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Abstract
Since 1979, the United Nations has maintained a list of drugs banned from sale in member countries. Interestingly, there are a number of pharmaceuticals on the market in the USA that have been banned elsewhere and similarly, there are some drug products that have been banned in the United States, but remain on the market in other countries. This report provides a look into the policies for banning drug sales internationally and the role of the United Nations in maintaining the master list for companies and countries to use for local decision guidance.

Background
At present, one of the leading causes of death in the U.S. is believed to be adverse drug reactions.[1-14] More than 20 million patients have taken at least 1 of the 5 drugs withdrawn from the market between September 1997 and September 1998. Seven drugs that were approved in 1993 and were withdrawn shortly later have contributed to 1002 deaths.[14] A study in 2002, showed that out of the 548 drugs that were approved in the U.S. between 1975-1999, fifty six (10.2 %) of them required a new black box warning or were withdrawn.[12] Thus, it is very important that the consumer as well as the practitioner become aware of dangerous drugs.

In 1979 the United Nations General Assembly first brought up the question of establishing a list of banned pharmaceutical products that could be exchanged between nations. Under resolution 37/137 (Annex I) of December 17 1982, the General Assembly requested the Secretary-General to organize the Consolidated List of Products Whose Consumption and/or Sale Have Been Banned, Withdrawn, Severely restricted or Not Approved by Governments. The List is a continuing effort by the United Nations to circulate information on products that are harmful to health and the environment.[2]

The first issue of the List covered less than 500 products regulated by 60 governments. The fifth issue which covered both pharmaceuticals and chemicals, included over 700 products regulated by 94 governments. By the eleventh and twelfth editions, the List had grown to include more than 1100 products regulated by 115 states.[2] At present the most recently updated issue is the fourteenth issue, which contains data on 66 new products with updated/new information on 22 existing products. An update of the fourteenth issue was published in 2010 adding 99 more products to the List by the actions of 38 governments.[3]

In 1985 the United Nations Secretariat, in conjunction with the World Health Organization (WHO) and the United Nations Environment Program (UNEP) met at the first inter-agency meeting and executed the first review of the List. The review outlined key points such as arrangements for the preparation of future issues, the need for criteria for determining the inclusion of products, the question of the legal and public health context of regulatory actions that were not included in the first issue of the List and the treatment of commercial data.[2] Ever since then the List has been updated annually making the information available to users through direct internet access.

Introduction
Since 1995 the List was divided into two separate issues, one focusing on pharmaceuticals and the other on chemicals, which are published in alternate years. The pharmaceuticals are further separated into monocomponent products, combination products and group products.[2] This paper will only focus on the 151 monocomponent pharmaceuticals that were withdrawn and why they were withdrawn by the U.N. and by specific countries such as the USA, Japan, UK, Sweden and Australia.

More specifically, this paper will compare the drugs banned in the U.S. versus the drugs banned in other prominent countries. Do we have similar policies on which drugs to withdraw or, does the U.S. act on its own when it comes to drug withdrawal?

While the U.N. may outlaw a certain drug, it is possible that the banned drug may be still available in certain countries. In

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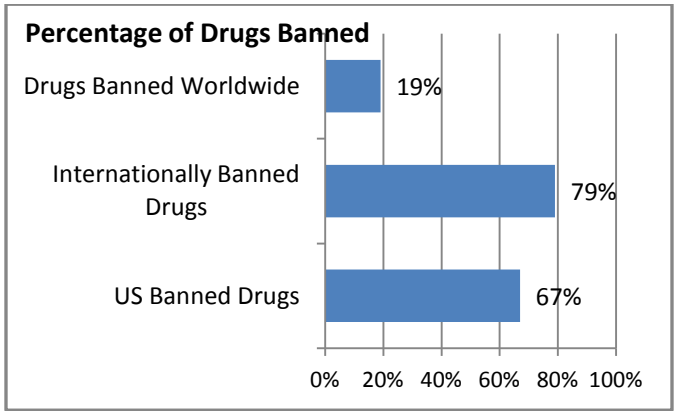
addition, this paper will investigate any lag time that may occur between the issue date of withdrawal by the U.N. and the actual date it was removed from the specific country. It is important to note that if a product is not listed as regulated by a country it does not necessarily mean that it is permitted in the country. It is highly possible that some information has not been communicated to the U.N.[2] as well.

Drugs Banned in the U.S.

In the United States of America, The Center for Drug Evaluation and Research (CDER) a part of the U.S. Food and Drug Administration (FDA) is in charge of evaluating new drugs for safety and effectiveness before they may be sold. After the drugs are on the market, CDER acts as a watchdog, monitoring for any side effects and for any unexpected health risks. Sometimes drugs have to be withdrawn from the market due to severe unwanted side effects that may be fatal. In 2005, new molecular entities (NME) such as valdecoxib, pemoline, and technetium (99m Tc) fanolesomab were all removed due to increased risk of serious adverse effects. Valdecoxib, a COX-2 selective inhibitor was removed from the market due to increased risk of skin reactions and cardiovascular events. Likewise pemoline, a CNS stimulant used for treatment of ADHD was removed because of fatal hepatoxicity[2] (See appendix for more drugs that were removed in the U.S., Internationally, and worldwide).

Figure 1 shows the percentage of the 151 drugs we studied that were removed in the U.S. compared to the drugs that were removed internationally and worldwide.

Figure 1.



Only 67 % of the 151 drugs that were on the List were banned by the U.S, while internationally 79 % were banned. This shows clearly that the U.S is not in complete agreement with the other countries on which drugs should be banned. There are many reasons why the policies of the U.S may differ from the international world. One reason might be a monetary benefit that drug companies/ government get from keeping a drug on the market. An example of a drug that has continued to be kept on the market is the anti-diabetic drug, rosiglitazone (Avandia). A drug might also be kept on the market in one country because it has a legitimate medical use, while in another country it may not be used medically and therefore is banned. For example, flunitrazepam, commonly known as the date rape drug "roofies", is used for the treatment of insomnia in many European countries. However, the FDA has not approved the use of flunitrazepam and it has deemed it an illegal substance.[2]

Figure 1 also shows that only 19% of drugs were banned worldwide. This shows the lack of agreement on which drugs should be banned globally. It seems as if drugs that were banned worldwide had to have severe fatal adverse effects before they reached the eyes of the entire world. Drugs such as Fen-Fen which contained fenfluramine and phentermine were mainly removed after 20 years in the U.S. market due to a lawsuit which totaled over $13 billion in legal damages and of course potential fatal pulmonary hypertension and heart valve problems.[10] Both fenfluramine and its d-enantiomer, dexafluramine (Redux) were withdrawn in September 1997 worldwide. The second drug that made up Fen-fen, phentermin was banned in Sweden and the United Kingdom in 1981 and 2000 respectively. However, it is still marketed widely in the U.S. [2]

Figure 2.

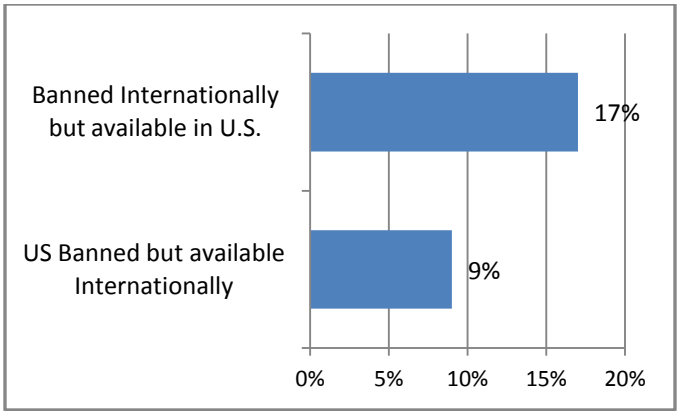


Figure 2 compares the drugs that were banned in the U.S. but are available internationally versus the drugs that are banned internationally but are available in the U.S. It shows that 9 % of the drugs banned by the U.S. are available in the international market. On the other hand, of the drugs banned internationally, 17 % are available in the U.S. This goes to show again that the policies of the U.S. may tend to be different than the rest of the World. Of the 17 % internationally banned drugs, three of the drugs are from the same class of drugs, the barbiturates. In Sweden, barbiturates

such as amobarbital, hexobarbital, pentobarbital and phenobarbital were all banned due to fatal intoxications and abuse potential. In April 2001, France suspended the production of phenobarbital due to reports of rare but severe cutaneous and mucosal reactions including Steven-Johnson Syndrome and Lyell Syndrome.[2] However, phenobarbital is still used vigorously in the U.S. for the treatment of epilepsy/ tonic-clonic seizures.

Another drug that is widely used in the U.S., but is banned internationally is the muscle relaxant, carisoprodol (Soma). In November 2007, the European Medicines Agency (EMA) recommended the suspension of marketing authorization after evidence of abuse and addiction from taking carisoprodol for back pain. Both Norway and Sweden have pulled carisoprodol off the market due to problems of dependence and intolerable side effects. As of 2008, the UK had planned to pull carisoprodol off the market due to increased risk of abuse, addiction, intoxication, and psychomotor impairment.[1]

As of March 26 2010, the abuse potential of carisoprodol was brought to light in the U.S, as the DEA issued a Notice of hearing discussing the plan to place carisoprodol as a controlled substance. However, as of today carisoprodol is not a controlled substance under federal regulations while certain states consider it to be a controlled substance. These states include Alabama, Arizona, Arkansas, Florida, Georgia, Hawaii, Indiana, Kentucky, Louisiana, Massachusetts, Minnesota, Mississippi, New Mexico, Nevada, Oklahoma, Oregon and Texas.[4] While it is not a controlled substance in many states carisoprodol is only approved for short term use and prescribers are encouraged not to prescribe the drug to people with a background of addiction. It is interesting to notice that cariosprodol's metabolite, meprobamate which has significant anxiolytic properties was banned in Sweden in 1981 due to potential for abuse and addiction.[2] The UK was also planning to remove meprobamate due to severe side effects.[1] In the U.S. it has been classified as C-IV and was the best-selling tranquilizer for a long time before being replaced by the benzodiazepines.

A very controversial drug that has caused 13,000 lawsuits, while bringing in annual sales peaking at approximately $2.5 billion for GlaxoSmithKline in 2006, was the antidiabetic drug, rosiglitazone (Avandia). Rosiglitazone has been associated with increased risk of heart failure by 64 % over a seven year period.[7] In September 2010, the EMA suspended the drug from the European market completely. [5] The U.S. however, continues to market the drug with a black boxed warning.

Only 9% percent of drugs banned by the U.S. are available internationally as shown in Figure 2. In November 2000, the FDA issued a public health advisory against the use of phenylpropanolamine, a psychoactive drug used as a stimulant, decongestant, and anorectic. Due to increased risk of strokes in young women, FDA requested the suspension of marketing of this drug and removed phenylpropanolamine from all OTC formulations in 2005.[11] While Canada has also withdrawn the drug, Europe continues to market it as a prescription and OTC drug. In the UK, it is sold in combinations with acetaminophen and caffeine as a cough and cold medication.

Another drug that has been banned in the U.S. but is available outside the U.S is pergolide (Permax), a dopamine receptor agonist used for the treatment of Parkinson's disease. Permax was approved in 1988 as an adjunctive therapy with levodopa in Parkinson's disease. Valvular heart disease was first described in association with pergolide in 2002. In 2003, the FDA asked Lilly to add valvulopathy (abnormality of cardiac valves) to the warnings section of Permax labeling. In 2006, the warning was upgraded to a black box warning, the FDA's strongest form of warning, because of new data concerning risks of heart valve damage. In 2007, it was removed from the U.S market due to increased rates of vavular dysfunction that were associated with using the drug. Pergolide is still used in other countries such as the UK and Australia for the treatment of Parkinson's disease, hyperprolactinemia and restless leg syndrome.[8]

Figure 3.

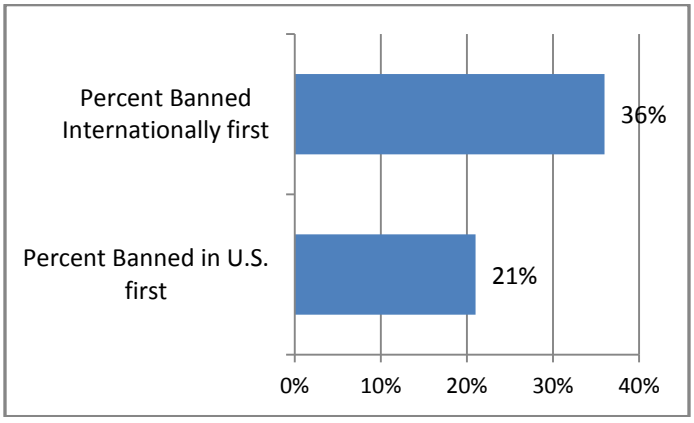


Figure 3 shows the percentage of the 151 drugs we studied that were banned in the U.S. first versus the percentage of drugs banned first in the other countries (UK, Australia, Sweden, and Japan). Approximately 36 % of the drugs banned were first banned internationally before they were banned in the U.S. Only 21 % of the drugs were banned by the U.S. first

before they were also banned by the rest of the world. For the remaining 43%, differences were not detected. This shows that the U.S. may no longer be leader in observing, reporting and removing dangerous drugs from the market. This might be because the drug might have been introduced first internationally before it became available in the U.S. Thus, the time for the FDA to see any adverse effects from the drug might have lagged in comparison to other countries. For example, troglitazone, a thiazolidinediones used to treat diabetes was first introduced by a Japanese company. Due to an idiosyncratic reaction leading to hepatitis it was only approved in January 1997 in the U.S. However, it was already on the world market years before and was voluntarily removed in December 1997 in the UK and Japan due to concerns of hepatotoxicity.[2] Since the U.S. was late to approve the drug, logically they were only able to withdraw the drug by 2000.

Another drug that the U.S. was slow in removing from the market was the well known prescribed pain killer, dextropropoxyphene also called as propoxyphene (Darvon-N). This drug was usually combined with acetaminophen under the brand, Darvocet. Dextropropoxyphene which has been on the marker for more than 25 years came under fire in 1978 by consumer groups who claimed it caused suicides in many of the patient. The manufacturing company, Eli Lilly minimized the news and persuaded doctors that dextropropoxyphene was safe as long it was not mixed with alcohol. In 2004, products containing only dextropropoxyphene were removed in U.K. and later in June 2009, the EMEA recommend gradual withdrawal of all products containing dextropropoxyphene from the European Union.[6]

A month later in the U.S., the FDA still decided to continue marketing dextropropoxyphene with a black box warning for the risk of overdose. On November 19 2010, the FDA finally pulled all forms of dextropropoxyphene from the market due to risk of heart arrhythmias. It is alarming that a drug such as dextropropoxyphene that had a high potential risk of causing heart problems was on the market for more than 20 years before it was completely removed. It is estimated that over 10 million people may have used these products.[9]

Conclusion

Drug withdrawal is an important task that involves continued surveillance and pharmacovigilance and is as important as the process of drug discovery and production. Since the establishment of the List, the dissemination of information on which drugs are banned has become easier. Nevertheless, countries tend to have different policies on which drugs to withdraw and when to withdraw them. The U.S. is on its own time course compared to other countries such as UK, Japan, Australia and Sweden and withdraws drugs based on the FDA's decisions. Likewise in order for a drug to be withdrawn globally, the side effects usually have to be severe enough to catch the attention of the entire world. In addition most of the time, drugs are kept on the market for many years before they are found to be more harmful than good. While there might be monetary benefits for each country in keeping these drugs on the market, the U.N. must step up the visibility of the withdrawal of dangerous drugs list.

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Appendix: Drugs Banned in the U.S., Internationally, and Worldwide

Drugs Banned in U.S.	Effective Date	Drugs Banned But Available in U.S.	Banned in other Countries (UK, Sweden, Japan, Australia)	Effective Date	Grounds for Removal
Acetanilide			JPN	Jul 1971	Aplastic anaemia
Acetylfuratrizine			JPN	Jul 1977	Superseded by safer and more effective preparations.
Alclofenac			UK	1979	Skin rashes and mutagenic activity
Amfepramone			SWE	Jan 1981	Potential for abuse
Amfepramone HCl			UK	Apr 2000	Risks outweigh benefits
Amfetamine	1973				High risk of abuse and dependence
Aminoglutethimide	1966				Serious toxic effects to thyroids, ovaries, adrenals and uteri of female rats caused sexual precocity and masculinization of young females
Aminophenazone	Nov 1977		AUS, JPN, UK SWE	1965, Dec 1977, 1989	Importation inhibited due to bone marrow suppression and fatal agranulocytosis Not known if marketed in U.S.
Amilprilose	Jan 1994				Lack of efficacy and safety
Amobarbital			SWE	July 1985	Fatal intoxications and abuse
Aphrodisiac drugs	Jan 1990				Unsafe and of doubtful effectiveness
Aprobarbital			SWE	July 1985	Fatal intoxications and abuse
Aristolochia			UK	July 1999	End-stage renal failure
		Aristolochic Acid	UK, AUS	Sept 2004	Nephrotoxic and carcinogenic
Astemizole	1999				QT prolongation
Azaribine	Aug 1976				Thromboembolism
Benzylpenicillin sodium (topical)	Feb 1972				Lack of effectiveness compared to risk
Benoxaprofen	1982				

Bithionol	Oct 1967		JPN	July 1971	Photosensitivity and cross-photosensitivity with other chemicals
Boric acid and borates (topical use in infants)	1985		UK JPN	July 1985	Dead in infants
Bromfenac	Jun 1998				Hepatic failure
Bromocriptine	Sep 1989				Risk of rebound effect and only 10 % benefit therapeutically
Bunamiodyl	1964		SWE	1964	Repeat doses may be associated with oliguria, renal tubular necrosis, and death
Calamus	Nov 1968				Animal carcinogenicity
Cerivastatin	Aug 2001		Worldwide	Aug 2001	Increased risk of rhabdomyolysis especially when used with gemifibrozil
Chloroform	Jul 1976		JPN,UK	May 1976	Liver cancer in mice and rats
Cisapride	Apr 2000		UK, JPN	Jul 2000, Oct 2000, Dec 2002	Cardiac events
Clioquinol	Nystaform removed (Clioquinol & nystatin)		JPN, SWE	Sep 1970, Jun 1975	Causes subacute myelo-optic neuropathy (SMON)
Cobalt (non-radioactive forms)	Jul 1967				Lack of effectiveness in treating iron deficiency anemia and causes severe toxicity
Coumarin			AUS	Aug 15 1996	Death from hepatotoxicity in women
Cyclandelate	Dec 1996				Not effective vasodilator
Dalkon shield	1974		UK	1985	Increase risk of PID
Dantron	Mar 30 1987		JPN, UK	Feb 1987, Apr 1987-May 2000	Carcinogenic and genotoxicity
Dexamfetamine	1973				Abuse and high risk of dependence
Dexfenfluramine hydrochloride/Fenluramine	Sept 1997		Worldwide		Heart valve problems and pulmonary hypertension
Dibenzepin hydrochloride			SWE	Jan 1983	Fatal suicidal attempts
Diethylaminoethoxyhexestrol			JPN	Dec 1970	Liver toxicity
Difurazone			JPN	Jul 1977	Superseded by safer and more effective products
Dihydrostreptomycin	Sep 1970				Otoxicity

Dihydroxymethylfuratrizine			JPN	July 1977	Superseded by safer and more effective products
Dilevalol	Aug 9 1990		JPN	Aug 9 1990	Worldwide removal- Liver toxicity
Dimazole	Jul 1977				Neurotoxic –avaliable in 40 countries
Dinoprostone			UK	July 19 1990	Uterine hypertonia and foetal distress
Domperidone(injectable)	Jan 31 1985		All	Jan 31 1985	Worldwide removal-cardiotoxicity
Droperidol			UK	Mar 2001	Cardiac events
Droxicam			E.U.	Dec 14 1994	Suspended marketing authorization due to hepatic damage
Ephedra	Jan 02 2004				Heart attack and stroke
Erythrityl tetranitrate	1998				Lack of efficacy for management, prophylaxis or treatment of angina
Erythromycin estolate			SWE		Severe cholestatic hepatitis and jaundice
Ethyl nitrite (spirit)	Jun 26 1980				Risk of fatal methaemoglobinaemia and poisoning in some infants
Factor IX			SWE	1984	Reports of infections with HIV (the AIDS virus) in patients treated with drug
Factor VIII			UK	Oct 1986	Reports of infections with HIV (the AIDS virus) in patients treated with drug
Fenclofenac	1980s		UK	1985	Fatal skin Rashes
Feprazone			UK	Mar 30 1984	Concern of risk/benefit ratio- only available in 7 countries
Flosequinan	October 1993		UK	Jul 1993	Increased hospitalization and death
Flunitrazepam	Not approved by FDA- illegal drug		Available in other countries for treatment of insomnia		
Furazolidone	1991		Japan	Jul 1977	Superseded by safer and more effective preparations
Glafenine			E.U. Worldwide	Jan 14 1992, May 1992	Risk of serious anaphylactic reactions
Grepafloxacin hydrochloride	Oct. 27, 1999		UK Worldwide	Oct 1999	Cardiac arrhythmias; QT prolongation

Guanofuracin	N/A		JPN	Jul 1977	Superseded by safer and more effective preparations.
Halogenated salicylanilides	Dec 1 1975		JPN	Jan 1976	Disabling skin disorders and photosensitivity in humans.
Heptabarb			SWE	Jul 1984	Fatal intoxication and abuse
		Hexachlorophene	JPN	Mar 1972	Banned in nursing powder preparations due to brain edema. Carcinogenic?
Hexobarbital			SWE	Oct 1984	Fatal intoxication and abuse
Hyoscine methonitrate			SWE	Jun 1981	Removed from appetite suppressant forumulations
Indoprofen	1984		UK Worldwide removal	Dec 1983, 1984	Severe GI reactions Carcinogenicity in rats
Iodinated casein strophanthin (neo-barine)	Oct 1964				Thyrotoxic side effects
Isocarboxazid			JPN	Nov 1974	Lack substantial evidence of efficacy and safety
Isoxicam	31 Oct 1985		Worldwide		Fatal skin reactions
Laetrile	24 Mar 1987		AUS	Feb 20 1986	Importation of drug prohibited due to lack of efficacy and toxicity; can be potentially fatal
Levacetylmethadol	23 Aug 2003		E.U.	2001	Pro-arrhythmic potential
Levamfetamine	1973				Evidence of abuse and high risk of dependence
Loperamide (Drop formulations)	1990		All	1990	Worldwide removal due to cases of paralytic ileus
L-Tryptophan	Nov 17 1989		UK,SWE, JPN	Dec 1989 May 1990	Eosinophilia-myalgia syndrome
Lynestrenol	1970		AUS	1980	Mammary tumours in the beagles
Mephenesin			JPN	Jul 1976	Lack of substantial evidence of efficacy and safety.
Meprobamate			SWE	Jan 1981	Potential for abuse and lack of effiacy
Metamizole sodium	Jun 27 1977		AUS SWE	1965, 1999	Prohibited the importation; fatal agranulocytosis
Methapyrilene	1992		UK,AUS	1979, 1980	Carcinogenicity in rodents
Methiodal sodium			SWE	Jan 1975	Induced muscle spasms, safer alternates available
Metofoline	Mar 1965		Not available outside U.S.		Eye changes and corneal opacities in dogs
Metrodin HP			UK	Feb 2003	Creutzfeldt-Jakob Disease

Mibefradil	1998		UK	Jul 1998	Numerous drug interactions
Nebacumab	1993		Worldwide		Increased mortality
Nialamide			JPN	Nov 1974	Lack substantial evidence of efficacy and safety
		Nifedipine	AUS	Mar 1996	10 mg withdrawn due to serious adverse effects related to rapid release and higher peaks. Committee has deferred ruling on 5 mg for 12 months
Nitrendipine			AUS		Registration refused on grounds of inadequate data on pharmacokinetics
Nitrofural			JPN	Jul 1977	Superseded by safer and more effective preparations
Nomifensine	Jan 1986		Worldwide		Haemolytic anaemia
Noscapine			UK	1991	Cough mixtures containing noscapine were withdrawn and all other noscapine products were placed under Rx only due to concerns of genotoxicity
Oxyphenbutazone			SWE, UK	Jan 1985	Blood dyscrasias. All products in UK have been revolved except eye ointment
Oxyphenisatine acetate	Feb 1972		AUS, JPN, UK	1972, 1978	Fatal liver disease, jaundice UK-all removed except suppositories for single-dose use
Pentobarbital			SWE	Jul 1985	Fatal intoxications and abuse
Pexiganan	Mar 2000				Not approved-lack of efficacy
Phenacetin	Nov 1983		UK,SWE,JPN,	Mar 1980, Jul 1982, Aug 1982	Carcinogenicity and renal damage, hemolytic anemia, methaemoglobinaemia
Phenformin	Nov 1978		SWE,UK	Oct 1978, 1982	Severe lactic acidosis
		Phenobarbital	SWE	Jul 1985	Abuse potential and fatal intoxication
Phenolphthalein			European Union, JPN	Dec 1997, Jan 1998	skin reactions, potassium loss and atonia
		Phentermine	SWE,UK	Jan 1981, Apr 2000	Potential for abuse; risk outweighs benefit
Phenylpropanolamine	Nov 2000				Hemorrhagic stroke; JPN, UK evidence is weak but package includes new warnings
Pipamazine	Jul 1969				Lack of proof of efficacy and safety
Piperazine			SWE	1983	Carcinogenic and mutagenic potential

Pirprofen	Sep 30 1990		Worldwide		Fatal liver toxicity
Pituitary-chorionic gonadotropin (injectable	Jul 1972				Risk of eliciting antibodies to animal protein, leading to allergic reactions
Polidexide sulfate			UK	1977	Oculo-mucocutaneous syndrome
Polyoxyethylated castor oil	Jun 1984		Worldwide		Severe anaphylactoid reactions and haematological changes including hyperlipidaemia, altered blood viscosity and erythrocyte aggregation
Practolol			SWE, UK	May 1975, 1977	Only IV preparation available others removed due to evidence of oculo-mucocutaneous syndrome
Prasterone	1985				Lack of efficacy and safety of long-term use
Prenylamine	1989		Worldwide		Polymorphic ventricular tachycardia
Pumactant			UK	Apr 2000	Higher mortality rate in neonates
Pyrrolizidine			UK	Mar 1993	Liver toxicity
Remoxipride	Mar 1994		Worldwide		Aplastic anaemia
Sertindole			UK	Dec 1998	Cardiac arrhythmias
Somatropin (pituitary-derived)	Aug 1985		UK	May 1985	Reports of death from development of Creutzfeldt-Jakob disease
Strychnine and salts			JPN	1987	No demonstrated therapeutic value
Sulfamethizole			SWE	Feb 1984	Adverse reactions and low sales; replaced by newer safer antibiotics
Sulfamethoxypyridazine			SWE	Feb 1984	Adverse reactions and low sales; renal toxicity, sometimes fatal exfoliative dermatitis and erythema multiforma, hemolytic anemia/aplastic anemia
Sulfathiazole	Sep 1970				Serious adverse reactions as listed above
Suloctidil	1985		Worldwide		Hepatitis
Suprofen	May 1987		Worldwide		Sales had diminished to point product was no longer economically viable

Temafloxacin	Jun 1992		Worldwide		Hypoglycaemia, haemolytic anaemia, renal failure, hepatitis and anaphylactic reactions
Terconazole			SWE	Jul 1991	Vaginal suppositories containing 80 mg and 160 mg terconazole was withdrawn due to febrile reactions
Terfenadine	1998				Associated with rare, but serious heart problems when taken with certain antibiotics and antifungals; JPN,UK available with warnings
Terodiline	1992		Worldwide		Ventricular tachycardia, heart block and bradycardia associated
Tetracycline (pediatric)	Jan 1979		AUS	1991	Stain teeth and retard bone growth
Thenalidine	Jul 1958		UK, SWE, AUS	1961, 1976,1980	Severe neutropenia
Tienilic acid	Jan 1980				Liver toxicity
Tolcapone			EME,UK, AUS,	Nov 1998, Feb 1999	Hepatotoxic
Tolrestat	Nov 1996		Worldwide		Hepatic necrosis and death
		Triazolam	AUS JPN UK	Apr 1986, Mar 1992, Jun 1993	0.50mg and 0.25mg triazolam were not approved due to risk of adverse effects. 0.125mg triazolam were approved for the treatment of insomnia. Dose should not exceed 0.5 mg. Reversible psychiatric adverse effects, particularly loss of memory and depression
		Troglitazone	UK, JPN	Dec 1997	Severe hepatocellular damage, hepatic necrosis and hepaticfailure
		Trovafloxacin mesilate	EME	May 1999	Marketing authorization suspended due to hepatic events
Urethane	Mar 1977		JPN	Jul 1975	Carcinogenicity
Vinarol and viga (dietary supplements)	Apr 2003				Unlabeled presence of sildenafil
Vinbarbital			SWE	Jul 1984	Fatal intoxications and abuse
Zimeldine	Jul 1983		Worldwide		Hypersensitivity reactions and neurological complications
Zomepirac	Mar 1983				Serious allergic reactions, including five deaths from anaphylaxis