## Off

### 1

#### The standard is maximizing expected well being – Prefer

#### [1] Pleasure and pain are intrinsic value and disvalue – everything else regresses. Evolutionary knowledge is reliable – broad consensus and 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.

#### [2] Actor specificity – state actors can only use util – outweighs since different actors have different obligations.

#### A – Aggregation – all policies benefit some and hurts others – only util can resolve these cuz it gives a clear weighing mechanism

#### B – Collectivism – States are composed of many actors who inevitably disagree about intent means they can only use consequentialism because they don’t have to agree

#### C – Bureaucrats aren’t philosophers – policymakers do not have experience with dense frameworks so they don’t understand how to apply them to specific instances but they do understand that pain is bad and pleasure is good because it’s intrinsic to existing.

#### [3] Extinction first –

#### a. Wager – if there is any chance of goodness existing, we ought to preserve our existence to maximize it.

#### b. Sequencing – if their framework is true, people dying is bad because it means those people can’t use their framework

#### c. Repugnance – if their framework cannot explain why people dying is bad – you should reject it because it cannot disavow of atrocities. You shouldn’t vote for a framework that can’t say the holocaust was a bad thing.

#### d. Performativity – us having a moral debate proves moral uncertainty because it means we are not certain about which framework is true - means we should preserve our ability to find the true framework

### 2

#### The California recall has given democrats optimal election strategy for the midterms to maximize gains – right-wing extremists winning primaries alienate moderates

Ronayne and Riccardi 9/15 (Kathleen Ronayne and Nicholas Riccardi; 9/15/21; AP News; *“Democrats see a midterm map in California recall success”*; accessed 9/19/21; <https://apnews.com/article/donald-trump-california-recall-california-campaigns-health-48a08f0362762dd53f8171c35c09f57b>; Kathleen Ronayne is a olitical reporter for The Associated Press with bylines from California to New Hampshire and swing states in between. Now covering the recall election of Gov. Gavin Newsom and California's influence on the national political debate; Nicholas is a political writer at the associated press) HB

Few Democrats were surprised to see Democratic Gov. Gavin Newsom swat down a Republican-driven recall campaign in bright-blue California. But they were pleased with how he did it. By making the race into a referendum on former President Donald Trump and his supporters’ “extreme” resistance to coronavirus precautions, Newsom offered a formula for survival that could translate to dozens of races in next year’s midterm elections, Democrats said. A healthy turnout, spurred by some late anxiety, showed Democrats remain eager to vote against the former president, even when he’s not on the ballot. California voters rejected the “Republican brand that is centered around insurrection and denying the pandemic,” said Rep. Sean Patrick Maloney, chairman of the Democratic Congressional Campaign Committee. Republicans said they saw nothing to worry about in the California results. Losing badly in a liberal stronghold isn’t much of a prediction of the party’s performance in battlegrounds like Florida or Georgia, they said. They argue they were saddled with a flawed candidate — talk radio host Larry Elder, the Republican frontrunner whom Democrats likened to a Trump clone in a state the former president lost by 30 percentage points and did little to appeal to moderate voters in swingy suburbs. But President Joe Biden and his party won’t have it as easy next year as Newsom did, said Ron Nehring, a former chairman of the California Republican Party who was harshly critical of Elder and worked for one of his rivals “Gavin Newsom had one opponent who he was able to define in the minds of enough swing voters,” he said. “No. 1, Biden himself is not going to be on the ballot and No. 2, he does not have a singular opponent.” On Wednesday, Biden embraced Newsom’s victory and his message. “This vote is a resounding win for the approach that he and I share to beating the pandemic: strong vaccine requirements, strong steps to reopen schools safely, and strong plans to distribute real medicines — not fake treatments — to help those who get sick,” Biden said in a statement. But there will be better test cases coming on how these messages play with voters. In November, voters in Virginia will choose between Democrat Terry McAuliffe, a former governor and longtime Democratic operative, and GOP businessman Glenn Youngkin. McAuliffe has been hammering Youngkin as too extreme for a state that has been growing more diverse, more suburban and more Democratic for years. California has similar demographic trends at play. In Orange County, long a GOP bastion, racial and ethnic diversity and the growing distaste higher-educated, wealthy voters have shown for Trump have opened the door to Democrats in the county — although the GOP won back two House seats there last year. The recall was failing in Orange County by 5 percentage points on Wednesday, although the vote count in California will go on for weeks and the final margins may change. Newsom and his Republican opponent John Cox essentially tied in the county in 2018. Even the incomplete the results buoyed Democrats. “We’re pretty excited about California, and it’s not because we thought we’re going to lose it — it’s because the margin is better than expected and it shows the Republican message is failing badly in swing districts,” Mahoney said. Still, it’s hard to draw too many conclusions from a single election in a state so liberal that Democrats held every statewide office even during Republican wave years of 2010 and 2014. “It’s like us boasting about beating a recall in Alabama,” quipped Matt Gorman, a former strategist with the National Republican Congressional Committee. Gorman said Democrats would only get so much mileage out of demonizing Republican nominees and trying to tie them to Trump. “Biden is the focus” of the midterms, Gorman said, noting how Republicans unsuccessfully tried to tie congressional Democrats to Nancy Pelosi in 2018, when she was only minority leader and didn’t control the House of Representatives. “It becomes less effective once they’re out of power.” “If inflation is high, gas prices are high and COVID is spiking, it’s going to be much harder” for Democrats to talk about Trump and Republican extremism in 2022, Gorman said. It will also be hard for Republicans not to talk about Trump. GOP primaries for Senate seats in Ohio, Georgia and Pennsylvania already are poised to be a competition for Trump’s base. House candidates have been clamoring for Trump’s endorsement. The former president hasn’t been shy about anointing favorites. Democrats are certain to use that against those candidates when they face a general election. “I think a sad reality of the modern GOP is that there are going to be a lot of Larry Elders on the ballot in 2022 because they’re going to win Republican primaries,” said Addisu Demissie, a Newsom campaign strategist. “When the alternative is extreme, you represent not just your base but the middle.”

#### The plan is politically unpopular – voters are divided which means that plans passage flips the major thin margins – vaccines proves

The Hill 5/4 (The Hill; 5/4/21; The Hill; *“Poll: Majority oppose proposal to temporarily waive intellectual property rights on COVID-19 vaccines”*; accessed 8/27/21; <https://thehill.com/hilltv/what-americas-thinking/551797-poll-majority-oppose-proposal-to-temporarily-waive-intellectual>) HB

A majority of voters oppose the proposal to temporarily waive intellectual property rights on COVID-19 vaccines, a new Hill-HarrisX poll finds. The survey comes as the Biden administration faces mounting pressure to support a proposal led by India and South Africa that would waive an international intellectual property agreement that protects pharmaceutical trade secrets. Backers of the move argue it would enable lower-income countries to manufacture the vaccines themselves while those opposed say it could make the vaccine less safe and damper production in existing locations. Fifty-seven percent of registered voters in the May 3-4 survey said they oppose the proposal to waive intellectual property rights on COVID-19 vaccines. By contrast, 43 percent of respondents said they support the proposal. Sixty-four percent of Republican voters along with 52 percent of both Democratic and independent voters said they oppose waiving the intellectual property rights of vaccines. "This is a complex issue with a remarkably sophisticated understanding by the public. The tension is as follows: On one hand you have the need to protect the intellectual property rights of the scientists and companies that brought about the fastest vaccine in history, and will likely need to produce new versions of the shot even faster to battle evolving strains," Dritan Nesho, chief researcher and CEO of HarrisX, told Hill.TV. "On the other hand there’s the need to save lives, reaching global heard immunity and providing access to the vaccine as broadly and equitably as as possible," Nesho continued. "Today a majority of 57 percent of U.S. voters would like to protect the intellectual property of vaccine makers, but as more and more people are vaccinated in advanced economies, voter pressure for broader and more equitable distribution will rise," Nesho added. "Already we see Democrats and independents here split on the issue of whether or not to waive IP rights to provide greater access to the vaccines." President Biden is expected to weigh in on the proposal at a World Trade Organization meeting on Wednesday. The most recent Hill-HarrisX poll was conducted online among 939 registered voters. It has a margin of error of 3.2 percentage points.

#### **A Republican win in 2022 shuts out climate action for decades**

Silverman 8/24 (Ellie Silverman; 8/24/21; The Washington Post; *“Climate activists fear this is the last chance to pass meaningful legislation”*; accessed 8/27/21; <https://www.washingtonpost.com/dc-md-va/2021/08/24/climate-biden-congress-protest/>; Ellie Silverman covers protest movements, activism and local news. At The Post, she has also covered local crime and courts. She has previously reported on retail, breaking news and general assignment stories for the Philadelphia Inquirer, her hometown paper. She graduated from the University of Maryland, where she reported for the Diamondback) HB

There is a rising frustration among many of those organizers, who say they helped turn out the vote in 2020 but are not seeing climate pledges translate into meaningful changes. They are worried that the opportunity to push through ambitious climate legislation will soon be gone — and that they may not have another chance. “He said he was the climate president,” Peltier — an Anishinaabe citizen of the Turtle Mountain Band of Chippewa and a member of the Indigenous environmental justice organization Honor the Earth — said outside the White House on Monday. “Now he doesn’t care.” Many climate activists have described an escalating sense of urgency to implement the sweeping changes needed to slow Earth’s warming, highlighted by the recent landmark report from the Intergovernmental Panel on Climate Change. U.N. Secretary General António Guterres called the report a “code red for humanity.” The pace of emissions shows the planet is on track to warm more than two degrees Celsius above preindustrial levels, which could trigger irreversible damage, according to the IPCC report. The Greenland ice sheet could collapse, and sea levels could rise more than six feet. There will be more of the climate-fed fires of this summer, deadly heat waves and devastating floods. Natalie Mebane read the IPCC report and thought of how much ground the climate movement in this country lost under President Donald Trump, whose administration allowed more pollution and weakened protections for wildlife. She worries Republicans will regain power in the 2022 midterms and thinks the slim window from now until then may be the final opportunity to see climate priorities passed through Congress. If not, it could be years before Democrats are in control — wasted time that Mebane fears could cause permanent devastation. “If the Democrats lose a single seat in the Senate, it’s over,” said Mebane, the associate director of U.S. policy for 350.org, an international climate group. “These years that we have right now is the last time that we can even make an impact and influence on climate change before it becomes runaway climate change that we have zero control over.” Biden has tackled greenhouse-gas emissions by proposing new federal goals and mandates to begin shifting the country toward electric cars, rejoined the Paris climate accord and revoked a federal permit for the Keystone XL oil pipeline. But activists point out Biden is still supporting Line 3, a tar-sands oil-pipeline expansion project that will be able to carry 760,000 barrels a day from Canada across northern Minnesota and into Wisconsin. They have called for him to revoke the permit, as he did with Keystone XL, and have protested for months, including on construction sites, chaining themselves to equipment and risking arrest. The White House did not respond to a request for comment. Earlier this month, the Senate approved the $1.2 trillion infrastructure bill with funding to tackle climate change, but many activists said the legislation has fallen short of dramatically addressing goals as lofty as this crisis demands. That does not mean Democrats should pass just any climate legislation, activists say — it has to include the right policies. Compromising on climate, they said, is not good enough. Though the bipartisan infrastructure bill apportions billions of dollars toward funding new public transit and electric-car charging stations, measures that are meant to cut climate-warming emissions, environmental organizations say it does not go far enough. They want to see legislation supporting Biden’s stated goal of replacing 100 percent of lead pipes and the replacement of all diesel school buses with clean electric ones. “It’s hard to square the scale of the problem with the solutions being discussed,” said Lukas Ross, program manager for the Climate and Energy Justice program at Friends of the Earth, another environmental group. “This is not the moment to bargain away the store in the name of passing anything.” Climate groups are focusing on the passage of a second bill through budget reconciliation, a process that would allow Democrats to pass more dramatic climate legislation without Republican support. Democrats in Congress are hoping to work in a clean-energy standard that would compel power providers to shift to wind, solar and other low-emission sources of energy to achieve 80 percent clean electricity by the end of the decade.

#### **US climate action is key to world wide action**

Beeler 19 (Carolyn Beeler; 9/18/19; PRI; *“Top US leadership is 'missing ingredient' in climate change action”*; accessed 8/27/21; <https://www.pri.org/stories/2019-09-18/top-us-leadership-missing-ingredient-climate-change-action>; Carolyn Beeler leads environment coverage for The World. She reports and edits stories focused on the people and places most impacted by climate change, and what they're doing to address it. She has reported from all seven continents and won national and regional awards for her breaking news and in-depth feature reporting. Before joining The World, Carolyn helped pilot the weekly health and science show, The Pulse, at WHYY in Philadelphia, and reported from Berlin for a year as a Robert Bosch Foundation fellow. She studied journalism at Northwestern University and got her start in radio as a Kroc fellow at NPR.) HB

World leaders will meet in New York next week for the United Nations Climate Summit, an event called by the Secretary-General to push for more and faster cuts to global greenhouse gas emissions. Notably missing at the summit: American leadership. Five years ago, a joint climate policy announcement from the US and China paved the way for the Paris climate accord to come to fruition after decades of failed attempts at an international climate pact. Then in June 2017, President Donald Trump announced that he would withdraw the US from the very same agreement his country had helped broker just a few years before. Under the rules of the accord, countries can announce the intention to leave, but must wait two years before being allowed to do so. Two years later, what impact has this policy whiplash had on the climate? Inside the US, that answer is relatively simple to quantify. Across the country, some 4,000 state and local governments, institutions and businesses have declared that, though the federal government intends to withdraw from the Paris climate agreement, they’re still on board with cutting emissions. One of those local governments is in Arlington, Massachusetts, where the town hall was illuminated green after Trump’s 2017 Paris withdrawal announcement. “We’ve come to the realization that if the federal government’s not going to do it, it’s going to fall to the local level,” said Adam Chapdelaine, Arlington’s town manager. “Somebody has to step up and be a leader.” Even before the Paris Agreement, the town has long worked to reduce its greenhouse gas emissions, from switching its street lights to LED bulbs to buying electric vehicles for its official fleet. Residents can opt-in to 100% renewable energy in their homes and the town is advocating for all-electric heating and cooling systems. Since the US federal government reversed its climate change policies, Arlington has gotten perhaps more ambitious: The town’s new high school is being designed to run on geothermal and solar energy and the whole town aims to go carbon-neutral by 2050. These state and local actions are being highlighted as “answering the global call to combat the climate crisis” by a coalition of sub-national actors formed by New York Mayor Michael Bloomberg and former California Gov. Jerry Brown. But these actions have only partly counteracted sweeping federal changes under the Trump administration. Trump has slashed regulations on emissions from power plants, air conditioners and refrigerators, and oil and gas drilling nationwide. He moved to revoke California’s ability to set its own strict vehicle emission rules on Wednesday, highlighting the limits of state-based action on climate change. So how does the emissions balance sheet tally up today, two years after the US backed away from the Paris agreement? Kate Larsen, a director at the independent research firm the Rhodium Group, said US carbon emissions are a few percentage points higher than they would have been if former President Barack Obama-era policies were in place. Projected forward five years, that gap will just grow. “Under the current set of Trump administration policies, the US is on track to achieve only about 14 to 17% emission reductions below 2005 levels in 2025,” Larsen said. That’s about half of the 26 to 28% emission reductions that the US promised in the climate accord. “[It's] a long way from the commitment that Obama reached in Paris,” Larsen said. Scientists say that to limit warming to 1.5 degrees Celsius and avoid the worst impacts of climate change, global emissions must be cut nearly in half by 2030. Inside the US, local action is partly, but not wholly, counteracting federal policies. The bigger question is how much global ambition to tackle the climate crisis will flag if the world’s largest historic emitter is no longer leading the push. Will countries, seeing the US doing less on climate change, do the same themselves? Under Obama, the US put its full diplomatic muscle into getting countries signed on to the Paris Agreement. “If you were a head of state from India, from China, or from anywhere and you were going to meet with the United States, you knew that you'd have to be prepared to speak about climate change and the Paris Agreement,” said Elan Strait, a former climate negotiator on the Paris Agreement who now works at the World Wildlife Foundation. By 2020, countries are requested to announce new carbon cuts as part of the Paris process. Those cuts have to be more ambitious if countries hope to meet the Paris Agreement goal of keeping warming “well below” 2 degrees Celsius and pursue efforts to limit warming to the scientist-recommended 1.5 degree Celsius. “I completely believe that the missing ingredient this time around is the United States leadership driving climate as a head-of-state agenda,” Strait said. Only when those 2020 climate pledges start rolling in will the international community start to see the full impact of the US climate policy reversal.

**Climate change causes extinction – ocean acidification, water and resource wars, econ collapse, and regional conflicts.**

Pachauri and Meyer 15 (Rajendra K. Pachauri Chairman of the IPCC, Leo Meyer Head, Technical Support Unit IPCC were the editors for this IPCC report, “Climate Change 2014 Synthesis Report” <http://epic.awi.de/37530/1/IPCC_AR5_SYR_Final.pdf> IPCC, 2014: Climate Change 2014: Synthesis Report. Contribution of Working Groups I, II and III to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change [Core Writing Team, R.K. Pachauri and L.A. Meyer (eds.)]. IPCC, Geneva, Switzerland, 151 pp)

SPM 2.3 Future risks and impacts caused by a changing climate Climate change will amplify existing risks and create new risks for natural and human systems. Risks are unevenly distributed and are generally greater for disadvantaged people and communities in countries at all levels of development. {2.3} Risk of climate-related impacts results from the interaction of climate-related hazards (including hazardous events and trends) with the vulnerability and exposure of human and natural systems, including their ability to adapt. Rising rates and magnitudes of warming and other changes in the climate system, accompanied by ocean acidification, increase the risk of severe, pervasive and in some cases irreversible detrimental impacts. Some risks are particularly relevant for individual regions (Figure SPM.8), while others are global. The overall risks of future climate change impacts can be reduced by limiting the rate and magnitude of climate change, including ocean acidification. The precise levels of climate change sufficient to trigger abrupt and irreversible change remain uncertain, but the risk associated with crossing such thresholds increases with rising temperature (medium confidence). For risk assessment, it is important to evaluate the widest possible range of impacts, including low-probability outcomes with large consequences. {1.5, 2.3, 2.4, 3.3, Box Introduction.1, Box 2.3, Box 2.4} A large fraction of species faces increased extinction risk due to climate change during and beyond the 21st century, especially as climate change interacts with other stressors (high confidence). Most plant species cannot naturally shift their geographical ranges sufficiently fast to keep up with current and high projected rates of climate change in most landscapes; most small mammals and freshwater molluscs will not be able to keep up at the rates projected under RCP4.5 and above in flat landscapes in this century (high confidence). Future risk is indicated to be high by the observation that natural global climate change at rates lower than current anthropogenic climate change caused significant ecosystem shifts and species extinctions during the past millions of years. Marine organisms will face progressively lower oxygen levels and high rates and magnitudes of ocean acidification (high confidence), with associated risks exacerbated by rising ocean temperature extremes (medium confidence). Coral reefs and polar ecosystems are highly vulnerable. Coastal systems and low-lying areas are at risk from sea level rise, which will continue for centuries even if the global mean temperature is stabilized (high confidence). {2.3, 2.4, Figure 2.5} Climate change is projected to undermine food security (Figure SPM.9). Due to projected climate change by the mid-21st century and beyond, global marine species redistribution and marine biodiversity reduction in sensitive regions will challenge the sustained provision of fisheries productivity and other ecosystem services (high confidence). For wheat, rice and maize in tropical and temperate regions, climate change without adaptation is projected to negatively impact production for local temperature increases of 2°C or more above late 20th century levels, although individual locations may benefit (medium confidence). Global temperature increases of ~4°C or more 13 above late 20th century levels, combined with increasing food demand, would pose large risks to food security globally(high confidence). Climate change is projected to reduce renewable surface water and groundwater resources in most dry subtropical regions (robust evidence, high agreement), intensifying competition for water among sectors (limited evidence, medium agreement). {2.3.1, 2.3.2} Until mid-century, projected climate change will impact human health mainly by exacerbating health problems that already exist (very high confidence). Throughout the 21st century, climate change is expected to lead to increases in ill-health in many regions and especially in developing countries with low income, as compared to a baseline without climate change (high confidence). By 2100 for RCP8.5, the combination of high temperature and humidity in some areas for parts of the year is expected to compromise common human activities, including growing food and working outdoors (high confidence). {2.3.2} In urban areas climate change is projected to increase risks for people, assets, economies and ecosystems, including risks from heat stress, storms and extreme precipitation, inland and coastal flooding, landslides, air pollution, drought, water scarcity, sea level rise and storm surges (very high confidence). These risks are amplified for those lacking essential infrastructure and services or living in exposed areas. {2.3.2} Rural areas are expected to experience major impacts on water availability and supply, food security, infrastructure and agricultural incomes, including shifts in the production areas of food and non-food crops around the world (high confidence). {2.3.2} Aggregate economic losses accelerate with increasing temperature (limited evidence, high agreement), but global economic impacts from climate change are currently difficult to estimate. From a poverty perspective, climate change impacts are projected to slow down economic growth, make poverty reduction more difficult, further erode food security and prolong existing and create new poverty traps, the latter particularly in urban areas and emerging hotspots of hunger (medium confidence). International dimensions such as trade and relations among states are also important for understanding the risks of climate change at regional scales. {2.3.2} Climate change is projected to increase displacement of people (medium evidence, high agreement). Populations that lack the resources for planned migration experience higher exposure to extreme weather events, particularly in developing countries with low income. Climate change can indirectlyincrease risks of violent conflicts by amplifying well-documented drivers of these conflicts such as poverty and economic shocks (medium confidence). {2.3.2} 2010 )

### 3

#### Text – States ought to individually domestically establish single-payer national health insurance.

#### Solves evergreening and drug prices while avoiding our innovation turns.

Narayanan 19 Srivats Narayanan 8-15-2019 "Medicare for All and Evergreening" <https://medium.com/@srivats.narayanan/medicare-for-all-and-evergreening-cb84c930e0ea> (UMKC School of Medicine)//Elmer

Drug companies rake in massive profits. The pharmaceutical industry has some of the largest profit margins among American industries. Unfortunately, pharmaceutical giants don’t always have patients’ best interests in mind — they make a big portion of their money by exploiting the patent process instead of making breakthrough drugs that would meaningfully improve patients’ lives. Pharmaceutical corporations aren’t as innovative as one might expect. Although the Food and Drug Administration (FDA) has been consistently approving new (and expensive) drugs every year, most of these drugs aren’t impacting healthcare much. Many studies have revealed that a whopping 85–90% of new drugs since the mid-1990s “provide few or no clinical advantages.” This is because pharmaceutical firms are spending their time and money on a technique known as “evergreening.” Evergreening is when drug companies produce redundant drugs that are nothing but minor modifications of old drugs. By making slight alterations to their medicines, biotech companies continue to hold patents for drugs with minimal spending on research and development (R&D). Pharmaceutical companies then use those patents to prevent competitors from selling generic versions of their drugs. Without any competition, these corporations get away with ridiculously high drug pricing and can thus make big profits on their drugs. The companies simultaneously justify their absurd drug prices by pointing to the inflated R&D costs of producing new drugs. This excuse has been used time and again by the profit-hungry pharmaceutical industry, and it’s coming at the expense of patients who struggle to afford their medicines. A well-known example of evergreening pertains to the anticonvulsant medication gabapentin, which was first sold by Pfizer under the brand name Neurontin. When the drug became available as a generic medication over a decade ago, Pfizer created a very similar medicine, pregabalin (Lyrica), that didn’t have any significant benefits over the original drug. As a result, Pfizer has kept a control over the market for anticonvulsant drugs with negligible innovation. The drug industry’s reliance on evergreening is undoubtedly stifling innovation. This is where **Medicare for All**, **which would impose the government as the only health insurer**, **would be useful**. **In our current system**, **there are many insurers** **and they each have** **little market power** **and** consequently **little negotiating power** **to reduce** treatment **prices**. **Since the government would have** **consolidated control over healthcare financing** under Medicare for All, **its stronger bargaining power would force drug companies to charge lower prices for their products**. In addition, prescription drugs would be paid for by the government and not by patients under Medicare for All. **Medicare for All would prevent evergreening**. **National healthcare financing** **would align** **how much the government pays a drug company with how much patients benefit** from the company’s drugs. **If a new drug had more clinical benefits** than an older version, **the government would pay more** for it. If a new drug produced the same results as an older version, the government wouldn’t pay more for the new drug. So, Medicare for All would **encourage** pharmaceutical **companies to pursue truly innovative drugs because such drugs would be more profitable**. The policy would incentivize companies to invest in R&D for more useful drugs, instead of just producing redundant and expensive medications. A national healthcare plan would prioritize “patient and community needs” and match up pharmaceutical companies’ interests with actually improving public health. Evergreening has become the name of the game for the pharmaceutical industry. A major solution to the evergreening problem is Medicare for All. **A single-payer system** like Medicare for All **would sharply curtail evergreening**, since drug companies wouldn’t be able to profit from it. Medicare for All would **usher** in **a new era of medical innovation**.

## On

### AT Framing

#### Extinction first under Kant

#### Sequencing – agents must exist to Reason in the first place which means living is a prior question

#### Logic – it would be a contradiction to determine any action’s goodness or badness if all action is impossible because there are not agents to perform those actions.

#### Kant collapses to util

#### Freedom - Maximizing freedom demands an aggregation to determine if an action minimizes or maximizes that freedom since otherwise it’s impossible to understand tradeoffs

#### Maxims - Universal maxims are good or bad based on the consequences of the world where that maxim is true i.e a world where everyone can murder is bad because everyone would die.

#### Kant is wrong

#### Schmagency – Agents can choose to act irrationally and be schmagents instead of agent

#### Tailoring Objection – universal maxims are not concrete which means agents can contort them to fit their specific situations and permit any action.

#### Actor-Specificity – Only util can decipher between tradeoffs, Kant has a weighing mechanism but it’s not enough – Kant freezes action when a perfect duty and a perfect duty are in conflict. Only util can solve for tradeoffs.

### More on framing

#### 2] Neg a priori’s do not negate a) they all assume I didn’t already meet my burden after the ac, b) Resolved is defined as[[1]](#footnote-1) firm in purpose or intent; determined and I’m determined, c) affirm means to express agreement[[2]](#footnote-2) and you already know I do.

#### Neg a priori’s affirm – denying the assumptions of a statement proves it valid – the aff is a set of conditionals since the offense being true relies on the framework b) if the aff is winning, they get the ballot is a tacit ballot conditional which means denying the premise proves the conclusion that I should get the ballot.

#### **Negating affirms because it assumes that the 1ac is a statement that is worthy of contestation which means are arguments are legitimate.**

### 1NC – AT: Pharma Advantage

#### Pharma innovation is high now and strong IP protection are the only incentive for drug innovation.

* Answers Evergreening/Me-Too Drugs

Stevens and Ezell 20 Philip Stevens and Stephen Ezell 2-3-2020 "Delinkage Debunked: Why Replacing Patents With Prizes for Drug Development Won’t Work" <https://itif.org/publications/2020/02/03/delinkage-debunked-why-replacing-patents-prizes-drug-development-wont-work> (Philip founded Geneva Network in 2015. His main research interests are the intersection of intellectual property, trade, and health policy. Formerly he was an official at the World Intellectual Property Organization (WIPO) in Geneva, where he worked in its Global Challenges Division on a range of IP and health issues. Prior to his time with WIPO, Philip worked as director of policy for International Policy Network, a UK-based think tank, as well as holding research positions with the Adam Smith Institute and Reform, both in London. He has also worked as a political risk consultant and a management consultant. He is a regular columnist in a wide range of international newspapers and has published a number of academic studies. He holds degrees from the London School of Economics and Durham University (UK).)//Elmer

The **Current System** Has **Produced a Tremendous Amount of Life-Sciences Innovation** The frontier for biomedical innovation is seemingly limitless, and the challenges remain numerous—whether it comes to diseases that afflict millions, such as cancer or malaria, or the estimated 7,000 rare diseases that afflict fewer than 200,000 patients.24 And while certainly citizens in developed and developing nations confront differing health challenges, those challenges are increasingly converging. For instance, as of this year, analysts expect that **noncommunicable** diseases such as cardiovascular disease and diabetes will account for 70 percent of natural fatalities **in developing countries**.25 Citizens of low- and middle-income countries bear 80 percent of the world’s death burden from cardiovascular disease.26 Forty-six percent of Africans over 25 suffer from hypertension, more than anywhere else in the world. Similarly, 85 percent of the disease burden of cervical cancer is borne by individuals living in low- and middle-income countries.27 To develop treatments or cures for these conditions, novel biomedical innovation **will be needed from everywhere**. Yet tremendous progress has been made in recent decades. To tackle these challenges, the global pharmaceutical industry invested over **$1.36 trillion in R&D** in the decade from 2007 to 2016—and it’s expected that annual R&D investment by the global pharmaceutical industry will reach $181 billion by 2022.28 In no small part due to that investment, **943 new active substances have been introduced** globally over the prior 25 years.29 The U.S. Food and Drug Administration (FDA) has approved more than **500 new medicines since 2000** alone. And these medicines are getting to more individuals: Global medicine use **in 2020 will reach 4.5 trillion doses**, up 24 percent from 2015.30 Moreover, there are an estimated 7,000 new medicines under development globally (about half of them in the United States), with 74 percent being potentially first in class, meaning they use a new and unique mechanism of action for treating a medical condition.31 In the United States, over 85 percent of all drugs sold are generics (only 10 percent of U.S. prescriptions are filled by brand-name drugs).32 And while some assert that biotechnology companies focus too often on “me-too” drugs that compete with other treatments already on the market, the reality is many drugs currently under development are meant to tackle some of the **world’s most intractable diseases**, **including cancer and Alzheimer’s**.33 Moreover, such arguments miss that many of the drugs developed in recent years have in fact been first of their kind. For instance, in 2014, the FDA approved **41 new medicines** (at that point, the most since 1996) many of which were first-in-class medicines.34 In that year, 28 of the 41 drugs approved were considered biologic or specialty agents, and 41 percent of medicines approved were intended to treat rare diseases.35 Yet even when a new drug isn’t first of its kind, it can still produce benefits for patients, both through **enhanced clinical efficacy** (for instance, taking the treatment as a pill rather than an injection, with a superior dosing regimen, **or better treatment** for some individuals who don’t respond well to the original drug) and by generating competition that exerts downward price pressures. For example, a patient needing a cholesterol drug has a host of statins from which to choose, which is important because some statins produce harmful side effects for some patients. Similarly, patients with osteoporosis can choose from Actonel, Boniva, or Fosomax. Or take for example Hepatitis C, which until recently was an incurable disease eventually requiring a liver transplant for many patients. In 2013, a revolutionary new treatment called Solvadi was released that boosted cure rates to 90 percent. This was followed in 2014 by an improved treatment called Harvoni, which cures the Hepatitis C variant left untouched by Solvadi. Since then, an astonishing six new treatments for the disease have received FDA approval, opening up a wide range of treatment options that take into account patients’ liver and kidney status, co-infections, potential drug interactions, previous treatment failures, and the genotype of HCV virus.36 “If you have to have Hepatitis C, now is the time to have it,” as Douglas Dieterich, a liver specialist at the Icahn School of Medicine at Mount Sinai Hospital in New York, told the Financial Times. “We have these marvellous drugs we can treat you with right now, without side effects,” he added. “And this time next year, we’ll have another round of drugs available.”37 Moreover, the financial potential of this new product category has led to multiple competing products entering the market in quick succession, in turn placing downward pressure on prices.38 As Geoffrey Dusheiko and Charles Gore write in The Lancet, “The market has done its work for HCV treatments: after competing antiviral regimens entered the market, competition and innovative price negotiations have driven costs down from the initially high list prices in developed countries.”39 As noted previously, opponents of the current market- and IP-based system contend patents enable their holders to exploit a (temporary) market monopoly by inflating prices many multiples beyond the marginal cost of production. But rather than a conventional neoclassical analysis, an analysis based on “innovation economics” finds it is exactly this “distortion” that is required for innovation to progress. As William Baumol has pointed out, “Prices above marginal costs and price discrimination become the norm rather than the exception because … without such deviations from behaviour in the perfectly competitive model, innovation outlays and other unavoidable and repeated sunk outlays cannot be recouped.”40 Or, as the U.S. Congressional Office of Technology Assessment found, “Pharmaceutical R&D is a risky investment; therefore, high financial returns are necessary **to induce companies to invest** in researching new chemical entities.”41 This is also why, in 2018, the U.S. Congressional Budget Office estimated that because of high failure rates, biopharmaceutical **companies would need to earn a 61.8 percent rate of return on their successful new drug R&D projects in order to match a 4.8 percent after-tax rate of return on their investment**s.42 Indeed, **it’s the ability to recoup fixed costs, not just marginal** costs, through mechanisms such as patent protection that lies at the heart of all innovation-based industries and indeed all innovation and related economic progress. If companies could not find a way to pay for their R&D costs, and could only charge for the costs of producing the compound, **there would be no new drugs developed**, just as there would be no new products developed in any industry. Innovating in the life sciences remains expensive, risky, difficult, and uncertain. Just 1 in 5,000 drug candidates make it all the way from discovery to market.43 A 2018 study by the Deloitte Center for Health Solutions, “Unlocking R&D productivity: Measuring the return from pharmaceutical innovation 2018,” found that “the average cost to develop an asset [an innovative life-sciences drug] including the cost of failure, has increased in six out of eight years,” and that the average cost to create a new drug has risen to $2.8 billion.44 Related research has found the development of new drugs requires years of painstaking, risky, and expensive research that, for a new pharmaceutical compound, takes an average of 11.5 to 15 years of research, development, and clinical trials, at a cost of $1.7 billion to $**3.2 billion**.45 IP rights—including patents, copyrights, and data exclusivity protections—give innovators, whether in the life sciences or other sectors, the **confidence** to undertake the risky and expensive process of innovation, secure in the knowledge they’ll be able to capture a share of the gains from their efforts. And these gains are often only a small fraction of the true value created. For instance, Yale University economist William Nordhaus estimated inventors capture just 4 percent of the total social gains from their innovations; the rest spill over to other companies and society as a whole.46 Without adequate IP protection, private investors would never find it viable to fund advanced research because lower-cost copiers would be in a position to undercut the legitimate prices (and profits) of innovators, even while still generating substantial profits on their own.47 As the report “Wealth, Health and International Trade in the 21st Century” concludes, “Conferring robust intellectual property rights is, in the pharmaceutical and other technological-development contexts, **in the global public’s long-term interests.** Without adequate mechanisms for directly and indirectly securing the private and public funding of medicines and vaccines, research and development communities across the world will lose future benefits that would far outweigh the development costs involved.”48 Put simply, the current market- and IP-based life-sciences innovation system is producing life-changing biomedical innovation. As Jack Scannell, a senior fellow at Oxford University’s Center for the Advancement of Sustainable Medical Innovation has explained, “I would guess that one can buy today, at rock bottom generic prices, a set of small-molecule drugs that has greater medical utility than the entire set available to anyone, anywhere, at any price in 1995.” He continued, “Nearly all the generic medicine chest was created by firms who invested in R&D to win future profits that they tried pretty hard to maximize; short-term financial gain building a long-term common good.”49 For example, on September 14, 2017, the FDA approved Mvasi, the first biosimilar for Roche’s Avastin, a breakthrough anticancer drug when it came out in the mid-1990s for lung, cervical, and colorectal cancer.50 In other words, a medicine to treat forms of cancer that barely existed 20 years ago is now available as a generic drug today. It’s this dynamic that enables us to imagine a situation wherein drugs to treat diseases that aren’t available anywhere at any price today (for instance, treatments for Alzheimer’s or Parkinson’s) might be available as generics in 20 years. But that will only be the case if we preserve (and improve where possible) a life-sciences innovation system that is generally working. The current system does not require wholesale replacement by a prize-based system that—notwithstanding a meaningful success here or there—has produced nowhere near a similar level of novel biomedical innovation.

#### Secondary and Follow-on patents are key.

IP Watch 18 9-21-2018 "Inside Views: Why Follow-On Pharmaceutical Innovations Should Be Eligible For Patent Protection" <https://www.ip-watch.org/2018/09/21/follow-pharmaceutical-innovations-eligible-patent-protection/> (a non-profit independent news service that provides professional coverage of global policymaking on intellectual property and innovation.)//Elmer

Why Protect Follow-On Innovation? The **attack on secondary** pharmaceutical **patents is based** in part **on** the **flawed premise** that **follow-on innovation is of marginal value** at best, and thus less deserving of protection than the primary inventive act of identifying and validating a new drug active ingredient. In fact, **follow-on innovation** **can play** a **critical role in transforming** **an interesting drug candidate into a safe and effective treatment option** for patients. A good example can be seen in the case of **AZT** (zidovudine), a drug ironically described in the Guidelines as the “first breakthrough in AIDS therapy.” AZT **began** its life **as a** failed attempt at a **cancer drug**, and it was **only years later** that its potential **application in the fight against AIDS** was realized. Follow-on research resulted in a method-of-use patent directed towards the use of AZT in the treatment of AIDS, and it was this patent that incentivized the investment necessary to bridge the gap between a promising drug candidate and a safe, effective, and FDA-approved pharmaceutical. Significantly, because of the long lag time between the first public disclosure of AZT and the discovery of its use in the treatment of AIDS, patent protection for the molecule per se was unavailable. In a world where follow-on innovation is unpatentable, there would have been no patent incentive to invest in the development of the drug, and without that incentive AZT might have languished on the shelf as simply one more failed drug candidate. Other examples of important drugs that likely never would have been made available to patients without the availability of a “secondary” patent include **Evista** (raloxifene, used in the treatment of osteoporosis and to reduce the risk of invasive breast cancer), **Zyprexa** (olanzapine, used in the treatment of schizophrenia), and an orally-administrable formulation of the antibiotic cefuroxime. **Pharmaceutical development** **is prolonged and unpredictable**, and frequently **a safe and effective drug** **occurs only as a result of** **follow-on innovation** occurring **long** **after the initial synthesis** and characterization of a pharmaceutically interesting chemical compound. The inventions protected by secondary patents can be just as critical to the development of drugs as a patent on the active ingredient itself. The Benefits of Follow-On Innovation The criticism of patents on follow-on pharmaceutical innovation rests on an assumption that follow-on innovation provides little if any benefit to patients, and merely serves as a pretense for extending patent protection on an existing drug. In fact, there are many examples of follow-on products that represent significant improvements in the safety-efficacy profile. For example, the original formulation of Lumigan (used to treat glaucoma) had an unfortunate tendency to cause severe hyperemia (i.e., redeye), and this adverse event often lead patients to stop using the drug, at times resulting in blindness. Subsequent research led to a new formulation which largely alleviated the problem of hyperemia, an example of the type of follow-on innovation that significantly benefits patients but that which would be discouraged by a patent regime that does not reward follow-on innovation. Follow-on pharmaceutical innovation can come in the form of an extended-release formulation that permits the drug to be administered at less frequent intervals than the original formulation. Critics of secondary patents downplay the significance of extended-release formulations, claiming that they represent nothing more than a ploy to extend patent protection without providing any real benefit to patients. In fact, the availability of a drug that can be taken once a day has been shown to improve patient compliance, a significant issue with many drugs, particularly in the case of drugs taken by patients with dementia or other cognitive impairments. Extended-release formulations can also provide a more consistent dosing throughout the day, avoiding the peaks and valleys in blood levels experienced by patients forced to take an immediate-release drug multiple times a day. Other examples of improved formulations that provide real benefits to patients are orally administrable formulations of drugs that could previously only be administered by more invasive intravenous or intramuscular injection, combination products that combine two or more active pharmaceutical agents in a single formulation (resulting in improved patient compliance), and a heat-stable formulation of a lifesaving drug used to treat HIV infection and AIDS (an important characteristic for use in developing countries with a hot climate).

#### Evergreening is an incoherent concept AND anti-trust solves it

IP Watch 18 9-21-2018 "Inside Views: Why Follow-On Pharmaceutical Innovations Should Be Eligible For Patent Protection" <https://www.ip-watch.org/2018/09/21/follow-pharmaceutical-innovations-eligible-patent-protection/> (a non-profit independent news service that provides professional coverage of global policymaking on intellectual property and innovation.)//Elmer

“Evergreening” – an Incoherent Concept Drug innovators are often accused of using secondary patents to “evergreen” the patent protection of existing drugs, based on an assumption that a secondary patent somehow extends the patent protection of a drug after the primary patent on the active ingredient is expired. As a general matter, this is a false assumption — a patent on an improved formulation, for example, is limited to that improvement and does not extend patent protection for the original formulation. Once the patents covering the original formulation have expired, generic companies are free to market a generic version of the original product, and patients willing to forgo the benefits of the improved formulation can choose to purchase the generic product, free of any constraints imposed by the patent on the improvement. Of course, drug innovators hope that doctors and their patients will see the benefits of the improved formulation and be willing to pay a premium for it, but it is important to bear in mind that ultimately it is patients, doctors, and third-party payers who determine whether the value of the improvement justifies the costs. Of course, this assumes a reasonably well-functioning pharmaceutical market. If that market breaks down in a manner that forces patients to pay higher prices for a patented new version of a drug that provides little real improvement over the original formulation, then it is the deficiency in the market which should be addressed, rather than the patent system itself. For example, if a drug company is found to have engaged in some anticompetitive activity to block generic competition in the market for the original product once it has gone off patent, then antitrust and competition laws should be invoked to address that problem. If doctors are prescribing an expensive new formulation of a drug that provides little benefit compared to a cheaper, unpatented original product, then that is a deficiency in the market that should be addressed directly, rather than through a broadside attack on follow-on innovation. In short, if is found that secondary patents are being used in a manner that creates an unwarranted extension of patent protection, it is that misuse of the patent system which should be addressed directly, rather than through what amounts to an attack on the patent system itself.

### 1N – Biowar Turn

#### Eliminating IPR greenlights access to dangerous information which could allow rogue actors to develop bioweapons immune to vaccines – viral vaccines in particular are high risk

Sandbrink et. al ’21

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There are three dimensions of biological dual-use risks: 1) misuse of ostensibly civilian facilities, 2) misuse of equipment and agents, and 3) generation and dissemination of scientific knowledge with risk of misuse [34]. Historically, the dual-use potential of vaccines was tied to the dual-use potential of vaccine production facilities and equipment for production of threat agents for traditional inactivated or attenuated vaccines. This dual-use potential is illustrated by the historical example of Iraq repurposing fermenters from a veterinary vaccine production plant for botulinum toxin production in 1988.[34], [35] The Soviet Union also planned to use ostensibly civilian vaccine production facilities to produce biological warfare agents in the event of a war with the United States [36].

While over recent decades dual-use risks have generally been considered a niche concern in vaccine development, the focus of dual-use risk from vaccine research has shifted from the misuse of civilian facilities to the generation and dissemination of scientific insights with dual-use potential. One prominent example of vaccine research leading to the dissemination of dual-use insights was the synthesis of horsepox virus and its publication in 2018. This research was directed at the development of a better smallpox vaccine. However, as this was the first account of the synthesis of an orthopoxvirus, a virus in the same family and closely related to variola virus, the agent that causes smallpox, this research has lowered the barrier for individuals seeking to acquire the variola virus which has been eradicated from nature and is only known to exist at two secure repositories in the United States and Russia [37].

The increased concern around dual-use knowledge is driven by the fact that rapid advances in molecular biology, including DNA synthesis and gene-editing, continue to lower the barrier for viral engineering and synthesis [34]. Therefore, the risk from dissemination of dual-use insights on the modification of viral properties like transmissibility and immune evasion is amplified, as such insights might allow actors to create transmissible agents posing global or even existential threats. In comparison, the ability to produce large batches of toxins and non-transmissible viruses could be used to create harm at large but limited scale. While large-scale production has long been considered a key barrier to the weaponisation of existing viruses on the basis of knowledge on historical biological weapons programs, the potential for misuse of production technology would be limited to the proprietor of the facility in question [38], [39]. In contrast, once released into the public, scientific knowledge may inform malicious actors around the globe.

Dual-use aspects of research on novel platform vaccine technologies, which leverage recent advances in viral and nucleic acid synthesis and modification, have not been evaluated sufficiently to date. Hence, we here assess and compare the dual-use risk of different novel and traditional vaccine approaches (Table 1) and propose strategies to minimise biosecurity risks posed by vaccine platform technologies.

Compared to other vaccine approaches, we identify research on viral vector-based platforms as exhibiting relatively high dual-use potential. This is in particular due to the high concern we associate with the generation of knowledge on the modification of viral properties. As we discuss in more detail below, research on viral vector-based vaccines involves viral engineering which may inform modification of concerning agents such as variola virus and creates incentives for the generation of potentially concerning insights on conferring viral immune evasion. We classify research on rational attenuation approaches, which aims to create live attenuated viral vaccines with better genomic stability, as exhibiting medium to high dual-use potential. Research on synonymous codon replacement may not only lead to potential insights on enhancement of virulence, but importantly generates the synthetic biology tools necessary to conduct such enhancement, for example the ability to introduce many mutations simultaneously with high precision [26].

In the following section, we examine the dual-use potential of virally vectored vaccines to identify which particular lines of research raise concerns and how these concerns may be mitigated. Virally vectored vaccines may increase biosecurity risk through two routes: (1) generating particular insights with more direct dual-use potential and (2) spreading viral engineering capabilities which could enable misuse. Assessing this danger means looking at the incremental risk of further research into virally vectored vaccines, but also at the pre-existing margin of similar work and research. If vaccine platforms are a small part of all viral engineering or all immune-evasive work, the additional risk is commensurately less.

The foremost source of biosecurity risk from research on virally vectored vaccines is the creation of insights and knowledge with dual-use potential. For instance, work on virally vectored vaccines may lead to insights into the evasion of pre-existing anti-vector immunity. Such knowledge may be leveraged to engineer pathogens to evade pre-existing, potentially vaccine-induced, immunity.

Pre-existing anti-vector immunity is one of the major limitations of viral vector-based vaccines and therapeutics. Pre-existing vector-specific antibodies may neutralise viral vectors before their entry of host cells and hence may prevent the induction of immune responses against the encoded antigens [[12]](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7904460/#b0060), [[13]](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7904460/#b0065). Such pre-existing immunity may be induced by natural infection or by previous administration of a vector-based vaccine or therapeutic, therefore limiting the reusability of a given vector-based platform [[14]](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7904460/#b0070). Accordingly, there exists a strong incentive to overcome this limitation, and many different approaches to circumventing pre-existing anti-vector immunity have been explored [[40]](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7904460/#b0200). For instance, while adenovirus serotype 5 (Ad5) features desirable properties as a vaccine vector with regard to immunogenicity, there is a high prevalence of pre-existing anti-Ad5 immunity in the human population [[41]](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7904460/#b0205). In order to circumvent this immunity, chimeric vectors have been created where hypervariable regions of Ad5 hexon protein are replaced with those from a less seroprevalent adenovirus serotype such as Ad48 ([Fig. 2](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7904460/figure/f0010/) ) [[15]](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7904460/#b0075). One could readily imagine how experience with and knowledge of the creation of chimeric vectors to evade pre-existing anti-vector immunity could be leveraged to create pathogens able to evade vaccine-induced immunity. The example of the creation of chimeric Ad5 may only be of limited concern from a dual-use perspective as adenovirus is a relatively less concerning pathogen and this approach of creating chimeric vectors is relatively pathogen specific. However, similar modifications of attenuated versions of highly pathogenic viruses may be readily translatable to modifying pathogenic versions of these viruses for evasion of pre-existing or vaccine-induced immunity. For instance, Miest et al created a recombinant oncolytic measles virus capable of evading pre-existing neutralising antibodies through exchange of envelope glycoproteins with those of canine distemper virus [[42]](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7904460/#b0210). Similar insights into the creation of new “serotypes” of pathogenic viruses may emerge from research on overcoming anti-vector immunity in the context of virally vectored vaccines. Furthermore, efforts to overcome pre-existing anti-vector immunity may lead to more universal insights into strategies for evading pre-existing immunity that are applicable and translatable to a wide range of pathogens.

1. http://www.dictionary.com/browse/resolved [↑](#footnote-ref-1)
2. http://www.dictionary.com/browse/affirm [↑](#footnote-ref-2)