### Advantage 1

#### 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."

#### 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.

### Advantage 2

#### Global health inequality threatens progress in fight vs COVID-19 encouraging vaccine resistant mutations

Fink 7-30-21

(Jenni, https://www.newsweek.com/who-warns-world-blind-understanding-covid-spread-hurting-ability-end-pandemic-1614722)

A lack of testing for COVID-19 in parts of the world is preventing countries from having a clear picture of how the virus is spreading and therefore hurting the world's chances at fighting the virus and ending the pandemic, according to the World Health Organization. Health inequities throughout the world have plagued the global response to COVID-19 from the outset and WHO has pushed higher income countries to help lower income countries in the interest of ending the pandemic. Along with restricted access to vaccines, lower income countries have struggled to have sufficient testing, meaning the virus is likely going undetected in certain areas, further enabling its ability to spread. Low testing rates is "leaving the world blind to understanding where the disease is and how it's changing," Dr. Tedros Adhanom Ghebreyesus, director general of the WHO said on Friday during a press briefing. Without improving global testing rates, Ghebreyesus said the world can't "fight the disease" or mitigate the risk it poses to people around the globe. who blind covid spread cases On Friday, the World Health Organization warned the world is "blind" to how COVID-19 is spreading because of a lack of testing in certain places. WHO Director-General Tedros Adhanom Ghebreyesus attends a daily press briefing on the new coronavirus dubbed COVID-19, at the WHO headquaters on March 2, 2020, in Geneva. FABRICE COFFRINI//AFP/GETTY IMAGES NEWSWEEK NEWSLETTER SIGN-UP > One of Ghebreyesus' biggest frustrations with the pandemic response is the failure to evenly distribute the vaccine around the world. In some countries, like the United States and other higher-income nations, significant portions of the population have been vaccinated. While those large vaccinated populations help reduce the spread of the virus in some areas, other countries, especially those in Africa, haven't been able to vaccinate even 10 percent of their population. This puts the entire world at risk because when the virus is able to spread throughout communities it has the ability to mutate, thereby increasing the possibility that a mutation could evade the vaccines. It's a scenario public health officials have been warning about for months and Ghebreyesus said on Friday that "hard won gains are in jeopardy" or have already been lost because the virus has been able to spread. Nearly 30 countries have high or rising oxygen needs and the shortage of life-saving oxygen could lead to increased deaths. More than 196 million cases of COVID-19 have been reported around the world, according to a Johns Hopkins University tracker, and more than 4.2 million people have died. Ghebreyesus suspected the number of cases would top 200 million within the next two weeks and warned that health systems in many countries are being overwhelmed. Preventing hospitals from exceeding capacity was a massive concern when the pandemic first broke out and a year later, parts of the U.S. are having their health systems strained as the more transmissible Delta variant spreads. On Thursday, Arkansas Governor Asa Hutchinson declared a public health emergency that allows the state to bring in health care workers from outside Arkansas and makes it easier for retired health care workers and medical students to become licensed. The goal is to help alleviate stress on health care systems and Hutchinson said they've had people waiting in ambulances because there wasn't an open spot in a hospital. That strain will only become more exacerbated if a mutation occurs that evades the vaccine, as inoculations have proven effective at helping to keep people out of the hospital. Ghebreyesus warned that more variants will emerge if global access to vaccines and testing doesn't improve. "The pandemic will end when the world chooses to end it. It is in our hands. We have all the tools we need. We can prevent this disease. We can test for it and we can treat it," Ghebreyesus said.

#### IP protections are the vital internal link to resolve vaccine deficiencies. Empirics disprove all pro patent arguments

Kumar, PhD, 7-12-21

(Rajeesh, Associate Fellow Manohar Parrikar Institute for Defence Studies and Analysis, https://www.idsa.in/issuebrief/wto-trips-waiver-covid-vaccine-rkumar-120721)

In October 2020, India and South Africa had submitted a proposal to the World Trade Organization (WTO), suggesting a waiver of certain provisions of the Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement for the “prevention, containment and treatment of COVID-19”. The proposal seeks the waiver of “the implementation, application, and enforcement of sections 1, 4, 5 and 7 of part II of the TRIPS agreement”, which are stipulations referring to copyright, industrial design, patents, and undisclosed information (trade secrets).1 The proponents of the proposal argue that a waiver will enable timely and equitable access to affordable health products and technologies, including vaccines. Though many member countries had supported and co-sponsored the proposal, a small but influential group of countries, mainly Australia, Canada, the European Union (EU), Japan, the United Kingdom (UK) and the United States (US), opposed it. They argued that existing exceptions under the TRIPS Agreement are sufficient to address the concerns mentioned in the proposal. This resulted in sidelining of the waiver proposal for months. However, on 5 May 2021, the Joseph Biden administration announced its support for waiving intellectual property protections for COVID-19 vaccines.2 It was a significant step towards breaking the seven-month gridlock, and led to many more countries modifying their position on the waiver proposal. On 25 May 2021, the co-sponsors of the waiver proposal submitted a revised proposal that specified the scope of the waiver as applying to “health products and technologies” and also added a section on the proposed duration of the waiver, i.e., three years.3 At present, more than 100 countries, including the US and China support this proposal. The principal opponent of the waiver is the EU and in June 2021, it submitted an alternative proposal to the TRIPS Council, which requested to keep TRIPS’ provisions intact and focused on compulsory licensing and removing vaccine export restrictions to address the concerns raised by India and South Africa.4 The EU proposal also stated that the TRIPS Agreement does not prevent countries from taking measures to protect public health.5 At the meeting of the TRIPS Council on 8–9 June 2021, the member states agreed to text-based negotiations focusing on two proposals tabled by members. The members also decided to hold a series of meetings till the end of July 2021 to take stock of the text-based negotiations. However, the latest developments show that the waiver discussions hit a hurdle due to a split between the developed and developing countries over the negotiation text. This brief discusses how TRIPS becomes a barrier to the equitable access of COVID-19 vaccines. It also examines how a waiver will help India in its fight against COVID-19 at home and abroad. TRIPS and its Exceptions TRIPS, a comprehensive multilateral agreement on Intellectual Property (IP), was an outcome of the Uruguay Round (1986–94) of negotiations of the General Agreement on Tariffs and Trade (GATT). The Agreement came into force on 1 January 1995 and offers a minimum standard of protection for Intellectual Property Rights (IPR).6 In WTO, IPR are divided into two main categories. First, copyright and related rights (Articles 9 to 14, Part II of the TRIPS Agreement). Second, industrial property that includes trademarks, geographical indications, industrial designs, patents, integrated circuit layout designs, and undisclosed information (Articles 15 to 38, Part II of the TRIPS Agreement).7 Article IX.3 and IX.4 of the Marrakesh Agreement Establishing the WTO deals with TRIPS waivers. Article IX.3 says that in “exceptional circumstances” the Ministerial Conference may waive off an obligation imposed on WTO member countries.8 Such a decision requires the support of three-fourths of the WTO membership. According to Article IX.4, any waiver granted for more than one year will be reviewed by the Ministerial Conference. Based on the annual review, the Conference may extend, modify, or terminate the waiver. The TRIPS Agreement provides some flexibility primarily in the form of compulsory licensing and research exceptions through Articles 30 and 31. While Article 30 permits WTO members to make limited exceptions to patent rights, Article 31 provides a detailed exception, provided certain conditions are met. Compulsory licensing is the process of granting a license by a government to use a patent without the patent holder's consent. Article 31 permits granting compulsory license under circumstances such as “national emergencies”, “other circumstances of extreme urgency”, “public noncommercial use”, or against “anti-competitive” practices.9 In addition to these original waivers, the Declaration on the TRIPS Agreement and Public Health, adopted at the 2001 Doha Ministerial Meeting, also recognises some exceptions, for instance, in situations of a public health emergency, member countries have the freedom to determine the grounds upon which compulsory licenses are granted. Similarly, under Article 66.1, the least developed countries (LDCs) are given waivers for implementing TRIPS on pharmaceuticals till 1 January 2033. COVID-19 and TRIPS Waiver Two significant factors rekindled the debate on TRIPS waiver for essential medical products—first, vaccine inequity, and second, the insufficiency of existing waiver provisions in fighting the COVID-19 pandemic. COVID-19 is an exceptional circumstance, and equitable global access to the vaccine is necessary to bring the pandemic under control. However, the world is witnessing quite the reverse, i.e., vaccine nationalism. Vaccine nationalism is “my nation first” approach to securing and stockpiling vaccines before making them available in other countries. A TRIPS waiver would be instrumental in addressing the growing inequality in the production, distribution, and pricing of the COVID-19 vaccines. Vaccine Inequity According to Duke Global Health Innovation Center, which monitors COVID-19 vaccine purchases, rich nations representing just 14 per cent of the world population have bought up to 53 per cent of the most promising vaccines so far. As of 4 July 2021, the high-income countries (HICs) purchased more than half (6.16 billion) vaccine doses sold globally. At the same time, the low-income countries (LICs) received only 0.3 per cent of the vaccines produced. The low and middle-income countries (LMICs), which account for 81 per cent of the global adult population, purchased 33 per cent, and COVAX (COVID-19 Vaccines Global Access) has received 13 per cent.10 Many HICs bought enough doses to vaccinate their populations several times over. For instance, Canada procured 10.45 doses per person, while the UK, EU and the US procured 8.18, 6.89, and 4.60 doses per inhabitant, respectively.11 Source:“Tracking COVID-19 Vaccine Purchases Across the Globe”, Duke Global Health Innovation Center, Updated 9 July 2021. Consequently, there is a significant disparity between HICs and LICs in vaccine administration as well. As of 8 July 2021, 3.32 billion vaccine doses had been administered globally.12 Nonetheless, only one per cent of people in LICs have been given at least one dose. While in HICs almost one in four people have received the vaccine, in LICs, it is one in more than 500. The World Health Organization (WHO) notes that about 90 per cent of African countries will miss the September target to vaccinate at least 10 per cent of their populations as a third wave looms on the continent.13 South Africa, the most affected African country, for instance, has vaccinated less than two per cent of its population of about 59 million. This is in contrast with the US where almost 47.5 per cent of the population of more than 330 million has been fully vaccinated. In Sub-Saharan Africa, vaccine rollout remains the slowest in the world. According to the International Monetary Fund (IMF), at current rates, by the end of 2021, a massive global inequity will continue to exist, with Africa still experiencing meagre vaccination rates while other parts of the world move much closer to complete vaccination.14 This vaccine inequity is not only morally indefensible but also clinically counter-productive. If this situation prevails, LICs could be waiting until 2025 for vaccinating half of their people. Allowing most of the world’s population to go unvaccinated will also spawn new virus mutations, more contagious viruses leading to a steep rise in COVID-19 cases. Such a scenario could cause twice as many deaths as against distributing them globally, on a priority basis. Preventing this humanitarian catastrophe requires removing all barriers to the production and distribution of vaccines. TRIPS is one such barrier that prevents vaccine production in LMICs and hence its equitable distribution. TRIPS: Barrier to Equitable Health Care Access The opponents of the waiver proposal argue that IPR are not a significant barrier to equitable access to health care, and existing TRIPS flexibilities are sufficient to address the COVID-19 pandemic. However, history suggests the contrary. For instance, when South Africa passed the Medicines and Related Substances Act of 1997 to address the HIV/AIDS public health crisis, nearly 40 of world’s largest and influential pharma companies took the South African government to court over the violation of TRIPS. The Act, which invoked the compulsory licensing provision, allowed South Africa to produce affordable generic drugs.15 The Big Pharma also lobbied developed countries, particularly the US, to put bilateral trade sanctions against South Africa.16 Similarly, when Indian company Cipla decided to provide generic antiretrovirals (ARVs) to the African market at a lower cost, Big Pharma retaliated through patent litigations in Indian and international trade courts and branded Indian drug companies as thieves.17 Another instance was when Swiss company Roche initiated patent infringement proceedings against Cipla’s decision to launch a generic version of cancer drug, “erlotinib”. Though the Delhi High Court initially dismissed Roche's appeal by citing “public interest” and “affordability of medicines,” the continued to pressure the generic pharma companies over IPR. 18 Likewise, Pfizer’s aggressive patenting strategy prevented South Korea in developing pneumonia vaccines for children.19 A recent document by Médecins Sans Frontières (MSF), or Doctors Without Borders, highlights various instances of how IP hinders manufacturing and supply of diagnostics, medical equipment, treatments and vaccines during the COVID-19 pandemic. For instance, during the peak of the COVID-19 first wave in Europe, Roche rejected a request from the Netherlands to release the recipe of key chemical reagents needed to increase the production of diagnostic kits. Another example was patent holders threatening producers of 3D printing ventilators with patent infringement lawsuits in Italy.20 The MSF also found that patents pose a severe threat to access to affordable versions of newer vaccines.21 Source:“COVID-19 Vaccine R&D Investments”, Global Health Centre, Graduate Institute, Geneva, Updated 9 July 2021. The opponents of the TRIPS waiver also argue that IP is the incentive for innovation and if it is undermined, future innovation will suffer. However, most of the COVID-19 medical innovations, particularly vaccines, are developed with public financing assistance. Governments spent billions of dollars for COVID-19 vaccine research. Notably, out of $6.1 billion in investment tracked up to July 2021, 98.12 per cent was public funding.22 The US and Germany are the largest investors in vaccine R&D with $2.2 billion and $1.5 billion funding. Source:“COVID-19 Vaccine R&D Investments”, Global Health Centre, Graduate Institute, Geneva, Updated 9 July 2021. Private companies received 94.6 per cent of this funding; Moderna received the highest $956.3 million and Janssen $910.6 million. Moreover, governments also invested $50.9 billion for advance purchase agreements (APAs) as an incentive for vaccine development. A recent IMF working paper also notes that public research institutions were a key driver of the COVID-19 R&D effort—accounting for 70 per cent of all COVID-19 clinical trials globally.23 The argument is that vaccines are developed with the support of substantial public financing, hence there is a public right to the scientific achievements. Moreover, private companies reaped billions in profits from COVID-19 vaccines. Source: Katharina Buchholz, “COVID-19 Vaccines Lift Pharma Company Profits”, Statista, 17 May 2021. One could argue that since the US, Germany and other HICs are spending money, their citizens are entitled to get vaccines first, hence vaccine nationalism is morally defensible. Nonetheless, it is not the case. The TRIPS Agreement includes several provisions which mandates promotion of technology transfer from developed countries to LDCs. For instance, Article 7 states that "the protection and enforcement of IP rights should contribute to the promotion of technological innovation and the transfer and dissemination of technology, to the mutual advantage of producers and users of technical knowledge and in a manner conducive to social and economic welfare, and to a balance of rights and obligations."24 Similarly, Article 66.2 also mandates the developed countries to transfer technologies to LDCs to enable them to create a sound and viable technological base. The LMICs opened their markets and amended domestic patent laws favouring developing countries’ products against this promise of technology transfer. Another argument against the proposed TRIPS waiver is that a waiver would not increase the manufacturing of COVID-19 vaccines. Indeed, one of the significant factors contributing to vaccine inequity is the lack of manufacturing capacity in the global south. Further, a TRIPS waiver will not automatically translate into improved manufacturing capacity. However, a waiver would be the first but essential step to increase manufacturing capacity worldwide. For instance, to export COVID-19 vaccine-related products, countries need to ensure that there are no IP restrictions at both ends – exporting and importing. The market for vaccine materials includes consumables, single-use reactors bags, filters, culture media, and vaccine ingredients. Export blockages on raw materials, equipment and finished products harm the overall output of the vaccine supply chain. If there is no TRIPS restriction, more governments and companies will invest in repurposing their facilities. Similarly, the arguments such as that no other manufacturers can carry out the complex manufacturing process of COVID-19 vaccines and generic manufacturing as that would jeopardise quality, have also been proven wrong in the past. For instance, in the early 1990s, when Indian company Shantha Biotechnics approached a Western firm for a technology transfer of Hepatitis B vaccine, the firm responded that “India cannot afford such high technology vaccines… And even if you can afford to buy the technology, your scientists cannot understand recombinant technology in the least.”25 Later, Shantha Biotechnics developed its own vaccine at $1 per dose, and the UNICEF (United Nations Children’s Emergency Fund) mass inoculation programme uses this vaccine against Hepatitis B. In 2009, Shantha sold over 120 million doses of vaccines globally. India also produces high-quality generic drugs for HIV/AIDS and cancer treatment and markets them across the globe. Now, a couple of Indian companies are in the last stage of producing mRNA (Messenger RNA) vaccines.26 Similarly, Bangladesh and Indonesia claimed that they could manufacture millions of COVID-19 vaccine doses a year if pharmaceutical companies share the know-how.27 Recently, Vietnam also said that the country could satisfy COVID-19 vaccine production requirements once it obtains vaccine patents.28 Countries like the United Arab Emirates (UAE), Turkey, Cuba, Brazil, Argentina and South Korea have the capacity to produce high-quality vaccines but lack technologies and know-how. However, Africa, Egypt, Morocco, Senegal, South Africa and Tunisia have limited manufacturing capacities, which could also produce COVID-19 vaccines after repurposing. Moreover, COVID-19 vaccine IPR runs across the entire value chain – vaccine development, production, use, etc. A mere patent waiver may not be enough to address the issues related to its production and distribution. What is more important here is to share the technical know-how and information such as trade secrets. Therefore, the existing TRIPS flexibilities, such as compulsory and voluntary licensing, are insufficient to address this crisis. Further, compulsory licensing and the domestic legal procedures it requires is cumbersome and not expedient in a public health crisis like the COVID-19 pandemic.

ever, requires recipient manufacturers to acquire the IP necessary for mRNA technologies— which is currently missing.

#### Failure to contain COVID-19 causes extinction

Guy R. **McPherson, PhD, 20** [PhD Range Science, Professor Emeritus, University of Arizona School of Natural Resources and Department of Ecology & Evolutionary Biology], “Will COVID-19 Trigger Extinction of All Life on Earth?” Eart & Envi Scie Res & Rev, Volume 3 Issue 2, 4-8-2020, <https://opastonline.com/wp-content/uploads/2020/04/will-covid-19-trigger-extinction-of-all-life-on-earth-eesrr-20-.pdf>

Small lives matter. Indeed, the “human body contains about 100 trillion cells, but only maybe one in 10 of those cells is actually — human” [1]. We are comprised of bacteria and other tiny living organisms, as well as non-living entities such as viruses. One such virus has captured the attention of the world, and with good reason. **The novel coronavirus could trigger extinction of humans, and therefore the extinction of all life on Earth**. I frequently hear and read that COVID-19 is a nefarious attempt by the so-called “elite” among us to depopulate the burgeoning human population on Earth. Other conspiracy theories abound, including COVID-19 as an attempt to further reduce human rights, promote expensive medical therapies, and otherwise enrich the wealthy at the expense of the bamboozled masses. I do not doubt the ability of the informed wealthy to fleece the ignorant masses. Nor do I doubt the ability of the informed wealthy to turn virtually any situation into an opportunity for monetary gain. A quick glance at the past two centuries provides plenty of examples. However, I doubt the monetarily wealthy among us are interested in accelerating human extinction, even for financial gain. As I explain below, **the ongoing** reduction in industrial activity **as a result of COVID-19 almost certainly leads to loss of habitat for human animals, hence putting us on the fast track to human extinction**. I doubt the knowledgeable “elite” are interested in altering the sweet deal they are experiencing with the current set of living arrangements. The aerosol masking effect, or global dimming, has been described in the peer-reviewed literature since at least 1929 [2, 3]. **Coincident with industrial activity adding to greenhouse gases that warm the planet, industrial activity simultaneously cools the planet by adding aerosols to the atmosphere. These aerosols block incoming sunlight, thereby keeping cool our pale blue dot. Reducing industrial activity by as little as 35 percent is expected to cause a global-average temperature rise of 1 degree Celsius within a few weeks**, according to research on the aerosol masking effect [4]. Such research was deemed collectively too conservative by a paper in the 17 January 2019 issue of Science [5]. As pointed out by the lead author of the latter paper on 22 January 2019 “Global efforts to improve air quality by developing cleaner fuels and burning less coal could end up harming our planet by reducing the number of aerosols in the atmosphere, and by doing so, diminishing aerosols’ cooling ability to offset global warming” [6]. The cooling effect is “nearly twice what scientists previously thought,” and the paper by Rosenfeld et al. [5] cites the conclusion by Levy et al. [4], indicating as little as 35% reduction in industrial activity drives a 1 C global-average rise in temperature, thereby suggesting that as little as a 20% reduction in industrial activity will drive a 1 C spike in temperature within a few weeks [7]. Additional, recent support for the importance of the aerosol masking effect comes from [8, 9]. Furthermore, loss of aerosols exacerbates heat waves [10]. Human extinction might have been triggered several years ago when the global-average temperature of Earth exceeded 1.5 C above the 1750 baseline. According to a comprehensive overview published by European Strategy and Policy Analysis System in April, an “increase of 1.5 degrees is the maximum the planet can tolerate; … at worst, [such a rise in temperature above the 1750 baseline will cause] the extinction of humankind altogether” [11, 12]. Earth’s global-average temperature hit 1.73 C above the 1750 baseline by April, 2018 the highest global-average temperature experienced by Homo sapiens on Earth [13, 14]. By 13 March 2020, 2 C above the 1750 baseline was crossed [11]. In other words, human extinction via the death-by-a-thousandcuts route might be locked in with no further heating of Earth. In light of the ongoing pandemic, the ongoing Mass Extinction Event, and abrupt, irreversible climate change, it is pleasantly surprising that humans still occupy Earth. The pandemic-induced reduction in industrial activity may have already reduced the aerosol masking effect sufficiently to trigger a 1 C temperature spike. The outcome is not yet obvious because the timing of the outbreak of the novel coronavirus was favorable for human habitat. Trees produced leaves in the Northern Hemisphere spring of 2020 as a result of carbohydrates stored the previous year and grain crops were harvested before the novel coronavirus emerged. Results of the recent and ongoing rise in temperature, which have already been reported in China and India, will become obvious to most humans when many more trees die. Large-scale die-off of trees likely will approximately correspond with catastrophic crop failure. This might occur by the end of this year, although I would rather it not. **Every civilization requires bread and circuses**. There is little doubt **the circuses attendant to industrial civilization will continue until the end of the planetary show for Homo sapiens. Bread, however, requires wheat. Wheat production requires a delicate balance of growing conditions that, like habitat for humans, teeters on the brink** [15]. **The path to near-term human extinction thus runs from a tiny virus underlying a pandemic through a reduction of industrial activity that overheats a planet already running a fever**. **The outbreak of COVID-19 could very well be the event that accelerates human extinction via reduction of industrial activity, hence loss of habitat for Homo sapiens. As a result of the rapid environmental change likely to follow, we are almost certain to lose all life on Earth** [16]. History is replete with examples of human hubris. We thought we were mighty, and we certainly have left our mark on Earth. **How embarrassing for the big-brained human species that a microscopic virus could pull the trigger on our extinction** [15].

#### Corona escalates security threats that cause extinction – cooperation thesis is wrong.

Recna 21 [Research Center for Nuclear Weapon Abolition; Nagasaki, Japan; “Pandemic Futures and Nuclear Weapon Risks: The Nagasaki 75th Anniversary pandemic-nuclear nexus scenarios final report,” Journal for Peace and Nuclear Disarmament; 5/28/21; <https://www.tandfonline.com/doi/full/10.1080/25751654.2021.1890867>] Justin

The Challenge: Multiple Existential Threats

The relationship between pandemics and war is as long as human history. Past pandemics have set the scene for wars by weakening societies, undermining resilience, and exacerbating civil and inter-state conflict. Other disease outbreaks have erupted during wars, in part due to the appalling public health and battlefield conditions resulting from war, in turn sowing the seeds for new conflicts. In the post-Cold War era, pandemics have spread with unprecedented speed due to increased mobility created by globalization, especially between urbanized areas. Although there are positive signs that scientific advances and rapid innovation can help us manage pandemics, it is likely that deadly infectious viruses will be a challenge for years to come.

The COVID-19 is the most demonic pandemic threat in modern history. It has erupted at a juncture of other existential global threats, most importantly, accelerating climate change and resurgent nuclear threat-making. The most important issue, therefore, is how the coronavirus (and future pandemics) will increase or decrease the risks associated with these twin threats, climate change effects, and the next use of nuclear weapons in war.5

Today, the nine nuclear weapons arsenals not only can annihilate hundreds of cities, but also cause nuclear winter and mass starvation of a billion or more people, if not the entire human species. Concurrently, climate change is enveloping the planet with more frequent and intense storms, accelerating sea level rise, and advancing rapid ecological change, expressed in unprecedented forest fires across the world. Already stretched to a breaking point in many countries, the current pandemic may overcome resilience to the point of near or actual collapse of social, economic, and political order.

In this extraordinary moment, it is timely to reflect on the existence and possible uses of weapons of mass destruction under pandemic conditions – most importantly, nuclear weapons, but also chemical and biological weapons. Moments of extreme crisis and vulnerability can prompt aggressive and counterintuitive actions that in turn may destabilize already precariously balanced threat systems, underpinned by conventional and nuclear weapons, as well as the threat of weaponized chemical and biological technologies. Consequently, the risk of the use of weapons of mass destruction (WMD), especially nuclear weapons, increases at such times, possibly sharply.

The COVID-19 pandemic is clearly driving massive, rapid, and unpredictable changes that will redefine every aspect of the human condition, including WMD – just as the world wars of the first half of the 20th century led to a revolution in international affairs and entirely new ways of organizing societies, economies, and international relations, in part based on nuclear weapons and their threatened use. In a world reshaped by pandemics, nuclear weapons – as well as correlated non-nuclear WMD, nuclear alliances, “deterrence” doctrines, operational and declaratory policies, nuclear extended deterrence, organizational practices, and the **existential risks** posed by retaining these capabilities – are all up for redefinition.

A pandemic has potential to destabilize a nuclear-prone conflict by incapacitating the supreme nuclear commander or commanders who have to issue nuclear strike orders, creating uncertainty as to who is in charge, how to handle nuclear mistakes (such as errors, accidents, technological failures, and entanglement with conventional operations gone awry), and opening a brief opportunity for a first strike at a time when the COVID-infected state may not be able to retaliate efficiently – or at all – due to leadership confusion. In some nuclear-laden conflicts, a state might use a pandemic as a cover for political or military provocations in the belief that the adversary is distracted and partly disabled by the pandemic, increasing the risk of war in a nuclear-prone conflict. At the same time, a pandemic may lead nuclear armed states to increase the isolation and sanctions against a nuclear adversary, making it even harder to stop the spread of the disease, in turn creating a pandemic reservoir and transmission risk back to the nuclear armed state or its allies.

In principle, the common threat of the pandemic might induce nuclear-armed states to reduce the tension in a nuclear-prone conflict and thereby the risk of nuclear war. It may cause nuclear adversaries or their umbrella states to seek to resolve conflicts in a cooperative and collaborative manner by creating habits of communication, engagement, and mutual learning that come into play in the nuclear-military sphere. For example, militaries may cooperate to control pandemic transmission, including by working together against criminal-terrorist non-state actors that are trafficking people or by joining forces to ensure that a new pathogen is not developed as a bioweapon.

To date, however, the COVID-19 pandemic has increased the isolation of some nuclear-armed states and provided a textbook case of the failure of states to cooperate to overcome the pandemic. Borders have slammed shut, trade shut down, and budgets blown out, creating enormous pressure to focus on immediate domestic priorities. Foreign policies have become markedly more nationalistic. Dependence on nuclear weapons may increase as states seek to buttress a global re-spatialization6 of all dimensions of human interaction at all levels to manage pandemics. The effect of nuclear threats on leaders may make it less likely – or even impossible – to achieve the kind of concert at a global level needed to respond to and administer an effective vaccine, making it harder and even impossible to revert to pre-pandemic international relations. The result is that some states may proliferate their own nuclear weapons, further reinforcing the spiral of conflicts contained by nuclear threat, with cascading effects on the risk of nuclear war.

### Framework

#### Ethics must begin a-posteriori:

#### 1 – We can’t obtain evidence of goodness without desire.

Sayre-McCord 01

Geoffrey Sayre-McCord, Philosophy, University of North Carolina, Chapel Hill, "Mill's “Proof” Of The Principle of Utility: A More Than Half-Hearted Defense", Social Philosophy and Policy, 2001, accessed: 1 April 2020, <https://www.cambridge.org/core/journals/social-philosophy-and-policy/article/mills-proof-of-the-principle-of-utility-a-more-than-halfhearted-defense/FDBE07CBE08D4E17523930BF8C7BBC32>, R.S.

How is the argument supposed to go, if not by way of these multiple fallacies? Let us start with the principle of evidence and the analogy Mill draws between visibility and desirability. What is the analogy supposed to be if not one that commits Mill to interpreting "desirable" as "capable of being desired"?

When it comes to visibility, no less than desirability, Mill explicitly denies that a "proof" in the "ordinary acceptation of the term" can be offered.25 As he notes, "To be incapable of proof by reasoning is com mon to all first principles; to the first premises of our knowledge, as well as to those of our conduct."26 Nonetheless, support -- that is, evidence, though not proof -- for the first premises of our **knowledge** is **provided by** "our **senses, and** our internal **consciousness.**" Mill's suggestion is that, when it comes to the first principles of conduct, desire play the same epistemic role that the senses play, when it comes to the first principles of knowledge.

To understand this role, it is important to distinguish the fact that someone is sensing something from what is sensed, which is a distinction mirrored in the contrast bet ween the fact that someone is desiring something and what is desired. In the case of our senses, the evidence we have for our judgments concerning sensible qualities traces back to what is sensed, to the content of our sense-experience. Likewise, Mill is suggesting, in the case of value, the evidence we have for our judgments concerning value traces back to what is desired, to the content of our desires. Ultimately, the grounds we have for holding the principles we do must, he thinks, be traced back to our experience, to our senses and desires. Yet the evidence we have is not that we are sensing or desiring something but what it is that is sensed or desired.

When we are having sensations of red, when what we are looking at appears red to us, we have evidence (albeit overrideable and defeasible evidence) that the thing is red. Moreover, if things never looked red to us, we could never get evidence that things were red, and would indeed never have developed the concept of redness. Similarly, when we are desiring things, when what we are considering appears good to us, we have evidence (albeit overrideable and defeasible evidence) that the thing is good. Moreover, **if we never desired** things, **we could never get evidence** that **things were good, and** would indeed **never have developed** the concept of **value.**

Recall that desire, for Mill, like taste, touch, sight, and smell, is a "passive sensibility." All of these, he holds, provide us with both the content that makes thought possible and the evidence we have for the conclusions that thought leads us to embrace. "Desiring a thing" and "thinking of it as desirable (unless for the sake of its consequences)" are treated by Mill as one an d the same, just as seeing a thing as red and thinking of it as red are one and the same. Accordingly, a person who desires x is a person who ipso facto sees x as desirable. Desiring something, for Mill, is a matter of seeing it under the guise of the good. This means that it is important, in the context of Mill's argument, that one not think of desires as mere preferences or as just any sort of motive. They constitute, according to Mill, a distinctive subclass of our motivational states, and are distinguished (at least in part) by t heir evaluative content. Thus, Mill is neither assuming nor arguing that something is good because we desire it; rather, he is depending on our desiring it as establishing that we see it as good.

At the same time, while desiring something is a matter of seeing it as good, one could, on Mill's view, believe that something is good without desiring it, just as one can believe something is red without seeing it as red. While desire is supposed to be the fundamental source of our concept of, and evidence for, desirability, once the concept is in place there are contexts in which we will have reason to think it applies even when the corresponding sensible experience is lacking. Indeed, in Chapter IV, Mill is concerned not with generating a desire, but with justifying the belief that happiness is desirable, and the only thing desirable, as an end, and so concerned with defending the standard for determining what should be desired.

Mill's aim is to take what people already, and he thinks inevitably, see as desirable and argue that those views commit them to the value of the general happiness (whet her or not their desires follow the deliverances of t heir reason). Those who, like Mill, desire the general happiness already hold the view that the general happiness is desirable. They accept the claim that Mill is trying to defend. As Mill knows, however, there are many who do not have this desire -- many who desire only their own happiness, and some who even desire that others suffer. These are the people he sets out to persuade, along with others who are more generous and benevolent, but who nonetheless do not see happiness as desirable, and the only thin g desirable, as an end. Mill's argument is directed at convincing t hem all -- whether their desires follow or not -- that they have grounds for, and are in fact already com mitted to, regarding the happiness of others as valuable as an end.

At the same time, while desiring something is a matter of seeing it as good, one could, on Mill's view, believe that something is good without desiring it, just as one can believe something is red without seeing it as red. While desire is supposed to be the fundamental source of our concept of, and evidence for, desirability, once the concept is in place there are contexts in which we will have reason to think it applies even when the corresponding sensible experience is lacking. Indeed, in Chapter IV, Mill is concerned not with generating a desire but with justifying the belief that happiness is desirable, and the only thing desirable, as an end, and so concerned with defending the standard for determining what should be desired. Mill recognizes that whatever argument he might hope to offer will need to appeal to evaluative claims people already accept (since he takes to heart Hume's caution concerning inferring an 'ought' from an 'is'). The claim Mill thinks he can appeal to -- that one's own happiness is a good (i.e. desirable) -- is something licensed as available by people desiring their own happiness. Yet he is not supposing here that the fact that they desire their own happiness, or anything else, is proof that it is desirable, just as he would not suppose that the fact that someone sees something as red is proof that it is. Rather, he is supposing that if people desire their own happiness, or see something as red, one can rely on t hem having available, as a premise for further argument, the claim that their own happiness is desirable or that the thing is red (at least absent contrary evidence). As he puts it in the third paragraph, "If the end which the utilitarian doctrine proposes to itself were not, in theory and in practice, acknowledged to be an end nothing could ever convince any person that it was so."

Thus, in appealing to the analogy bet ween judgments of sensible qualities and judgments of value, Mill is not trading on an ambiguity, nor does his argument here involve identifying being desirable with being desired or assuming that "desirable" means "desired." He is instead relying consistently on an empiricist account of concepts and their application -- on a view according to which we have the concepts, evidence, and knowledge we do only thanks to our having experiences of a certain sort. In the absence of the relevant experiences, he holds (with other empiricists), we would not only lack the required evidence for our judgments, we would lack the capacity to make the judgments in the first place. **In** the **presence of** the relevant **experience**s, though, **we have** both the concepts and the required **evidence** -- "not only all the proof which the case admits of, but all which it is possible to require."

#### 2 – Indifference – Even if there are apriori moral truths, I can choose to ignore them. Cognition is binding – if I put my hand on a hot stove, I can’t turn off my natural aversion to it.

#### The standard is maximizing expected wellbeing.

#### Prefer:

#### 1 – Pleasure and pain *are* intrinsic value and disvalue – everything else *regresses* – robust neuroscience.

Blum et al. 18

Kenneth Blum, 1Department of Psychiatry, Boonshoft School of Medicine, Dayton VA Medical Center, Wright State University, Dayton, OH, USA 2Department of Psychiatry, McKnight Brain Institute, University of Florida College of Medicine, Gainesville, FL, USA 3Department of Psychiatry and Behavioral Sciences, Keck Medicine University of Southern California, Los Angeles, CA, USA 4Division of Applied Clinical Research & Education, Dominion Diagnostics, LLC, North Kingstown, RI, USA 5Department of Precision Medicine, Geneus Health LLC, San Antonio, TX, USA 6Department of Addiction Research & Therapy, Nupathways Inc., Innsbrook, MO, USA 7Department of Clinical Neurology, Path Foundation, New York, NY, USA 8Division of Neuroscience-Based Addiction Therapy, The Shores Treatment & Recovery Center, Port Saint Lucie, FL, USA 9Institute of Psychology, Eötvös Loránd University, Budapest, Hungary 10Division of Addiction Research, Dominion Diagnostics, LLC. North Kingston, RI, USA 11Victory Nutrition International, Lederach, PA., USA 12National Human Genome Center at Howard University, Washington, DC., USA, Marjorie Gondré-Lewis, 12National Human Genome Center at Howard University, Washington, DC., USA 13Departments of Anatomy and Psychiatry, Howard University College of Medicine, Washington, DC US, Bruce Steinberg, 4Division of Applied Clinical Research & Education, Dominion Diagnostics, LLC, North Kingstown, RI, USA, Igor Elman, 15Department Psychiatry, Cooper University School of Medicine, Camden, NJ, USA, David Baron, 3Department of Psychiatry and Behavioral Sciences, Keck Medicine University of Southern California, Los Angeles, CA, USA, Edward J Modestino, 14Department of Psychology, Curry College, Milton, MA, USA, Rajendra D Badgaiyan, 15Department Psychiatry, Cooper University School of Medicine, Camden, NJ, USA, Mark S Gold 16Department of Psychiatry, Washington University, St. Louis, MO, USA, “Our evolved unique pleasure circuit makes humans different from apes: Reconsideration of data derived from animal studies”, U.S. Department of Veterans Affairs, 28 February 2018, accessed: 19 August 2020, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6446569/>, R.S.

**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.

#### 4] Extinction outweighs –

#### a] Prerequisite – if we’re all dead then no conception of moral value can exist and it procedurally precludes us from acting according to other ethical frameworks so it comes first.