing consisting of three phases. The first phase (Phase I) involves "preliminary studies, usually on healthy subject to see how the drug is handled in the body and whether compound raises safety issues. [51]. Phase II, after being shown that the drug is "reasonably safe to take"[52] in Phase I studies, "involves studies in small patient groups . . . . . to determine effectiveness"[53]. After successful completion of Phases I and II, a drug candidate is tested in "larger size clinical trials designed to substantiate whether the drug is safe and effective for its intended purpose"[54]. The cumulative data is subject to scientific and regulatory review by the FDA. Upon approval by the FDA, the manufacturer of the drug has the right to market the drug.

Over-the Counter Drugs: Certain drugs can be legally purchased by a patient can legally without a prescription; these drugs are called over-the –counter (OTC) drugs. Such drugs are defined as "generally recognized as safe and effective (GRASE)[55]. Sometimes OTC drugs called "old" drugs, though there is no such official definition; this is, most likely, a reference to the 1938 FDCA, which exempted drugs marketed prior to 1938 from the NDA provision[56]**.** An over-the counter (OTC) monograph is available for every drug defined by law as to be GRASE and can be marketed without prior FDA approval.

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[48] See Anon., *Primer on Food and Drug Law and Regulation Food and Law Institute Summer Internship Program (June 19-23, 2000)* at 34 (henceforth Primer)

[49] Id. also see Timothy R. Covington, *Self-Care and Nonprescription Drugs*, in Handbook of prescription Drugs, American Pharmaceutical Association, Washington D.C. (1995) (henceforth Covington)

[50] Primer (These are also called "pre-clinical Investigations")

[51] Id

[52] Id

[53] Id

[54] Id

[55] See Covington

[56] Id

Reclassification of Prescription-only Drugs to OTC status.

According to the Durham-Humphrey amendments in 1951 to the Food Drug and Cosmetic Act, only those drugs that cannot be safely used without medical supervision need a prescription[57]. To state this differently, prescription-only drugs are an exception than the rule..

OTCness has been defined as[58]:

> . . . the wide spread availability of safe and effective non-prescription medicines for responsible self care by the consumer according to label directions, pursuant to applicable laws, regulations, and voluntary industry codes affecting manufacturing, packaging, labeling, distribution, and sales of quality products and the advertising of those products in all media

The FDA started meeting its statutory mandate for OTCness in 1972 by "defining not only safety but also the effectiveness of all marketed OTC ingredients[59]". Safety criteria for switching from prescription-only to OTC status are a relative standard. The switch is allowed if the drug has " a low incidence of adverse reactions . . . low potential for harm may result from abuse"[60]. In this context, effectiveness means "a reasonable expectation of . . . clinically significant relief".[61]

Criteria for reclassification include[62]:

i. Is the disease self-diagnosable?
ii. Is the disease self-treatable?
iii. What are the adverse effects of the drug? This may include unique toxicity such as Viagra® and nitrates.
iv. Is the drug habit-forming?
v. Do benefits outweigh risks?[63]
vi. Can warnings against inappropriate and/or unsafe use be written?
vii. Can labeling be read and understood by an ordinary person?
viii. Has the prescription-only drug been on the market long enough to provide full information about its safety profile? The regulatory standard is "used for a material time and extent"

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[57] See R. William Soller. The Over-The-Counter Scientific/Regulatory Paradigm 33 Drug Inf. J. 799 (1997)
[58] Id
[59] Id
[60] Id
[61] Id
[62] Id at 10
[63] See Prescription Drug Conversion, http://www.americangeriatrics.org/products/positionpapers/conversi.html (visited April 19, 2002). (This position paper by the American Geriatric Society discusses potential risks of elderly patients to drug toxicity including a request that the FDA require that drug labels be understandable and readable (large print).

There are three ways to accomplish this reclassification:[64] (1) the manufacturer provides additional data in support of a request for the switch, (2) the FDA may authorize the switch, sua sponte[65]or (3) the manufacture may petition the FDA for switching from prescription-only to OTC status[66]. Providing additional data is the most common current practice for accomplishing this switch because of economic incentives.[67]

Part II: Risk of Drug Toxicity in Supervised[68] and Unsupervised [69] Drug Therapy

Available data in this area is quite limited. Drug therapy is mainstay of patient care. It has been estimated that about 3.5 billion health problems are treated annually; about 50% of these problems are treated using prescription drugs; the other 50% by OTC drugs.[70] It is generally believed that patient safety is assured if the patient uses a prescription-only drug based on a valid prescription (one written the patient's physician after an in-person evaluation). However, clinical experience with drugs does not support this assumption. It has been estimated that about 100,000 hospitalized patients died in 1994 in the United States of the adverse drug reactions (ADRs)[71]. An ADR is defined by the World Health Organization as "any noxious, unintended and undesired effect of a drug, which occurs at doses used in humans for prophylaxis, diagnosis or therapy"[72]. Even more alarming is that many of these ADRs are preventable[73]. This death toll can be put in perspective by comparison with death rates from other causes: heart disease (743, 460); cancer (529904), stroke (150108) pulmonary disease (101077) and accidents (90523)[74]. These statistics show that fatalities from ADRs are the fifth leading cause of death in the US. This has understandably drawn much public attention and the drug makers are encouraged to provide toxicity information to patients[75]. While hospitalized patients and outpatients

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[64] 21 C.F.R. § 314.70-.71
[65] Id. Pt. 330
[66] Id. § 310.200(6)
[67] See David g. Adams et. Al., *Fundamentals of Law and Regulation* Vol. II, Food and Drug Law Institute, Washington, D.C, (1995) at 197
[68] For the purposes of this discussion, supervised drug therapy deals with (1) an out-patient who is on a drug treatment program prescribed by a physician following a in-person diagnosis of the patient or (2) in-patient hospitalized.
[69] Unsupervised deals with situations where the patient is self-treating his or her illness
[70] Covington at 4

[71] See Jason Lazarou et al., *Incidence of Adverse Drug Reactions in Hospitalized Patients: A Meta Analysis of Prospective Studies*, 279 JAMA 1200 (1998).

[72] See Anon. *World Health Organization. International Drug Monitoring: The Role of Hospital*. Geneva, Switzerland: World Health organization, 1996. Technical Report Series no. 425
[73] Paula Kwalbrun, *Eradicating Medical Errors: Can it be Done*? Pharmacy Times at 53 (2000, October)
[74] Jason Lazarou, Incidence *of Drug Reactions in Hospitalized Patients: A Meta-Analysis of Prospective Studies.* 279 JAMA 1200, 1204 (1998)
[75] J. Gray. Bill would Force Drug Makers to Give Customers Data on Risks. New York Times (1996) (July 25, A11)

on a prescription-drug under the supervision of a physician are situated in different settings, the similarity between the two situations is that they are under supervised drug therapy. Therefore, regulating Internet drug prescribing is unlikely to enhance drug safety.

The tragic experiences with Viagra® further show that patients, receiving a prescription-only drug dispensed based on a valid prescription from his physician , can still suffer fatal ADRs. Within months after its approval in March 1998, reports started to appear about fatalities in men who had used the drug[76]. The FDA has confirmed that about 130 Americans had died after taking these pills by November of 1998. There is evidence that these fatalities included patients who had received Viagra® from their physicians or from Internet sources. In one specific example, a 65-year patient had received the drug from his urologist[77]. Another urologist confessed, "He did not consider possible cardiac effects"[78]. One death, that of a 52-year old patient, followed the use of Viagra® purchased on the Internet[79]. Another drug that caused fatalities was cisapride[80], used to treat a non-life threatening condition (gastroesophageal reflux) in adults. When pediatricians prescribed the drug to infants with the same condition, it was reported that 24 of them died[81]. It has also been reported that about 1000 patients have died because of ADRs from seven drugs that were approved since 1993 but later recalled from the market.[82]

The reasons for deaths in hospitalized patients[83] and outpatients on Viagra®[84] and cisapride[85] point to the complex nature of ADRs, and often defy a clear explanation. However, it is important to identify plausible explanations for these reported ADR-related fatalities, so that proposals to either reduce, if not eradicate, ADRs can be proposed. Some potential explanation for drug-related ADRs are listed below:

> Limited Pre-approval Clinical Testing: Undetected drug interactions are a serious problem of drug therapy. One major reason why a drug's toxicity remains unknown, especially during the "initial"[86] period after its approval, is related to the drug approval process. Under FDCA, a prescription drug is approved by the FDA only after the manufacturer submits data to convince the FDA that the new drug is "safe and effective".[87] . Though results from extensive[88] animal (pre-

[76] See Shannon Brownlee and Stacey Schultz, Dying for Sex, http://www.usnews.com/usnews/nycu/helath/articles/99011/nucu/11viag.htm (visited April 1, 2002)
[77] Id
[78] Id
[79] See John Barry, *Online Pharmacies: Should We be Free to Buy Drugs Without the Advice of A Doctor?*, http://speakout.com/activism/issue_briefs/1339b-1html
[80] See FN 32
[81] Id
[82] Id.
[83] FN 12
[84] FN 14
[85] See FN 32
[86] One major factor affecting the duration of the initial period is the number and variety of patients treated with the drug.
[87] See Primer (FN 47)

clinical) and clinical (normal subjects and patients) studies (the NDA application, *see supra*) are submitted by the manufacturer to prove "safety and efficacy", clinical data is obtained only from a in a relatively small number of patients[89] for economic reasons. The following examples will illustrate the point. Terfenadine (many know it by its trade name Seldane®), the first non-sedative anti-histamine drug) was tested in 5000 patients prior to approval; 7.5 million patients were exposed to this drug before it was recalled from the market due to newly discovered toxicities. [90] The popular weight control combination, consisting of fenfluramine and dexfenfluramine (known as fen-phen), was tested separately only in a total of 1540 patients prior to approval; at the time of its recall because of the damage it caused to heart valves, a total of 9.2 million patients had been exposed to this drug[91]. Therefore, if a small percentage of patients are susceptible to an adverse drug reaction to a prescription-only drug, then such dangers will become known only as more patients over time are exposed to the drug[92]. In addition to a relatively small sample size in clinical trials, patients are also screened to exclude certain other conditions[93]. This additional constraint further limits the wider applicability of clinical results submitted in the NDA.

Voluntary Post-Marketing Surveillance: The FDA has mandated that a manufacturer report ADRs of a prescription-only drug after it initiates sale of the drug[94]. The major objectives of this Surveillance is to detect previously unknown ADRs, further understand the known risks of the drug, discover interactions with other drugs, uncover patient populations that are more likely to suffer ADRs and identify causation between drug use and patient problems.[95] . However, in practice this program is essentially a voluntary effort because a drug manufacturer "is not required to actively seek out safety information about their products"[96]. Only when " a healthcare professional or consumer spontaneously notifies it (the manufacturer] of any adverse event associated with the use of the drug in humans', is the manufacture required to report such events to the FDA[97].

Inadequate Physician Education in Drug Therapy

Pharmacology is defined as "[t]he science, which deals with the study of drugs in all its aspects"[98]. Therapeutics is defined as " [t]he branch of medical science

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[88] FN 14 (In the case of Viagra®, "several boxes" of clinical data was submitted to the FDA)

[89] See Michael A. Friedman, *The Safety of Newly Approved Medicines: Do Recent Market Removals Mean There is a Problem,* and 281 JAMA 1728. Only a relatively small number of patients are tested prior to approval for economic reasons. The current estimate of the average cost of bring a new drug to market is about $ 800 million.

[90] Id

[91] Id

[92] FN 32 ('Many serious ADRs are discovered only after a drug has been on the market for years")

[93] See FN 14 at 6

[94] See Barbara A. Noah and David B. Brushwood, *Adverse Drug Reactions in Elderly Patients: Alternative Approaches to Postmarket Surveillance, 33* J. Health L. 383, 390 (2000)

[95] Id at 396

[96] Id at 397

[97] 21 C.F.R. § 314.80 (1999).

[98] Blakiston's Gould Medical Dictionary 3rd Edn., McGraw-Hill Co. (1972)

dealing with treatment of disease"[99]. Pharmacology is one of the less emphasized areas in medical school curriculum[100]. The average number of required hours of preclincial instruction in Pharmacology at a US Medical School for the MD degree is 99.0[101]. Therapeutics is not listed as a separate area of instruction. A Time article more than 20 years ago stated[102]:

> Pharmacists get three to four years of training, almost exclusively about drugs. Many of them know more than doctors [medical doctors] do about potentially dangerous drug interactions. Medical schools usually give only one formal course in pharmacology. Physicians, in fact, pick up their practical drug knowledge on the job and by reading medical journals. A hotly debated but durable criticism of physicians is that they rely heavily on drug-company literature and advertising, both sometimes misleading.

It is now widely known patients[103] on nitrates[104] who engage in sexual activity[105], after using Viagra® are at high risk of sudden death due severe hypotension (reduced blood pressure). The original label warned about the risk of simultaneous ingestion of Viagra® and nitrates, and stated, "There is a degree of cardiac risk associated with sexual activity". However, there was no information on the safety of the drug in patients with heart disease or who recently had heart attacks or strokes. In view of the fatalities, the label has been revised to include information on these additional risks.[106]

In addition, "[i] t has been documented that physicians often ignore "warnings on package inserts and the possibility of drug interaction when prescribing drugs"[107]. This statement was made subsequent to a commentary on the withdrawal of 5 approved prescription-only drugs between September 1997 and September 1998[108]. In addition, other factors that exacerbates the problem of ADRs problem are misprescribing, medication errors and undetetcted interactions"[109].

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[99] Id

[100] See Jordan J. Cohen, Curriculum Directory 2000 (28th Edition), Association of American Medical Colleges (For example, the average requirements for Pathology and Pathophysiology are 201.5 and 220.7 hours, respectively).

[101] Id.

[102] See Anon. *More Than Just Pill Counters: Clinically Trained Pharmacists Begin Prescribing for Patients*. TIME (October 12, 1981)

[103] It should be noted that most patients who take Viagra® are older and may have underlying heart disease (e.g. angina, history of heart attacks)

[104] A class of drugs taken to reduce blood pressure (anti-hypertensive)

[105] FN 14 (A 65-year old " began shaking and passed out, just as the couple was finishing having sex"

[106]

[107] See Eric P. Brass, *Changing the Status of Drugs from Prescription to Over-the Counter Availability,* 345 *New* Engl. J. Med., 810, 814 (2001)

[108] Id

[109] Id

Ignoring warnings by physicians of potential side effects of drugs when prescribing them is particularly unsettling in view of the learned intermediary doctrine[110]. This principle exempts pharmaceutical companies from having to warn the patient directly of dangers inherent with the drug[111]; instead, this doctrine limits the duty to warn of a manufacturer of a prescription-only drug to "an obligation to advise the prescribing physician of any potential dangers that may result from the drug's use"[112]. The Fifth Circuit explained the physician's role as follows[113]:

> Prescription drugs are likely to be complex medicines, esoteric in formula and varied in effect. As a medical expert, the prescribing physician can take into account the propensities of the drug, as well as the susceptibly of his patient. His is the task of weighing the benefits of any medication against its potential dangers. The choice he makes is an informed one, an individual medical judgment bottomed on knowledge of both patient and palliative.

A patient is falsely reassured of a drug's safety when the prescribing physician fails to convey manufacture provided drug information to the patient. Such reassurance exacerbates the situation because the patient is not likely to seek additional information of potential side effects of the drug

The Self-Care Revolution[114]: Sweeping changes have been or are being made with respect to re-classification of drugs so that many more prescription-only drugs are now reclassified as OTC drugs[115] The term "switch" in this paper refers to this reclassification of existing "prescription-only" drugs as OTC drugs. To-date, about 40 prescriptions – only drugs has been reclassified to OTC status[116]. The obvious effect of this reclassification effect is to make more drugs available to a patient without the supervision of a physician or other health care provider. This change runs contrary to the intent of proponents of regulating Internet prescribing which in essence is to limit access to prescription drugs under supervised conditions.

Patients are taking an active and more informed role in their own health care[117]. This is supported by the availability of abundance of health care information in varied forms such as hundreds of health related self-help books, newspapers articles, television and radio programs and Internet web sites. The term "lifestyle' medicine" was coined by Art

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[110] See Chester Chuang, *Is There a Doctor in the House? Using Failure- to-Warn Liability to Enhance Safety of Online Prescribing*, 75 N.Y.Y.L. Rev. 1452

[111] Id

[112] See Reyes v. Wyeth Lab., 498 F.2d 164, 1276 (5th cir. 1974); see also Restatement (Third) of Torts: Product Liability §6(d) (1997).

[113] Id.

[114] See Covington, page 5

[115] See Covington

[116] See Charles Marwick, *From Rx to OTC; More Drugs Make the Switch*. 278 JAMA 103 (between 1984 to 1994, only 9 drugs were switched for prescription-only to OTC status. In 1995, 5 drugs underwent this switch and in 1996, 13 drugs were switched)

[117] Id

Ilene to describe the "partnership between informed health care consumers and health care providers"[118].

This revolution might be the result of (1) certain attitudes and beliefs such as appreciation of wellness and preventive action, acceptance of self responsibility for one's health, (2) demographic issues such as age, size of family gender differences and socioeconomic status and (3) economics of health care such as cost, convenience and availability of health care services and products and (4) education and knowledge such as educational level of the patient, knowledge of the disease and treatment regimen and the ability to understand health information.

Patient Risk with Reclassification of Prescription-only drugs to OTC status.

In many instances, when a prescription-only drug is reclassified as an OTC drug, it is available as tablets but at a lower dose. For example, the active ingredient of Motrin® tablets is ibuprofen, a drug well known to the public for its analgesic and anti-inflammatory properties. The amount (dose) of ibuprofen contained in a Motrin® tablet 800 milligrams. At this dosage, the drug is a prescription-only drug. . In 1984, the FDA approved it as an OTC drug[119]. Since then, a patient can readily buy 200 milligrams ibuprofen tablets (e.g. Advil®), since at the strength it is classified as an OTC drug. Therefore, a patient can easily "acquire" the prescription-only Motrin® by taking four Advil® tablets. Emerging data suggest that this reclassification of ibuprofen has caused some incidence of toxicity. After reports of serious injuries to children with ibuprofen since its reclassifications as an OTC drug, the U.S. Consumer Product Safety Commission has mandated child resistant (C-R) packaging for all OTC produced approved after January 29, 2002[120]. As indicated (see infra), patient education of drug, both prescription-only and OTC should be an integral part of any regulatory effort to reduce drug related toxicities.

Part III: Suggestions to Improve Patient Safety

This problem of ensuring patient safety and efficacy of drug therapy with prescription-only and OTC drugs places a heavy burden on the shoulder of all health care providers. Regulation of Internet drug prescribing may appear at first blush to be the solution Reasons are discussed why regulation is not the optimal solution. Other solutions are proposed that are more likely to be effective in optimizing drug therapy and minimize, if not avoid, ADRs.

Regulation of Internet Drug Prescribing is not the Answer: Such efforts are unlikely to be a satisfactory solution since successful enforcement will require the co-ordination of

[118] Id
[119] See George Misko: *Oral RX to dugs going O-T-C need C-R Packaging, Food & Drug Packaging (March 2002) at 12*
[120] Id

several Federal and state agencies. Federal agencies that have jurisdiction over drugs include the FDA, The Federal Trade Commission, the Department of Justice and the United States Customs [121]. In addition, corresponding agencies of each of the States are also involved[122]. In addition, practice of medicine and pharmacy are regulated by the States. Such attempts are likely to fail because (1) an offending Internet pharmacy site that has been closed, can be reopened in a matter of hours[123], (2) more than half the Internet sites that provide prescription-only drugs are foreign and hence, outside US jurisdiction. While the prescription volume from foreign sites will be almost impossible to determine, unknown, "[t] he U.S. Customs reported intercepted hat it intercepted 9725 unauthorized prescriptions . . . in 1998 [124] and (3) many Americans, especially the elderly, most of whom happen to be on fixed incomes, are seeking to save money on their medications reasons[125]. There is concern such regulatory efforts might "become another bottomless pit for taxpayer money like the 'War on Drugs'"[126].

The issue of what constitutes a "valid prescription" could make regulation of Internet drug prescribing difficult to enforce. Current federal law does not indicate who has the authority to prescribe[127]. In general, physicians are recognized to have the authority to prescribe. For example, New York defines the practice of medicine as "diagnosing, treating, operating or prescribing for any human disease, pain, injury, deformity or physical condition"[128]. This authority is not exclusively vested with physicians. Connecticut defines a prescribing practitioner as a " physician, dentist, veterinarian, podiatrist, osteopath, scientific investigator or other person licensed, or otherwise permitted to distribute, dispense or to administer a controlled substance in the course of registered professional practice"[129].

The need for regulating Internet drug prescribing is minimized in view of the reports that Internet pharmacies have not become commercially as successful as expected due to competition.[130] The prescription-only drug market "is tightly controlled by insurance companies and health maintenance organizations (HMOs)[131]. It has also been predicted, "online retailers are unlikely to succeed as stand-alone businesses".[132]

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[121] See Kara M. Friedman, *Internet Prescribing Limitations and Alternatives.* 10 Annals Health L. 139
[122] Id
[123] See Chet Dembeck, *Is Regulation of Online Pharmacies Doomed to Failure,* http://ecommercetimes.com/perl/story/2315.html (last visited April 1, 20020
[124] Id
[125] Id.
[126] Id
[127] See William Hoffman, Hubert Humphrey: Retrospective of a Living Room Shoot, The Doric Column (April 3, 2001), available at http://mbnet.umn.edu/doric/humphery.html (citing 10 Annals Health Law, 139, 175)
[128] N.Y. Educ. Law § 6521 (Mckinney 2000)
[129] Conn. Gen. Stat § 21a-240(430(2000)
[130] See Anon., *A Dose of Reality*. 353 Economist 56 (1999)
[131] Id.
[132] Id.

Patient Education: Many factors, other than the drug and dose, affect drug safety and efficacy[133]. These factors include other medications, both prescription-only and OTC, the patient is taking, the patient's age, sex and clinical history. Therefore, patient responsibility and active participation with respect to his/her drug therapy is crucial in enhancing safety of drug therapy and decreasing drug toxicity. Results of surveys show that patients would be receptive in assuming such responsibility. These surveys have shown (1) 94% of those surveyed recognized the need to exercise caution when using drugs, even if they are available without a prescription (2) 93% of those surveyed stated that they read instructions of OTC drugs and (3) 54% believed that reclassification of prescription-only to OTC drugs would be economical with respect to time and money. Therefore, Federal and state government should take out public service announcements in print and on-air media to warn patients of issues to consider when buying prescription-only drugs on line. The FDA has an easy to understand on-line "DOs and DONTs" guide for patients wishing to buy medicines on-line[134]. However, it should also include a special caution for new[135]drugs on the market drugs (using Viagra as a example) in plain English:

> *Viagra is a new prescription-only drug. Do not use this drug without first taking to your physician and pharmacist. All its toxicities are not fully understood. The interaction(s) of this drug with other drugs are also not fully known. Therefore it is important for the drug to work properly and your safety that you inform your physician and/or pharmacist[136] (1) how much of the drug do you take (2) how often do you take this drug and (3) all other medications including g vitamins and nutritional supplements you are taking*

Patient education on proper use and risks of prescription drugs has been a politically contested issue[137]. Historically, during the Carter Administration, the FDA had issued a regulation requiring drug manufacturers to provide more information on prescription-only drugs to patients[138]. This order was revoked by the succeeding Reagan Administration in 1981; manufacturers would be 'encouraged" to make such information available to patients[139]. The US Senate revived the idea and moved to require that pharmaceutical companies provide "detailed information on the use and risks of prescription drugs"[140].

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[133] See generally PDR 2002
[134] http://www.fda.gov/cder/drug/consumer/buyonline/guide.htm (last visited April 30, 2002)
[135] See FN 32 (about 50% of undiscovered safety problems were identified only with a 7 -year period of use)
[136] See next section
[137] Jerry Gray, *Senate Backs Bill to Require Data on Drugs for Consumers.* The New York Times (July 25, 1996) at A19.
[138] Id.
[139] Id
[140] Id

In addition, the availability of approved sites such as the VIPPS program, operated by the National Boards of Pharmacy need to be widely publicized[141]. Dissemination of such information should educate the patient on the serious risk of using prescription-only drugs purchased from uncertified Internet sites, especially foreign pharmacies. It would assist them with questions they should ask of the Internet pharmacy operator before making a purchase.

Changing State Laws to Give Pharmacists Independent Prescribing Authority

The principle behind this recommendation is a well-recognized standard and may be stated as "use the best available talent for the job". Training of pharmacists recently has undergone major changes[142] with emphasis on patient drug therapy. The American Council on Pharmaceutical Education (ACPE) proposed major curricular competencies to achieve this goal[143] Specifically, five areas were emphasized; (1) biomedical sciences (2) pharmaceutical sciences, (3) behavioral, social and administrative pharmacy sciences, (4) pharmacy practice and (5) pharmacy practice experience.[144]
Pharmaceutical care, as defined by the American Pharmaceutical Association is:
The patient centered outcomes oriented pharmacy practice that requires the pharmacist to work in concert with the patient and the patient's other healthcare providers to promote health, to prevent disease and to assess, monitor, initiate and modify medications to assure that drug therapy regimens are safe and effective[145].

The goal of pharmaceutical care "is to optimize the patient's health-related quality of life, and achieve positive outcomes, with realistic economic expenditures"[146].
"The management of drug therapy is one of the important challenges in the health care management"[147]. Cost of adverse drug reactions (ADRs) during hospitalization was

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[141] See David B. Brushwood, *Responsive Regulation of Internet Pharmacy Practice*, 10 *Annals* of Health L. 75, 101 (such programs as the VIPPS are of limited value to the patient if their existence is not widely known in the Internet user community). Also, see Chet Dembeck; *Is Regulation of Online Pharmacies Doomed to Failure? (htpp://www.ecoomercetimes.com/perl/story/2315.html* (The FDA had indicated that it would use part of the $10 million that the Clinton Administration had proposed for regulating Internet Pharmacy to "urge consumers to buy drugs only from Web sites that display such verifications as the . . . (VIPPS) seal".

[142] In 1995, the American Association of Colleges of Pharmacy enhanced the requirements for the pharmacist. The 5-year (post-high school). BS degree was increased to the 6-year Doctor of Pharmacy (Pharm. D.) degree

[143] Wayne K. Anderson, Pharmacists *in the Health Care System* Http://pharamcy.buffalo.edu/about/paper.shtml (last visited May 1, 2002) ("key professional competencies [of the pharmacist] . . . are an ability to (a) evaluate drug orders or prescriptions,. . . (f) design, implement, monitor, evaluate and modify or recommend modifications in drug therapy to insure effective, safe, and economical patient care, . . . (k) recommend, counsel and monitor patient use of nonprescription drugs, . . ."

[144] Id

[145] Daniel B. Brushwood and C.D. Hepler. Redefining Pharmacist Professional Responsibility', in Pharmaceutical Care; CH Knowlton and Richard P. Penna, (Eds), Chapman and Hall, New York, (1996) p. 195

[146] Id

[147] Wayne K. Anderson, Pharmacists *in the Health Care System*, http://pharamcy.buffalo.edu/about/paper.shtml (last visited May 1, 2002)

estimated to range from $ 2- 4 billion[148]; the cost of preventable ADRs was about $1-2 billion. This economic burden of ADRs excludes the costs of malpractice[149] and patient care related to the ADRs. Experiences from a 3-year study in one hospital involving ADRs showed that they increased the risk of death by 2-fold[150].

In contrast to the Medical curriculum[151], a typical pharmacy school curriculum for the Doctor of Pharmacy degree[152] requires about 135 hours of Pharmacology and about 200 hours of therapeutics[153]. In addition, they are required to takes courses in pharmacokinetics[154] (about 120 hours). In addition, requirements include about 120 hours of education in the study of various dosage forms[155]. Though the dose (amount of drug) contained in two dosage forms is identical, how it is delivered from the dosage form can influence the effect(s) of that that dose. A recent report comments on the problems associated with the practice of "pill splitting"[156] among physicians[157].

Pharmacist intervention in patient drug therapy has reduced ADRs. Two examples are given in support. In the first example, pharmacists reviewed the medication orders prior to dispensing over a 6-month period.[158]. An order was considered in error when both the physician and pharmacist agreed that the order needed to be changed[159]. Errors were classified as potentially lethal, serious, significant, depending on the potential of the ordered drug, dose, route of administration to cause death, non-life threatening ADRs or be ineffective, respectively. During the 6 months, there were 479 errors; the distribution for lethal, serious and significant errors was 5.6%, 30.3% and 64.1 % respectively [160].

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[148] Id

[149] David W. Bates, *the Cost of Adverse Drug Events in Hospitalized Patients.* 277 JAMA 307 (1997)

[150] See David C. Classen, Adverse *Drug Events in Hospitalized Patients* 277 JAMA 301 (1997)

[151] See FN 99

[152] In 1995, the American Association of Colleges of Pharmacy enhanced the requirements for the pharmacist. The 5-year (post-high school). BS degree was increased to the 6-year Doctor of Pharmacy (Pharm.D.) degree

[153] Shelly M. Janasz, Pharmaphacts 2000, School of Pharmacy, University of Missouri-Kansas City.

[154] In practical terms, pharmacokinetics can be defined as the study of the rates of entry of the drug following into the body its administration the body the distribution of the drug into various sites in the body after entry and the removal from the body. These rates can significantly influence the effectiveness and toxicity of certain drugs. Since affected by many physiological (e.g. age of the patients) and disease (e.g. congestive heart failure), pharmacokinetics principles are sued to tailor drug dosages to individual patient needs.

[155] Dosage forms refer to the various drug products such as rapid and controlled release capsules and tablets, elixirs, tablets.

[156] Pill splitting refers to breaking a tablet into smaller portions

[157] Pamela Gaynor, *Pill Splitting Lowers Costs, but Raises Health Concerns.* http://www.post-gazette.com/helathscience/20020430hsplit0430p5.asp (last visited April 30, 2002)

[158] Hugo L. Folli, et al., *Medication Error Prevention by Clinical Pharmacists in Two Children's Hospitals*

[159] Id.

[160] Id (Potentially lethal error was defined as one where the prescribed dose was (i) in the "severe toxicity range", (ii) the prescribed dose of the drug had a " high potential to cause cardiopulmonary arrest", (iii) "the drug being administered had high potential to cause a life-threatening adverse reaction . . ." given the patient's medical history, (iv) the prescribed dose of a potential life-saving drug was "too low . . . " and (v) the dose of drug was "too high (10 times the normal dose) a serious error was defined as one in which (1) the route was inappropriate with potential of resulting the "patient to suffer a severe toxic reaction", (ii) the prescribed drug dose was too low for "a patient . . . who is in acute distress", (iii) the prescribed dose

In spite of their knowledge based on their educational background and clinical training, pharmacists have no unsupervised authority to prescribe In 24 states; they have limited authority to prescribe[161] under what is called collaborative practice arrangements between pharmacists and physicians. [162]. Washington, the first state to legalize such arrangements, define practice of pharmacy as:

> Practice of pharmacy includes . . . the initiating or modifying drug therapy in accordance with written guidelines or protocols previously established and approved for his or her practice by a practitioner authorized to prescribe drugs; . . . ."[163]

While such pharmacist participation in a patient drug therapy has the potential to improve patient drug therapy, recent studies casts doubt on such optimism because physicians in general have not been supportive of collaborative arrangements[164].

Recent reports show that granting of prescribing authority to pharmacists is being discussed in other countries[165]. In the United Kingdom, Health Minister Lord Hunt said "Pharmacists are an untapped resource for the NHS [National Health Service]. . . . by harnessing their skills we can deliver rapid access to medicines and improved patient care"[166]. Chief Pharmaceutical Officer said, " The proposal launched today will improve patients' access to the medicines they need and make the best us of pharmacists' skills. Pharmacists are a highly skilled and extensively trained profession. . . . For the first time, pharmacists will be able to make use of their training to prescribe for NHS patients"[167]

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was 4-10 times the normal dose, (iv) the drug would results in toxic amounts in the body (5) the "ordered drug could exacerbate the patients condition", and (vi) the drug ordered was misspelled, increasing the risk that the wrong drug would be dispensed. A significant error was defined as (i) the dose was 50 to 400% the normal dose, (ii) the dose was "too low " (iii) the wrong laboratory tests to monitor drug side-effects (iv) the incorrect route of administration was ordered and (v) errors were made in ordering intravenous fluids

[161] See Anon., *Twenty-four States Allow Collaborative Practice Arrangements*. http://www.ncbop.org/jan99-4.asp.

[162] Lori A. Ferro, et. al., *Collaborative Practice Agreements between Pharmacist and Physicians*. http://www.aphanet.org/education/dcpm/collaboartive.pdf (such agreements allow pharmacists to renew prescriptions, change drug dosages, initiate patient therapy or immunization without prior further approval) Also sees Kathy Riley, *Collaborative Prescribing Authority for Pharmacists Gains Momentum,* the Consultant Pharmacist, 1 (September 1996).

[163] West's Revised Code of Washington Annotated (WA ST. 18.64.011)(11)

[164] SJ Bradshaw and WR Doucette. *Community Pharmacists as Patient Advocates: Physician Attitudes*. 38 J. Am. Pharm. Assoc. 598 (1998); GR Bailie, B. Romeo. New York Sate Primary Care Physicians' Attitudes to Community Pharmacists' Clinical Services. 156 Arch. Intern. Med. 1437 (1996)

[165] Anon., *Groundbreaking New Consultation Aims to Extend Prescribing Powers of Prescribing For Pharmacists and Nurses.* http://tap.ccta.gov.uk/doh/intpress.nsf/page/2002-0189?OpenDocument

[166] Id

[167] Id

Therefore, modification of existing federal and state laws is needed. The practice of pharmacy should be defined to include prescribing of drugs without physician supervision. This will be major change in the practice of drug treatment. Since federal guidelines do not prohibit other health professions from prescribing, states can enact legislation to provide pharmacists with the authority to prescribe. Such authority should be made contingent on additional post -graduate training of pharmacists in drug therapy.

Mandatory Post-marketing Surveillance

As discusses (see *supra*), the present Surveillance program is essentially voluntary. It is based "on the assumption that "a drug is safe unless reports of adverse effects call the assumption into question"[168]. It has been estimated that less than 10% of all ADRs are reported to the FDA[169]. This has been attributed partly the fact that "the medication use system and the drug regulatory system function separately"[170]. A "systems approach to ADR detection " has been proposed to improve reporting of such events.[171]

It has been recommended that a Drug Safety Board, similar to the National Transportation Safety Board, be established to investigate drug 'disasters"[172]. Though much fewer people die of Airline accidents, they are investigated much more thoroughly.[173]. It is hoped that information to be gathered during such investigations would be invaluable in "improving the quality of drug therapy in medical practice"[174]

In conclusion, ADRs related to drug therapy, especially the large number of fatalities is a serious public health challenge. Recent clinical experience with a given drug can illustrate the complexity of the problem of preventing ADRs. It was reported on February 2, 2002 that, most likely, the widely used anti-allergy medicine Claritin®, currently a prescription-only drug would be available as an over-the-counter (nonprescription) drug[175]. On April 25, 2002 it was reported that the European drug regulatory agency is concerned about potential for Claritin ®) to cause birth defects[176]. In one setting, namely the US, the drug is being made readily accessible to patients with out any medical supervision. In a different setting, namely Europe, there is concern about its toxicity. Effective solutions to optimize drug therapy should be based on a "team effort", which includes patient education, specialized training of health care

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[168] See Alastair J. Wood et al., *Making Medicine Safer- the Need for an Independent Drug Safety Board.* 339 New Engl. J. Med. 1851 (1998)
[169] See FN 32
[170] see FN 93
[171] Id at 419
[172] See Alastair J. Wood et al., *Making Medicine Safer- the Need for an Independent Drug Safety Board.* 339 New Engl. J. Med. 1851 (1998)

[173] Id
[174] Id
[175] See Mathew Herper, *Will Claritin is Sold Without a Prescription? http://www.forbes.comm/2002/02/01/0201sgp.html*
[176] See Anon., *Europe Drug Agency Reviewing Claritin Safety,* http://www.chron.com/cs/CDA/story.hts/health/1383430 (last visited April 30, 2002)

providers responsible for making therapeutic decisions, such as physicians and pharmacists, and modifying regulations to restrict therapeutic decisions to those with the necessary training and mandatory post-marketing surveillance.