ADDITIONAL EXCLUSIVITY FOR BIOLOGIC DRUGS IN THE TPP: A NEED OR GREED?

Public Citizen's Global Access to Medicines Program

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INTRODUCTION

The brand-name pharmaceutical industry has been campaigning to include a lengthy period of exclusivity for biological products in the Trans-Pacific Partnership (TPP). The argument focuses on the complexity of biological drugs, the consequences of their high monopolist prices for budgets and for people's health, and whether there is a need for a special exclusivity rule, separate from patent protections, to recoup the research and development (R&D) costs put into development of these pharmaceutical products.[1]

Industry claims that insufficient intellectual property (IP) protection delays introduction of new medicines into the market.[2] However, there seems to be no correlation between IP protection and submission lag in emerging markets and little reason to think that submission lag would be significantly reduced if stronger IP protections were in place.

The Biotechnology Industry Organization (BIO) also argues that long exclusivity periods are essential for the promotion of innovation.

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BIOLOGICS & BIOSIMILARS: AN OVERVIEW WHAT ARE BIOLOGIC MEDICINES?

A biologic medicine consists of a large molecule typically derived from living cells, which can include therapeutic proteins, DNA vaccines, monoclonal antibodies and fusion proteins. These medicines have provided major advances in the treatment of cancer, autoimmune diseases (such as rheumatoid arthritis), and many other diseases.[3]

Biosimilar medicines are biological drugs that are similar, but not exactly the same as an originator biologic.[4] Unlike generic medicines where the active ingredients are identical, biosimilars are similar to, but not identical copies of, the originator biologic.[5] Biosimilars made by different manufacturers differ from the original product and from each other.[6] A biosimilar is a therapeutic alternative to an innovator, or originator, biologic medicine and can potentially offer access to the therapy at a reduced cost.

In traditional, small molecule chemical entities, under the U.S. Hatch-Waxman Act, generic manufacturers must show that their product has the same active ingredients (bioequivalence) and the same strength[7] and dosage form as the originator (pharmaceutical equivalence).[8] By contrast, sameness cannot be established in biologics and biosimilars due to the nature of the large complex molecules, which involve sugars, proteins, and, in some cases, may be living entities.[9] Thus, in the Biologics Price Competition and Innovation Act (BPCIA), Congress set the standard for follow-on biologics to be substantially similar to the originator product, rather than equivalent.[10] A biosimilar must also exhibit "no clinically meaningful structural differences from a brand-name biologic."[11] The BPCIA permits approval of follow-on biologics based on "solid evidence of structural similarity, with only small confirmatory clinical trials - much smaller than the trials traditionally required for approving new drugs."[12]

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Table 1: Overview of the main differences between chemical and biological drugs	
Chemical	**Biological**
Produced by chemical synthesis	Produced by living cell cultures
Low molecular weight	High molecular weight
Well-defined structure	Complex, heterogeneous structure
Mostly process-independent	Strongly process-dependent
Completely characterised	Impossible to fully characterise the molecular composition and heterogeneity
Stable	Unstable, sensitive to external conditions
Mostly non-immunogenic	Immunogenic

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In 2015, the U.S. Food and Drug Administration (FDA) granted approval to Sandoz for the first follow-on biologic, or biosimilar, of the anti-cancer biologic filgrastim (brand name Neupogen). This is the first biosimilar approved through the BPCIA pathway and offers hope to patients who otherwise would not have been able to afford the originator drug.[14]

Before many countries created regulatory pathways for biosimilars, a biosimilar growth hormone drug called Omnitrope (otherwise known as somatropin, non-proprietarily), approved by the European Commission (EC) on April 12, 2006,[15] had already entered the market. Omnitrope gained initial approval in Australia, 2004, and was launched a year later for pediatric indications. Omnitrope was also approved under the Public Health Services Act 505(b)(2) in the U.S., 2006, before the Biologics Price Competition and Innovation Act was passed.[16] Omnitrope is approved in Australia, Japan, Canada, New Zealand and the EU.

Although only roughly 1% of prescriptions dispensed in the United States are biologics, they account for 28% of American drug spending, with their cost and use forecasted to grow sharply.[17] In response, payers are imposing greater out-of-pocket costs on patients, requiring more stringent preauthorization requirements, or simply refusing to cover certain biological products. This is placing substantial burdens on patients suffering from critical diseases and has made biologics a luxury for many.[18]

Global spending on biologics is projected to reach $1.3 trillion in 2018. This is a 30% increase from 2013.[19] This steady rise in drug spending will be painful and budget busting for wealthy countries and regions such as the United States and the EU, and even worse for developing countries, such as Vietnam, whose health care resources are already stretched thin.[20] Biosimilar competition is an essential component to reducing exorbitant prices. Countries must be able to provide affordable access to life-saving drugs.[21] Unnecessarily long monopolies would have devastating consequences.

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PHARMACEUTICAL COMPANIES UNNECESSARILY PUSH FOR LONG EXCLUSIVITY IN THE TPP

Pharmaceutical companies have their sights set on emerging markets, and companies are revising their market entry strategies to maintain high profit margins. China's pharmaceutical market is growing at more than twice the global rate and has been projected to be the world's second largest by 2015.[22] Pharmaceutical markets in the other components of the BRICs–Russia, India, and Brazil–are expected to grow at a rate between 9 percent and 16 percent.[23] Elsewhere, countries like Argentina, Turkey, Venezuela, Vietnam, and South Africa all exhibit substantial pharmaceutical market growth potential, driven by rapid economic expansion, rising incomes, and growing populations.[24] Interestingly, these countries are also the most heavily criticized countries in the U.S. Trade Representative's Special 301 Reports[25] for supposedly inadequate intellectual property protections.

Nevertheless, the vast majority of emerging market growth consists of sales of generics.[26]

This complication means that, in order to seek the highest possible profit margins in these emerging markets, the pharmaceutical industry must find a way to delay or prevent follow-on products from entering the market in these countries. By imposing a minimum standard of 12 years exclusivity for biological products, the industry can keep biosimilars out of the market, thus keeping prices (and industry profits) high.

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INDUSTRY CRIES LAG TIME PROBLEMS BUT MAKES NO CONNECTION BETWEEN LAG TIME AND IP PROTECTIONS

Drug lag is any delay in making a drug available in a particular market. The pharmaceutical industry argues that there is a lag time problem, but does not, or cannot, equate this issue to IP protection or market or data exclusivity periods. Pharmaceutical companies already have an exclusivity period of at least five years in many jurisdictions (separate from and in addition to patent protections), but insist on substantially more exclusivity for biologics.[27] While companies say IP protection is important to them, the available evidence does not support a conclusion that IP protection is a major factor in actual market entry decisions. Instead, market size is the key determinant.

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SUBMISSION LAG TIME IS A PRODUCT OF MARKET SIZE, NOT IP

While industry claims that it is reluctant to enter markets that it perceives as having weak IP protection, such as China and India,[28] this is contradicted by the evidence. A 2010 study found that the primary reason for drug lag time in Brazil, Russia, and India is submission lag, i.e. the pharmaceutical company lagging in submitting their drug for approval.[29] The study found that a "decrease in relative lag is a consequence of the rapid reduction in submission lag over the decades" which was a "key result of the increase in commercial interest towards the BRIC and N-11 countries from pharmaceutical companies."[30]

In 2012 the Center for Innovation in Regulatory Science (CIRS) conducted a study that specifically addresses submission lag, meaning delay in drug companies' filing for registration, as distinguished from regulatory lag. The study defines "lag time" as "that time period in calendar days from first-world approval to the time that the product is submitted for regulatory review in another country".[31] CIRS indicates that Singapore, a major transshipment hub for the Asian market with robust IP protection, has a similar submission lag time as India, a country the industry has heavily criticized for its supposedly "anti-innovation" IP regime.[32] Submission lag time exists even in emerging markets that implement strong IP strategies.[33] India has no data exclusivity for small molecules or biologics,[34] yet still a relatively short submission lag time.

The same trend can be seen in South Africa. The study indicates that South Africa has an extremely short average submission lag time of 57 days (much shorter than that of Singapore, whose market is smaller with stronger IP protections), however South Africa has been heavily criticized for having weak IP protections for branded pharmaceuticals.[35]

Further, industry claims that more than two-thirds of new drugs are approved in the U.S. first due to the United States' streamlined process of regulatory approval and robust IP standards,[36] while unsatisfactory IP standards in countries like India and China prevent companies from entering the market.[37] This argument substantively fails, however, given that nearly every pharmaceutical that is available in the U.S. market is also sold in the Chinese market. Once again, it seems that the decision to enter a market has more to do with market size than IP protection.[38]

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STRONGER IP DOES NOT ACTUALLY ADDRESS THE LAG TIME ISSUE

In a 2006 survey conducted by CIRS, drug companies said that they "need to be confident that technical data submitted to regulatory agencies will remain confidential and that IP legislation will protect patent violations and the marketing of pirated products".[39] Further, "deficiencies in IP protection are major disincentives to companies planning the registration of products in new markets."[40] This, the industry argues, ultimately leads to companies strategically delaying entry into countries with lax IP protections.

But in 2012, CIRS studied the factors that actually influenced market entry in certain countries. For the majority of countries cited in the study, including India, the major factor influencing a company's decision to enter a particular market is the "size of the country's population and nature of its market".[41]

Pharmaceutical companies do not seem to consider IP protection in countries in their determinations over when to enter a market, despite proclamations to the contrary. Strategically the pharmaceutical industry repeatedly indicates that market access is about providing "the right data, to the right stakeholders, for the right customers, communicated in the right language and at the right time".[42] Pharmaceutical companies focus on individual components (price, market size, payers, and government agencies) of market access, but there is no holistic approach to deal with all components together.[43] Pharmaceutical companies consider public funding and reimbursement as a high priority when deciding whether to enter into emerging markets, whereas lack of IP protection has been seen as less relevant.[44]

The Special 301 Report listed Turkey as Priority Foreign Country, and claimed that industry group the Pharmaceutical Researchers and Manufacturers of America (PhRMA) and its member companies "face significant market access barriers in Turkey, including deficiencies in Turkey's intellectual property framework, slow and unpredictable government product registration" and a "non-transparent" and "unrealistic" reimbursement and pricing system.[45] However, Turkey attracts a large amount of pharmaceutical company investment. Increasing income, aging demographics and widespread access to health care contribute to the industry's perception of potential in the Turkish pharmaceutical market. The Economist Intelligence Unit (EIU)[46] forecasts that the healthcare sector in Turkey is set to boom

STRONGER IP DOES NOT ACTUALLY ADDRESS THE LAG TIME ISSUE

by per Capita Growth (CAGR) of 5.6% between 2013 and 2017. Pharmaceutical companies are entering the Turkish market relatively quickly according to the CIRS report, regardless of the lengthy regulatory lag due to the "slow and unpredictable" registration process. Turkish submission lag is 123 days, whereas the regulatory lag (or time it takes for the regulatory agency to approve the drug for market entry) is 871 days.[47] While the extensive time required for regulatory approval in Turkey is cause for concern, it doesn't seem to deter companies from submitting their products for approval in Turkey relatively soon after its first global regulatory submission.

The same Special 301 Report claims that India, a suggested "Priority Watch List" country, places significant trade barriers on the pharmaceutical industry due to inefficient intellectual property protections.[48] However, the issues cited in the report have failed to stop pharmaceutical companies from entering the Indian market in a timely fashion. As noted above, despite industry gripes, the regulatory submission lag time in India is relatively short at 275 days. Between 2005 and 2014, India had granted over 77% of a total 4,614 patents in the pharmaceutical sector to foreign companies.[49]

HIGH RETURNS ON INVESTMENTS

Pharmaceutical companies are attempting to place an unreasonable chasm between small-molecule and large-molecule pharmaceuticals.[50] Pharmaceutical companies claim that they need more exclusivity for biologics due to the much higher cost of the biologics R&D process, as compared to chemically synthesized drugs. It may be true that the biologic discovery and development process is more expensive than small molecule drug development, with BIO claiming that biotechnology companies spent $30 billion on R&D in 2008. However, the prices of biologic drugs are also much higher, as seen below in the comparison chart of five blockbuster small molecule drugs, five blockbuster biologics and their corresponding prices.

It should be noted that this is a new age in drug development. In the 20th century, pharmaceutical companies thrived with a steady stream of relatively simple chemical compounds that could treat a large number of people.[51] These compounds could easily obtain a patent, resulting in branded pharmaceutical companies making a fortune.[52] In the 21st century, however, it has become significantly harder for drug makers to find new cures, and they have sought salvation in biotechnology.[53] As these biologic drugs are increasing their market share, the pricing and efficacy for these complex molecules is coming under greater scrutiny. The demand for biologic products is inelastic with respect to price. Demand for these drugs is not consumer based; rather prescribers direct the demand.[54] Since the demand for biologics is less sensitive to price than small molecule drugs, the margin between price and cost is often much higher.[55] As the chart below demonstrates, patients pay substantially more for biologic drugs. Even though the cost of drug development is high for biologics, companies have high returns on their investments in R&D for biologics.

Biologics are like any other pharmaceutical product in that they undergo substantially the same discovery and trial phases. They should not be treated with extra protection of exclusivity not afforded to small molecule compounds in a way that extends the monopoly and reduces access to affordable versions of these life-saving compounds for patients.[56]

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HIGH RETURNS ON INVESTMENTS

Blockbuster Small Molecule Drug Prices[57]		Blockbuster Biologic Drug Prices[58]	
Abilify (Bristol-Myers Squibb)	$17,976 per year per patient	Humira (Abbott)	$63,168.00 per year per patient
Plavix (Bristol-Myers Squibb)	$10,293.26 per year per patient	Remicade (Merck)	$55,104 per year per patient
Advair (GlaxoSmithKline)	$4,200 per year per patient	Rituxan (Roche)	$32,280.00 per year per patient
Lipitor (Pfizer)	$4,032 per year per patient	Enbrel (Amgen)	$26,580.00 per year per patient
Nexium (AstraZeneca)	$3,912 per year per patient	Lantus (Sanofi)	$15,888.00 per year per patient

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INDUSTRY INFLATES R&D COST ESTIMATES

The pharmaceutical industry often argues that strong intellectual property protection is a necessary incentive to biomedical innovation. "Profits earned from one generation of biomedical innovation" are necessary "for investment in the next generation of biomedical innovation" and that "this dynamic is vital for true innovation-based industries".[59] A confidential, unverifiable study conducted in 2003 claims that to incentivize pharmaceutical industries to innovate a "new chemical entity" or "new molecular entity", they would need to recoup nearly $802 million per new drug.[60] This study was updated in 2014 to claim new pharmaceutical discovery now costs companies $2.6 billion.[61]

This data, however, is flawed on a number of levels and the study has been debunked by numerous scholars, notably Jerry Avorn in the New England Journal of Medicine article entitled "The $2.6 Billion Pill - Methodologic and Policy Considerations".[62] In another debunking article, James Love points out that this number does not account for taxpayer subsidies or tax credits specifically tied to R&D expenditures. In fact, the 2014 study fails to mention that, in 2010, the amount of money claimed through the Orphan Drug tax credit, which covers roughly 50 percent of the costs of clinical testing, was less than $650 million for 14 approvals.[63] Considering that clinical trials are one of the largest cost burdens in the pharmaceutical R&D process, this suggests that the $2.5 billion is significantly inflated. Staggering costs presented in the studies are not the net R&D costs for a pharmaceutical company.[64]

Another argument made in industry-funded reports is that the companies, in assessing R&D costs, must account for 5,000-10,000 compounds tested during the discovery process for every single drug that eventually enters the market.[65] However, this number doesn't address the fact that high-speed computer screenings consume a small percentage of R&D costs and that only about one in five drugs that enter human trials (where a bulk of the R&D expenditures happen) receive U.S. FDA approval.[66] In other words, a large portion of failed products whose high development costs must be recouped through high prices on successful products (or so industry claims), are abandoned before onerous development costs hit.

In sum, the $802 million figure (as

INDUSTRY INFLATES R&D COST ESTIMATES

well as the $2.5 billion figure) is based on an incomplete and unbalanced assessment of data funded, at least in part, by the industry itself. A more realistic estimate of R&D costs per "average new drug" is considerably lower.[67]

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CONCLUSION

The continued development of biologic products is both essential and necessary in the fight against cancer and other diseases. While the costs associated with R&D might be high, pharmaceutical companies can recoup the financial burden without enshrining rules granting unnecessarily long monopolies in the TPP. Long monopolies place an unnecessary burden on those who are meant to benefit from these innovations, the patients. The cost for payers and out-of-pocket costs associated with these new drugs is extremely high and makes treatment a luxury out of reach for most in developing countries. Increased IP protection will not address this issue, nor will it expedite the company's strategic entry into a particular market.

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REFERENCES

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Notes

[1] *The Trans-Pacific Partnership and Innovation in the Bioeconomy: The Need for 12 Years of Data Protection for Biologics*, BIO TPP White Paper, *available at* https://www.bio.org/sites/default/files/TPP%20White%20Paper%20_2_.pdf.

[2] Patrick Kilbride, *Weak Intellectual Property Protection is a Barrier for Innovators*, U.S. Chamber of Commerce (Aug. 27, 2014), *available at* https://www.uschamber.com/blog/weak_intellectual_property_protection_barrier_innovators.

[3] Ameet Sarpatwari, et al, *Progress and Hurdles for Follow-on Biologics*, N. Engl. J. Med. (May 6, 2015).

[4] *Biologics and Biosimilars: An Overview*, Amgen.

[5] *Id.*

[6] *Id.*

[7] Lawrence Kogan, *The U.S. Biologics Price Competition and Innovation Act of 2009 Triggers Public Debates, Regulatory/Policy Risks, and International Trade Concerns*, 6 Global Trade and Customs Journal 513, 514 (2011).

[8] *Id.*

[9] *Id.* at 515.

[10] Sarpatwari, *supra* note 3.

[11] *Id.*

[12] *Id.*

[13] Paul Declerck, *Biologicals and Biosimilars: A Review of the Science and its Implications*, GaBI J. (2012), *available at* http://gabi-journal.net/biologicals_and_biosimilars_a_review_of_the_science_and_its_implications.html.

[14] *Id.*

[15] European Medicines Agency, *Omnitrope*, *available at* http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000607/human_med_000946.jsp&mid=WC0b01ac058001d124.

[16] See Wikinvest, *Omnitrope for Novartis_AG (NVS)*, *available at* http://www.wikinvest.com/stock/Novartis_AG_(NVS)/Omnitrope.

[17] Sarpatwari, *supra* note 3.

[18] *Id.*

[19] IMS Institute for Healthcare Informatics. Global Outlook for Medicines Through 2018. 2014. http://static.correofarmaceutico.com/docs/2014/12/01/informe_ims.pdf

[20] OECD. Health at a Glance: Asia/Pacific 2012. http://dx.doi.org/10.1787/9789264183902-en (note that Vietnam drug spending accounts for half

REFERENCES

of all health spending in the country).

[21]IMS Institute for Healthcare Informatics . Global Outlook for Medicines Through 2018. 2014. http://static.correofarmaceutico.com/docs/2014/12/01/informe_ims.pdf. (nearly half of all drugs in the late stage oncology pipeline are biologics)

[22]Thomas Baker, *The Big Sell: Biologics in Emerging Markets*, PharmExe.com (Sept. 1, 2012), *available at* http://www.imshealth.com/deployedfiles/ims/Global/Content/Innovation/Powering%20Client%20Transformation/Emerging%20Markets/Biologics_in_emergingmarkets.pdf.

[23]*Id.*

[24]*Id.*

[25]Note: The Special 301 Report is an annual report published by the Office of the U.S. Trade Representative (USTR) in which USTR outlines grievances with other countries' intellectual property policies (and sometimes health-related policies that have nothing to do with IP, such as pharmaceutical reimbursement schemes). It is used a pressure tactic by industry and its champions in the U.S. government to pressure countries into adopting industry's preferred policy options.

[26]Baker, *supra* note 22.

[27]BIO, *supra* note 1.

[28]See PhRMA Special 301 Submission 2015 (which places India on a priority watch list for inadequate IP protection).

[29]Harriet Wileman and Arun Mishra, *Drug Lag and Key Regulatory Barriers in Emerging Markets*, Perspect Clin. Res. (2010).

[30]*Id.*

[31]*Id.* at 2.

[32]*Id.*

[33]Lawrence Libert, et al, *Influencers of Lag Time in the Emerging Markets*, CIRS R&D Briefing 51 (2012), *available at* http://www.cirsci.org/sites/default/files/CIRS_R&D_Briefing_51_Lag_Time_in_EM.pdf.

[34]India has a system for protection of test data, in compliance with TRIPS Article 39, which does not establish anexclusivity over data and requires protection, against disclosure unless steps are taken to ensure that the data is protected against "unfair commercial use."

[35]Libert, et al, *supra* note 33.

[36]Matthew Howes, *The Global Drug-Lag Problem*, CenterWatch News Online (May 26, 2015), *available at* http://www.centerwatch.com/news_online/article/7981/the_global_drug_lag_problem#sthash.

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REFERENCES

zjauPTOF.dpbs.

[37]PhRMA Special 301 Submission 2015, *available at* http://www.phrma.org/sites/default/files/pdf/PhRMA-2015-Special-301-Rev.pdf (stating that "PhRMA...remain[s] concerned over barriers to market access such as the lack of effective regulatory data protection and patent enforcement").

[38]See *An Inside Look at Eli Lilly and Company's Emerging Market Strategy*, Forbes (May 11, 2015), *available at* http://www.forbes.com/sites/medidata/2015/05/11/an_inside_look_at_eli_lilly_and_companys_emerging_markets_strategy/(stating that "[Eli] Lilly believes that China is a huge opportunity for its products").

[39]Neil McAuslane, et al, *A cross-regional comparison of the regulatory environment in emerging markets*, CIRS R&D Briefing 50 (2006), *available at* http://www.cirsci.org/sites/default/files/RD%2050%20Feb06%20EM%20Cross%20Regional%20Compar.pdf.

[40]*Id.* at 8.

[41]*Id.* at 12.

[42]*Market Access: Please, No More Talk of 'Hurdles' and 'Obstacles'*, Pharmafile (July 2, 2013), *available at* http://www.pharmafile.com/news/178236/market_access_please_no_more_talk_hurdles_and_obstacles.

[43]Anuj Kumar, et al, *Pharmaceutical Market Access in Emerging Markets: Concepts, Components, and Future*, Journal of Market Access and Health Policy (2014), *available at* http://www.jmahp.net/index.php/jmahp/article/view/25302.

[44]Dr. Mattias Buente, et al, *Pharma and Emerging Markets 2.0: How Emerging Markets are Driving the Transformation of the Pharmaceutical Industry*, Strategy& (2013), *available at* http://www.strategyand.pwc.com/media/file/Strategyand_Pharma_Emerging_Markets_2.0.pdf.

[45]PhRMA Special 301 Submission 2015, *available at* http://www.phrma.org/sites/default/files/pdf/PhRMA-2015-Special-301-Rev.pdf.

[46]EIU is an independent business within the Economist Group providing forecasting and advisory services through research and analysis, such as industry report and five-year country economic forecasts. http://www.eiu.com/home.aspx.

[47]Libert, et al, *supra* note 33.

[48]See PhRMA Special 301 Submissions 2014 & 2015, *available at* http://www.phrma.org.

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[49]Press Trust of India, *77% patents in Indian pharma sector granted to foreign companies*, Dec 2014, *available at* http://www.business_standard.com/article/pti_stories/77_pc_patents_in_indian_pharma_sector_granted_to_foreign_cos_114122800173_1.html.

[50]See *The Trans-Pacific Partnership and Innovation in the Bioeconomy: The Need for 12 Years of Data Protection for Biologics*, BIO

[51]*Going Large: A Wave of New Medicines Known as Biologics Will be Good for Drugmakers, but May Note be so Good for Health Budgets*, The Economist (Jan. 3, 2015), *available at* http://www.economist.com/news/business/21637387_wave_new_medicines_known_biologics_will_be_good_drugmakers_may_not_be_so_good.

[52]*Id.*

[53]*Id.*

[54]Thomas Fulda, Handbook of Pharmaceutical Public Policy, 63 (2007).

[55]*Id.*

[56]See *generally*, Gargi Chakrabarti, *The Need of Data Exclusivity: Impact on Access to Medicine*, 19 JIPR 325 (Aug. 2014) (data exclusivity "acts as an extra layer of protection for the originator company").

[57]Price of CVS Pharmacy, *available at* http://www.goodrx.com/ (note that the estimates for per year per patient were derived for the per month estimates).

[58]Kimberly Holland, *Lower RA Medication Costs with Patient Assistance Programs*, Healthline (June 23, 2014), *available at* http://www.healthline.com/health/ (note that the estimates for the per year per patient were derived from the per month estimates).

[59]Stephen Ezell, *The Imperative of Protecting Life Science Innovation in the TPP*, Information Technology & Innovation Foundation (March 2015).

[60]Donald Light and Rebecca Warburton, *Demythologizing the High Costs of Pharmaceutical Research*, The London School of Economics and Political Science (2011).

[61]Joseph DiMasi, et al, *Innovation in the Pharmaceutical Industry: New Estimates of R&D Cost*, Tufts Center for the Study of Drug Development (Nov. 18, 2014). *available at* http://csdd.tufts.edu/files/uploads/Tufts_CSDD_briefing_on_RD_cost_study_Nov_18,_2014..pdf.

[62]See Jerry Avorn, *The $2.6 Billion Pill Methodologic and Policy Considerations*, 372 N Engl J Med 1877 (May 2015),

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REFERENCES

available at http://www.nejm.org/doi/full/10.1056/NEJMp1500848#t\unhbox\voidb@x\bgroup\let\unhbox\voidb@x\setbox\@tempboxa\hbox{a\global\mathchardef\accent@spacefactor\spacefactor}\accent22a\egroup\spacefactor\accent@spacefactorrticle.

[63] James Love, *KEI Comment on the New Tufts Study on Drug Development Costs, Knowledge Ecology International* (Nov. 2014), *available at* http://keionline.org/node/2127.

[64] *Id.* at 4.

[65] *Drug Discovery and Development: Understanding the R&D Process*, PhRMA (2007).

[66] *Id.*

[67] Light, *supra* note 60

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