## 1AC

### Framework

**Pleasure and pain are intrinsic value and disvalue**

**Blum et al. 18**

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

**Actor Spec— States must use util. Any other standard dooms the moral theory**

**Goodin 90.** Robert Goodin 90, [professor of philosophy at the Australian National University college of arts and social sciences], “The Utilitarian Response,” pgs 141-142 //RS

My larger argument turns on the proposition that there is something special about the situation of public officials that makes utilitarianism more probable for them than private individuals. Before proceeding with the large argument, I must therefore say what it is that makes it so special about public officials and their situations that make it both more necessary and more desirable for them to adopt a more credible form of utilitarianism. Consider, first, the argument from necessity. Public officials are obliged to make their choices under uncertainty, and uncertainty of a very special sort at that. All choices – public and private alike – are made under some degree of uncertainty, of course. But in the nature of things, private individuals will usually have more complete information on the peculiarities of their own circumstances and on the ramifications that alternative possible choices might have for them. Public officials, in contrast, are relatively poorly informed as to the effects that their choices will have on individuals, one by one. What they typically do know are generalities: averages and aggregates. They know what will happen most often to most people as a result of their various possible choices, but that is all. That is enough to allow public policy-makers to use the utilitarian calculus – assuming they want to use it at all – to choose general rules or conduct.

**Extinction comes first under any framework.**

**Pummer 15** [Theron, Junior Research Fellow in Philosophy at St. Anne's College, University of Oxford. “Moral Agreement on Saving the World” Practical Ethics, University of Oxford. May 18, 2015] AT

There appears to be lot of disagreement in moral philosophy. Whether these many apparent disagreements are deep and irresolvable, I believe there is at least one thing it is reasonable to agree on right now, whatever general moral view we adopt: that it is very important to reduce the risk that all intelligent beings on this planet are eliminated by an enormous catastrophe, such as a nuclear war. How we might in fact try to reduce such existential risks is discussed elsewhere. My claim here is only that we – whether we’re consequentialists, deontologists, or virtue ethicists – should all agree that we should try to save the world. According to consequentialism, we should maximize the good, where this is taken to be the goodness, from an impartial perspective, of outcomes. Clearly one thing that makes an outcome good is that the people in it are doing well. There is little disagreement here. If the happiness or well-being of possible future people is just as important as that of people who already exist, and if they would have good lives, it is not hard to see how reducing existential risk is easily the most important thing in the whole world. This is for the familiar reason that there are so many people who could exist in the future – there are trillions upon trillions… upon trillions. There are so many possible future people that reducing existential risk is arguably the most important thing in the world, even if the well-being of these possible people were given only 0.001% as much weight as that of existing people. Even on a wholly person-affecting view – according to which there’s nothing (apart from effects on existing people) to be said in favor of creating happy people – the case for reducing existential risk is very strong. As noted in this seminal paper, this case is strengthened by the fact that there’s a good chance that many existing people will, with the aid of life-extension technology, live very long and very high quality lives. You might think what I have just argued applies to consequentialists only. There is a tendency to assume that, if an argument appeals to consequentialist considerations (the goodness of outcomes), it is irrelevant to non-consequentialists. But ***that is a huge mistake.*** Non-consequentialism is the view that there’s more that determines rightness than the goodness of consequences or outcomes; ***it is not the view that the latter don’t matter***. Even John Rawls wrote, “All ethical doctrines worth our attention take consequences into account in judging rightness. One which did not would simply be irrational, crazy.” ***Minimally plausible versions of deontology and virtue ethics must be concerned in part with promoting the good***, from an impartial point of view. They’d thus imply very strong reasons to reduce existential risk, at least when this doesn’t significantly involve doing harm to others or damaging one’s character. What’s even more surprising, perhaps, is that even if our own good (or that of those near and dear to us) has much greater weight than goodness from the impartial “point of view of the universe,” indeed even if the latter is entirely morally irrelevant, we may nonetheless have very strong reasons to reduce existential risk. Even egoism, the view that each agent should maximize her own good, might imply strong reasons to reduce existential risk. It will depend, among other things, on what one’s own good consists in. If well-being consisted in pleasure only, it is somewhat harder to argue that egoism would imply strong reasons to reduce existential risk – perhaps we could argue that one would maximize her expected hedonic well-being by funding life extension technology or by having herself cryogenically frozen at the time of her bodily death as well as giving money to reduce existential risk (so that there is a world for her to live in!). I am not sure, however, how strong the reasons to do this would be. But views which imply that, if I don’t care about other people, I have no or very little reason to help them are not even minimally plausible views (in addition to hedonistic egoism, I here have in mind views that imply that one has no reason to perform an act unless one actually desires to do that act). To be minimally plausible, egoism will need to be paired with a more sophisticated account of well-being. To see this, it is enough to consider, as Plato did, the possibility of a ring of invisibility – suppose that, while wearing it, Ayn could derive some pleasure by helping the poor, but instead could derive just a bit more by severely harming them. Hedonistic egoism would absurdly imply she should do the latter. To avoid this implication, egoists would need to build something like the meaningfulness of a life into well-being, in some robust way, where this would to a significant extent be a function of other-regarding concerns (see chapter 12 of this classic intro to ethics). But once these elements are included, we can (roughly, as above) argue that this sort of egoism will imply strong reasons to reduce existential risk. Add to all of this Samuel Scheffler’s recent intriguing arguments (quick podcast version available here) that most of what makes our lives go well would be undermined if there were no future generations of intelligent persons. On his view, my life would contain vastly less well-being if (say) a year after my death the world came to an end. So obviously if Scheffler were right I’d have very strong reason to reduce existential risk. ***We should also take into account moral uncertainty.*** What is it reasonable for one to do, when one is uncertain not (only) about the empirical facts, but also about the moral facts? I’ve just argued that there’s agreement among minimally plausible ethical views that we have strong reason to reduce existential risk – not only consequentialists, but also deontologists, virtue ethicists, and sophisticated egoists should agree. But even those (hedonistic egoists) who disagree should have a significant level of confidence that they are mistaken, and that one of the above views is correct. Even if they were 90% sure that their view is the correct one (and 10% sure that one of these other ones is correct), they would have pretty strong reason, from the standpoint of moral uncertainty, to reduce existential risk. Perhaps most disturbingly still, even if we are only 1% sure that the well-being of possible future people matters, it is at least arguable that, from the standpoint of moral uncertainty, reducing existential risk is the most important thing in the world. Again, this is largely for the reason that there are so many people who could exist in the future – there are trillions upon trillions… upon trillions. (For more on this and other related issues, see this excellent dissertation). Of course, it is uncertain whether these untold trillions would, in general, have good lives. It’s possible they’ll be miserable. It is enough for my claim that there is moral agreement in the relevant sense if, at least given certain empirical claims about what future lives would most likely be like, ***all minimally plausible moral views would converge on the conclusion that we should try to save the world***. While there are some non-crazy views that place significantly greater moral weight on avoiding suffering than on promoting happiness, for reasons others have offered (and for independent reasons I won’t get into here unless requested to), they nonetheless seem to be fairly implausible views. And even if things did not go well for our ancestors, I am optimistic that they will overall go fantastically well for our descendants, if we allow them to. I suspect that most of us alive today – at least those of us not suffering from extreme illness or poverty – have lives that are well worth living, and that things will continue to improve. Derek Parfit, whose work has emphasized future generations as well as agreement in ethics, described our situation clearly and accurately: “We live during the hinge of history. Given the scientific and technological discoveries of the last two centuries, the world has never changed as fast. We shall soon have even greater powers to transform, not only our surroundings, but ourselves and our successors. If we act wisely in the next few centuries, humanity will survive its most dangerous and decisive period. Our descendants could, if necessary, go elsewhere, spreading through this galaxy…. Our descendants might, I believe, make the further future very good. But that good future may also depend in part on us. If our selfish recklessness ends human history, we would be acting very wrongly.” (From chapter 36 of On What Matters)

### Advantage 1

**Pharmaceutical innovation is *declining***

**Mata, 19** (Nathan Mata, 11-18-2019, accessed on 8-23-2021, Halloran Consulting Group, "Declining Innovation in the Pharmaceutical Industry | Halloran Consulting Group", https://www.hallorancg.com/2019/11/18/declining-innovation-in-the-pharmaceutical-industry/)WWPP

Despite the increasing demand for new drugs to address unmet and underserved medical needs, innovation within the pharmaceutical industry has not proceeded at the same pace. Data from numerous credible sources have shown that over past 10 years there has been very little breakthrough innovations in the large pharma sector. For example, data from the FDA revealed that from 2006-2014, there had been no increase in the average number of new drug applications (NDAs) and biologics license applications (BLAs) submitted for novel drugs. Submission numbers for novel drugs have remained relatively constant at about 35 NDAs and BLAs filed during each year (NDA and BLA Submissions). Moreover, in the first comprehensive study of evergreening—defined as artificially extending the intellectual property (IP) protection cliff—it was determined that 78% of the patents approved during the period from 2005-2015 corresponded to medications already on the market (Feldman, 2018). Therefore, rather than create new medicines, companies are largely recycling and repurposing old ones. This finding is a startling departure from the classic concept of IP protection for pharmaceuticals and is emblematic of the declining innovation in the industry. One possibility for the apparent lack of innovation to meet medical needs is an underlying scarcity of good ideas: as knowledge advances, it becomes more difficult to discover new ideas. In this case, slowdowns in productivity and innovation would be difficult to prevent or reverse. Yet, other factors may also limit innovation. For example, good ideas may not be scarce but they may be riskier to develop, and large pharma companies may prefer to focus instead on safer, but more marginal, projects. The finding that 64% of FDA-approved drugs in 2018 originated from emerging biopharma companies, not large pharma, suggests that scarcity of good ideas is not a factor underlying the declining innovation. A comprehensive analysis of innovation and R&D productivity in the large pharma sector has been conducted by Dr. Kelvin Stott (Director of R&D Portfolio Management, Novartis). In this two-part blog-post entitled “Pharma’s broken business model, An industry on the brink of terminal decline” (Part 1, Part 2), actual historic profit & loss (P&L) performance data obtained from EvaluatePharma was used to calculate Pharma’s return on R&D investment (ROI) among several large pharmaceutical companies. Dr. Stott’s analysis shows a clear downward trend for R&D ROI over the past 20+ years. A similar finding has been reported by both BCG and Deloitte in 2016 and 2018, respectively. Because the business practices of large pharma show no sign of change, it is likely that this downward trajectory will continue. Trends and Practices Underlying Declining Innovation Growing competition and decreased ROI from R&D programs are the primary reasons for down-sizing of non-core business processes among large pharmaceutical companies. Thus, companies may be prevented from pursuing innovative therapies because they lack the cash to turn their financially riskier ideas into reality. Because down-sizing in the pharmaceutical industry has typically taken essential resources away from discovery and early-stage research, the end result is reduced innovation and productivity. Another important aspect of the innovation/productivity decline is the practice of utilizing the patent system to extend existing patents beyond the initial 20-year protection (in the U.S.), rather than reinvesting profits to foster innovation and create new drugs to meet medical needs. What further exacerbates the problem is the issuance of patents with overly-wide claims that block knowledge creation and patents for what are essentially existing drugs. For example, Losec (AstraZeneca), which was developed to treat heartburn and ulcers, was later reformulated and rebranded. This enabled the company to issue a new patent with new claims for the barely modified medication, effectively extending the company’s monopoly on this type of drug well beyond the period granted by the original patent. Finally, the practice of large pharmaceutical companies to implement share buybacks to boost share prices (and stock options for executives) rather than reinvest in R&D further diminishes the opportunity for innovation. To put things in perspective, a Reuters Special Report noted that pharmaceuticals maker Pfizer spent $139 billion on share buybacks and dividends and just $82 billion on R&D over the past decade. Implications for Stakeholders and Taxpayers The trends and practices within large pharmaceutical companies noted above should be alarming not just to stakeholders in drug development, but also to taxpayers as they are largely footing the bill for drug research while pharmaceutical companies are reaping all the rewards. The development of Sofosbuvir, which treats hepatitis C, is a representative example. Sofosbuvir emerged from over 10 years of basic research science and $62.4 million of U.S. taxpayer-funded research (through the Department of Veterans Affairs and the National Institutes of Health, NIH). But when Gilead Sciences later acquired the drug (labeled as Sovaldi), it priced a 12-week course of pills at $84,000 in the U.S. market, even though a 12-week treatment course costs less than $200 to produce. By the end of 2017, Sofosbuvir had generated over $50 billion in sales. According to Bryn Gay, Hepatitis C Project Co-Director at the Treatment Action Group, “Companies have raked in profits of over $70 billion from hep C medicines, yet companies like Gilead and Janssen have walked away from additional hep C research, such as for a preventative vaccine.”. Gay further stated, “The impact of NIH-funded research again demonstrates that we need to increase government funding for infectious and neglected diseases. We can’t rely on Pharma to set R&D agendas shaped by how much profit can be generated.” Sofosbuvir is not an exception. Taxpayers in the U.S. have funded research via congressional appropriations to NIH funding for every single one of the 210 new drugs that the FDA approved from 2010-2016 (Cleary et al., 2018). Findings from the study by Cleary et al. show that the NIH contribution to research associated with new drug approvals is greater than previously appreciated. This report also highlights the risk of reducing federal funding for basic biomedical research as this would further hinder innovation in both small and large pharmaceutical sectors. Collectively, these facts lead to the inescapable conclusion that the current practice of establishing patent monopolies and price-hiking by large pharma cannot be justified by expenditures related to noble and innovative R&D endeavors.

#### Global IPR laws founded upon the TRIPS agreement exacerbate global inequality. You should reject neg args – they are probably based on unfounded assumptions

Ranjan 18 [Rajiv Ranjan is an Assistant Professor, CMS Business School, Bangalore, Karnataka, India. “Politics of Intellectual Property Rights (IPRs)

in Medicine: The Dichotomies” <https://journals.sagepub.com/doi/abs/10.1177/2319714518789762?journalCode=fiba>] //aaditg

Introduction The health care costs are the single major impediment in pushing people out from the vicious web of poverty (Bartlett, 2011; Briesacher et al., 2010; Kent, 2002; Leone, James, & Padmadas, 2012). Poor people have neither access to a clean environment nor choices which can help them prevent diseases as they cannot afford ‘curative’ health care in the form of medicines. Lack of choice (exit mechanism as in a well-functioning market) to bargain with the companies and voice (as in a well-functioning democracy) to decide the development path and climate change policies their country follows (Ebi & Semenza, 2008; Haines, Kovats, Campbell-Lendrum, & Corvalán, 2006; Kunkel, Pielke Jr., & Changnon, 1999; McCarthy, 2001; Patz, Campbell-Lendrum, Holloway, & Foley, 2005; Patz, Epstein, Burke, & Balbus, 1996) work as a health care impediment. Environmental pollution and climate change impact health of individuals, and poor people are more vulnerable to such health impacts. Thus, there is a denial of a healthy environment to them and hence lack of ‘preventive’ health care by design. Four of the eight UN Millennium Development Goals (MDGs) pertain to health directly. The deadline for the achievement of MDGs has already come to an end in 2015 with many goals not realized and more so in the developed world. UN (2013) had forewarned of such failure. A retrospective analysis of what went wrong is an important international policy question worth inquiry. The existence of Intellectual Property Rights (IPRs) in medicine for many critical life-saving drugs, lack of generic drugs for deadly diseases and lack of research and development (R&D) for diseases related to the poor are some of the possible impediments in achievement of health-related MDG goals (Love & Hubbard, 2007; Stiglitz, 2002, 2004, 2006, 2007, 2008, 2010; Viana, 2001; Williams, 2012). Williams (2012) shows that there are a lot of market failures and government failures in case of health care. In health care, 82% of R&D happens in government organizations and publicly funded research institutions. Companies invest only 1.2% of their revenue on R&Ds. Under these conditions, the logic of existence of IPRs becomes questionable. The logic for the existence of IPRs is based on a number of untested and unverified assumptions about human behaviour. The next section discusses the global health problems through a description of the UN MDG goals related to health and their progress status. This is followed by a section on about government and market failures in health care and the present understanding of public health as an issue, and some understanding of the possible understanding on the solutions front. Public–private partnership (PPP) as an instrument for health care providers and the challenges and preconditions for its successful working as an intervention is discussed. The next section describes the rich–poor dichotomy with regards to health care and how power operates in that, followed by a section on logic of the existence of IPRs, in which what are the possible assumptions of the IPR model for providing incentives to promote medical research in the context of the adverse conditions of health care especially in the poorer developing world and non-existence of a competitive market is identified. Next, the analysis of health care R&D expenditure sharing between public and private organizations is done. Then, in the following section, the power and politics dimensions and how faces of power get reflected in this story of IPRs in medicine is discussed. The public interest versus private gains and poor versus rich debates can be found out in the previous sections. It is revealed that there are boundaries between the developed and the developing world by existence of agreements like agreement on TradeRelated Aspects of Intellectual Property Rights (TRIPS) where the developed countries have high bargaining power as opposed to the developed countries among a host of other issues that clearly show the exercise of power in one way or the other. This is followed by a section on globalization phenomenon and IPRs, the power and politics dimensions revealed and conclusions and future work that can follow from this work, respectively. MDG Goals and their Progress: A Description of the Global Health Scenarios and Mitigation Strategies This article focuses on the four goals that are concerned with health and related issues. These would be a reduction of child mortality, improvement of maternal health, combat HIV/ AIDS and other diseases, and eradicate extreme poverty and hunger. This section gives the progress on these goals as of June 2013 as shown by a report on their progress (UN, 2013). 1. Eradicate extreme poverty and hunger 2. Reduce child mortality 3. Improve maternal health 4. Combat HIV/AIDS, malaria and other diseases To comment on the overall progress of MDGs related to health care, it would not be inappropriate to say that the progress has been concentrated to the developed countries while the developing countries and regions still lack behind in terms of MDGs. It can also be seen that access to health facilities still continues to be an issue in most of the UN member states. Government and Market Failures in Health Care and Complexity of the Problem The whole health care debate is on whether the government should intervene or not, despite the understanding that there are both market failures and government failures. Neither of the two, that is, market failures and government failure, are mutually exclusive scenarios in all situations so that one can serve as a plausible answer to the other. The present understanding is that there is a need for collaborative participation of both public and private entities to address the challenges of health care. The emergence of a third entity called civil society organizations which acts as a liaison for moderation between the public welfare goals versus the private profitmaking objectives reveal the interplay of power between the different stakeholders in the health care since public policymaking is less of a technocracy and more of a social construction of politically valued ends. And hence the questions of the emergence of civil societies and NGOs and how they arose, what were the forces behind its formation and day-to-day financial requirements become critical to understand whether their pushing for a social change of the social service exercise is just a worldly exhibition of a co-optation strategy of the more powerful against the lesser as pointed out by Kivel (2007). There are mainly two types of the health care system. One, free market-based system. Second, governmentbased socialized health care system. There is the prevalence of mixed system as well with countries scattered on the continuum of the two extremes, but how the partnership gets strengthened for delivery of better public services is still a question of enquiry. In a market-based health care system, the logic is that government should not intervene as it prevents the efficient allocation of resources, that is, the efficiency criterion. The rhetoric is that invisible hand of the market will take care of resource allocation. The larger assumption is that health care market fulfils all necessary conditions of an ideal perfectly competitive market. But the ideal efficient market is hard to find and especially so in case of products and services pertaining to the poor who do not have the want due to knowledge (the verifiability of which needs to be tested) that is to say that they are unconcerned about their own health which seems implausible. If they do have the want, they lack the purchasing power to convert it into demand which is a precondition for market provisioning. The understanding of the government’s role is to plug the gaps left behind due to market failures. This is under the assumption that the people in the government are only concerned about public welfare as opposed to private benefits as the government’s critics point out and empirical evidence of corruption reveal. Health for all is a public good according to this discourse. This is motivated by Tobin’s (1970) description of specific egalitarianism and the redistributive objectives of the governments, that is, the justice and equity dimensions. Cash transfer versus direct delivery, better targeting, imposing policymakers’ preferences become some of the major debates. Government failure like market failure also happens at several counts. If the market has information failure, the government is no better. The government also does not know the exact gap due to market failures. Then there is also hypothesis and plausible evidence of markets being more efficient than the government. There are problems of moral hazard, economic sustainability, that is, concern about level and rate of growth of health spending, opportunity cost of spending, relative benefits reduction with more expenditure, fiscal sustainability, that is—ability to recover costs incurred—cost recovery ratio (which is 1.55% average across all the states of India). The challenges are ways to reduce burden, that is, reduce health expenditure, increase revenues from health services, make health services more efficient, etc. Though government intervention is needed as the ideal market is not a reality. The different levels of intervention can be: • Knowledge imparting activities • Regulation of private markets • Mandate something • Finance health care with public funds • Provide health care dire ctly In case of private, there is a misalignment of interest; in case of government, there are accountability issues and perverse incentive with no proper responsibility mechanisms to ensure proper services. The emergence of civil society organizations do offer a hope but their mode of arrival, the source of sustenance and ways of working needs to be ascertained before jumping on the conclusion that they are proper representatives of the societal preferences. Thus, both existences of public and private institutions in health care and a representative civil society are what the current state of literature suggests as important stakeholders for health care provision ing. PPPs as an Instrument for Health Provi sion The complexity of health care problems has posed several challenges in the provision of health care for the less endowed. PPPs have emerged as one of the solutions to address some of these issues. But it has been questioned on equity and distributional grounds. Though PPP is not the panacea for all ills, but with proper ownership, power, risk and responsibility sharing between the public and the private players, better health outcomes for all can be achieved as indicated by the UN MDGs. Moreover, one thing is easily agreeable that both private and public need to join hands to meet the challenge of providing quality health care services to all considering the financial and incentive lacunae faced by both of them respectively. And, most importantly it must be seen as a supplement to the public provisioning system rather than a substit ute. The reasons for the introduction of PPPs in health care provisioning are that it leads to an increased level of finance in the sector as a whole. It supplements government provision and hence leads to a reduction of pressure on government finances. It also provides for a learning curve for the private sector in the provision of health care for the poor at low cost and offers scope for innovation coming from private sector. The government authorities need to focus on their key strengths of policy, planning, regulation and quality assurance, and private in provision where they are better. There needs to be a focus on outputs and outcomes monitoring from a provider rather than only input focus. The longer time horizon leads to a better alignment of interests of the public and private. It also leads to a reduction of politicization of issues and corrupt ion. The downsides of PPP can be loss of control by public health authorities and hence lead to loss of public accountability, if not properly designed. It can lead to full privatization. The distributional aspects of benefits can be questioned leading to inequalities in provision and exclus ion. But PPPs involve a very complex design in terms of strategy, system and processes. The idea of PPPs in health care is a recent phenomenon. Public sector’s role is to define the scope of business, to specify the priorities, targets and outputs, and also to set the performance regime by which the management of the PPP is given incentives to deliver. The role of private sector is in delivering on the objectives of PPP creating value for money for the public sector. PPPs must not be confused with privatization because the former is a collaborative effort to promote financial as well as service delivery improvements without increasing the role of private over the public or the other way round. In case of primary health care, it becomes all the more important because there is a degree of public good characteristics attached to the intrinsic nature of the good. The main aim of introducing PPPs in health care is to ensure efficiency, effectiveness, quality, equity and accountabil ity. This analysis only shows the complexities involved in health care provisioning and hence jumping to solutions based on models might not be the best way to go as models are not full representation of reality and are freight with a lot of assumptions whose validity needs to be ascertained before being romanticized by the ideas expressed in the most eloquent manner and jumping into act ion. The Rich–Poor Dicho tomy As pointed out by Paul (1992) in his accountability framework that the less-endowed people are faced with lack of various ‘exit mechanisms’ such as money, vouchers and grants, lost-cost health care services, etc., and they have to resort to ‘voice mechanisms’ such as seeking NGOs help, etc. Figure A3 can be referred to see how the exit and voice mechanisms availability plays out between the poor and the rich wherein the former is not able to demand even the primary health care for him in contrast to the latter who can even demand his cosmetic needs. The contrasting reality becomes all the starker when the same medicine which can have been used for the treatment of Kalajar, a fatal disease 72 FIIB Business Review 7(2) mostly affecting poor people is sold as a hair removal cream to serve the cosmetic needs of the rich when people are dying of the Kalajar. Kivel (2007) and Chossudovsky (2010) point out the hidden dangers in seeing NGOs as representative of the societal needs without ascertaining facts about their mode of arrival, the source of sustenance and ways of working. The co-optation strategy by legitimization of NGOs as representatives of societal concerns does not help the cause of low voice of the poor with regards to health care among other basic needs. Moreover, the poor people, especially the tribal are not allowed to indulge in preventive healthcare. Also norms for curative healthcare are defined by society. People who do not follow are labelled as dissenters. The framing of the whole health care debate as curative and not preventive, which a widespread debate even in the developed world groups, especially in the US, only reveals the interplay of power between the people who can afford versus the less endowed in terms of resources. This is an exhibition of the various faces of power, namely pluralistic tradition, non-decision-making, ideological and disciplinary powers as mentioned in by Healey and Hinson (20 10). The Logic of IPR Demysti fied IPRs by definition are appropriate benefits emerging from intellect to a private entity as opposed to the public in large. For IPRs to be a part of public policy, they have to be seen as serving a public purpose, that is, helping achieve goals that are considered legitimate for and by the public. Therefore, the claims that are made in favour of IPRs are that they are necessary to incentivize innovation. The nature of claims and assumptions behind IPRs need to be investigated fully before talking about them as the only legitimate way to ensure health care innovation as it is freight with behavioural assumpti ons. Refer to Figure A4 for understanding the flow diagram of the rationale. The fundamental claim is: IPRs are necessary to incentivize innovation by private actors. Incentivizing private innovation with IPRs leads to a greater innovation. More innovation is good for the society. Therefore, public policies should support IPRs. The assumption is more innovation (regardless of kind) is good for soci ety. Plausible concern relating to IPRs in medicine is companies protect their IPRs by incremental innovations which prevents their conversion into generic medicine rasing distributional concerns (Henry & Stiglitz, 2010). By ignoring these, goals of public policy are delegitimized/reprioritized. One of the nested claim is that in the absence of IPRs, sufficient incentives for innovation would not exist, and therefore lead to reduced innovation. Which might not be true always or else Alexander Fleming would not have had incentive to discover penicillin which he did. Other assumptions are that innovation is costly, most of these costs are private, and therefore the private benefits of innovation must exceed the private costs of innovation for sufficient incentives. The concerns are ignoring costs of innovation borne by the public. There is also ignorance of non-pecuniary motives for innovation. By ignoring these, more attention to certain kinds of incentives and costs is paid. Therefore, certain kinds of innovation, the kind which was done by those with pecuniary interests and the kind which was done where there are clear pecuniary rewards, are encouraged. Thus, the whole logic is freight with a lot of assumptions about human behaviour and motivation which needs to be verif ied. Discussion R&D in Health Care Expenditures: The Public–Private De bate There is a need to analyze the extent of spending that takes place on R&D for the health care industry in comparison to other expenditures. Looking at the industry investment budget on R&D as a percentage of sales, it has stayed in the range of 1%–1.5% for a long time now (Derek, 2013). Referring to Booz for their annual survey of ‘Global Innovation 1000’, it is agreeable that semiconductor industry and the drug industry are the two largest industries where most of the money is reinvested in the l abs. The big companies have expenditures at the level of the semiconductor industry. Roche spends over 19%, Merck spends over 17% and AstraZenca spends over 16%. Other biggies such as Sanofi and GSK spend over 14% and Pfizer spends over 13%. But Pfizer spends the highest in terms of magnitude. Johnson & Johnson (J&J) and Abbott have their spending a bit lower than the biggies. But there is rarely a drug company that spends in a single-digit percentage. So nearly half of the top 20 R&D spending companies are in the drug domain. Also, the only domain surpassing them is the semiconductor industry. Referring to Figure A1 and A2, it can be seen that super drugs get cheaper and generic as times passes. The productivity of research comes down. The only way to get spikes is a discovery of new disease and not a new drug. But what really needs to be thought is that, is the spending more significant than the other expenditures of the drug companies. Finding R&D expenditures is easy because the drug companies list them as a line item in their financial reports. To compare them with the marketing expenditures, the sales, general and administration expenses, that is, SG&A, have to be looked into. The SG&A component comprises elements other than sales and marketing spend ing. For drug companies, SG&A spending is way higher than their R&D expenditures in most of the cases (Derek, 2013; Staton, 2013). The case of Biogen can be intuitively seen as an exception as specialty drugs will not require the magic of sales representatives to convince the practitioners. • Merck spends on SG&A 27%, whereas on R&D 17.3% • Pfizer spends on SG&A 33%, whereas on R&D 14.2% Ranjan 73 • AstraZeneca spends on SG&A 31.4%, whereas on R&D 15.1% • BMS spends on SG&A 28%, whereas on R&D 22% • Biogen spends on SG&A 23%, whereas on R&D 24% • J&J spends on SG&A 31%, whereas on R&D 12.5% Comparing it to the other industries like airlines where the SG&A expenditure is nearly only 5% of their revenue, a lot of time needs to be spent on why cannot drug compa nies lower their marketing and adminis trative costs and spend more on research or price discrimination to make drugs affordable to the poor. For 60 years, the AIDS drugs did not get public by renewal through incremental patents which do show the private profit-making for incentives turning into a profiteering exercise. This shows how private incentives become perverse and a mechanism to wield resource and power as the resource dependence theory (Hillman, Withers, & Collins, 2009) suggests. The TRIPS Agreement: The Developed versus Developing World Powe r Dynamics TRIPS Agreement TRIPS stands for Trade-Related Aspects of Intellectual Property Rights. The TRIPS agreement of the World Trade Organization (WTO) requires all member countries to adhere to minimum standards of intellectual property protection (e.g., all technological inventions must be protected for at least 20 years). It serves as one of the three pillars on which the WTO now rests, along with trade in goods and trade in services. The minimum standards of protection in TRIPS cover different kinds of intellectual property, including patents (which grand market exclusivity for technological inventions), copyright (for artistic and literary works) and trademarks (for names and symbols). It requires that these standards be effectively implemented by all WTO members. This means that countries should have legal and administrative procedures under the national courts that would allow holders of property rights, domestic and foreign, to seek and obtain redress in the event that their rights are infringed. If a WTO member fails to represent these standards in national law or to implement them, it can be challenged by trading partners under the WTO dispute settlement p rocedures. TRIPS and Pharm aceuticals For developing countries, the most important aspect of TRIPS agreement relates to its provisions on patents, especially because they affect pharmaceuticals industry. Prior to TRIPS, most developing countries had ‘weak protection’ for pharmaceutical patents (Subramanian, 2004). This constitutes of short patent terms, the narrow scope for definition, the invention to facilitate ease of imitation and relatively tolerant use of compulsory licensing to dilute the monopoly power of the patent holder. In the Uruguay round, which offered scope for bargaining and the exchange of concessions between nations, developing countries sought compensation for the likely negative impact of TRIPS. Thus, higher standards of protection for intellectual property in exchange for better access for clothing and agricultural goods thus constituted the grand bargain in this round between industrial and developing countries. Impact on Developi ng Nations In the TRIPS negotiations, developing countries were asked to strengthen their patent protection to levels prevailing in industrial countries. But it had an economic impact on the developing nations. According to economic theory, stronger patent protection has two conflicting effects on economic welfare. • In short run, it confers monopoly power on patent holders, reducing competition and increasing prices in the market in which the patented product is sold. • In the long run, by providing economic rents or monopoly profits, it increases the incentive to undertake R&D, by allowing the fixed costs of R&D to be recouped. For developing countries, the economic effects are different. As net users rather than net exporters of R&Dintensive products, they do not benefit from the monopoly profits that are created by patent protection. The profits directly benefit the multinational corporations instead and the consumers suffer from higher prices. Further, because the markets are small in relation to global demand, actions taken by developing countries to strengthen patent protection have little impact on the incentive to undertake additional R&D. Thus, a combination of higher costs in the short run and likely absence of dynamic gains overtime means that raising levels of protection would not benefit developin g countries.

#### Pharma patent practices serve to keep drug prices high: evergreening, product hopping, patent thickets, pay for delay

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Practices [https://fas.org/sgp/crs/misc/R46221.pdf 2/11/2020](https://fas.org/sgp/crs/misc/R46221.pdf%202/11/2020) Congressional Research Service ] // aaditg

Intellectual property (IP) rights in pharmaceuticals are typically justified as necessary to allow manufacturers to recoup their substantial investments in research, development, and regulatory approval. IP law provides exclusive rights in a particular invention or product for a certain time period, potentially enabling the rights holder (e.g., a brand-name drug manufacturer) to charge higher-than-competitive prices. If rights holders are able to charge such prices, they have an incentive to lengthen the period of exclusive rights as much as possible. Indeed, some commentators allege that pharmaceutical manufacturers have engaged in patenting practices that unduly extend the period of exclusivity. These critics argue that these patenting practices are used to keep drug prices high, without any benefit for consumers or innovation. Criticisms center on four such practices:  “Evergreening”: So-called patent “evergreening” is the practice of filing for new patents on secondary features of a particular product as earlier patents expire, thereby extending patent exclusivity past the original twenty-year term. Later-filed patents may delay or prevent entry by competitors, thereby allowing the brand-name drug manufacturer (the brand) to continue charging high prices.  “Product Hopping”: Generic drug manufacturers allege that as patents on a particular product expire, brand manufacturers may attempt to introduce and switch the market to a new, similar product covered by a later-expiring patent—a process known as “product hopping” or “product switching.” This practice takes two forms: a “hard switch,” where the older product is removed from the market, and a “soft switch,” where the older product is kept on the market with the new product. In either case, the brand will focus its marketing on the new product in order to limit the market for any generic versions of the old product.  “Patent Thickets”: Generic and biosimilar companies also allege that the brands create “patent thickets” by filing numerous patents on the same product. These thickets allegedly prevent generics from entering the market due to the risk of infringement and the high cost of patent litigation.  “Pay-for-Delay” Settlements: Litigation often results when a generic or biosimilar manufacturer attempts to enter the market with a less expensive version of a branded pharmaceutical. Core issues usually include whether the brand’s patents are valid, and whether the generic or biosimilar product infringes those patents. Rather than litigate these issues to judgment, however, the parties will often settle. Such settlements may involve the brand paying the generic or biosimilar to stay out of the market—referred to as “reverse payment” or “pay-for-delay” settlements. These settlements are allegedly anticompetitive because they allow the brand to continue to charge high prices without risking invalidation of its patent, thus unjustifiably benefiting the settling companies at the expense of the consumer.

#### That fuels monopolies stifling innovation.

Bryan Mercurio 14, Law Professor at The Chinese University of Hong Kong, “TRIPs, Patents, and Innovation: A Necessary Reappraisal?” <https://e15initiative.org/wp-content/uploads/2015/09/E15-Innovation-Mercurio-FINAL.pdf>

Identifying the factors that stimulate innovation is difficult (Lemley 2000), and attention must be paid to the different kinds of innovation--cumulative innovation; horizontal (basic) innovation; and vertical (applied) innovation. The impact of patent protection can differ on each of these types of innovation. For instance, where cumulative innovation occurs--that is, where a single product may rely on inventions owned by a number of firms--“there is good reason to think that the patent system may discourage innovation overall rather than encouraging it” (Bessen and Maskin 2009; Chu et al. 2012). Shapiro (2001) finds that “with cumulative innovation and multiple blocking patents, stronger patent rights can have the perverse effect of stifling, not encouraging innovation.” In such a situation, multiple licences have to be purchased; uncertainty regarding the status of the technology persists; and the value of patent licensing is questioned (Heller 2008; Boldrin and Levine 2008). Lawsuits become the norm; costs rise as firms defend claims and play the game by defensively purchasing patents; and innovation suffers (Boldrin and Levine 2013; Bessen and Muerer 2008). One only needs to look at the present situation in the high-tech sector to see this cycle playing out, where as much as US$20 billion was spent in 2010-11 on patent litigation and purchases, and where a “patent tax” of up to 20 percent of R&D costs exists (Duhigg and Lohr 2012). That a limited monopoly can stifle innovation should not come as a surprise given that competition is generally seen as a positive force in a market economy. Competition is widely thought to provide incentives for the efficient use of resources; motivation for constant progress; and protection for consumers (Vickers 1995). To some, there is an inherent contradiction between innovation and patent protection, as the latter impedes diffusion and obviates potential gains to be made from collaboration and competition (Rothbard 1962; Mises 1966; Palmer 1989; Lemley 2000; Stiglitz 2008). Thus, while Shumpeter acknowledges that competition for innovation led to temporary monopolies and argues that these monopolies were in turn replaced when new firms further innovated (1976), Stiglitz demonstrates that the established monopolies became entrenched as costs and externalities reduced incentives for displacement (Stiglitz and Walsh 2005). In turn, insufficient diversity among patent holders (a lack of so-called “equilibrium diversity”) encourages them to focus R&D on improving existing technologies through incremental improvements, as opposed to investing in R&D to develop new technologies and products (Acemoglu 2011).In essence, this is what the European Commission alleged in its prosecution of Microsoft for anti-competitive behaviour. There, the Commission deemed Microsoft to be a dominant player, which used its near-monopoly power to reduce “talent and capital invested in innovation” in a manner that “limits the prospects for ... competitors to successfully market innovation and thereby discourages them from developing new products” (2004). The negative effect on innovation is exacerbated by a number of factors, including the growing problem of patent thickets. Owing to the“difficulty of determining the boundaries” of patent claims, there are often multiple and competing claims over one or more aspects of an invention- -situations which, Stiglitz states, “especially impede innovation” (2008). While patent thickets have existed for more than a hundred years (a patent thicket impeded the development and commercialization of the airplane), they have more recently become particularly widespread in the electronics industry (GAO 2013). Other factors, such as defensive patenting and the extortion-like practices of socalled patent trolls, have likewise substantially increased the risk of net welfare loss and less innovation (Bessen et al. 2011; Tucker 2011). Recent studies even find that patent pool arrangements result in reduced innovation by member-firms (Lampe and Moser 2010; Joshi and Nerkar 2011; Lampe and Moser 2012). Evidence also exists to show that stronger patent protection leads not to enhanced innovation or an improvement in overall welfare, but to firms protecting their interests by advocating even more protection (Landes and Posner 2003). In so doing, firms divert resources away from R&D, and into lobbyists and lawsuits. Boldrin and Levine (2013) refer to this as the political economy effect, where patent protection keeps increasing due to the lobbying efforts of entrenched firms, and without regard to the system as a whole. In their view, such behavior distorts the optimum range of protection and unbalances the entire system. In conclusion, while it is a certainty that patent protection increases patent applications and the number of patents granted, there is little to no solid evidence that it leads to increased innovation (Boldrin and Levine 2013; Scherer 2009; Lerner 2009; Gallini 2002; Jaffe 2000). Since the evidence suggests that “policy changes that strengthen patent protection … [do] not spur innovation” (Lerner 2002; UNCTAD 2011), it is unsurprising that “there is widespread unease that the costs of stronger patent protection may exceed the benefits” (Jaffe 2002). POTENTIAL RESPONSES To establish the economic significance and value of patents, it is necessary to weigh their social costs against their social benefits. Hall et al. (2012) explain, In principle a patent will function to increase fixed (and most likely sunk) costs of entry into a market where the invention protected by the patent is practiced. This will reduce entry and therefore competition. From a welfare perspective, this is the price society pays in order to encourage invention and innovation by the initial entrant. What results is a trade‐off between the interests of the incumbent holding the patent and the potential entrant excluded by it. In the case of patents, policy makers need to come to a view of how much protection to afford the patentee in order to create incentives for R&D. Given the trade-off between innovation and access, policy should be designed to reach the “optimal scope of IPRs protection”--that is, a “balance between the social benefit of innovation and the social cost of monopolistic distortion” (Nordhaus 1969). It is this balance that some believe is now lopsided. This section focuses on what can be done within the confines of the WTO to ensure that patent protection stimulates innovation and that the benefits are in balance with social costs. It goes beyond merely describing the available flexibilities offered by TRIPS to Members or analyzing the use of such tools. This work has been done (Mercurio 2013; Declaration on Patent Protection 2014), but does not go to the heart of the issue-- that of the link between IPRs and innovation. Moreover, given the definitional vagueness and uncertainty of the boundaries of patent claims and rights, countries have become risk averse and are unlikely to take action that may be viewed as inconsistent with the TRIPS Agreement. The discussion and debate must now move beyond the well-known but little used flexibilities to encompass the broader and more fundamental issue of whether IPRs--and correspondingly the TRIPS Agreement-- actually encourage innovation. In a sense, all the potential responses are radical in that they all require a shift from the status quo and amendment to the TRIPS Agreement. For this reason, none are likely to be feasible in the short, and perhaps even medium, term. This does not mean that potential responses should not be discussed. As the economic data and evidence against the current form and level of patent protection mounts, alternatives will become more realistic options. Radical proposals aimed at promoting innovation deserve to feature in the debate. The remainder of this section raises four alternatives to the status quo for discussion.

#### Err aff – offensive patents are more likely to be used than defensive patents

Gubby 19 (Helen Gubby, Is the Patent System a Barrier to Inclusive Prosperity? The Biomedical Perspective, Wiley Online Library, 06 September 2019, <https://onlinelibrary.wiley.com/doi/full/10.1111/1758-5899.12730)//ww> pbj

Patent system manipulation The patent system has become the context in which many innovations reach society. Patented inventions are everywhere: from everyday kitchen items like coffee machines and cleaning products to inventions that have a significant global impact, such as advances in medicinal drugs, systems to purify water and increasing the harvest from crops. In return for disclosing the information necessary for others ‘skilled in the art’ to make the invention, inventors of new and useful products and processes are rewarded with a monopoly, usually for 20 years. The patent is the legal instrument that protects that monopoly. The ideology behind the development of the patent system was to create a win-win situation: increased prosperity for inventors as they could make use of their market monopoly position to establish their reputation, recover research costs and make a profit, and increased prosperity and welfare for society which could benefit from these new inventions. But does the patent system deliver a win-win result? The patent application must describe how to make the invention and this information is published during the patent application process. Typically applicants will keep this information to the absolute minimum necessary in order to obtain the patent. Patenting only selected aspects of an invention can obscure the overall configuration of the invention. The use by corporations of patents as strategic tools has further undermined the original goals of the patent system and skewered the patent bargain in favour of the inventor. Biomedical innovations are vital to healthcare: they should not be controlled by private companies through patent monopolies. 1 The patent monopoly The monopoly awarded to the patentee gives the patent holder the right to exclude all others from making, using, selling, offering to sell, keeping the product or importing anything covered by the patent claims in all countries where patent protection has been granted. In general, this exclusionary right persists (if renewal fees are paid) until the expiration of the patent protection period. This yields the patent owner significant power. Even Adam Smith, who considered most exclusive privileges to be detrimental to society, did not consider this to be the case with respect to patent monopolies. These, Smith considered, ‘are harmless enough’: For if the legislature should appoint pecuniary rewards for the inventors of new machines, etc., they would hardly ever be so precisely proportioned to the merit of the invention as this is. For here, if the invention be good and such as is profitable to mankind, he will probably make a fortune by it; but if it be of no value he also will reap no benefit. (Smith, 1762-3, p. 83) This too was Jeremy Bentham's justification of the patent system: the utilitarian ground of efficiency. An exclusive privilege, Bentham argued, is ‘of all rewards the best proportioned’ (Bentham, 1843, p. 71). If the invention were not useful there would be no reward; if it was useful then the reward would be proportionate to its utility. 2 The distortion of the patent system: the patent as a strategic tool As the economy has largely shifted from industrial manufacturing to high-tech, life science and information processing industries, intellectual property has become more and more important. Corporations have become increasingly aware of the potential of the patent, not just as a shield to protect against imitation, but as a strategic tool to block competition and dominate markets. Patents have come to have a broader strategic function in which innovation may only play a small part. Although many patents do not produce any income: ‘In terms of strategy, though, the patent can be much more valuable’ (Macdonald, 2004, p. 143). Patent strategy is directly related to the business context. The Carnegie Mellon Survey of the US manufacturing sector in 1994 revealed that firms often used patents as strategic tools, rather than as simply a means of protecting an invention from wrongful imitation (Cohen et al., 2000). In their examination of motives to patent, Blind et al. (2009) recognised that, although protection from imitation was still the most important factor, ‘the importance of the strategic motives to patent are confirmed’ (Blind et al., 2006, p. 671). Patent strategies The decision to patent has become in part uncoupled from the original core purpose of the patent: to protect an invention from unfair imitation by other market participants. Larger firms, with the capital assets to pay for the cost of patenting, use their patent portfolios strategically. Patents have become useful as bargaining chips; they provide leverage. Large patent portfolios are a means to get access to important co-operations or cross-licensing arrangements (Blind et al., 2009, p. 431). Yet while building the portfolio requires enormous legal costs, it contributes little to research incentives. Furthermore, these portfolios can be used not just to oblige competitors to take licences, but also the terms of these licences can restrict competitors to certain areas of technology (Barton, 2000). Larger firms can afford to play the ‘wrap around’ strategy. Instead of applying for a single patent to cover an invention, other patents are filed around the main patent. These related patents lock down the discrete features of an invention. The tactic hinders entry to the market. Competitors will be put to time, effort and cost to fight their way through all the relevant patents covering the technology. Furthermore, the chance that the competitor's invention may infringe one of the many claims in one of the many patents is high. Not only can damages be awarded for infringement, but also an injunction. Injunctions prevent the party accused of infringement from producing any products that require the use of the technology covered by the infringed patent and all infringing products are removed from the market. Patents may be used simply to block competitors. Using a patent as a blocking strategy is common practice (Neuhäusler, 2012). Defensive blocking is used to protect a firm's own freedom to operate: it does not want to be shut out by the patents of its rivals. An offensive blocking strategy is where patents are filed to cover products or processes that the firm does not intend to practice itself, but which could be viable alternatives to competitors. By patenting all conceivable alternatives, research by competitors that might threaten their own technological lead can be thwarted. As in general a patentee is under no obligation to license out its technology to another, the strategy can deter market entry or new product launch. This offensive blocking of competitors by means of patents, ‘is clearly a case of the patent system being used for purposes other than for which it was originally intended’ (Blind, 2009, p. 436). However, both defensive and offensive blocking should be a policy concern, as they can reduce economic efficiency. Defensive patenting increases cost to firms without necessarily producing any benefit and offensive patenting can reduce technological progress and increase consumer costs by reducing competition (Thumm, 2004, p. 533). Using data from a large-scale survey of patent applications, Torrisi discovered that a substantial share of patents remained unused and a substantial number of patent applications were filed to block other patents. There were institutional differences; there were more unused patents in Japan and the EU than in the USA. Although cautious to make generalisations about unused patents, as some unused patents are there to ensure freedom to operate or simply because of management inefficiency, Torrisi et al. did conclude that: ‘[o]ur results highlight that there might be substantial benefits that patent owners draw from being able to keep patent rights unused. These would have to be balanced against possible harm imposed on other economic agents’ (Torrisi et al., 2016; , p. 1384). These strategies show a disconnect with the original purpose of the patent system. Patent strategies impact on innovation, and this in turn impacts on society. Concern was already expressed quite forcibly some years ago by Turner: Surely when the framers of the [US] Constitution empowered Congress to grant monopolies to ‘promote the progress of science and the useful arts’, they did not envision the beneficiaries of this grant would use it to bury new technologies to protect market share or capital investments. (Turner, 1998, p.209) Administrative failures Patent offices have been struggling to cope with the increasing number of patent applications: in 2017, more than 3 million patent applications were filed worldwide (WIPO, 2018). This influx has resulted in substantial application backlogs, with an increasingly long time between the patent filing and the patent grant: five years is not unusual. Complaints of poor quality control have been made concerning the US Patent and Trademark Office as well as the European Patent Office (Abbott, 2004; Mabey, 2010). The WIPO recognised a consistent upward trend in patent filings is putting patent offices under enormous pressure (WIPO, 2017, p. 13). Why are these administrative failings dangerous from a societal perspective? Patents grant a monopoly that can impact innovative processes for 20 years or more. Patents have been granted that should not have been granted. When an overly broad patent is granted, this can block further innovation by others. Broad patents may mean that access to vital research is not available because the results of that research are covered by patent claims. In particular, broad basic patents on fundamental research can block and deter follow-on research. The incentive to innovate is reduced (Barton, 2000; Henry and Stiglitz, 2010).1 Back in 1966, the societal implication of overly broad grants was expressed clearly by the US Supreme Court when it rejected a broad claim covering a group of chemicals: ‘Such a patent may confer power to block off whole areas of scientific development without compensating benefits to the public.’2 3 The exclusionary effects of patent system manipulation: the biomedical sector Biotechnical inventions have a fundamental impact on healthcare, with applications in medical diagnosis, research tools and pharmaceutical drugs. Knowledge has become a very valuable asset. Its commercialisation opens up lucrative business opportunities. The strategic use of patents in the biomedical sector is intended to protect those business interests. However, those patent strategies have societal repercussions. Intellectual property rights and biomedical research A common argument is that there is a distinction between fundamental research and the application of that research; fundamental research should remain in the public domain, while applications can be the province of patents. That is a misguided distinction. As Eisenberg and Nelson point out, the conventional view that basic research is a public enterprise while applied technology is a private enterprise conducted in the hope of earning profits, ignores the ways in which basic science and applied technology can frequently overlap: public and private interest may then conflict (Eisenberg and Nelson, 2002). Fundamental research can become proprietary. A patent should only give protection to an invention. According to US law, this invention must be ‘useful’ (35 US Code, Section 101) and the European Patent Convention 1973 (EPC) requires that an invention is capable of ‘industrial application’ (Art. 52, EPC). Patent law therefore mandates that there must be a practical application. Consequently, a patent does not extend to a discovery, the terrain of fundamental research, as this is explicitly excluded from patentability. The line between ‘discovery’ and ‘invention’ has, however, become exceedingly thin, if non-existent, with respect to molecular technology. The current position with regard to genes and DNA sequences in effect marks a departure from the traditional doctrine that excluded discoveries from patentability. Genes are not new products; they exist in nature and therefore cannot be invented. Yet today, genes and gene sequences are patented as inventions, being regarded as ‘products’. Even if a use of the gene or sequence is speculative, if a use is plausible at the time the patent is filed the utility requirement is fulfilled. The EPC was amended to be brought into line with the terms of the European Directive on the legal protection of biotechnological inventions. This Directive states: An element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element.3 Taking an apparently different track, in 2013 the US Supreme Court stated that the mere act of isolating a gene from its surrounding genetic material was not an act of invention. The court did accept synthetic cDNA as patentable, as this was created in the laboratory.4 Scientists have voiced concern that what is often patented has not so much been produced but rather discovered, and is human genetic information rather than an invention (see for a summary of some of these arguments Bergel, 2015). These developments in patent law have created a very real danger: researchers could be barred from accessing fundamental research, which in turn could hinder new knowledge and further innovation. Back in 1998, Heller and Eisenberg warned policy makers to be alert: more upstream rights could block downstream innovation. In this way, the private ownership of biomedical research could lead to fewer useful products for improving human health (Heller and Eisenberg, 1998). If genes and DNA sequences are patent protected, then the patent owner has the right to exclude all others from using that technology. This breach of the discovery/invention distinction is symptomatic of the expansion of patentable subject matter at a global level, extending property claims deep into biology and limiting the scope for accessible treatment and future research (David and Halbert, 2017). The danger of private ownership of fundamental research became apparent with the commencement of the Human Genome Project in the 1990s. The project turned into a struggle between publically funded scientists and private companies. Publically funded scientists worked hard to ensure that all their research would remain in the public domain and therefore published all their findings to prevent patent applications blocking access to research. Their attempts were not always successful. For example, one day before Mike Stratton was due to publish his paper on cancer genes in the journal Nature in 1995, the private company Myriad Genetics applied for a patent on BRCA1 and BRCA2, which were associated with breast cancer. The patents allowed it to charge for tests at a cost of $2,500 per patient. Licences for the use of its simpler tests for breast cancer by other labs cost several hundred dollars per patient, a cost that, given the nature of the American healthcare system, meant the test was not available for all female patients in the USA. By 2015, Myriad was worth over $3bn (Pollock, 2018, p. 64). The leading patent offices, those in the USA, Europe and Japan, have granted thousands of patents claiming human DNA. Patent thickets have already emerged, with many of the sequences claimed in patents overlapping. For example, a gene with 15 exons could have a separate patent on each exon; there could be a claim on the complete sequence, as well as a claim on the promoter sequence. One illustration of the complexity of these overlapping patents is the difficulties encountered by researchers from the PATH foundation when they were trying to develop a malaria vaccine: they had to negotiate research use for the 39 different patents involved (Thomas et al., 2002). Thomas also points to the dangers of broad patents grants: ‘Furthermore, because the majority of patents covering DNA sequences are what are termed per se claims, the applicant, in making the first claim, gains the right to all uses, including those that are as yet undiscovered’ and ‘[a]n excessively broad patent that contains claims to all conceivable diagnostic tests creates a monopoly, such that there is little incentive to develop improved tests’ (Thomas et al., 2002, pp. 1186–1187). Some commentators are not convinced that patent monopolies have hindered follow-up research. Clark states that there is a lack of evidence that intellectual property protection measures have had a significant negative impact on academic biomedical research: ‘In the face of no empirical evidence, the myth that patents inhibit biomedical research, publication and dissemination of knowledge is promulgated’ (Clark, 2011, pp. 79–80). Caulfield et al. (2006), while acknowledging that there have been good reasons for concern, like Clark concludes ‘the feared problems have not widely manifested’. However, Caulfield et al.'s research does point to one important exception: gene patents that cover a diagnostic test. Patent owners have asserted exclusivity or licence terms ‘widely viewed as inappropriate’ (Caulfield et al., 2006;, pp. 1892–1893). The assertion of ‘no empirical evidence’ is certainly too strong. Examples of problematic access to fundamental technology do bubble to the surface. One such example is the position regarding zinc-finger proteins (ZFPs), which can bind almost all DNA sequences. The ZFP patent portfolio has been dominated by one firm in particular: Sangamo. Researchers found that Sangamo was highly selective in its choice of collaborators. Academic scientists therefore often took the risk of using the technology without a licence, hoping that Sangamo would not sue academics. However, even this did not solve the problem. The patents did not disclose all the necessary information. Vital knowledge remained in the Sangamo database and design rule set. Without this proprietary information scientists could not practice the claimed invention: ‘More complete patent disclosure might also have obviated the need to generate various open science alternatives to the Sangamo platform’ (Chandrasekharan et al., 2009). These examples should not be dismissed as ‘anecdotes’; they are important. They indicate that access by academics to fundamental research can be hampered. Nor do we know how many innovative start-ups or small firms have been hindered by blocking patents, too expensive licences, restrictive licence terms or threats of being sued for patent infringement. An assessment of the situation cannot be made simply by looking at litigated cases: litigated cases are always the tip of the iceberg. The pharmaceutical industry Pharma companies stress that medicinal drugs take years of research and development. The venture is also far from risk free: the drug may be a failure either because clinical trials fail, so approval is not given, or because it is not a commercial success. Based on a study at the Tufts Center, it has been estimated that the time needed for the development of a new drug, from initial stages through to approval, takes on average 11.8 years and will cost in the range of $802 million to $1.8 billion (DiMasi et al., 2003; Barazza, 2014). It is these costs, the industry argues, that justify the high price of the drugs. In a critique of the methodology used by the Tufts Center to explain a cost of $802 million, and the lack of public access to the data used for the study, Light and Warburton argue that such estimates should be treated with scepticism; these are ‘mythical costs’ to try to justify the high prices of drugs (Light and Warburton, 2011). What is clear is that if the drug survives the patent process and the authorisation process, and turns out to be a blockbuster, huge profits can be reaped. For example, the Danish company Lundbeck grew rapidly in the 1990s primarily because of its anti-depression drug, Citalopram. Citalopram alone accounted for around 80 per cent of the company's sales by the end of the twentieth century, with large sales figures for Europe and the USA at that time bringing in kr. 720 million.5 Similarly, Losec, a medicine for stomach ulcers, was so successful that it is estimated to have brought in between $15–30 billion for AstraZeneca, making AstraZeneca one of the largest global pharmaceutical companies (Granstrand and Tietze, 2014). Many pharmaceutical companies have not been reticent to exert their monopoly position to ensure market dominance and satisfy their investors. However, with some exceptions, a patent expires after 20 years. When the patent expires, the market for the drug opens up to generic drug companies. These generic drug manufacturers have not had to sustain the costs in development of the original brand manufacturers. This means that they can sell generic medicines considerably cheaper: on average 25% lower than the price of the brand drugs at the time of generic entry and 40% lower two years after entry. The share of the market by generic companies after two years is estimated at 45% (European Commission, 2009: paragraph 1560). It is not surprising, given the huge profits that a blockbuster drug can make for a company, that pharma companies will look to manipulate the patent system to prolong their market dominance. The brand name drug companies have various strategies they can employ. They can wrap many patents around the original patent, resulting in patent clusters. Patents are filed for certain specific aspects of a single product, such as dosing, delivery systems and combinations. For example, depending on the medicine, the medicine may come with a proprietary inhaler or injector that is integrated into the product. Yet these combinations will be patented separately. Consequently, even after all the patents on the medicine expire, the remaining patents on the associated device, or parts of the device, can be sufficient to prevent generic entry (Beall et al., 2016). The ‘evergreening’ strategy is a form of blocking mainly used in the pharmaceutical industry. As the patent system allows improvements and additions to be patented, inventions that are really just slight modifications of the old drug are patented. These secondary patents, usually filed just before the patent on the original drug expires and competition can start, each gain 20 years protection. The weaker patents are an attempt to prolong the patent protection of the original, much stronger patent. Although from the technical perspective only minor improvements may be involved, from an economic perspective these can be significant as patents for incremental improvement processes can be filed almost continually. Building and maintaining a patent network of new medical applications, improvements and substitutions is an effective evergreening strategy, also cutting down possibilities for ‘invent around’ attempts (Granstrand and Tietze, 2014). As Dwivedi et al. (2010, p. 324) notes: ‘While most of these evergreening strategies conform to the letter of the law, very often they seem to undermine the spirit in which patent laws were created’. Even when generic products do enter the market, patients will not always opt for the cheaper drug. Why? What should not be underestimated is the scope and intensity of the marketing campaigns of the brand name companies. Their aim is to ensure that patients switch to the second generation product by convincing them that the newer version is worth the extra money. Strategies include convincing marketing authorisation and pricing and reimbursement bodies, as well as doctors, that the generic product is less safe, less effective or of inferior quality (European Commission, 2009). Another major strategy used by brand name companies is the so-called ‘pay-for-delay’ practice. This practice was one of the concerns that prompted the European Commission to launch its enquiry into the pharmaceutical industry in 2008. In a ‘pay-for-delay’ agreement, a generic manufacturer agrees to delay entry to the market in exchange for a value transfer. Instead of the claimant brand name company demanding damages from the generic company for infringement of its existing secondary patents, in reverse payment settlements the one accused of infringement is the one receiving payment. The generic company is basically paid simply to keep out of the patent owner's market, often also agreeing not to challenge the validity of the claimant's (secondary) patents. The parties can reach a settlement by in effect sharing part of the monopoly profit, the consequence being that prices are kept high (Choi et al., 2014). Following the sector enquiry, the European Commission issued a number of decisions against brand name companies and those generic companies that had entered into agreements with them. In 2013, Lundbeck and four generic firms were fined €145 million, a decision confirmed by the General Court of the European Union in 2016: the agreement was per se illegal being a violation of EU competition law. Other pharma companies fined included Johnson & Johnson, Novartis and Servier. The Final Report by the European Commission observed: ‘The additional costs caused by delays to generic entry can be very significant for the public health budgets and ultimately the consumer.’ (European Commission, 2009, p. 1558). These ‘pay-for-delay’ agreements have also been challenged in the USA. The Federal Trade Commission (FTC) was of the opinion that these agreements were infringements of competition law and that ‘[a]lthough both the brand name companies and generic firms are better off with such settlements, consumers lose the possibility of earlier generic entry’.6 In the lawsuit the FTC brought against Actavis for agreeing to delay bringing its version of Solvay's AndroGel to market, the US Supreme Court did not categorise the agreement as per se illegal. It mandated that a ‘rule of reason’ approach should be used, reviewing such settlements on a case by case basis.7 The FTC has remained committed to scrutinising pay-for-delay agreements. The monopoly position has made it possible for pharma companies to charge high prices for their medicines. At times this has caused public outrage, particularly when the price of a drug rose considerably from one day to another. For example, the price of tablets containing the drug Daraprim, when acquired by Turing Pharmaceuticals, rose from $13.50 a tablet to $750 a tablet overnight, bringing the cost of treatment per annum for some patients to thousands of dollars. Cycloserine increased in price from $500 for 30 pills to $10,800 for 30 pills after it was acquired by Rodelis Therapeutics (Pollack, 2015). The high price of some medications has caused concern in Europe too. Governments struggle in their negotiations with pharma companies. In the Netherlands, the government has expressed its dissatisfaction with the current situation in a report. One of the problems highlighted in this report is the patent monopoly: Another important cause of high prices is the extensive protection manufacturers obtain on their patents. This process was originally intended to stimulate innovation, but is currently used by the industry to maintain a monopoly – and thereby a high price - on new medications for as long as possible. This has a significant impact on society: The way the pharmaceutical market works has led to innovation and new medicines which are extremely valuable for patients. But those patients, and in fact all Dutch people who pay insurance premiums, find themselves at a disadvantage because pharmaceutical companies have a monopoly when it comes to new medicines. Therefore, we need to seek a healthy balance between rewarding innovation and the affordability of medicinal care. (Ministry of Public Health, Welfare and Sport, the Netherlands, 2016: pp. 4, 13) The price of medicines has become a matter of critical importance even for wealthier countries. The pharmaceutical industry and developing countries However, perhaps the largest group of patients excluded from the potential benefits of biomedical research are those in developing countries. Exclusion can originate in the very choice of which drugs pharma companies decide to develop. Their research tends to be market orientated. By the end of the twentieth century, only about one per cent of newly developed drugs were for tropical diseases, such as African sleeping sickness, dengue fever and leishmaniosis (Maurer et al., 2004). Companies aim to make a profit and satisfy shareholders. It is therefore not surprising that expensive R&D will be more geared up to the types of illnesses prevalent in developed countries, as these countries have more capital resources to pay the price for these drugs. As Stiglitz (2006: p. 1279) observed: ‘Poor people cannot afford drugs, and drug companies make investments that yield the highest returns’. Not only does the choice of which drug is developed significantly impact on developing countries: the imposition of stringent requirements for intellectual property protection under the TRIPS agreement is also a factor in access to treatment. This was made explicit in the World Bank report: Nothing is more controversial in TRIPS. It is conceivable that patent protection will increase incentives for R&D into treatments for diseases of particular concern to poor countries. However because purchasing power is so limited in the poorest countries, there is little reason to expect a significant boost in such R&D. Accordingly, many developing countries see little potential benefit from introducing patents. In contrast, potential costs could be significant. (World Bank, 2001, p. 137) The Doha Declaration on the TRIPS Agreement in 2001 did confirm the right of countries to use compulsory licences to gain access to medicines. By issuing a compulsory licence, the government gives permission to a third party to produce the patented product or process without the consent of the patent owner. The drug so produced is much cheaper than the brand name drug at the monopoly price. This right has already been exercised on various occasions, for example by the South African authorities in 2003 in order to create more general access to AIDS medicines. Does compulsory licensing therefore deal with any negative impact of TRIPS for developing countries, given that TRIPS hindered the use of cheaper, domestic generic versions of brand name patented drugs? Compulsory licensing is not without undesirable side effects. It has the potential to reduce incentives for pharma companies to innovate, and for tensions between the government authorising the compulsory licences and the governments of the patentees, which can have both political and economic implications (Flynn et al., 2009; Reichman, 2009). There have been indications that the USA is not entirely at ease when states order compulsory licensing of American pharmaceuticals (Nagan et al., 2017). Compulsory licensing may be an instrument to alleviate the strictures of the patent system to some extent, but it is not the entire solution.

#### three impacts:

#### [1] Only pharma innovation solves global pandemics that risk extinction

Jeffrey Sachs 14, Professor of Sustainable Development, Health Policy and Management @ Columbia University, Director of the Earth Institute @ Columbia University and Special adviser to the United Nations Secretary-General on the Millennium Development Goals) “Important lessons from Ebola outbreak,” Business World Online, August 17, 2014, http://tinyurl.com/kjgvyro

Ebola is the latest of many recent epidemics, also including AIDS, SARS, H1N1 flu, H7N9 flu, and others. AIDS is the deadliest of these killers, claiming nearly 36 million lives since 1981. Of course, even larger and more sudden epidemics are possible, such as the 1918 influenza during World War I, which claimed 50-100 million lives (far more than the war itself). And, though the 2003 SARS outbreak was contained, causing fewer than 1,000 deaths, the disease was on the verge of deeply disrupting several East Asian economies including China’s. There are four crucial facts to understand about Ebola and the other epidemics. First, most emerging infectious diseases are zoonoses, meaning that they start in animal populations, sometimes with a genetic mutation that enables the jump to humans. Ebola may have been transmitted from bats; HIV/AIDS emerged from chimpanzees; SARS most likely came from civets traded in animal markets in southern China; and influenza strains such as H1N1 and H7N9 arose from genetic re-combinations of viruses among wild and farm animals. New zoonotic diseases are inevitable as humanity pushes into new ecosystems (such as formerly remote forest regions); the food industry creates more conditions for genetic recombination; and climate change scrambles natural habitats and species interactions. Second, once a new infectious disease appears, its spread through airlines, ships, megacities, and trade in animal products is likely to be extremely rapid. These epidemic diseases are new markers of globalization, revealing through their chain of death how vulnerable the world has become from the pervasive movement of people and goods. Third, the poor are the first to suffer and the worst affected. The rural poor live closest to the infected animals that first transmit the disease. They often hunt and eat bushmeat, leaving them vulnerable to infection. Poor, often illiterate, individuals are generally unaware of how infectious diseases -- especially unfamiliar diseases -- are transmitted, making them much more likely to become infected and to infect others. Moreover, given poor nutrition and lack of access to basic health services, their weakened immune systems are easily overcome by infections that better nourished and treated individuals can survive. And “de-medicalized” conditions -- with few if any professional health workers to ensure an appropriate public-health response to an epidemic (such as isolation of infected individuals, tracing of contacts, surveillance, and so forth) -- make initial outbreaks more severe. Finally, the required medical responses, including diagnostic tools and effective medications and vaccines, inevitably lag behind the emerging diseases. In any event, such tools must be continually replenished. This requires cutting-edge biotechnology, immunology, and ultimately bioengineering to create large-scale industrial responses (such as millions of doses of vaccines or medicines in the case of large epidemics). The AIDS crisis, for example, called forth tens of billions of dollars for research and development -- and similarly substantial commitments by the pharmaceutical industry -- to produce lifesaving antiretroviral drugs at global scale. Yet each breakthrough inevitably leads to the pathogen’s mutation, rendering previous treatments less effective. There is no ultimate victory, only a constant arms race between humanity and disease-causing agents.

#### [2] Pharma is key to biotech

Garth JS Cooper 6, independent medical scientist at the University of Auckland, “Fates Intertwined,” March 2006, <https://library.wur.nl/WebQuery/file/cogem/cogem_t4505194e_001.pdf>

Biotechnology and pharmaceuticals are inextricably intertwined. Although biotech companies often rely upon the resources of larger pharma companies, the converse is also true. Among other things, biotechs require funding, validation, and access to expertise and markets. Big pharma continues to need ideas and products, and places to outsource risk. The pharmaceutical industry faces uncertainties driven by falling innovation 1,2, its relevance to reducing the global burden of disease , and the equity of access to its products3. If biotechs are not embraced by pharma—they cannot be copied —then as competitors they will increasingly come to dominate the industrial nexus. The issues of both industries need to be addressed together. Apart, biotech and pharma will continue to struggle with the self-determining issues that they currently confront. Working together, the fabric of these industries will be transformed and the world of human therapeutics will flourish.

#### Biotech collapse wrecks the economy

Carlson 16, Robert Carlson is the managing Director at Bioeconomy Capital, “Estimating the biotech sector's contribution to the US economy”, Nature Biotechnology 34, 247–255 (2016), http://www.nature.com/nbt/journal/v34/n3/full/nbt.3491.html?WT.feed\_name=subjects\_business&foxtrotcallback=true#author-information

Biotech is now a major contributor to the US economy. When considered as an industry in itself, biotech and its economic impact rivals mining, utilities, chemicals and computing and electronics. Internationally, at least 20 countries have articulated strategies that explicitly identify biotech as critical to their future economic and employment growth1. Given this focus on economic development, it is crucial to better define the current systemic role of biotech. Moreover, ongoing discussions of funding and investment, benefit and risk, and opportunity and threat all would benefit from a more detailed understanding of where biotech is and where it is headed. In this article, I use data collected from a variety of public and private sources to assemble an initial economic assessment of biotech in the United States as a test case for an analysis at the global level. What emerges is a picture of a sector already making a remarkable and accelerating transformation of the US economy. By my estimate, total domestic US revenues generated by biotech in 2012 reached at least $324 billion—the equivalent of >2% of gross domestic product (GDP; for comparison, see Supplementary Table 1 for a list of selected industries and their contributions to US GDP). The estimate is intended to be conservative; the actual total could be 10–20% higher. Total revenues comprise three biotech subsectors: biologics (drugs), at $91 billion; crops (and seeds), at $128 billion; and industrial products (biofuels, enzymes, biomaterials and biochemicals), at >$105 billion. Over the past decade, aggregate revenues have grown on average at annual rates >10%, much faster than the economy as a whole. Remarkably, biotech revenue growth was the equivalent of >5% of annual US GDP growth every year between 2007 and 2012. It is difficult to project exactly how large the biotech sector might ultimately become, but the trends indicate that biological technologies are likely to generate an increasing share of both GDP and annual GDP growth. What is biotech, and how can it be measured? Current understanding of the biotech sector is hampered by inconsistencies in usage and definition of 'biotechnology' and 'bioeconomy' in public discussion and in print. These words may be used in reference only to pharmaceuticals (or biopharmaceuticals or biologics, depending on one's definition), genetically modified (GM) crops, or public companies whose primary revenues rely on biological technologies, thereby muddling an integrated description of the industry (Box 1). Beyond linguistic imprecision, a lack of data resulting from inadequate characterization of the economy hampers any assessment of the economic size and scope of biotech. Even in the United States, the country with the largest biotech sector, there is no official mechanism to distinguish between products made through biology and products manufactured through other technologies. At present, for example, a chemical manufactured through biological technologies is treated identically to one derived from fossil petroleum. The biological product may displace the petroleum product from the market on the basis of price or preference, yet revenues now accrue to a category that includes petrochemicals. Under the current classification system, even revenues from novel biomolecules, including those that may outperform petroleum products, will be misattributed to fossil sources. The approach I take here differs from the frequently employed tactic of describing 'biotech industry' revenues on the basis only of financial reporting from public companies. For example, this journal's 'What's Fueling the Biotech Engine' series2 focuses exclusively on the metric of domestic US sales of drug products. Another annual Feature, 'Public Biotech by the Numbers'3, defines the biotech industry as including only the companies whose revenues are derived primarily from sales of biotech products, an approach similar to that of the annual 'Beyond Borders' reports by consultants Ernst and Young (New York). Defining the biotech sector on the basis of financial reporting of qualifying companies works only as long as those companies fit the scope of that definition. If a biotech company is acquired by a company outside the biotech sector (e.g., a big pharma or a chemical company), the relevant revenues from the biotech company's products 'disappear' from estimates based on companies in the industry—for example, in these analyses, product revenues from Genentech (S. San Francisco, CA, USA) are no longer counted toward the biotech industry because Genentech is now part of Roche (Basel, Switzerland), which is classified as a large pharmaceutical company. More broadly, the above industry analyses often focus predominantly on biotech enterprises engaged in biomedical markets; companies involved in crops (and seeds) or industrial bioproducts are often given comparatively scant attention. Quantifying biotech's economic contribution The economic impact of an industry is often based on its contribution to GDP (Supplementary Table 1). GDP is a national measure of economic output, which in the United States is calculated by the government using survey and census data. According to the US Census Bureau, “the North American Industrial Classification System (NAICS) is the standard used by Federal statistical agencies in classifying business establishments for the purpose of collecting, analyzing, and publishing statistical data related to the US business economy” (http://www.census.gov/eos/www/naics/index.html). The NAICS is used to segment the economy according to a list of six-digit codes that are reevaluated every five years. The resulting data serve as the basis for constructing GDP in one of three ways: the value added to the economy for each industry, total domestic income earned and final sales of domestic products to purchasers. The algorithms used to calculate GDP are adjusted over time, with refinements intended to sharpen understanding of how goods and services are exchanged to create value. In principle, then, biotech innovations can, like any other component of the US economy, be assessed through changes in the NAICS and GDP calculations. However, there is at present no means to calculate the contribution of biotech to GDP on the basis of the value added, total income or final sales methods. Despite the intention that “producing units that use the same or similar production processes are grouped together in NAICS,” the only NAICS code for biotech-related businesses is specifically meant to identify research and development entities, and it is associated with a very broad definition of biotech (Box 2 and http://www.census.gov/eos/www/naics/reference\_files\_tools/NAICS\_Update\_Process\_Fact\_Sheet.pdf). The only code associated with biological manufacturing of any kind is a subset of pharmaceutical production. Although biotech may nominally be used in various industries that do not obviously overlap (e.g., in the production of fuels or drugs), it comprises a coherent set of tools, skills and practices that together constitute similar production processes that are very different from synthetic chemistry or resource mining. At present, the vast majority of biotech product and service revenues are evidently collected into generic categories such as chemicals, agriculture and pharmaceuticals. Consequently, among other shortcomings, in the NAICS system, what is identified as 'biochemicals' (Fig. 1) conflates chemicals produced largely via fermentation with chemicals produced from petroleum or mining. This is but one example of misaggregation of biotech revenues with those generated from entirely unrelated production processes. n lieu of standardized data classified via the NAICS, how might one estimate the contribution of biotech to GDP? One starting point is industry revenue, corrected as is feasible to remove double counting (Box 1 and Supplementary Methods). For the present analysis, I relied largely on data from the following sources: corporate financial reporting, US Department of Agriculture (USDA) crop price and GM seed usage reporting, and private consulting firms. Because these data are of varying quality and quantity, I combined available hard data with trends and anecdotes to develop estimates. I argue here that the result is a reasonable approximation of the contribution of biotech to GDP. US biotech revenues The quantitative data used were derived primarily from financial reporting and market prices, and the estimates primarily from surveys, private consulting reports and numerical interpolation of sparse time series data (sources of uncertainty are detailed in Box 3). Because of differences in the regulatory structure and financing and, consequently, the pace of innovation across the industry, the biotech sector naturally breaks down into three subsectors: biologics (biotech drugs), GM crops or seeds and industrial biotech. Although biologics development is said to run faster than small-molecule pharmaceuticals, the cost for each is frequently estimated to be >$1 billion per drug, spent over 10 years of development and clinical trials4. GM crops may cost between $500 million and $700 million to develop, with field trials running 3–5 years, depending on whether those trials are conducted simultaneously in the southern and northern hemispheres4. Finally, industrial products may cost anywhere from tens to hundreds of millions of dollars to develop—depending in part on whether the physical infrastructure (i.e., 'steel in the ground') is included in the costs—and US regulatory barriers may be so low that only a notification letter to relevant authorities is required, meaning products can be marketed as soon as they are produced4, 5. Biologics. For this analysis, I define biologics as drugs produced using GM organisms; I explicitly exclude drugs purified from nonmodified organisms. On the basis of reporting from publicly traded companies, global 2012 revenues from biologics reached at least $125 billion; McKinsey and Company (New York) estimated that 2012 global biopharmaceuticals revenues may have been as high $168 billion6 (http://www.mckinsey.com/insights/health\_systems\_and\_services/rapid\_growth\_in\_biopharma) (Supplementary Table 2). Of that total, domestic US revenues from biologics reached $91 billion. This figure includes ~$28 billion in revenues accruing to such companies as Genentech and Genzyme (Cambridge, MA, USA) that are now wholly owned by overseas entities—Roche and Sanofi (Paris), respectively. Domestic US clinical sales of biologics rose >18%, reaching $63.6 billion in 2012 (ref. 2). Beyond drugs that are produced biologically, the contemporary development and testing of virtually all small-molecule prescription drugs is highly dependent on biotech. Of the ~$337 billion in total 2012 US pharmaceutical revenues, a large fraction of the small-molecule revenues relied heavily on biotechnologies used in discovery, validation and trials7. Further complicating this estimate is the challenge of accounting for the potential double-counting of 'biologics feedstocks' produced in the United States, as some fraction of those revenues is produced from exports, and ~75% of pharmaceutical ingredients used in the United States are imported from China8. Consequently, in the interest of simplicity and of using data that are relatively easy to come by, I have chosen to include here only 'nameplate' biologics revenues that are directly attributable to biological production, even though this probably underestimates the total relevant revenues by a substantial amount. GM crops. Global planting of GM crops increased by 6% in 2012, reaching a total of 170 million hectares9. In the United States, where farmers planted 40% of the total global GM crop area, GM corn, cotton and soy continued to have ~90% penetration, with GM sugar beets at 95%. Using average crop revenue figures and the fractions of crops planted in GM seed as compiled by the USDA, I estimate that the sum of farm-scale domestic US revenues, seeds and licensing revenues reached $128 billion (Fig. 2 and Supplementary Table 3). On the basis of the global acreage of GM crops as reported by the International Service for the Acquisition of Agri-biotech Applications, and assuming approximately uniform global prices, I estimate that 2012 global farm-scale revenues for GM crops were at least $300 billion9. How should the biotechnological contribution to GM crop revenues be valued? Until 2009, revenues from GM seeds alone were widely misreported as total “revenues from GM crops”10. Seeds, however, grow into larger organisms with greater value. Some of that value would be realized without the GM component. The US National Research Council (NRC) estimates that by planting GM crops, US farmers receive an additional economic benefit that ranges between 6% and 20% of total crop revenues, depending on the crop, where it is planted and how closely farmers follow recommended practices11. Cumulative 2000–2012 GM crop and seed revenues (Fig. 3) amount to $802 billion, suggesting that US farmers received between $50 billion and $160 billion in additional economic benefit over those years. These figures substantially exceed the benefits estimated by Brookes and Barfoot12 for 1996–2011. This difference highlights the complexity of the analysis and the need to develop standards and consistency. For example, a fraction of the economic benefit estimated by the NRC is indirect, in that farmers who plant GM crops are able to spend less time tending to those crops. That time can be used in other pursuits, including earning additional income, a factor that Brooks and Barfoot intentionally exclude owing to the complexity of gathering and analyzing such data in a global context12. More recently, Klümper and Qaim found that “on average, GM technology adoption has reduced chemical pesticide use by 37%, increased crop yields by 22%, and increased farmer profits by 68%”13. Beyond the direct benefits to farmers planting GM crops, there are benefits to conventional crops in proximity to GM crops. Multiple lines of evidence demonstrate that insect-resistant crops produce area-wide pest suppression—also known as the 'halo effect'—reducing losses in nearby conventional crops. This effect both reduces pesticide requirements for conventional crops and increases their yield; consequently, by one estimate, more than 70% of the cumulative benefits of Bt corn adoption over a period of 14 years accrued to nonadopters in the US Midwest14. The economic benefits of GM crops to nonadopting farmers are difficult to assess broadly, but they should be attributed in some way to the total economic contribution GM crops. I do not attempt to include this value in the present revenue estimate. Going forward, a more thorough accounting of what revenues are produced by which crops might provide a mechanism to include only the fraction of revenues attributable to GM traits. This metric should include the value provided by nearby GM crops to farmers of conventional crops and would thereby contribute to solidifying conversations about the utility and value of various integrated pest-management approaches. This accounting strategy could be the product of work in the public or private sector, but it should be adopted at the federal level to facilitate data gathering and analysis. For simplicity, here I use the total farm-scale revenues from GM crops and seeds. This may well constitute an overestimate of GM crop revenues, but its contribution to estimated total biotech revenues is arguably offset by my use of only 'nameplate' biologics revenues, described above. Industrial biotech. The industrial subsector appears to be the fastest-growing portion of the biotech sector (Fig. 3), and the lack of resolution of this component at the level of the NAICS masks a large and accelerating shift in the US economy. US revenues from industrial biotech reached at least $105 billion in 2012. The accuracy of the industrial revenue estimate continues to suffer in comparison to estimates for biologics and GM crops, owing to the quantity and quality of available data (Fig. 3). My previous efforts have required reverse engineering of reports from private consulting firms who rarely describe data sources and methods4. For the present set of estimates, I first excluded the value of corn from annual US ethanol revenues, which I then used as a lower bound for total US revenues. To these figures I added a conservatively scaled fraction of the international industrial biotech revenue figures reported by consulting firms (Box 1 and Supplementary Table 4). For the 2012 data, I relied on data provided by by Agilent Technologies (Santa Clara, CA, USA), of $125 billion15. Although it would be preferable to categorize industrial biotech products under biofuels, enzymes, biomaterials and biochemicals (biologically derived chemicals), the Agilent report categorizes revenues differently. Its internal breakdown of the $125 billion in business-to-business sales for 2012 was as follows: $66 billion in biochemicals, $30 billion in biofuels, $16 billion in biologics feedstocks (active pharmaceutical ingredients), $12 billion in food and agricultural applications (including enzymes) and $1 billion in new markets. Darlene Solomon, senior vice-president and CTO of Agilent, later clarified that the “industrial biotechnology market analysis was developed via analysis of corporate financial reports, equity analyst reports, private consulting firms reports, and third party market research reports” (personal communication).No further information is available at present. For the revenue estimate reported here, I have scaled the 2012 Agilent biofuels revenues to avoid double counting the substantial contribution of corn feedstocks (on average, ~68% of the wholesale cost of ethanol) (Supplementary Table 4). This reduces the 2012 value added of biofuels production to no more than $10 billion. Notably, biochemicals have eclipsed fuels as the largest component of industrial biotech revenues. The magnitude of the disparity between biofuel and biochemical revenues is informative for understanding the state of the bioeconomy and may inform ongoing policy debates about the relative levels of federal support received by each type of product. The estimates presented here suggest that biochemicals may already generate the equivalent of ~0.4% of the US GDP (compared with ~3% for petrochemicals; see below and Supplementary Table 4). Last, the ultimate contribution of industrial biotech to GDP could be 10–15% larger than that quoted here, depending on the actual retail margin and value added for consumers by biotech beyond business-to-business transactions. The total 2012 impact on the US economy could therefore have been as much as $155 billion, which would bring the total 2012 biotech revenues to >$374 billion. Contribution to US GDP To what extent is it sensible to refer to a 'biotech industry' and its contribution to GDP? Just as cell culture and fermentation are quite different from mining or petroleum refining, so are they different from agriculture. But biological production methods, and their underlying bioengineering techniques and tools, are similar in many ways, particularly when contrasted with mining and refining. These distinctions are likely to be of increasing importance in policy discussions around renewable biological manufacturing and its potential to replace processes and manufacturing based on fossil energy and materials. Moreover, aggregate revenues from GM organisms are now a large and rapidly growing contribution to the US economy (Fig. 3). How well does the sum of biotech revenues in Figure 3 approximate the contribution of biotech to GDP? The overall quality of the data available supports treating any aggregate as only an estimate. As argued above, 'nameplate' biologics revenues are probably a substantial underestimate of subsector revenues. Similarly, although use of total GM crop revenues overestimates the value added to these crops by genetic modification, the total impact is probably underestimated, owing to the direct benefits for conventional crops via the halo effect. Historically, industrial revenues are the least precise owing to the quantity and quality of data, although I eliminated obvious double counting where feasible. In all three cases I sought to produce conservative estimates whenever possible. Taken together, until better data are available, the resulting revenue figure is a reasonable proxy for a direct measure of 'GM domestic product' (GMDP). Therefore, it is arguably both useful and approximately correct to aggregate the revenues from GM organisms as the GMDP to assess the economic impact of biotech. With this approximation in hand, the interpolation in Figure 3 enables a direct historical comparison of biotech revenues to GDP and GDP growth in the United States over the past three decades. This comparison reveals that the US economy, and in particular annual US GDP growth, is becoming increasingly dependent on biotech. Biotech revenues have increased as a fraction of GDP gradually since 1980, reaching the equivalent of at least 2% in 2012. This development is driven by annual increases in biotech revenues that, by 2012, contributed the equivalent of at least 5.4% of annual GDP growth. The apparent peak between 2007 and 2011 is due to the poor overall performance of the US economy rather than any particular trend in biotech. This phenomenon, also visible in 1991 and 2001–2003, suggests that biotech as a sector is relatively robust in the face of general economic downturn. Now, as the broader economy recovers, the annual biotech revenue growth contribution appears to be realigning with the multidecadal trend; several more years may yet be required to resolve the actual annual rate. The model is sensitive to the size of the 2012 industrial biotech revenues; using a biotech revenue estimate of $350 billion would raise the contribution of biotech to GDP to 2.26% and the 2012 contribution to GDP growth to 8.6% (data not shown). The code used to generate historical estimates can also be used to project future revenues. However, because of both the uncertainty in the size of 2012 biotech revenues (between $324 billion and $374 billion) and the sensitivity of the revenue interpolation and growth rates to the size of 2012 industrial revenues, I will not speculate on the magnitude of more recent revenues or quantitatively predict future performance. The code used to generate Figures 3 and 4 is available is available from Biodesic (http://www.biodesic.com). Better tracking of the bio-based economy Box 2 summarizes how NAICS could be used to track biotech products and revenues. Looking forward, one necessary change to the NAICS would be to institute a 'nonpharmaceutical, cell-based manufacturing' code. This code would capture the majority of industrial biotech revenues, which even at the business-to-business 2012 total of $105 billion exceeded the $101 billion in direct contribution to GDP claimed by the mining industry (Supplementary Table 4 compares the contributions to GDP of biotech and selected manufacturing and extractive industries)16. An additional code could be used to specify cell-based manufacturing that relies on modified genomes. These updates for biotech would not constitute a departure from previous practices; indeed, there is precedent to fine grain the measurement of any industry, and there are multiple NAICS codes to characterize aspects of mining and mineral processing, as well as related services and equipment manufacturing. The US government should examine the bioeconomy at a similar resolution. The current NAICS codes either miss substantial biotech revenues and employment or misaggregate them with entirely dissimilar means of production. Of more general concern, the misattribution of sector revenues obscures the broader raw economic contribution of biotech. The resulting ignorance impedes quantitative assessment of key features of sector growth and health, such as the number of firms, the rate of firm creation and destruction, firm longevity, employment and returns on public and private sector investment. I hope that, by calling attention to these and other shortcomings, this analysis will encourage private and public sector efforts to gather and share data that support a more detailed understanding of the biotech sector and its contributions to innovation and physical and economic security. The NAICS is under review for an update in 2017. New codes specifically designed to elicit information about biological production would address serious shortcomings in the way the US government assesses its economy. The continued use of NAICS codes adopted in previous years will explicitly confuse chemicals directly produced through biological systems with those refined from fossil sources and ores. For example, a recent attempt by the Battelle Memorial Institute (Columbus, OH, USA) to use the NAICS to define 'bioscience-related' employment was hampered by antiquated industrial groupings that not only excluded many companies that derive revenue from biotech products (including GM seeds, nonagricultural industrial chemicals and industrial enzymes) but also included companies that manufacture farm equipment and irradiation instruments that are clearly not biotech related17. Consequently, using the current NAICS to estimate biotech employment is a difficult proposition, because the current codes do not map well onto existing and emerging bioproduction methods18. Modernizing the NAICS must be a priority of both the public and private sectors to enable accurate economic analyses, employment measurements and appropriate marshaling and allocation of resources. The mechanisms to better characterize the bioeconomy throughout North America appear to exist in the form of NAICS and the North American Product Classification System (NAPCS). Ongoing revisions to industrial coding and classification provide opportunities to untangle biotech revenues from other industries and to clarify the contribution of biological production to the economy. The broader bioeconomy The estimates of the economic contribution of the biotech sector provided here are relatively inaccurate compared with those describing other parts of the US economy. Not only are there whole areas of biotech activity for which no data are collected, there is also a lack of detail for biotech products where data are available. A critical question for any analysis of the 'biotech sector' is that of what falls within the scope of biotech. For example, in excess of the biologics estimate provided here, there are almost certainly additional billions of dollars in revenues attributable to the creation, maintenance and production of GM model animals, such as knockout microbes and rodents, which are increasingly sold as services to industry and academia. Similarly, companies produce many types of modified cells and antibodies for sale, and vaccines are increasingly produced via biotechnological techniques such as reverse genetics. Marketing reports for sale on the Internet suggest that sales of chemically synthesized peptides, oligonucleotides and genes generate between hundreds of millions and several billion dollars annually. Other reports (http://www.bccresearch.com/market-research/biotechnology/synthetic-biology-bio066c.html; http://www.transparencymarketresearch.com/synthetic-biology-market.html) define a new category of 'synthetic biology' that is putatively already worth several billion dollars a year and that will purportedly climb to tens of billions by 2020. In principle, all of these contributions could be tracked with appropriate NAICS codes, because the value provided by biotech tools should be reflected in their price and thus in the revenues of the vending companies. Properly accounting for these contributions could add tens of billions of dollars in additional revenue to the biotech tally provided here, but such a calculation is not obviously feasible with current data. Clearly defined metrics are critical for formulating policy and allocating resources for research, development and market incentives. For example, policy discussions about alternatives to fossil fuels and reducing carbon emissions should consider metrics not only on biofuels but also on the contribution of biochemicals to plastics and solvents, given that ~15% of a barrel of petroleum is processed into such materials (http://www.eia.gov/energyexplained/index.cfm?page=oil\_refining and http://www.eia.gov/dnav/pet/PET\_PNP\_PCT\_DC\_NUS\_PCT\_A.htm). In other words, although the energy content of petroleum might be replaced by many sources, more consideration should be given to replacing the atoms in petroleum, given their crucial role as materials in the existing economy. Addressing the shortcomings of present data through better measurement would benefit strategy development and policy-making across the public and private sectors. For example, adequate planning to educate an appropriate labor force requires understanding the current skill base and overall sector employment. More broadly, accurate and precise historical revenue estimates would facilitate efforts to understand the long-term return on public and private investments in the bioeconomy and would benefit conversations both practical and political. Beyond the United States, better data would help governments assess biotech's contributions to their own economies. Yet assessing the specific economic roles of modified DNA and biomanufacturing should be undertaken as part of a larger effort. It is often said that this is the century of biology and that biology is the technology of the twenty-first century. Private investments continue to flow into biotech, motivated by hopes of developing new medical treatments, crops, chemicals and production processes.Public investments seek the same returns, with additional expectations for education, employment and economic development. How can the returns from these investments be tallied, and how should this tally be used to assess the contribution of biology to the larger economy? It is well past time for governments around the world to collaborate in developing a standardized and comprehensive understanding of the role of biology in their economies. Standardized data would be invaluable in an assessment of the economic importance of biotech and would enable a direct comparison with GDP. In the long term, it would be ideal to have an industry-wide reference metric that is comparable to GDP. Some governments track—to varying degrees—healthcare, domestic agricultural productivity and biofuels production, but data collection and analytical standards are far from uniform (e.g., see the variable quality and quantity of data in the European Commission's Bioeconomy Observatory (http://biobs.jrc.ec.europa.eu/)). As a step toward clarity, nascent efforts are under way to assemble a unified picture of the value provided by biological goods and services in the form of the biobased economy. The definition of 'biobased economy' varies internationally. In the United States, it is typically defined as “economic activity and jobs generated by the use and conversion of agricultural feedstocks to higher value products; the use of microbes and industrial enzymes as transformation agents or for process changes; and the production of bio-based products and biofuels”19. Responding to a mandate from the US Congress, the USDA has elaborated a list of potential “biobased economy indicators” and also described the difficulties in fleshing out those metrics20. Yet even in the current data-poor environment, the biobased economy was recently valued at an estimated $1.25 trillion in the United States for 2012, the equivalent of about 7% of the GDP21. As impressive as these numbers are, they may still exclude a wide variety of economically important biological goods and services. The preceding definition of biobased economy, and the one used by the USDA, omit fisheries, forestry and agriculture20. Depending on who is counting, those industries generate between $300 billion and $800 billion in revenue annually, bringing even a conservative estimate of the total size of the broader US bioeconomy to nearly 10% of GDP4. For comparison, a recent estimate of the European Union's bioeconomy sectors that included all biobased activity put the total at >$2 trillion and 9% of GDP22. Yet even if a more detailed and thorough accounting were to raise the total bioeconomy to 15% or 20% of GDP, that number would underestimate the larger importance of biological systems in supporting countries and their economies. Without biological production in the form of food, water, oxygen and raw materials, the rest of the economy would be worthless. Precisely because the biobased economy is intertwined with, and depends on, agriculture and natural resources, a thorough understanding of the relationship between biological systems and the economy requires a broader systematic accounting that extends across land and water resources, agriculture, food, textiles and paper, to cutting-edge products of metabolic engineering. Simply put, we should measure everything better.

#### Economic decline causes global war---the current confluence of tech disruption, nationalism, polarization, and declining multilat make escalation likely

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The next economic crisis is closer than you think. But what you should really worry about is what comes after: in the current social, political, and technological landscape, a prolonged economic crisis, combined with rising income inequality, could well escalate into a major global military conflict. The 2008-09 global financial crisis almost bankrupted governments and caused systemic collapse. Policymakers managed to pull the global economy back from the brink, using massive monetary stimulus, including quantitative easing and near-zero (or even negative) interest rates. But monetary stimulus is like an adrenaline shot to jump-start an arrested heart; it can revive the patient, but it does nothing to cure the disease. Treating a sick economy requires structural reforms, which can cover everything from financial and labor markets to tax systems, fertility patterns, and education policies. Policymakers have utterly failed to pursue such reforms, despite promising to do so. Instead, they have remained preoccupied with politics. From Italy to Germany, forming and sustaining governments now seems to take more time than actual governing. And Greece, for example, has relied on money from international creditors to keep its head (barely) above water, rather than genuinely reforming its pension system or improving its business environment. The lack of structural reform has meant that the unprecedented excess liquidity that central banks injected into their economies was not allocated to its most efficient uses. Instead, it raised global asset prices to levels even higher than those prevailing before 2008. In the United States, housing prices are now 8% higher than they were at the peak of the property bubble in 2006, according to the property website Zillow. The price-to-earnings (CAPE) ratio, which measures whether stock-market prices are within a reasonable range, is now higher than it was both in 2008 and at the start of the Great Depression in 1929. As monetary tightening reveals the vulnerabilities in the real economy, the collapse of asset-price bubbles will trigger another economic crisis – one that could be even more severe than the last, because we have built up a tolerance to our strongest macroeconomic medications. A decade of regular adrenaline shots, in the form of ultra-low interest rates and unconventional monetary policies, has severely depleted their power to stabilize and stimulate the economy. If history is any guide, the consequences of this mistake could extend far beyond the economy. According to Harvard’s Benjamin Friedman, prolonged periods of economic distress have been characterized also by public antipathy toward minority groups or foreign countries – attitudes that can help to fuel unrest, terrorism, or even war. For example, during the Great Depression, US President Herbert Hoover signed the 1930 Smoot-Hawley Tariff Act, intended to protect American workers and farmers from foreign competition. In the subsequent five years, global trade shrank by two-thirds. Within a decade, World War II had begun. To be sure, WWII, like World War I, was caused by a multitude of factors; there is no standard path to war. But there is reason to believe that high levels of inequality can play a significant role in stoking conflict. According to research by the economist Thomas Piketty, a spike in income inequality is often followed by a great crisis. Income inequality then declines for a while, before rising again, until a new peak – and a new disaster. Though causality has yet to be proven, given the limited number of data points, this correlation should not be taken lightly, especially with wealth and income inequality at historically high levels. This is all the more worrying in view of the numerous other factors stoking social unrest and diplomatic tension, including technological disruption, a record-breaking migration crisis, anxiety over globalization, political polarization, and rising nationalism. All are symptoms of failed policies that could turn out to be trigger points for a future crisis. Voters have good reason to be frustrated, but the emotionally appealing populists to whom they are increasingly giving their support are offering ill-advised solutions that will only make matters worse. For example, despite the world’s unprecedented interconnectedness, multilateralism is increasingly being eschewed, as countries – most notably, Donald Trump’s US – pursue unilateral, isolationist policies. Meanwhile, proxy wars are raging in Syria and Yemen. Against this background, we must take seriously the possibility that the next economic crisis could lead to a large-scale military confrontation. By the logic of the political scientist Samuel Huntington , considering such a scenario could help us avoid it, because it would force us to take action. In this case, the key will be for policymakers to pursue the structural reforms that they have long promised, while replacing finger-pointing and antagonism with a sensible and respectful global dialogue. The alternative may well be global conflagration.

#### [3] Ag biotech innovation key to keep up with food demands – regulatory failures undermine U.S. ag, and result in increased global famines that risk instability

Redick 14, Thomas, JD (1985) from the University of Michigan and is chair of the American Bar Association Section on Environment, Energy & Resources (ABA-SEER) Committee on Agricultural Management, “The “Stacked” Pipeline of Biotech Specialty Crops and Regulatory/Market Barriers to Coexistence,” pg online @ <http://nabc.cals.cornell.edu/Publications/Reports/nabc_25/25_6_1_Redick.pdf>

Biotech Benefits and the Upcoming Pipeline It is now clear that agricultural biotechnology has provided benefits both to human health and to the environment. This continues to be clear, despite what activists say, since growers are using fewer chemicals such as pesticides. Some of the major US-based environmental groups are starting to get behind agricultural biotechnology. In a speech to a European audience in 2012, the vice president of the Worldwide Fund for Nature (WWF-US) in the United States said, “I’m convinced that modern genetic technology could help get better yields from local and regional crops in Africa and South-East Asia” (McEwan, 2012) We have improved food safety through use of biotech corn. Iowa State University has done excellent research showing that mycotoxin formation is reduced in certain Bt-corn varieties. It is unhealthy to eat known carcinogens. If other nations struggling to cope with mycotoxin-related effects (cancer, birth defects, etc.), simply by approving planting of Bt corn those nations would reduce those effects and bring health benefits through biotechnology. (Murillo-Williams and Munkvold, 2008). Moreover, time has trumped the early concerns expressed by Al Gore about biotech crops exacerbating over-supply; we know now that the world has become too needy to be cavalier in dismissing innovation in agricultural biotechnology. With people around the world asking for more and more corn, soy and other foods at reasonable prices, and rioting to overthrow their governments, we know that yields actually matter. While many factors were contributory, the recent violent protests in North Africa and the Middle East coincided with sudden peaks in global food prices. Researchers suggest that a given food- price threshold may exist, above which protests become likely (Lagi et al., 2011). With such social unrest making the world an increasingly unstable place, we do not have the luxury of tinkering with the highly productive US agricultural system that makes food for the world without risking serious negative impacts overseas. The pipeline for biotech crops is becoming more interesting with each innovation in plant breeding. Genes are being silenced with no “plant pest” DNA to regulate or test for, making regulation more complex. Such new plant-breeding methods involve: • RNA-interference. • Oligo-RNA etc—Cibus, Keygene, etc. • Public-academic breeding coming on fast? • USDA does not see a plant pest, EPA sees resistance issues, etc. The pipeline of biotech commodity crops promises new approaches to food and agriculture, and, finally, direct consumer benefits, not just improved production traits (e.g. herbicide and pest resistance) enabling more-efficient production. These include: • Improved consumer health (high oleic, omega-3 soy, etc.) • Stress-tolerant cultivars, possibly N2 -fixing corn • Environmental impact management—lower GHG emissions • Feeds to reduce feedlot waste (by manipulating genes for phytase to increase efficiency of consumption of phosphates) • More crop from a drop—drought-tolerance in time for climate-disrupted agriculture. Although some proposed innovations may prove to be mere pipedreams, people are working on N2 fixation in corn with symbiotic microorganisms and also making corn photosynthesis work for soy (i.e. “C4 soy”) (Buchanan et al., 2010). There will be more room for public and academic breeding tools in the smaller specialized sector of agriculture. All of this innovation has environmental and economic benefits. This has led the World Wildlife Fund, Environmental Defense Council, and even the Natural Resources Defense Council to start talking about technology neutrality vis-à-vis biotech crops. Opposition to GMOs keeps coming and coming, however. The recently withdrawn French Séralini study, which showed tumors in rats, serves to demonstrate the commitment of certain researchers to bend scientific rules to achieve anti-GMO results. Although the study was badly flawed, it has caused governments to say, “Well, that’s peer-reviewed science. Let’s ban it and make nations stop exporting it to us.” While the high cost of regulatory compliance has led to oligopoly power with a “concentration” in the biotech-seed marketplace, the coming decade may see more new players entering the marketplace (e.g. Okanagan Specialty Crops with its Arctic® Apple2, and J.R. Simplot with its “Innate®” potato1).

#### Food shortage extinction

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Weapons of Mass Destruction Detonating just 50–100 out of the global arsenal of nearly 15,000 nuclear weapons would suffice to end civilisation in a nuclear winter, causing worldwide famine and economic collapse affecting even distant nations, as we saw in the previous chapter in the section dealing with South Asia. Eight nations now have the power to terminate civilisation should they desire to do so – and two have the power to extinguish the human species. According to the nuclear monitoring group Ploughshares, this arsenal is distributed as follows: – Russia, 6600 warheads (2500 classified as ‘retired’) – America, 6450 warheads (2550 classified as ‘retired’) – France, 300 warheads – China, 270 warheads – UK, 215 warheads – Pakistan, 130 warheads – India, 120 warheads – Israel, 80 warheads – North Korea, 15–20 warheads.11 Although actual numbers of warheads have continued to fall from its peak of 70,000 weapons in the mid 1980s, scientists argue the danger of nuclear conflict in fact increased in the first two decades of the twenty-first century. This was due to the modernisation of existing stockpiles, the adoption of dangerous new technologies such as robot delivery systems, hypersonic missiles, artificial intelligence and electronic warfare, and the continuing leakage of nuclear materials and knowhow to nonnuclear nations and potential terrorist organisations. In early 2018 the hands of the ‘Doomsday Clock’, maintained by the Bulletin of the Atomic Scientists, were re-set at two minutes to midnight, the highest risk to humanity that it has ever shown since the clock was introduced in 1953. This was due not only to the state of the world’s nuclear arsenal, but also to irresponsible language by world leaders, the growing use of social media to destabilise rival regimes, and to the rising threat of uncontrolled climate change (see below).12 In an historic moment on 17 July 2017, 122 nations voted in the UN for the first time ever in favour of a treaty banning all nuclear weapons. This called for comprehensive prohibition of “a full range of nuclear-weapon-related activities, such as undertaking to develop, test, produce, manufacture, acquire, possess or stockpile nuclear weapons or other nuclear explosive devices, as well as the use or threat of use of these weapons.”13 However, 71 other countries – including all the nuclear states – either opposed the ban, abstained or declined to vote. The Treaty vote was nonetheless interpreted by some as a promising first step towards abolishing the nuclear nightmare that hangs over the entire human species. In contrast, 192 countries had signed up to the Chemical Weapons Convention to ban the use of chemical weapons, and 180 to the Biological Weapons Convention. As of 2018, 96 per cent of previous world stocks of chemical weapons had been destroyed – but their continued use in the Syrian conflict and in alleged assassination attempts by Russia indicated the world remains at risk.14 As things stand, the only entities that can afford to own nuclear weapons are nations – and if humanity is to be wiped out, it will most likely be as a result of an atomic conflict between nations. It follows from this that, if the world is to be made safe from such a fate it will need to get rid of nations as a structure of human self-organisation and replace them with wiser, less aggressive forms of self-governance. After all, the nation state really only began in the early nineteenth century and is by no means a permanent feature of self-governance, any more than monarchies, feudal systems or priest states. Although many people still tend to assume it is. Between them, nations have butchered more than 200 million people in the past 150 years and it is increasingly clear the world would be a far safer, more peaceable place without either nations or nationalism. The question is what to replace them with. Although there may at first glance appear to be no close linkage between weapons of mass destruction and food, in the twentyfirst century with world resources of food, land and water under growing stress, nothing can be ruled out. Indeed, chemical weapons have frequently been deployed in the Syrian civil war, which had drought, agricultural failure and hunger among its early drivers. And nuclear conflict remains a distinct possibility in South Asia and the Middle East, especially, as these regions are already stressed in terms of food, land and water, and their nuclear firepower or access to nuclear materials is multiplying. It remains an open question whether panicking regimes in Russia, the USA or even France would be ruthless enough to deploy atomic weapons in an attempt to quell invasion by tens of millions of desperate refugees, fleeing famine and climate chaos in their own homelands – but the possibility ought not to be ignored. That nuclear war is at least a possible outcome of food and climate crises was first flagged in the report The Age of Consequences by Kurt Campbell and the US-based Centre for Strategic and International Studies, which stated ‘it is clear that even nuclear war cannot be excluded as a political consequence of global warming’. 15 Food insecurity is therefore a driver in the preconditions for the use of nuclear weapons, whether limited or unlimited. A global famine is a likely outcome of limited use of nuclear weapons by any country or countries – and would be unavoidable in the event of an unlimited nuclear war between America and Russia, making it unwinnable for either. And that, as the mute hands of the ‘Doomsday Clock’ so eloquently admonish, is also the most likely scenario for the premature termination of the human species. Such a grim scenario can be alleviated by two measures: the voluntary banning by the whole of humanity of nuclear weapons, their technology, materials and stocks – and by a global effort to secure food against future insecurity by diverting the funds now wasted on nuclear armaments into building the sustainable food and water systems of the future (see Chapters 8 and 9). Climate Change The effects of food and war on climate change as it is presently predicted to occur were described in Chapter 3: in brief, the stable climate in which agriculture arose over the past 6000 years is now becoming increasingly unstable as a result of the billions of tonnes of carbon that humans are injecting into the atmosphere and oceans, forming a colossal heat engine to drive more frequent, violent weather. This in turn impairs food production in regions of the world already facing severe stresses from population growth and resource depletion. Military analysts describe climate change as a ‘threat multiplier’, augmenting the tensions, conflict and instability which already exist. In reality it is a feedback loop, in which worsening climate conditions cause greater food insecurity, which is met by measures (like increased land clearing and use of fossil fuels and chemicals), which in turn worsen climate conditions, which worsen food security, which cause wars, which inflict more eco-damage... Two degrees (2 C) of global warming – described as the danger point for humanity – are predicted to occur well before 2050 because of our collective failure to curb our carbon emissions.16 Those 2 C of warming portend bad things for any food system that depends on the weather – but just how bad cannot easily be forecast as both the climate state and the response of the global food system are governed by human behaviour, which is fairly unpredictable. Current estimates suggest crop losses of the order of 20–50 per cent at the very time we are trying to raise food output by 50–70 per cent. What can be confidently predicted, however, is that there will be an increase in both the frequency and scale of harvest failures and agricultural disease outbreaks around the world as we approach the mid century – and that beyond 2 C of warming it will become very hard indeed to maintain a stable outdoors, agriculture-based system to meet an anticipated doubling in world demand for food by the 2060s. The ‘worst case’ risk of this, as previously outlined, would be ten billion people having to subsist on enough food to feed only four billion. That, however, is by no means the worst case of the climate story. There are ominous signs that humans have already unleashed planetary forces over which we have absolutely no control – and that these, should they become large enough, will take charge of the Earth’s climate engine and drive it into a superheated condition of +9–10 C or even higher. Today, more people are aware that global warming may lead to complete melting of all glaciers and the polar ice-caps, thereby raising sea levels by 65 metres and inundating almost all of the world’s seaboard cities, fertile river deltas and coastal plains.17 This would clearly have a devastating effect on coastal food production. However, this process will probably take several centuries, allowing populations ample time to relocate inland. That sea levels previously rose by a similar quantum at the end of the last Ice Age, flooding part of Australia, severing Britain from Europe and America from Asia, is proof enough that such events occur as a regular part of the Earth’s warming and chilling cycles. The great existential threat to humanity lies in vast stores of frozen methane gas (CH4) locked into the soils of the tundra regions of Canada and Siberia, in colossal deposits of frozen methane on the continental seabed surrounding the Arctic Ocean, and in massive stores of methane submerged in peat deposits and swamps in places such as the Amazon and the wet tropical forests of Southeast Asia and Africa. Methane is a gas with 20–70 times the climate-forcing power of carbon dioxide. These deposits are the accumulation of the slow decomposition of planet and animal matter in the Earth’s sediments over several hundred million years – they are identical in origin to the gas bubbles that surface when we stir the bed of a pond or lake. The actual volume of these methane deposits is still being assessed by science. Recent estimates suggest: • seabed deposits – between 500–2500 billion tonnes of frozen carbon;18 • tundra deposits – potentially emitting 180–420 million tonnes of carbon a year by 2100; and • tropical peat swamps – could emit 480–870 million tonnes of carbon a year by 2100.19 That carbon released from peat swamps, tundra and possibly the oceans can have a catastrophic effect on the Earth’s climate is foreshadowed by an event known as the Palaeocene–Eocene Thermal Maximum (PETM), which took place some 55 million years ago, when Earth took a sudden fever and its temperature rocketed upwards by +5–9 C. This ‘heat spike’ caused a lesser extinction event involving widespread loss of ocean life and a smaller toll of land animals.20 However, the heating occurred over a much longer period – 100–200,000 years, compared with human-driven heating (50–100 years) – and is thought to have been mainly caused by the drying out and burning of tropical peat swamps as the climate warmed. However, the volume of carbon which caused this sharp planetary heat spike in the past is estimated to be barely a tenth of that released by humanity today.21 Today, human activity in clearing rainforests, draining swamps and burning the world’s forests to open them up for farming and food production is releasing vast amounts of methane and CO2. Explosion craters have been reported across Canada and Siberia as frozen methane deposits well up and erupt with the melting of the tundra. And scientists from Sweden, Russia, Canada and America have reported methane bubbling from the seabed of the Arctic Ocean, though not yet in massive volumes. The risk in all this is that, by warming the planet by only 1–2 C, we have set in train natural processes that we are powerless to control, setting ourselves on an inescapable trajectory to a Hothouse Earth, 5–10 C or more above today’s levels. Although it is hard to estimate, some scientists are of the view that fewer than one billion humans would survive such an event22 – in other words, nine people out of every ten may perish in the cycle of famines, wars, heatwaves and pandemic diseases which global overheating would entail. This underlies the deadly urgency of ceasing to burn all fossil fuels, locking up as much carbon as possible and re-stabilising the Earth’s climate. In that, food production can and will play a central role. Poisoned Planet ‘Earth, and all life on it, are being saturated with man-made chemicals in an event unlike anything which has occurred in all four billion years of our planet’s story. Each moment of our lives, from conception unto death, we are exposed to thousands of substances, some deadly in even tiny doses and most of them unknown in their effects on our health and wellbeing or upon the natural world. These enter our bodies with every breath, each meal or drink, the clothes we wear, the products with which we adorn ourselves, our homes, workplaces, cars and furniture, the things we encounter every day. There is no escaping them. Ours is a poisoned planet, its whole system infused with the substances humans deliberately or inadvertently produce in the course of extracting, making, using, burning or discarding the many marvellous products on which modern life depends. This explosion in chemical use and release has all happened so rapidly that most people are blissfully unaware of its true magnitude and extent, or of the dangers it now poses to us all as well as to future generations for centuries to come.’ This is a summation of the chemical crisis facing all of humanity, as well as all life on Earth, which I wrote in Surviving the 21st Century, and which is based on the extensive scientific research reported in Poisoned Planet.23 It is a crisis with profound impact for everyone. According to the medical journal The Lancet, nine million people – one in six – die every year from chemical pollution of their air, water, food and living environment.24 A further 40 million die from the so-called noncommunicable or ‘lifestyle’ diseases (NCDs), cancer, heart disease, diabetes and lung disease, which are mostly diet-related.25 Food production, as we have seen, is deeply implicated in the chemical deluge. However, it is also an existential threat to human health, both in terms of infectious disease and the new ‘lifestyle’ diseases. No-one to my knowledge has compiled an accurate assessment of the total chemical effusion of humanity or presented a realistic impression of its true scale. Box 6.1 represents my own best estimate, drawn from various reliable sources. From this it can easily be seen that the scale of humanity’s chemical assault on ourselves and on the planet is many times the scale of our climate assault – yet this issue commands nowhere near the political or scientific priority that it should. It is arguably the most under-rated, under-investigated and poorly understood of all the existential threats to humanity. The poisoning of the Earth by human activities has grave implications for the health and safety of the global food chain and its eight billion consumers. It is not only the use of chemicals in food production that is of concern, but also the contamination of water, soils and livestock by industrial pollutants from other sources, such as mining or manufacturing. It is also the disruption of vital services such as pollination by insects of a [[BOX 6.1 OMITTED]] third of the world’s food crops and 90 per cent of wild plants.26 It is the contamination of up to three quarters of the world fish catch with microscopic plastic particles and clothing microfibres made by the petrochemical industry.27 The ending of this flood of poisons is a prerequisite for a safe, healthy and sustainable global food supply in future. And, since government regulation has largely failed to stem the worldwide flood, the task now falls to consumers – to choose foods which have been produced by safe methods and shun foods produced by unsafe methods. That is the only way that the food industry can be encouraged (and penalised) into doing the right thing by humanity and the planet: by consumers rewarding it for producing clean food and punishing it for toxic food. Otherwise it will continue to pollute as profitably as it can. It follows that the urgent global education of consumers about which foods are safe and which are toxic is also a pre-requisite. Food Security Our demand for food is set to double by the 2060s – potentially the decade of ‘peak people’, the moment in history when the irresistible human population surge may top out at around 10 billion. However, as we have seen, many of the resources needed to supply it agriculturally could halve and the climate for the growing of food outdoors become far more hostile. Why food insecurity is an existential threat to humanity should, by now, be abundantly clear from the earlier chapters of this book: present systems are unsustainable and, as they fail, will pose risks both to civilization and, should these spiral into nuclear conflict, to the future of the human species. The important thing to note in this chapter is that food insecurity plays into many, if not all, of the other existential threats facing humanity. The food sector’s role in extinction, resource scarcity, global toxicity and potential nuclear war has already been explained. Its role in the suppression of conflict is discussed in the next chapter. Its role in securing the future of the megacities, and of a largely urbanised humanity, is covered in Chapter 8. And its role in sustaining humanity through the peak in population and into a sustainable world beyond is covered in Chapter 9.

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