# Bioterror 1AC v11

## Advantage

#### [Maassen] Terrorists have long wanted to steal and unleash bioweapons on vulnerable populations.

Maassen 20

Lara Maassen Bioterrorism: A Clear and Imminent Threat [BIOTERRORISM](https://www.counterextremism.com/newsfreetags/bioterrorism) June 25, 2020 [Lara Maassen](https://www.counterextremism.com/people/lara-maassen) — Research Intern The Counter Extremism Project (CEP) is a not-for-profit, non-partisan, international policy organization formed to combat the growing threat from extremist ideologies. <https://www.counterextremism.com/blog/bioterrorism-clear-and-imminent-threat> -CAT

The ongoing COVID-19 pandemic has made the dangers of biological pathogens undeniable to the general public. However, long before this global outbreak, bioterrorism was recognized as a credible threat. Current global events have highlighted that biological warfare is not a myth but a harsh reality. Successive outbreaks caused by newly emerging diseases, transferred from animals to humans through zoonotic spillover, such as Ebola, SARS, and now COVID-19, as well as recent advances in biotechnology giving rise to dual-use biological agents have highlighted the need for greater capacity in public health preparedness, enhanced rigor of bioengineering research guidelines and potential stricter regulations. According to the Centers for Disease Control and Prevention (CDC), bioterrorism is the planned and deliberate release of a pathogenic strain of a microorganism such as a virus, bacteria, or biological toxins, that can sicken or kill people, livestock, or crops. An attack against humans could have the aim of illness, death, fear, societal disruption, and economic damage. Targeting livestock and crops has the potential to destabilize food supply chains, resulting in far reaching consequences on human health and economic output of the agricultural sector. The CDC characterizes biothreat agents according to the severity of impact they would have if released during a bioterror attack. For the purpose of understanding the different kinds of mechanisms that can be implemented as control measures, it is also useful to distinguish biological agents based on their means of transmission. Transmissible agents are those which can spread between humans (e.g. Ebola, SARS, smallpox) or between animals (e.g. foot and mouth disease). A subcategory of this classification includes zoonotic diseases, which are infectious agents that have the ability to “spill over” from animals into humans. Non-transmissible agents can cause severe infections but cannot be spread between infected and susceptible individuals. Bioterrorism is not new. The 2001 Anthrax attacks in the U.S., in which letters laced with anthrax were mailed to U.S. government officials, are no doubt the most famous example of past bioterror attacks. Assaults of this nature, however, date back to the 1300s when Europeans threw plague-infected cadavers over city walls to infect those within. The threat to food supply is no longer an abstract concept either: in the months following the 9/11 attacks, American troops found hundreds of pages of U.S. agricultural documents in al-Qaeda camps. Furthermore, a substantial part of the terrorists’ training manual was reportedly devoted to agricultural terrorism such as the destruction of crops and livestock through pathogens. While these outbreaks would most definitely have far reaching impacts, those that scientists fear most may come from within our own laboratories. The concern of many scientists, including Professor Julia Higgins of the Royal Society in the U.K., is that the findings of life science research could be used to engineer deadly viruses. Initially it seemed as though cutting-edge work such as targeted genetic modifications of microorganisms were out of reach of those who wanted to misuse these technologies. However, as these technologies have progressed, they have become far cheaper and more accessible. Incredibly rapid and profound changes in genetic modifications in bio-molecular engineering and enhanced bio-production technology may make it easier than ever for terrorists to overcome the barriers that prevented the acquisition of biological weapons in the past. Reflecting the seriousness of this threat, in 2005 the National Institute of Allergy and Infectious Disease (NIAD) received funding of $73 million to study the immune response to infectious agents that could be used as potential bioterror agents. Due to the multidisciplinary nature of the field, bioterrorism countermeasures require the skills of experts with vastly different backgrounds and knowledge bases. A multilevel defensive strategy to mitigate the threat of a bioterror attack should be undertaken. This should include legal deterrence, prevention and surveillance, medical management, and dissemination of information to the public. While this is still an emerging field of research and policy development, there are many difficult questions that should be addressed when countering the risk of dual-use biological research. These include: “Should there be regulations on who can access an education in bioengineering or what research the scientific community can publish or even conduct?” There is no easy or clear cut answer to many of these issues, but it is obvious that effective bioterrorism countermeasures must include expertise from a wide range of fields, including medical, security, military, and regulatory countermeasures. The expansion of large corporate biotech companies have made genome editing tools available, even to those without any scientific knowledge or laboratory training. Moving forward, regulations on their products will need to be implemented. Companies as well as research institutions must be expected to carry part of the burden of ensuring that these technologies do not fall into the hands of future bioterrorists. Furthermore, creating awareness among the public and doctors, stock-piling drugs and vaccines, and establishing protocols for preparedness are all key elements of countermeasures but the magnitude of research that is yet to be done in this field should not be cause for panic but rather cause for serious, deliberate and long-term international cooperation. This is by no means a comprehensive summary of the field of bioterrorism, nor was it intended to be. Rather I hope readers have gained an overview of a threat that may have seemed abstract to many. Here I have provided an outline of the main issues surrounding bioterrorism and in the following weeks I will add more entries on specific topics that I have touched on. These will include a more in-depth analysis of the countermeasures that have already been implemented and how these could be further developed, what likely agents of bioterrorism are, what modes of dissemination may be most threatening, and the emerging dangers of dual-use research.

#### [Marx] And now they can.

Marx 20

Willem Marx, 4-22-2020, "COVID-19 has shown U.S., U.K. are vulnerable to biological terrorism, experts say," NBC News, <https://www.nbcnews.com/politics/national-security/experts-covid-19-has-shown-u-s-u-k-are-n1207776> -recut CAT

Former officials in the U.S. and the U.K. warn that the devastating impact of the coronavirus on health care infrastructures and economies may act as a "neon light" for terrorist groups looking to unleash pathogens on Western nations. The pandemic has shown that the West has trouble testing, tracking and treating a pandemic or sustaining a supply of protective equipment for health care workers. It has also raised questions about the security of pathogen research labs worldwide. "Many of the very worst-case characteristics of an intentional event are also being seen in this naturally occurring pandemic," said Dr. Robert Kadlec, the assistant secretary for preparedness and response at the U.S. Department of Health and Human Services. Kadlec, a retired Air Force colonel and surgeon who has spent much of the past two decades focused on biodefense policy and legislation inside the White House, the Defense Department and the Senate, helped the FBI with its investigation into the 2001 "Amerithrax" attacks. The perpetrator in the attacks, which killed five people and infected 17 others, used anthrax from a government lab. "We've come a long way in 20 years, and yet there is so much more that needs to be done," he said. The Trump administration's repeated assertion that the virus may have escaped from a Chinese laboratory has placed the security measures at such facilities worldwide under a microscope. Over the past century, only a couple of dozen countries have developed biological weapons programs. But security experts expressed concern about "dual use" laboratories — where scientists examine pathogens for research purposes and to develop vaccines. Full coverage of the coronavirus outbreak Legislation signed by President Barack Obama obliged the incoming Trump administration to develop a national biodefense strategy, which was published in September 2018. It sought to centralize a federal response team to handle naturally occurring, accidental and deliberate biological threats and to build on previous experiences, including the 2001 anthrax attacks, a 2009 influenza pandemic, the 2014 Ebola epidemic and the more recent fallout from the Zika virus. But it also highlighted the dangers of storing lethal pathogens in laboratories that might lack "appropriate biosecurity measures," which would mean that "actors who wish to do harm" could divert them. The number of these "biosafety level 4" labs, where scientists research easily transmitted pathogens, has multiplied rapidly in recent years. And to many security experts, the locations of some facilities and their insufficient safeguards represent a substantial threat. "You've got to start thinking about the mind of the terrorist or the criminal," said Chris Phillips, the former head of the British government's National Counter Terrorism Security Office, a police unit housed inside the country's domestic intelligence agency, MI5, with responsibility for safeguarding the facilities in the U.K.

#### [Bar-Yam] That risks extinction – global transportation networks and variants prevent burnout and lead to superspreaders.

Bar-Yam 16

Yaneer Bar-Yam 16, physicist and complex systems scientist, Founding President of the New England Complex Systems Institute, Ph.D., S.B., physics, Massachusetts Institute of Technology, “Transition to extinction: Pandemics in a connected world,” NECSI, 7-3-2016, <http://necsi.edu/research/social/pandemics/transition> -recut CAT

[ FIGURE 1 OMITTED ] The video (Figure 1) shows a simple model of hosts and pathogens we have used to study evolutionary dynamics. In the animation, the green are hosts and red are pathogens. As pathogens infect hosts, they spread across the system. If you look closely, you will see that the red changes tint from time to time — that is the natural mutation of pathogens to become more or less aggressive. Watch as one of the more aggressive—brighter red — strains rapidly expands. After a time it goes extinct leaving a black region. Why does it go extinct? The answer is that it spreads so rapidly that it kills the hosts around it. Without new hosts to infect it then dies out itself. That the rapidly spreading pathogens die out has important implications for evolutionary research which we have talked about elsewhere [1–7]. In the research I want to discuss here, what we were interested in is the effect of adding long range transportation [8]. This includes natural means of dispersal as well as unintentional dispersal by humans, like adding airplane routes, which is being done by real world airlines (Figure 2). [ FIGURE 2 OMITTED ] When we introduce long range transportation into the model, the success of more aggressive strains changes. They can use the long range transportation to find new hosts and escape local extinction. Figure 3 shows that the more transportation routes introduced into the model, the more higher aggressive pathogens are able to survive and spread. [ FIGURE 3 OMITTED ] As we add more long range transportation, there is a critical point at which pathogens become so aggressive that the **entire host population** dies. The pathogens die at the same time, but that is not exactly a consolation to the hosts. We call this the phase **transition to extinction** (Figure 4). With **increasing levels of global transportation**, human civilization may be **approaching such a critical threshold**.



Figure 4: The probability of survival makes a sharp transition (red line) from one to zero as we add more long range transportaion (horizontal axis). The right line (black) holds for different model parameters, so we need to study at what point the transition will take place for our world.

In the paper we wrote in 2006 about the dangers of global transportation for pathogen evolution and pandemics [8], we mentioned the risk from Ebola. Ebola is a horrendous disease that was present only in isolated villages in Africa. It was far away from the rest of the world only because of that isolation. Since Africa was developing, it was only a matter of time before it reached population centers and airports. While the model is about evolution, it is really about which pathogens will be found in a system that is highly connected, and Ebola can spread in a highly connected world. The traditional approach to public health uses **historical evidence analyzed statistically** to assess the potential impacts of a disease. As a result, many were surprised by the spread of Ebola through West Africa in 2014. As the connectivity of the world increases, **past experience is not a good guide** to future events. A key point about the phase **transition to extinction** is its **sudden**ness. Even a system that seems stable, can be destabilized by a **few more** long-range connections, and connectivity is continuing to increase. So how close are we to the tipping point? We don’t know but it would be good to find out before it happens. While Ebola ravaged three countries in West Africa, it only resulted in a handful of cases outside that region. One possible reason is that many of the airlines that fly to west Africa stopped or reduced flights during the epidemic [9]. In the absence of a clear connection, public health authorities who downplayed the dangers of the epidemic spreading to the West might seem to be vindicated. As with the choice of airlines to stop flying to west Africa, our analysis didn’t take into consideration how people respond to epidemics. It does tell us what the outcome will be unless we respond fast enough and well enough to stop the spread of future diseases, which may not be the same as the ones we saw in the past. As the world becomes more connected, the dangers increase. Are people in western countries safe because of higher quality health systems? Countries like **the U.S.** have highly skewed networks of social interactions with some very highly connected individuals that can be “**superspreaders**.” The chances of such an individual becoming infected may be low but events like a mass **outbreak pose a much greater risk** if they do happen. If a sick food service worker in an airport infects 100 passengers, or a contagion event happens in mass transportation, an outbreak could very well prove **unstoppable**. Watch this mock video of a pathogen spreading globally through land and air transportation. Long range transportation will continue to pose a threat of pandemic if its impacts cannot be contained.

#### And patent laws delay an effective response to bioterror – 4 warrants

#### A] [Lindsey] Patent trolling

Lindsey 21

Brink Lindsey; Lindsey is a vice president at the Niskanen Center, where his research focuses on policy responses to slow growth and high inequality. Prior to joining Niskanen, Lindsey was vice president for research at the Cato Institute. From 2010 to 2012, he was a senior scholar in research and policy at the Ewing Marion Kauffman Foundation.; 6-3-2021; "Why intellectual property and pandemics don’t mix"; https://www.brookings.edu/blog/up-front/2021/06/03/why-intellectual-property-and-pandemics-dont-mix/, Brookings, accessed 7-31-2021; JPark – recut CAT

When we take the longer view, we can see a fundamental mismatch between the policy design of **intellectual property protection and** the policy requirements of **effective pandemic response**. Although patent law, properly restrained, constitutes one important element of a well-designed national innovation system, the way it goes about encouraging technological progress is singularly ill-suited to the emergency conditions of a pandemic or other public health crisis. Securing a TRIPS waiver for COVID-19 vaccines and treatments would thus establish a salutary precedent that, in emergencies of this kind, governments should employ other, more direct means to incentivize the development of new drugs. Here is the basic bargain offered by patent law: encourage the creation of useful new ideas for the long run by slowing the diffusion of useful new ideas in the short run. The second half of the bargain, the half that imposes costs on society, comes from the temporary exclusive rights, or monopoly privileges, that a patent holder enjoys. Under U.S. patent law, for a period of 20 years nobody else can manufacture or sell the patented product without the permission of the patent holder. This allows the patent holder to block competitors from the market, or extract licensing fees before allowing them to enter, and consequently charge above-market prices to its customers. Patent rights thus slow the diffusion of a new invention by restricting output and raising prices. The imposition of these short-run costs, however, can bring net long-term benefits by sharpening the incentives to invent new products. In the absence of patent protection, the prospect of easy imitation by later market entrants can deter would-be innovators from incurring the up-front fixed costs of research and development. But with a guaranteed period of market exclusivity, inventors can proceed with greater confidence that they will be able to recoup their investment. For the tradeoff between costs and benefits to come out positive on net, patent law must strike the right balance. Exclusive rights should be valuable enough to encourage greater innovation, but not so easily granted or extensive in scope or term that this encouragement is outweighed by output restrictions on the patented product and discouragement of downstream innovations dependent on access to the patented technology. Unfortunately, the U.S. **patent** **system** at present **is out of balance.** Over the past few decades, the expansion of patentability to include software and business methods as well as a general relaxation of patenting requirements have led to wildly excessive growth in these temporary monopolies: the number of patents granted annually has skyrocketed roughly fivefold since the early 1980s. One unfortunate result has been the rise of “non-practicing entities,” better known as **patent trolls**: firms that make nothing themselves but buy up patent **portfolios** and monetize them through aggressive litigation. As a result, a law that is supposed to encourage innovation h**as turned into a legal minefield** for many would-be innovators. In the pharmaceutical industry, firms have abused the law by **piling up patents for** trivial, therapeutically **irrelevant “innovations” that allow them to extend** their **monopolies and keep raising prices** long beyond the statutorily contemplated 20 years. Patent law is creating these unintended consequences because policymakers have been caught in an ideological fog that conflates “intellectual property” with actual property rights over physical objects. Enveloped in that fog, they regard any attempts to put limits on patent monopolies as attacks on private property and view ongoing expansions of patent privileges as necessary to keep innovation from grinding to a halt. In fact, patent law is a tool of regulatory policy with the usual tradeoffs between costs and benefits; like all tools, it can be misused, and as with all tools there are some jobs for which other tools are better suited. A well-designed patent system, in which benefits are maximized and costs kept to a minimum, is just one of various policy options that governments can employ to stimulate technological advance—including tax credits for R&D, prizes for targeted inventions, and direct government support.

#### B] [Bateman] Blocking patents

Bateman 19

Julie Bateman, USE OF BENEFIT CORPORATIONS TO ACCELERATE ACCESS TO AFFORDABLE VACCINES, Boston College Intellectual Property and Technology Forum, 2019. Copyright © Boston College Intellectual Property & Technology Forum, Julie Bateman \* J.D. Candidate, Boston College Law School (expected 2021); B.S., Civil & Environmental Engineering, B.S., International Natural Resource Studies, University of Michigan (2012). -CAT

Although patents incentivize vaccine development, they also introduce barriers to producing generic versions of newly patented vaccines and to developing novel vaccines that rely on existing technologies.57 The twenty-year limited monopoly provided by a patent is often crucial for vaccine developers to recoup their investment from long and expensive development cycles.58 Since the 1990s, developers have increasingly protected their vaccines with patents, such as those covering vaccine compositions, process technologies, methods of using the vaccine, and dose regimens. 59 Patent holders in the vaccine market include academic and research institutions as well as government entities and for-profit companies. 60 There are often dozens of patents held by various entities for a single vaccine. 61 For example, the HPV vaccine is covered by at least **eighty-one U.S. patents held by eighteen entities**, creating an extremely complex patent landscape. 62 Oftentimes, the patent holder licenses the patent for limited uses.63 1. Patents & Licensing for Generic Vaccines Post-TRIPS, DCVMs cannot infringe on patents without permission. 64 As such, to create a generic version of a vaccine, a DCVM must navigate complex patent landscapes and obtain the necessary licenses.65 Generally, pharmaceutical companies voluntarily license their technology to DCVMs for the development of generic versions.66 In such a voluntary licensing agreement, a pharmaceutical company licenses the relevant technologies to the DCVM and transfers know-how for manufacturing processes.67 In exchange, the DCVM usually pays royalties to the pharmaceutical company and is restricted to selling the generic version in its own country or a specific geographic region.68 On the other hand, advocates for greater vaccine accessibility have proposed alternatives such as compulsory licenses and market-based licenses. 69 Some global health professionals have advocated for the issuance of compulsory licenses when pharmaceutical companies refuse to voluntarily license critical technologies, which is authorized by TRIPS at a country’s discretion. 70 Thailand, for example, issued a compulsory license for antiretroviral drugs to combat the AIDS epidemic. 71 Currently, compulsory licenses have not yet been issued for patents covering vaccines. 72 Some have argued that these licenses should be issued for HPV vaccines because HPV disproportionally impacts LMICs and a duopoly has maintained a relatively high price for the vaccines. 73 As a compromise between voluntarily licensing by pharmaceutical companies and compulsory licensing, some have proposed market-based licensing to expand access to affordable vaccines while still compensating developers for their research and development.74 For example, the “Generic Open (GO) License,” a market-based licensing system, proposes that DCVMs should automatically produce generic versions of patented vaccines exclusively in LMICs in exchange for a royalty paid to the innovator company, based on profits within that country.75 2. Patent Blocking for New Vaccines & Product Development Partnerships Patents can impede the development of new vaccines when such vaccines depend on unexpired patented technologies. 76 These patents are often referred to as “blocking patents.”77 This issue arises when universities, national institutes of health, and pharmaceutical companies hold patents on a particular technology that is critical to develop a particular new vaccine.78

**C]** [Mullowney & Harris 1] **Negotiations**

**Mullowney and Harris 13**

Jared Mullowney (Texas Tech University School of Law) and Neil Harris (Texas Tech University School of Law). “Patent Protectability or Public Health?—An Examination of the Patent Compulsory License and Bioterrorism.” Journal of Biosecurity, Biosafety, and Biodefense Law 4(1). June 2013. JDN. https://doi.org/10.1515/jbbbl-2012-0011

If a patent holder sues over royalty amounts and delays the granting of a compulsory license, then the second problem becomes even clearer: in the situation of a bioterrorism attack or a national public health emergency, time is of the essence. Not only would the compensation disputes take up time, but under the TRIPS Agreement, parties are required (unless exempted) to make efforts to reach an agreement on a voluntary license.107 Furthermore, under TRIPS, a compulsory license is not to be granted until “such efforts have not been successful within a reasonable period of time.”108 Here, we run into the similar situation where “reasonable period of time” is not defined. It has been suggested that a reasonable period of time is anywhere from ninety days to six months.109 The timing problem, thus, becomes obvious: in the event of a bioterrorism attack or a public health emergency, waiting ninety days to six months before granting a compulsory license is simply unreasonable. It appears, then, that the patent holder could bring suit for a better royalty determination or the patent holder could delay negotiations; either situation ultimately delays the issue of a compulsory license, potentially leaving the general public at risk of the effects of a bioterrorism attack. While it is unlikely that a pharmaceutical company would willingly delay negotiations, it should be noted that neither the United States Code nor the TRIPS Agreement sets out an express requirement that the negotiations be done in good faith.110

#### D] [Morton and Duan 1] Holdouts

Morton and Duan 20

Christopher J. Morten, Charles Duan Copyright 2020 Christopher J. Morten and Charles Duan. Morten is the deputy director of the Technology Law and Policy Clinic and a Fellow at the Engelberg Center on Innovation Law & Policy at New York University School of Law. He is also a Visiting Fellow of the Yale Global Health Justice Partnership and an Affiliated Fellow of the Information Society Project at Yale Law School. Duan is a Senior Fellow at the R Street Institute, Washington, D.C. Order of authorship was determined by coin flip. P WHO'S AFRAID OF SECTION 1498? A CASE FOR GOVERNMENT PATENT USE IN PANDEMICS AND OTHER NATIONAL CRISES 23 Yale J. L. & Tech. 1 Yale Journal of Law and Technology Fall, 2020 <https://www.kiip.re.kr/webzine/2103/file/kiip_43_file5.pdf> -CAT

In the two months following the September 11 attacks, Congress, the Bush Administration, and the public became aware of a likely possibility of bioterrorism, specifically in the form of anthrax spores being blanketed over a large population.105 At the time, the only approved antibiotic for treating anthrax was ciprofloxacin, sold under the brand name Cipro. The drug quickly became a household name after news anchor Tom Brokaw, himself the recipient of an anthrax-laden letter, ran a television segment ending with the line, “in Cipro we trust.”106 Calls for a federal \*27 stockpile of the drug, however, met a roadblock: the German firm Bayer AG held a patent on ciprofloxacin, but was unable to meet the government's requisition amount for a sufficient stockpile; the company reported that it would require almost two years to manufacture enough.107 While generic manufacturers estimated that they could fulfill the requisition in three months, Bayer refused to license the patent.108 Bayer's patent standoff led to numerous calls to invoke § 1498 to enable generic manufacturing of the drug. Alfred Engelberg, a “smart and tough-as-nails attorney” known for his role in the Hatch-Waxman Act governing pharmaceuticals,109 authored a memorandum to Senator Chuck Schumer, laying out the case for invoking the law and a procedure for doing so. Engelberg proposed that the Department of Health and Human Services provide a blanket government authorization for generic firms to submit federal \*28 bids for procurement.110 Just days later, the senator called for invocation of the law in a press conference,111 leading to national interest in the possibility of invoking government use of Bayer's patent.112 Engelberg's memorandum is succinct in its analysis of § 1498. It simply observes “ample authority” and “overwhelming precedents” supporting the use of § 1498 to procure a stockpile of ciprofloxacin,113 quotes a few cases, and moves on to more detailed analysis of practical questions of regulatory approval and dismissal of ongoing patent infringement litigation. The memorandum does not discuss effects on incentives to innovate or other policy implications of invoking government patent use at all. One can imagine a variety of reasons for this summary treatment of § 1498, but the likeliest is the prior context. In the decades prior to 2001, the appropriateness of § 1498 in the context of federal procurement--in both emergency and non-emergency situations--was settled. A 1958 decision of the Comptroller General addressed the question of whether procurement officers should consider patent or patent license holdings in the course of choosing among bids.114 The Comptroller General's answer was no, based on an understanding that any standard procurement invitation automatically provided the requisite authorization and consent under § 1498. 115 The U.S. government was, and still is, free to procure whatever it needs from whomever it wants without permission from patent holders. The Comptroller General's decision \*29 sparked a wave of patentee-friendly legislative proposals across the 1960s to restrict the U.S. government's patent-blind procurement practice; none of the bills succeeded.116 As government procurement officers purchased patented technologies again and again in subsequent decades, case law confirmed repeatedly that § 1498 is automatically invoked and “the patentees' sole remedy [is] a suit against the United States in the Court of Claims.”117 Given this long-settled federal policy of using § 1498 as a routine part of government contracting, there was no need to treat in depth the question of using § 1498 for procuring ciprofloxacin. In the wake of Senator Schumer's call, Bayer rapidly moved to oppose any invocation of § 1498. Bayer immediately launched a comprehensive branding campaign (including a $3 million buy for full page advertising in all the major papers) promising that the company would “stand ready to support the United States government providing Cipro to meet emergency needs.”118 Bayer and other pharmaceutical industry representatives also lobbied Congress and the administration heavily “to provide reassurance of Bayer's commitment.”119 Bayer also attempted to paint government patent use as misguided, even illegitimate, “emphasiz[ing] the importance of patents for research and investment.”120 Remarkably, the Bush Administration initially sided with Bayer on the aptness of § 1498. Likely concerned about contradicting its international opposition to compulsory patent licensing--having rejected calls to invoke compulsory licensing on HIV/AIDS drug patents in the Global South as the landmark 2001 Doha Declaration was being \*30 negotiated121--the Bush administration publicly rebuked calls to invoke the statute. A spokesman for HHS said that “[w]e don't feel there's a need to lift the patent at this time,”122 and HHS Secretary Tommy Thompson more bluntly rejected calls to “break” Bayer's patent: “No. 1, it's illegal,” the Wall Street Journal quoted him as saying.123 As pressure mounted, though, the government appeared to change course: Secretary Thompson “threatened to bypass Bayer's patent” and was “ready to ask Congress for special legislation that would make the government exempt from paying any damages to Bayer for breaking the patent.”124 Ultimately, Bayer agreed to make substantial concessions in negotiations with the government, including massive increases in manufacturing and a price cut on ciprofloxacin to $0.95 or less per pill, compared to $1.83 that the government had been paying previously and the wholesale price of $4.67.125 What role § 1498 played in that ultimate deal is a Rashomon question with at least three possible answers. The majority view, as reported by almost all commentators at the time and subsequently, was that Thompson did indeed threaten to invoke § 1498, which “provide[d] the government with the necessary leverage” to force Bayer into a concession.126 Indeed, Bayer's financial statements \*31 noted that “in response to anthrax bioterror attacks in the United States in 2001, the U.S. and Canadian governments contemplated compulsory licensing of our ciprofloxacin antibiotic,” which seems to confirm that § 1498 did come up in Bayer's negotiations.127 Thompson's general counsel Alex Azar, on the other hand, contended that Thompson “never threatened to break Bayer's patent,” though Thompson did advise Bayer that he was willing to ask Congress for “authority to procure generics” in a manner that was “hardly the same thing as threatening a company.” Azar repeated that statement at his 2018 nomination for HHS Secretary.128 Bayer's CEO Helge Wehmeier advanced a third view and claimed that Thompson had not even gone that far--according to Wehmeier, the negotiation over Cipro took “less than ten minutes” with no invocation of leverage, from § 1498 or Congress.129 The Wehmeier and Azar views that § 1498 played no role in the negotiations have found little traction among historians. Even those critical of § 1498 generally accept that HHS invoked it or some other threat of government patent use en route to negotiating a favorable \*32 deal for the government,130 and Azar's letter appears to not to have been cited in any subsequent literature.131 But Bayer's massive public relations push, coupled with the Bush Administration's initial vocal disavowal of the appropriateness of § 1498, seems to have had an important (and underacknowledged) legacy, shifting views of § 1498 from a routine, beneficial government power commonplace in federal procurement to a dramatic incursion too extreme for use even in the face of a credible terrorist threat--or even “illegal.” Legal observers at the time were left “scratching their heads” over this change.132 This history suggests that contemporary views of § 1498 are of relatively recent vintage, rather than being any long-held understanding about the statute. The now widespread “conventional wisdom” that § 1498 is an “exceptional” remedy to be used only in a vanishingly small set of circumstances133 seems to be a product of just the last two out of the eleven decades the statute has been on the \*33 books. For much more of our nation's history, § 1498 was used routinely, especially in times of national emergency. At the same time, if Engelberg and Schumer had not put § 1498 on the table, Bayer may not have made that massive public relations push or been as conciliatory to the federal government as it eventually was.

## Plan

#### The member nations of the World Trade Organization ought to reduce intellectual property protections for medicines through compulsory licensing of bioterror countermeasures without consultation or compensation to the holder.

## Solvency

#### 1] [Park] That cuts through obstacles and enables rapid responses – we have a bivalent vaccine against anthrax and smallpox ready to go right now, but it would infringe on multiple national and international patents that don’t expire until 2036.

Park et al 21

Deok Bum Park, Bo-Eun Ahn, Hosun Son, Young-Ran Lee, Yu-Ri Kim, Su Kyoung Jo, Jeong-Hoon Chun, Jae-Yon Yu, Myung-Min Choi & Gi-eun Rhie Construction of a bivalent vaccine against anthrax and smallpox using the attenuated vaccinia virus KVAC103 BMC Microbiology volume 21, Article number: 76 (2021) <https://bmcmicrobiol.biomedcentral.com/articles/10.1186/s12866-021-02121-5> -CAT

Anthrax and smallpox are high-risk infectious diseases, and considered as potential agents for bioterrorism. To develop an effective countermeasure for these diseases, we constructed a bivalent vaccine against both anthrax and smallpox by integrating a gene encoding protective antigen (PA) of Bacillus anthracis to the genome of the attenuated vaccinia virus strain, KVAC103. Results Immunization with this bivalent vaccine induced antibodies against both PA and vaccinia virus in a mouse model. We also observed that the efficacy of this vaccine can be enhanced by combined immunization with immunoadjuvant-expressing KVAC103. Mouse groups co-immunized with PA-expressing KVAC103 and either interleukin-15 (IL-15) or cholera toxin subunit A (CTA1)-expressing KVAC103 showed increased anti-PA IgG titer and survival rate against B. anthracis spore challenge compared to the group immunized with PA-expressing KVAC103 alone. Conclusions We demonstrated that the attenuated smallpox vaccine KVAC103 is an available platform for a multivalent vaccine and co-immunization of immunoadjuvants can improve vaccine performance. Background Bacillus anthracis and Variola virus are causative agents of anthrax and smallpox, respectively, and representative pathogens that can be possibly utilized as bioterrorism or biological weapons. Development of effective medical countermeasures against these pathogens is a national task of high priority [1, 2]. The biological attack in 2001 by B. anthracis spores via the US postal system has prompted the need to develop vaccines and therapeutics against anthrax [1]. Protective antigen (PA) is one of the major component of anthrax toxin, and also a principal ingredient of two licensed anthrax vaccines, Anthrax Vaccine Adsorbed (AVA) and Anthrax Vaccine Precipitated (AVP) [3]. Recently, a recombinant PA protein vaccine is being developed by Korea Centers for Disease Control (KCDC), and clinical trials are in progress [4, 5]. Although endemic smallpox was declared eradicated since the last case observed in 1977, Variolar virus still remains a potential biological weapon [2], and smallpox vaccines have been stockpiled for strategic use in some nations. To reduce side effects of conventional smallpox vaccines, attenuated vaccinia virus strains have been investigated in various ways [6]. KVAC103 is an attenuated vaccinia virus developed by KCDC [7]. Interleukin-15 (IL-15) is a cytokine involved in the proliferation and maintenance of CD8+ memory T cells, and has been suggested as an effective vaccine adjuvant [8, 9]. Previous studies on HIV-1 vaccine demonstrated that co-immunization of IL-15 strongly increased antigen-specific memory T cells and long-term immunity [10, 11]. Smallpox vaccines with integrated IL-15, tested in a mouse model, showed increased and prolonged cellular and humoral immunity [12]. This IL-15-containing smallpox vaccine also has been applied in a multivalent influenza vaccine [13]. Co-administration of IL-15 with staphylococcal enterotoxin B vaccine increased the number of dendritic cells in a mouse model [14]. Cholera toxin (CT) also has long been investigated as an efficient immunoadjuvant. The toxin is composed of subunit A and B, and subunit A contains two fragments, A1 and A2 [15]. The ADP-ribosyltransferase activity of cholera toxin subunit A1 (CTA1) is known to be important for enhancing immune responses [16]. The effect of CTA1 as an immunoadjuvant has been demonstrated against numerous pathogens, such as influenza A virus, HIV, Helicobacter pylori, and Mycobacterium tuberculosis [17,18,19,20]. Vaccinia virus is a popular platform for gene transfer and multivalent vaccine against various diseases [21, 22]. In a previous study, a dual vaccine for smallpox and anthrax has been developed by inserting PA gene of B. anthracis into Wyeth or modified vaccinia Ankara (MVA) strain [23]. A viral vector system that utilizes KVAC103 as a gene delivery system and a multivalent vaccine has been previously invented [7, 24]. In this study, we constructed a bivalent vaccine candidate against both smallpox and anthrax, by integrating a recombinant anthrax PA-encoding gene into KVAC103, using a viral vector pVVT1-EGFP-C7L. We examined the protective efficacy of KVAC103-derived bivalent vaccine in a mouse model. In addition, we observed that the vaccine supplemented with immunoadjuvant-expressing vaccinia viruses can increase immune response against anthrax. Results A human codon-optimized PA was cloned into viral vector pVVT1 to generate smallpox/anthrax dual vaccine candidate. A signal peptide derived from the tissue plasminogen activator was attached to the N-terminal of PA (thPA). We also constructed viral vector clones encoding a human IL-15 (hIL15) or a human codon-optimized CTA1 (hCTA1) gene. The viral vectors were integrated into the KVAC103 genome by homologous recombination at the thymidine kinase (TK) gene site (Fig. 1). Fig. 1 figure1 A diagram of viral vector construction. Human codon-optimized genes encoding PA with a signal peptide (MDAMKRGLCCVLLLCGAVFVSP) derived from the tissue plasminogen activator polypeptide (thPA), IL-15 (hIL15), or CTA1 (hCTA1) were cloned into pVVT1-EGFP-C7L. The GeneBank sequence ID for PA, IL-15, and CTA1 are AAA22637.1, NP\_000576.1, and CAA24995.1, respectively. The expected molecular weight of integrated thPA, IL-15, and CTA1 are 81 kDa (757 aa), 18 kDa (162 aa), and 29 kDa (258 aa), respectively. Viral vector constructs are integrated into KVAC103 genome by homologous recombination at TK gene site Full size image Protein expression of PA and CTA1 in the dual vaccine candidate viruses were confirmed by immunoblot assay (Fig. 2)a. PA and CTA1 were detected in virus-infected cell lysates. This indicates that cells infected by KVAC-thPA-C7L or KVAC-hCTA1-C7L viruses properly express PA or CTA1, respectively. The IL-15 ELISA result shows that cells infected by KVAC-hIL15-C7L also secreted IL-15 in vitro (Fig. 2b). Fig. 2 figure2 Expression of integrated proteins in vitro. a The expression of PA and CTA1 was detected by immunoblot assay in cell lysates. Vero cells were infected with KVAC-thPA-C7L and KVAC-CTA1-C7L for 48 h, and 50 μg of cell lysates from the infected cells were analyzed. The molecular weights from a size marker are indicated on the left. b The expression level of IL-15 was detected by ELISA. The IL-15 expression levels of infected Vero cells with KVAC103 derivatives were determined by the IL-15 ELISA kit (Biolegend). The bars on the graph indicates means of IL-15 expression levels from duplicated results in the same experiments, and the error bars stand for the standard error of the mean (\*\*\*P < 0.001). NS, not significant. One-way ANOVA was applied for analysis Full size image In a preliminary experiment, we observed that repeated vaccination in 3 week interval increased the anti-PA antibody titer around 10-fold compared to single vaccination (data not shown). The in vivo efficacy of the dual vaccine candidate with or without adjuvant-expressing viruses was estimated in a mouse model (Fig. 3). We immunized A/J mice (n = 8) with our vaccine candidate KVAC-thPA-C7L with or without adjuvant expressing viruses 2 times with a 3-week interval. The anti-PA antibody levels of all groups immunized with KVAC-thPA-C7L were increased compared to the groups immunized with the adjuvant only (KVAC-hIL15-C7L or KVAC-hCTA1-C7L). Mouse groups vaccinated with KVAC-thPA-C7L plus an immunoadjuvant-containing strain (KVAC-hIL15-C7L or KVAC-CTA1-C7L) exhibited higher mean values of antibody titers compared to the group immunized with KVAC-thPA-C7L only (Fig. 3a). Except the two outliers which are extraordinarily high in the group immunized with KVAC-thPA-C7L only in Fig. 3a (29,800 and 30,600), the mean values of anti-PA antibody titer are significantly increased in the mouse groups immunized with both KVAC-tPA-C7L and adjuvant-expressing strains (One-way ANOVA, p value < 0.01). Fig. 3 figure3 Immunogenicity and protective efficacy of the bivalent vaccine with or without adjuvant-expressing viruses in a mouse model. a Anti-PA IgG titers of individual mice in 5 groups (n = 8 for each group) were determined by ELISA. The Y-axis represents EC50 values. The horizontal bars indicate mean of individual groups (for KVAC-thPA-C7L, the mean value calculated except the two outliers). The error bars represent standard error of the mean. The asterisks (\*\*) represent significant differences between indicated groups in statistical analysis (\*\*P < 0.01). NMS, normal mouse sera. b Anti-viral antibody titers were determined by PRNT assay. The Y-axis represents PRNT50, the reciprocal of the dilution factor of sera reducing plaque formation in half. The bars represent arithmetic means of results from two independent assays with pooled sera of individual groups (eight mice per group) and the error bars represent standard error of the mean (\*\*\*P < 0.001). NS, not significant. NMS, normal mouse sera. c Immunized mice were challenged with 50 × LD50 of B. anthracis Sterne spores by s.c. injections. Survival rates of 5 groups (n = 8 for each group) were observed for 14 days. The p-value between KVAC-thPA-C7L and KVAC-C7L with immunoadjuvant only (KVAC-hIL-C7L, KVAC-hCTA1-C7L) is lower than 0.001 and indicated as \*\*\*. The p-value between KVAC-thPA-C7L and both KVAC-C7L with PA and immunoadjuvant (KVAC-thPA-C7L + KVAC-hIL-C7L, KVAC-thPA-C7L + KVAC-hCTA1-C7L) is lower than 0.05 and indicated as \* Full size image Neutralizing antibodies against vaccinia virus in mouse sera were measured by PRNT assay. Unlike the anti-PA antibodies, production of neutralizing antibodies against vaccinia virus does not appear to be significantly affected by the presence of immunoadjuvant (Fig. 3b). In a previous study, IL-15 expressing vaccinia virus induced increased neutralizing antibodies compared to the control vaccinia virus in a mouse model [12]. In our experiment, the effect of adjuvants was not observed and all the sera immunized with the constructs induced similar level of neutralizing antibodies. Immunized mice were challenged with B. anthracis Sterne spores 3 weeks after the final vaccination. Survival rates were monitored for 2 weeks. Mice immunized with adjuvant only were all dead within a week. In the group immunized with KVAC-thPA-C7L only, 62.5% of mice survived, while groups immunized with both KVAC-thPA-C7L and immunoadjuvant expressing virus (KVAC-hIL15-C7L or KVAC-CTA1-C7L) were fully protected from the challenge (Fig. 3c). The result indicates that enhanced immunity achieved by co-expression of adjuvant can protect the mice more effectively against anthrax. Discussion Poxviruses have been often used as a vector system for vaccines because of their large DNA genome and convenience in manipulation [21, 22]. In a previous study, engineered vaccinia strains expressing both PA and IL-15 showed enhanced immunogenicity against B. anthracis compared to the conventional anthrax vaccine AVA in animal test [23]. Our result presented that the co-expression of IL-15 in KVAC103 also enhanced protective efficacy of our bivalent vaccine. Co-expression of CTA1 induced immune response against the PA-expressing vaccine in the similar level to IL-15. Our result demonstrated that co-immunization of CTA1, as well as IL-15, was effective enough to enhance the immune responses against PA and reconfirmed that CTA1 is a suitable adjuvant for multivalent vaccines derived from KVAC103. This result is the first observation of the effect of CTA1 as an immunoadjuvant in a viral vaccine system. Conclusion In summary, we explored the possibility of developing a bivalent vaccine using KVAC103, an attenuated vaccinia virus strain. Like other vaccinia virus strains previously utilized, it is confirmed that KVAC103 also can serve as a useful platform for multivalent vaccines. In addition, the vaccine can be further effective with the supplement of cytokines or adjuvants. Methods Cell and virus Vero cell (African green monkey kidney cell) was purchased from the American Type Culture Collection (ATCC, USA). Cells were grown in Opti-Eagle’s Minimum Essential Medium (Opti-MEM, Invitrogen) supplemented with 2% heat-inactivated fetal bovine serum (FBS, Invitrogen), incubated at 37 °C, and humidified with 5% CO2. The attenuated vaccinia virus strain KVAC103 and the viral vector pVVT1-EGFP-C7L were provided by Korea National Institute of Health (KNIH). This vector contains the vaccine virus C7L gene which encodes interferon antagonist, and this is one of the 26 genes defective in KVAC103 compared to its ancestor strain. This gene is required for enhanced viral reproduction [24]. Construction of anthrax/smallpox dual vaccine candidate vectors Viral vector constructs were generated using the pVVT1-EGFP-C7L vector [24] as a template (Fig. 1). Human IL-15 gene and human codon-optimized B. anthracis PA and CTA1 genes were synthesized (Bioneer). The synthesized genes were cloned into the vector using SfiI restriction enzyme site. The constructed vectors were mixed with Lipofectamine (Invitrogen) and transfected into KVAC103-infected Vero cells. Single plaques were isolated from the original infected cells and verified using PCR. The primer sequences used for verification were 5′-TTT GAA GCA TTG GAA GCA ACT-3′ and ‘5’-ACG TTG AAA TGT CCC ATC GAG T-3′. Virus preparation Viruses were infected to mono-layered Vero cells with 0.01 MOI. The virus-infected cell media were harvested when more than 80% of total cells showed cytopathic effect. From the harvested culture supernatant, viruses were collected by ultra-centrifugation. The pellet was resuspended in 1× PBS, pH 7.0 (Gibco). The concentration of viral particles was determined by the standard plaque assay. The viruses were infected the Vero cells overlaid on 6-well plates for 2 days. The plate were staining with crystal violet and the plaque numbers on each well were counted. Western blot analysis Virus-infected Vero cells or their culture supernatants were lysed in 1× RIPA buffer (G-Bioscience) containing 1% PMSF (Theromfisher Scientific) at 4 °C. Fifty μg of protein from each cell lysate was resolved on denaturing polyacrylamide gel electrophoresis (PAGE) and transferred to polyvinylidene difluoride (PVDF) membrane (Amersham). Expression levels of PA and CTA1 proteins were detected using mouse monoclonal antibodies against PA and cholera toxin, respectively (Abcam, 1:1000), and horse radish peroxide (HRP)-conjugated secondary antibodies (Abcam, 1:3000). Mouse immunization and serum collection Female A/J mice (5-week old) were purchased from SLC, Inc. (Japan) and housed in an animal biosafety level 2 (ABL2) facility in KCDC. Mice were immunized with the vaccine candidate virus (5 × 107 pfu/mouse) with or without the adjuvant-expressing virus (5 × 107 pfu/mouse) 2-times at 3-week intervals subcutaneously (s.c.) with 8 mice as a group. Mice sera were collected 20 days after final immunization to measure anti-PA IgG and vaccinia virus plaque reduction neutralizing antibody titers. The schematic view of mouse immunization and serum collection is in Fig. 4. Fig. 4 figure4 A Schematic view of the animal experiment. Mice were immunized two times with 3 weeks interval and sera were collected by bleeding 20 days after the last vaccination. One day after bleeding, mice were challenged with anthrax spores. Survival was observed for 14 days Full size image Enzyme-linked immunosorbent assay (ELISA) The anti-PA IgG titers of mice sera were determined by ELISA as previously described with some modifications [25]. Briefly, 96 well plates were coated with 1 μg/ml of recombinant PA (Green Cross, Korea). Mouse sera were diluted from 1:100 to 1:204800 and loaded to each well, incubated for 1 h at 37 °C. Horseradish peroxidase-conjugated anti-mouse IgG goat antibody (Invitrogen) and 3,3`,5,5`-tetramethylbenzidine (TMB) substrate were used for detection. The optical density of each well was measured at 450 nm and the half maximal effective concentration (EC50) was calculated by 4-parameter logistic equation regression using SoftMaxPro5.3 (Molecular Device, USA). The data were analyzed and visualized using GraphPad Prism 5. The IL-15 expression level of KVAC103 derivatives were determined by the IL-15 ELISA kit (Biolegend) according to the manufacturer’s protocol. Vero cells were infected with viruses of 0.01 MOI. Cell lysates were collected 2 days after infection and analyzed. Plaque reduction neutralization test (PRNT) Serial two-fold dilutions of heat-inactivated mouse sera were mixed with vaccinia virus Lister strain of approximately 50 plaque forming units (PFU). After 2 h incubation at 37 °C, the serum and virus mixtures were inoculated onto monolayered Vero cells. After two days incubation at 37 °C with 5% CO2, cells were fixed and stained using a mixture of crystal violet and formalin for 10 min. Stained plates were dried in air at room temperature and the plaque numbers were counted. The neutralizing antibody titer was defined as the reciprocal of dilution factor that reduced plaque numbers in half (50%) compared to a serum-free control (PRNT50). B. anthracis spore challenge Immunized mice were challenged with 50-fold of lethal dose 50 (LD50) of B. anthracis Sterne spore by s.c. injections. Survival of the mice was monitored for 14 days as described in Fig. 4. Spores were prepared according to a previous study [26]. The LD50 determined by Reed-Muench method [27] in A/J mice model via s.c. route was 1794 spores. Survived animals were euthanized using CO2 gas. Animal study protocols (KCDC-102-16-2A and KCDC-039-17-2A) were approved by the Institutional Animal Care and Use Committee (IACUC) of Korea Centers for Disease Control and Prevention (KCDC). All procedures involved in the housing and care of animal strictly followed guidelines and requirements of the IACUC. Statistical analysis The Statistical analysis was performed using GraphPad Prism 5. To analyze the anti-PA ELISA titer, One-way ANOVA followed by Tukey’s post hoc test were used to evaluate the difference between groups. To analyze the survival rate, Kaplan-Meier survival plots were evaluated with the log-rank test. Availability of data and materials The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request. References 1. Russell PK. Project BioShield: What It Is, Why It Is Needed, and Its Accomplishments So Far. Clin Infect Dis. 2007;45(Supplement\_1):S68–72. Article Google Scholar 2. Cieslak TJ, Christopher GW, Kortepeter MG, Rowe JR, Pavlin JA, Culpepper RC, Eitzen EM Jr. Immunization against potential biological warfare agents. Clin Infect Dis. 2000;30(6):843–50. CAS Article Google Scholar 3. Cybulski RJ Jr, Sanz P, O'Brien AD. Anthrax vaccination strategies. Mol Asp Med. 2009;30(6):490–502. CAS Article Google Scholar 4. Rhie GE, Park YM, Chun JH, Yoo CK, Seong WK, Oh HB. Expression and secretion of the protective antigen of Bacillus anthracis in Bacillus brevis. FEMS Immunol Med Microbiol. 2005;45(2):331–9. CAS Article Google Scholar 5. Kang CK, Kim NH, Kim CJ, Rhie GE, Jo SK, Ahn M, Kang J, Choe PG, Park WB, Kim NJ, et al. Immunogenicity and safety of a novel recombinant protective antigen anthrax vaccine (GC1109), a randomized, single-blind, placebo controlled phase II clinical study. Vaccine. 2019;37:3820–4. CAS Article Google Scholar 6. Kennedy RB, Lane JM, Henderson DA, Poland GA. 54 - Smallpox and Vaccinia. In: Plotkin SA, Orenstein WA, Offit PA, Edwards KM, editors. Plotkin's Vaccines (Seventh Edition): Elsevier; 2018. p. 1001–30. e1012. https://doi.org/10.1016/B978-0-323-35761-6.00054-7. https://www.sciencedirect.com/science/article/pii/B9780323357616000547. 7. Lee YJ, Son HS, Yeo SG, Yoo JS, Lee SW. Development of viral vector using attenuated Vaccinia virus strain, KVAC103. Public Health Weekly Report, KCDC. 2016;9(38):755–9. Google Scholar 8. Tovey MG, Lallemand C. Adjuvant activity of cytokines. Methods Mol Biol. 2010;626:287–309. CAS Article Google Scholar 9. Perera PY, Lichy JH, Waldmann TA, Perera LP. The role of interleukin-15 in inflammation and immune responses to infection: implications for its therapeutic use. Microbes Infect. 2012;14(3):247–61. CAS Article Google Scholar 10. Calarota SA, Dai A, Trocio JN, Weiner DB, Lori F, Lisziewicz J. IL-15 as memory T-cell adjuvant for topical HIV-1 DermaVir vaccine. Vaccine. 2008;26(40):5188–95. CAS Article Google Scholar 11. Oh S, Berzofsky JA, Burke DS, Waldmann TA, Perera LP. Coadministration of HIV vaccine vectors with vaccinia viruses expressing IL-15 but not IL-2 induces long-lasting cellular immunity. Proc Natl Acad Sci U S A. 2003;100(6):3392–7. CAS Article Google Scholar 12. Perera LP, Waldmann TA, Mosca JD, Baldwin N, Berzofsky JA, Oh S. Development of smallpox vaccine candidates with integrated interleukin-15 that demonstrate superior immunogenicity, efficacy, and safety in mice. J Virol. 2007;81(16):8774–83. CAS Article Google Scholar 13. Valkenburg SA, Li OT, Mak PW, Mok CK, Nicholls JM, Guan Y, Waldmann TA, Peiris JS, Perera LP, Poon LL. IL-15 adjuvanted multivalent vaccinia-based universal influenza vaccine requires CD4+ T cells for heterosubtypic protection. Proc Natl Acad Sci U S A. 2014;111(15):5676–81. CAS Article Google Scholar 14. Saikh KU, Kissner TL, Nystrom S, Ruthel G, Ulrich RG. Interleukin-15 increases vaccine efficacy through a mechanism linked to dendritic cell maturation and enhanced antibody titers. Clin Vaccine Immunol. 2008;15(1):131–7. CAS Article Google Scholar 15. Agren L, Lowenadler B, Lycke N. A novel concept in mucosal adjuvanticity: the CTA1-DD adjuvant is a B cell-targeted fusion protein that incorporates the enzymatically active cholera toxin A1 subunit. Immunol Cell Biol. 1998;76(3):280–7. CAS Article Google Scholar 16. Agren LC, Ekman L, Lowenadler B, Nedrud JG, Lycke NY. Adjuvanticity of the cholera toxin A1-based gene fusion protein, CTA1-DD, is critically dependent on the ADP-ribosyltransferase and Ig-binding activity. J Immunol. 1999;162(4):2432–40. CAS PubMed Google Scholar 17. Eliasson DG, El Bakkouri K, Schon K, Ramne A, Festjens E, Lowenadler B, Fiers W, Saelens X, Lycke N. CTA1-M2e-DD: a novel mucosal adjuvant targeted influenza vaccine. Vaccine. 2008;26(9):1243–52. CAS Article Google Scholar 18. Sundling C, Schon K, Morner A, Forsell MNE, Wyatt RT, Thorstensson R, Hedestam GBK, Lycke NY. CTA1-DD adjuvant promotes strong immunity against human immunodeficiency virus type 1 envelope glycoproteins following mucosal immunization. J Gen Virol. 2008;89(Pt 12):2954–64. CAS Article Google Scholar 19. Akhiani AA, Stensson A, Schon K, Lycke N. The nontoxic CTA1-DD adjuvant enhances protective immunity against helicobacter pylori infection following mucosal immunization. Scand J Immunol. 2006;63(2):97–105. CAS Article Google Scholar 20. Andersen CS, Dietrich J, Agger EM, Lycke NY, Lovgren K, Andersen P. The combined CTA1-DD/ISCOMs vector is an effective intranasal adjuvant for boosting prior Mycobacterium bovis BCG immunity to Mycobacterium tuberculosis. Infect Immun. 2007;75(1):408–16. CAS Article Google Scholar 21. Altenburg AF, Kreijtz JH, de Vries RD, Song F, Fux R, Rimmelzwaan GF, Sutter G, Volz A. Modified vaccinia virus Ankara (MVA) as production platform for vaccines against influenza and other viral respiratory diseases. Viruses. 2014;6(7):2735–61. CAS Article Google Scholar 22. Gomez CE, Najera JL, Krupa M, Esteban M. The poxvirus vectors MVA and NYVAC as gene delivery systems for vaccination against infectious diseases and cancer. Curr Gene Ther. 2008;8(2):97–120. CAS Article Google Scholar 23. Merkel TJ, Perera PY, Kelly VK, Verma A, Llewellyn ZN, Waldmann TA, Mosca JD, Perera LP. Development of a highly efficacious vaccinia-based dual vaccine against smallpox and anthrax, two important bioterror entities. Proc Natl Acad Sci U S A. 2010;107(42):18091–6. CAS Article Google Scholar 24. Son HS, Yeo SG, Lee SW: Recombinant Vaccinia Virus Derived From Kvac103 Strain. In. US patent 9,879,281: Korea centers for disease control and prevention; 2016. 25. Chun JH, Choi OJ, Cho MH, Hong KJ, Seong WK, Oh HB, Rhie GE. Serological correlate of protection in Guinea pigs for a recombinant protective antigen Anthrax vaccine produced from Bacillus brevis. Osong Public Health Res Perspect. 2012;3(3):170–6. Article Google Scholar 26. Ivins B, Fellows P, Pitt L, Estep J, Farchaus J, Friedlander A, Gibbs P. Experimental anthrax vaccines: efficacy of adjuvants combined with protective antigen against an aerosol Bacillus anthracis spore challenge in Guinea pigs. Vaccine. 1995;13(18):1779–84. CAS Article Google Scholar 27. Reed LJ, Muench H. A simple method of estimating fifty per cent endpointS12. Am J Epidemiol. 1938;27(3):493–7.

#### 2] [Morton and Duan 2] It’s feasible–even the threat of CL exemptions to pharmaceutical patents incentivized increased distribution and lower prices; Bayer proves.

Morton and Duan 20

Christopher J. Morten, Charles Duan Copyright 2020 Christopher J. Morten and Charles Duan. Morten is the deputy director of the Technology Law and Policy Clinic and a Fellow at the Engelberg Center on Innovation Law & Policy at New York University School of Law. He is also a Visiting Fellow of the Yale Global Health Justice Partnership and an Affiliated Fellow of the Information Society Project at Yale Law School. Duan is a Senior Fellow at the R Street Institute, Washington, D.C. Order of authorship was determined by coin flip. P WHO'S AFRAID OF SECTION 1498? A CASE FOR GOVERNMENT PATENT USE IN PANDEMICS AND OTHER NATIONAL CRISES 23 Yale J. L. & Tech. 1 Yale Journal of Law and Technology Fall, 2020 <https://www.kiip.re.kr/webzine/2103/file/kiip_43_file5.pdf> -CAT

In the two months following the September 11 attacks, Congress, the Bush Administration, and the public became aware of a likely possibility of bioterrorism, specifically in the form of anthrax spores being blanketed over a large population.105 At the time, the only approved antibiotic for treating anthrax was ciprofloxacin, sold under the brand name Cipro. The drug quickly became a household name after news anchor Tom Brokaw, himself the recipient of an anthrax-laden letter, ran a television segment ending with the line, “in Cipro we trust.”106 Calls for a federal \*27 stockpile of the drug, however, met a roadblock: the German firm Bayer AG held a patent on ciprofloxacin, but was unable to meet the government's requisition amount for a sufficient stockpile; the company reported that it would require almost two years to manufacture enough.107 While generic manufacturers estimated that they could fulfill the requisition in three months, Bayer refused to license the patent.108 Bayer's patent standoff led to numerous calls to invoke § 1498 to enable generic manufacturing of the drug. Alfred Engelberg, a “smart and tough-as-nails attorney” known for his role in the Hatch-Waxman Act governing pharmaceuticals,109 authored a memorandum to Senator Chuck Schumer, laying out the case for invoking the law and a procedure for doing so. Engelberg proposed that the Department of Health and Human Services provide a blanket government authorization for generic firms to submit federal \*28 bids for procurement.110 Just days later, the senator called for invocation of the law in a press conference,111 leading to national interest in the possibility of invoking government use of Bayer's patent.112 Engelberg's memorandum is succinct in its analysis of § 1498. It simply observes “ample authority” and “overwhelming precedents” supporting the use of § 1498 to procure a stockpile of ciprofloxacin,113 quotes a few cases, and moves on to more detailed analysis of practical questions of regulatory approval and dismissal of ongoing patent infringement litigation. The memorandum does not discuss effects on incentives to innovate or other policy implications of invoking government patent use at all. One can imagine a variety of reasons for this summary treatment of § 1498, but the likeliest is the prior context. In the decades prior to 2001, the appropriateness of § 1498 in the context of federal procurement--in both emergency and non-emergency situations--was settled. A 1958 decision of the Comptroller General addressed the question of whether procurement officers should consider patent or patent license holdings in the course of choosing among bids.114 The Comptroller General's answer was no, based on an understanding that any standard procurement invitation automatically provided the requisite authorization and consent under § 1498. 115 The U.S. government was, and still is, free to procure whatever it needs from whomever it wants without permission from patent holders. The Comptroller General's decision \*29 sparked a wave of patentee-friendly legislative proposals across the 1960s to restrict the U.S. government's patent-blind procurement practice; none of the bills succeeded.116 As government procurement officers purchased patented technologies again and again in subsequent decades, case law confirmed repeatedly that § 1498 is automatically invoked and “the patentees' sole remedy [is] a suit against the United States in the Court of Claims.”117 Given this long-settled federal policy of using § 1498 as a routine part of government contracting, there was no need to treat in depth the question of using § 1498 for procuring ciprofloxacin. In the wake of Senator Schumer's call, Bayer rapidly moved to oppose any invocation of § 1498. Bayer immediately launched a comprehensive branding campaign (including a $3 million buy for full page advertising in all the major papers) promising that the company would “stand ready to support the United States government providing Cipro to meet emergency needs.”118 Bayer and other pharmaceutical industry representatives also lobbied Congress and the administration heavily “to provide reassurance of Bayer's commitment.”119 Bayer also attempted to paint government patent use as misguided, even illegitimate, “emphasiz[ing] the importance of patents for research and investment.”120 Remarkably, the Bush Administration initially sided with Bayer on the aptness of § 1498. Likely concerned about contradicting its international opposition to compulsory patent licensing--having rejected calls to invoke compulsory licensing on HIV/AIDS drug patents in the Global South as the landmark 2001 Doha Declaration was being \*30 negotiated121--the Bush administration publicly rebuked calls to invoke the statute. A spokesman for HHS said that “[w]e don't feel there's a need to lift the patent at this time,”122 and HHS Secretary Tommy Thompson more bluntly rejected calls to “break” Bayer's patent: “No. 1, it's illegal,” the Wall Street Journal quoted him as saying.As pressure mounted, though, the government appeared to change course: Secretary Thompson “threatened to bypass Bayer's patent” and was “ready to ask Congress for special legislation that would make the government exempt from paying any damages to Bayer for breaking the patent.”124 Ultimately, Bayer agreed to make substantial concessions in negotiations with the government, including massive increases in manufacturing and a price cut on ciprofloxacin to $0.95 or less per pill, compared to $1.83 that the government had been paying previously and the wholesale price of $4.67.125 What role § 1498 played in that ultimate deal is a Rashomon question with at least three possible answers. The majority view, as reported by almost all commentators at the time and subsequently, was that Thompson did indeed threaten to invoke § 1498, which “provide[d] the government with the necessary leverage” to force Bayer into a concession.126 Indeed, Bayer's financial statements \*31 noted that “in response to anthrax bioterror attacks in the United States in 2001, the U.S. and Canadian governments contemplated compulsory licensing of our ciprofloxacin antibiotic,” which seems to confirm that § 1498 did come up in Bayer's negotiations.127 Thompson's general counsel Alex Azar, on the other hand, contended that Thompson “never threatened to break Bayer's patent,” though Thompson did advise Bayer that he was willing to ask Congress for “authority to procure generics” in a manner that was “hardly the same thing as threatening a company.” Azar repeated that statement at his 2018 nomination for HHS Secretary.128 Bayer's CEO Helge Wehmeier advanced a third view and claimed that Thompson had not even gone that far--according to Wehmeier, the negotiation over Cipro took “less than ten minutes” with no invocation of leverage, from § 1498 or Congress.129 The Wehmeier and Azar views that § 1498 played no role in the negotiations have found little traction among historians. Even those critical of § 1498 generally accept that HHS invoked it or some other threat of government patent use en route to negotiating a favorable \*32 deal for the government,130 and Azar's letter appears to not to have been cited in any subsequent literature.131 But Bayer's massive public relations push, coupled with the Bush Administration's initial vocal disavowal of the appropriateness of § 1498, seems to have had an important (and underacknowledged) legacy, shifting views of § 1498 from a routine, beneficial government power commonplace in federal procurement to a dramatic incursion too extreme for use even in the face of a credible terrorist threat--or even “illegal.” Legal observers at the time were left “scratching their heads” over this change.132 This history suggests that contemporary views of § 1498 are of relatively recent vintage, rather than being any long-held understanding about the statute. The now widespread “conventional wisdom” that § 1498 is an “exceptional” remedy to be used only in a vanishingly small set of circumstances133 seems to be a product of just the last two out of the eleven decades the statute has been on the \*33 books. For much more of our nation's history, § 1498 was used routinely, especially in times of national emergency. At the same time, if Engelberg and Schumer had not put § 1498 on the table, Bayer may not have made that massive public relations push or been as conciliatory to the federal government as it eventually was.

**3]** [Mullowney & Harris 2] **That’s K2 accessibility to countermeasures**

**Mullowney and Harris 13**

Jared Mullowney (Texas Tech University School of Law) and Neil Harris (Texas Tech University School of Law). “Patent Protectability or Public Health?—An Examination of the Patent Compulsory License and Bioterrorism.” Journal of Biosecurity, Biosafety, and Biodefense Law 4(1). June 2013. JDN. https://doi.org/10.1515/jbbbl-2012-0011

As mentioned earlier, the United States Code does not lay out guidelines that must be followed if a **c**ompulsory **l**icense is to be granted.87 But when should it be used? No doubt, it should be used in a situation similar to the anthrax attacks seen in 2001. As mentioned earlier, Bayer still held a valid patent over the cipro drug during the anthrax attacks. There were two major issues surrounding the public reaction to the anthrax attacks: the first dealt with the price of cipro and the second dealt with the availability of cipro.88 In essence, the situation was that there have been two reported anthrax attacks on America. Following these attacks, the general public and the government go into a **widespread panic** of a large scale bioterrorism attack. People rush out to buy, and the government hopes to stockpile, an antibiotic called cipro. Bayer, the patent holder of cipro, indicates that it can only produce about 200 million of the 1.2 billion tablets in the timeframe that the Government projects will be necessary. Cipro is expensive, and the cost of anthrax treatment for a single individual ranges from $500 to $700 or more. Congress has placed a compulsory license scheme for patents within the United States Code. So then, how could it have helped? Although the compulsory license ultimately was not needed, analysis should not be done with the gift of hindsight. The **c**ompulsory **l**icense could have solved the two problems the country faced surrounding the attacks: it would have **increased** the **availability** of cipro and would have **reduced the price.** It would have increased the availability because as discussed earlier, Bayer would only be able to provide 200 million tablets,89 and at least three other pharmaceutical manufacturers were **ready and willing** to make the generic form of cipro.90 This, at least, would have provided the government with more than 200 million tablets. Furthermore, the potential licensees would have offered cipro at **drastically reduced prices.**91 While it is now known that the situation surrounding Bayer and cipro resolved itself without major issue, this must not be a reason to disregard similar future situations.

#### 4] [Oriola] The most credible studies agree specific CL exemptions for pharmaceutical patents are key to distributing the necessary resources for bioterror countermeasures.

Oriola 07

Taiwo A. Oriola (Cardiff Law School, and the ESRC Centre for Business Relationships, Accountability, Sustainability, & Society, University of Cardiff, United Kingdom). “AGAINST THE PLAGUE: EXEMPTION OF PHARMACEUTICAL PATENT RIGHTS AS A BIOSECURITY STRATEGY.” JOURNAL OF LAW, TECHNOLOGY & POLICY. 2007. JDN. <http://illinoisjltp.com/journal/wp-content/uploads/2013/10/05-05-08_Oriola_AHW_Formatted_FINAL.pdf> -recut CAT

This Article proposes the inclusion of a bioterrorism-specific pharmaceutical patents appropriation clause in national and international patent regimes. The thesis is predicated on the impropriety of the current bureaucracy-prone access to medicines paradigms in international and national patent regimes for bioterrorism-induced public health crises situations. Using highly plausible, worst-case scenarios of bioterrorism attacks, this Article argues that vast swathes of the population could become simultaneously vulnerable to deadly bioweapons, exposing millions of people to inevitable deaths, in override patents on crucial drugs or vaccines without the consent of patent 426. Audrey R. Chapman, Approaching Intellectual Property as a Human Right: Obligations Related to Article 15 (1) (c), COPYRIGHT BULL., July-Sept. 2001, at 4, 6-7, http://unesdoc.unesco.org/images/0012/ 001255/125505e.pdf#page=4. 427. See PERELMAN, supra note 219 at 2-3 (acquiescing to the creativity promotion rationale for intellectual property protection, but railing at the regime’s degeneration into a system which now “threatens to exhaust creative activity”). 428. Lawrence O. Gostin, When Terrorism Threatens Health: How Far Are Limitations on Human Rights Justified?, 55 FLA. L. REV. 1105, 1168 (2003) 429. LAWRENCE O. GOSTIN, PUBLIC HEALTH LAW: POWER, DUTY, RESTRAINT 20 (2000). 430. George G. Djolov, Patents, Price Controls, and Pharmaceuticals: Considerations from Political Economy, 6 J. WORLD INTELL. PROP. 611, 611-31 (2003); James Thuo Gathii, Rights, Patents, Markets and the Global Aids Pandemic, 14 FLA. J. INT’L L. 261, 263-351 (2002); Faizel Ismail, The Doha Declaration on Trips and Public Health and the Negotiations in the WTO on Paragraph 6: Why PhRMA Needs to Join the Consensus!, 6 J. WORLD INTELL. PROP. 393, 393-401 (2003); Nadia Natasha Seeratan, The Negative Impact of Intellectual Property Patents Rights on Developing Countries: An Examination of the Indian Pharmaceutical Industry, 3 SCHOLAR 339, 339 (2001). No. 2] AGAINST THE PLAGUE 343 holders, thus avoiding lengthy ight be destined for failure. Moreover, this Article deems a bioterrorism-specific appropriation clause in global negotiations that patents regimes expedient, in light of the pervasive and dominant propatents forces intent on a stronger intellectual property regime. This regime rationalizes patent protection solely on utilitarianism, and would cast attempts at proportionality of rights as campaigns against innovation. A fortiori, absent a bioterrorism-specific pharmaceutical patent appropriation clause, authorities could be bogged down by political and economic expediencies of pharmaceutical patent appropriation, fostering indecision that would make securing critical medicines in bioterrorism pandemics situations nigh impossible. This Article justifies the case for bioterrorism-specific pharmaceutical patents appropriation on ethical grounds, overriding public interests, and fundamental rights to health and life.

#### 5] [Avedissian] Avoiding compensation debates is key - patentholders are incentivized to circumvent existing legal structures because they profit from bioterror

Avedissian 02

Avedissian, Grace K (J.D. Candidate, May 2003, American University, Washington College of Law; B.A., Political Science, 1997, Rutgers College). "Global Implications of a Potential U.S. Policy Shift Toward Compulsory Licensing of Medical Inventions in a New Era of "Super-Terrorism"." American University International Law Review 18, no. 1 (2002): 237-294. <https://digitalcommons.wcl.american.edu/cgi/viewcontent.cgi?article=1188&context=auilr> -CAT

C. IMPLICATIONS OF A U.S. COMPULSORY LICENSING LAW ON GLOBAL COUNTERTERRORISM EFFORTS House Bills 1708 and 3235 primarily address the high cost of prescription drugs in the United States. 96 However, if Congress enacts the bills into law, compulsory licensing arrangements for prescription drugs in the United States would also increase global access to therapeutic drugs to treat victims of biological or chemical terrorism. 197 1. Impact on Worldwide Availability of Pharmaceutical Products to Combat Super-Terrorism House Bills 1708 and 3235 would facilitate access to counterterrorism drugs for foreign nations that are victimized by biological or chemical warfare in two ways.98 First, House Bill 3235 would allow compulsory licensees to export therapeutic drugs immediately to foreign countries following a biological or chemical attack.'99 195. See id. (suggesting that House Bill 3235 could be used to rush life-saving medicines to countries with inadequate access to health related products in case of an act of biological terrorism in that country). 196. See Statement of Congressman Brown, supra note 132 (attributing the inflation in employee health plan premiums and the curtailment of Medicare coverage to an excessive increase in prescription drug costs in the United States since 1993). Brown also notes that the primary incentive for introducing compulsory licensing bills in Congress is to reduce the cost of prescription medications for U.S. citizens. Id. 197. See CPT's Letter to Secretary Thompson, supra note 11l (urging the Bush Administration to provide a legal framework for acquiring critical medicines immediately). 198. See CPT's Comments on H.R. 3235, supra note 184 (determining that House Bill 3235 would facilitate the use of compulsory licensing by addressing two controversial issues-the amount of remuneration due to a patent holder and the ability to export products pursuant to a compulsory license). 199. See infra notes 204-25 and accompanying text (discussing the global benefits of allowing one country to use compulsory licensing to export health related products to another country). [18:237 2002] COMPULSORYLICENSING OF MEDICAL INVENTIONS Second, both House Bills 3235 and 1708 provide a compensation framework that would expedite the compulsory licensing process. 200 The export provision of House Bill 3235 is necessary to facilitate foreign access to therapeutic drugs that pharmaceutical companies patent in the United States.20 Most developing countries do not have the factories to produce vaccines or antibiotics that would alleviate the suffering and reduce the casualties from biological or chemical warfare.20 2 Following the bioterrorism attacks in the United States in October 2001, many governments focused on methods of improving the response to such future events in their own countries. 23 However, in terms of preparation for responding to super-terrorism, the United States is in the best position to provide public health disaster relief in case of an international incident.20 4 Without House Bill 3235, it is unclear how much time would pass before the U.S. government would render aid to a foreign country facing a public health crisis from super-terrorism. For example, it took years of pressure by interest groups to convince the U.S. authorities to permit the use of compulsory licenses for alleviating the HIV/AIDS pandemic, even while thousands of infected people worldwide were dying of AIDS.2 °6 House Bill 3235 provides an implementation mechanism that would expedite the process of providing humanitarian assistance to poor countries experiencing health emergencies.2 7 Clearly, the Secretary of HHS may still be reluctant to issue compulsory licenses due to pressure from the pharmaceutical industry. 20 8 However, the media, the public, public health interest groups, and some politicians would also likely exert pressure on the Secretary, compelling him to exercise his authority under House Bill 3235.29 Furthermore, the passage of House Bill 3235 would serve the best interests of American citizens living abroad in a country targeted for super-terrorism.2 0 If a foreign country has an inadequate supply of medicines, American lives could depend on the availability of drugs exported from the United States. 21 ' The U.S. government has an Mokhiber & Weissman, supra note 112 (alleging that the U.S. government allied itself with the pharmaceutical industry to protect patent rights rather than public health, even when American lives were at risk during the Cipro patent dispute). 206. See Gathii, supra note 18, at 733 (reporting that, by 1999, at least fifteen million Africans had died of AIDS, even though AIDS can be treated with a combination of drugs). 207. See CPT's Comments on H.R. 3235, supra note 184 (proposing that the provision for exports of medicines in House Bill 3235 would allow the United States to rush medicines to a foreign country during a public health emergency generated by an act of biological warfare). 208. See Dolmo, supra note 30, at 143 (discussing the pharmaceutical industry's powerful influence on U.S. trade policies with respect to patent rights). 209. See id. at 143-44 (noting that public pressure, together with successful lobbying efforts by public health and consumer rights interest groups, influenced U.S. officials to change the trade policy regarding the use of compulsory licensing for HIV/AIDS drugs). 210. See Letter to USTR Zoellick, supra note 52 (contending that House Bill 3235 could save the lives of many Americans living in developing countries with inadequate access to pharmaceutical drugs). 211. See id. (reasoning that under House Bill 3235, the Secretary of HHS could authorize generic manufacturers in the United States to produce and export patented medicines to countries in which American lives may be at risk in a public health crisis). 276 [18:237 COMPULSORY LICENSING OF MEDICAL INVENTIONS obligation to aid American citizens living on foreign soil.212 However, without the export provision of House Bill 3235, the U.S. government does not have an adequate legislative vehicle to ensure that Americans in foreign countries receive supplies of antibiotics for treatment against exposure to biological or chemical agents.2 13 The United States also needs the proposed compulsory licensing bills to provide clarity as to the remuneration entitlements of patent holders who do not authorize the government's licensing of their patents.2 "4 Presently, the United States may issue compulsory licenses for patents to address public health concerns under its eminent domain authority in 28 U.S.C. § 1498.15 However, section 1498 is an inadequate provision for compulsory licensing because it does not provide a legal framework for determining the royalty fees to which patent holders are entitled for the use of their patents.21 6 The 212. See Madeleine K. Albright, Countering Terrorism Abroad, in SUPER TERRORISM, supra note 1, at 113 (stating that the United States must provide the best security possible to U.S. citizens living all around the world, even to diplomatic personnel, who according to international law are legally under the protection of their host countries). 213. See CPT's Comments on H.R. 3235, supra note 184 (implying that the export of patented medicines is discouraged under the current U.S. patent regime). 214. See infra notes 215-20 and accompanying text (discussing the problems under current U.S. law regarding compensation for the issuance of a compulsory license law and the need to address them in order to increase access to essential medicines in case of a public health emergency). 215. See 28 U.S.C. § 1498(a) (1994) (permitting the federal government to use or license a patent without the authorization of the patent owner); see also Memorandum from Al Engelberg, former U.S. Justice Department attorney, to Senator Charles Schumer (explaining, with reference to Cipro, that the government may assert the same defenses to the patent infringement allegation that are available to a private party, i.e., the patent is invalid, not infringed, or unenforceable), at http://lists.essential.org/pipermail/ip-health/2001 - October/002105.html (last visited Sept. 5, 2002). 216. See Press Release, U.S. Congressman Sherrod Brown, GOP Bioterrorism Plan Neglects Key Points (Nov. 15, 2001) [hereinafter GOP Bioterrorism Plan] (commenting that the Bush Administration would not invoke its eminent domain authority to override Bayer's patent for Cipro because the amount of compensation to be decided later by a judge may be too high, and contending that House Bill 3235 has an administrative compensation process that would eliminate that element of uncertainty), available at http://www.house.gov/sherrodbrown/bioterror 1115.html (last visited Sept. 5, 2002). 2002] AM. U. INT'LL. REV. statute allows patent owners to sue the government for compensation for patent infringement, but only after the government issues a compulsory license. 7 Consequently, since the amount of compensation is unclear at the outset, a judicial holding could subject the government to high compensatory liability.218 The unpredictability of this compensation process under 28 U.S.C. § 1498 deters the use of compulsory licensing.2 9 House Bills 1708 and 3235 would mitigate this problem by providing clear criteria for an administrative determination of reasonable compensation at the time of the licensing.220 Under the remuneration provisions of the bills, public officials would determine a "reasonable" remuneration for use of a patent based on numerous factors. 22 Among the factors to consider are the risks and costs associated with the R&D of the product, the degree of 217. See 28 U.S.C. § 1498(a) (granting a patent owner the right to sue the government for the non-voluntary use of its patent and receive compensation in an amount determined by a judge). But see W.L. Gore & Associates, Inc. v. Garlock, Inc., 842 F.2d 1275, 1282-83 (Fed. Cir. 1988) (holding that 28 U.S.C. § 1498(a) prevents a patent holder from enjoining a compulsory licensee from selling the patented product to the federal government and from suing the licensee for patent infringement). 218. See GOP Bioterrorism Plan, supra note 216 (stating that Secretary Thompson of HHS argued against invoking 28 U.S.C. § 1498 to override Bayer's patent on Cipro because the amount of damages for which the government would be liable could be too excessive). 219. See CPT's Comments on H.R. 3235, supra note 184 (fearing that the uncertainty surrounding the compensation issue for compulsory licensing under 28 U.S.C. § 1498 influenced the U.S. government's reluctance to use compulsory licensing to obtain an adequate stockpile of Cipro). 220. See H.R. 1708, sec. 2(a)(d) (2001) (providing a list of considerations for the Secretary of HHS and the FTC to evaluate the "reasonableness of ... the remuneration" to be paid to a patent owner for the authorized use of its patent); see also H.R. 3235, sec. 2(a)(b) (2001) (granting the Secretary of HHS the right to determine "reasonable remuneration for use of the patent"); see also CPT's Comments on H.R. 3235, supra note 184 (stating that "HR 3235 is needed to introduce more predictability and certainty in the compensation process, so that public health officials can act fast and confidently, to address a crisis as it happens"). 221. See H.R. 1708, sec. 2(a)(d) (listing six factors to consider in determining remuneration for the compulsory licensing of a patent); see also H.R. 3235, sec. 2(a)(b) (enumerating nine factors that the Secretary of HHS may take into account when determining a reasonable compensation amount to a patent holder for the unauthorized use of its patent). 278 [18:237 2002] COMPULSORY LICENSING OF MEDICAL INVENTIONS 279 importance of the invention to public health, the degree to which the government funded the research and development of the invention, and the public health benefits arising from increased access to the product.2 2 In stark contrast, the amount of damages under the current compensation system of 28 U.S.C. § 1498 may be based on the financial loss of the patent owner resulting from the compulsory license.223 Under this formula, the government could end up paying the same amount as it would have originally paid for the brand-name drug before issuing the compulsory license, and additionally, it would incur legal expenses from the litigation.224 This result would defeat the purpose of the compulsory license, which is to increase the availability of essential drugs at a reasonable cost.225 2. Impact on R&D of Pharmaceutical Products that Combat SuperTerrorism Compulsory licensing legislation in the United States would not hinder the pharmaceutical industry's ability to develop new medicines that counter biological or chemical agents.226 The 222. H.R. 1708, sec. 2(a)(d); H.R. 3235, sec. 2(a)(b); see also Mokhiber & Weissman, supra note 112 (discussing the compensation criteria of House Bill 3235). 223. See Correa, supra note 145, sec. 3.1 (explaining that remuneration under 28 U.S.C. § 1498 may be based on the amount of loss incurred by the patent owner, not the amount gained by the licensee); see also, e.g., Leesona Corp. v. U.S., 599 F.2d 958, 969 (Ct. Cl. 1979) (holding that in an eminent domain case, the proper measure of damages is "what the owner has lost, not what the taker has gained"). 224. See Todd Zwillich, Bill Would Allow Emergency Bypass of Drug Patents, REUTERS, Nov. 8, 2001 (reporting that supporters of House Bill 3235 claim that under the current system, a potential suit for patent infringement against the government could be very costly to the government), available at http://lists.essential.org/pipermail/ip-helath/200 1 -November/002366.html (last visited Sept. 5, 2002). 225. See id. (indicating that the compensation process of 28 U.S.C. § 1498 frustrates the purpose of compulsory licenses). 226. See Dolmo, supra note 30, at 160-61 (presenting the microeconomic theory that compulsory licensing will increase drug sales when prices decrease, and therefore compulsory licensing does not harm sales revenue to the extent that drug industries contend); see also Statement of Congressman Brown, supra note 132 (noting that drug companies whose patents are under compulsory licenses would still reap the financial rewards of marketing their products first, and would be entitled to royalties from generic producers); Médecins Sans Frontières, MSF AM. U. INT'L L. REV. pharmaceutical industry and other opponents of compulsory licensing allege that revenue from drug sales is necessary to maintain investments and recoup R&D costs. 227 The occasional use of compulsory licensing by the government, however, would not likely dissuade investors from participating in a highly lucrative industry.228 Even if private investments in the industry decrease slightly, it would not drastically affect R&D financing.229 Pharmaceutical companies finance less than half of the R&D for new products. 230 The majority of R&D funding comes from American tax dollars, private foundations, and state and local governments. 23 I Also, the companies receive generous tax breaks on their portion of the R&D expenditure.232 Moreover, the government offers drug companies Response to 'Boys from Brazil' (asserting that "[w]ith Africa accounting for only one percent of drug sales, it is ludicrous to suggest that the use of generics in Africa diminishes the economic incentive for multinationals to conduct research"), at http://www.msf.org/content/page.cfm?articleid=826FCC89-E I EC-4E25- 99DE3E9BB3FAC3D7 (last visited Sept. 5, 2002). 227. See Carroll, supra note 29, at 2469 (discussing developed countries' argument that investors would consider the pharmaceutical industry a risky investment because compulsory licensing would preclude drug companies from recovering their R&D expenditures). 228. See Statement of Congressman Brown, supra note 132 (highlighting the fact that profits in the pharmaceutical industry are at least five percent higher than profits in any other industry and will increase by sixteen to eighteen percent over the next four years); see also U.S. CONGRESS, OFFICE OF TECHNOLOGY ASSESSMENT, PHARMACEUTICAL R&D: COSTS, RISKS AND REWARDS 104 (1993) (finding that, throughout the 1980s, the net returns on pharmaceutical R&D well exceeded the cost of capital investments, including the time and risks incurred by investors), avaiable at http://www.wws.princeton.edu/-ota/diskl/1993/9336\_n.htm (last visited Feb. 28, 2002). 229. See Statement of Congressman Brown, supra note 132 (indicating that compulsory licensing would not impair R&D capabilities of drug companies because a large proportion of R&D is subsidized through non-industry funding). 230. See id. (presenting data that show drug companies contribute less than half of the overall pharmaceutical R&D expenditures in the United States). 23 1. See id. (stating that taxpayers fund forty-two percent of pharmaceutical R&D, while other non-pharmaceutical sources generate eleven percent of R&D financing). 232. See PUBLIC CITIZEN, Rx R&D MYTHS: THE CASE AGAINST THE DRUG INDUSTRY'S R&D "SCARE CARD" ii [hereinafter RX R&D MYTHS] (highlighting that in addition to obtaining federal funding, pharmaceutical companies receive tax advantages for conducting research and developing new drugs), available at [18:237 COMPULSORYLICENSING OF MEDICAL INVENTIONS additional financial incentives for testing the safety of drugs for children.233 The enactment of House Bill 1708 would ensure that drug prices accurately reflect the costs incurred by drug companies for R&D. 34 Section 3 of the bill requires pharmaceutical companies to provide the Secretary of HHS with annual disclosure of their audited financial information relating to the pricing of their drugs. 235 The Secretary evaluates the pricing schemes based on the reported cost of R&D for a specific drug, as well as overall R&D activities. 236 This financial reporting system is the best challenge to the industry's persistent claim that compulsory licensing inhibits R&D of future medical inventions. 237 http://www.citizen.org/publications/print-release.cfm?ID=7065 (last visited Sept. 5, 2002). 233. See id. (noting that as a result of the "pediatric exclusivity" incentive for testing the effects of drugs on children, the drug industry generates an additional $600 million in profits per year, while incurring costs of less than $100 million a year). 234. See H.R. 1708, sec. 3(a) (mandating that drug companies submit annual financial reports to the Secretary of HHS). The Secretary may penalize any drug company that fails to meet the reporting requirement by assessing a maximum fine of $25,000 for each day that passes the reporting deadline, but only after the Secretary provides a written notice of delinquency and gives the company an opportunity to request a judicial hearing. See id. sec. 3(b)(1) - (2); see also Statement of Congressman Brown, supra note 132 (urging that it is time to hold the pharmaceutical companies accountable for their drug pricing and purported expenses). 235. See H.R. 1708 sec. 3(a) (requiring a financial report from drug companies disclosing costs associated with the research and development of a new drug and costs allocated to all research and development activities of the company). 236. See Statement of Congressman Brown, supra note 132 (expressing the importance of a reporting system that would allow authorities to ascertain the true costs incurred by the pharmaceutical industry). 237. Compare Press Release, Pharmaceutical Research and Manufacturers of America, Health Care Advocates to Fight Efforts by Generic Industry to Jeopardize the Progress in Medical Research (Feb. 25, 2002) (claiming that any attempt to weaken the patent protections under the current law will harm research efforts for new drugs), available at http://www.phrma.org/press/newsreleases//2002-02-25.347.phtml (last visited Sept. 5, 2002) with Statement of Congressman Brown, supra note 132 (challenging the pharmaceutical industry's assertion that drug companies could not produce new drugs if the government institutes compulsory licensing laws). 2002] AM. U. INT'L L. REV. Given the ongoing tension between the pharmaceutical industry and developed countries on one side, and developing countries on the other side, the following section suggests ways in which the WTO and the Unites States can alleviate some of the problems associated with the compulsory licensing debate. 238 The international community must take immediate steps to address this issue before the use of biological and chemical agents becomes a prevalent means of global terrorism. 23 9 JII.RECOMMENDATIONS Compulsory licensing is an essential legal and legislative tool in the fight against global super-terrorism. 240 The U.S. opposition to compulsory licensing permits pharmaceutical companies to profit from bioterrorism, 241 and poses an unacceptable health risk to populations exposed to biological or chemical agents.242 In light of the effects of globalization, the United States and other developed countries cannot afford to ignore global health concerns. 243 A large- scale super-terrorist attack on any country would result in devastating human loss and would create regional or global panic, with rippling effects on the global economy.244 Accordingly, the WTO must add breadth to the compulsory licensing provisions of the TRIPS Agreement. 245 Also, the U.S. government must facilitate the use of compulsory licensing by addressing concerns regarding remuneration to patent holders and the effects of compulsory licensing on research and development. 246 This policy shift would recognize the need to assist the developing world during health emergencies, particularly those arising from the acts of super- terrorism. 2 47 A. THE WTO MUST RECOGNIZE ITS MEMBERS' RIGHT TO OBTAIN COMPULSORY LICENSED PRODUCTS FROM FOREIGN MARKETS In the event of a biological or chemical disaster, developing countries that lack the capacity to manufacture essential drugs must be able to exercise their legitimate right to use compulsory licensing without the fear of economic or legal reprisal from developed countries.2 48 The WTO must acknowledge this right by adopting an interpretation of the TRIPS Agreement that protects public health.2 In the Doha Declaration, the WTO Ministers instructed the TRIPS Council to find a solution to the problem arising from the inadequate manufacturing capacity of some developing nations.25 ° As an integral part of the solution, the Council must allow countries to either (1) grant a compulsory license to a generic drug manufacturer in a foreign market under Article 31 (f) of the TRIPS Agreement,25 ' or (2) import medicines that are the product of a compulsory license issued by the exporting country-as permitted under House Bill 3235.252 A contrary interpretation would simply defeat the fundamental purpose and premise of compulsory licensing under the TRIPS Agreement, that is, increasing global access to life-saving drugs.253 Without a proper implementation mechanism for compulsory licensing, the TRIPS Agreement offers empty benefits to poor countries in dire need of affordable drugs.254 Although the WTO could permit Members to issue compulsory licenses under either Article 30 or Article 31(f) of the TRIPS Agreement, it is more feasible to employ Article 3 1(0.255 Since Article 31 is the technical provision that authorizes compulsory licensing, it contains various terms and conditions that grant some protection to patent holders. 256 For instance, under Article 31, a compulsory license expires when the circumstances requiring it cease to exist, and the licensee must pay the patent holder "adequate remuneration" for the license.257 On the other hand, Article 30 does not offer such specific protections to patentees.258 Consequently, developed countries are more likely to oppose the use of this provision as the basis for permitting compulsory licensing for exports. 259 These countries, however, may be more receptive to a broad interpretation of Article 31(f), whereby a WTO Member can export medicines under a compulsory license to a Member that lacks or has an insufficient manufacturing capacity for pharmaceuticals.26 ° The enactment of House Bill 3235 would be significant for the development of a WTO resolution regarding the scope of compulsory licensing under the TRIPS Agreement. 6 In the past, the U.S. government acted strategically to prevent the WTO from adopting a flexible interpretation of the TRIPS Agreement by exerting economic and political pressure on developing countries.262. See Abbott, supra note 42, at 12 (stating that despite the United States' public endorsement of the need to address global public health issues, trade representatives continue to exert political and economic pressures on developing 285 AM. U. INT'L L. REV. It is time for the United States to reverse its policy. 263 In light of the recent anthrax attacks in the United States and the potential for greater harm from biological or chemical warfare, the United States must acknowledge the importance of global cooperation and worldwide access to counterterrorism antibiotics. 264 Congress should pass House Bill 3235 to clearly indicate the United States' support for allowing exports of medicines to address public health crises in developing countries.265 B. THE UNITED STATES MUST FACILITATE THE REMUNERATION PROCESS OF COMPULSORY LICENSING UNDER U.S. LAW The recent controversy over the potential compulsory licensing of the Cipro patent demonstrates that Congress must amend U.S. patent law to incorporate compulsory licensing provisions.266 The Cipro countries that advocate for a liberal interpretation of the TRIPS Agreement); see also Letter to USTR Zoellick, supra note 52 (criticizing the U.S. government's strategy of proposing language at TRIPS conferences that appears to benefit the poorer countries, but which would actually restrict protections for public interests and advance the interests of pharmaceutical companies). 263. See Letter to USTR Zoellick, supra note 52 (accusing the U.S. government of harming foreign relations and its own standing in the international community through its abuse of power with regard to intellectual property issues). 264. See International Centre for Trade and Sustainable Development, Draft Declaration on TRIPS and Health Highlights Divisions in the WTO, BRIDGES WKLY. TRADE NEWS DIG., Oct. 30, 2001 (quoting Justin Forsyth, Oxfam GB Policy Director as saying, "We had hoped that the issue of access to the patented anti-Anthrax drug, Cipro, would make rich country governments more sensitive to the needs in developing countries ... But the latest reports from the WTO in Geneva indicate that the US has not budged an inch"), available at http://www.ictsd.org/weekly/01-10-30/story2.htm (last visited Sept. 19, 2002); see also, International Centre for Trade and Sustainable Development, Anthrax Scare Draws New Focus on JPRs and Access to Medicines, BRIDGES WKLY. TRADE NEWS DIG., Oct. 23, 2001 [hereinafter Anthrax Scare] (quoting Paulo Teixeira, Director of the Brazilian government's AIDS program as saying, "The anthrax outbreak is very distressing but I hope it will make [the United States and Canada] reflect more about our position that compulsory licensing is an entirely legitimate instrument if there is a problem of access to a crucial drug"), available at http://www.ictsd.org/weekly/O1 - 10-23/story2.htm (last visited Sept. 19, 2002). 265. See Anthrax Scare, supra note 264 (urging the USTR to take the lead in changing trade policy to reflect public interest rather than the interests of large pharmaceutical companies and lobbyists). 266. See GOP Bioterrorism Plan, supra note 216 (stating that the anthrax attacks and the subsequent dispute over the Cipro patent demonstrates the need for a 286 [18:237 2002] COMPULSORYLICENSING OF MEDICAL INVENTIONS dispute indicates that the uncertainty over amounts of compensation to be paid to patent holders may be a factor in the U.S. government's reluctance to use compulsory licensing. 67 As long as government officials are uncomfortable with allowing courts, to determine the government's liability for issuing compulsory licenses under 28 U.S.C. § 1498, they will continue to choose the conservative approach of avoiding the use of compulsory licensing to eliminate the risk of liability.268 Congress should enact House Bills 1708 and 3235 to address the concerns regarding compensation for the non-voluntary use of a patent.269 The administrative compensation process proposed in the bills should mitigate the fear of exposing the government to future litigation and liability upon the issuance of compulsory licenses. 7 ° The factors enumerated in the bills for determining compensation to statutory basis for compulsory licensing other than eminent domain authority to effectively address the threat of bioterrorism). 267. See Other Anthrax Drugs, N.Y. TIMES, Oct. 28, 2001 (publishing a letter from Bernard A. Schwetz, the Acting Principal Deputy Commissioner of the Food and Drug Administration, in which he defends the Bush Administration's decision to not exercise its eminent domain authority to override the Cipro patent because "if the government overrode the patent, Bayer could bill the Treasury for lost revenues"); see also CPT's Comments on H.R. 3235, supra note 184, paras. 2-3 (asserting that Secretary Thompson's reluctance to obtain essential antibiotics through compulsory licensing, simply because damage payments for patent infringement could be expensive, will subject the public to higher health risks). 268. See CPT's Comments on H.R. 3235, supra note 184, para. 3 (fearing that "[b]ureaucrats will cut comers with the public health" due to concerns about unpredictable liability costs). 269. See GOP Bioterrorism Plan, supra note 216 (arguing that House Bills 1708 and 3235 would prevent extensive litigation and unnecessary costs that could otherwise arise under 28 U.S.C. § 1498). 270. Regarding the Bush Administration's plan to address bioterrorism, Congressman Brown stated in his address to Secretary Tommy Thompson of HHS and Director Jeffrey Koplan of the Centers of Disease Control and Prevention: The spread of anthrax has already taken a significant toll on the nation's sense of security. Unencumbered access to drugs is an essential element in our response to bioterrorism. Establishing the statutory and regulatory framework now to secure generic drugs on an expedited and affordable basis simply makes sense. Taking that step now will help ensure that the priority of doing what's best for the public is not subsumed by cost concerns, red tape, or legal haggling. I'd like to work with you to ensure you have this [sic] compulsory licensing tool available to you before another 'Cipro situation' arises. 287 AM. U. INT'L L. REV. patentees are fairly comprehensive and should generate reasonable royalty fees. 27 The remuneration provisions, however, should also include such considerations as the domestic market share for the licensed product, general royalty rates in the pharmaceutical sector, and royalty rates that licensees would pay for a voluntary license of the product.27 2 This administrative procedure will allow public officials to act more promptly and decisively in issuing compulsory licenses, which would be particularly important in the aftermath of a biological or chemical attack.273 It would permit the government to immediately increase the production and distribution of generic drugs in times of national and international public health disasters.274 C. THE U.S. GOVERNMENT SHOULD AGGRESSIVELY ADDRESS PURPORTED R&D CONCERNS THAT IMPEDE COMPULSORY LICENSING The most practical challenge to the pharmaceutical industry's claim that compulsory licensing impedes R&D is to implement a system by which officials can scrutinize the R&D records of pharmaceutical companies.275 At present, the government does not 271. See H.R. 1708, sec. (2)(a)(d) (listing such factors as the costs of R&D, the importance of the product to public health, the amount of public funding received for R&D, the need for providing incentives for new inventions, public interest considerations, and public health benefits from increased access to the product); see also H.R. 3235 sec. 2(a)(b) (listing the same five factors as H.R. 1708 and including additional factors, such as the benefits of increased availability of the product to working families and retired persons, and the need to remedy anticompetitive behavior). 272. See Correa, supra note 145, ch. X, sec. 3.1 (discussing various methods used by U.S. federal courts for determining "reasonable" royalty rates). 273. See GOP Bioterrorism Plan, supra note 216 (noting that the rapid availability of therapeutic drugs is essential to saving thousands of lives in the event of a release of a biological agent like anthrax). 274. See CPT's Comments on H.R. 3235, supra note 184 (emphasizing that legislation providing more predictability in the compensation process of compulsory licensing would facilitate the government's ability to address both domestic and foreign public health emergencies as they arise). 275. See Statement of Congressman Brown, supra note 132 (arguing that a requirement that pharmaceutical companies provide audited, detailed information regarding their expenses is a necessary component of challenging the industry's threat that drug companies will cease to produce new drugs if legislators compel price reductions for marketed drugs); see also Rx R&D MYTHS, supra note 232, at 288 [18:237 2002] COMPULSOR YLICENSING OF MEDICAL INVENTIONS attempt to verify or explore the industry's claim that drug prices merely reflect the high risks and costs associated with R&D.276 The pharmaceutical industry has refused for years to disclose its R&D records to congressional investigators and independent auditors.277 Nevertheless, the drug companies still receive substantial governmental subsidies, generous tax incentives, and other financial incentives to engage in R&D of new pharmaceutical products.278 Section 3 of House Bill 1708 would be an effective legal tool for exposing the true costs incurred by the drug companies, since it requires both the Secretary of HHS and Congress to review the financial reports submitted by the companies. 279 The financial reporting requirements of the bill are also useful to the authorities in determining whether a patent holder is engaging in monopolistic 23-24 (advocating for the disclosure to Congress of R&D costs by the drug industry). 276. See Why Do Medicines Cost So Much?, supra note 36 (alleging that R&D costs for each new drug brought to the market total on average $500 million). But see Rx R&D MYTHS, supra note 232, at ii (exposing the falsehoods of the industry's claims by scrutinizing government studies, companies' financial filings with the U.S. Securities and Exchange Commission, and other documents obtained through the Freedom of Information Act). In the 1990s, the actual after-tax R&D costs for each new drug ranged from $57 million to $71 million, not $500 million. Id. Also, pharmaceutical R&D is not as risky as the industry claims, given the fact that only twenty-two percent of the new drugs on the market over the past two decades were actually innovative rather than mere replicas of existing drugs. Id. 277. See Rx R&D MYTHS, supra note 232, at ii (noting that the pharmaceutical industry won a nine-year legal battle to limit the ability of congressional investigators from the General Accounting Office to review the industry's R&D records). Although Congress has the authority to subpoena the industry's R&D records, it has never invoked that authority. Id. Congress' failure to act may be attributed to the fact that the pharmaceutical industry makes generous financial contributions to political campaigns. Id. For example, in 1999-2000, the pharmaceutical industry spent $262 million on federal lobbying, campaign contributions, and "issue" advertisements for candidates. Id. 278. See Statement of Congressman Brown, supra note 132 (criticizing the fact that prescription drug prices are soaring, even though the drug industry receives tax breaks, and is well-funded by taxpayers, private foundations, state and local governments, and other non-industry sources); see also RX R&D MYTHS, supra note 232, at ii (recognizing that the federal government provides various financial incentives to drug companies in connection with their R&D activities, and arguing that R&D risks and costs are significantly reduced by taxpayer-funded research). 279. See H.R. 1708, sec. 3(a) (mandating that drug companies submit annual audited financial reports related to drug pricing to the Secretary of HHS, who would provide a copy of the reports to Congress). 289 AM. U. INT'L L. REV. practices (i.e., excessive pricing) and whether compulsory licensing is a proper remedial course of action.280 Some commentators argue that drug companies still rely heavily on revenue from products they have already placed on the market in order to cover their half of the R&D budget.28' The industry, however, could clearly compensate for lower sales revenues by curtailing certain expenditures.282 Drug companies allocate exorbitant sums of money for inordinate expenses, such as generous employee compensation packages, marketing, and advertising.283 The ability to incur expenses of such magnitude casts doubt on the assertion that pharmaceutical companies cannot afford lost revenues because it would reduce their R&D capacities.284 House Bill 1708 should serve as a mechanism to regulate private drug companies by subjecting their financial reports to scrutiny by the Secretary of HHS and 280. See id. sec. 2(b)(3) (providing that anti-competitive conduct by a patent holder could subject the patent of products at issue to compulsory licensing); see also Statement of Congressman Brown, supra note 132 (accusing the drug industry of price-gouging). 281. See Litovsky, supra note 127, at 22 (arguing that despite government funding, drug companies need to raise sufficient revenue from drug sales to cover total R&D costs). Commentators reason that the introduction of lower-priced products in the marketplace through compulsory licensing would lead to fewer sales for patent holders and lower profits for investors. Id. Commentators argue that reduced earnings would have adverse consequences on R&D financing by the patent holding drug companies. Id. 282. See, e.g., Rx R&D MYTHS, supra note 232, at 20 (attributing an increase in drug prices to increased advertising since 1997). But cf Fisch, supra note 39, at 311 (arguing that cutting back on pharmaceutical drug advertisements would harm patient care because the advertisements inform patients about a potential treatment and encourage them to contact a physician). 283. See Statement of Congressman Brown, supra note 132 (illustrating that drug companies allocate excessive amounts of money to non-essential expenses). For example, in 2000, Bristol-Myers Squibb dispensed $1.2 million for the CEO's salary, $1.9 million for his bonuses, and $30.4 million in stock options. Id. Furthermore, pharmaceutical companies spent $8.3 billion in 2000 for marketing and advertising. Id. 284. Compare Litovsky, supra note 127, at 22 (alleging that increasing competition in the generic drug market will discourage private investments and will significantly reduce the R&D budgets of brand-name drug companies) with Statement of Congressman Brown, supra note 132 (arguing that brand-name drug companies must account for all their expenditures if they continue to maintain that high drug prices are necessary to cover their R&D expenditures). 290 [18:237 COMPULSORY LICENSING OF MEDICAL INVENTIONS Congress.2 5 Consequently, drug company executives may adopt a more conservative fiscal policy with regard to their expenses.286 Such curtailed expenditures, coupled with the availability of public funding for R&D, would limit the effect of compulsory licensing on the total R&D budget for future pharmaceutical innovations.287 D. COMPULSORY LICENSING LEGISLATION is NEEDED TO FACILITATE GLOBAL PREPAREDNESS FOR SUPER-TERRORISM The U.S. Congress should pass compulsory licensing legislation in order to demonstrate a willingness to provide humanitarian aid and international cooperation during a foreign public health crisis.288 Although the world has not yet witnessed a major bioterrorism or chemical terrorism incident, super-terrorism is a global threat and warrants global preparation. 289 National security is clearly a priority for the Bush Administration, which has initiated domestic 285. See H.R. 1708, sec. 3(a) (requiring pharmaceutical companies to submit annual financial reports on drug costs and sales to the Secretary of HHS). 286. See Statement of Congressman Brown, supra note 132 (supporting the notion that drug companies should account for their expenses). 287. Cf Rx R&D MYTHS, supra note 232, at 20 (contrasting the expenditures on marketing and administrative costs-thirty percent of revenue, by Fortune 500 drug companies in 2000-with the expenditure on research and development twelve percent of revenue). 288. See Albright, supra note 212, at 110 (acknowledging that the United States must assist foreign nations that are victimized or threatened by terror, and stating that "[i]t is not enough for Americans to be concerned only about attacks against Americans"). 289. See Pan American Health Organization ("PAHO"), Latin America, Caribbean Urged to Plan for Bioterrorism (reporting that experts on bioterrorism and emergency response who met at a PAHO conference after the bioterrorist attacks in the United States urged Latin American and Caribbean countries to prepare to respond to bioterrorism), at http://www.paho.org/English/DPI/pr01026.htm (last visited Sept. 5, 2002). At a meeting of Health ministers from the Americas at PAHO, U.S. Secretary of HHS Thompson stated: Given the evolving opportunities and the reality of an uncertain future, we must work together if we really want to make a difference .... Although each country has a responsibility to meet the health needs of its people, there are few issues countries working alone can fully resolve. The need to build partnerships and alliances has never been more compelling. 20021 AM. U. INT'L L. REV. preparedness programs to prevent and respond to bioterrorism and chemical terrorism.2 9° However, it is insufficient for the United States to adopt an isolationist attitude towards health.291 Super-terrorism requires global preparedness because it has significant international repercussions.292 A healthy population is a vital aspect of any country's economic welfare, since the loss of human capital reduces the country's labor and intellectual workforce. 293 Also, the economic shortfall resulting from an emerging public health crisis in developing countries has detrimental effects on international trade and global markets. 94 290. See Press Release, U.S. Department of Health and Human Services, Secretary Thompson Testifies on HHS Readiness and Role of Vaccine Research and Development (Oct. 23, 2001) (noting that following the anthrax attacks in October 2001, the Bush Administration requested $1.2 billion for production of vaccines and antibiotics and $643 million for expansion of the National Pharmaceutical Stockpile), available at http://www.hhs.gov/news/press/2001pres/20011023.html (last visited Sept. 5, 2002). 291. See Global Health Core Messages, supra note 8 (acknowledging that American health and economic prosperity is "inextricably linked" to the health of the world population and the prosperity of its trading partners); see also PAHO, supra note 289 (reporting that experts on bioterrorism and emergency response at the PAHO conference noted that "[g]iven the global economy, an outbreak anywhere in the world may be considered a threat to virtually all nations"). 292. See American Medical Association, AMA Urges Global Ban of Biological Weapon Development (warning that exposure to a communicable biological agent anywhere in the world would have global health repercussions due to globalization and the ease and frequency of travel), at http://www.amaassn.org/ama/pub/article/2403-5338.html (last visited Sept. 5, 2002); see also Symposium, Bioterrorism: Homeland Defense Symposium: The Next Steps, Threat Panel (Feb. 8, 2000) (analyzing the destabilizing effects of agriculture bioterrorism (i.e., animal and crop disease from exposure to biological agents) on global public health, political and social welfare, and the economy), available at http://www.rand.org/nsrd/bioterr/chalk.htm (last visited Sept. 5, 2002). 293. See Global Health Core Messages, supra note 8 (noting that there is a critical link between healthy individual growth and the development of intellectual capital of a nation, and that intellectual capital is a universal currency). 294. See id. (stating that "[h]ealthy populations and healthy economies are vital for a healthy world economy and strong markets"). 292 [18:237 2002] COMPULSORY LICENSING OF MEDICAL INVENTIONS Compulsory licensing is an important component of global preparedness. 295 If a developing country falls prey to super-terrorism, it would need medical assistance to treat its infected population with antibiotics.296 The international community, and especially the United States-the largest source for pharmaceutical products-has a moral and ethical obligation to provide affordable therapeutic drugs to developing countries that do not have the resources to combat super-terrorism. 297 The failure to act when thousands of lives are at risk is unacceptable.298 Consequently, the export provision of House Bill 3235 is particularly crucial in light of the potential for alarmingly high mortality rates from biological or chemical terrorism.299 CONCLUSION The increased threat of bioterrorism since September 11, 2001, refocused the attention of the international community on the need to address problems in the compulsory licensing provisions of the TRIPS Agreement.300 In this new era of super-terrorism, compulsory 295. See GOP Bioterrorism Plan, supra note 216 (declaring that the U.S. government should have compulsory licensing legislation before the occurrence of another bioterrorism incident). 296. See Abbott, supra note 42, at 12-13 (explaining that for poor countries with inadequate local manufacturing capacities, the only means of gaining access to essential drugs is through importation). 297. See Letter to USTR Zoellick, supra note 52 (indicating that the U.S. government should provide humanitarian aid to a foreign nation facing a public health emergency). 298. See Gilmore, supra note 2, at 15 (finding that the release of 1,000 kilograms of the nerve gas Sarin in open air would kill approximately 10,000 people); see also Federation of American Scientists, Biological Warfare Agents (reporting that one hundred kilograms of anthrax "released from a low-flying aircraft over a large city on a clear, clam night, could kill one to three million people"), at http://www.fas.org/nuke/intro/bw/agent.htm (last visited Sept. 5, 2002). 299. See H.R. 3235, sec. 2(a)(c) (establishing an administrative authority with power to issue a compulsory license for exportation of generic medicines to a country with urgent public health needs). 300. See Anthrax Scare, supra note 264 (observing that Canada's decision to issue a compulsory license for Cipro and the United States' consideration of purchasing generic versions of the antibiotic rekindled debates on the issues of compulsory licensing and access to essential medicines). 293 AM. U. INT'L L. REV. licensing is an essential legal mechanism for saving thousands of lives.30' It is imperative that the WTO and the TRIPS Council continue to interpret the TRIPS Agreement in a way that supports the protection of public health and implements the Doha Declaration in good faith.30 2 Also, the United States must cease its abuse of economic power to influence the TRIPS negotiations.3 3 It is time for the United States to recognize that a change in its patent protection policy is necessary to mitigate the threat of biological or chemical terrorism on public health. The adoption of compulsory licensing legislation in the United States would be a monumental step toward facilitating access to life-saving medicines in a time of national or foreign public health crisis resulting from super-terrorism.

## Framing

#### The standard is maximizing expected wellbeing. Prefer:

#### 1] Degrees of wrongness – If I break a promise to meet for lunch, that’s not as bad as breaking one to take a dying person to the hospital. Only the consequences explain why the second one is so much worse than the first.

#### 2] Aggregation – States lack unified intent. Because different people have different ethical systems, the only non-arbitrary way to aggregate is to help the most people.

#### 3] [Blum] Util’s a prerequisite to all other moral theories; robust neuroscience proves – pleasure and pain are the only intrinsic values and disvalues – everything else regresses

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. -recut CAT

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] [Bostrom] Extinction first – You can’t be 100% sure about any framework, so you must keep people alive to make future ethical determinations.

Bostrom 12

[Nick Bostrom, Faculty of Philosophy & Oxford Martin School University of Oxford. “Existential Risk Prevention as Global Priority”. 2012. www.existential-risk.org/concept.html]

These reflections on moral uncertainty suggest an alternative, complementary way of looking at existential risk; they also suggest a new way of thinking about the ideal of sustainability. Let me elaborate. Our present understanding of axiology might well be confused. We may not now know — at least not in concrete detail — what outcomes would count as a big win for humanity; we might not even yet be able to imagine the best ends of our journey. If we are indeed profoundly uncertain about our ultimate aims, then we should recognize that there is a great option value in preserving — and ideally improving — our ability to recognize value and to steer the future accordingly. Ensuring that there will be a future version of humanity with great powers and a propensity to use them wisely is plausibly the best way available to us to increase the probability that the future will contain a lot of value. To do this, we must prevent any existential catastrophe.

## U/V

#### 1] [Shah] We don’t take a stance – but if they do, permissibility and presumption affirm - affirming is harder so all theory arguments have an implicit aff flex standard because of huge side bias – outweighs neg fairness arguments unless they prove how it uniquely outweighs the disparity since it’s structural.

Shah 19 Sachin Shah, Grant Brown, 11-22-2019, "A Statistical Analysis of Side-Bias on the 2019 November-December Lincoln Douglas Debate Topic by Sachin Shah," NSD Update, <http://nsdupdate.com/2019/a-statistical-analysis-of-side-bias-on-the-2019-november-december-lincoln-douglas-debate-topic-by-sachin-shah/?fbclid=IwAR2dksMH6SK-_CQmFOUZz7_1Ay1HbX6oBDcjnKD4RipVozgkNSkfk1Ye3E4> SJCP//JG

There is sufficient evidence that the negative is able to overcome this skew more often than the affirmative. This further indicates negative side bias. Conclusion This analysis is statistically rigorous and relevant in several aspects: (A) The p-value is less than the alpha. (B) The data is on the current November-December topic, meaning it’s relevant to rounds these months [4]. (C) The data represents a diversity of debating and judging styles across the country. (D) This analysis accounts for disparities in debating skill level. (E) Multiple tests confirm the results. As a final note, it is also interesting to look at the trend over multiple topics. In the rounds from 117 TOC bid-distributing tournaments (September 2017 – 2019 YTD), the negative won 52.88% of ballots (p-value < 0.0001). This suggests the bias might be structural, and not topic specific, as this data spans eight different topics [5]. Therefore, this analysis confirms that affirming is in fact harder again on the 2019 November-December topic. So, once again, don’t lose the flip!

#### Prefer our ev with super-low p-values to their analytics.

**2] I get RVIs on theory - otherwise it’s a NIB, and time skew amplifies any abuse including ableism – I’m always behind on prep because of cognitive disabilities and I read and process slowly**

**3] I-meets justify RVIs – deters future abuse**

**4] CX checks**

#### 5] No innovation loss.

Son 19

Kyung-Bok Son (College of Pharmacy, Ewha Womans University). “Importance of the intellectual property system in attempting compulsory licensing of pharmaceuticals: a cross-sectional analysis.” Globalization and Health volume 15, Article number: 42 (2019). JDN. <https://globalizationandhealth.biomedcentral.com/articles/10.1186/s12992-019-0485-7-recut> CAT

Methods We used a multivariate logistic model to regress attempts to issue compulsory licensing on the characteristics of the intellectual property system, controlling for macro context variables and other explanatory variables at a country level. Results A total 139 countries, selected from members of the World Trade Organization, were divided into a CL-attempted group (N = 24) and a non-CL-attempted group (N = 115). An attempt to issue compulsory licensing was associated with population (+) and a dummy variable for other regions, including Europe and North America (−). After controlling for macro context variables, mature intellectual property system was positively associated with attempting compulsory licensing. Conclusions Our study provided evidence of an association between attempting compulsory licensing and matured patent systems. This finding contradicts our current understanding of compulsory licensing, such as compulsory licensing as a measure to usurp traditional patent systems and sometimes diametrically opposed to the patent system. The findings also suggest a new role of compulsory licensing in current patent systems: compulsory licensing could be a potential alternative or complement to achieve access to medicines in health systems through manufacturing and exporting patented pharmaceuticals.

#### 6. No alt-agent fiat.

Strait and Wallace 08

L. Paul Strait, University of Southern California and Brett Wallace, George Washington University. “ACADEMIC DEBATE AS A DECISIONMAKING GAME: INCULCATING THE VIRTUE OF PRACTICAL WISDOM”. Contemporary Argumentation and Debate. The Journal of the Cross Examination Debate Association, Vol. 29 (2008): 1-36.

Like all arguments in the negative’s arsenal, counterplans have the burden to be relevant to the question posed by the affirmative plan (disadvantages accomplish this by having a compelling ‘link’). For this reason, counterplans must be competitive but we argue that competition is necessary but not sufficient to demonstrate relevance. Lichtman and Rohrer (1975) observe that negative fiat should have a limited scope, relating to the logic of who is making the decision: It is assumed, of course, that decision-makers being addressed have the power to put a counterplan into effect. An individual or governmental unit can reasonably be asked to reject a particular policy if an alternative promises greater net benefits. If, however, a counterplan must be adopted by another individual or unit of government, the initial decision-maker must consider the probability that the counterplan will be accepted. Debate propositions often affirm that a particular policy should be adopted by the federal government. Even if adoption of this policy by the individual state governments would be more beneficial, a reasonable critic would still affirm the resolution if state adoption were highly unlikely. The federal government should refrain from acting only when the net benefits of state and local action, discounted by the probability that such action will occur, are greater than the net benefits of federal action. (p. 74, footnote 13). Expanding upon this common sense approach, Korcok (2002) reasons that advantages and disadvantages relating to political ramifications, resources, policy effectiveness, enforcement, and so on, all depend upon whose task it is to take the desired action. Therefore, questions of the substantive desirability of the affirmative, along with questions of the educational value of learning general governmental processes, are incoherent without first specifying who is making the decision. Consider what it means when a judge votes affirmative or negative. Supposing the affirmative has presented a topical plan, the judge votes affirmative when the plan is shown to be net-advantageous when compared to the status quo or a competitive alternative, and the judge votes negative when the plan is shown to be less desirable than the status quo or a competitive alternative. If testifying before Congress, this judge could reasonably say: “Based on the arguments I have heard over the last hour and a half, it would be better for you to do X than Y.” In other words, after the debate is concluded, one entity could make a decision based on the information presented. This is not to say that Congress (or anyone else) should make decisions based on the outcomes of scholastic debate rounds. What matters is that the debaters will have made an informed decision. This is utterly impossible if the negative advocates action by some agent other than the affirmative’s. Since the point of fiat is to bracket off questions of ‘would’ in order to focus completely on questions of ‘should,’ questions of probability never get discussed (Broda-Bahm, 2002). From the perspective of the agent identified in the plan, the probability is 100%: if the agent decides to adopt the mandates of the plan, there is an absolute guarantee that it will in fact do so. Yet, if the plan is compared to a counterplan in which Japan, rather than the United States, attempts to solve the advantage(s), there is never a situation where the United States could make a decision based on a 100% probability that Japan would take action if the United States did not. Thus, if Congress failed to consider the chance that that decision-making body would not in fact take the desired action, it would hardly be engaging in what Aristotle (c. 330bce/1941a) calls “correctness of thinking,” the substance of practical wisdom.

#### 7. Roleplaying the state doesn’t endorse it but teaches the language of power to enable internal resistance strategies

Coverstone 05

Alan Coverstone (masters in communication from Wake Forest, longtime debate coach) “Acting on Activism: Realizing the Vision of Debate with Pro-social Impact” Paper presented at the National Communication Association Annual Conference November 17th 2005 <https://www.natcom.org/> -CAT

An important concern emerges when Mitchell describes reflexive fiat as a contest strategy capable of “eschewing the power to directly control external actors” (1998b, p. 20). Describing debates about what our government should do as attempts to control outside actors is debilitating and disempowering. Control of the US government is exactly what an active, participatory citizenry is supposed to be all about. After all, if democracy means anything, it means that citizens not only have the right, they also bear the obligation to discuss and debate what the government should be doing. Absent that discussion and debate, much of the motivation for personal political activism is also lost. Those who have co-opted Mitchell’s argument for individual advocacy often quickly respond that nothing we do in a debate round can actually change government policy, and unfortunately, an entire generation of debaters has now swallowed this assertion as an article of faith. The best most will muster is, “Of course not, but you don’t either!” The assertion that nothing we do in debate has any impact on government policy is one that carries the potential to undermine Mitchell’s entire project. If there is nothing we can do in a debate round to change government policy, then we are left with precious little in the way of pro-social options for addressing problems we face. At best, we can pursue some Pilot-like hand washing that can purify us as individuals through quixotic activism but offer little to society as a whole. It is very important to note that Mitchell (1998b) tries carefully to limit and bound his notion of reflexive fiat by maintaining that because it “views fiat as a concrete course of action, it is bounded by the limits of pragmatism” (p. 20). Pursued properly, the debates that Mitchell would like to see are those in which the relative efficacy of concrete political strategies for pro-social change is debated. In a few noteworthy examples, this approach has been employed successfully, and I must say that I have thoroughly enjoyed judging and coaching those debates. The students in my program have learned to stretch their understanding of their role in the political process because of the experience. Therefore, those who say I am opposed to Mitchell’s goals here should take care at such a blanket assertion. However, contest debate teaches students to combine personal experience with the language of political power. Powerful personal narratives unconnected to political power are regularly co-opted by those who do learn the language of power. One need look no further than the annual state of the Union Address where personal story after personal story is used to support the political agenda of those in power. The so-called role-playing that public policy contest debates encourage promotes active learning of the vocabulary and levers of power in America. Imagining the ability to use our own arguments to influence government action is one of the great virtues of academic debate. Gerald Graff (2003) analyzed the decline of argumentation in academic discourse and found a source of student antipathy to public argument in an interesting place. I’m up against…their aversion to the role of public spokesperson that formal writing presupposes. It’s as if such students can’t imagine any rewards for being a public actor or even imagining themselves in such a role. This lack of interest in the public sphere may in turn reflect a loss of confidence in the possibility that the arguments we make in public will have an effect on the world. Today’s students’ lack of faith in the power of persuasion reflects the waning of the ideal of civic participation that led educators for centuries to place rhetorical and argumentative training at the center of the school and college curriculum. (Graff, 2003, p. 57) The power to imagine public advocacy that actually makes a difference is one of the great virtues of the traditional notion of fiat that critics deride as mere simulation. Simulation of success in the public realm is far more empowering to students than completely abandoning all notions of personal power in the face of governmental hegemony by teaching students that “nothing they can do in a contest debate can ever make any difference in public policy.” Contest debating is well suited to rewarding public activism if it stops accepting as an article of faith that personal agency is somehow undermined by the so-called role playing in debate. Debate is role-playing whether we imagine government action or imagine individual action. Imagining myself starting a socialist revolution in America is no less of a fantasy than imagining myself making a difference on Capitol Hill. Furthermore, both fantasies influenced my personal and political development virtually ensuring a life of active, pro-social, political participation. Neither fantasy reduced the likelihood that I would spend my life trying to make the difference I imagined. One fantasy actually does make a greater difference: the one that speaks the language of political power. The other fantasy disables action by making one a laughingstock to those who wield the language of power. Fantasy motivates and role-playing trains through visualization. Until we can imagine it, we cannot really do it. Role-playing without question teaches students to be comfortable with the language of power, and that language paves the way for genuine and effective political activism. Debates over the relative efficacy of political strategies for pro-social change must confront governmental power at some point. There is a fallacy in arguing that movements represent a better political strategy than voting and person-to-person advocacy. Sure, a full-scale movement would be better than the limited voice I have as a participating citizen going from door to door in a campaign, but so would full-scale government action. Unfortunately, the gap between my individual decision to pursue movement politics and the emergence of a full-scale movement is at least as great as the gap between my vote and democratic change.