### 1AC – FW

#### The standard is maximizing expected wellbeing.

#### Prefer:

#### 1] Pleasure and pain are intrinsic value and disvalue-- robust neuroscience prove.

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**Pleasure** is not only one of the three primary reward functions but it also **defines reward.** As homeostasis explains the functions of only a limited number of rewards, the principal reason why particular stimuli, objects, events, situations, and activities are rewarding may be due to pleasure. This applies first of all to sex and to the primary homeostatic rewards of food and liquid and extends to money, taste, beauty, social encounters and nonmaterial, internally set, and intrinsic rewards. Pleasure, as the primary effect of rewards, drives the prime reward functions of learning, approach behavior, and decision making and provides the **basis for hedonic theories** of reward function. We are attracted by most rewards and exert intense efforts to obtain them, just because they are enjoyable [10]. Pleasure is a passive reaction that derives from the experience or prediction of reward and may lead to a long-lasting state of happiness. The word happiness is difficult to define. In fact, just obtaining physical pleasure may not be enough. One key to happiness involves a network of good friends. However, it is not obvious how the higher forms of satisfaction and pleasure are related to an ice cream cone, or to your team winning a sporting event. Recent multidisciplinary research, using both humans and detailed invasive brain analysis of animals has discovered some critical ways that the brain processes pleasure [14]. Pleasure as a hallmark of reward is sufficient for defining a reward, but it may not be necessary. A reward may generate positive learning and approach behavior simply because it contains substances that are essential for body function. When we are hungry, we may eat bad and unpleasant meals. A monkey who receives hundreds of small drops of water every morning in the laboratory is unlikely to feel a rush of pleasure every time it gets the 0.1 ml. Nevertheless, with these precautions in mind, we may define any stimulus, object, event, activity, or situation that has the potential to produce pleasure as a reward. In the context of reward deficiency or for disorders of addiction, homeostasis pursues pharmacological treatments: drugs to treat drug addiction, obesity, and other compulsive behaviors. The theory of allostasis suggests broader approaches - such as re-expanding the range of possible pleasures and providing opportunities to expend effort in their pursuit. [15]. It is noteworthy, the first animal studies eliciting approach behavior by electrical brain stimulation interpreted their findings as a discovery of the brain’s pleasure centers [16] which were later partly associated with midbrain dopamine neurons [17–19] despite the notorious difficulties of identifying emotions in animals. Evolutionary theories of pleasure: The love connection BO:D Charles Darwin and other biological scientists that have examined the biological evolution and its basic principles found various mechanisms that steer behavior and biological development. Besides their theory on natural selection, it was particularly the sexual selection process that gained significance in the latter context over the last century, especially when it comes to the question of what makes us “what we are,” i.e., human. However, the capacity to sexually select and evolve is not at all a human accomplishment alone or a sign of our uniqueness; yet, we humans, as it seems, are ingenious in fooling ourselves and others–when we are in love or desperately search for it. It is well established that modern biological theory conjectures that **organisms are** the **result of evolutionary competition.** In fact, Richard Dawkins stresses gene survival and propagation as the basic mechanism of life [20]. Only genes that lead to the fittest phenotype will make it. It is noteworthy that the phenotype is selected based on behavior that maximizes gene propagation. To do so, the phenotype must survive and generate offspring, and be better at it than its competitors. Thus, the ultimate, distal function of rewards is to increase evolutionary fitness by ensuring the survival of the organism and reproduction. It is agreed that learning, approach, economic decisions, and positive emotions are the proximal functions through which phenotypes obtain other necessary nutrients for survival, mating, and care for offspring. Behavioral reward functions have evolved to help individuals to survive and propagate their genes. Apparently, people need to live well and long enough to reproduce. Most would agree that homo-sapiens do so by ingesting the substances that make their bodies function properly. For this reason, foods and drinks are rewards. Additional rewards, including those used for economic exchanges, ensure sufficient palatable food and drink supply. Mating and gene propagation is supported by powerful sexual attraction. Additional properties, like body form, augment the chance to mate and nourish and defend offspring and are therefore also rewards. Care for offspring until they can reproduce themselves helps gene propagation and is rewarding; otherwise, many believe mating is useless. According to David E Comings, as any small edge will ultimately result in evolutionary advantage [21], additional reward mechanisms like novelty seeking and exploration widen the spectrum of available rewards and thus enhance the chance for survival, reproduction, and ultimate gene propagation. These functions may help us to obtain the benefits of distant rewards that are determined by our own interests and not immediately available in the environment. Thus the distal reward function in gene propagation and evolutionary fitness defines the proximal reward functions that we see in everyday behavior. That is why foods, drinks, mates, and offspring are rewarding. There have been theories linking pleasure as a required component of health benefits salutogenesis, (salugenesis). In essence, under these terms, pleasure is described as a state or feeling of happiness and satisfaction resulting from an experience that one enjoys. Regarding pleasure, it is a double-edged sword, on the one hand, it promotes positive feelings (like mindfulness) and even better cognition, possibly through the release of dopamine [22]. But on the other hand, pleasure simultaneously encourages addiction and other negative behaviors, i.e., motivational toxicity. It is a complex neurobiological phenomenon, relying on reward circuitry or limbic activity. It is important to realize that through the “Brain Reward Cascade” (BRC) endorphin and endogenous morphinergic mechanisms may play a role [23]. While natural rewards are essential for survival and appetitive motivation leading to beneficial biological behaviors like eating, sex, and reproduction, crucial social interactions seem to further facilitate the positive effects exerted by pleasurable experiences. Indeed, experimentation with addictive drugs is capable of directly acting on reward pathways and causing deterioration of these systems promoting hypodopaminergia [24]. Most would agree that pleasurable activities can stimulate personal growth and may help to induce healthy behavioral changes, including stress management [25]. The work of Esch and Stefano [26] concerning the link between compassion and love implicate the brain reward system, and pleasure induction suggests that social contact in general, i.e., love, attachment, and compassion, can be highly effective in stress reduction, survival, and overall health. Understanding the role of neurotransmission and pleasurable states both positive and negative have been adequately studied over many decades [26–37], but comparative anatomical and neurobiological function between animals and homo sapiens appear to be required and seem to be in an infancy stage. Finding happiness is different between apes and humans As stated earlier in this expert opinion one key to happiness involves a network of good friends [38]. However, it is not entirely clear exactly how the higher forms of satisfaction and pleasure are related to a sugar rush, winning a sports event or even sky diving, all of which augment dopamine release at the reward brain site. Recent multidisciplinary research, using both humans and detailed invasive brain analysis of animals has discovered some critical ways that the brain processes pleasure. Remarkably, there are pathways for ordinary liking and pleasure, which are limited in scope as described above in this commentary. However, there are **many brain regions**, often termed hot and cold spots, that significantly **modulate** (increase or decrease) our **pleasure or** even **produce the opposite** of pleasure— that is disgust and fear [39]. One specific region of the nucleus accumbens is organized like a computer keyboard, with particular stimulus triggers in rows— producing an increase and decrease of pleasure and disgust. Moreover, the cortex has unique roles in the cognitive evaluation of our feelings of pleasure [40]. Importantly, the interplay of these multiple triggers and the higher brain centers in the prefrontal cortex are very intricate and are just being uncovered. Desire and reward centers It is surprising that many different sources of pleasure activate the same circuits between the mesocorticolimbic regions (Figure 1). Reward and desire are two aspects pleasure induction and have a very widespread, large circuit. Some part of this circuit distinguishes between desire and dread. The so-called pleasure circuitry called “REWARD” involves a well-known dopamine pathway in the mesolimbic system that can influence both pleasure and motivation. In simplest terms, the well-established mesolimbic system is a dopamine circuit for reward. It starts in the ventral tegmental area (VTA) of the midbrain and travels to the nucleus accumbens (Figure 2). It is the cornerstone target to all addictions. The VTA is encompassed with neurons using glutamate, GABA, and dopamine. The nucleus accumbens (NAc) is located within the ventral striatum and is divided into two sub-regions—the motor and limbic regions associated with its core and shell, respectively. The NAc has spiny neurons that receive dopamine from the VTA and glutamate (a dopamine driver) from the hippocampus, amygdala and medial prefrontal cortex. Subsequently, the NAc projects GABA signals to an area termed the ventral pallidum (VP). The region is a relay station in the limbic loop of the basal ganglia, critical for motivation, behavior, emotions and the “Feel Good” response. This defined system of the brain is involved in all addictions –substance, and non –substance related. In 1995, our laboratory coined the term “Reward Deficiency Syndrome” (RDS) to describe genetic and epigenetic induced hypodopaminergia in the “Brain Reward Cascade” that contribute to addiction and compulsive behaviors [3,6,41]. Furthermore, ordinary “liking” of something, or pure pleasure, is represented by small regions mainly in the limbic system (old reptilian part of the brain). These may be part of larger neural circuits. In Latin, hedus is the term for “sweet”; and in Greek, hodone is the term for “pleasure.” Thus, the word Hedonic is now referring to various subcomponents of pleasure: some associated with purely sensory and others with more complex emotions involving morals, aesthetics, and social interactions. The capacity to have pleasure is part of being healthy and may even extend life, especially if linked to optimism as a dopaminergic response [42]. Psychiatric illness often includes symptoms of an abnormal inability to experience pleasure, referred to as anhedonia. A negative feeling state is called dysphoria, which can consist of many emotions such as pain, depression, anxiety, fear, and disgust. Previously many scientists used animal research to uncover the complex mechanisms of pleasure, liking, motivation and even emotions like panic and fear, as discussed above [43]. However, as a significant amount of related research about the specific brain regions of pleasure/reward circuitry has been derived from invasive studies of animals, these cannot be directly compared with subjective states experienced by humans. In an attempt to resolve the controversy regarding the causal contributions of mesolimbic dopamine systems to reward, we have previously evaluated the three-main competing explanatory categories: “liking,” “learning,” and “wanting” [3]. That is, dopamine may mediate (a) liking: the hedonic impact of reward, (b) learning: learned predictions about rewarding effects, or (c) wanting: the pursuit of rewards by attributing incentive salience to reward-related stimuli [44]. We have evaluated these hypotheses, especially as they relate to the RDS, and we find that the incentive salience or “wanting” hypothesis of dopaminergic functioning is supported by a majority of the scientific evidence. Various neuroimaging studies have shown that anticipated behaviors such as sex and gaming, delicious foods and drugs of abuse all affect brain regions associated with reward networks, and may not be unidirectional. Drugs of abuse enhance dopamine signaling which sensitizes mesolimbic brain mechanisms that apparently evolved explicitly to attribute incentive salience to various rewards [45]. Addictive substances are voluntarily self-administered, and they enhance (directly or indirectly) dopaminergic synaptic function in the NAc. This activation of the brain reward networks (producing the ecstatic “high” that users seek). Although these circuits were initially thought to encode a set point of hedonic tone, it is now being considered to be far more complicated in function, also encoding attention, reward expectancy, disconfirmation of reward expectancy, and incentive motivation [46]. The argument about addiction as a disease may be confused with a predisposition to substance and nonsubstance rewards relative to the extreme effect of drugs of abuse on brain neurochemistry. The former sets up an individual to be at high risk through both genetic polymorphisms in reward genes as well as harmful epigenetic insult. Some Psychologists, even with all the data, still infer that addiction is not a disease [47]. Elevated stress levels, together with polymorphisms (genetic variations) of various dopaminergic genes and the genes related to other neurotransmitters (and their genetic variants), and may have an additive effect on vulnerability to various addictions [48]. In this regard, Vanyukov, et al. [48] suggested based on review that whereas the gateway hypothesis does not specify mechanistic connections between “stages,” and does not extend to the risks for addictions the concept of common liability to addictions may be more parsimonious. The latter theory is grounded in genetic theory and supported by data identifying common sources of variation in the risk for specific addictions (e.g., RDS). This commonality has identifiable neurobiological substrate and plausible evolutionary explanations. Over many years the controversy of dopamine involvement in especially “pleasure” has led to confusion concerning separating motivation from actual pleasure (wanting versus liking) [49]. We take the position that animal studies cannot provide real clinical information as described by self-reports in humans. As mentioned earlier and in the abstract, on November 23rd, 2017, evidence for our concerns was discovered [50] In essence, although nonhuman primate brains are similar to our own, the disparity between other primates and those of human cognitive abilities tells us that surface similarity is not the whole story. Sousa et al. [50] small case found various differentially expressed genes, to associate with pleasure related systems. Furthermore, the dopaminergic interneurons located in the human neocortex were absent from the neocortex of nonhuman African apes. Such differences in neuronal transcriptional programs may underlie a variety of neurodevelopmental disorders. In simpler terms, the system controls the production of dopamine, a chemical messenger that plays a significant role in pleasure and rewards. The senior author, Dr. Nenad Sestan from Yale, stated: “Humans have evolved a dopamine system that is different than the one in chimpanzees.” This may explain why the behavior of humans is so unique from that of non-human primates, even though our brains are so surprisingly similar, Sestan said: “It might also shed light on why people are vulnerable to mental disorders such as autism (possibly even addiction).” Remarkably, this research finding emerged from an extensive, multicenter collaboration to compare the brains across several species. These researchers examined 247 specimens of neural tissue from six humans, five chimpanzees, and five macaque monkeys. Moreover, these investigators analyzed which genes were turned on or off in 16 regions of the brain. While the differences among species were subtle, **there was** a **remarkable contrast in** the **neocortices**, specifically in an area of the brain that is much more developed in humans than in chimpanzees. In fact, these researchers found that a gene called tyrosine hydroxylase (TH) for the enzyme, responsible for the production of dopamine, was expressed in the neocortex of humans, but not chimpanzees. As discussed earlier, dopamine is best known for its essential role within the brain’s reward system; the very system that responds to everything from sex, to gambling, to food, and to addictive drugs. However, dopamine also assists in regulating emotional responses, memory, and movement. Notably, abnormal dopamine levels have been linked to disorders including Parkinson’s, schizophrenia and spectrum disorders such as autism and addiction or RDS. Nora Volkow, the director of NIDA, pointed out that one alluring possibility is that the neurotransmitter dopamine plays a substantial role in humans’ ability to pursue various rewards that are perhaps months or even years away in the future. This same idea has been suggested by Dr. Robert Sapolsky, a professor of biology and neurology at Stanford University. Dr. Sapolsky cited evidence that dopamine levels rise dramatically in humans when we anticipate potential rewards that are uncertain and even far off in our futures, such as retirement or even the possible alterlife. This may explain what often motivates people to work for things that have no apparent short-term benefit [51]. In similar work, Volkow and Bale [52] proposed a model in which dopamine can favor NOW processes through phasic signaling in reward circuits or LATER processes through tonic signaling in control circuits. Specifically, they suggest that through its modulation of the orbitofrontal cortex, which processes salience attribution, dopamine also enables shilting from NOW to LATER, while its modulation of the insula, which processes interoceptive information, influences the probability of selecting NOW versus LATER actions based on an individual’s physiological state. This hypothesis further supports the concept that disruptions along these circuits contribute to diverse pathologies, including obesity and addiction or RDS.

#### Extinction first –

#### 1] Objectivity, easier to weigh than [Their Impact]– body count is the most objective way to calculate impacts because comparing suffering or [THEIR IMPACT] is unethical and irresolvable

#### 2] Moral uncertainty – if we’re unsure about which interpretation of the world is true – we ought to preserve the world to keep debating about it

#### 3] No intent foresight distinction, you are culpable for consequences that you foresee because it’s part of your mental deliberation to act upon it

#### A] Philosophers would prevent extinction if they knew it would happen otherwise they are culpable for it

#### Util is the best theoretically justified framework

#### 1] Ground – Util cares about all impacts which ensures link and impact turn ground for both sides. Util impacts are easy to contextualize and allows for all types of ground with work debaters have to do.

#### 2] Novice Accessibility – Util is fairer and more educational for novice debaters since contention/LARP ground is what they learn you crowd out novice debaters by debating up and guts accessibility for trad debate. B] Encourages tricking novices and preventing clash and engagement on your offense. OW on participation to the activity

### 1AC: Innovation

#### Advantage 1 is Innovation

#### We are in an innovation crisis – new drugs are not being developed in favor of re-purposing old drugs to infinitely extend patent expiration.

Feldman 1 Robin Feldman 2-11-2019 "‘One-and-done’ for new drugs could cut patent thickets and boost generic competition" <https://www.statnews.com/2019/02/11/drug-patent-protection-one-done/> (Arthur J. Goldberg Distinguished Professor of Law, Albert Abramson ’54 Distinguished Professor of Law Chair, and Director of the Center for Innovation)//SidK + Elmer

Drug companies **have brought great innovations** to market. Society rewards innovation with patents, or with non-patent exclusivities that can be obtained for activities such as testing drugs in children, undertaking new clinical studies, or developing orphan drugs. The rights provided by patents or non-patent exclusivities provide a defined time period of protection so companies can recoup their investments by charging monopoly prices. When patents end, lower-priced competitors should be able to jump into the market and drive down the price. **But that’s not happening**. Instead, drug companies build massive patent walls around their products, extending the protection **over and over again**. Some modern drugs have an avalanche of U.S. patents, with expiration dates **staggered across time**. For example, the rheumatoid arthritis drug Humira is **protected by more than 100 patents**. Walls like that **are insurmountable**. Rather than rewarding innovation, our patent system is now largely repurposing drugs. Between 2005 and 2015, **more than three-quarters** of the drugs associated with new patents **were not new ones** coming on the market but existing ones. In other words, we are mostly churning and recycling. Particularly troubling, new patents can be **obtained on minor tweaks** such as adjustments to dosage or delivery systems — a once-a-day pill instead of a twice-a-day one; a capsule rather than a tablet. Tinkering like this may have some value to some patients, but it nowhere near justifies the rewards we lavish on companies for doing it. From society’s standpoint, incentives should drive scientists back to the lab to look for new things, not to recycle existing drugs for minimal benefit.

#### We control Uniqueness – up to 80% of all new patents are not new drugs but old ones.

Feldman 2 Robin Feldman 18, May your drug price be evergreen, Journal of Law and the Biosciences, Volume 5, Issue 3, December 2018, Pages 590–647, <https://doi.org/10.1093/jlb/lsy022> Arthur J. Goldberg Distinguished Professor of Law, Albert Abramson ’54 Distinguished Professor of Law Chair, and Director of the Center for Innovation (Study Notes: Presenting the first comprehensive study of evergreening, this article examines the extent to which evergreening behavior—which can be defined as artificially extending the protection cliff—may contribute to the problem. The author analyses all drugs on the market between 2005 and 2015, combing through 60,000 data points to examine every instance in which a company added a new patent or exclusivity.)//sid

The study results demonstrate definitively that the pharmaceutical industry has strayed far from the patent system's intended design. The patent system is not functioning as a time-limited opportunity to garner a return, followed by open competition. Rather, companies throughout the industry seek and obtain repeated extensions of their competition-free zones. Moreover, the incidence of such behavior has steadily increased between 2005 and 2015, especially on the patent front and for certain highly valuable exclusivities. Most troubling, the data suggest that the current state of affairs **is harming innovation** in tangible ways. Rather than creating new medicines—sallying forth into new frontiers for the benefit of society—drug companies are focusing their time and effort extending **the patent life of old products**. This, of course, is not the innovation one would hope for. The greatest creativity at pharmaceutical **companies should be in the lab, not in the legal department**.115 The following sections describe the results obtained through our analysis in detail, but below are the key takeaways from the study: Rather than creating new medicines, pharmaceutical companies are recycling and repurposing old ones. In fact, 78% of the drugs associated with new patents in the FDA’s records **were not new drugs** coming on the market, but existing drugs. In some years, the percentage reached as high as 80%. Adding new patents and exclusivities to extend the protection cliff is particularly pronounced among blockbuster drugs. Of the roughly 100 best-selling drugs, more than 70% extended their protection at least once, with more than 50% extending the protection cliff more than once. Looking at the full group, almost 40% of all drugs available on the market created additional market barriers by **having patents or exclusivities added** to them. Many of the drugs adding to the Orange Book are ‘serial offenders’—returning to the well repeatedly for new patents and exclusivities. Of the drugs that had an addition to the Orange Book, 80% of those had an addition to the Orange Book on more than one occasion, and almost half of these drugs had additions to the Orange Book on four or more occasions. The number of drugs with a high quantity of added patents in a single year has substantially increased. For example, the number of drugs with three or more patents added to them in one year has doubled. Similarly, the number of drugs with five or more added patents has also doubled. Overall, the quantity of patents added to the Orange Book has more than doubled, increasing from 349 patents added in the year 2005 to 723 in 2015. The number of drugs that had a patent added to them in the Orange Book almost doubled. There were striking increases in certain exclusivities, such as orphan drug exclusivity, new patient population exclusivity, and new product exclusivity. In particular, the number of drugs with an added orphan drug exclusivity tripled. In addition, the number of times a use code was added to a patent more than tripled, suggesting that this has become a new favored game. To provide a broad sense of the types of metrics we are using, some could be characterized as ‘intensity’ measures, which capture the breadth and depth of patent and exclusivity activity in the industry. Another set of our metrics can be characterized as ‘temporal’ measures, which evaluate whether there are any trends in the behavior under examination across time during our 11-year timeframe from 2005 to 2015.

#### The only major study confirms our Internal Link – Evergreening decimates competition by resulting in functional monopolies

Arnold Ventures 20 9-24-2020 "'Evergreening' Stunts Competition, Costs Consumers and Taxpayers" <https://www.arnoldventures.org/stories/evergreening-stunts-competition-costs-consumers-and-taxpayers/> (Arnold Ventures is focused on evidence-based giving in a wide range of categories including: criminal justice, education, health care, and public finance)//Elmer

In 2011, Elsa Dixler was diagnosed with multiple myeloma. That August, she was prescribed Revlimid, a drug that had come on the market six years earlier. By January 2012, she went into full remission, where she has remained since. So long as Revlimid retains its effectiveness, she will take it for the rest of her life. “I was able to go back to work, see my daughter receive her Ph.D, and have a pretty normal life,” said Dixler, a Brooklyn resident who is now 74. “So, on the one hand, I feel enormously grateful.” But Dixler’s normal life has come at a steep financial cost to her family and to taxpayers. Revlimid typically costs nearly $800 per capsule, and Dixler takes one capsule per day for 21 days, then seven days off, and then resumes her daily dose, requiring 273 capsules a year. Since retiring from The New York Times at the end of 2017, she has been on Medicare. Dixler entered the Part D coverage gap (known as the donut hole) “within minutes,” she said. She estimates that adding her deductible, her copayment of $12,000, and what her Part D insurance provider pays totals approximately $197,500 a year. Revlimid should have **been subject to competition** from generic drug makers starting in 2009, bringing down its cost by many orders of magnitude. But by obtaining **27 additional patents**, eight orphan drug exclusivities and 91 total additional protections from the U.S. Food and Drug Administration (FDA) since Revlimid’s introduction in 2005, its manufacturer, Celgene, has extended the drug’s **monopoly** **period** **by 18 years** — through March 8, 2028. “I cannot fathom the immorality of a business that relies on **squeezing people with cancer**,” Dixler said, noting her astonishment that Revlimid has obtained orphan drug protections when it treats a disease that is not rare and does not serve a very limited population. She also observed that Revlimid’s underlying drug is thalidomide, which has been around for decades. “They didn’t invent a new drug, rather, they found a new use for it,” she said. “The cost of Revlimid has imposed constraints on our retirement,” Dixler said, “but when I hear other people’s stories, I feel very lucky. A lot of people have been devastated financially.” Revlimid is a case study in a process known as “evergreening” — artificially sustaining a monopoly for years and even decades by manipulating intellectual property laws and regulations. Evergreening is most commonly used with blockbuster drugs generating the highest prices and profits. **Of the roughly 100 best-selling drugs, more than 70 percent have extended their protection** from competition at least once. More than half have extended the protection cliff multiple times. The true scope and cost of evergreening has been brought into sharper focus by a groundbreaking, publicly available, comprehensive database released Thursday by the Center for Innovation at the University of California Hastings College of Law and supported by Arnold Ventures. **The Evergreen Drug Patent Search is the first database to exhaustively track the patent protections filed by pharmaceutical companies**. Using data from 2005 to 2018 on brand-name drugs listed in the FDA’s Orange Book — a listing of relevant patents for brand name, small molecule drugs — it demonstrates the full extent of how evergreening has been used by Big Pharma to prolong patents and delay the entry of generic, lower-cost competition. “Competition is the backbone of the U.S. economy,” said Professor Robin Feldman, Director of the UC Hastings Center for Innovation, who spearheaded the database’s creation. “But it’s not what we’re seeing in the drug industry. “With evergreening, pharmaceutical companies repeatedly make slight, often trivial, modifications to drugs, dosage levels, delivery systems or other aspects to obtain new protections,” she said. “They pile these protections on over and over again — so often that 78 percent of the drugs associated with new patents were not new drugs coming on the market, but existing drugs.” Competition is the backbone of the U.S. economy. But it’s not what we’re **seeing in the drug industry**. Professor Robin Feldman Director of the UC Hastings Center for Innovation In recent decades, evergreening has systematically undermined the Drug Price Competition and Patent Term Restoration Act of 1984, which created the generic drug industry. Commonly known as the Hatch-Waxman Act, it established a new patent and market exclusivity regime in which new drugs are protected from competition for a specified period of time sufficient to allow manufacturers to recoup their investments and earn a reasonable profit. When that protection expires, generic drug makers are incentivized to enter the market through a streamlined regulatory and judicial process. Drug prices typically drop by as much as 20 percent when the first generic enters the market**, and with more than one generic manufacturer, prices can plummet by 80 to 85 percent**. “Hatch-Waxman created an innovation/reward/competition cycle, but it’s been distorted into an innovation/reward/more reward cycle,” Feldman said. “To paraphrase something a former FDA commissioner once said, the greatest creativity in Big Pharma should come from the research and development departments, not from the legal and marketing departments.” Feldman led the development of the Evergreen Drug Patent Search in response to repeated requests from Congressional committees, members of Congress, state regulators and journalists for information about specific drugs and companies. “We want to make it so anyone can have the question about drug protections at their fingertips whenever they want,” Feldman said. “It’s designed to be easy and user-friendly, and to enhance public understanding about how competition may be limited rather than enhanced through the drug patent system.” The **database** was **created through** a painstaking process of **combing** through **160,000 data points** **to examine every instance where a pharmaceutical company added a new drug patent or exclusivity**. “Most of it was done by hand,” Feldman said, “with multiple people reviewing it at every stage. And along the way we repeatedly made conservative choices. **We erred on the side of underrepresenting the evergreen gain** to be sure we were as fair and reasonable as possible.” Among the 2,065 drugs covered in Evergreen Drug Patent Search, there are many examples of the evergreening strategy used by pharma to delay the entry of competition, especially generics, often for widely prescribed drugs, including those used to treat heartburn, chronic pain, and opioid addiction. Nexium Before Nexium, there was Prilosec, a popular drug to treat gastroesophageal reflux disease (GERD). But its patent exclusivity was due to expire in April 2001. In the late 1990s, with a precipitous drop in revenue looming, Prilosec’s manufacturer, AstraZeneca, decided to develop a replacement drug. Using “one-half of the Prilosec molecule — an isomer of it,” the result was Nexium, which received approval in February 2001. Essentially an evergreened version of Prilosec, Nexium’s exclusivity was then extended by more than 15 years, as AstraZeneca received 97 protections stemming from 16 patents. These included revised dosages, compounds, and formulations. Feldman said that tinkering changes such as Nexium’s do not involve the substantial research and development required for a new drug, nor do they constitute true innovations, yet for a decade and a half, patients and taxpayers were forced to pay far more than was warranted for GERD relief. In fact, in 2016 — one year after patent exclusivity expired — Nexium still topped all drugs in Medicare Part D spending, totaling $1.06 billion. Suboxone Use of this combination of buprenorphine and naloxone for treating opioid addiction has exploded in the wake of the opioid epidemic. Since its approval, Suboxone’s manufacturer, Reckitt Benckiser (now operating as Indivior), extended its protection cliff eight times, gaining nearly two extra decades of exclusivity through early 2030. The drug maker gained six patents for creating a film version of the drug — notably around the time protection was expiring for its tablet version. (The therapeutic benefits of the film and tablet are identical.) An earlier version of Suboxone also obtained an orphan drug designation, despite an opioid epidemic that has expanded Suboxone’s customer base to millions of potential customers. Suboxone generates more than $1 billion in annual revenue and ranks among the 40 top-selling drugs in the U.S. Truvada When Truvada, commonly referred to as PrEP, was approved in 2004, this HIV-prevention drug was a breakthrough. But 16 years later — and 14 years after its original exclusivity was to expire — it retains its monopoly status. Truvada’s manufacturer, Gilead, has received 15 patents and 120 protections since it came on the market, extending its exclusivity for more than 17 years, until July 3, 2024. In countries where generic Truvada is available, PrEP costs $100 or less per month, compared to $1,600 to $2,000 in the U.S. As a result, Truvada is unaffordable to many people **who need protection from HIV**. Barred from access, they are left vulnerable to infection. “We’re establishing a precedent that a pharmaceutical company can charge whatever it wants even as it allows an epidemic to continue, and the government refuses to intervene,” said James Krellenstein, co-founder of the group PrEP4All. “That should scare every American. If it’s HIV today, it will be another disease tomorrow.” EpiPen First approved in 1987, the EpiPen has saved the lives of countless numbers of people with deadly allergies. But it is protected from competition until 2025 — 38 years after its introduction — because its owner, Mylan, has filed five patents, four since 2010, all involving tweaks to the automatic injector. The actual medication used, epinephrine, has existed for more than a century — the innovation here is in the delivery device. Because these small changes to the injector have maintained its monopoly for so long, the cost of an EpiPen package (containing two injectors) has risen from $94 when Mylan purchased the device to between $650 and $700 today. For many people, especially parents of children with severe reactions to common allergens like peanuts, EpiPen’s increasing price tag imposes an onerous financial burden. What Can Be Done As the Evergreen Drug Patent Search makes clear, the positive impact of Hatch-Waxman has been steadily and severely eroded by a regulatory system vulnerable to increasingly sophisticated forms of manipulation. “You might say that the patent and regulatory system has been weaponized,” Feldman said. “When billions of dollars are at stake, there’s a lot of money available to look for ways to exploit the legal system. And companies have become adept at this, as our work has found.” There are several key steps that Congress could take to restore the balance between innovation and competition that is the key to a successful prescription drug regulatory process. These may include: Imposing restrictions on the number of patents that prescription drug manufacturers can defend in court to discourage the use of anticompetitive patent thickets. Limiting the patentability of so-called secondary patents — which don’t improve the safety or efficacy of a drug — through patent and exclusivity reform. Reforming the 180-day generic exclusivity, which can currently be abused to block other competitive therapies. “**The Evergreen Drug Patent Search provides the publicly available, evidence-based foundation that defines the extent of the problem**, and it can be used to develop policies that solve the problem of anti-competitive patent abuses,” said Kristi Martin, VP of Drug Pricing at Arnold Ventures. “Our incentives have gotten out of whack,” Martin said. “The luxury of monopoly protection should only be provided to innovations that provide meaningful benefits in saving lives, curing illnesses, or improving the quality of people’s lives. It should not be provided to those gaming the system. If we can change that, we can save consumers, employers, and taxpayers many billions of dollars while increasing the incentives for pharmaceutical companies to achieve breakthroughs."

#### Reject Negative Turns – they’re pharmaceutical lies – the Plan isn’t anti-Patent, just pro-innovation – breaking down secondary patents is key.

* AT Advantage CPs to solve Drug Prices

Radhakrishnan 16 Priti Radhakrishnan 6-14-2016 "Pharma’s secret weapon to keep drug prices high" <https://www.statnews.com/2016/06/14/secondary-patent-gilead-sovaldi-harvoni/> (Priti Radhakrishnan is cofounder and director of the Initiative for Medicines, Access & Knowledge (I-MAK), a US-based nonprofit group of scientists and lawyers working globally to get people lifesaving medicines. Before founding I-MAK, she worked as a health attorney in the US, Switzerland, and India.)//Elmer

Skyrocketing drug prices are forcing states to take **unprecedented measures** to rein in health care spending. Vermont just became the nation’s first state to require prescription drug pricing transparency. The New York and Massachusetts attorneys general have launched investigations into major pharmaceutical companies’ and insurers’ drug pricing policies and strategies. These **are important steps**. **But** they **ignore a key driver of the problem: secondary patents**. Familiar to only a few people inside the insular world of intellectual property law, secondary patents work like this: Companies file for additional, defensive patents to thicken the protection around their original base patents. These additional patents **rarely represent anything new in terms of science**. Instead, their **purpose is to** **prolong** **a** company’s **monopoly** and, along with that, its ability to charge high prices for its drugs. Some drugs have dozens of secondary patents. Abbott Labs, for example, has over 108 patents on its HIV drug Kaletra. Take the case of Sovaldi, a treatment for hepatitis C developed by Gilead Sciences. In the United States, Gilead prices Sovaldi at up to $1,000 a pill, or about $84,000 for a complete course of treatment. This pricing strategy helped Gilead clear $18 billion in profits last year, while taxpayer-funded Medicaid programs, state health programs, and patients have trouble affording this astronomically priced drug. Sovaldi is comprised of a base compound — sofosbuvir — for which the pharma giant has filed three patents. On top of that, Gilead has pursued an additional 24 patents, with more likely to come. My organization, the Initiative for Medicines, Access & Knowledge (I-MAK), aims to ensure that people with hepatitis C and HIV around the world get the medicines they need to survive and lead healthy lives. We have evaluated Gilead’s patent portfolio and found that, based on US and international patent law, Gilead does not deserve any of its 27 patents for Sovaldi. Both the base and secondary patents for the drug are based on old science and commonly known techniques. Yet because of its defensive patenting strategy, Gilead will maintain an iron lock on its market share and charge exorbitantly high prices to Americans with hepatitis C until well into the 2030s. Harvoni, another medication that treats hepatitis C, combines sofosbuvir and a drug called ledipasvir. Currently, Harvoni has 27 secondary patents. If these were removed, people in the US could access far cheaper versions of the same drug as soon as 10 years earlier. Based on I-MAK’s conservative estimates, this could open access to treatment for millions of people in the US, saving patients and payers like Medicare and Medicaid $5 billion over an eight-year period. In the US, Harvoni is priced at $94,000 for a course of treatment. In middle-income, high-population countries like Argentina, Brazil, and China, people are forced to pay thousands of dollars for sofosbuvir. Stripping away unmerited patents would reduce drug costs and increase access for millions of people in the US and around the world. **Pharmaceutical companies love to claim that winnowing** their armada of pate**nts would be a disincentive to innovation** and would limit research into new drugs. **Don’t believe it**. **The industry devotes shockingly little funding to research and development**. Companies **spend** roughly **one-third** of their revenues **on marketing** **and only half as much on research** and development, while spending big on armies of lawyers to devise and defend secondary patents and other so-called “life cycle management” strategies. Drug **research funding** has been **declining for more than a decade**, **while** strategies of **secondary patenting have steadily increased.** We support patents — just not those that are unmerited and that unjustly prolong companies’ market power and prevent legitimate competition.

#### Only innovation now solves AMR super-bugs -- timeframe’s key.

Sobti 19 [Dr. Navjot Kaur Sobti is an internal medicine resident physician at Dartmouth-Hitchcock-Medical Center/Dartmouth School of Medicine and a member of the ABC News Medical Unit. May 1, 2019. “Amid superbug crisis, scientists urge innovation”. <https://abcnews.go.com/Health/amidst-superbug-crisis-scientists-urge-innovation/story?id=62763415>] Dhruv

[The United Nations](https://abcnews.go.com/Politics/amal-clooney-angelina-jolie-speak-us-weighed-vetoing/story?id=62574726) has called antimicrobial resistance a “global crisis.” With the [rise in superbugs](https://abcnews.go.com/Health/superbug-fungus-global-health-threat-600-us-infected/story?id=62297532) across the globe, common infections are becoming harder to treat, and lifesaving procedures riskier to perform. Drug-resistant infections result in about 700,000 deaths per year, with at least 230,000 of those deaths due to multidrug resistant tuberculosis, [according to a groundbreaking report from the World Health Organization (WHO).](https://www.who.int/antimicrobial-resistance/interagency-coordination-group/IACG_final_report_EN.pdf?ua=1) Given that antibiotic resistance is present in every country, antimicrobial resistance (AMR) now represents a global health crisis, according to the UN, which has urged immediate, coordinated and global action to prevent a potentially devastating health and financial crisis. With the rising rates of AMR -- including antivirals, antibiotics, and antifungals -- estimates from the WHO show that AMR may cause 10 million deaths every year by 2050, send 24 million people into extreme poverty by 2030, and lead to a financial crisis as severe as the on the U.S. experienced in 2008. Antimicrobial resistance develops when germs like bacteria and fungi are able to “defeat the drugs designed to kill them,” according to the Centers for Disease Control and Prevention. Through a biologic “survival of the fittest,” germs that are not killed by antimicrobials and continue to grow. WHO explains that “poor infection control, inadequate sanitary conditions and inappropriate food handling encourage the spread” of AMR, which can lead to “superbugs.” Those superbugs require powerful and oftentimes more expensive antimicrobials to treat. Examples of superbugs are far and wide, and can range from drug-resistant bacteria like Pseudomonas aeruginosa and Staphylococcus aureus to fungi like Candida. These bugs can cause illnesses that range from pneumonia to urinary tract and sexually transmitted infections. According to the WHO, AMR has caused complications for nearly 500,000 people with tuberculosis, and a number of people with HIV and malaria. The people at the [highest risk for AMR](https://www.who.int/news-room/detail/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed) are those with chronic diseases, people living in nursing homes, hospitalized in the ICU or undergoing life-saving treatments such as organ transplantation and cancer therapy. These people often develop infections, which can become antimicrobial-resistant, rendering them difficult, if not impossible, to treat. [(MORE: Melissa Rivers talks about her father's suicide with Dr. Jennifer Ashton)](https://abcnews.go.com/Health/melissa-rivers-talks-fathers-suicide-dr-jennifer-ashton/story?id=62733179&cid=clicksource_26_null_headlines_hed) The CDC notes that “antibiotic resistance has the potential to affect people at any stage of life,” including the “healthcare, veterinary, and agriculture industries, making it one of the world’s most urgent public health problems." AMR can cause prolonged hospital stays, billions of dollars in healthcare costs, disability, and potentially, death. “The most important thing is to understand and embrace the interconnectedness of all of this,” said Dr. Robert Redfield, director of the CDC, in a recent interview with ABC News’ Dr. Jennifer Ashton. It’s not just our countries that are connected.” Research has shown that superbugs like Candida auris “came from multiple places, at the same time. It wasn’t just one organism that [evolved]” in a single location, Redfield added. Given longstanding concerns about antimicrobial misuse leading to AMR, physicians have embraced a medical approach called antibiotic stewardship. This encourages physicians to carefully evaluate which antibiotic is most appropriate for their patient, and discontinue it once it is no longer medically needed. WHO has also highlighted that the inappropriate use of antimicrobials in agriculture -- such as on farms and in animals -- may be an underappreciated cause of AMR. Noting these trends, the WHO has urged for “coordinated action...to minimize the emergence and spread of antimicrobial resistance.” It urges all countries to make national action plans, with a focus on the development of new antimicrobial medications, vaccines, and careful antimicrobial use. Redfield emphasized the importance of vaccination during the global superbug crisis, stating that “the only way we have to eliminate an infection is vaccination.” He added that investing in innovation is key to solving the crisis. While WHO continues to advocate for superbug awareness, they warn that AMR has reversed “a century of progress in health.” The WHO added that “the challenges of antimicrobial resistance” are “not insurmountable,” and that coordinated action will “help to save millions of lives, preserve antimicrobials for generations to come and secure the future from drug-resistant diseases.”

#### Extinction - generic defense doesn’t apply.

Srivatsa 17 Kadiyali Srivatsa 1-12-2017 “Superbug Pandemics and How to Prevent Them” <https://www.the-american-interest.com/2017/01/12/superbug-pandemics-and-how-to-prevent-them/> (doctor, inventor, and publisher. He worked in acute and intensive pediatric care in British hospitals)//Elmer

It is by now no secret that the human species is locked in a race of its own making with “**superbugs**.” Indeed, if popular science fiction is a measure of awareness, the theme has pervaded English-language literature from Michael Crichton’s 1969 Andromeda Strain all the way to Emily St. John Mandel’s 2014 Station Eleven and beyond. By a combination of massive inadvertence and what can only be called stupidity, we must now invent new and effective antibiotics faster than deadly bacteria evolve—and regrettably, they are rapidly doing so with our help. I do not exclude the possibility that bad actors might deliberately engineer deadly superbugs.1 But even if that does not happen, humanity faces an existential threat largely of its own making in the absence of malign intentions. As threats go, this one is entirely predictable. The concept of a “black swan,” Nassim Nicholas Taleb’s term for low-probability but high-impact events, has become widely known in recent years. Taleb did not invent the concept; he only gave it a catchy name to help mainly business executives who know little of statistics or probability. Many have embraced the “black swan” label the way children embrace holiday gifts, which are often bobbles of little value, except to them. But the threat of inadvertent pandemics is not a “black swan” because its probability is not low. If one likes catchy labels, it better fits the term “gray rhino,” which, explains Michele Wucker, is a high-probability, high-impact event that people manage to ignore anyway for a raft of social-psychological reasons.2 A pandemic is a quintessential gray rhino, for it is no longer a matter of if but of when it will challenge us—and of how prepared we are to deal with it when it happens. We have certainly been warned. The curse we have created was understood as a possibility from the very outset, when seventy years ago Sir Alexander Fleming, the discoverer of penicillin, predicted antibiotic resistance. When interviewed for a 2015 article, “The Most Predictable Disaster in the History of the Human Race, ” Bill Gates pointed out that one of the costliest disasters of the 20th century, worse even than World War I, was the Spanish Flu pandemic of 1918-19. As the author of the article, Ezra Klein, put it: “No one can say we weren’t warned. And warned. And warned. A pandemic disease is the most predictable catastrophe in the history of the human race, if only because it has happened to the human race so many, many times before.”3 Even with effective new medicines, if we can devise them, we must contain outbreaks of bacterial disease fast, lest they get out of control. In other words, we have a social-organizational challenge before us as well as a strictly medical one. That means getting sufficient amounts of medicine into the right hands and in the right places, but it also means educating people and enabling them to communicate with each other to prevent any outbreak from spreading widely. Responsible governments and cooperative organizations have options in that regard, but even individuals can contribute something. To that end, as a medical doctor I have created a computer app that promises to be useful in that regard—of which more in a moment. But first let us review the situation, for while it has become well known to many people, there is a general resistance to acknowledging the severity and imminence of the danger. What Are the Problems? Bacteria are among the oldest living things on the planet. They are masters of survival and can be found everywhere. Billions of them live on and in every one of us, many of them helping our bodies to run smoothly and stay healthy. Most bacteria that are not helpful to us are at least harmless, but some are not. They invade our cells, spread quickly, and cause havoc that we refer to generically as disease. Millions of people used to die every year as a result of bacterial infections, until we developed antibiotics. These wonder drugs revolutionized medicine, but one can have too much of a good thing. Doctors have used antibiotics recklessly, prescribing them for just about everything, and in the process helped to create strains of bacteria that are resistant to the medicines we have. We even give antibiotics to cattle that are not sick and use them to fatten chickens. Companies large and small still mindlessly market antimicrobial products for hands and home, claiming that they kill bacteria and viruses. They do more harm than good because the low concentrations of antimicrobials that these products contain tend to kill friendly bacteria (not viruses at all), and so clear the way for the mass multiplication of surviving unfriendly bacteria. Perhaps even worse, hospitals have deployed antimicrobial products on an industrial scale for a long time now, the result being a sharp rise in iatrogenic bacterial illnesses. Overuse of antibiotics and commercial products containing them has helped superbugs to evolve. We now increasingly face microorganisms that cannot be killed by antibiotics, antifungals, antivirals, or any other chemical weapon we throw at them. Pandemics are the major risk we run as a result, but it is not the only one. Overuse of antibiotics by doctors, homemakers, and hospital managers could mean that, in the not-too-distant future, something as simple as a minor cut could again become life-threatening if it becomes infected. Few non-medical professionals are aware that antibiotics are the foundation on which nearly all of modern medicine rests. Cancer therapy, organ transplants, surgeries minor and major, and even childbirth all rely on antibiotics to prevent infections. If infections become untreatable we stand to lose most of the medical advances we have made over the past fifty years. And the problem is already here. In the summer of 2011, a 43-year-old woman with complications from a lung transplant was transferred from a New York City hospital to the Clinical Center at the National Institutes of Health (NIH), in Bethesda, Maryland. She had a highly resistant superbug known as Klebsiella pneumoniae carbapenemase (KPC). The patient was treated and eventually discharged after doctors concluded that they had contained the infection. A few weeks later, a 34-year-old man with a tumor and no known link to the woman contracted KPC while at the hospital. During the course of the next few months, several more NIH patients presented with KPC. Doctors attacked the outbreak with combinations of antibiotics, including a supposedly powerful experimental drug. A separate intensive care unit for KPC patients was set up and robots disinfected empty rooms, but the infection still spread beyond the intensive care area. Several patients died and then suddenly all was silent on the KPC front, with doctors convinced they had seen the last of the dangerous bacterium. They couldn’t have been more mistaken. A year later, a young man with complications from a bone marrow transplant arrived at NIH. He became infected with KPC and died. This superbug is now present in hospitals in most, if not all U.S. states. This is not good. This past year an outbreak of CRE (carbapenem-resistant enterobacteriaceae) linked to contaminated medical equipment infected 11 patients and killed two in Los Angeles area hospitals. This family of bacteria has evolved resistance to all antibiotics, including the powerful carbapenem antibiotics that are often used as a last resort against serious infections. They are now so resilient that it is virtually impossible to remove them from medical tools such as catheters and breathing tubes placed into the body, even after cleaning. Then we have gonorrhea, chlamydia, and other sexually transmitted diseases that we cannot treat and that are spreading all over the world. Anyone who has sex can catch these infections, and because most people may not exhibit any symptoms they spread infections without anyone knowing about it. Sexually transmitted diseases used to be treatable with antibiotics, but in recent years we have witnessed the rise of multi-drug resistant STDs. Untreated gonorrhea can lead to infertility in men and women and blindness and other congenital defect in babies. As is well known, too, we have witnessed many cases of drug-resistant pneumonia. These problems have arisen in part because of simple mistakes healthcare professionals repeatedly make. Let me explain. Neither superbugs nor common bacterial infections produce any special symptoms indicative of their cause. Rashes, fevers, sneezing, runny noses, ear pain, diarrhea, vomiting, coughing, fatigue, and weakness are signs of common and minor illnesses as well as uncommonly deadly ones. Therefore, the major problem for clinicians is to identify a common symptom that may potentially be an early sign of a major infection that could result in an epidemic. We know that dangerous infections in any given geographical area do not start at the same time. They start with one victim and gradually spread. But that victim is only one among hundreds of patients a doctor will typically see, so many doctors will miss patients presenting with infections that are serious. They will probably identify diseases that kill fast, but slow-spreading infections such as skin infections that can lead to septicemia are rarely diagnosed early. In addition, I have seen doctors treating eczema with antibiotic cream, even though they know that bacteria are resistant to the majority of these drugs. This sort of action encourages simple infections to spread locally, because patients are therefore not instructed to take other, more useful precautions. On top of that, some people are frivolous about infections and assume doctors are exaggerating the threat. And some people are selfish. Once I was called to see a passenger during a flight who had symptoms consistent with infection. He boarded the plane with these symptoms, but began to feel much worse during the flight. I was scared, knowing how infections such as Ebola can spread. This made me think about a way to screen passengers before they board a flight. Airlines could refund a traveler’s ticket, or issue a replacement, in case of sickness—which is not the policy now. We currently have no method to block infectious travelers from boarding flights, and there are no changes in the incentive system to enable conscientious passengers to avoid losing their money if they responsibly miss a flight because of illness. Speaking of selfishness, I once saw a mother drop her daughter off at school with a serious bout of impetigo on her face. When I asked her why she had brought her daughter to school with a contagious infection, she said she could not spare the time to keep her at home or take her to the doctor. By allowing this child to contact other children, a simple infection can become a major threat. Fortunately, I could see the rash on the girl’s face, but other kids in schools may have rashes we cannot see. Incorrect diagnosis of skin problems and mistaken use of antibiotics to treat them is common all over the world, and so we are continually creating superbugs in our communities. Similarly, chest infections, sore throats, and illnesses diagnosed as colds that unnecessarily treated with antibiotics are also a major threat. By prescribing antibiotics for viral infections, we are not only helping bacteria develop resistance, but we are also polluting the environment when these drugs are passed in urine and feces. All of this helps resistant bacteria to spread in the community and become an epidemic. Ebola is very difficult to transmit because people who are contagious have visible and unusual symptoms. However, the emerging infections and pandemics of the future may not have visible symptoms, and they could break out in highly populous countries such as India and China that send thousands of travelers all over the world every day. When a person is infected with a contagious disease, he or she can expect to pass the illness on to an average of two people. This is called the “reproduction number.” Two is not that high a number as these things go; some diseases have far greater rates of infection. The SARS virus had a reproduction number of four. Measles has a reproduction number of 18. One person traveling as an airplane passenger and carrying an infection similar to Ebola can infect three to five people sitting nearby, ten if he or she walks to the toilet. The study that highlighted this was published in a medical journal a few years ago, but the airline industry has not implemented any changes or introduced screening to prevent the spread of infections by air travel passengers, a major vehicle for the rapid spread of disease. It is scary to think that nobody knows what will happen when the world faces a lethal disease we’re not used to, perhaps with a reproduction number of five or eight or even ten. What if it starts in a megacity? What if, unlike Ebola, it’s contagious before patients show obvious symptoms? Past experience isn’t comforting. In 2009, H1N1 flu spread around the world before we even knew it existed. The Questions Remains Why do seemingly intelligent people repeatedly do such collectively stupid things? How did we allow this to happen? The answer is disarmingly simple. It is because people are incentivized to prioritize short-term benefits over long-term considerations. It is what social scientists have called a “logic of collective action” problem. Everyone has his or her specialized niche interest: doctors their patients’ approval, business and airline executives their shareholders’ earnings, hospitals their reputations for best-practice hygienics, homemakers their obligation to keep their own families from illness. But no one owns the longer-term consequences for hundreds of millions of people who are irrelevant to satisfying these short-term concerns. Here is an example. At a recent Superbug Super Drug conference in London that I attended, scientists, health agencies, and pharmaceutical companies were vastly more concerned with investing millions of dollars in efforts to invent another antibiotic, claiming that this has to be the way forward. Money was the most pressing issue because, as everyone at the conference knew, for many years pharmaceutical companies have been pulling back from antibiotics research because they can’t see a profit in it. Development costs run into billions of dollars, yet there is no guarantee that any new drug will successfully fight infections. At the same conference Dr. Lloyd Czaplewski spoke about alternatives to antibiotics, in case we cannot come up with new ones fast enough to outrun superbug evolution. But he omitted mention of preventive strategies that use the internet or communication software to help reduce the spread of infections among families, communities, and countries. It is madness that we don’t have a concrete second-best alternative to new antibiotics, because we need them and we need them quickly. Of course, this is why we have governments, which have been known occasionally in the past as commonwealths. Governments are supposed to look out for the wider, common interests of society that niche-interested professionals take no responsibility for, and that includes public health. It is why nearly every nation’s government has an official who is analogous to the U.S. Surgeon General, and nearly every one has a public health service of some kind. Alas, national governments do not always function as they should. Several years ago physician and former Republican Senator Bill Frist submitted a proposal to the Senate for a U.S. Medical Expeditionary Corps. This would have been a specialized organization that could coordinate and execute rapid responses to global health emergencies such as Ebola. Nothing came of it, because Dr. Frist’s fellow politicians were either too shortsighted or too dimwitted to understand why it was a good idea. Or perhaps they simply realized that they could not benefit politically from supporting it. Plenty of mistakes continue to be made. In 2015, a particularly infectious form of bird flu ripped through 14 U.S. states, leading farmers to preventively slaughter nearly 40 million birds. The result of such callous and unnecessary acts is that, instead of exhausting themselves in the host population of birds, the viruses quickly find alternative hosts in which to survive, and could therefore easily mutate into a form that can infect humans. Earlier, during the 1980s, AIDS garnered more public attention because a handful of rich and famous people were infected, and because the campaign to eradicate it dovetailed with and boosted the political campaign on behalf of homosexual rights. Methicillin resistant Staphylococcus aureus (MRSA) in hospitals, by far the bigger threat at the time, was virtually ignored. Some doctors knew that MRSA would bring us to our knees and kill millions of people worldwide, but pharmaceutical companies and device and equipment manufacturers ignored these doctors and the thousands of patients dying in hospitals as a result of MRSA. They prioritized the wrong thing, and government did not correct the error. And that is partly how antibiotic-resistant infection went from an obscure hospital problem to an incipient global pandemic. Politics well outside the United States plays several other roles in the budding problem that we are confronting. Countries often will not admit they have a problem and request help because of the possible financial implications in terms of investment and travel. Guinea did not declare the Ebola epidemic early on and Chinese leaders, worried about trade and tourism, lied for months in 2002 about the presence of the SARS virus. In 2004, when avian influenza first surfaced in Thailand, officials there displayed a similar reluctance to release information. Hospitals in some countries, including India, are managed and often owned by doctors. They refuse to share information about existing infections and often categorically deny they have a problem. Reporting infections to public health authorities is not mandatory, and so hospitals that fail to say anything are not penalized. Even now, the WHO and the CDC do not have accurate and up-to-date information about the spread of E. coli or other infections, and part of the reason is that for-profit hospitals are reluctant to do anything to diminish their bottom line. Syria and Yemen are among those countries that are so weak and fragmented that they cannot effectively coordinate public healthcare. But their governments are also hostile to external organizations that offer relief. Part of the reason is xenophobia, but part is that this makes the government look bad. Relatedly, most poor-nation governments do not trust the efficacy of international institutions, and think that cooperating with them amounts to a re-importation of imperialism. They would rather their own people suffer and die than ask for needed help. That brings us to the level of international public health governance. Alas, sometimes poor-country governments estimate the efficacy of international institutions accurately. The WHO’s Ebola response in 2014-15 was a disaster. The organization was slow to declare a public health emergency even after public warnings from Médecins Sans Frontières, some of whose doctors had already died on the front line. The outbreak killed more than 28,000 people, far more than would have been the case had it been quickly identified. This isn’t just an issue of bureaucratic incompetence. The **WHO is under-resourced for the problems it is meant to solve. Funding comes from voluntary donations, and there is no mechanism by which it can quickly scale up its efforts during an emergency. The result is that its response to the next major disease outbreak is likely to be as inadequate as were its responses to Ebola, H1N1, and SARS**. Stakeholders admit that we need another mechanism, and most experts agree that the world needs some kind of emergency response team for dangerous diseases. But no one knows how to set one up amid the dysfunctional global governance structures that presently exist. Maybe they should turn to Bill Frist, whose basic concept was sound; if the U.S. government will not act, perhaps some other governments will, and use the UN system to do so. But as things stand, we lack a health equivalent of the military reserve. Neither government leaders nor doctors can mobilize a team of experts to contain infections. People who want to volunteer, whether for government or NGO efforts, are not paid and the rules, if any, are sketchy about what we do with them when they return from a mission. Are employers going to take them back? What are the quarantine rules? It is all completely ad hoc, meaning that humanity lacks the tools it needs to protect itself. And note, by the way, the contrast between how governments prepare for facing pandemics and how they prepare for making war. War is not more deadly to the human race than pandemics, but national defense against armed aggression is much better planned for than defense against threats to public health. There is a wealth of rules regarding it, too. Human beings study and plan for war, which kills people both deliberately and accidentally, but they do not invest comparable effort planning for pandemics, which are liable to kill orders of magnitude more people. To the mind of a medical doctor, this is strange. Creating Conditions for Infections to Spread Superbug infections spread for several interlocking reasons. Some are medical-epidemiological. Most of the infections of the past thirty years have started in one place and in one family. As already noted, they spread because many infectious diseases are highly contagious before the onset of symptoms, and because it is difficult to prevent patients who know they are sick from going to hospitals, work, and school, or from traveling further afield. But again, one reason for the problem is political, not medical. Many governments have no strategies in place to prevent pandemics because they are unwilling to tell their people how infections spread. They don’t want to worry people with such talk; it will make them, they fear, unpopular. So governments may have mountains of bureaucracy with great heaps of rules and regulations concerning public health, but they are generally unwilling to trust their own citizens to use common sense on their own behalf. This, too, seems very strange. Until now, no one has come forward to help us develop strategies to educate people how to identify and prevent the spread of infection to their families and communities. The majority of stakeholders have also been oblivious to the use of new technologies to help reduce the spread of these infections. There are some exceptions. In a fun blog post called Preparedness 101: Zombie Apocalypse, the CDC uses the threat of a zombie outbreak as a metaphor to encourage people to prepare for emergencies, including pandemics. It is well meaning and insightful, yet when my colleagues and I try to discuss ways of scaling up the CDC’s example with doctors and nurses, they shut down. Nobody plans for an actual crisis partly because it is too scary and hence paralyzing to think about. But it is also because it is not most health professionals’ job; it is not what they are trained and paid to do. It is always someone else’s job, except that it has turned out to be nobody’s job. Worse, the situation is not static. While we sit paralyzed, superbugs are evolving. Epidemiological models now predict how an algorithmic process of disease spread will move through the modern world. All urban centers around the entire globe can become infected within sixty days because we move around and cross borders much more than our ancestors did, thanks to air travel. A new pandemic could start crossing borders before we even know it exists. A flu-like disease could kill more than 33 million people in 250 days.3

#### Pharma spills-over – has cascading global impacts that are necessary for human survival.

NAS 8 National Academy of Sciences 12-3-2008 “The Role of the Life Sciences in Transforming America's Future Summary of a Workshop” //Re-cut by Elmer

Fostering Industries to Counter Global Problems The life sciences have applications in areas that range far beyond human health. Life-science based approaches could **contribute to advances in** many industries, from energy production and pollution remediation, to clean manufacturing and the production of new biologically inspired materials. In fact, biological systems could provide the basis for new products, services and industries that we cannot yet imagine. Microbes are already producing biofuels and could, through further research, provide a major component of future energy supplies. Marine and terrestrial organisms extract carbon dioxide from the atmosphere, which suggests that biological systems could be used to help manage climate change. Study of the complex systems encountered in biology is decade, it is really just the beginning.” Advances in the underlying science of plant and animal breeding have been just as dramatic as the advances in genetic can put down a band of fertilizer, come back six months later, and plant seeds exactly on that row, reducing the need for fertilizer, pesticides, and other agricultural inputs. Fraley said that the global agricultural system needs to adopt the goal of doubling the current yield of **crops while reducing key inputs like pesticides, fertilizers, and water** by one third. “It is more important than putting a man on the moon,” he said. Doubling agricultural yields would “change the world.” Another billion people will join the middle class over the next decade just in India and China as economies continue to grow. And all people need and deserve secure access to food supplies. Continued progress will require both basic and applied research, The evolution of life “put earth under new management,” Collins said. Understanding the future state of the planet will require understanding the biological systems that have shaped the planet. Many of these biological systems are found in the oceans, which cover 70 percent of the earth’s surface and have a crucial impact on weather, climate, and the composition of the atmosphere. In the past decade, new tools have become available to explore the microbial processes that drive the **chemistry of the oceans**, observed David Kingsbury, Chief Program Officer for Science at the Gordon and Betty Moore Foundation. These technologies have revealed that a large proportion of the planet’s genetic diversity resides in the oceans. In addition, many organisms in the oceans readily exchange genes, creating evolutionary forces that can have global effects. The oceans are currently under great stress, Kingsbury pointed out. Nutrient runoff from agriculture is helping to create huge and expanding “dead zones” where oxygen levels are too low to sustain life. Toxic algal blooms are occurring with higher frequency in areas where they have not been seen in the past. Exploitation of ocean resources is disrupting ecological balances that have formed over many millions of years. Human-induced changes in the chemistry of the atmosphere are changing the chemistry of the oceans, with potentially catastrophic consequences. “If we are not careful, we are not going to have a sustainable planet to live on,” said Kingsbury. Only by understanding the basic biological processes at work in the oceans can humans live sustainably on earth.

#### Expanding breadth of Pharma Innovation into neglected diseases results in global linkages that revitalizes global health diplomacy.

Hotez 16, Peter J. Blue marble health: an innovative plan to fight diseases of the poor amid wealth. JHU Press, 2016. (Sabin Vaccine Institute and Texas Children’s Hospital Center for Vaccine Development, Departments of Pediatrics and Molecular Virology and Microbiology)//Elmer

We also need to better understand how these NTDs are actually transmitted within US borders, and I think it is extremely important to learn more about the links between these diseases and poverty. As I noted earlier, a drive through Houston’s Fifth Ward provides some insights, as one can quickly identify predisposing risk factors, including stray animals, dilapidated houses without window screens, standing water and discarded tires, and other evi- dence of environmental degradation, but we need to conduct careful epidemiological studies to really understand the links between poverty and NTDs, as well as animal reservoirs for illnesses such as Chagas disease and others. All of this presents an important research and development agenda for the **NTDs** in the United States. There are no point-of-care diagnostic tests available for most of the NTDs endemic to the nation, so blood from pa- tients must be sent to the CD С or other specialty research laboratories in order to establish a diagnosis for these conditions. As I sometimes point out to general audiences, when you go to your physician and get blood work done, there is no box to check off for toxocariasis or Chagas disease as there is for blood chemistries or other routine tests. We need diagnostic tests that are easily accessible to physicians and nurses. We also need new and improved treatments and vaccines. Because the NTDs are poverty-related diseases, they often fly below the radar screen of the major pharmaceutical companies and are not prioritized. Thus, the drugs used to treat these illnesses are not widely available, so typically the CDC has to be contacted in order to access them. In addition, many of these medicines were developed decades ago and produce a lot of side effects. For instance, the two medicines for Chagas disease—benznidazole and nifurtimox—cause skin rashes, diarrhea, and other unpleasant or even dangerous symptoms and illnesses. Patients using these medications have to interrupt their treatments up to 20% of the time. Moreover, these drugs cannot be used by pregnant women. Currently, new innovations for NTDs like Chagas dis- multinational ease still rely on nonprofit PDPs. The Geneva-based Drugs pharmaceutical for Neglected Diseases Initiative is leading efforts to de- companies have velop new and safer Chagas disease medicines [60], while shown little or modest at our National School of Tropical Medicine the Sab in interest in American Vaccine Institute and Texas Childrens Hospital Center for NTDs. As a result, new Vaccine Development (Sabin PDP) is working to develop products are being a therapeutic vaccine that could be used alongside exist- developed in the ing treatments [61]. These efforts rely on major philan- nonprofit sector. thropic donors. In our case at the Sabin PDP, they include the Kleberg Foundation, the Carlos Slim Foundation, the Southwest Electronic Energy Medical Research Institute, and Texas Childrens Hospital. Summary Points 1. In the United States, 45.3 million people live below the poverty line, roughly the same number of impoverished Americans alive during the early 1960s when Michael Harrington wrote The Other America. Approximately 20 million Americans now live in extreme poverty at one-half the US poverty level, and approximately 5 million are living on less than $2 per day 2. American poverty concentrates in specific areas, especially in southern states, with Texas having the largest numbers who live in poverty Important areas in the South include the Gulf Coast, border areas with Mexico, the Mississippi Delta, and Appalachia. 3. Approximately 12 million Americans are infected with NTDs, led by toxocariasis and trichomoniasis—which disproportionately affect African Americans—and Chagas disease (American trypanosomiasis) and cysticercosis—which disproportionately affect people of Hispanic origin. Toxoplasmosis is another important NTD. Toxocariasis, cysticercosis, and toxocariasis exert important mental health effects on impoverished Americans. Many of these NTDs are transmitted within US borders (autochthonous infections). 4. Arboviral infections are also important NTDs, led by dengue fever in Gulf Coastal areas and West Nile virus infection. WNV can cause chronic, persistent viral infections linked to chronic neurologic and renal disease. 5. There is an urgent need to promote awareness about the NTDs, especially for physicians and other health-care providers. 6. New policies are needed to expand surveillance for the NTDs affecting the United States. New legislation has been adopted in Texas, while additional bills are being introduced in the US Congress. Epidemiological studies are also needed to better understand how these diseases are transmitted and how they are linked to extreme poverty in the American South and elsewhere. 7. There is an urgent need for new “control tools” for American NTDs, including point-of-care diagnostics, antiparasitic and antiviral drugs, and vaccines. Many of these products are being developed by nonprofit PDPs rather than pharmaceutical companies. he G20 "A Theory of Justice" In his landmark 1971 book A Theory of Justice, the Harvard political philosopher John Rawls articulates two overriding principles of a just and fair society, namely, (1) “equality in the assignment of basic rights and duties” and (2) allowance of some social and economic inequalities, but only if they ultimately benefit “the least advantaged members of society” [1]. In terms of Rawls’s worldview, I believe that finding widespread NTDs among the extreme poor (and least-advantaged) who live amidst wealth—the central tenet of blue marble health—might represent one of the most jarring affronts to what he terms “justice as fairness” Because NTDs are now widespread among the leastadvantaged members of the worlds wealthiest economies, and they represent a major basis for thwarting their future growth, it is urgent for these nations, especially the G20 countries, to adopt strong internal policies to combat these diseases. I envision a three-pronged strategy to best address the G20 s (and Nigeria’s) poorest citizens afflicted by NTDs: 1. Each of the G20 nations and Nigeria has the capacity to fully understand the extent of these diseases within their own borders and then provide their own impoverished populations access to essential medicines used in mass drug administration to target helminth infections, in addition to trachoma, leprosy, yaws and scabies, and to provide treatments for other high-disease burden NTDs, including leishmaniasis and Chagas disease. The G20 countries and Nigeria Three major steps are required to effectively address blue marble health. 141 142 Blue Marble Health need to allocate resources and implement programs to achieve universal coverage for these diseases. 2. Each of the G20 nations and Nigeria has the capacity to conduct research and development for new NTD biotechnologies; they need to allocate resources toward this goal. 3. Both activities should be conducted within an overall framework of health system strengthening. Mass Drug Administration in the G20 A good place to revisit MDA among the G20 countries is to more closely examine the six G20 countries with positive worm indices—Brazil, China, India, Indonesia, Mexico, and South Africa—in addition to Nigeria. Together these countries account for one-half of the worlds helminth infections [2]. An analysis of WHO s PCT database reveals that most of these nations are severely underachieving when it comes to providing MDA for people who require regular and periodic treatment for their intestinal helminth infections, schistosomiasis, and LF. Shown in table 11.1 is WHO’s estimate of the percentage that received treatment in 2013 [3-5]. Overall, the G20 nations affected by helminth infections and Nigeria perform poorly when it comes to treating their affected populations through MDA. In terms of specific countries in Latin America, Brazil is reaching only approximately one-third of its children and population at risk. And although Mexico provides complete coverage for intestinal worms, it—as previously mentioned—neither diagnoses nor treats hundreds of thousands (and possibly millions) of people with Chagas disease. In Africa, Nigeria’s MDA reaches less than 25% of its children at risk for helminth infections, and there is no information about schistosomiasis coverage in South Africa forthcoming from WHO. However, as Dr. Eyrun Kjetland (who works extensively in South Africa) has pointed out, female genital schistosomiasis remains widespread there, in part because praziquantel has been mostly unavailable in the country, owing to its drug importation laws. Schistosomiasis and other NTDs are still found among the poor in the Kingdom of Saudi Arabia. The entire MENA region severely underdiagnoses most of its NTDs, including leishmaniasis. In Asia, Indonesia largely does not promote widespread deworming for its children, and only a small percentage of its population receives treatment for LF, while India does only marginally better. Indonesia also suffers from high rates of yaws, which can also be targeted by MDA using the antibiotic azithromycin. Similarly in India, the vast majority of its children do not have access to regular and periodic deworming, and only about one-half of the population receives MDA for LF. India also has the worlds largest numbers of leprosy cases. This disease can also be attacked through MDA using a multidrug therapy regimen. WHO does not present information on China, either because it has not been determined or is unavailable. However, China has made great strides in reducing its schistosomiasis prevalence since 1949, and it has eliminated LF. Similarly, Japan and South Korea have achieved significant success both in economic development and in reducing or eliminating its NTDs. 144 Blue Marble Health Key common factors for poor performance in meeting MDA targets are vast geographies, decentralization of health care, inadequate resource allocation, and lack of political will. Overall, the six G20 countries with positive worm indices, together with Nigeria, have the means and capacity to eliminate LF within their own borders, while greatly reducing the disease burdens of their intestinal helminth infections and schistosomiasis through MDA. Some of the key common factors for poor performance in meeting MDA targets are vast geographies, decentralization of health care that results in fragmentation of drug delivery, inadequate resource allocation, and lack of political will and commitment. What about G20 countries affected by NTDs but without a positive worm index? In the United States, the 12 million Americans infected and living with NTDs are largely unrecognized, undiagnosed, and untreated. The United States also does very little in terms of conducting active surveillance for Chagas disease (and other major NTDs), and only a tiny percentage of its population receives access to diagnosis and treatment—the same is true for Argentina. In both North America and Europe, toxocariasis and other parasitic zoonotic infections are seldom diagnosed and treated. Minimal information is available on eastern ------------------- Europeans, Turks, and Russians with intestinal worms or zoonotic NTDs or their access to diagnosis and treatment. NTDs remain widespread among Aboriginal Australians, including intestinal helminth infections and scabies—both of which can be targeted through MDA. Thus, the current status of access to essential medicines for people living in poverty and with NTDs among the G20 countries and Nigeria can be summarized as abysmal. The fact that so few are being treated through MDA programs is especially sad, given its low costs. As previ- ------------------- ously mentioned, there are approximately 1.07 billion treatments required among the populations at greatest risk in the G20 countries and Nigeria. At a cost of 50 cents per person per year, approximately $500 million would be required—that is, a dollar amount representing a tiny percentage (<0.001%) of the $65 trillion combined economy of these countries. The bottom line is that each of these nations has the internal capacity to provide these low-cost treatments to its impoverished populations. WHO has now launched a Universal Health Coverage (UHC) initiative that builds on its 1978 “Health for All” Alma-Ata declaration and the MillenThe current status of access to essential medicines for people living in poverty and with NTDs among the G20 countries and Nigeria can be summarized as abysmal. The G20 145 nium Development Goals, with a focus on protecting the health of the worlds most economically vulnerable populations. The activities highlighted here clearly fall within WHO s UHC mandate. Research and Development for New Control Tools and Biotechnologies For many of the leading NTDs—including vector-borne diseases such as dengue, leishmaniasis, Chagas disease, African sleeping sickness, and malaria, and also some helminth infections such as hookworm, schistosomiasis, onchocerciasis, and foodborne trematodiases—there are equally urgent needs to develop new drugs, diagnostics, and vaccines. Each year, the Australian policy group known as Policy Cures publishes an annual G-FINDER Report that measures the global investment in new technologies for neglected diseases, defining them broadly to include both the NTDs and the “big three” diseases: HIV/ AIDS, ТВ, and malaria [6]. For the year 2014, G-FINDER determined that approximately $3.37 billion was invested globally in neglected disease R&D technology, with most of that support going toward the big three diseases [6]. A look at total government support for neglected disease R&D, almost all of it from G20 countries, is also interesting. The public sector provided 64% of the total funding, and the United States provided two-thirds of that funding, mostly from the US National Institutes of Health [6]. In all, 71% of the total government funding for neglected diseases comes from the United States, European Commission, and United Kingdom. However, as the G-FINDER Report points out, these absolute numbers do not consider the GDPs of these nations. In terms of public funding relative to GDP ratios, countries such as Ireland, Denmark, Norway, and Argentina do particularly well in this regard [6]. Shown in table 11.2 are selected estimates from G-FINDER of the percentage of their GDP that various governments have devoted to R&D on Of government funding for neglected diseases R&D, a whopping 71% comes from the United States, European Commission, and United Kingdom. We need greater involvement and support from the remainder of the G20 countries, including positive worm index G20 countries— Brazil, China, India, Indonesia, Mexico, and South Africa, in addition to Nigeria. 146 Blue Marble Health Although NTDs and other poverty-related diseases account for almost 14% of the global disease burden, they receive only a bit more than 1% of the global health-related R&D funds. neglected diseases. Using data from the G-FINDER Report combined with GDP information, I calculate that the world spends approximately 0.0028% of its GDP on neglected diseases R&D. Only three G20 countries—United States, United Kingdom, and Australia—match or exceed that percentage, ------------------- although India and France come close to it. The worstperforming countries were China and Japan. However, in 2013 the Japanese government, together with Japans major pharmaceutical companies and the Bill & Melinda Gates Foundation, formed a partnership known as the Global Health Innovative Technology (GHIT) Fund for supporting PDPs and other entities to develop and shape new biotechnologies for neglected diseases, with an emphasis on NTDs [7, 8]. China is a different matter. The New York Times has reported that China paid out $86.3 billion in foreign investments in the year 2013 [9], with much of that spent in fragile nations where health systems are broken and NTDs are widespread. Clearly, China needs to allocate some of those funds to neglected diseases, either for MDA or new technologies. In addition, the nation of Brazil could easily increase its global contribution to NTD technologies by ю -fold in order to match higher-performing nations in this regard. Germany is now looking at supporting NTD technologies as part of an overarching G7 initiative on NTDs. In 2011, the German government launched a policy roadmap for neglected and poverty-related diseases [10]. Indeed, a recent analysis conducted by German investigators has found although NTDs ------------------- and other poverty-related diseases account for almost 14% of the global disease burden, they receive only a bit more than 1% of the global health-related R&D funds [11]. As shown in figure 11.1, by presenting R&D expenditures for a particular disease divided by the disability adjusted life years (DALYs) it is possible to get a sense of ------------------- diseases that are especially underfunded—even compared with other NTDS—such as the intestinal helminth infections and other neglected enteric diseases, as well as rheumatic fever [11]. Such data argue for the great urgency needed in addressing these health disparities by increasing R&D funding and support. Recently, the Dutch and German governments and the European Union (EU) have established important initiatives to support NTD R&D. The Dutch Ministry of Foreign Affairs, for instance, has been a major partner in our human hookworm vaccine initiative, while the EU has an important Frameworks Program 7 (FP7) for supporting new technologies [12], including a HOOKVAC Consortium of partners organized through the Amster dam Institute of Global Health and Development [13]. Most recently, the EU has established an ambitious Horizon 2020 program for expanding R&D in Europe, including NTD R&D activities [14], on top of a European and Developing Countries Clinical Trials Partnership (EDCTP) for clinically evaluating new NTD technologies [15]. New German government funding for NTD R&D funding was just announced. These Dutch, German, and EU initiatives represent an important advance for shaping the next generation of products to treat and prevent NTDs. Yet another aspect of blue marble health is the rise in comorbid conditions between the NTDs, the big three diseases, and the noncommunicable diseases. Impoverished and neglected populations in the G20 countries and Nigeria are facing a double hit resulting from the convergence of NTDs and NCDs. For instance, in Texas, Mexico, and India (but presumably elsewhere) they include both ТВ and diabetes interactions and, lately, dengue and diabetes interactions. In South Africa, HIV/AIDS now flourishes amidst the high prevalence of female genital schistosomiasis. Studying the pathogenesis and epidemiology of these comorbid interactions will also be an important theme in the coming years. Shaping a Policy for the G20 The G20 began meeting in 2008 in response to that years global recession and have since convened in a summit each year to discuss the major policy issues of the day [16]. At the 2015 G20 Summit held in Turkey, the major areas of broad emphasis included strengthening the global recovery and enhancing resilience, while ensuring sustainability [17]. Clearly, lifting the bottom segments of their populations out of poverty through NTD control and elimination could fall within the G20 remit. It is imperative that the six member nations with positive worm indices commit to providing total MDA coverage for their populations affected by the major helminth infections, and also that the four Western Hemispheric countries step up surveillance, diagnosis, and treatment for Chagas disease. Leishmaniasis, both kala-azar and the cutaneous form, also represent major NTDs affecting the G20, and these diseases need to be targeted for control and elimination. The US, Dutch, German, and Japanese governments, along with the EU, stand out for their contributions toward supporting product development to counter NTDs, 150 Blue Marble Health Equally important is the R&D agenda. There are some obvious underachievers among the G20 countries that must step up and contribute to R&D for new drug, diagnostic, and vaccine products to fight the neglected diseases [18]. Toward that aim, several investigators have proposed the establishment of R&D funds to support neglected disease research. They include a global vaccine development fund [19] and a general biomedical R&D fund focused on antimicrobial resistance, emerging infectious diseases, and neglected diseases [20]. Both proposals are thoughtful, have a lot of merit, and need to be considered, but I offer an alternative or complementary solution. In 2013, the World Health Assembly passed a resolution (66.22) that proposes a “strategic work plan” to achieve sustainable funding for health R&D that could emphasize NTDs. The plan commits the director-general of the World Health Organization to establish a global “observatory” in order to identify gaps and opportunities for health R&D related to neglected diseases [21]. Through a pooled fund managed by WHO-TDR (a special program on tropical disease research and training), several pilot projects are now being supported [22]. Given that todays neglected disease R&D support comes mostly from the United States—and indeed mostly from a single agency, the National Institutes of Health—it is difficult to envision how such a fund would be created without calling on the NIH yet again. Realistically, it is unlikely the NIH leadership or the well-established community of US scientists would be willing to cede control of NIH budgets to an international body. Instead, I think it is worth considering the possibility of having each of the G20 countries establish its own version of the Japanese GHIT Fund, which builds on indigenous scientists and academic institutions and their own pharmaceutical industries. A Chinese or South Korean version of GHIT for example could become a vital and important institution. Creating twenty separate innovation funds could achieve the same goals as a global fund, while simultaneously ensuring national ownership and capacity building for indigenous academic and industrial institutions. Many of them could develop and shape new biotechnologies in collaboration with the 16 international PDPs. This approach would be especially useful for the less developed G20 countries, including Brazil, Global funds for R&D are an option. An attractive alternative is to create national funds for product development R&D in each of the G20 countries and Nigeria—ones that resemble those put forward by the Dutch and Japanese governments. The G20 151 India, Indonesia, and Mexico. These nations have indigenous vaccine manufacturers, which are represented by the Developing Country Vaccine Manufacturers Network, and therefore have a level of sophistication for producing next-generation NTD vaccines. Still another option is for smaller groups of G20 countries to come together to support R&D investments. The EU’s programs for new NTD technologies highlighted above represent important examples. In addition, if institutions from China and India (both rivals and neighbors) collaborated in the area of neglected diseases [23], some important NTD problems affecting Asia could be solved in the coming years. The United States has potential to extend its outreach on NTDs by collaborating with other G20 nations in the Americas or other countries [24]. As a UN agency, WHO could certainly partner with one or more of these G20 NTD R&D investment funds, especially through its global health R&D observatory mechanism. Another key United Nations agency might include WIPO—the World Intellectual Property Organization. Through the Patent Cooperation Treaty mechanism, the Geneva-based WIPO represents one of the few revenue-generating UN agencies. In 2011, in collaboration with BIO Ventures for Global Health, it established WIPO Re:Search to facilitate the development of products to combat NTDs by bringing together major pharmaceutical companies and academic investigators working on these diseases [25]. As a revenue-generating UN agency under the charismatic leadership of Francis Gurry, WIPO has the potential to expand this remit to support NTD product R&D. Looking beyond the G20 The major NTDs linked to wealthy countries and blue marble health could also be addressed by nongovernmental organizations, including faith-based groups. For example, in 2011 the Pew Research Centers Forum on Religion and Public Life reported that the center of the worlds Christian-majority countries has shifted from Europe and North America to the Global South, meaning Africa, Asia, and Central and South America [26]. Thus, countries such as Brazil, Philippines, Angola, Democratic Republic of Congo, and Papua New Guinea now have some of the highest percentages of Christian populations. As shown in table 11.3, from an analysis published in PLOS NTDs I found that almost all of the world s Chagas disease cases and African trypanosomiasis (sleeping sickness) can be found in Christian-majority countries, in addition to almost one-half of the schistosomiasis cases [26]. These findings suggest the possibility of bringing in new actors to combat NTDs. They could include the Vatican and Pope Francis, especially given the new popes renewed commitment to impoverished populations [19]. The Orthodox Christian Church also has opportunities to highlight NTDs in countries such as Ethiopia or those in the Middle East, as do many Christian faith-based organizations and universities. The G20 153 Summary Points 1. The six G20 countries with positive worm indices—Brazil, China, India, Indonesia, Mexico, and South Africa, together with Nigeria, have the means and capacity to eliminate LF within their own borders, while greatly reducing the disease burdens of their intestinal helminth infections and schistosomiasis through MDA. 2. G20 countries without classical worm indices, including the United States, also need to find mechanisms for promoting surveillance and access to essential medicine options for the poor living with NTDs within their own borders. 3. The G20 countries also have important biotechnology capabilities, which have yet to be adequately tapped for producing new NTD diagnostics, drugs, and vaccines. Beyond the United States, European nations, Australia, and Japan, they also include Brazil, China, India, Indonesia, Mexico, Russian Federation, Saudi Arabia, South Africa, and South Korea. 4. Yet another aspect of blue marble health is the rise in comorbid conditions between the NTDs, the big three diseases, and the NCDs. 5. The EU and the Dutch and German governments have launched important NTD technology initiatives, as has the Japanese government and its partners through a new GHIT Fund. These activities support PDPs committed to NTDs as well as indigenous academic institutions and industrial organizations. 6. Large G20 economies such as Brazil and China must increase their global commitment to support new NTD technologies and R&D. 7. There are opportunities to link these new investments with parallel activities ongoing at two UN agencies, namely, WHO and WIPO. 8. These topics should be highlighted at future G20 summits. 9. Faith-based organizations could have a future role. For instance, the Vatican and related entities have opportunities to expand commitments to control those NTDs that are found to be prevalent among Christian-majority countries. Central to the blue marble health concept is that each of the G20 nations and Nigeria need to take greater responsibility for their own neglected diseases and neglected populations. Doing so could result in the control or elimination of one-half or more of the planets NTDs, with substantial gains made against HIV/AIDS, ТВ, and malaria. Thus, while programs of overseas development assistance devoted to health, such as PEPFAR, GFATM, PMI, and USAID’s NTD Program, in which the worlds richest countries provide support to the poorest nations for their neglected diseases, must continue and should even expand, we need increasingly to recognize the hidden burden of neglected diseases among the poor living in wealthy countries. As a first step, we must expand initiatives that raise awareness about the problem of NTDs within each of the G20 countries and Nigeria. The Global Network for NTDs linked to the Sabin Vaccine Institute has been working closely with the governments of India and Nigeria, respectively, in order to explain the opportunity for mass drug administration and its potential impact on health and economic development. MDA coverage rates are disappointingly low in these nations, especially for intestinal helminth infections and LF, as well as for schistosomiasis in the case of Nigeria. An extraordinary finding is that at least three nations with positive worm indices—India, Pakistan, and China—also maintain nuclear stockpiles [1]. Could the scientific horsepower of these nuclear states be partly redirected toward reducing endemic NTDs at home? 154 A Framework for Science and Vaccine Diplomacy 155 Outside of India and Nigeria, there is a need to promote NTD awareness in each of the G20 countries. For example, in the United States, our National School of Tropical Medicine has been highlighting the plight of some 12 million Americans living with NTDs. We have now worked with the Texas Legislature to enact a bill for NTD surveillance in suspected high-prevalence areas. However, similar initiatives need to be enacted across the G20 nations, including the European Union. In addition, international cooperation between the different G20 nations and Nigeria could be critical in achieving higher population coverage for MDA. For instance, China, despite its billions of dollars of business investments in sub-Saharan Africa, has not yet promoted NTD control efforts there. Yet China has tre- mendous expertise in MDA for NTDs and could provide Africa with valuable advice in this area. China was the first country to eliminate LF and has achieved successes in re- ducing its burden of schistosomiasis more than ю -fold since the 1949 revolution. China could also share its best practices with neighboring India, where NTDs remain practically ubiquitous [ 2]. Similarly, Japan and South Korea have made great gains toward eliminating intestinal helminth infections, while the former has also successfully eliminated LF and schistosomiasis. International cooperation between these three East Asian nations and Nigeria, or with the G20 countries with positive worm indices, especially India, Indonesia, and Brazil (where they are the highest), could result in important, positive health and economic gains. Each of these activities represents examples of what some refer to as global health diplomacy. Global Health Diplomacy My former colleague at Yale University, Ilona Kickbusch, currently the director of the Global Health Programme at the Graduate Institute of International and Development Studies in Geneva, has provided several working definitions of global health diplomacy, including efforts to “position health in foreign policy negotiations,” together with the establishment of global health governance initiatives [3]. Indeed, the creation of the GAVI Alliance, GFATM, UN AIDS, and other Geneva-based organizations might be considered vital examples of organizations created under the auspices of global health diplomacy, with the first two created following the 2000 Millennial Development Goals. The MDGs themselves represent an important framework for global health diplomacy, and arguably the most successful. Since 2005, several global health diplomacy initiatives have been enacted that could facilitate NTD activities among the G20 and Nigeria, although most of these actions are more focused on emerging viral infections of pandemic potential rather than the widespread chronic and debilitating NTDs. The International Health Regulations (IHR) were enacted in 2005 as a binding legal mechanism for all member states of WHO and focused on responses to acute public health emergencies [4]. IHR demands that countries report outbreaks and other public health events, while WHO responds with measures to uphold and enforce global health security [4]. IHR also establishes an emergency committee that advises the WHO director-general on whether an unexpected event should be considered a public health emergency. It also provides recommendations on initial steps for travel restrictions, surveillance, and infection control. With the possible exception of dengue fever, it is not clear how IHR will substantively address the NTDs or other blue marble health conditions. Moreover, even with IHR in place, the global response to the 2014 emergence of Ebola in West Africa was slow and inadequate and led to a catastrophic outbreak in the fall of that year [5]. This failure may require future revisions in the IHR, as recently recommended in a 2015 Lancet article by Lawrence Gostin and his colleagues at Georgetown University [6]. The Global Health Security Agenda (GHSA) is an interagency initiative of the US government conducted in partnership with other nations and international organizations, including WHO [7]. GHSA is also focused on preventing or reducing the impact of epidemics and outbreaks of pandemic potential, such as H7N9 influenza virus or MERS coronavirus, as well as detecting emerging threats and implementing rapid and effective responses. In some respects, GHSA represents the US component or response to IHR. It also covers intentional or accidental releases of dangerous infectious disease pathogens. Global Health 203s and The Lancet Commission were launched in 2013, coinciding with the twentieth anniversary of a landmark 1993 World Development Report that helped to ignite international efforts to link investments in health with economic development [8]. The Lancet Commission identifies four key messages and actions: (1) the substantial economic return on investing in health, which can be as much as 24% in low- and middle-income countries; (2) implementation of a “grand convergence” in global health through scale-up of health technologies and strengthening health systems by the year 2035; (3) fiscal policies such as taxation of tobacco and reduction of subsidies for fossil fuels, which represent powerful forces or “levers” for elected leaders; and (4) universal health coverage as an efficient mechanism to improve health as well as to provide “financial protection” [8]. The Addis Ababa Action Agenda (AAAA) is the product of the first of three international meetings for implementing the UN s 2015 Sustainable Development Goals. However, health is at present only a minor component of the AAAA. Indeed, the SDGs have been criticized because health is now only 1 of the 17 goals, whereas it was front and center among the 2000 MDGs. So far, the AAAAs recommendations have included the promotion of the health systems strengthening component of the GFATM and GAVI Alliance and the establishment of a Global Financing Facility (GFF) for womens and childrens health that would go hand-inhand with the UN secretary generals new Global Strategy for Every Woman Every Child [9]. The emphasis of these initiatives is to reduce preventable maternal, child, and adolescent deaths by 2030. Despite the evidence that hookworm infection and Chagas disease rank among the leading complications of pregnancy among women living in poverty in low- and middle-income countries, while female genital schistosomiasis is among sub-Saharan Africa’s most common gynecologic condition, there is not yet a specific mention of NTDs in the AAAA or GFF. Ultimately, the G20 nations can identify ways to address blue marble health disparities under the auspices of the SDGs or the global health diplomacy initiatives highlighted above. However, at present there is no specific mandate for them to do so. Vaccine Science Diplomacy Concurrently, the G20 nations have opportunities to collaborate in scientific activities leading to the development of new drugs, diagnostics, and vaccines. I have used the term “vaccine science diplomacy” to refer to inter- national scientific codevelopment of lifesaving vaccines between scientists of different nations, but particularly from nations with strained or evenly openly contentious international relations. The best historical example of vaccine science diplomacy is the codevelopment of the oral polio vaccine, led on the American side by Dr. Albert B. Sabin, and his Soviet virologist counterparts, including Dr. Mikhail Petrovich Chumakov [3]. In modern times there is potential interest in explor ing vaccine science diplomacy opportunities between the United States and some of the worlds Muslim-majority nations belonging to the Organisation of Islamic Cooperation [10,11]. OIC countries include most of the Middle East and North Africa, as well as some highly populated Southeast Asian nations, including Bangladesh, Indonesia, and Malaysia, as well as most of central Asia. New estimates that we published in PLOS NTDs in 2015 indicate that the 30 most-populated OIC countries account for 35% of the worlds helminth infections comprising the global Worm Index, including 50% of the worlds children who require MDA for schistosomiasis [11]. Given that approximately 1.5 billion people live in OIC countries, or about 20% of the global population, helminth infections appear to disproportionately affect the health and economic development of Muslim-majority countries, as does leishmaniasis, trachoma, and possibly other NTDs [11]. As shown in figure 12.1, there is also tight inverse association between the worm index and human development index in the Muslim world [11]. OIC nations with strong infrastructures in science and biotechnology are potentially attractive candidates to pursue joint vaccine science diplomacy initiatives with the United States. Here the idea would be to promote scientific collaborations between US scientists and scientists from selected OIC countries in order to create new NTD technologies for some of the worst-off Muslim-majority countries. The “worst-off” might include OIC countries at the high end of the worm index, including Mali, Cote d’Ivoire, Mozambique, Cameroon, Burkina Faso, and Niger, as well as Nigeria [11].

### 1AC: Plan

#### Plan – The member nations of the World Trade Organization ought to reduce intellectual property protections for medicines by implementing a one-and-done approach for patent protection.

#### The Plan solves Evergreening.

Feldman 3 Robin Feldman 2-11-2019 "‘One-and-done’ for new drugs could cut patent thickets and boost generic competition" <https://www.statnews.com/2019/02/11/drug-patent-protection-one-done/> (Arthur J. Goldberg Distinguished Professor of Law, Albert Abramson ’54 Distinguished Professor of Law Chair, and Director of the Center for Innovation)//SidK + Elmer

I believe that one period of protection **should be enough**. We should make the legal changes necessary to prevent companies **from building patent walls** and piling up mountains of rights. This could be accomplished **by a “one-and-done” approach** for patent protection. Under it, a drug would receive just one period of exclusivity, and no more. The choice of which “one” could be left entirely in the hands of the pharmaceutical company, with the election made when the FDA approves the drug. Perhaps development of the drug went swiftly and smoothly, so the remaining life of one of the drug’s patents is of greatest value. Perhaps development languished, so designation as an orphan drug or some other benefit would bring greater reward. The choice would be up to the company itself, based on its own calculation of the maximum benefit. The result, however, is that a pharmaceutical company chooses whether its period of exclusivity would be a patent, an orphan drug designation, a period of data exclusivity (in which no generic is allowed to use the original drug’s safety and effectiveness data), or something else — but **not all of the above** and more. Consider Suboxone, a combination of buprenorphine and naloxone for treating opioid addiction. The drug’s maker has extended its protection cliff eight times, including obtaining an orphan drug designation, which is intended for drugs that serve only a small number of patients. The drug’s first period of exclusivity ended in 2005, but with the additions its protection now lasts until 2024. That makes almost two additional decades in which the public has borne the burden of monopoly pricing, and access to the medicine may have been constrained. Implementing a one-and-done approach in conjunction with FDA approval underscores the fact that these problems and solutions are designed for pharmaceuticals, not for all types of technologies. That way, one-and-done could be implemented through **legislative changes to the FDA’s drug approval system**, and would apply to patents granted going forward. One-and-done would apply to both patents and exclusivities. A more limited approach, a baby step if you will, would be to invigorate the existing patent obviousness doctrine as a way to cut back on patent tinkering. Obviousness, one of the five standards for patent eligibility, says that inventions that are obvious to an expert or the general public can’t be patented. Either by congressional clarification or judicial interpretation, many pile-on patents could be eliminated with a ruling that the core concept of the additional patent is nothing more than the original formulation. Anything else is merely an obvious adaptation of the core invention, modified with existing technology. As such, the patent would fail for being perfectly obvious. Even without congressional action, a more vigorous and robust application of the existing obviousness doctrine could significantly improve the problem of piled-up patents and patent walls. Pharmaceutical companies have become adept at maneuvering through the system of patent and non-patent rights to create mountains of rights that can be applied, one after another. This behavior lets drug companies keep competitors out of the market and beat them back when they get there. We shouldn’t be surprised at this. Pharmaceutical companies are profit-making entities, after all, that face pressure from their shareholders to produce ever-better results. If we want to change the system, we must change the incentives driving the system. And right now, the incentives for creating patent walls are just too great.

#### Reforming the Patent Process would lower Drug Prices and incentivize Pharma Innovation by revitalizing the Market.

Stanbrook 13, Matthew B. "Limiting “evergreening” for a better balance of drug innovation incentives." (2013): 939-939. (MD (University of Toronto) PhD (University of Toronto))//Elmer

At issue in the Indian case was “evergreening,” a now widespread practice by the pharmaceutical industry designed to extend the monopoly on an existing drug by modifying it and seeking new patents.2 Currently, half of all drugs patented in Canada have multiple subsequent patents, extending the lifetime of the original patent by about 8 years.3 Manufacturers, in defence of these practices, predictably tout the advantages of new versions of their products, which often represent more potent isomers or salts of the original drugs, longer-lasting formulations or improved delivery systems that make adherence easier or more convenient. But the new versions are by definition “**me too” drugs**, and demonstration that the resulting **incremental benefits** in efficacy and safety are clinically meaningful **is often lacking**. Moreover, the original drugs have often been “blockbusters” used for years to improve the health of millions of patients. It seems hard to argue convincingly why such beneficial drugs require an upgrade, often just before their patents expire. Rather than the marginal benefits accrued from tinkering with already effective agents, patients worldwide are in desperate need of new classes of pharmaceuticals for the great many health conditions for which treatments are presently inadequate or entirely lacking. But developing truly innovative drugs is undeniably a high-risk venture. It is important and necessary that pharmaceutical companies continue to take these risks, because they are usually the only entities with sufficient resources to do so. Therefore, companies must continue to perceive **sufficient incentives** to continue investing in innovation. Indeed, there is evidence that the prospect of future evergreening has become part of the incentive calculation for innovative drug development.4 But surely it is perverse to extend unpredictably a period of patent protection that the government intended to be clearly defined and predictable, and to maintain incentives that drive companies to divert their **drug-development resources away from innovation**. **Current patent legislation may not be optimal** for striking the right balance between encouraging innovation and facilitating profiteering. Given the broad societal importance of patent legislation, ongoing research to enable active governance of this issue should be a national priority. In the last decade, Canada’s laws have been among the friendliest toward evergreening in the world.5 We should now reflect on whether this is really in our national interest. Governments, including Canada’s, would do well to take inspiration from India’s example and tighten regulations that currently facilitate evergreening. This might involve **denying future patents for modifications** that currently would receive one. An overall reduction in the duration of all secondary patents on a therapy might also be considered. Globally, a more flexible and individualized approach to the length of drug patents might be a more effective strategy to align corporate incentives with population health needs. Limits on evergreening would likely reduce the **extensive patent litigation** that contributes to the **high prices of generic drugs** in Canada.3 Reducing economic pressure on generic drug companies may facilitate current provincial initiatives to lower generic drug prices. As opportunities to generate revenue from evergreening are eliminated, research-based pharmaceutical companies would be left with no choice but to invest more in innovative drug development to maintain their profits.

#### Only reinvigorating innovation solves high drug prices -- topples drug monopolies.

Engelberg 19 [Alfred B. Engelberg is a retired intellectual property lawyer and philanthropist. During his legal career, he was a patent examiner at the US Patent Office, a patent trial attorney at the US Department of Justice, and a member of the New York City law firm of Amster, Rothstein, and Engelberg. February 28, 2019. “A Shortfall In Innovation Is The Cause Of High Drug Prices”. <https://www.healthaffairs.org/do/10.1377/hblog20190228.636555/full/>] Dhruv

A System That Generates Profits Rather Than Research And Innovation

Each year the drug industry loses revenues because the monopolies on older medicines expire and they become available as low-cost generics. For at least the [last decade, revenue declines](https://www.nytimes.com/2011/03/07/business/07drug.html) have been large because blockbuster drugs for treating cholesterol, blood pressure, diabetes, depression and acid reflux have all become generic. Generic versions of Lipitor, Nexium, Prozac and many other blockbusters are now taken by millions of patients every day. In contrast, new drugs launched during the last decade are mostly specialty and orphan drugs that are taken by far fewer patients.  Despite their high initial prices, these drugs don’t generate enough revenue to replace the revenue lost from blockbuster monopoly expirations.

To avoid reporting lower revenue and profits, drug manufacturers have been imposing large annual price increases, often 10 percent or more, on all drugs that remain protected by monopolies.  The cumulative effect has been to double or triple the price of top-selling branded drugs such as Humira, Lyrica, Lantus and many others. That is why US drug prices are the highest in the world.   Here is what the IQVIA (formerly IMS) annual [reports](https://structurecms-staging-psyclone.netdna-ssl.com/client_assets/dwonk/media/attachments/590c/6aa0/6970/2d2d/4182/0000/590c6aa069702d2d41820000.pdf?1493985952) on medicine use show for the decade from 2008-2017:

Lost revenue from monopoly expirations was [$185 billion](http://www.piapr.org/clientuploads/PRESENTATIONS/IQVIA_Institute_2018_and_Beyond.pdf) whereas revenue gained from new medicines was only $169 billion.

Increases in invoice prices – the list prices often used to determine patient cost-sharing -- generated $187 billion. Net revenue -- the revenue remaining after deducting rebates and other price concessions -- increased by $106.

Undiscounted spending on prescription pharmaceuticals grew $167 billion (58 percent) from $286 to $453 billion, while the number of prescriptions filled with a brand-name medicine fell 59 percent, from over 1 billion to fewer than 450 million per year.

Generic drug use rose from 72 percent to 90 percent of all prescriptions.

Many commentators, including an article by [Hernandez et. al](https://www.healthaffairs.org/doi/10.1377/hlthaff.2018.05147) in the January 2019 issue of Health Affairs, have noted that price increases have been an important factor in the rising cost of drugs. What this data makes clear is that without the enormous price increases on a shrinking market for new medicines, the industry’s revenues and profits would have remained essentially flat for a decade.  In addition, but for these price increases, the overall cost of prescription drugs would have declined over the last decade as a result of the large increase in the percentage of prescriptions filled with a generic medicine.

Price increases largely fueled profits rather than additional research spending. According to the [GAO](https://www.gao.gov/assets/690/688472.pdf), profit margins grew to over 20 percent for the largest drug companies, more than double the average profit margin of the largest 500 industrial companies. Yet, from 2008 to 2014 research spending increased by only $8 billion and PhRMA companies [report](https://www.statista.com/statistics/265085/research-and-development-expenditure-us-pharmaceutical-industry/) a total of $18 billion in increases from 2015 to 2017. Moreover, the bulk of the industry’s spending was on later-stage development of new drugs acquired from 3rd parties. This suggests that drug manufacturers have become increasingly dependent on federally funded research at academic medical centers to seed a drug development pipeline.

Over the past 40 years, drug manufacturers successfully lobbied for longer monopolies, claiming that this would spur greater investment in research.  Legislation providing for patent term extensions of up to 5 years and market exclusivities of 5 to 12 years have lengthened the average monopoly period from less than 8 years to [over 14 years](https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2109854) for the top-selling drugs.  The length of these monopolies has been augmented by a variety of monopoly abuses including pay-for-delay patent settlements, denying generic manufacturers access to the samples needed to gain approval for competitive products, and “patent evergreening,” i.e. obtaining numerous secondary patents of dubious quality to delay competition.   Longer monopolies appear to be a substitute rather than an incentive for innovation because they make it easier for manufacturers to earn profits without the risk and cost of investing in the discovery of new medicines.