The title reflects the ‘half-joking’ beliefs of some physicians that if a drug is so widely needed, so completely safe, and so ultimately effective, then it should be added to the water. With the hugely expanding power and influence of today’s drug industry, the previous comment reflects more of a clever and creative, yet deeply disturbing suggestion to a companies’ marketing department than of a passing joke. Sometimes it’s difficult to tell if someone is joking.

However, what this statement more likely reflects is the extent to which we are now comfortable as a society with the use of drugs, and many of them are often prescribed and taken without a second thought. As patients, many of us even feel dissatisfied with the competence and capability of our physicians if we leave the clinic without a drug prescription in hand, and subsequently, many of us would rather take a drug to treat what ails us than to employ a natural remedy or simply let our bodies heal themselves as they have so eloquently evolved to do. As physicians and medical students, many of us have also become so comfortable and familiar with drugs that we may prescribe them with an equal sense of indifference, or even look forward to the day when we can write our very first prescription. In both cases there is a seeming lack of respect, both for the unpredictability and potential consequences that any and all drugs pose to patients. Considering this, joking about putting statins in the water not only reflects how ‘casual’ we have become with the drug industry, but it also reflects, to a much larger degree, the prominent and growing influence the drug industry has on society as a whole.

For many years the drug industry has done its utmost to shape how the medical community defines disease, how physicians prescribe the drugs they manufacture, and how the public becomes aware of, and more recently makes requests for specific drugs from their doctors. The previous two installments of Health Care and the Drug Industry examined these influences, and now in the third paper, we take a step back and look at how these influences play out on a much larger scale. In this last paper we’ll examine how research is often driven by marketing objectives rather than real health needs; how the patent, which gives the drug industry the legal ‘right’ to demand enormous prices for its drugs, is often manipulated, stretched and abused to satisfy the drug industry’s insatiable drive for profit; and how diseases are literally ‘manufactured’ with the sole intent of opening new ‘disease markets’ to derive and obtain maximum profitability, and a hefty jump on the local competition. The effects of these misguided activities on society are real and immense, but they also may be much more difficult to observe, and above all quantify. This last installment of Health Care and the Drug Industry hopes to shed some light on what really motivates the behaviour of our less-than-noble drug industry.

Drug research: improving health or making money?

When it comes to research, the drug industry has made some impressive discoveries, and subsequently has developed some truly incredible and very helpful drugs. To some degree because of this work, we are now witnessing an era in medicine that allows many who suffer from illness and disease to overcome odds that previously would have been insurmountable. We are able to improve the quality of life, and increase the lifespan of those with heart conditions, diabetes, cancer, epilepsy and many other health conditions. Drug industry-funded research has allowed many of these advancements to take place and for this we are thankful. However, with all of this improvement there are costs to be considered as well.

Currently, a lot of new research is being motivated by the potential for financial reward, not real patient need. Many are questioning the extensive funding that drug industry pours into scientific studies because of the inherent conflict of interest that arises out of a positive result for their drug. A recent and comprehensive study in the Canadian Medical Association Journal found that industry-funded research is more likely to be associated with statistically significant pro-industry findings than non-industry funded research. These studies are then used by the drug industry to gain regulatory approval for their drug,
and then in many cases by physicians in their clinical decisions regarding patients.

Many times we, as a society, are too quick to applaud such studies and too eager to incorporate the new and ‘remarkably effective’ drug into the medical mainstream. In the case of anti-depressants for children, the medical community could not have learned a more critical message of just how easily the drug industry can make us believe a treatment is good, as well as how eager and willing we are to go along with it. Despite repeated claims by researchers and physicians that there were significant health-risk for children using selective serotonin reuptake inhibitor (SSRI) anti-depressants, they were marketed, supported and prescribed for millions. In February of this year, Health Canada released a public warning against the pediatric use of 7 antidepressant drugs including paroxetine (Paxil), bupropion (Wellbutrin), citalopram (Celexa), fluvoxamine (Luvox), mirtazapine (Remeron), sertraline (Zoloft), and venlafaxine (Effexor). Six of these are SSRI’s.

Not only are we finding out about the potentially dangerous effects of these drugs on children, but disturbing evidence has also recently surfaced indicating that earlier research had been withheld by those that stood to gain financially from their use. The drug giant GlaxoSmithKline is currently facing increasing legal costs over what many are calling corrupt corporate practices. A report in CMAJ cites “an internal document [that] advised staff at GlaxoSmithKline to withhold clinical trial findings in 1998 that indicated the antidepressant paroxetine (Paxil in North America and Seroxat in the UK) had no beneficial effect in treating adolescents.”

One study, #329, was conducted between 1993 and 1996, and was the largest trial using an SSRI antidepressant on the pediatric population for its time. The results showed paroxetine to be no more effective than placebo. Another study, #377, actually showed the placebo to be more effective than paroxetine. Despite this, the SmithKline Central Medical Affairs team (CMAt) distributed a document which described the results as “insufficiently robust” and recommended the company “effectively manage the dissemination of these data in order to minimize any potential negative commercial impact.” With all this concern over commercial impact, it is interesting that the internal document makes no mention of any potential health impact paroxetine might have on the millions of children who were encouraged to use it.

Academic researchers are often well aware that working with drug companies can be like ‘dancing with the devil.’ While their financial support may be crucial, there is often pressure to provide results that are favourable towards their drug. Any evidence that suggests otherwise is as important, if not more important for public safety, yet researchers ‘under contract’ are often prevented from publishing these results. In 1988 Betty Dong, a professor of clinical pharmacology at the University of California was approached by Flint Pharmaceuticals because she had published a small study which showed their thyroid replacing medication Synthroid might have a clinical advantage over other drugs. Flint funded her to complete another study, and even used company scientists to help design it. When subsequent results showed Synthroid to be no different than the competing thyroid drugs, Dong was blocked from publishing her research. For seven years attempts were made to discredit her and in 1995 when she tried to publish her results in JAMA, legal threats were made against her.

Knoll pharmaceuticals, which acquired Flint in the same year, hired a doctor to ‘reinterpret’ and publish the results. It was not until 1997 when Dong was finally able to publish her work and Knoll was immediately sued by Synthroid users who had paid out approximately $365 million in extra costs for a drug they were led into believing was more effective. During the seven years it took to finally publish the truth regarding Synthroid, its manufacturers had collected an estimated $2.45 billion in sales.

The patent, profits and human suffering

When a new drug is being developed companies are sure to apply for patent protection. The patent, which originally saw its roots develop in Europe during the late 1800’s, gave inventors a right to the rewards, financial or otherwise, for a period of 6 months following the release of their new product. Essentially, it gave the inventor a monopoly over the production and sale of their product during this time. Since then, the patent has become a tool the drug industry uses to lever immense profits from patients and health care plans across the world. Not long ago, drug patents extended for a period of 4 years. However, following intense lobbying by drug companies through a US delegation at the NAFTA negotiations, the Canadian government unwisely extended the patent deadline by an astonishing 16 years. That gave, and continues to give drug companies exclusive rights to manufacture and sell their product for a full 20 years following patent approval. With a newly approved drug and the patent in place, a company will be able to charge ‘sky high’ prices protected by patents.

Proponents for the patent, which not surprisingly include the drug industry, as well as researchers for pro-industry think-tanks like the Fraser Institute argue that higher drug prices protected by patents are an excellent way for manufacturers to recoup the money spent for research and development (R&D). A commonly quoted value for the cost of bringing a drug to the market is around $800 million, however a large part of this value is an estimate of ‘lost capital,’ or what a
company might have made were it not spending money on the drug in question. Also, this amount doesn’t include the tax breaks companies get for R&D which can reduce expenses substantially. Consequently, other drug development estimates have been much lower.\textsuperscript{7} Whatever the case, when you look at the numbers it is clear that patents definitely allow for these expenses to be repaid many, many times over. In 2002, the top 2 drug companies GlaxoSmithKline and Pfizer both had revenues of almost $30 billion\textsuperscript{8} with Pfizer posting R&D expenses during that same time at approximately $5 billion. Interestingly, the money spent on marketing was up around $11 billion, more than double their R&D expenses for the year.\textsuperscript{9}

One of the fundamental problems with high, patent-protected drug prices is that they place many beneficial and life-saving medications out of reach for many people. Millions in the US have no health insurance and are thus unable to afford the huge costs of prescription drugs when they need them. Many, like the American elderly population, are being hit hard by inflated drug prices, and consequently have turned to buying their prescription drugs at a significantly reduced cost from other countries over the internet. A 1999 US House of Representatives report found that “older Americans and others who pay for their own drugs are charged far more for their prescription drugs than are the drug companies’ most favored customers, such as health maintenance organizations and the federal government. The report finds that a senior citizen in the United States paying for his or her own prescription drugs must pay, on average, more than twice as much for the drugs as the drug companies’ favored customers…In effect, the pricing strategies of drug manufacturer victimize those who are least able to afford it. As a result of price discrimination, large corporate and governmental customers with market power are able to buy their drugs at low prices while senior citizens, who often have the greatest need and the least ability to pay, are forced to pay the highest prices for prescription drugs."\textsuperscript{10} Business economists have stated that the problem of high drug prices is solved by the fact that “drug makers, in a free market with patent protection, have an incentive to charge higher prices only to higher earners, while giving discounts to lower earners.”\textsuperscript{11} Apparently this ‘incentive’ doesn’t yet seem to be strong enough.

**Protecting the patent, and “evergreening”**

Not only is the patent used to protect hugely inflated drug prices, but it is also abused by the drug industry in several other ways. When a patented drug is up for expiration, drug companies are quick to replace it with another newly patented drug very similar to the previous one. Then with a hugely aggressive marketing campaign where patients and doctors are ‘alerted’ to the new, and better drug, a company may get to cash in for another 20 years. This practice is actually so common it has been given the name ‘evergreening.’ Less expensive generic versions barely gain a corner of the market and their companies have little chance to compete with the ‘new’ drug.

Recently, the drug industry has taken advantage of the ‘new drug-better drug’ myth with the proton-pump inhibitor omeprazole (Prilosec) and its ‘new’ and freshly patented replacement drug esomeprazole (Nexium). This virtually indistinguishable enantiomer is now called ‘the Purple Pill,’ and its maker AstraZeneca has been forking out half a billion dollars a year in an enormous public advertising campaign to try and convince patients and doctors that it’s better. Unlike the generic omeprazole, the ‘new’ Purple Pill sells for just as much as its predecessor, at roughly $4 a pill.\textsuperscript{12} With the corporate drug machines in full gear, no wonder prescription drug costs are spiralling out of control.

Often drug companies exploit their financial and judicial power to give their patents as much of an extension as possible so that profits can be maximized. Companies regularly submit patent infringement suits, which cause an immediate 24-30 month delay in the filing of generic drug approval applications. Drug industry lawyers will also attempt virtually anything to patent there way out of losing a ‘blockbuster’ drug. To illustrate this point, consider the following example from *Wall Street Journal* staff reporter Gardiner Harris: Astra’s attorneys were constantly alert to chances to file patents on Prilosec. For instance, when outside scientists figured out that ulcers are often the result of bacterial infection, Astra obtained patents on the idea of combining Prilosec with antibiotics. The company then argued that generic competitors couldn’t launch copycat versions of Prilosec because doctors might prescribe them with antibiotics, in violation of its patent on the combination. Astra also patented a substance that briefly forms in the human body when Prilosec is swallowed. Then it claimed that patients who took generic versions of Prilosec would violate this patent, so that generics themselves were illegal. The company also patented the way it manufactured the drug and claimed generic competitors were illegally using identical techniques. And it patented the idea of putting two coatings on the drug’s active ingredient. Prilosec’s active ingredient can survive only about 8 minutes in stomach acid – not enough time for it to get through to the intestine for absorption. So it needs a so-called enteric coating that resists stomach acid. Unfortunately, most such coatings are also slightly acidic. So Astra’s scientists decided to add a thin middle coat to keep the enteric coating from damaging the drug. This
problem is so common that standard industry textbooks describe it and chemical companies sell middle coatings to solve it. Yet Astra’s lawyers persuaded patent clerks in Europe and the U.S. that its scientists had made a novel discovery when they came up with this triple-layering. It was like patenting the discovery that hamburgers are best served with the tomato slice sandwiched between the lettuce and the meat so the bread doesn’t get soggy.12

Protecting the profits, losing our trust

Often attempts at evergreening go well beyond the ridiculous and result in cases of clear-cut fraud. In the late 1990’s the drug company Schering-Plough, enjoyed global sales of three billion a year for its patented drug Claritin (loratadine), but was nearing the end of its 20-year patent monopoly. Since Claritin had supplied them with almost 40% of their revenue, they decided a patent extension was in order. The company’s lawyers claimed the US FDA had unfairly delayed initial approval of the drug, and eventually they managed to secure a four year extension. The FDA had required Schering-Plough to submit over 37 amendments to its original approval application due to inadequate evidence, as well as concerns of carcinogenicity in test animals. However, the tactics did not end there. In 1999, a bill was introduced in the US Congress by Senator Torricelli which would allow Claritin (and six other drugs) another patent extension. The day before the bill was introduced Schering had made a $50,000 donation to the Democratic Senatorial Campaign Committee of which Torricelli was Chair. Another Senator who presided over hearings on the bill was known to have flown several times with his staff on the Schering-Plough executive jet. Fortunately, the public found out about the story, and the bill was scrapped.13

Whether or not a patient has access to a drug such as Claritin certainly carries with it no implications of life or death. However in the world of life saving drugs, fierce patent control costs lives. For cancer patients, the stress of illness and for some the prospect of succumbing to the disease must be an incredible burden to bear. It goes without saying that the affordability of drugs like Taxol and Platinol make a significant difference, especially for those who lack medical coverage. Last year Bristol-Myers Squibb, the makers of Taxol and Platinol, were found guilty on major antitrust charges after generic manufacturers sought FDA approval for less expensive versions following the expiration of the original patent. A report from The Wall Street Journal explains how Bristol-Myers Squibb “illegally sought to extend patent protection on three blockbuster drugs, blocking competition from less-costly medications.” The Federal Trade Commission, which headed up the investigation, alleged “a decade-long pattern of regulatory abuse by Bristol-Myers, shielding more than $2 billion in annual sales from competition by generic drugs and forcing cancer patients and others to overpay hundreds of millions of dollars for medications. The case is the latest in a string of suits alleging that drug makers game Food and Drug Administration rules to extend patent protection, allowing them to reap higher prices and stifle competition.” In January, the company agreed to pay $670 million to resolve related lawsuits filed by states, generic drug makers and pharmacies.14 However, many feel that for an industry which is so profitable, financial penalties are an inadequate deterrent for future injustices against the public.

Creating diseases creates patients

Crucial to any commercial strategy that attempts to sell a product is the need to locate appropriate markets. Often, if there is no ‘real’ need for your product then companies will opt to create the demand instead, and it is for this reason that some of the worst products with regard to human health are also some of the most heavily marketed. If you are in the business of selling drugs it sure helps to have people to sell them to, and for the drug industry finding people means finding diseases. When business is slow and the monumental life-saving drug creations are few and far between, the drug industry focuses its energy and enormous financial wealth on opening new ‘disease markets’ where previously they did not exist. From an industry that brought us adult attention deficit hyperactivity disorder (aADHD) for those that meet 10 points on a list that includes “procrastination, a need to seek high stimulation activities, and a lack of attention to detail,” or pre-menstrual dysphoric disorder (PMDD), which ‘conveniently’ calls for the use of a newly patented and re-packaged version of Prozac named Sarafem, or ‘Prozac in Pink,’ we see the emergence of a steady stream of disorders, dysfunctions, and diseases.

Daniel Berman, the Geneva-based coordinator for Médecins Sans Frontières’ Access to Essential Medicines Campaign, used to work for the drug industry. He describes how academics and public ‘education’ agencies are used to help create ‘new’ diseases: “You find a professor working in a university and fund that professor to write a book or to do a media tour around the country. Or you find a public figure, a sports figure or an actor, to go around and meet and work with journalists, and to do work with public forums, so you literally create this need.”15 Barry Brand, a product director for GlaxoSmithKline confirms this strategy: “Every marketers dream is to find an unidentified or unknown market and develop it.”16 Brand, who spearheaded the approval and subsequent extension of Glaxo’s patented drug
paroxetine (Paxil) for ‘social anxiety disorder’ or SAD, appears to have achieved his dream.

Whether or not we realize it, society is being influenced on a large scale when it comes to the drug industry’s influence in defining disease. Millions of healthy people are being turned into patients due to an industry-sponsored decrease in the threshold for high blood pressure, now called ‘pre-hypertension.’ Millions of aging men with declining testosterone levels are also now being marketed into the notion of a ‘male menopause,’ complete with industry supported clinics that classify aging as a ‘treatable condition’ and are poised to provide hormone replacement therapy as a means to treat it.17 Not only has Health Canada approved testosterone therapy for a condition which has not yet even been defined and accepted by the medical community, but it is doing so on the basis of very questionable research.

Joel Lexchin, a Toronto emergency physician and professor of health policy at York University describes the state of research on ‘andropause’: “Nobody knows whether or not these declining testosterone levels in otherwise normal men really represent a pathology, or mean anything at all. There have been no long-term studies that show testosterone replacement is beneficial, and some of the short-term studies are really very equivocal.”18 Dr. John McKinley, director of the Massachusetts Male Aging Study also confirms these comments: “There isn’t a single well-designed clinical trial on hormone replacement therapy for men that has been done anywhere in the world…I know all the players involved and most of the work has been done by researchers who are paid for by the industry that benefits from positive findings.”19 In November of last year the US Institute of Medicine published a 217-page report on testosterone: “The committee was unable to find conclusive evidence regarding the efficacy of testosterone therapy for older men…”20 In fact, if the industry-motivated marketing machine continues as it is, we could very likely be setting ourselves up to repeat what happened to women when two major Women’s Health Initiative studies were cut short after hormone replacement therapy was found to be increasing the risk of heart disease, strokes, and breast cancer.

**Profit-seeking behaviour disorder (PSBD)**

Inspired by the drug industry’s ability and aptitude for manufacturing disease, it has now become evident that a new area of disease might be ready for development. It has had a high prevalence in society for many years, but alarmingly, is now reaching epidemic proportions. While not yet qualifying as a disease, it is most certainly a disorder, and is now specifically referred to as profit seeking behaviour disorder, or PSBD. This disorder shows itself in many ways, but ultimately it is a behaviour best characterized by the consistent and often pathologic pursuit of financial profit above all else. In making a diagnosis of PSBD, physicians cannot as yet rely on any defined clinical assessment tools, and therefore, they must pay particular attention to the patient history. To illustrate this point, those involved in the following two examples would qualify for a PSBD diagnosis:

“In a recent US Medicaid fraud settlement, Bayer pharmaceuticals agreed yesterday to pay the government $257 million and pleaded guilty to a criminal charge after engaging in what federal prosecutors said was a scheme to overcharge for the antibiotic Cipro. According to documents turned over to the government by a whistle-blower, Bayer was coached in the scheme by a purchasing manager from Kaiser Permanente, one of the nation's largest health care organizations. The fraud involved selling Cipro to Kaiser at prices lower than the company was charging Medicaid, in violation of a federal law that requires drug makers to give the Medicaid program the lowest price charged to any customer. To cover up the fraud, the Cipro bottles sold to Kaiser were relabeled with Kaiser's name and given a different drug identification number.”19

“Prosecutors also announced yesterday that GlaxoSmithKline had agreed to pay $87.6 million to settle civil charges that it had overcharged the Medicaid program for Paxil, an antidepressant, and Flonase, an allergy spray. That deal also involved re-labelling medicines for Kaiser, prosecutors said.”19

**Preventative medicine: Are you at risk?**

Not only are new ‘diseases’ literally being created by the drug industry, but they are also sponsoring, supporting, and even driving a recent increase in the treatment of risk factors for diseases as conditions unto themselves. This risk-factor-as-disease model uses surrogate markers to evaluate a patient’s state of health, and includes examples like hypercholesterolemia, or high blood cholesterol as a risk for future heart disease; osteopenia and osteoporosis as a risk factor for future bone fracture; and ‘pre-hypertension’ as a risk factor for a risk factor, since hypertension (high blood pressure) is linked to higher incidence of strokes and heart disease.

The approach commonly follows a ‘test - treat - retest’ sequence, and enables the drug industry to target increasing numbers of ‘patients’ with drug treatments, and thereby increase sales substantially. It also causes people to view themselves more and more as being sick rather than healthy. We end up discussing our cholesterol levels or bone mineral densities as though a heart attack may be imminent, or a life-threatening hip fracture inevitably around the corner. In this regard, “social studies of medicine have repeatedly demonstrated how market forces may create and capitalize on a climate of risk and reassurance, which
then drives the use of health technologies regardless of whether they lead to improved health outcomes.\textsuperscript{20} Notwithstanding, this is what is now called preventative medicine. Take for instance the example of osteoporosis, where common medical belief is that by measuring women’s bone densities, and in many cases Initiating expensive and potentially dangerous drug treatment before they develop osteoporosis, we are attacking the problem before it develops. Research funded by the makers of Fosamax (alendronate), a commonly used drug to prevent fractures, found that fracture incidence was reduced by an infinitesimal 1% (absolute risk reduction) in women with a previous history of fractures or osteoporosis. So, over a period of four years, 100 women would have to take Fosamax, at a cost of up to $700/yr in order for one to avoid a hip fracture. Between 1995 and 2000, Canadians spent $56 million on ‘preventative therapy’ using a drug that, in 1996, topped the US FDA list for the most reported adverse effects.\textsuperscript{20}

However, if we are really the kind of person that likes to get at the root of a problem, and design an ultimate and long-lasting solution, then a real preventative approach might look quite different. If we’re talking about women and bone density, there is a preventative approach to health requires time and commitment on behalf of the physician as well as the patient. These things however, do not result in medical “busy-ness,”\textsuperscript{26} and they certainly fail to result in the continuous sale of drugs so desperately ‘needed’ by the drug industry. According to Alex Hittle, a biotech analyst at AG Edwards in St. Louis, “we sometimes joke that when you’re doing a clinical trial, there are two possible disasters. The first disaster is if you kill people. The second disaster is if you cure them. The truly good drugs are the ones you can use chronically for a long, long time.”\textsuperscript{15}

With what we have seen of drug company trends lately, this quote is rather easy to believe. However, if this is truly so, why is it we see ads from drug companies like Pfizer that say things like: “It is our greatest hope that someday soon, the only place you’ll find cancer will be on a history exam, or that Alzheimer’s, the disease that robs memories, will itself fade into the past.” If that isn’t enough the ad then describes how “at Pfizer, we look to the future with the knowledge that the only thing that is incurable is our passion.”\textsuperscript{27} If the public relations department has done their job properly you’ll not only be shedding tears of joy by now, but if you’re not careful you might also find yourself believing the message. In fact many have been lulled into a false sense that the drug industry shares equally their commitment to the patient above all else, and the vast profits they earn are merely an extra benefit.

One should also bear in mind that for the drug industry, making a statement about curing disease is suspect. One cannot believe such a statement simply because it is made by an industry which is absolutely dependent on the presence of disease in order to sell drugs and be profitable. To achieve such a goal would...
mean that everyone is healthy, and a healthy society wouldn’t presumably require the use of drugs. No drugs mean no drug industry, and this doesn’t fit. The only way in which this statement could work is if the cures all lie with the use of drugs. This obviously isn’t, and most certainly shouldn’t be the case. But if it was, many would question their use of the word ‘cure,’ especially if patients end up having to endure a lifetime of drug treatment as would be the ideal situation described by Hittle. Maybe putting statins in the water would be one way in which the drug industry might want to seek out its ‘cure.’

Over 25 years ago, *Fortune* magazine did a story on Merck CEO Henry Gadsden. In the interview, Mr. Gadsden described his goal of freeing his company from a market limited to sick people. He said he wanted Merck to be just like the chewing gum company Wrigley’s and sell to everyone.28 Maybe we’d be better off if the drug industry started making chewing gum instead.

**Useful resources**

The Stop Patient Abuse Now (SPAN) website:
- [http://www.spancoalition.org/](http://www.spancoalition.org/)

The Alliance for Human Research Protection:

The Patented Medicines and Pricing Review Board and the number of patented drugs in circulation:

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