PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA (P*h*RMA)

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PhRMA 2019 SPECIAL 301 OVERVIEW

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The Pharmaceutical Research and Manufacturers of America (PhRMA) appreciates the opportunity to provide this submission for the *2019 Special 301 Report*. Established by the Trade Act of 1974, the Special 301 review gives the Administration a critical tool to address damaging market access and intellectual property barriers abroad that harm America's leading innovative and creative industries and the more than 45 million jobs they support across the country.[1]

Urgent action is required to address serious market access and intellectual property barriers in the 24 overseas markets named in this submission. As explained further below, biopharmaceutical innovators in the United States face a wide array of damaging pricing policies abroad that threaten billions of dollars in lost sales and put American jobs and exports at risk. Medicines discovered and manufactured by PhRMA member companies are the constant target of compulsory licensing and other harmful practices that deny the most basic intellectual property protections necessary to drive discovery and bring new treatments and cures to patients around the world.

The Office of the U.S. Trade Representative and other federal agencies should prioritize action to reverse compulsory licensing in **Malaysia** and to end damaging pricing policies in several markets, including **Canada**, **Japan**, **South Korea**. Government price controls imposed in many markets are non-tariff barriers to trade that substantially eliminate incentives to invest in the development of new medicines for patients. They deny American inventors and workers the ability to compete on fair and equitable terms in foreign markets and undermine the expected benefit of intellectual property protections. Ending damaging pricing policies in these markets and others could add billions of dollars to research and development for new medicines and lower overall health care costs around the world.[2]

I. The Innovative Biopharmaceutical Sector

The U.S. biopharmaceutical industry is the world leader in medical research – producing more than half the world's new molecules in the last decade.[3] Innovators in this critical sector depend on strong intellectual property protection and enforcement, and

[1] U.S. Department of Commerce, *Intellectual Property and the U.S. Economy: 2016 Update*, September 2016, available at https://www.uspto.gov/sites/default/files/documents/IPandtheUSEconomySept2016.pdf (last visited Feb. 7, 2019).

[2] See Council of Economic Advisors, "Reforming Biopharmaceutical Pricing at Home and Abroad," February 2018, available at https://www.whitehouse.gov/wp-content/uploads/2017/11/CEA-Rx-White-Paper-Final2.pdf (last visited Feb. 7, 2019); and U.S. Department of Commerce, International Trade Administration, Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Consumers, Pricing, Research and Development, and Innovation, December 2004.

[3] Battelle Technology Partnership Practice, *The Biopharmaceutical Research and Development Enterprise: Growth Platform for Economies around the World*, Battelle Memorial Institute, May 2012, available at http://www.phrma.org/sites/default/files/pdf/phrma_growthplatformforeconomiesaroundtheworld_20120508.pdf (last visited Feb. 7, 2019).

on fair and equitable access to overseas markets. With the right policies and incentives in place at home and abroad, they can continue to bring valuable new medicines to patients and contribute powerfully to the American economy and jobs.

A. Biopharmaceutical innovation delivers value for patients and economies

PhRMA member companies and the more than 800,000 women and men they employ across the United States are devoted to inventing, manufacturing and distributing valuable medicines that enable people to live longer, healthier, and more productive lives.[4] They work in partnership with universities, clinical researchers, patient organizations, health care providers and others to bring new treatments and cures to patients who need them at home and abroad – introducing nearly 600 new therapies since 2000[5] and investing in many of the over 7,000 new drugs currently in development worldwide,[6] with about three quarters having the potential to be first-in-class treatments.[7]

Pioneering work by biopharmaceutical innovators in the United States contributes significantly to economic growth and supports good-paying jobs in all 50 states. In 2015, biopharmaceutical research and development activity added more than $1.3 trillion to the U.S. economy and supported nearly 4.8 million American jobs, including indirect and induced jobs.[8] For all occupations involved in the biopharmaceutical industry, the average total compensation per direct employee is twice the average compensation in any other U.S. private sector industry.[9] In 2017, the industry exported almost $56 billion in biopharmaceuticals,[10] making the sector one of the top U.S. exporters among intellectual property-intensive industries.[11]

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[4] TEConomy Partners, *The Economic Impact of the U.S. Biopharmaceutical Industry*, Oct. 2017, available at http://phrma-docs.phrma.org/files/dmfile/PhRMA_GoBoldly_Economic_Impact.pdf (last visited Feb. 7, 2019).

[5] U.S. Food and Drug Administration, "New Drugs at FDA: CDER's new molecular entities and new therapeutic biological products," available at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugInnovation/ucm20025676.htm (last visited Feb. 7, 2019); and U.S. Food and Drug Administration, "Biological approvals by year," available at http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/BiologicalApprovalsbyYear/default.htm (last visited Feb. 7, 2019).

[6] *Adis R&D Insight database*, accessed Jan. 4, 2019.

[7] Long G., The Biopharmaceutical Pipeline: Innovative Therapies in Clinical Development. Analysis Group; 2017.

[8] TEConomy Partners, *The Economic Impact of the US Biopharmaceutical Industry*, Oct. 2017, , available at http://phrma-docs.phrma.org/files/dmfile/PhRMA_GoBoldly_Economic_Impact.pdf (last visited Feb. 7, 2019).

[9] Id.

[10] TradeStats Express™: National Trade Data for NAICS Code 3254 Pharmaceuticals and Medicines, available at http://tse.export.gov/TSE/TSEHome.aspx (accessed January 2019).

[11] Industry R&D data from National Science Board of the National Science Foundation, *Science and Engineering Indicators 2012*, 2012; Industry export data from PhRMA analysis of data from U.S. ITA, *TradeStats Express: National Export Data*; Software publishers data from the International Intellectual Property Alliance.

Even more important than the biopharmaceutical sector's role in the U.S. economy is its contribution to global patient health. Biopharmaceutical innovation extends lives, improves worker productivity and cuts health care costs. Between 1950 and 2016, life expectancy for women and men in the United States increased by more than a decade[12] – adding trillions of dollars to the U.S. economy.[13] New medicines are responsible for much of this increase. According to a National Bureau of Economic Research working paper, new treatments accounted for three-quarters of life expectancy gains in the United States and other high-income countries between 2000 and 2009.[14]

For example, the AIDS death rate has dropped nearly 87% since the approval of antiretroviral treatments in 1995.[15] Today, a 20-year old diagnosed with HIV can expect to live another 50 years.[16] New medicines have cut heart disease deaths by 38%, according to the Centers for Disease Control and Prevention.[17] More than 80% of the increase in life expectancy of cancer patients since 1980 is attributable to new treatments.[18] New hepatitis C therapies approved since 2013 cure over 90% of patients – a more than two-fold increase from previously available treatment options.[19]

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[12] U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics, *Health, United States, 2017*, Table 15, May 2018, available at https://www.cdc.gov/nchs/data/hus/hus17.pdf (last visited Feb. 7, 2019).

[13] Between 1970 and 2000, increased longevity added about $3.2 trillion per year to national wealth in the United States. See Murphy, K.M. and R.H. Topel, "The Value of Health and Longevity," National Bureau of Economic Research, June 2005, available at http://www.nber.org/papers/w11405 (last visited Feb. 7, 2019).

[14] Lichtenberg, F.R., "Pharmaceutical Innovation and Longevity Growth in 30 Developing and High-income Countries, 2000-2009," *National Bureau of Economic Research*, July 2012, available at http://www.nber.org/papers/w18235 (last visited Feb. 7, 2019).

[15] U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics, *Health, United States, 2014*, Table 29, May 2015, available at http://www.cdc.gov/nchs/data/hus/hus14.pdf (last visited Feb. 7, 2019).

[16] Id.

[17] U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, "New CDC Vital Signs: CDC finds 200,000 heart disease deaths could be prevented," Dec. 2013, available at https://www.cdc.gov/media/releases/2013/p0903-vs-heart-disease.html (last visited Feb. 7, 2019); and U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, "Vital Signs: Avoidable Deaths from Heart Disease, Stroke, and Hypertensive Disease—United States, 2001-2010," Sep. 2013, available at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6235a4.htm (last visited Feb. 7, 2019).

[18] Sun, E., D. Lakdawalla et al., "The determinants of recent gains in cancer survival: an analysis of the surveillance, epidemiology and end results [SEER] database," *Journal of Clinical Oncology*, 2008, available at http://ascopubs.org/doi/abs/10.1200/jco.2008.26.15_suppl.6616 (last visited Feb. 7, 2019); A more recent article by the American Cancer Society (dated Jan. 7, 2016) reported that cancer death rates have been reduced nearly 23% since 1991. See http://www.cancer.org/cancer/news/news/cancer-statistics-report-death-rate-down-23-percent-in-21-years (last visited Feb. 7, 2019).

[19] See, for example, Tracey Walker, "FDA approves Viekira Pak to treat hepatitis C," Dec. 19, 2014, available at http://formularyjournal.modernmedicine.com/formulary-journal/news/fda-approves-viekira-pak-treat-hepatitis-c?page=full (last visited Feb. 7, 2019).

PhRMA member companies are building on these achievements and pioneering new treatments and cures for some of the world's most devastating diseases. Researchers are developing more than 1,200 new medicines for infectious diseases, including viral, bacterial, fungal, and parasitic infections such as the most common and difficult-to-treat form of hepatitis C, a form of drug-resistant malaria, a form of drug-resistant MRSA, and a novel treatment for smallpox.[20] Advances in biotechnology and genomics are propelling the discovery of new medicines to treat a range of chronic and infectious diseases. Made using living organisms, biologic medicines are revolutionizing the treatment of cancer and autoimmune disorders. Biologics are critical to the future of the industry and promise progress in the fight against conditions like Alzheimer's, which today lack effective treatments.[21]

New medicines can lower the overall cost of treating these and other devastating diseases by reducing medical complications, hospitalizations and emergency room visits. For example, the use of cholesterol-lowering statin drugs has cut hospitalizations and saved the U.S. health care system at least $5 billion.[22] Every $24 spent on new medicines for cardiovascular diseases in OECD countries saves $89 in hospitalization costs.[23] Treating high blood pressure according to clinical guidelines would result in annual health system savings of about $15.6 billion.[24] In addition to lowering overall health care costs, appropriate use of medicines can increase worker productivity by reducing rates of absenteeism and short-term disability.[25] A recent study demonstrated that appropriate use of diabetes medicines saved 15% and 20% per month in medical spending after one year of initiating treatment[26] and an estimated reduction of more than one million

[20] PhRMA, 2013 Medicines in Development – Infectious Diseases Report, Pharmaceutical Research and Manufacturers of America, Dec. 2013, available at http://phrma.org/sites/default/files/pdf/MedsInDevInfectiousDiseases2013.pdf (last visited Feb. 7, 2019).

[21] Id.

[22] Grabowski, D., D. Lakdawalla et al., "The Large Social Value Resulting From Use Of Statins Warrants Steps To Improve Adherence And Broaden Treatment," *Health Affairs*, Oct. 2012, available at https://www.healthaffairs.org/doi/pdf/10.1377/hlthaff.2011.1120 (last visited Feb. 7, 2019).

[23] Lichtenberg, F., "Have newer cardiovascular drugs reduced hospitalization? Evidence from longitudinal country-level data on 20 OECD countries, 1995-2003," National Bureau of Economic Research, May 2008, available at http://www.nber.org/papers/w14008 (last visited Feb. 7, 2019).

[24] Cutler, D.M., G. Long et al., "The Value of Antihypertensive Drugs: A Perspective on Medical Innovation," *Health Affairs*, Jan. 2007, available at https://www.healthaffairs.org/doi/pdf/10.1377/hlthaff.26.1.97 (last visited Feb. 7, 2019).

[25] Carls G.S., M.C. Roebuck et al., "Impact of medication adherence on absenteeism and short-term disability for five chronic diseases," *Journal of Occupational and Environmental Medicine*, July 2012, available at http://journals.lww.com/joem/Abstract/2012/07000/Impact_of_Medication_Adherence_on_Absenteeism_and.7.aspx (last visited Feb. 7, 2019).

[26] Jha A.K., Aubert R.E., Yao J., Teagarden J.R., Epstein R.S., "Greater adherence to diabetes drugs is linked to less hospital use and could save nearly $5 billion annually," *Health Affairs*, Aug. 2012, available at https://www.healthaffairs.org/doi/10.1377/hlthaff.2011.1198 (last visited Feb. 7, 2019).

emergency department visits and hospitalizations annually, for an annual savings of up to $8.3 billion.[27]

PhRMA members are working to overcome significant systemic challenges that can prevent the poorest patients from accessing medicines. Together with governments, academia and others, they are leading more than 300 initiatives with more than 1,000 partners to help shape sustainable solutions that improve the health of all people.[28]In 2017, more than 20 biopharmaceutical companies joined the World Bank and the Union for International Cancer Control to launch Access Accelerated – a first-of-its-kind global initiative to address cancer and other non-communicable diseases that cause more than 28 million deaths per year in low and lower-middle income countries.[29]

Between 2000 and 2011, biopharmaceutical innovators contributed an estimated $98.4 billion dollars toward achieving health-related Millennium Development Goals.[30] Despite a three percent drop in public funding for neglected disease (excluding Ebola) research and development in 2014, biopharmaceutical industry funding increased by 28% during the same period.[31]

B. Policies that power prevention, treatments and cures

Strong protection and enforcement of patents, regulatory test data and other intellectual property, and fair and transparent market access to overseas markets provide powerful incentives that drive and sustain substantial investments in valuable treatments and cures. Where markets are open and intellectual property is protected and enforced, biopharmaceutical innovators have the predictability and certainty they need to collaborate with partners, compete successfully and accelerate the launch of new medicines.

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[27] Slejko J.F., Ho M., Anderson H.D., Nair K.V., Sullivan P.W., Campbell J.D., "Adherence to statins in primary prevention: yearly adherence changes and outcomes," *J Manag. Care Pharm*. Jan. 2014, available at https://www.jmcp.org/doi/10.18553/jmcp.2014.20.1.51 (last visited Feb. 7, 2019).

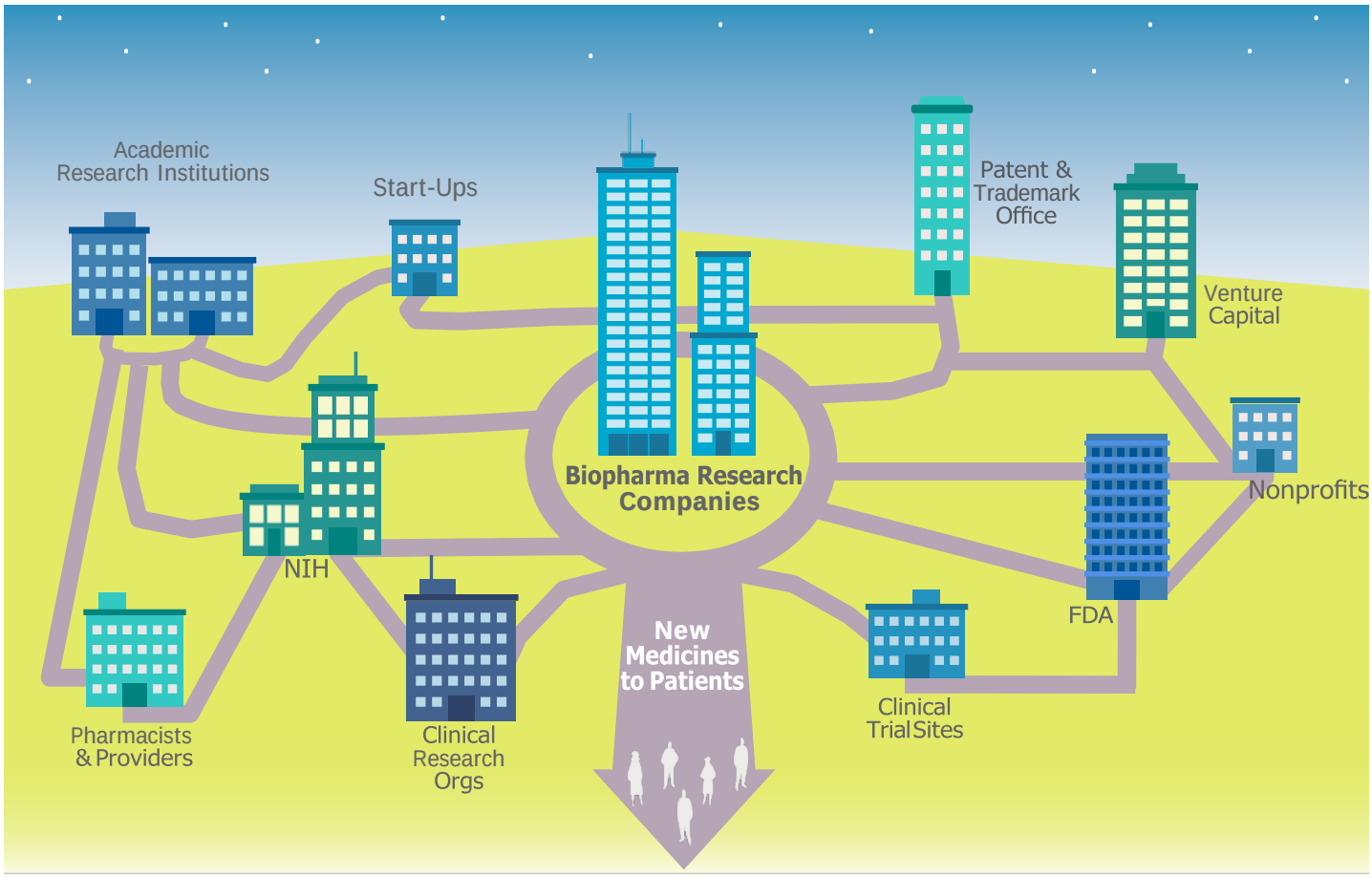
[28] See Global Health Progress, available at http://www.globalhealthprogress.org (last visited Feb. 7, 2019).

[29] Access Accelerated, "Biopharma Companies Partner and Launch First-of-its-Kind Global Initiative to Address Rise of Non-Communicable Diseases," Jan. 2017, available at https://accessaccelerated.org/22-biopharma-companies-partner-launch-first-kind-global-initiative-address-rise-non-communicable-diseases/ (last visited Feb. 7, 2019).

[30] Morris, Jeremiah et al., *The Pharmaceutical Industry's Contributions to the United Nations Millennium Development Goals*, Hudson Institute, May 2013, available at http://www.hudson.org/content/researchattachments/attachment/1260/the_pharmaceutical_industry_s_contributions_to_the_un_millennium_development_goals.pdf (last visited Feb. 7, 2019).

[31] Global Funding of Innovation for Neglected Diseases: G-Finder, available at https://gfinder.policycuresresearch.org/ (last visited Feb. 7, 2019).

Figure 1: Collaboration and the biopharmaceutical R&D process



As highlighted in Figure 1 above, research, development and distribution of innovative medicines increasingly involves collaboration and the exchange of commercially sensitive information between multiple partners across borders and around the world. Strong intellectual property protection and enforcement enable innovators to license their patented inventions to others with the certainty that valuable information disclosed is secure. Thanks to the technology transfer framework established by the Bayh-Dole Act, licensing of intellectual property is also enabling collaboration among industry, university and public sector researchers in the development of new medicines and other products – adding close to $591 billion to the U.S. economy and supporting about 4.2 million American jobs between 1996 and 2015.[32] Such collaboration is delivering similar benefits in other countries. Recent research in the United Kingdom

[32] See Association of University Technology Managers, Statistics Access for Technology Transfer (STATT) database, available at https://autm.net/surveys-and-tools/databases/statt (last visited Feb. 7, 2019); and Pressman, L., D. Roessner et al., "The Economic Contribution of University/Nonprofit Inventions in the United States: 1996-2013," Mar. 2015, available at https://www.bio.org/sites/default/files/files/BIO_2015_Update_of_I-O_Eco_Imp.pdf (last visited Feb. 7, 2019).

found that public expenditure on biomedical and health research leveraged even greater private sector investment, delivering a total rate of return to public biomedical and health research of up to 28%.[33]

Patents and market-based pricing policies promote competition and greater treatment options. In exchange for the limited period of protection patents provide, innovators must fully disclose their inventions to the world. That disclosure accelerates innovation and empowers potential competitors to build on those inventions. Competition means more medicines in the same therapeutic class, more options for patients and even lower prices.[34] For example, less than a year after market entry of the first in a new class of hepatitis C treatments, there were multiple suppliers that competed both on price and clinical benefits. Indeed, competition was so fierce that the largest U.S. pharmacy benefit manager claimed hepatitis C treatment is less expensive in America than in other western countries.[35] European countries have seen similar gains from competition.[36]

Today, biopharmaceutical innovators face competition faster – both from other innovators and from generic drug companies. In the 1970s, a new medicine might remain the only innovative treatment available in its therapeutic class for ten years or more. By the 2000s, that period had declined to about two years.[37] Generic competitors now challenge patents earlier and more frequently – even as early as four years after the launch of an innovative medicine.[38] Today, over 94% of innovative medicines experience at least one patent challenge prior to generic entry – compared to 25% in 1995.[39]

[33] Sussex, J., Y. Feng et al., "Quantifying the economic impact of government and charity funding of medical research on private research and development funding in the United Kingdom," *BMC Medicine*, Feb. 2016, available at http://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-016-0564-z (last visited Feb. 7, 2019).

[34] International Federation of Pharmaceutical Manufacturers and Associations, *The New Frontiers of Biopharmaceutical Innovation, 2012*, available at http://www.ifpma.org/wp-content/uploads/2016/01/IFPMA_New_Frontiers_Biopharma_Innovation_2012_Web.pdf (last visited Feb. 7, 2019).

[35] LaMattina, J., "For Hepatitis C Drugs, U.S. Prices are Cheaper Than in Europe," Forbes, Dec. 2015, available at http://www.forbes.com/sites/johnlamattina/2015/12/04/for-hepatitis-c-drugs-u-s-prices-are-cheaper-than-in-europe/#1483772d64bb (last visited Feb. 7, 2019).

[36] Berdud, M. et al., "R&D, Competition and Diffusion of Innovation in the EU: The Case of Hepatitis C," Office of Health Economics, July 2018, available at https://www.ohe.org/publications/rd-competition-and-diffusion-innovation-eu-case-hepatitis-c (last visited Feb. 7, 2019).

[37] Tufts Center for the Study of Drug Development, "First-in-class drugs in competitive development races with later entrants," Impact Report, Dec. 2015, available at https://csdd.tufts.edu/impact-reports/ (last visited Feb. 7, 2019).

[38] Grabowski, H., G. Long et al., "Updated trends in US brand-name and generic drug competition," Journal of Medical Economics, Sep. 2016, available at https://www.ncbi.nlm.nih.gov/pubmed/27064194 (last visited Feb. 7, 2019).

[39] Id.

Increasing competition from biosimilars is driving down the cost of cutting-edge treatments.[40]

Patents promote faster access to new medicines. A major 2014 study found firms launch innovative medicines sooner in countries where there is effective patent protection and enforcement. The study looked at data from the launch of more than 600 drugs in almost 80 countries between 1983 and 2002. It showed that strong patent protection accelerates new product launches in higher and lower income countries alike.[41] Launching a medicine in a particular country also has important effects on the whole health care system. For instance, when a new medicine is introduced, biopharmaceutical companies invest in educating health care providers on the science and appropriate use of that medicine.[42] This investment later enables accelerated acceptance of generic versions once relevant patents expire.

Strong intellectual property protection and enforcement has long been a critical goal of America's trade policy agenda. Strong intellectual property protection and enforcement at home and abroad provides essential incentives for investment in the biopharmaceutical sector and in all of the innovative industries that today account for nearly 40% of U.S. gross domestic product.[43] For each of these industries, developing and bringing new products and processes to market is a risky endeavor; it requires time and substantial resources. In most cases, new products will fail to deliver returns that meet or exceed investment. Some three-quarters of all venture capital-backed internet startups fail.[44] And even those that succeed often fail to make a profit. Biopharmaceutical firms face similar challenges. Just two of every ten marketed medicines achieve returns that match or exceed average research and development costs.[45] Of the approximately 1,200 biopharmaceutical companies in the United States, more than 90% do not earn a profit.[46]

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[40] *See*, *e.g.*, Sagonowsky, E., "As competition heats up, U.S. prices for Remicade and biosims slip: analyst," FiercePharma, Dec. 2018, available at https://www.fiercepharma.com/pharma/amid-biosim-competition-remicade-prices-gradually-slipping-analyst (last visited Feb. 7, 2019).

[41] Cockburn, I.M. et al., "Patents and the Global Diffusion of New Drugs," *National Bureau of Economic Research*, Sep. 2014, available at http://nber.org/papers/w20492 (last visited Feb. 7, 2019).

[42] Wilsdon, Tim and Glyn Chambers, "The wider value delivered to patients, healthcare systems and competitors when innovators launch new products," *Charles River Associates*, Apr. 2013.

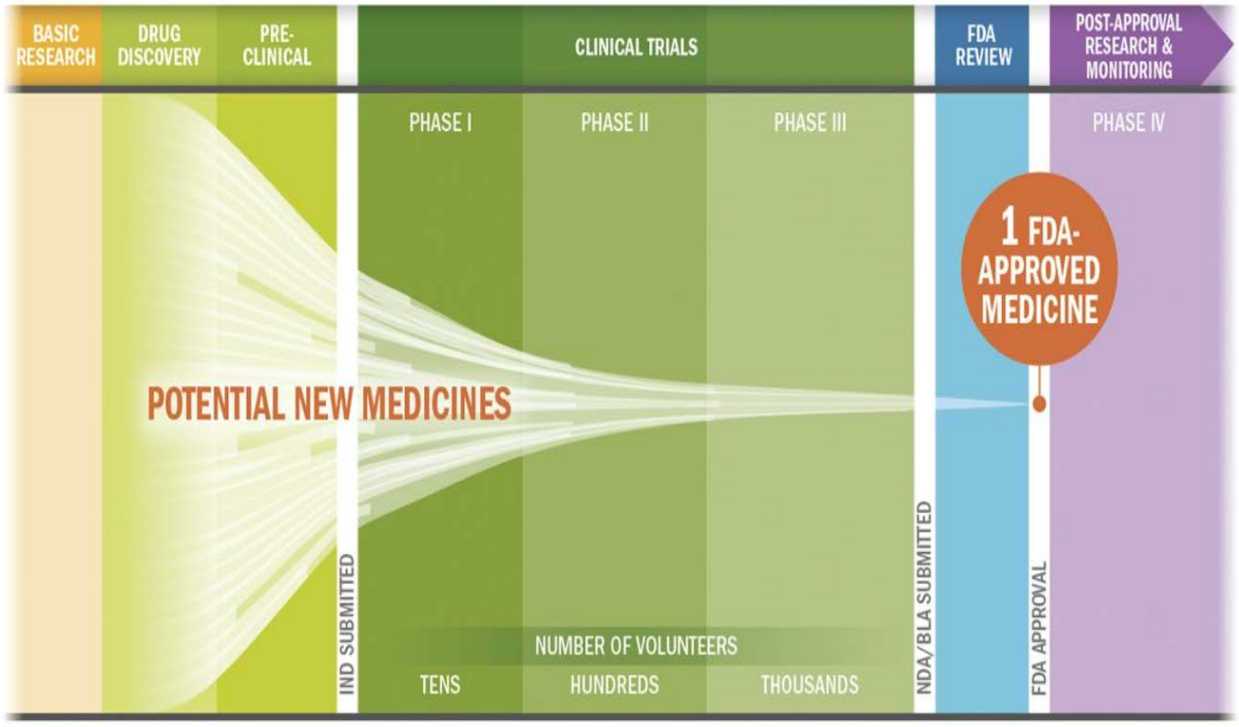
[43] U.S. Department of Commerce, *Intellectual Property and the U.S. Economy: 2016 Update*, Sep. 2016, available at https://www.uspto.gov/sites/default/files/documents/IPandtheUSEconomySept2016.pdf (last visited Feb. 7, 2019).

[44] Gage, D., "The Venture Capital Secret: 3 Out of 4 Start-Ups Fail," *The Wall Street Journal*, Sep. 2012, available at http://www.wsj.com/articles/SB10000872396390443720204578004980476429190 (last visited Feb. 7, 2019).

[45] Vernon, J.A., J.H. Golec and J.A. DiMasi, "Drug development costs when financial risk is measured using the fama-french three-factor model," *Health Economics*, Aug. 2010, available at http://onlinelibrary.wiley.com/doi/10.1002/hec.1538/abstract (last visited Feb. 7, 2019).

[46] Biotechnology Industry Organization, *Unleashing the Next Generation of Biotechnology Innovation*, available at https://www.bio.org/sites/default/files/files/Whitepaper-Final_0.pdf (last visited Feb. 7, 2019).

Figure 2: The biopharmaceutical research and development process



Key: IND: Investigational New Drug Application, NDA: New Drug Application, BLA: Biologics License Application

The lengthy approval process for new products makes the research-based biopharmaceutical sector particularly reliant on the temporary protection intellectual property rights provide.[47] Unlike products made by other innovative industries, new medicines are not market-ready at the time they are developed. As highlighted in Figure 2 above, biopharmaceutical firms rigorously test and evaluate potential therapies through a series of clinical trials to demonstrate they are safe and effective for treatment of a particular disease or condition.[48] In 2013, the innovative biopharmaceutical industry sponsored nearly 6,200 clinical trials across all 50 states.[49] Test data generated through those trials is then submitted to national regulatory agencies for marketing approval.

[47] Without patent protection, an estimated 65% of pharmaceutical products would not have been brought to market, compared with an average of eight percent across all other industries. *See* Mansfield, E., "Patents and Innovation: An Empirical Study," *Management Science*, Feb. 1986, available at https://www.jstor.org/stable/2631551?seq=1#page_scan_tab_contents (last visited Feb. 7, 2019).

[48] PhRMA adaptation based on Dimasi J.A., "Cost of Developing a New Drug," Tufts Center for the Study of Drug Development, *R&D Cost Study Briefing* available at https://static1.squarespace.com/static/5a9eb0c8e2ccd1158288d8dc/t/5ac66afc6d2a732e83aae6bf/1522952963800/Tufts_CSDD_briefing_on_RD_cost_study_-_Nov_18%2C_2014..pdf (last visited Feb. 7, 2019); and U.S. Food and Drug Administration, *Development and Approval Process (Drugs)*, available at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ (last visited Feb. 7, 2019).

[49] Battelle Technology Partnership Practice, *Biopharmaceutical Industry-sponsored Clinical Trials: Impact on State Economies*, Battelle Memorial Institute, Mar. 2015, available at

For these reasons and others, research and development is more capital intensive in the innovative biopharmaceutical sector than in other industries. Firms in this sector invest twelve times more in research and development per employee than the average of all other manufacturing industries.[50] In 2016 alone, American biopharmaceutical companies invested more than $90 billion in research and development.[51] Clinical trials can account for more than 60% of the total cost of bringing a new medicine to market, and there is no guarantee promising molecules and proteins that enter clinical trials will result in a new treatment or cure.[52] The process of evaluating potential new therapies is so exacting that less than 12% of all potential new drugs entering clinical trials result in an approved medicine.[53]

Advances in the treatment of diseases typically are not driven by large, dramatic developments, but more commonly build on a series of continuous improvements over time. The best clinical role and full value of a particular therapy typically emerges years after initial approval as further research is conducted and physicians and other health care providers gain real-world experience. These improvements and the further development of therapeutic classes of medicines often lead researchers to explore new treatments in related areas – restarting the research and development cycle. Indeed, nearly a quarter of existing therapeutic indications are treated by medicines initially developed to address a different concern.[54] And more than 60% of therapies on the World Health Organization's (WHO's) Essential Medicines List relate to improvements on older

http://www.phrma.org/sites/default/files/pdf/biopharmaceutical-industry-sponsored-clinical-trials-impact-on-state-economies.pdf (last visited Feb. 7, 2019).

[50] Pham, N., *IP-Intensive Manufacturing Industries: Driving U.S. Economic Growth, NDP Analytics*, Mar. 2015, available at http://www.ndpanalytics.com/ip-intensive-manufacturing-industries-driving-us-economic-growth-2015/ (last visited Feb. 7, 2019).

[51] PhRMA, PhRMA Annual Membership Survey, 2017, available at http://phrma-docs.phrma.org/files/dmfile/PhRMA_membership-survey_2017.pdf (last visited Feb. 7, 2019).

[52] Research!America, U.S. Investments in Medical and Health Research and Development, 2013-2016, Arlington, VA, Fall 2017, available at https://www.researchamerica.org/sites/default/files/RA-2017_InvestmentReport.pdf (last visited Feb. 7, 2019).

[53] PhRMA adaptation based on Dimasi JA. Cost of developing a new drug. Tufts Center for the Study of Drug Development (CSDD). R&D Cost Study Briefing (Nov. 18, 2014), available at https://static1.squarespace.com/static/5a9eb0c8e2ccd1158288d8dc/t/5ac66afc6d2a732e83aae6bf/1522952963800/Tufts_CSDD_briefing_on_RD_cost_study_-_Nov_18%2C_2014..pdf (last visited Feb. 7, 2019).

[54] Jin, G. and S. Wong, "Toward better drug repositioning: prioritizing and integrating existing methods into efficient pipelines," *Drug Discovery Today*, Jan. 2014, available at http://www.sciencedirect.com/science/article/pii/S1359644613003991 (last visited Feb. 7, 2019).

treatments.[55] This step by step transformation in knowledge has led to increased survival, improved patient outcomes and enhanced quality of life for many patients.[56]

II. Practices that Undermine Innovation and Access to New Treatments

To research, develop and deliver new treatments and cures for patients who need them around the world, biopharmaceutical innovators must be able to secure and effectively enforce patents and protect regulatory test data. They must be able to obtain timely marketing approval for new medicines and make those therapies available to patients according to reimbursement rules and procedures that are fair, transparent, reasonable and non-discriminatory, and that appropriately value and reward patented pharmaceuticals.

For well over a century, governments have recognized the need for global minimum standards that enable inventors to effectively and efficiently protect and share their inventions in a territorial system of intellectual property rights. Signed in 1883, the Paris Convention for the Protection of Industrial Property allowed inventors, regardless of nationality, to claim priority for their inventions and to take advantage of the intellectual property laws in each member country. To facilitate the process of filing patent applications around the world, many members of the Paris Convention established the Patent Cooperation Treaty (PCT) in 1970. Today, more than 90% of all countries are members of the Paris Convention and the PCT.

The World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), which entered into force in 1994, was a major achievement in strengthening the worldwide protection and enforcement of intellectual property rights by creating an international minimum standard of protection for intellectual property rights. TRIPS was premised on the view that its obligations, if faithfully implemented by the diverse WTO Membership,[57] would create the policy and legal framework necessary for innovation-based economic development of WTO Members by rewarding innovation with reliable rights-based systems and permitting the flow of its attendant commercial benefits. Because it concerns both the definition and enforcement of rights, TRIPS is one of the single most important steps toward effective protection of intellectual property globally. WTO Members, including the United States, have an important role to play not only in fully and effectively implementing, but also in reiterating and enforcing, TRIPS minimum standards.

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[55] See Cohen, J. and K. Kaitin, "Follow-On Drugs and Indications: The Importance of Incremental Innovation to Medical Practice," *American Journal of Therapeutics*, Jan.-Feb. 2008, available at http://journals.lww.com/americantherapeutics/Citation/2008/01000/Follow_On_Drugs_and_Indications__The_Importance_of.15.aspx (last visited Feb. 7, 2019).

[56] Goss, T.F., E.H. Picard, and A. Tarab, *Recognizing the Value in Oncology Innovation*, Boston Healthcare Associates, June 2012, available at http://www.phrma.org/sites/default/files/flash/phrma_innovation_oncology.pdf (last visited Feb. 7, 2019).

[57] 164 members as of July 29, 2016.

Critically, the United States and other countries have promoted, given effect to and built on the global minimum standards of protection provided by these international rules through eligibility criteria for trade preference programs, WTO accessions and regional and bilateral trade agreements that establish strong intellectual property protections and require fair and equitable market access. However, certain U.S. trading partners maintain or are considering acts, policies or practices that are harming or would harm the ability of biopharmaceutical innovators to research, develop and deliver new treatments and cures for patients around the world. These acts, policies or practices deny or would deny adequate and effective intellectual property protection and/or fair and equitable market access for innovative medicines. In many cases, they appear to be inconsistent with global, regional and bilateral rules.

Multilateral organizations that once served as custodians of the international rules-based system increasingly are seeking to undermine and even eliminate intellectual property protections that drive and sustain biopharmaceutical innovation in the United States and around the world. By reinterpreting international agreements and through meetings, reports, guidelines and training programs, the WHO, the United Nations Development Program (UNDP), the United Nations Conference on Trade and Development (UNCTAD), Unitaid and other organizations are promoting acts, policies and practices globally and in specific countries that prevent biopharmaceutical innovators from securing and maintaining patents, protecting regulatory test data and from enjoying fair and equitable market access.[58]

The following sections highlight the most serious challenges facing PhRMA members around the world. The acts, policies and practices of specific countries are described further below. PhRMA members urge USTR and other federal agencies to highlight these challenges, acts, policies and practices in the 2019 Special 301 Report and to use all available tools to address and resolve them.

A. Practices that deny fair and equitable market access

The Special 301 statute requires USTR to identify countries that deny fair and equitable market access to U.S. persons who rely on intellectual property protection. PhRMA members increasingly encounter acts, policies and practices abroad that deny fair and equitable market access. Through arbitrary and often discriminatory government price controls, unnecessary regulatory delays and high tariffs and taxes, countries across Europe, Asia and beyond are limiting market competition, increasing costs and undermining the ability of biopharmaceutical innovators in the United States to bring new medicines to patients who need them.

In recent years, America's biopharmaceutical sector has witnessed a surge in the number and severity of arbitrary and discriminatory government price controls abroad that

[58] Hudson Institute, "The Patent Truth about Health, Innovation and Access," 2016, available at https://s3.amazonaws.com/media.hudson.org/files/publications/20160706ThePatentTruthAboutHealthInnovationandAccess.pdf (last visited Feb. 7, 2019).

threaten U.S. exports and jobs. Such measures cause serious damage in the countries that maintain them by rationing patient access to health care. They can have significant ripple effects across other markets. For example, price setting implemented in one country can directly and indirectly harm access to medicines in many other markets due to international reference pricing. These policies can restrict competition and artificially depress prices below market value (and even below the cost of production), ultimately delaying and denying access to new medicines that patients need.[59]

A 2004 Commerce Department study[60] found that international reference pricing and other such schemes that "rely heavily on government fiat to set prices rather than competition in the marketplace" put short-term government objectives ahead of long-term strategies that would ensure continued R&D into medicines that patients need most. The report showed that moving to market-based systems would add billions to research and development for new medicines and lower overall health care costs around the world by promoting greater efficiencies in off-patent markets. Urgent action is needed to address and resolve the following government price control regulations, policies and practices that are limiting market access for medicines researched and developed in the United States:

- *Government price control measures*. In many countries, governments are the primary payer of medicines and in effect dictate prices. This dominant position often results in U.S. trading partners failing to appropriately recognize the value of innovation in their pricing and reimbursement policies, instead engaging in actions that distort markets and artificially depress prices below what a competitive market would provide. Foreign governments are increasingly employing a range of regulatory measures, including international reference pricing, therapeutic reference pricing, mandatory price cuts, clawback taxes, and flawed health technology assessments. These measures are often layered to exert maximum pressure. **Korea** employs several price control measures – including health technology assessments that require unreasonable thresholds for "cost-effectiveness," international reference pricing of inappropriate off-patent and generic comparators, and ad hoc measures – to systematically cut prices. Last year, **Japan** approved sweeping changes to pricing policies that significantly undermine efforts to carry a fair share of the costs of global research and development. In particular, the eligibility criteria for the new Price Maintenance Premium (PMP) program as well as other price-cutting measures such as newly proposed health technology assessments will mean that some of America's most innovative medicines will be significantly undervalued. In **Canada**, the Patented Medicine Prices Review Board regulates the maximum allowable price that a manufacturer can charge for a patented medicine to public or private payers. The Board has proposed draconian changes intended to set prices at levels paid by less wealthy countries. Examples of other highly-developed countries that

[59] PhRMA analysis of IQVIA Analytics Link and FDA, EMA and PMDA data on new active substances launched globally, Jan. 2019.

[60] U.S. Department of Commerce, International Trade Administration, Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Consumers, Pricing, Research and Development, and Innovation, Dec. 2004.

undervalue innovative medicines include **Australia**, **Austria**, **Belgium**, the **Czech Republic**, **Denmark**, **Finland**, **France**, **Germany**, **Greece**, **Ireland**, **Italy**, the **Netherlands**, **New Zealand, Switzerland** and the **United Kingdom**.

- *Discrimination against American innovators*. In many countries, governments have policies that benefit domestic drug companies and wholesalers at the expense of innovators in the United States. For example, last year **Japan** revised its pricing policies to allow premium pricing based on company criteria that appears to be inherently biased towards domestic companies (*e.g.*, number of local clinical trials and whether the product was launched first in Japan), and recently proposed new health technology assessments that will subject imported products to greater scrutiny and price cuts than domestic products. These new company and country-of-origin criteria call into question Japan's commitment to fair and non-discriminatory policies, including that of national treatment.

Other acts, policies and practices delay or limit market access for America's biopharmaceutical innovators and the benefits patients overseas could realize from faster access to medicines and greater competition between treatments in the same therapeutic class. These barriers include:

- *Import barriers.* High tariffs and taxes can limit U.S. biopharmaceutical exports and prevent access to new treatments in overseas markets.[61] Under the WTO Pharmaceutical Agreement, the United States and the 33 other countries do not impose any import duties on a wide range of medicines and other health products.[62] However, biopharmaceutical innovators in the United States do not benefit from the same access to China, India and other emerging economies that are leading producers and net exporters of drugs[63] and active pharmaceutical ingredients[64] but are not parties to the WTO Pharmaceutical Agreement. Between 2006 and 2013, the value of worldwide biopharmaceutical trade in countries that are not parties to that Agreement increased at a compound annual growth rate of more than 20%. This means that a larger proportion of medicines distributed

[61] Bate, R. et al., "Still Taxed to Death: An Analysis of Taxes and Tariffs on Medicines, Vaccines and Medical Devices," AEI-Brookings Joint Center for Regulatory Studies, February 2006, available at https://www.researchgate.net/publication/46454258_Still_Taxed_to_Death_An_Analysis_of_Taxes_and_Tariffs_on_Medicines_Vaccines_and_Medical_Devices (last visited Feb. 7, 2019).

[62] General Agreement on Tariffs and Trade, "Trade in Pharmaceutical Products" (L/7430), Mar. 1994, available at https://ustr.gov/sites/default/files/WTO%20Pharmaceutical%20Agreement%20March%201994.pdf (last visited Feb. 7, 2019).

[63] WHO, WIPO and WTO, *Promoting Access to Medical Technologies and Innovation: Intersections between public health, intellectual property and trade*, 2012, available at https://www.wto.org/english/res_e/booksp_e/pamtiwhowipowtoweb13_e.pdf (last visited Feb. 7, 2019).

[64] China is the world's leader in active pharmaceutical ingredient manufacturing and exports. *See* Huang, Y., "Chinese Pharma: A Global Health Game Changer?," Council on Foreign Relations, Mar. 2015, available at http://www.cfr.org/china/chinese-pharma-global-health-game-changer/p36365 (last visited Feb. 7, 2019).

around the world are potentially subject to tariffs.[65] For example, the United States is by far the largest market for Indian generic drug exports,[66] but **India**'s basic import duties on biopharmaceutical products and active ingredients average about ten percent.[67] Additional duties and assessments can raise the effective import duty to as high as 20% or more.[68] Federal and state taxes on medicines in **Brazil** can add nearly 34% to the retail price of medicines – among the highest tax burdens on medicines in the world.[69] Other countries that maintain high tariffs and taxes on imported medicines include **Argentina**, **Russia** and **Thailand**.

- *Regulatory approval delays.* **China** is making significant strides in reforming and strengthening its regulatory framework, but remains an outlier in the drug approval process compared to other regulatory authorities, with new medicines typically taking three to five years longer to reach the China market than other major markets. In other words, a "drug lag" remains in China. Other markets with complex and lengthy regulatory approval processes include **Korea**, **Russia** and **Turkey**. Accelerating regulatory approval in these countries and others will improve the efficiency of global drug development, facilitate U.S. exports and reduce the time it takes for new medicines to reach patients.

- *Government pricing and reimbursement delays.* Restrictive government pricing and reimbursement policies delay market access for biopharmaceutical innovators in the United States and prevent timely patient access to new treatments and cures that have received regulatory approval. These processes vary by country with the result that government reimbursement decisions can be almost immediate in some countries to several years in others. For example, prior to 2017, **China** had only undertaken two substantive updates (2004 and 2009) to the National Reimbursement Drug List which delayed reimbursement by up to seven years. In **Mexico**, delays can stretch as long as 1,500 days or more, on average, compared to 230 days in other countries.[70] PhRMA is encouraged by efforts China and

[65] Banik, N. and P. Stevens, "Pharmaceutical tariffs, trade flows and emerging economies," Geneva Network, Sep. 2015, available at http://geneva-network.com/wp-content/uploads/2015/09/GN-Tariffs-on-medicines.pdf (last visited Feb. 7, 2019).

[66] Pharmaceuticals Export Promotion Council of India, *12th Annual Report 2015-16*, 2016, available at http://www.pharmexcil.com/annual-report (last visited Feb. 7, 2019).

[67] Banik, N. and P. Stevens, "Pharmaceutical tariffs, trade flows and emerging economies," Geneva Network, Sep. 2015, available at http://geneva-network.com/wp-content/uploads/2015/09/GN-Tariffs-on-medicines.pdf (last visited Feb. 7, 2019).

[68] Olcay, M. and R. Laing, "Pharmaceutical Tariffs: What is their effect on prices, protection of local industry and revenue generation," World Health Organization, May 2005, available at http://www.who.int/intellectualproperty/studies/TariffsOnEssentialMedicines.pdf (last visited Feb. 7, 2019).

[69] Globally, on average, taxes account for 6.3% of the retail price of medicines. See EMIS, "Pharmaceutical Sector in Brazil," Dec. 2013, available at https://www.emis.com/sites/default/files/EMIS%20Insight%20-%20Brazil%20Pharmaceutical%20Sector.pdf (last visited Feb. 7, 2019).

[70] Mexico data provided by the Asociación Mexicana de Industrias de Investigación Farmacéutica. Comparison data from the European Federation of Pharmaceutical Industries and Associations (EFPIA) *Patients' W.A.I.T. Indicator Report*, available at http://studylib.net/doc/7634123/patients--w.a.i.t.-indicator--

Mexico have made to accelerate updates to their reimbursement lists. However, patients would be better served by a model that allows new drugs to be reviewed for reimbursement on a regular, or rolling, basis.

- *Lack of transparency and due process.* Lack of transparency, due process, and delayed reimbursement decisions are widespread across the world. In **Japan**, the government continues to make significant pricing policy reforms without adequate consultation with the industry. In **Mexico**, excessive regulatory approval delays are compounded by consolidated procurement processes that lack transparency and are applied inconsistently. In **Turkey**, reimbursement decision criteria are not clearly defined, the process is non-transparent, and unpredictable delays in decision-making significantly postpone patient access to innovative medicines.

PhRMA members recognize the efforts undertaken by the U.S. Government to address these barriers, including eliminating tariffs and promoting fair, reasonable and non-discriminatory pricing and reimbursement policies in trade agreements and addressing regulatory approval delays and other market access challenges in bilateral forums. PhRMA also welcomes the Administration's continued focus on the problem of advanced economies undervaluing U.S. innovative medicines.[71] As more countries enact price controls, the burden for financing medical advances will be increasingly borne by U.S. patients and biopharmaceutical innovators, while patients abroad will suffer decreased access to improved therapies over the long term. It remains critical for the U.S. Government to engage on these issues with its trading partners, and to require immediate and meaningful steps to resolve existing barriers and to ensure patients have faster access to new treatments and cures, including through effective enforcement of U.S. trade agreements.

B. Practices that undermine biopharmaceutical innovation

The six intellectual property challenges described below and highlighted in Figure 3 are having the most serious and immediate impact on the ability of PhRMA members to invest in discovering and transforming promising molecules and proteins into useful new medicines for patients around the world. These challenges hinder or prevent

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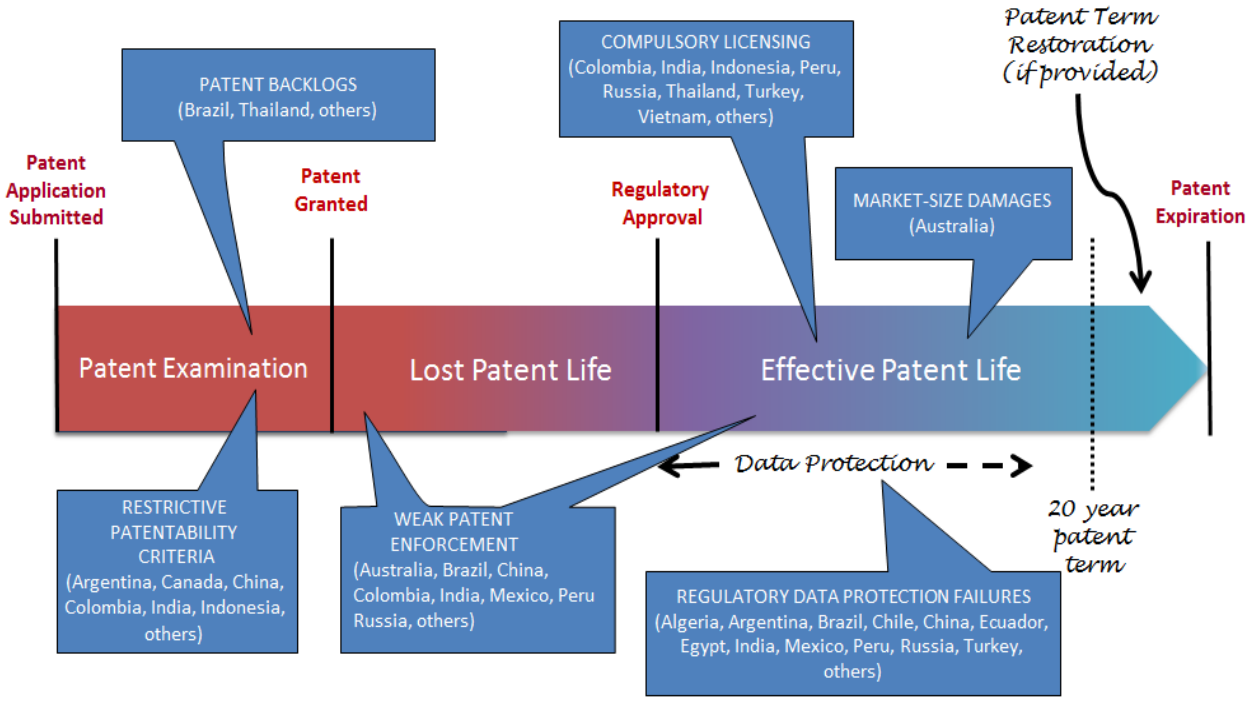
[71] Office of the U.S. Trade Representative, *2018 Special 301 Report*, Apr. 2018, available at https://ustr.gov/sites/default/files/files/Press/Reports/2018%20Special%20301.pdf (last visited Feb. 7, 2019); Office of the U.S. Trade Representative, *USTR Engagement on Pharmaceutical and Medical Device Issues*, Apr. 2018, available at https://ustr.gov/about-us/policy-offices/press-office/fact-sheets/2018/april/ustr-engagement-pharmaceutical-and (last visited Feb. 7, 2019); The Council of Economic Advisors, *Reforming Biopharmaceutical Pricing at Home and Abroad*, Feb. 2018, available at https://www.whitehouse.gov/wp-content/uploads/2017/11/CEA-Rx-White-Paper-Final2.pdf, (last visited Feb. 7, 2019); U.S. Department of Health and Human Services, *American Patients First: The Trump Administration Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs*, May 2018, available at https://www.hhs.gov/sites/default/files/AmericanPatientsFirst.pdf (last visited Feb. 7, 2019).

biopharmaceutical innovators from securing patents (restrictive patentability criteria and patent backlogs), maintaining and effectively enforcing patents (market-size damages, weak patent enforcement and compulsory licensing), and protecting regulatory test data (regulatory data protection failures).

Figure 3: Biopharmaceutical intellectual property challenges



Restrictive Patentability Criteria

To bring valuable new medicines to patients, biopharmaceutical innovators must be able to secure patents on all inventions that are new, involve an inventive step and are capable of industrial application.[72] National laws, regulations or judicial decisions that prohibit patents on certain types of biopharmaceutical inventions or impose additional or heightened patentability criteria restrict patient access to valuable new medicines and undermine investment in future treatments and cures. These restrictions prevent innovators from building on prior knowledge to develop valuable new and improved

[72] See, generally, TRIPS Article 27.1.

treatments that can improve health outcomes[73] and reduce costs[74] by making it easier for patients to take medicines and by improving patient adherence to prescribed therapies. Some of the most serious examples of restrictive patentability criteria challenges facing PhRMA members in countries around the world include:

- *Patentability restrictions and additional patentability criteria.* A number of countries maintain laws and regulations that, *per se*, prevent the patenting of a wide range of specific improvements to existing medicines[75] – improvements that are valuable to patients and payers and that require significant investment and research to develop. For example, **Argentina** issued regulations in 2012 that prevent biopharmaceutical innovators from securing patents on certain types of inventions, including new dosage forms and combinations. In the **Philippines**, national law limits patentability of new forms and new uses of existing medicines. **Indonesia** adopted a new patent law in 2016 that similarly prohibits patents for news forms and new uses of existing medicines. **India**'s Patent Law harms its own domestic

[73] New improvements to existing treatments, such as new dosage forms and combinations, are of tremendous value to patients. They can make it easier for patients to take medicines and increase patient adherence. Specifically, they make it more likely patients will take their medicines consistently and as prescribed. Such improvements might allow patients to take an oral medication instead of an injection or reduce the number of doses required. Adherence is inversely proportional to the number of times a patient must take their medicine each day. The average adherence rate for treatments taken once daily is nearly 80%, compared to about 50% for medicines that must be taken four times a day. Patient adherence to prescribed courses of treatment leads to better health outcomes and is particularly important for the management of chronic, non-communicable diseases like diabetes, heart disease and cancer. According to the WHO, "[a]dherence to therapies is a primary determinant of treatment success." See Shrank, William H. et al., "A Blueprint for Pharmacy Benefit Managers to Increase Value," *American Journal of Managed Care*, Feb. 2009, available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2737824/ (last visited Feb. 7, 2019).

[74] Encouraging patients to take their medicines consistently and as prescribed can lower overall health care costs. The cost of non-adherence has been estimated at $100 billion to $300 billion annually, including the costs of avoidable hospitalizations, nursing home admissions and premature deaths. Making patents available for improvements and new indications can also drive price competition for medicines by encouraging the development of alternative treatments – leading to multiple drugs in a single therapeutic class and increasing the range of options for patients and health care providers. See Osterberg, Lars and Terrence Blaschke, "Adherence to Medication," *New England Journal of Medicine*, Aug. 2005, available at http://www.nejm.org/doi/full/10.1056/NEJMra050100 (last visited Feb. 7, 2019); and DiMatteo, M. Robin, "Variations in Patients' Adherence to Medical Recommendations: A Quantitative Review of 50 Years of Research," *Medical Care*, Mar. 2004, available at http://journals.lww.com/lww-medicalcare/Abstract/2004/03000/Variations_in_Patients__Adherence_to_Medical.2.aspx (last visited Feb. 7, 2019); and DiMasi, Joseph A., *Price Trends for Prescription Pharmaceuticals 1995-1999*, background report prepared for the Department of Health and Human Services Conference on Pharmaceutical Pricing Practices, Utilization and Costs, Aug. 2000, available at https://aspe.hhs.gov/basic-report/price-trends-prescription-pharmaceuticals-1995-1999 (last visited Feb. 7, 2019).

[75] Examples of improvements include enantiomers and combination treatments. See Stevens, P. and J. Ellis, "Enantiomer Patents," Geneva Network, June 2017, available at https://geneva-network.com/wp-content/uploads/2017/07/enantiomer-patents.pdf (last visited Feb. 7, 2019); and Stevens, P. and J. Ellis, "The Power of Combination Drugs," Geneva Network, June 2017, available at https://geneva-network.com/wp-content/uploads/2017/07/Combination-drugs-patentability.pdf (last visited Feb. 7, 2019).

drug companies[76] by prohibiting patents on new forms and new uses of known substances, unless applicants can demonstrate they meet an additional "enhanced therapeutic efficacy" test. **Ukraine** is currently considering legislation that would restrict the patentability of new forms and uses.

In addition, multilateral organizations such as **UNDP** and **Unitaid** advocate actively for patentability restrictions and additional patentability requirements that are inconsistent with international practice. For example, although UNDP does not appear to have specialized expertise on intellectual property matters, it issued patent examination guidelines in 2016 that, if followed, would prevent innovators from securing patents on many kinds of biopharmaceutical inventions.[77] Similarly, Unitaid partnered with various non-governmental organizations in 2018 to launch a campaign to erode intellectual property policies and laws globally.

- *Restrictions on post-filing submissions.* Unlike patent offices in the United States, Europe, Japan, Korea and other major markets, **China**'s National Intellectual Property Administration (CNIPA) does not consistently accept data generated after a patent is filed during patent prosecution to describe inventions or satisfy inventive step requirements. This practice, contrary to China's December 2013 U.S.-China Joint Commission on Commerce and Trade (JCCT) commitment to allow patent applicants to submit additional data after filing patent applications, has caused significant uncertainty about the ability to obtain and maintain biopharmaceutical patents in China and caused denials of patents on new medicines in that country that received patents in other jurisdictions.

Restrictive patentability criteria in many of these countries and others appear to be contrary to WTO rules and U.S. trade agreements, which require parties to make patents available for inventions that are new, involve an inventive step and are capable of industrial application.[78] These laws also appear to apply solely to pharmaceutical products, either expressly by law or in a *de facto* manner as applied. This is not consistent with the obligations of WTO Members and U.S. trade agreement partners to make patents available without discrimination as to the field of technology.

PhRMA members appreciate steps USTR and other federal agencies have taken to address restrictive patentability criteria and look forward to continuing to work closely with these agencies to secure concrete progress and real results. Effective enforcement

[76] Geneva Network, "Copy or Compete: How India's patent law harms its own drug industry's ability to innovate," December 2018, available at https://geneva-network.com/article/section-3d/ (last visited Feb. 7, 2019).

[77] United Nations Development Program, "Guidelines for the Examination of Patent Applications relating to Pharmaceuticals," 2016, available at http://www.undp.org/content/undp/en/home/librarypage/hiv-aids/guidelines-for-the-examination-of-patent-applications-relating-t.html (last visited Feb. 7, 2019).

[78] Hollman, C.M. et al., "Patentability Standards for Follow-On Pharmaceutical Innovation," *Biotechnology Law Report*, June 2018, available at https://www.liebertpub.com/doi/pdf/10.1089/blr.2018.29073.cmh (last visited Feb. 7, 2019).

of U.S. trade agreements is needed to resolve these challenges in particular countries and to prevent others from adopting similar practices.

Patent Backlogs

Long patent examination and approval backlogs harm domestic and overseas inventors in every economic sector. Backlogs undermine incentives to innovate, prevent timely patient access to valuable new treatments and cures, and impose huge societal costs.[79] Because the term of a patent begins on the date an application is filed, unreasonable delays can directly reduce the value of granted patents and undermine investment in future research. For biopharmaceutical companies, patent backlogs can postpone the introduction of new medicines.[80] They create legal uncertainty for research-based and generic companies alike, and can increase the time and cost associated with bringing a new treatment to market.

Patent backlogs are a challenge around the world, but a few countries stand out for persistently long delays. In **Brazil** and **Thailand**, for example, it can take ten years or more to secure a patent on a new medicine.[81] In Brazil, the patent backlog challenge is compounded by an unnecessary dual examination process for biopharmaceutical patent applications. The Brazilian Health Surveillance Agency (ANVISA) may review all patent applications for new medicines, in addition to the formal patent examination process conducted by the Brazilian Patent Office.[82] Thailand approved a patent application filed by one PhRMA member six weeks before the patent expired. The situation is only somewhat better in markets like **India**, where it takes an average of six years to secure a patent,[83] and yet in 2015, India granted one patent based on an application filed 19 years earlier.[84]

[79] Schultz, M. and K. Madigan, "The Long Wait for Innovation: The Global Patent Pendency Problem," George Mason University, Center for the Protection of Intellectual Property, 2016, available at https://sls.gmu.edu/cpip/wp-content/uploads/sites/31/2016/10/Schultz-Madigan-The-Long-Wait-for-Innovation-The-Global-Patent-Pendency-Problem.pdf (last visited Feb. 7, 2019).

[80] Business Standard, Delay in Patents Can Slow Down Improvements in Medicines: Experts, October 2016, available at http://www.business-standard.com/article/news-ians/delay-in-patents-can-slow-down-improvement-in-medicine-experts-116101600452_1.html (last visited Feb. 7, 2019).

[81] Schultz, M. and K. Madigan, "The Long Wait for Innovation: The Global Patent Pendency Problem," George Mason University, Center for the Protection of Intellectual Property, 2016, available at https://sls.gmu.edu/cpip/wp-content/uploads/sites/31/2016/10/Schultz-Madigan-The-Long-Wait-for-Innovation-The-Global-Patent-Pendency-Problem.pdf (last visited Feb. 7, 2019).

[82] Cipriano, M., "Biodiversity Law Reform Spurs Innovation, But Patent Backlog Remains," Oct. 2016, available at https://pink.pharmamedtechbi.com/PS119423/Biodiversity-Law-Reform-Spurs-Innovation-But-Patent-Backlog-Remains (last visited Feb. 7, 2019).

[83] Id.

[84] IndiaSpend, *Patent Delays Threaten 'Make In India'*, Jan. 2016, available at http://www.indiaspend.com/cover-story/patent-delays-threaten-make-in-india-67033 (last visited Feb. 7, 2019).

Long patent examination delays cause significant damage. A London Economics study estimated the value of lost innovation due to increased patent pendency at £7.6 billion per year.[85] Patent backlogs are a particular challenge for small start-up firms that are playing an increasingly important role in biopharmaceutical innovation. According to a U.S. Patent and Trademark Office (PTO) Economic Working Paper, for every year an ultimately-approved patent application is delayed, a start-up firm's employment growth decreases by 21% and its sales growth decreases by 28% on average over the following five years.[86] Each year a patent application is delayed, the average number of subsequent patents granted decreases by 14%, and the probability that a startup will go public is cut in half.[87]

PhRMA members support patent term restoration provisions in trade agreements and national laws to address unreasonable patent examination delays. They support initiatives to increase the efficiency of patent prosecution and reduce patent backlogs, including the PCT and work sharing arrangements through the IP5 and Patent Prosecution Highway (PPH) programs. Through these and other initiatives, national and regional patent offices in the European Union, Japan, Korea, Mexico and elsewhere are succeeding in reducing patent examination delays. However, damaging proposed legislation in the **European Union** threatens to weaken patent term restoration mechanisms in Europe by reducing safeguards provided by Supplementary Protection Certificates. Further work is needed to consolidate gains in patent protections and to extend effective models to other countries.

Compulsory Licensing

Biopharmaceutical innovators support strong national health systems and timely access to safe, effective, and high-quality medicines for patients who need them. Patents drive and enable research and development that delivers new treatments and cures. These limited and temporary intellectual property rights are not a barrier to access to medicines[88] – particularly when governments and the private sector partner to improve health outcomes.

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[85] London Economics, *Patent Backlogs and Mutual Recognition report to the UK Intellectual Property Office,* Jan. 2010, available at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/328678/p-backlog-report.pdf (last visited Feb. 7, 2019).

[86] Farre-Mensa, J., D. Hegde, and A. Ljungqvist, "What Is a Patent Worth? Evidence from the U.S. Patent 'Lottery'," USPTO Economic Working paper No. 2015-5, Dec. 17, 2015, available at http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2704028 (last visited Feb. 7, 2019).

[87] Id.

[88] For example, see Attaran, A. and L. Gillespie-White, "Do Patents for Antiretroviral Drugs Constrain Access to AIDS Treatments in Africa?" *Journal of the American Medical Association*, Oct. 2001, available at https://jamanetwork.com/journals/jama/fullarticle/194301 (last visited Feb. 7, 2019); and Attaran, A. "How Do Patents and Economic Policies Affect Access to Essential Medicines in Developing Countries," *Health Affairs*, May 2004, available at https://www.healthaffairs.org/doi/full/10.1377/hlthaff.23.3.155 (last visited Feb. 7, 2019).

Compulsory licenses (CLs) have been issued in several countries, including **India**, **Indonesia, Russia** and **Malaysia**, that allow local companies to make, use, sell or import particular patented medicines without the consent of the patent holder. Other governments, including **Chile**, **Colombia**, **El Salvador**, **Peru**, **Turkey, Ukraine** and **Vietnam**, have adopted or considered resolutions, laws or regulations that promote or provide broad discretion to issue such licenses. PhRMA believes governments should grant CLs in accordance with international rules and only in exceptional circumstances and as a last resort. Decisions should be made on public health grounds through fair and transparent processes that involve participation by all stakeholders and consider all relevant facts and options.

Experience and recent research demonstrates that compulsory licensing is not an effective way to improve access or achieve other public health objectives. It does not necessarily lower prices[89] or speed access[90] in the short-term, or provide sustainable or comprehensive solutions to longer-term challenges. It does not address systemic barriers to access[91] – from weak health care delivery systems to low national health care funding and high taxes and tariffs on medicines. Compulsory licensing is particularly ineffective relative to the many alternatives available. Biopharmaceutical innovators support different tools and programs that make medicines available to patients who could not otherwise afford them, including drug donation and differential pricing programs, voluntary licensing and non-assert declarations.[92] In sub-Saharan Africa, for example, the majority of antiretrovirals are manufactured under voluntary licenses to local generic drug companies.[93]

Unfortunately, some countries appear to be using CLs to promote the local production of medicines at the expense of manufacturers and jobs in the United States and elsewhere.[94] For example, Malaysia issued a CL in 2017 in a move that appears

[89] Beall, R.F. et al., "Compulsory Licensing Often Did Not Produce Lower Prices for Antiretrovirals Compared to International Procurement," *Health Affairs*, Mar. 2015, available at http://content.healthaffairs.org/content/34/3/493.abstract?etoc (last visited Feb. 7, 2019).

[90] When Brazil issued a CL for an antiretroviral treatment in 2007, it took the local manufacturer two years to launch production of a generic version. See Bond, E. and K. Saggi, "Compulsory licensing, price controls, and access to patented foreign products," Vanderbilt University, Apr. 2012, available at http://www.wipo.int/edocs/mdocs/mdocs/en/wipo_ip_econ_ge_4_12/wipo_ip_econ_ge_4_12_ref_saggi.pdf (last visited Feb. 7, 2019).

[91] Vesper, I., "Cheap drugs not enough to fight hepatitis C in Asia," SciDevNet, July 2018, available at https://www.scidev.net/global/disease/news/drugs-fight-hepatitis-asia.html?utm_source=link&utm_medium=rss&utm_campaign=/global/global_rss.xml& (last visited Feb. 7, 2019).

[92] IFPMA Policy Position, *Voluntary Licenses and Non-Assert Declarations,* available at http://www.ifpma.org/wp-content/uploads/2016/03/IFPMA-Position-on-VL-and-Non-Assert-Declarations-18FEB2015.pdf (last visited Feb. 7, 2019).

[93] Chien, C., "HIV/AIDS Drugs for Sub-Saharan Africa: How Do Brand and Generic Supply Compare?" *PLoS One*, Mar. 2007, available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1805689/ (last visited Feb. 7, 2019).

[94] See, for example, Drugs for Neglected Diseases Initiative, "DNDi welcomes Malaysia's move to secure access to more affordable treatments for hepatitis C," Sep. 2017, available at

designed to facilitate the local development and marketing of a competing combination product. Indonesia's patent law enables the government to grant CLs on the grounds that an inventor is not manufacturing a patented product in Indonesia within three years after the patent was granted. In 2013, India's Intellectual Property Appellate Board affirmed a CL for a patented oncology medicine, based in part on a finding that the patented medicine was not being manufactured in India.[95]

In its 2018 Special 301 Report, USTR rightly highlighted concerning actions by "trading partners to unfairly issue, threaten to issue, or encourage others to issue, compulsory licenses" and committed to "engage, as appropriate, with trading partners". PhRMA members welcomed these statements and urge USTR and other federal agencies to engage to address serious and growing compulsory licensing threats across Latin America, Southeast Asia and elsewhere.

Weak Patent Enforcement

To continue to invest in the research and development of new medicines, biopharmaceutical innovators must be able to effectively enforce patents. Mechanisms such as patent linkage that provide for the early resolution of patent disputes before potentially infringing follow-on products enter a market are essential for effective enforcement. The premature launch of a product that is later found to infringe a patent may disrupt patient treatment and require governments to adjust and re-adjust national formularies and reimbursement policies. For biopharmaceutical innovators, it may cause commercial damage that is impossible to repair later.

At a minimum, effective early resolution mechanisms (1) require governments to notify the holder of a patent on a biopharmaceutical product if another party applies for marketing approval for a generic or biosimilar versions of that product, (2) enable the holder of a patent on a biopharmaceutical product to seek provisional enforcement measures, such as a stay, preliminary injunction or interlocutory injunction, to prevent the marketing of a potentially infringing generic or biosimilar version of that product, and (3) provide for the timely resolution of patent disputes before marketing approval is granted for a generic or biosimilar.

PhRMA members welcomed bold proposed intellectual property reforms **China** announced in 2017, including planned implementation of a patent linkage system. However, the draft Chinese patent law amendments circulated in January 2019 did not include provisions to facilitate patent linkage. PhRMA members were pleased to see that the proposed amendments anticipate the provision of patent term restoration (Article 43),

https://www.dndi.org/2017/media-centre/press-releases/dndi-welcomes-malaysia-move-access-affordable-treatments-hepc/ (last visited Feb. 7, 2019).

[95] Chatterjee, P., "India's First Compulsory License Upheld, But Legal Fights Likely to Continue," Intellectual Property Watch, Apr. 2013, available at http://www.ip-watch.org/2013/03/04/indias-first-compulsory-licence-upheld-but-legal-fights-likely-to-continue/ (last visited Feb. 7, 2019).

but these proposals will need to be refined and further developed in implementing regulations in order to achieve their goal of promoting the development of medicines.

Biopharmaceutical innovators strongly supported passage of patent linkage legislation in **Taiwan** in late 2017. We welcomed regulations issued on January 30, 2019, to implement patent linkage for both biologic and chemically synthesized medicines. We urge Taiwan to quickly finalize these regulations as issued. Such action would promote effective patent enforcement and demonstrate that Taiwan is ready for closer economic engagement with the United States and other leading economies. Further delay or partial implementation would be a significant missed opportunity and could dramatically reduce expected benefits.

U.S. trade agreements generally require parties to notify patent holders, to act expeditiously on requests for provisional enforcement measures and to prevent the marketing of generic or biosimilar products during the patent term without the consent of the patent holder. However, some U.S. trade agreement partners do not comply with these obligations. For example, biopharmaceutical innovators in the United States do not ordinarily receive any notice of a third party's intention to obtain marketing approval in **Australia,** so as to enable final resolution of patent claims before marketing approval, and are unable to quickly secure effective preliminary injunctions in **Mexico**.

Saudi Arabia has knowingly facilitated the infringement of the patent on a medicine formulated and exported from the United States by giving a local company approval to produce a competing product during the patent term. Similarly, in 2017 the **United Arab Emirates** has recently approved the sale of patent infringing generics despite the government's pharmaceutical patent commitments in Ministerial Decree No. 404 and reciprocal patent recognition obligations under the Gulf Cooperation Council. Effective early resolution mechanisms are also needed in **China**, **India**, **Russia** and other countries, where innovators are not notified of marketing approval applications filed for potentially infringing products and generally are unable to secure provisional enforcement measures.

PhRMA urges USTR and other federal agencies to enforce intellectual property commitments in existing U.S. trade agreements and to continue to promote effective patent enforcement abroad, including through the JCCT, the U.S.-India Trade Policy Forum and other bilateral dialogues.

Excessive and Punitive Damages

Biopharmaceutical innovators must be able to rely on and enforce patents issued by competent government authorities. Laws or policies that allow governments or other non-parties to a patent dispute to collect excessive and punitive damage awards after the fact from innovators that pursue unsuccessful patent claims unfairly penalize and discourage the use of provisional enforcement measures as part of well-functioning early resolution mechanisms. These policies undermine legal certainty, predictability and the incentive provided by patents to invest in new treatments and cures.

The ability to enforce patents in **Canada** continues to weaken. Canada's current policies discourage and penalize innovators from seeking patent enforcement actions by enabling generic litigants to recover excessive and punitive damage awards. Pending court decisions could make that situation far worse – increasing the potential that innovators forfeit patents prematurely in Canada rather than defend them. Section 8 of the Patented Medicines (Notice of Compliance) Regulations (PM(NOC) Regulations) is intended to compensate generic drug companies that bring successful patent disputes against innovators for actual losses suffered during the stay period. But, Canada's courts are granting generic litigants damages in excess of 100 percent of the total generic market.

Canada's implementing regulations of the Comprehensive Economic and Trade Agreement (CETA) further expose innovators to excessive liability under Section 8. These regulations enable competitors to claim indefinite future loses and to seek compensation for production "ramp-up" costs they may have incurred before the stay was granted and after it was lifted. In addition, Canada's courts are now contemplating even more excessive damage awards for generic litigants using obscure legal theories under the "Statute of Monopolies" to seek **treble** damages from innovators that unsuccessfully enforced their patent(s) against a generic litigant. An Ontario trial court decision awarding a generic litigant damage under this statute is currently under appeal.

Australia's Therapeutic Goods Act passed as part of legislation implementing the U.S.-Australia Free Trade Agreement,[96] provided for "market-size damages" in certain instances. Since 2012, the Australian government has stated its intent to seek – and has sought – market-size damages from biopharmaceutical innovators that have pursued unsuccessful patent claims. Those damages are designed to compensate Australia's pharmaceutical reimbursement scheme (PBS) for any higher price paid for a patented medicine during the period of a provisional enforcement measure. The PBS imposes automatic price cuts on medicines as soon as competing versions enter the market, but the policy entails no corresponding mechanism to compensate innovators for losses if an infringing product is launched prematurely.

By pursuing market-size damages, Australia is unfairly tipping the scales in commercial patent disputes – encouraging competitors to launch at risk and discouraging innovators from enforcing their patents. This action creates an inappropriate conflict of interest by permitting the same government that examined and granted a patent to seek damages if that patent is later ruled invalid or not infringed. It exposes innovators to significant additional compensation claims that are difficult to quantify and were not agreed to at the time provisional enforcement measures were granted. The size of these additional claims equates legitimate patent enforcement with patent abuse. Allowing governments or other non-parties to a patent dispute to collect market-size damages undermine legal certainty, predictability and the incentives patents provide for investment in new treatments and cures. Australia's practice appears to be inconsistent with the U.S.-

[96] See Schedule 7 of the U.S. Free Trade Agreement Implementation Act 2004, available at http://www.wipo.int/wipolex/en/text.jsp?file_id=206375 (last visited Feb. 7, 2019).

Australia Free Trade Agreement and with WTO intellectual property rules, including with respect to provisional measures.

In a 2004 letter[97] to Australia's trade minister, USTR raised concerns about the significant and negative impact that the Therapeutic Goods Act amendments permitting market-size damages could have on patent rights and the consistency of those amendments with Australia's international obligations. The letter stated that the "United States reserves its right to challenge the consistency of these amendments with such obligations." PhRMA members urge USTR and other federal agencies to prioritize actions to address Australia's pursuit of market-size damages.

Regulatory Data Protection Failures

Regulatory data protection (RDP) complements patents on innovative medicines. By providing temporary protection for the comprehensive package of information biopharmaceutical innovators must submit to regulatory authorities to demonstrate the safety and efficacy of a medicine for marketing approval, RDP provides critical incentives for investment in new treatments and cures.

RDP is a carefully balanced mechanism that improves access to medicines of all kinds. Prior to 1984, generic drug companies in the United States were required to generate their own test data for marketing approval. The Hatch-Waxman Act introduced abbreviated pathways that enabled generic drug companies to rely on test data developed by innovators.[98] In exchange, innovators received a period of protection for test data gained through substantial investments in clinical trials over many years. As a result of this and other provisions of Hatch-Waxman, the percentage of prescription drugs filled by generics soared from 19% in 1984 to 74% in 2009. Today, generics account for approximately 90% of all prescriptions filled in the United States.[99]

RDP is particularly critical for biologic medicines, which may not be adequately protected by patents alone. Made using living organisms, biologics are so complex that it is possible for others to produce a version – or "biosimilar" – of a medicine that may not be covered within the scope of the innovator's patent. For this reason and others, U.S. law provides twelve years of RDP for biologics. This was not an arbitrary number, but rather the result of careful consideration and considerable research on the incentives

[97] Letter from U.S. Trade Representative Robert B. Zoellick to Australian Minister of Trade Mark Vaile, Nov. 17, 2004, available at https://ustr.gov/archive/assets/Trade_Agreements/Bilateral/Australia_FTA/Implementation/asset_upload_file393_6951.pdf (last visited Feb. 7, 2019).

[98] Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended at 21 U.S.C. §355 and 35 U.S.C. §156, 271 and 282).

[99] PhRMA analysis based on IQVIA National Sales Perspective and Quintiles, IMS Institute MIDAS™ audited data, 2017.

necessary to ensure biopharmaceutical innovators and the associated global scientific ecosystem are able to sustainably pursue groundbreaking biomedical research.[100]

Unfortunately, many U.S. trading partners do not provide RDP. Others, like **Saudi Arabia**, provide RDP but have allowed local companies to rely on data submitted by American innovators during the period of protection. This is contrary to WTO rules, which require parties to protect regulatory test data submitted as a condition of obtaining marketing approval against both disclosure and unfair commercial use. Examples, some of which are described further in the country profiles below, include **Algeria**, **Argentina**, **Brazil**, **China**, **Egypt**, **India** and **Turkey**. U.S. trade agreements generally require parties to provide RDP for a specified period of time, but some partner countries have not fully honored their commitments. For example, **Mexico** and **Peru** provide RDP for small-molecule treatments, but not for biologics. **Canada** passed legislation in 2014 that gives the Health Minister broad discretion to share undisclosed test data without safeguards to protect against unfair commercial use. Other countries provide RDP in a manner that discriminates against foreign innovators.

PhRMA urges USTR and other federal agencies to enforce intellectual property commitments in existing U.S. trade agreements, to address RDP failures in bilateral forums and to seek and secure RDP commitments in trade agreement negotiations that reflect the high standards found in U.S. law.

C. Localization barriers – A cross-cutting challenge

Like businesses in many other sectors of the U.S. economy, PhRMA members are witnessing a proliferation of acts, policies and practices abroad that are designed to benefit local producers at the expense of manufacturers and their employees in the United States and elsewhere around the world. In countries like **Argentina**, **China**, **India**, **Indonesia**, **Russia**, **Turkey**, and **Vietnam** these localization barriers have become so pervasive that they are now a routine part of many transactions between businesses and governments – from securing patents, regulatory approval and market entry to the most minor administrative formalities.

These discriminatory measures put American jobs at risk and appear to violate the most basic principles of the global trading system found in the General Agreement on Tariffs and Trade, TRIPS and the WTO Agreements on Technical Barriers to Trade and Trade-Related Investment Measures. They deny adequate and effective intellectual property protection for biopharmaceutical innovators in the United States and fair and equitable market access for new medicines, vaccines and other health technologies. Some examples of the most serious localization barriers that are undermining the ability of PhRMA members to develop and deliver new treatments and cures include:

[100] See, for example, Grabowski, H. et al., "Data exclusivity for biologics," *Nature Reviews – Drug Discovery*, Jan. 2011, available at https://fds.duke.edu/db/attachment/1592 (last visited Feb. 7, 2019).

- *Market entry or other benefits conditioned on local manufacturing.* While many economies provide positive incentives for businesses to conduct research and development and to manufacture in their markets,[101] an alarming number are seeking to grow their economies by discriminating against innovators in the United States and other countries. For example, **Turkey** is once again pursuing a policy that would remove from the reimbursement list products that are not produced in Turkey. **Algeria** prohibits imports of virtually all biopharmaceutical products that compete with similar products manufactured domestically. **Russia**'s Law on the Federal Contract System allows government medicines procurement agencies to ban foreign goods in public procurement tenders. Moreover, Russia is implementing legislation that limits national medicine procurement to manufacturers in the Eurasian Economic Union (EAEU) if there are two or more manufacturers for a particular class of medicine. **Indonesia**'s new Patent Law permits the government to compulsory license patented medicines if the patent holder does not begin manufacturing that medicine in Indonesia within three years after the patent is granted.[102]

- *Mandatory technology transfer.* In **Indonesia** and other countries, local manufacturing requirements are coupled with other policies that directly expropriate sensitive intellectual property and know-how. For example, a foreign biopharmaceutical company may import medicines into Indonesia only if it partners with an Indonesian firm and transfers relevant technology so that those medicines can be domestically produced within five years. Requiring technology transfer to import medicines into Indonesia creates a windfall for domestic firms and artificially distorts the market.

- *De facto bans on imports.* Manufacturing licensing requirements generally are intended to ensure that companies meet globally recognized standards – such as good manufacturing practices (GMP). Some countries exploit these licensing requirements by adopting policies that virtually prevent market entry. For example, **Turkey** does not recognize internationally accepted GMP certifications from other countries unless they have mutual recognition agreements (MRAs) on inspections with Turkey. Given, however, the many steps that would need to be satisfied before an MRA could be pursued between the United States and Turkey, this policy serves as a *de facto* ban on imports from biopharmaceutical innovators in the United States. Turkey has stated publicly that the purpose of this policy is to promote Turkish drug companies.

[101] Pugatch Consilium, "Separating Fact From Fiction – How Localization Barriers Fail Where Positive Non-Discriminatory Incentives Succeed: A Global Assessment of Localization Policies and Incentivizing Life Science Investment and Innovation," 2016, available at http://www.pugatch-consilium.com/reports/Localization%20Paper_US_FINAL.pdf (last visited Feb. 7, 2019).

[102] Cory, N., "The Worst Innovation Mercantilist Policies of 2016," Information Technology and Innovation Foundation, Jan. 2017, available at http://www2.itif.org/2017-worst-innovation-mercantilist-policies.pdf?_ga=1.176855585.581989633.1484510758 (last visited Feb. 7, 2019).

Recent research[103] is demonstrating the significant and widespread damage localization barriers can inflict on the global economy and on markets that put such barriers in place. They cost businesses and their employees in the United States and other leading nations by cutting tens of billions of dollars in global trade and by reducing global income and innovation. They do not increase biopharmaceutical investment or knowledge-intensive employment in countries that adopt localization barriers. In fact, they can even reduce employment – particularly for the less skilled – by raising input costs and severing connections to global value chains.[104]

PhRMA members appreciate the attention USTR and other federal agencies have given to localization barriers in recent reports and publications. However, action is urgently needed to remove these barriers and to discourage other countries from adopting similar acts, policies and practices. Biopharmaceutical innovators in the United States look forward to concrete progress and real results in 2019.

III. Addressing Challenges and Securing the Benefits of Biopharmaceutical Innovation

To address these pressing challenges and ensure biopharmaceutical innovators in the United States can continue to research, develop and deliver new treatments and cures for patients who need them around the world, PhRMA members urge USTR and other federal agencies to take the following five actions. These actions can help ensure access to quality, safe and effective medicines at home and abroad by promoting high standards of protection for patents and regulatory test data, effective enforcement of these and other intellectual property rights and transparent and predictable legal and regulatory regimes.

A. Enforce and defend global, regional and bilateral rules

USTR and other federal agencies should use all available tools and leverage to ensure America's trading partners live up to their obligations in global, regional and bilateral trade and investment agreements. Modernizing existing trade agreements and stepping up enforcement activity in the months ahead will be critical to end discriminatory

[103] See, for example, Stone, S., J. Messent and D. Flaig, "Emerging Policy Issues: Localisation Barriers to Trade," OECD Trade Policy Papers, No. 180, 2015, available at http://www.oecd-ilibrary.org/trade/emerging-policy-issues_5js1m6v5qd5j-en;jsessionid=ai5pr32hanqoq.x-oecd-live-03 (last visited Feb. 7, 2019); Ezell, S.J., R.D. Atkinson and M.A. Wein, "Localization Barriers to Trade: Threat to the Global Innovation Economy," Information Technology and Innovation Foundation, Sep. 2013, available at http://www2.itif.org/2013-localization-barriers-to-trade.pdf?_ga=1.136058805.581989633.1484510758 (last visited Feb. 7, 2019). Hufbauer, G.C., J.J. Schott et al., *Local Content Requirements: A Global Problem*, Peterson Institute for International Economics, Sep. 2013, available at http://bookstore.piie.com/book-store/6802.html (last visited Feb. 7, 2019).

[104] Pugatch Consilium, "Separating Fact From Fiction – How Localization Barriers Fail Where Positive Non-Discriminatory Incentives Succeed: A Global Assessment of Localization Policies and Incentivizing Life Science Investment and Innovation," 2016, available at http://www.pugatch-consilium.com/reports/Localization%20Paper_US_FINAL.pdf (last visited Feb. 7, 2019).

pricing policies and to address longstanding intellectual property challenges around the world – particularly in countries that are U.S. trade and investment agreement partners, that have made important unfulfilled WTO accession commitments and that benefit from U.S. trade preference programs.

U.S. regional and bilateral trade agreements affirm globally accepted standards for the patentability of biopharmaceutical and other inventions and require countries to protect regulatory test data, provide mechanisms that enable innovators to resolve patent disputes prior to the marketing of potentially infringing products, and establish a stronger intellectual property framework. Some also include government pricing and reimbursement and transparency commitments. However, **Australia**, **Canada**, **Chile**, **Colombia**, **Korea** and other U.S. trading partners fail to adequately comply with some or all of these obligations. USTR and other federal agencies should consider a process to systematically review compliance with trade and investment agreements and take steps necessary to ensure agreed rules are followed.

On joining the WTO in 2001, **China** committed to provide six years of protection for clinical test and other data submitted for regulatory approval of biopharmaceutical products containing a new chemical ingredient.[105] China has never implemented this obligation, despite agreement to do so during the 2012 U.S.-China Joint Commission on Commerce and Trade meeting.[106] In light of these deficiencies, we strongly welcomed the CFDA draft Circular 55 (Relevant Policies on Protecting Innovators' Rights to Encourage New Drug and Medical Device Innovation) and draft "Implementing Provisions on Protection of Drug Trial Data" (April 2018), which propose up to twelve years of RDP for therapeutic biologics, orphan and pediatric medicines and six years of RDP for new small molecule drugs. These proposals represent a strong first step toward reform in this area, but it is now imperative that these proposed policy revisions are transparently and expeditiously implemented in a manner that provides for effective protection for U.S. biopharmaceutical companies and is consistent with China's international obligations and commitments.

The Generalized System of Preferences (GSP) program provides unilateral duty-free access to the U.S. market for more than 3,500 products.[107] Before granting GSP benefits to an eligible country, the President must take into account a number of factors, including the extent to which the country is willing to "provide equitable and reasonable access to its markets" and is "providing adequate and effective protection of intellectual

[105] World Trade Organization, "Report of the Working Party on the Accession of China" (WT/ACC/CHN/49), Oct. 2001, available at https://www.wto.org/english/thewto_e/acc_e/completeacc_e.htm (last visited Feb. 7, 2019).

[106] Office of the U.S. Trade Representative, "Fact Sheet: 23rd U.S.-China Joint Commission on Commerce and Trade," Dec. 2012, available at https://ustr.gov/about-us/policy-offices/press-office/fact-sheets/2012/december/23rd-JCCT (last visited Feb. 7, 2019).

[107] Office of the United States Trade Representative, *U.S. Generalized System of Preferences Guidebook*, Sep. 2016, available at https://ustr.gov/sites/default/files/GSP-Guidebook-September-16-2016.pdf (last visited Feb. 7, 2019).

property rights."[108] However, GSP beneficiaries like **Argentina**, **Brazil**, **India**, **Indonesia** and **Turkey** do not provide adequate and effective protection of intellectual property rights or fair and equitable market access.

The Special 301 Report is an important tool to identify and prioritize acts, policies and practices in these and other overseas markets that are harming America's creative and innovative industries by denying adequate and effective intellectual property protection and fair and equitable market access. PhRMA members urge USTR and other federal agencies to ensure this tool is used effectively. Action plans required by the Trade Facilitation and Trade Enforcement Act of 2015 should be developed for countries listed on the Priority Watch List with input from relevant stakeholders.[109] Out-of-cycle reviews announced in the Special 301 Report should be conducted and should involve the participation of relevant stakeholders.

USTR should prioritize actions to fill key enforcement positions, including the position of Chief Innovation and Intellectual Property Negotiator. Where necessary, USTR should consider bringing dispute settlement cases to secure compliance with trade and investment agreement commitments.

B. Secure strong commitments in global, regional and bilateral negotiations

PhRMA members strongly support the U.S.-Mexico-Canada Agreement (USMCA) and look forward to its swift passage and implementation. Global, regional and bilateral trade and investment negotiations like the USMCA provide critical opportunities to build on the existing foundation of international rules and to secure commitments necessary to drive and sustain 21st Century biopharmaceutical innovation. Ending discriminatory pricing policies, eliminating restrictive patentability criteria, addressing unreasonable patent examination and approval delays, providing for the early and effective resolution of patent disputes, ensuring robust protection of regulatory test data, and reducing unnecessary regulatory barriers can promote biopharmaceutical innovation and improve market access.

PhRMA supports trade agreements that include strong protections for intellectual property, ensure fair and equitable market access and enable biopharmaceutical innovators in the United States to export lifesaving medicines to patients around the world. Free and fair trade agreements open new markets. They help grow our economy and create better, higher-paying jobs. PhRMA members look forward to continuing to work with USTR and other federal agencies to modernize existing trade agreements and to consider opportunities to further improve public health and grow American

[108] See Title V of the Trade Act of 1974 (19 U.S.C. 2461 et seq.), as amended.

[109] See Section 182 of the Trade Act of 1974 (19 U.S.C. 2242), as amended.

manufacturing exports and jobs through additional trade agreements, including with leading U.S. biopharmaceutical export markets.[110]

C. End discrimination in pricing and reimbursement

PhRMA members are, and seek to be, partners in solutions to health care challenges facing patients and their communities around the world. However, some governments have proposed or implemented pricing and reimbursement policies that discriminate against medicines made in America, do not appropriately value innovation and lack predictable, transparent, and consultative processes. Such measures can undermine the ability of biopharmaceutical innovators to bring new medicines to patients who need them and to invest in future treatments and cures.

The biopharmaceutical industry is unique in that most foreign governments, as sole or primary health care providers, impose burdensome and often discriminatory price controls and regulations on the sector. Others have resorted to improperly using national compulsory licensing provisions to threaten or coerce manufacturers to accept pricing agreements on unreasonable commercial terms and conditions. As a result, market access for pharmaceuticals is not only dependent on innovators meeting strict regulatory approval standards and obtaining necessary intellectual property protections, but also on obtaining positive government pricing and reimbursement determinations. It is imperative, therefore, that regulatory procedures and decisions regarding the approval and reimbursement of medicines are governed by fair, transparent and verifiable rules guided by science-based decision making. There should be meaningful opportunities for input from manufacturers and other stakeholders to health authorities and other regulatory agencies and a right to appeal government pricing and reimbursement decisions to an independent, objective court or administrative body.

The U.S. government can play a critical role in ensuring transparency and due process of pricing and reimbursement policies, as well as in highlighting the global benefits to patients that result from a reduction in trade barriers. The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 called for the Administration to develop a strategy to address foreign price controls on pharmaceuticals and related practices through bilateral and multilateral trade negotiations. PhRMA believes that the cornerstone of any such strategy must be a proactive U.S. trade policy focused on: (i) addressing discriminatory government price controls and related practices; and (ii) highlighting the global benefits for patients from the potential groundbreaking research that could result from a reduction in key trade barriers. Unfortunately, governmental policies around the globe over the last year have continued to harm patient access to innovative medicines.

[110] U.S. Department of Commerce, International Trade Administration, "2016 Top Markets Report: Pharmaceuticals," 2016, available at http://trade.gov/topmarkets/pdf/Pharmaceuticals_Executive_Summary.pdf (last visited Feb. 7, 2019).

PhRMA members appreciate steps USTR and other federal agencies have taken to ensure fair and equitable market access for innovative medicines in overseas markets, including seeking and securing commitments in trade agreements that ensure pricing and reimbursement policies abroad are fair, reasonable, and non-discriminatory, and appropriately value patented pharmaceuticals. PhRMA urges USTR and other federal agencies to continue to promote the full implementation of these commitments and to build on them in future trade negotiations by ensuring future trade agreements meet the Trade Promotion Authority objective to "ensure that government regulatory reimbursement regimes are transparent, provide procedural fairness, are non-discriminatory, and provide full market access for United States products."[111]

In particular, proposed laws, regulations and procedures concerning how medicines are approved, priced, and reimbursed should be:

- Promptly published or otherwise made available to enable interested parties to become acquainted with them.
- Published prior to adoption in a single official journal of national circulation, with an explanation of the underlying purpose of the regulation. In addition, interested parties (including trading partners) should be provided a reasonable opportunity to comment on the proposed measures. Those comments and any revisions to the proposed regulation should be addressed in writing at the time that the agency adopts its final regulations. Finally, there should be reasonable time between publication of the final measures and their effective date so that the affected parties can adjust their systems to reflect the new regulatory environment.

In turn, specific regulatory determinations or pricing and reimbursement decisions should be:

- Based on fair, reasonable, consistent and non-discriminatory procedures, rules and criteria that are fully disclosed to applicants.
- Completed within a reasonable, specified timeframe. In some countries, there are no deadlines for making decisions on whether to approve new medicines. In others, deadlines exist, but are regularly not met. These delays impede market access, deplete the patent term, and are detrimental to patients waiting for life-saving medicines.
- Conducted so that they afford applicants timely and meaningful opportunities to provide comments at relevant points in the decision-making process.
- Supported by written reports which explain the rationale for the decision and include citations to any expert opinions or academic studies relied upon in making the determination.
- Subject to an independent review process.

[111] Section 102(b)(7)(G) of the Bipartisan Congressional Trade Priorities and Accountability Act of 2016 (P.L. 114-26).

D. Combat the worldwide proliferation of counterfeit medicines

PhRMA members view counterfeit medicines as a critical public health and safety concern threatening patients around the world. Counterfeit medicines may deprive patients of the medicines they need and contribute to drug-resistant forms of tuberculosis and other serious diseases and contain impurities or toxins that can cause harm or even death.[112] This challenge is exacerbated by the ease with which counterfeiters can offer fake medicines over the Internet[113] and ship them by mail[114] to patients and consumers worldwide.[115]

Counterfeit medicines are a potential danger to patients everywhere, including in the United States. During fiscal year 2017, U.S. Customs and Border Protection seized more than 2,200 shipments of counterfeit pharmaceuticals at America's borders.[116] Using a broader measure that includes counterfeiting, illegal diversion and theft, the Pharmaceutical Security Institute documented more than 3,500 incidents of pharmaceutical crime in the United States in calendar year 2017 – an all-time high.[117] Across all sectors, the Organization for Economic Cooperation and Development (OECD)

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[112] Testing reported in *The Lancet* found one-third of anti-malarial medicines in sub-Saharan Africa and South East Asia lacked active ingredients. See Guarvika, M.L.N. et al., "Poor-quality antimalarial drugs in southeast Asia and sub-Saharan Africa," *The Lancet*, June 2012, available at http://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2812%2970064-6/fulltext (last visited Feb. 7, 2019). See also testimony of Howard Sklamberg, U.S. Food and Drug Administration Deputy Commissioner for Global Regulatory Operations and Policy, before the House Energy and Commerce Subcommittee on Oversight and Investigations, "Counterfeit Drugs: Fighting Illegal Supply Chains," Feb. 2014, available at https://www.gpo.gov/fdsys/pkg/CHRG-113hhrg88828/pdf/CHRG-113hhrg88828.pdf (last visited Feb. 7, 2019).

[113] Of more than 11,000 web sites selling prescription medicines to patients in the United States, the National Association of Boards of Pharmacy® has found approximately 96% of them are operating illegally. See National Association of Boards of Pharmacy, "Internet Drug Outlet Identification Program: Progress Report for State and Federal Regulators," Aug. 2017, available at https://nabp.pharmacy/wp-content/uploads/2016/08/Internet-Drug-Outlet-Report-August-2017.pdf (last visited Feb. 7, 2019).

[114] An OECD study published last year found that more than 60% of counterfeit goods seized around the world between 2011 and 2013 were shipped by mail or express carrier. See OECD, "Trade in Counterfeit and Pirated Goods: Mapping the Economic Impact," 2016, available at http://www.keepeek.com/Digital-Asset-Management/oecd/governance/trade-in-counterfeit-and-pirated-goods_9789264252653-en#.WHv5mpcraBc#page1 (last visited Feb. 9, 2019).

[115] Institute of Medicine (IOM), *Countering the Problem of Falsified and Substandard Drugs*, February 2013, available at https://iom.nationalacademies.org/~/media/Files/Report%20Files/2013/Substandard-and-Falsified-Drugs/CounteringtheProblemofFalsifiedandSubstandardDrugs_RB.pdf (last visited Feb. 7, 2019). The IOM notes that "because the internet facilitates easy international sales, online drug stores have spread the problem of falsified and substandard drugs…."

[116] Homeland Security, "Intellectual Property Rights Seizure Statistics: Fiscal Year 2017," April 2018, available at https://www.cbp.gov/sites/default/files/assets/documents/2018-Apr/ipr-seizure-stats-fy2017.pdf (last visited Feb. 7, 2019).

[117] Pharmaceutical Security Institute, "Incident Trends," available at http://www.psi-inc.org/incidentTrends.cfm (last visited Feb. 7, 2019).

found that global counterfeiting and piracy accounts for 2.5% of world trade and disproportionately harms innovators in the United States.[118]

China and **India** are leading sources of fake medicines seized at ports of entry in the United States[119] and elsewhere,[120] though many other jurisdictions are involved – particularly in online sales.[121] According to the WHO, regions where protection and enforcement systems are weakest also see the highest incidence of counterfeit medicines. In these jurisdictions and others, customs and other law enforcement officials often are not able to seize counterfeit medicines, particularly goods in transit, goods in free trade zones and goods offered for sale on the Internet. Violations of limited laws on the books often are not effectively enforced or do not come with sufficient penalties to deter counterfeiting.[122]

PhRMA member companies work to maintain the safety of their manufacturing facilities and the security of their global supply chains. They currently employ and routinely enhance a variety of anti-counterfeiting technologies, including covert and overt features on the packaging of high-risk prescription medicines. They have adopted a range of business processes to better secure prescription drug supply chains and facilitate the early detection of criminal counterfeiting activity. They partner with law enforcement officials around the world.

To combat the global proliferation of counterfeit medicines and active pharmaceutical ingredients, PhRMA supports strengthening training and collaboration with U.S. trading partners to adopt and implement a comprehensive regulatory and enforcement framework that: (i) subjects drug counterfeiting activity to effective administrative and criminal remedies and deterrent penalties; (ii) adequately regulates and controls each link in the legitimate supply chain; (iii) trains, empowers and directs drug regulators, law enforcement authorities and customs to take effective and coordinated action, including against exports and online activity; and (iv) educates all stakeholders about the inherent dangers of counterfeit medicines.

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[118] OECD, "Trade in Counterfeit and Pirated Goods: Mapping the Economic Impact," 2016, available at http://www.keepeek.com/Digital-Asset-Management/oecd/governance/trade-in-counterfeit-and-pirated-goods_9789264252653-en#.WHv5mpcraBc#page1 (last visited Feb. 7, 2019).

[119] Homeland Security, "Intellectual Property Rights Seizure Statistics: Fiscal Year 2017," April 2018, available at https://www.cbp.gov/sites/default/files/assets/documents/2018-Apr/ipr-seizure-stats-fy2017.pdf (last visited Feb. 7, 2019).

[120] See, for example, European Commission, "Report on EU customs enforcement of intellectual property rights: Results at the EU border," 2015, available at http://ec.europa.eu/taxation_customs/sites/taxation/files/2016_ipr_statistics.pdf (last visited Feb. 7, 2019).

[121] United States Government Accountability Office, "Internet Pharmacies: Federal Agencies and States Face Challenges Combatting Rogue Sites, Particularly Those Abroad," (GAO-13-560), July 2013, available at http://www.gao.gov/assets/660/655751.pdf (last visited Feb. 7, 2019).

[122] Office of the U.S. Intellectual Property Enforcement Coordinator, "Supporting Innovation, Creativity & Enterprise: Charting a Path Ahead," U.S. Joint Strategic Plan on Intellectual Property Enforcement, FY2017-2019, available at https://obamawhitehouse.archives.gov/blog/2016/12/12/supporting-innovation-creativity-and-enterprise-charting-path-ahead (last visited Feb. 7, 2019).

E. Build and strengthen global cooperation

Finally, PhRMA members urge USTR and other federal agencies to further build and strengthen partnerships with countries around the world that also have a critical stake in a strong and effective intellectual property system that values and protects innovation. Federal agencies should promote full implementation and ensure effective enforcement of global, regional and bilateral commitments and support training of regulators, law enforcement officials, judges and other court personnel overseas to enforce those commitments.

PhRMA members appreciate the steps USTR and other federal agencies are already taking to strengthen cooperation with other governments. Bilateral forums like the Transatlantic IPR Working Group have helped to build understanding and to identify and advance common priorities. They can be a model for similar engagement with other countries. The network of PTO intellectual property attachés around the world is a vital resource for American inventors and should be expanded. Cooperation between PTO and other leading patent offices through the PCT, the IP5 and PPH programs is cutting costs, improving the efficiency of patent examination in overseas markets and helping to reduce stubbornly high patent examination backlogs.

All this provides a valuable foundation on which to build in the coming year and beyond. Fostering and strengthening coalitions that support innovation will be particularly critical in multilateral organizations, such as the WHO, the World Intellectual Property Organization (WIPO), the WTO, UNDP, UNCTAD and Unitaid, where work can be inappropriately focused on limitations and exceptions to intellectual property rights, if not actively seeking to undermine and even eliminate the intellectual property protections that drive America's innovation economy. This is even the case at WIPO – an organization that was created to "encourage creative activity" and to "promote the protection of intellectual property throughout the world."[123]

As a leading contributor to multilateral organizations, the United States must remain vigilant in these forums and work with other like-minded countries to advocate for robust intellectual property protection and fair and equitable market access. Federal agencies should ensure intellectual property matters are addressed in organizations with the appropriate mandate and expertise. They should strengthen interagency coordination and ensure officials with intellectual property expertise are part of U.S. delegations to relevant global meetings. They should enable all stakeholders to engage in discussions underway in multilateral organizations.

[123] See, generally, Convention Establishing the World Intellectual Property Organization, July 14, 1967, available at http://www.wipo.int/treaties/en/text.jsp?file_id=283854 (last visited Feb. 7, 2019).

IV. Country Designation Index

A. Priority Foreign Country

PhRMA urges USTR to designate **Canada**, **Japan**, **Korea** and **Malaysia** as Priority Foreign Countries. Market access and/or intellectual property acts, policies and practices in these four countries are the most onerous and egregious. They are having or could have the greatest adverse impact on medicines developed and manufactured in the United States. USTR and other federal agencies should use all available tools to remedy serious concerns in these countries.

B. Priority Watch List

PhRMA recommends that **13** countries be included on the Priority Watch List. We further recommend that **China** continue under Section 306 Monitoring. The detailed information presented in the country-specific sections below demonstrates that the acts, policies and practices of these countries are denying adequate and effective intellectual property protection or fair and equitable market access. They are harming biopharmaceutical innovators and their employees in the United States and limiting their ability to bring new treatments to patients around the world. In many cases, they appear to be inconsistent with relevant global, regional and bilateral trade and investment agreement rules. To evaluate progress and secure action and real results, PhRMA recommends that USTR conduct meaningful **Out-of-Cycle Reviews** for **Chile** and **Colombia**.

C. Watch List

PhRMA recommends that **seven** markets be included on the Watch List. We urge USTR and other federal agencies to include all these countries in the *2019 Special 301 Report* – particularly Australia and other countries that are current or potential U.S. bilateral trade agreement partners. To evaluate progress and secure action and real results, PhRMA recommends that USTR conduct a meaningful **Out-of-Cycle Review** for **Peru**. USTR and other federal agencies should monitor developments in these countries and address specific intellectual property and market access concerns through bilateral and multilateral engagement.

PRIORITY FOREIGN COUNTRY

CANADA

PhRMA and its member companies operating in Canada are extremely concerned about Canada's intellectual property (IP) protections for patented products and the pricing environment. While progress on strengthening IP is being made through the conclusion of the U.S.-Mexico-Canada Agreement (USMCA), the government's pricing reforms significantly undermine that progress and continue to be characterized by significant uncertainty and instability for U.S. innovative biopharmaceutical companies. Of particular concern are Canada's proposed new pricing policies for patented products that would significantly undermine the practical benefits to U.S. companies of Canada's trade-related intellectual property commitments and which create uncertainty for patients. In addition, Canada's IP regime continues to lag behind that of other developed nations in several significant respects.

Recognizing these challenges, PhRMA and its members commend the U.S. Government for its conclusion of the USMCA, which marks a historic point for U.S. trade policy and cements critical IP and other standards that will pave the way for the next generation of treatments and cures. PhRMA stands ready to work with the U.S. Government to secure full and faithful implementation of the USMCA and thereby address several of the issues raised below.

Key Issues of Concern:

- **The Patented Medicine Prices Review Board (PMPRB)**: In December 2017, Canada proposed regulatory changes to the current mandate of the PMPRB from ensuring "non-excessive" prices to ensuring "affordable" prices, and to change its pricing regulations accordingly. An initial analysis of the potential impacts of proposed changes to the PMPRB regulations estimated that industry revenues could be reduced by a minimum of $2.2 billion annually, or 25% of the Canadian market for innovative medicines.[124] An updated analysis conducted in July 2018 found that the proposals would lead to dramatic ceiling price reductions ranging from 40% to 90%, depending upon the medicine and, so, an even sharper decline in revenues than originally estimated.[125] Key proposals would amend the basket of reference countries (including the removal of the U.S. from the basket) with the intent of setting prices of patented medicines at the OECD median, introduce various new factors to determine whether a price is "excessive," and require manufacturers to report all indirect price reductions. These proposed changes could have a serious negative impact on U.S. biopharmaceutical companies operating in Canada, the availability of new medicines to Canadian patients, and the competitiveness of Canada for research-based pharmaceutical investment.

[124] PCDI Market Access, Proposed Amendments to the Patented Medicines Regulations: A Critical Appraisal of the Cost-Benefit Analysis, January 2018, available at http://www.pdci.ca/wp-content/uploads/2018/01/20180129_PDCI-Critical-Assessment-PM-Regs-Amendments_Report-Final.pdf (last visited Feb. 7, 2019).

[125] Ernst & Young, Analysis of impacts of PMPRB Pharmacoeconomic factors analysis, July 2018.

- **Weak patent enforcement**: The Canadian Patented Medicines (Notice of Compliance) Regulations (the PM(NOC) Regulations) include several key deficiencies that weaken Canada's enforcement of patents, including excessive and windfall damage awards to generic litigants, and limitations and inequitable eligibility requirements on the listing of patents in the Patent Register. Recent jurisprudence under the regulations has also resulted in a heightened level of liability for patent owners akin to punitive damages. PhRMA and its member companies are also troubled to see that Canada has used implementation of the Canada-EU Comprehensive Economic and Trade Agreement (CETA)[126] to implement reforms not required by that Agreement, which expose innovators to even greater potential liability under Section 8 of the PM(NOC) Regulations. PhRMA members are also concerned about potential damage awards which could stem from various common law theories within the Canadian provincial courts.

- **Inadequate patent term restoration**: Under CETA, Canada is required to provide innovators with some compensation for delays in obtaining marketing approval for pharmaceuticals. The USMCA also requires Canada to provide patent term restoration (PTR). However, in its CETA implementing regulations, Canada has chosen to implement an "export" exception that is inconsistent with the fundamental purpose of restoring a portion of the patent term lost due to the marketing approval process and has only adopted the minimum term of PTR negotiated under CETA further deviating from global standards. Furthermore, Canada's adoption of restrictive time limits and eligibility criteria will unduly and unreasonably limit patent term restoration eligibility in Canada in a manner that is contrary to the intent of the negotiation and the CETA text itself. PhRMA's member companies believe Canada should support innovation by ensuring that its PTR system effectively ameliorates the effects of lengthy regulatory processes, which can significantly erode the duration of the IP rights of innovators.

- **Standard for the disclosure of confidential business information (CBI)**: In November 2014, Canada enacted legislation to update its Food and Drugs Act (Bill C-17). Provisions in that law granted the Health Minister discretion to disclose a company's CBI without notice to the owner of the CBI and in accordance with a standard that is both inconsistent with other similar Canadian legislation and Canada's treaty obligations under NAFTA and TRIPS. Additionally, on July 9, 2018, the Federal Court of Canada issued a decision ordering Health Canada to release vast amounts of pharmaceutical clinical trial data on five medications to a researcher, undercutting the federal government's attempts to keep the information confidential. The decision, which was not appealed by Health Canada, has the potential to exacerbate the negative impacts of the draft regulations and guidelines on biopharmaceutical innovators.

[126] *See* CETA, Final Text, as published by the Government of Canada, available at http://www.international.gc.ca/trade-commerce/trade-agreements-accords-commerciaux/agr-acc/ceta-aecg/text-texte/toc-tdm.aspx?lang=eng (last visited Feb. 7, 2019).

- **Regulatory barriers to patient access to new medicines**: Bureaucratic barriers exist in Canada that extend the time between submission to the federal government of newly discovered medicines and vaccines for safety approval, and their ultimate availability through public formularies to benefit Canadian patients. This results in significant delays in access to innovative medicines, while also decreasing the time that innovative companies have to recoup their investments.

For these reasons, PhRMA requests that Canada be designated a **Priority Foreign Country** in the 2019 Special 301 Report, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protection and Pricing of Patented Products

The Patented Medicine Prices Review Board (PMPRB)

The PMPRB is a quasi-judicial body, created under the Canadian *Patent Act*.[127] The legislative mandate of the Board is to ensure that patented prices are not "excessive." Due to its power in shaping the real-world benefits of IP property protections, the PMPRB is an important institution within Canada's broader IP regime for pharmaceuticals. The PMPRB regulates the maximum allowable price that a manufacturer can charge for all patented medicines in Canada. The Board does not make decisions about the amount of reimbursement for a product, which is appropriately the responsibility of separate federal and provincial/territorial government agencies, or private insurers.

On December 2, 2017, Health Canada proposed Regulations Amending the *Patented Medicines Regulations* in Canada Gazette, Part I.[128] The PMPRB changes were initiated as part of the Board's professed role as a "counterweight to the patent rights of pharmaceutical manufacturers."[129] The proposed changes could negatively impact the innovative biopharmaceutical industry, the availability of new medicines to Canadian patients, and the competitiveness of Canada for research-based pharmaceutical investment.

Recent analysis found that patented drugs accounted for only 6.7 percent of the $232.9 billion reported by the Canadian Institute for Health Innovation for total health spending in Canada in 2016.[130] Moreover, patented drugs have experienced near *zero*

[127] *Patent Act*, R.S.C. 1985, c.P-4, ss.79-103.

[128] Canada Gazette, Part I, Regulations Amending the Patented Medicines Regulations, Vol. 151, No. 48, December 2, 2017, available at http://www.gazette.gc.ca/rp-pr/p1/2017/2017-12-02/html/reg2-eng.html (last visited Feb. 7, 2019).

[129] PMPRB 2015–16 Report on Plans and Priorities, http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1163 (last visited Feb. 7, 2019).

[130] Brett Skinner, Editorial, "How Ottawa's using a fake drug crisis to force through damaging pharmaceutical policy," Vancouver Sun, Jan. 16, 2018, available at

real cost growth for the last decade.[131] These data suggest that patented medicines are not the primary cost driver of Canadian health expenditure, so we question whether the reforms will generate benefits to outweigh the potential risks to access and innovation that will be created. Low prices should not be the *only* goal of pharmaceutical policy and we urge the government to take a more holistic view. It is crucial to carefully consider the impact of pricing policy on access to new medicines, clinical studies, launch of new treatments, investment, jobs, and the research ecosystem as a whole.

One conservative analysis of the proposed changes to the PMPRB estimated that industry revenues could be reduced by a minimum of $2.2 billion annually, or 25% of the Canadian market for innovative medicines.[132] An updated analysis completed in July 2018 indicates that the PMPRB's proposed changes could result in dramatic ceiling price reductions ranging from 40% to 90%, depending upon the medicine and, so, an even sharper decline in revenues.[133] These analyses do not account for the full scope of the potential impacts to the innovative industry and the Canadian economy. Depending on how the reforms are implemented, the financial and non-financial impacts could be more severe.[134] Moreover, taken as a whole, the proposed PMPRB changes will increase Canada-U.S. regulatory asymmetries, and may also create new border enforcement challenges by incenting inappropriate cross-border trade in innovative medicines.

Canada proposes to amend the PMPRB's basket of reference countries with the goal of setting ceiling prices of patented medicines in Canada at the Organization for Economic Cooperation and Development (OECD) median. Specifically, the PMPRB proposes to remove the U.S. and Switzerland, with the new basket consisting of: Australia, Belgium, France, Germany, Italy, Japan, the Netherlands, Norway, South Korea, Spain, Sweden and the United Kingdom. Despite being at the forefront of OECD economies, Canada would amend its list of referenced countries to replace the U.S. with countries which are poorer and/or have onerous price control policies. The U.S. is Canada's largest trading partner and the pharmaceutical markets in both countries share many common features. Any pricing determinations in Canada based on reference to other countries should include the U.S. and other countries with pro-innovation pharmaceutical policies.

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http://business.financialpost.com/opinion/how-ottawas-using-a-fake-drug-crisis-to-force-through-damaging-pharmaceutical-policy (last visited Feb. 7, 2019).

[131] *Id.*

[132] PCDI Market Access, Proposed Amendments to the Patented Medicines Regulations: A Critical Appraisal of the Cost-Benefit Analysis, January 2018, available at http://www.pdci.ca/wp-content/uploads/2018/01/20180129_PDCI-Critical-Assessment-PM-Regs-Amendments_Report-Final.pdf (last visited Feb. 7, 2019).

[133] Ernst & Young, Analysis of impacts of PMPRB Pharmacoeconomic factors analysis, July 2018.

[134] Ernst & Young, Innovative Medicines Canada Data Analytics and Members' Economic Footprint and Impact in Canada, September 2017, available at http://innovativemedicines.ca/wp-content/uploads/2017/10/20171030_EY-REPORT_IMC_FINAL.pdf (last visited Feb. 7, 2019).

Canada also proposes to introduce new factors to determine whether a price is "excessive." New proposed factors to regulate prices would include pharmacoeconomic evaluation based on an arbitrary monetary threshold of the value of an additional year of life; price ceilings based on projected market size; and the proportion of gross domestic product spent on patented medicines. Such cost-effectiveness thresholds could impact the future viability of many drugs for rare diseases and oncology treatments in Canada. While cost-effectiveness thresholds are used downstream in other nations in making reimbursement decisions, their utilization as part of a binding regulatory price ceiling would be unique in the world.

In the thirty years since the PMPRB was established, a variety of mechanisms have emerged in Canada for the government and industry to effectively address the affordability of medicines. These mechanisms include the Canadian Agency for Drugs and Technologies in Health (CADTH), the Common Drug Review and pan-Canadian Oncology Drug Review, the pCPA, and confidential product listing agreements, among others. Indeed, the specific change to include a cost-effectiveness factor as part of PMPRB's price evaluation overlaps with and duplicates the work of existing publicly funded agencies (*e.g.*, CADTH), and its major beneficiary would be for-profit private insurers as opposed to patients. Any expansion of the PMPRB's mandate to include "affordability" is therefore unnecessary and would harm U.S. innovative biopharmaceutical companies through additional downward pricing pressures.

In addition, Canada proposes to require manufacturers to report all indirect price reductions given as a promotion or in the form of rebates, discounts, refunds, free goods, free services, gifts, or any other benefit in Canada. Given the lack of information on the purpose and use of this information, potential legal concerns and the risk of significant and negative consequences for public payers and other market participants, PhRMA opposes the mandatory submission of indirect price reduction information to the PMPRB.

It appears that the PMPRB is also considering an unprecedented level of intervention into competitive markets, through "tiered" pricing for similar patented products, forcing some new products to a price lower than previously launched products. While few details are currently available, this would treat many innovative products in a similar manner to non-patented generic drugs and would pose barriers to important innovations and the range of therapeutic alternatives available to Canadians.

The proposed Regulations were scheduled to be finalized in early 2019, and it was anticipated that the proposals would apply to new and existing medicines for sales that occur after January 1, 2020. Due to ongoing discussions and consultations, it is unclear when these regulations will be finalized. In addition to the Regulations, the way in which they are to be implemented through changes to the PMPRB's Guidelines raise many additional points of uncertainty and risk for U.S. biopharmaceutical innovators. In particular, the proposed retroactive application of the new regulatory framework to products that have already been determined to be non-excessive under the PMPRB's current framework would be both inequitable and immensely disruptive for patentees.

PhRMA recommends that the U.S. Government urge the Government of Canada to not move forward with any changes to the PMPRB's mandate that would harm U.S. innovative biopharmaceutical companies and undermine the competitiveness of Canada's innovative medicines sector. Any PMPRB policy changes must ensure that the PMPRB's role is placed in its proper context with the many other agencies already active in the Canadian pharmaceutical marketplace. Any changes to the PMPRB's basket of comparator countries or other pricing methods, likewise, must be based on evidence, only made after a sound consultative process, and must include reasonable transitional measures to avoid or minimize disruptions to existing business arrangements.

The PMPRB is also required to report to the Federal Minister of Health on pharmaceutical trends and on R&D spending by pharmaceutical patentees. Due to the antiquated 1987 tax law formula used to measure R&D spending included in its governing regulations, PMPRB has consistently and systematically under-reported the R&D levels of innovative pharmaceutical companies operating in Canada for many years, underestimating the industry's contribution to private sector R&D spending and lessening the government's willingness to address the myriad issues described above. To the extent that PMPRB should have a mandate to report on R&D spending in Canada, PhRMA members urge the U.S. Government to encourage the Government of Canada to update the regulatory R&D definition in order that the PMPRB can more accurately calculate the significant R&D contributions made by pharmaceutical patentees to the Canadian knowledge-based economy.

Weak Patent Enforcement

In 1993, the PM(NOC) Regulations were promulgated for the stated purpose of preventing the infringement of patents by the premature market entry of generic drugs as a result of the "early working" exception. In 2015, the Canadian government helped resolve significant difficulties related to inappropriate court decisions that prevented the listing of patents relevant to combination inventions, which seriously undermined patent enforcement actions relevant to those inventions. However, serious and systemic deficiencies remain with the PM(NOC) Regulations. The regulations do not reliably provide "expeditious remedies to prevent infringements and remedies which constitute a deterrent to further infringements," as required under the TRIPS Agreement and NAFTA. For example:

1. Proceedings under the PM(NOC) Regulations and appeal rights

The negotiated CETA text stipulates that "patent linkage" systems must provide all litigants with "equivalent and effective rights of appeal." The intention behind this negotiated outcome was to address the asymmetry in legal rights that flowed from Canada's previous restrictive PM(NOC) Regulations regime under which a patent owner did not have an equal ROA as that afforded to a generic drug producer. CETA simply

required Canada to correct this imbalance. The changes to the PM(NOC) Regulations,[135] however, have proven to be far more extensive than necessary to comply with Canada's CETA obligations in a manner that prejudices existing innovator rights.

For example, despite adopting significantly more procedural complexity under the new regime, including full pleadings, discovery and trials in order to make final patent determinations in a single proceeding, Canada has maintained the same 24-month statutory stay that governed the old summary system. Given that 90% of patent infringement/invalidity actions in Canada in recent years have taken over two years to be determined, the innovative industry is concerned that patentees will now be forced to choose between the surrender of procedural rights and obtaining any kind of meaningful injunction under the new regime, contrary to Canada's many other related international obligations to protect intellectual property rights.

2. Limitation on Listing of Valid Patents and Inequitable Listing Requirements

Patent owners continue to be prevented from listing their patents on the Patent Register established under the PM(NOC) Regulations if the patents do not meet certain arbitrary timing requirements that are not present in the United States under the Hatch-Waxman Act. The effect of these rules is to deny innovative pharmaceutical companies access to enforcement procedures in the context of early working for any patent not meeting these arbitrary listing requirements.

3. Excessive Level of Liability for Lost Generic Profits

The PM(NOC) Regulations allow an innovator to seek an order preventing a generic manufacturer from obtaining Notice of Compliance, on the basis that the innovator's patent covers the product and is valid. When the innovator seeks such an order, but is ultimately unsuccessful, Section 8 provides the generic manufacturer the right to claim damages in the form of lost profits for the period of time they could have been selling the product, but for the innovator's action.

PhRMA members are concerned that Canadian courts have taken an approach to Section 8 damages that allows for excessive damages. Subsection 8(1) compensates for all losses actually suffered in the period during which the second person/company was held off the market – a provision that, as currently interpreted by the courts, has led to instances of overcompensation. The Courts have granted damages in excess of 100% of the total generic market, despite holdings that the provision is meant to be compensatory

[135] Regulations Amending the Patented Medicines (Notice of Compliance) Regulations, 2017, available at http://www.gazette.gc.ca/rp-pr/p2/2017/2017-09-07-x1/html/sor-dors166-eng.php (last visited Feb. 7, 2019).

and not punitive in nature. Such overcompensation is contrary to the law of damages and reflects a punitive as opposed to a compensatory theory of damages.[136, 137]

Recent CETA implementing regulations established new rules that further expose innovators to excessive liability under Section 8. The amended PM(NOC) regulations eliminate previous language specifying that the period during which the innovator is liable to the competitor for any losses suffered ends on the date the stay is withdrawn or discontinued by the innovator or is dismissed or reversed by the court. This unwarranted change is likely to result in excessive damages awards by enabling competitors to claim indefinite future loses and to seek compensation for production "ramp-up" costs they may have incurred before the stay was granted and after it was lifted. In addition, innovators are now "jointly and severally" liable for any damages. Expanding the scope of liability in this manner will enable competitors to claim damages from local subsidiaries or licensees, as well as their licensors or corporate partners in the United States.

Also in the area of excessive damage liability, PhRMA members are concerned about ongoing litigation under various common law theories within the provincial courts. In spite of Canadian PM(NOC) regulations governing compensatory damages for generic companies held off the market due to patent litigation, other proceedings have been allowed to proceed under various common law theories (Statute of Monopolies, Trademarks Act, unjust enrichment and others). These cases could result in damages liability for PhRMA members which exceeds the compensatory threshold.

Therefore, PhRMA members request that the U.S. Government urge Canada to implement amendments to the PM(NOC) Regulations to address this issue.

Inadequate Patent Term Restoration

Patent Term Restoration (PTR) seeks to compensate for a portion of the crucial effective patent life lost due to clinical trials and the regulatory approval process. Most of Canada's major trading partners, including the United States, the European Union and

[136] The Supreme Court of Canada granted leave with respect to a Section 8 damages case, but in April 2015 dismissed this case from the bench, stating that it did so substantially for the reasons of the majority in the Federal Court of Appeal. *Sanofi-Aventis, et al. v. Apotex Inc., et al.*, SCC. 35886, available at http://www.scc-csc.gc.ca/case-dossier/info/dock-regi-eng.aspx?cas=35886 (last visited Feb. 7, 2019). The dismissal of the appeal provided parties to Section 8 damages litigation with no meaningful higher court guidance with respect to how these damages are to be calculated in future lower court decisions, which means any clarity must come from regulatory amendments by the Government of Canada.

[137] On April 23, 2018, Eli Lilly Canada (Lilly) applied to the Supreme Court of Canada for leave to appeal in respect of a March 2018 decision of the Federal Court of Appeal. The Federal Court of Appeal had dismissed Lilly's appeal of a trial decision awarding more than $70 million to Teva Canada (Teva) under Section 8. The Federal Court of Appeal granted Teva's cross-appeal seeking to add to its recovery lost pipefill sales and an adjustment to account for an under-reporting of sales in the data relied on by both parties' experts: *Eli Lilly Canada Inc v Teva Canada Limited*, 2018 FCA 53, available at https://decisions.fct-cf.gc.ca/fca-caf/decisions/en/307557/1/document.do (last visited Feb. 7, 2019). Lilly was denied leave by the Supreme Court of Canada on November 8, 2018.

Japan, offer forms of PTR which generally allow patent holders to recoup a valuable portion of a patent term where time spent in clinical development and the regulatory approval process has kept the patentee off the market. In these countries, up to five years of lost time can be recouped.

By way of implementing CETA, Canada has made a potentially significant step to provide innovators with some compensation for delays in obtaining marketing approval for pharmaceuticals. Under CETA, Canada agreed to implement a "*sui generis* protection" period of between 2 to 5 years for pharmaceuticals to compensate for delays in drug marketing approval, subject to certain specified conditions.

However, PhRMA has concerns with Canada's implementation of this commitment under the new *Certificate of Supplemental Protection Regulations (CSP) Regulations.*[138] At a fundamental level, the *sui generis* protection provided by the CSP does not appear to grant the full patent protections that PTR is intended to provide, and instead appears to be implemented subject an exception for "manufacture for export." While this is permitted by the CETA text, this is not consistent with PTR in other jurisdictions and appears to be inconsistent with the text of U.S. free trade agreements.[139] Such an implementation of PTR that does not confer full patent rights, *e.g.*, that would provide an exception for "manufacturing for export" or other infringing activities, is not consistent with the fundamental purpose of restoring patent term lost due to marketing approval delays and should be avoided.

Moreover, having only adopted the minimum term of patent term restoration negotiated under CETA (*i.e.*, Canada's term is capped at two years of a possible five), Canada's further adoption of restrictive time limits and eligibility criteria will unduly and unreasonably limit CSP eligibility in Canada in a manner that is contrary to the intent of the negotiation and the CETA text itself.

In particular, the *CSP Regulations* introduce a new and complex CSP application requirement whereby only those Canadian NDSs filed within 1 year of any first international drug submission filed for the same drug (in any of EU, US, Australia, Switzerland or Japan) will be CSP eligible (the "Timely Submission Requirement"). The Timely Submission Requirement is a novel requirement in Canada that is unprecedented amongst the patent term restoration regimes of Canada's major trading partners, including the United States. PhRMA is concerned that the 1-year time limit being enforced under the Timely Submission Requirement will inappropriately bar otherwise deserving and eligible innovative medicines from benefiting from the period of *sui generis* protection.

Moreover, Canada's new PTR regime requires that CSP-eligible medicinal ingredients be "first" approvals. Unlike other jurisdictions, Canada has further

[138] Available at http://www.gazette.gc.ca/rp-pr/p2/2017/2017-09-07-x1/html/sor-dors165-eng.php (last visited Feb. 7, 2018).

[139] *See* Solovy, E., "A Manufacturing-for-Export Exception to Patent Protection: A Proposal for Exporting Violations of the TRIPS Agreement and Beyond," Journal of IP Law and Practice (Sep. 2017).

implemented a list of "variations" of medicinal ingredients and other prior drug approvals that will automatically exclude new drug submissions from possible CSP eligibility. Neither the U.S. nor EU patent term extension regimes provide enumerated lists of excluded variations ineligible for CSP.

PhRMA members urge the U.S. Government to engage with the Government of Canada on this issue in all available fora, and encourage Canada to join the ranks of other industrialized countries who are champions of IP protection internationally and to provide for effective and competitive PTR measures in Canada. CSP eligibility should not be circumscribed by overly restrictive enumerated exclusions on medicinal ingredients and patents.

Standard for the Disclosure of Confidential Business Information

PhRMA members are concerned with amendments to the Food and Drugs Act,[140] which could allow for an unprecedented disclosure of CBI contained in clinical trial and other data submitted by pharmaceutical companies to Health Canada in the course of seeking regulatory approval for medicines. The amendments could significantly impact incentives for drug innovation and are inconsistent with Canada's international treaty obligations.

There is particular concern surrounding issues of confidentiality, the broad definition of CBI (broad enough to also cover trade secrets), and the threshold for the disclosure of CBI by Health Canada to governments and officials, as well as to the public. These amendments are inconsistent with the standards set out in other Canadian federal health and safety legislation, are inconsistent with Canada's treaty obligations under NAFTA and TRIPS, and are also inconsistent with the standards and practices of other national health regulators, including the FDA.

Both NAFTA and the TRIPS Agreement require that CBI be protected against disclosure except where necessary to protect the public. For disclosure to the public, the amendments require a "serious risk," but it does not reach the standard set out in the treaty language since subjective and discretionary language has been included: the Minister may disclose CBI "if the Minister believes that the product may present a serious risk of injury to human health." (Emphasis added.) In other words, it is not necessary that there be a serious risk of injury to justify the disclosure; rather the amendments merely require that the Minister believes the disclosure to be necessary.

The amendments also state that the Minister may disclose CBI to a person who "carries out functions relating to the protection or promotion of human health or safety of the public" and this can be done "if the purpose of the disclosure is related to the protection or promotion of health or safety of the public." There is no necessity

[140] *See* http://www.parl.gc.ca/HousePublications/Publication.aspx?Language=E&Mode=1&DocId=6676418&File=4 (last visited Feb. 7, 2019).

requirement for the disclosure to occur, only that it be related to protecting or promoting health. NAFTA and TRIPS do not refer to disclosure for the promotion of health, but rather to disclosure needed to protect the health of the public.

Finally, the amendments provide inadequate protections to ensure that there is no unfair commercial use of the disclosed CBI as required by TRIPS Article 39.3. The potential recipients of the disclosed CBI are very broad, and there is no mechanism, such as a confidentiality agreement, to ensure that those recipients (or anyone else to whom they disclose that data) are not able to use the divulged CBI to secure an unfair commercial advantage.

In July 2015, a final guidance document was issued by Health Canada with respect to the administration of its powers to require and disclose CBI.[141] PhRMA and its member companies are pleased that the document provides some reassurances with respect to the administration of Health Canada's new powers under the amended Food and Drugs Act. However, the document is a non-binding guidance as opposed to binding law or regulations.

In September 2015, a pharmaceutical company was subjected to a disclosure by Health Canada of CBI related to its pharmaceutical product, representing the first known usage of the new legislative disclosure powers. Following a request made under the new mechanisms in the *Food and Drugs Act*, approximately 35,000 pages of raw trial data were released, demonstrating the potential prejudice to U.S. innovative biopharmaceutical companies that could result from future CBI disclosures.[142]

More recently, in December 2017, Health Canada released a draft regulatory package that would amend the Food and Drug Regulations (Regulations) and facilitate automatic public access to manufacturer submitted clinical information following the issuance of a final Health Canada regulatory decision.[143]

The proposed amendments to the Regulations specify the scope of clinical information in drug submissions that would cease to be CBI following the issuance of a

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[141] *See* Amendments to the Food and Drugs Act: Guide to New Authorities (power to require and disclose information, power to order a label change and power to order a recall), available at http://www.hc-sc.gc.ca/dhp-mps/legislation/unsafedrugs-droguesdangereuses-amendments-modifications-eng.php (last visited Feb. 7, 2019).

[142] *See* selected media reports on the CBI disclosure: David Bruser and Jesse McLean, "Health Canada Hands Over Documents But Muzzles Doctor," *Toronto Star* (Oct. 14, 2016), available at https://www.thestar.com/news/canada/2015/10/14/health-canada-hands-over-documents-but-muzzles-doctor.html (last visited Feb. 7, 2019); Anne Kingston, "Health Canada OKs research into popular morning-sickness drug" *Macleans* (Nov. 23, 2015), available at http://www.macleans.ca/society/health/health-canada-oks-research-into-popular-morning-sickness-drug/ (last visited Feb. 7, 2019).

[143] Canada Gazette, Part I, Regulations Amending the Food and Drug Regulations (Public Release of Clinical Information), Vol. 151, No. 49, December 9, 2017, available at http://gazette.gc.ca/rp-pr/p1/2017/2017-12-09/html/reg3-eng.html (last visited Feb. 7, 2019).

final regulatory decision (Notice of Compliance, Notices of Non-Compliance – Withdrawal, or Notice of Deficiency – Withdrawal). The amendments would authorize the Minister to release information that has ceased to be CBI to the public without notifying or receiving consent from the originator. Clinical information provided in drug submissions would continue to be treated as confidential during the regulatory review process. In addition, the proposed amendments would apply to drugs for human use and medical devices, and would apply to clinical information in drug submissions filed with Health Canada both before and after the coming into force of the Regulations. The intention appears to be to include previously submitted information, even from years or decades prior, within the scope of automatic public disclosure.

Health Canada has not yet released final amendments to the Regulations, but has consulted on draft guidelines to implement the proposed regulatory changes.

Further complicating matters, on July 9, 2018, the Federal Court of Canada issued a decision ordering Health Canada to release vast amounts of pharmaceutical clinical trial data on five medications, undercutting the federal government's attempts to keep the information confidential.[144] The effect of this decision, which Health Canada chose not to appeal, on the Regulations and/or the guidelines document is unknown at present, but it presents the risk that the scope of clinical information susceptible to public release will be made even broader than under the current regulatory and guidance document proposals.

PhRMA members therefore urge the U.S. Government to press the Government of Canada to ensure that regulations to implement these amendments to the Food and Drugs Act are consistent with Canada's international treaty obligations.

Market Access Barriers

Regulatory Barriers to Patient Access to New Medicines

Beyond the Health Canada safety approval process, there are additional time-consuming market access hurdles that significantly delay Canadian patients' ability to access new medicines and vaccines. These include the PMPRB review, health technology assessments, price negotiations through the pan-Canadian Pharmaceutical Alliance (pCPA), and, finally, the negotiation of product listing agreements with individual public drug plans.

Most recent (2016) data indicates that it takes an average of 449 days after Health Canada approval before a patient can access a new medicine through a Canadian public drug plan.[145] This delays access to the benefits of new medicines and vaccines for Canadian citizens, and also erodes the already limited time that innovative companies

[144] *Doshi v. Canada (Attorney General)*, 2018 FC 710.

[145] Canadians Facing Delayed Access to New, Innovative Medicines: Report (May 24, 2016), available at http://innovativemedicines.ca/canadians-facing-delayed-access-to-new-innovative-medicines-report/ (last visited Feb. 7, 2019).

have to recoup their significant investments in R&D, clinical trials and regulatory approval processes. PhRMA and its members urge the U.S. Government to engage with the Government of Canada on these growing delays that are hindering patient access to new medicines.

JAPAN

Over the past decade, Japan has made important reforms in the areas of drug pricing, drug evaluation and approval, and vaccine policy that have made the system more transparent, more supportive of innovation, and more conducive to innovative biomedical research and development. These changes have increased patient access to life-saving medicines and reduced regulatory delays in the introduction of new drugs, making Japan the second largest market in the world for innovative medicines.[146] However, over the past two years, the Japanese government has pursued, and the Central Social Insurance Medical Council (Chuikyo) has approved a number of new pricing efforts that significantly undermine Japan's pro-innovation environment and its efforts to carry its fair share of the costs of global R&D efforts. Further, these reforms to the system are being developed with limited meaningful opportunities for stakeholders to provide timely input which has raised serious questions about the fairness, transparency and predictability of the reform process.

Key Issues of Concern:

- **Inappropriate and Discriminatory Revisions to the Price Maintenance Premium System**: The new drug pricing package announced in December 2017, included several new pricing policies that run counter to the government's pledge to fuel innovation in Japan and efforts to appropriately value innovation. PhRMA member companies are concerned that the number of innovative products that qualify for the PMP have been reduced dramatically and fewer PhRMA member companies qualify for the full benefit of the PMP under the new company requirements for the PMP. According to the Ministry of Health, Labor and Welfare (MHLW), approximately 30 percent of patented medicines no longer qualify.[147] This move is severely and inappropriately undervaluing U.S. intellectual property. Further, the PMP eligibility criteria appear to be inherently biased towards domestic companies and seriously call into question Japan's commitment to fair and non-discriminatory policies.

- **Health Technology Assessment**: The Japanese government plans to implement a new Health Technology Assessment (HTA) system in April 2019. In 2018, the Japanese government cut the prices of several leading innovative products that were subject to an ongoing cost-effectiveness assessment pilot program. For these products, the price premium granted at launch was reduced based on an arbitrary cost-effectiveness threshold of 5 million yen per quality-adjusted life year, ignoring many other elements of a product's value. Given the challenges experienced during the pilot program, the Japanese government decided to re-review the outcome of the pilot program for several products. In January 2019, the Japanese government announced its proposed new HTA system which is broader

[146] IQVIA MIDAS™, 2017.

[147] Ministry of Health, Labor and Welfare, Official Notification, Mar. 5, 2018.

in scope than originally proposed, has discriminatory elements that clearly target foreign firms for additional price cuts, and is out of line with international norms and best practices. Further, the system has been developed without meaningful opportunities for interested stakeholders, including the innovative industry, to provide input. PhRMA remains very concerned about the current direction of the new HTA system in Japan and its potential to significantly undervalue U.S. innovation and ultimately harm patient access to new medicines.

- **Other Concerning Government Pricing Reforms**: Other changes to the pricing rules such as "huge seller repricing" and "optimal use guidelines" that have been imposed suddenly and without meaningful stakeholder involvement by the Japanese government reduce the predictability and transparency of the drug pricing system in Japan and threaten to undervalue U.S. products.

- **Lack of Predictability in the Japanese Marketplace**: Another issue of serious concern is the stated intention by the Japanese government to move from the current biennial price revision system to an annual revision system. Furthermore, the Japanese government has indicated that it plans to develop and implement by early 2019 a new Health Technology Assessment (HTA) system for the sole purpose of repricing patented medicines. These lingering elements of the reform that remain undecided continue to make the Japanese market highly unpredictable and make planning for the future for companies extremely difficult.

- **Reform Initiative Continues to Lack Transparency**: As the Japanese government developed its detailed plans to carry out the drug pricing reform initiative over the last two years, there were few formal attempts by the decision-making bodies to seek input from stakeholders, including the innovative pharmaceutical industry. For example, despite the key policy issues being debated by the government throughout 2018, the industry was only invited to testify in front of the Chuikyo on three occasions. Details on the topics for discussion at important meetings of the Chuikyo are not always shared with stakeholders in advance. Further, except for the formal hearings at which industry was invited to testify, industry representatives were only able to attend Chuikyo meetings as observers. Aside from the limited opportunities to testify before the Chuikyo, discussions this year on a possible move to annual repricing for innovative products, starting with an *ad hoc* price cut to be implemented in 2019 in conjunction with the planned consumption tax increase and implementation of a new HTA system continued to be conducted largely behind closed doors. Moving forward, PhRMA's member companies request more regular and meaningful opportunities to provide input regarding the development of further reforms to Japan's government pricing and reimbursement system.

- **Regulatory Policies**: The Japanese Government continues to seek to accelerate and expand drug development in Japan, ensure that patients have prompt access to the newest drugs, and support the pharmaceutical industry as a key driver of

economic growth in Japan. To achieve these goals, further flexible approaches are needed in the approval and regulatory process to promote simultaneous global development, including Japanese sample size for multi-regional clinical trials and long-term clinical studies, and to increase the number of drugs designated and approved early under the Sakigake designation and conditional early approval systems so they are equivalent to similar systems in the U.S. and EU.

- **Vaccines**: In order to ensure that Japanese citizens have access to the world's newest and most innovative vaccines, Japan needs to execute the National Vaccine Plan and to develop a system that provides for permanent and full funding of all recommended vaccines, transparency in the evaluation and adoption of new vaccines into the recommended (*i.e.*, funded) vaccination schedule, and a science-based process to determine the benefits of vaccines and to manage adverse events.

- **Patent Term Restoration**: PhRMA members appreciate Japan's patent term restoration laws, as they provide term extensions for subsequent marketing approvals for additional indications or medical uses, or modifications of previously approved products. The Japanese law acknowledges the value that additional approvals can provide to patients. However, the laws as currently interpreted by the Japanese Patent Office (JPO) often result in extensions for subsequent marketing approvals which are shorter in term than the extensions for the original approval, and can thus act as a disincentive to conduct research on additional medical uses and indications for an approved product.

For these reasons, PhRMA requests that Japan be designated a **Priority Foreign Country** in the 2019 Special 301 Report, and that the U.S. Government continue to work on an immediate basis to ensure that the problems described herein are quickly and effectively resolved in all available fora, including as part of the recently initiated trade agreement negotiations.

Market Access Barriers

<u>Pharmaceutical Pricing and Reimbursement</u>

1. Price Maintenance Premium

The introduction of the PMP in 2010 as a two-year pilot project (followed by its renewal in 2012, 2014 and 2016), has been a critical factor in promoting innovation in Japan, eliminating the drug lag, ensuring that Japanese patients have timely access to innovative medicines, and ensuring that U.S. and other innovative products were appropriately valued. This system has demonstrably led to increased R&D and applications and approvals for new drugs and indications, even though the net benefit of the price maintenance premium has been somewhat reduced by the 80% ceiling on the premium under certain circumstances and the continued use of the market expansion and other re-pricing rules.

Investment in drug innovation is a long-term endeavor, such that any unpredictability in the PMP could lead to slower development of new drugs. Therefore, the top public policy priority of PhRMA's member companies over the years has been to advocate for the PMP to be made a permanent part of the government's pricing and reimbursement system without reducing the scope of products eligible for the premium.

However, under the government pricing reforms announced in December 2017, products eligible to receive the PMP are those that either: (1) received a price premium at launch or post-launch; (2) meet certain criteria for new mechanisms of action; (3) are second- or third-in-class and launched within three years of a comparator product in the above groups; (4) received an orphan designation or; (5) were developed in response to an open request from MHLW. In essence, this new system equates "innovativeness" with the speed and the order in which products launch. PhRMA is opposed to such a non-science-based evaluation of innovation, and notes that several U.S. global best-selling products have been deemed "non-innovative" under the new criteria and stripped of their PMP eligibility. This clearly demonstrates that the new system fails to appropriately value U.S. innovation.

Companies with products eligible to receive the PMP were ranked and sorted into three tiers based on: (1) the number of phase 2+ clinical trials conducted in Japan; (2) the number of new products launched in Japan within the past five years; (3) the number of new products developed in response to open requests from MHLW; and (4) the number of products with a Sakigake designation. The number of companies eligible for Tier 1 status was limited to "25% but not exceeding 30%, even if there are many companies with the same score." All of the eligible products from these companies were awarded the full premium. Eligible products marketed by the middle tier or bottom tier of companies were awarded 90% or 80% of the premium, respectively. PhRMA believes that limiting the number of companies eligible for the full PMP cannot be seen as a true test of innovativeness. Further, these criteria inappropriately favor larger companies, and specific elements of the PMP company eligibility criteria appear to be inherently biased towards domestic companies, seriously calling into question Japan's commitment to fair and non-discriminatory policies pursuant to its WTO obligations.

In addition to the failure to provide adequate meaningful opportunities for interested stakeholders, including the U.S. industry to provide input into the development of these policies, the Japanese government has also failed to publish clear rules on how some of the new policies are being implemented.

2. Health Technology Assessment

PhRMA agrees that appropriate HTA systems have the potential to assist governments in making informed decisions about allocating resources. However, deficient HTA processes can run counter to their key objectives and risk denying or delaying patients' appropriate access to medical technologies, inefficiently allocating resources, constraining clinical freedom, and harming innovation through pure cost containment methods.

The Japanese government plans to implement a new Health Technology Assessment (HTA) system in April 2019. In 2018, the Japanese government cut the prices of several leading innovative products that were subject to an ongoing cost-effectiveness assessment pilot program. For these products, the price premium granted at launch was reduced based on an arbitrary cost-effectiveness threshold of 5 million yen per quality-adjusted life year, ignoring many other elements of a product's value. Given the challenges experienced during the pilot program, the Japanese government decided to re-review the outcome of the pilot program for several products.

In January 2019, the Japanese government announced its proposed new HTA system which is broader in scope than originally proposed, has discriminatory elements that clearly target foreign firms for additional price cuts, and is out of line with international norms and best practices. Further, the system has been developed without meaningful opportunities for interested stakeholders, including the innovative industry, to provide input. PhRMA remains very concerned about the current direction of the new HTA system in Japan and its potential to significantly undervalue U.S. innovation and ultimately harm patient access to new medicines.

Other Government Pricing Policies of Concern

Other changes to the pricing rules such as "huge seller repricing" and "optimal use guidelines" that have been imposed suddenly and without meaningful stakeholder involvement by the Japanese government reduce the predictability and transparency of the drug pricing system in Japan and threaten to undervalue U.S. products. Reform of the pricing system should be done via a fully fair and transparent system and should avoid reactive short-term, *ad hoc* re-pricing mechanisms that fail to appropriately value innovation. The huge seller repricing program should be revisited and the effect of optimal use guidelines on the health insurance system should be strictly limited so that patients' early access to innovative medicines is ensured.

The industry also recommends that other unfair or unreasonable rules in Japan's drug pricing and reimbursement system be corrected as follows:

1. *Limit Scope of the Repricing for Market Expansion Rule (including huge seller repricing)*: The repricing for market expansion rule was introduced decades ago to address significant market changes since the initial drug price was established. As such, it should be limited to products of which the preconditions on initial pricing have clearly changed and that have considerable fiscal impact. To the extent that it has deviated from this intent, the modality of repricing for market expansion, including huge seller repricing, should be revisited.

2. *Apply Innovation and Usefulness Premiums*: Under the comparator pricing method of new drugs, certain premiums may be granted where the drug shows greater innovation or usefulness than its comparator. PhRMA welcomes recent increases in the range of allowable premiums. However, as it is being applied, most new drugs eligible for the price premium still receive no, or relatively low, premiums.

PhRMA's members continue to support full use of the sliding scale in the application of premiums.

3. *Relax the 14-day Limit Rule for New Drug Prescriptions*: Prescriptions for newly approved drugs can only be written for a 14-day supply during the first year after approval. This restriction imposes a physical and financial burden on patients who are forced to visit their doctors twice a month for the first year simply to receive a prescription. It also imposes a burden on overworked doctors who have to see a patient as many as 26 times during this first year simply to renew a prescription.

Lack of Predictability in the Japanese Marketplace

Another issue of serious concern is the stated intention by the Japanese government to move from the current biennial price revision system to an annual revision system. In December 2017, the government postponed a decision on the criteria to be used to determine those products subject to annual price revisions. While the Japanese government has stated that the first annual repricing under the new system will take place in 2021, it has already announced that on top of the regular biennial price revisions in 2018 and 2020, there will be a price revision in 2019 linked to the planned increase of the consumption tax in 2019 This is of serious concern to the innovative pharmaceutical industry. PhRMA and its members believe that the current system should be maintained, and that if annual price revisions need to be conducted, products subject to revisions in off-years should be limited to those with a significant price discrepancy rate between the NHI price and the current market price.

Pharmaceutical Regulatory Reform and Related Issues

1. Simultaneous Global Development of Drugs

PhRMA welcomes the government's continued support of simultaneous global development and efforts to promote multiregional clinical trials (MRCT) in order to eliminate the drug lag and expedite the availability of life-saving and life-enhancing drugs to patients. Therefore:

- PhRMA encourages the government to increase its global and regional regulatory harmonization efforts, especially to include the reduction of market-specific requirements that can delay simultaneous global development. In particular, PhRMA hopes the MHLW and Pharmaceuticals and Medical Devices Agency (PMDA) will be increasingly flexible in the approval and regulatory process for promoting simultaneous global development, including Japanese sample size for multi-regional clinical trials and long-term clinical studies.

- PhRMA encourages harmonization of the following CMC data points:

    - Requirement to provide detailed description in the application form about manufacturing and manufacturing control;

- Bio-equivalency (BE) data requirements for drug products under development, including adherence to ICH M9 guidelines; and

- CMC data requirements for biological products.

- The industry appreciates the continuing efforts of the PMDA to report metrics on the number of simultaneous global development protocols and consultations. The commitment of PMDA to transition to using the 80 percent level rather than the median in reporting progress is a welcome development.

- PhRMA encourages PMDA to continue to ensure consistency across its review offices as they consider drug development strategies based upon the scientific aspects of each drug.

- The threat of drug-resistant pathogens to antibacterial drugs is becoming a worldwide issue. In the U.S., the Generating Antibiotic Incentives Now (GAIN) Act is being implemented to provide incentives such as an exclusivity period and fast track approval for new drugs against drug-resistant pathogens. The gap in drug development in this area between the U.S. and Japan may lead to a future drug lag in this area. PhRMA encourages the Japanese government to consider measures to promote drug development for Antimicrobial Resistance (AMR), and stands ready to cooperate to accelerate drug development in this area in support of the G7 Health Ministers' declaration on AMR.

2. Improved Efficiencies at PMDA

PhRMA appreciates and applauds the significant efforts made by PMDA to meet its review performance goals for standard and priority files, as well as its efforts to meet the demands for consultations in an expeditious manner. PhRMA values its participation in PMDA's Expert Working Groups on consultations and review practices. PhRMA looks forward to continuing its active participation in these groups and hopes that its participation will lead to the development and implementation of concrete process improvements that will aid PMDA in continuing to meet its performance goals.

3. Revision of Post-Approval Change Process and Reduction in Review Times

PhRMA appreciates the opportunity to discuss Japan's post-approval changes to manufacturing and control processes and will continue to provide constructive recommendations based on global best practices for revising the system so that it is more aligned with those systems used by other major regulatory agencies. PhRMA further appreciates the efforts to reduce the review times of partial change applications and encourages PMDA to include biologic products, especially those arising from recombinant technology, in those review targets.

4. Risk Management Plan (RMP)

Reform of the safety system and risk management is an important undertaking by the government, and PhRMA has supported the government's preparation and implementation of its Risk Management Plan. The RMP went into effect on April 1, 2013. Global standardization of risk minimization measures is critical. PhRMA looks forward to continuing to engage collaboratively with academia and regulatory authorities on the implementation of this process.

5. AMED – the Japan Agency for Medical Research and Development

PhRMA welcomes the creation of AMED in April 2015 as a new agency designed to enhance translational research, to support drug development from the laboratory through the clinical development process and into the marketplace, and to coordinate the national government's health care research and development budgets now assigned to different ministries without strategic coordination. PhRMA emphasizes the need to ensure that AMED's programs will be open to all pharmaceutical companies, whether Japanese or foreign-based.

6. Sakigake Program and Conditional Early Approval System

PhRMA welcomes the creation of the "Sakigake" program and the conditional early approval system which will encourage the early evaluation and approval of important new drugs. To avoid a drug lag for innovative products in Japan, PhRMA encourages the government to adopt a flexible approach to the acceptance requirements for applications in order to increase the number of drugs designated and approved early under the Sakigake designation and conditional early approval systems. This will ensure Japan's expedited approval pathways are equivalent to similar systems in the U.S. and EU. Further, the industry recommends that the Sakigake program be formally implemented from the current pilot phase as soon as possible and applauds the government's recent efforts to expand the program by increasing the number of reviewers.

Preventive Health Care and Vaccines

Prevention plays a critical role in protecting a population's health and well-being. However, more effective and efficient awareness initiatives aimed at the public should be undertaken. Vaccines are particularly important in reducing disease burden and medical expenses, as well as improving the quality of life. The past several years have seen some important changes, including a revision in 2013 of the Preventive Vaccination Law, implementation of National Vaccine Plan and adoption of six vaccines into the national immunization program (NIP). PhRMA applauds the government for these efforts, as well as for co-hosting six annual, high-level, important, and very successful Vaccine Policy Exchanges with the U.S. Department of Commerce, the U.S. Department of Health and Human Services, and the U.S. Centers for Disease Control and Prevention (CDC). However, outstanding issues continue to require attention:

- Although the revision of the Preventive Vaccination Law provided for full national funding for most recommended vaccines, including several foreign-origin vaccines, the changes did not apply to several other vaccines that are already approved. The value of vaccines should be recognized by a funding system and an NIP process that incentivize manufacturers to develop and bring new vaccines to Japan as quickly as possible, together with a nationwide program to educate citizens, and especially parents, about the importance of vaccinations.

- It is critical that decisions related to vaccines be based on science. This is especially important in any evaluation of adverse events and attendant actions.

- The current recommendation (and reimbursement) process is not transparent as it relates to the evaluation and adoption of new vaccines. As a result, vaccine manufacturers lack crucial information as to what data are necessary to receive a national recommendation and when the data should be presented.

- Furthermore, the vaccination decision-making process is unclear. While a Vaccination Policy Committee under MHLW exists, the timeline of a new vaccine's evaluation, the criteria by which it is evaluated, and the committee's ability to change vaccination policy, are not transparent.

- PhRMA welcomes the beginning of a National Vaccine Plan in Japan and the creation of a Japan version of the U.S. Advisory Committee on Immunization Practices (ACIP). PhRMA supports this and urges that the Committee on Immunizations be given the maximum possible responsibility and autonomy to make recommendations based on scientific evidence. A priority should be full execution of the National Vaccine Plan.

- Japan faces sporadic outbreaks due in part to shortage of available vaccines. The most recent example is rubella that started in the summer of 2018 and prompted the issuing of a warning for pregnant women traveling to Japan by foreign governments, including the CDC. Introduction of vaccines from outside Japan is one effective option in such circumstances, and in order to facilitate and accelerate this, there should be a more harmonized regulatory system, including modernization of various requirements such as Minimum Requirements for Biological Products (MRBP).

- Quality standards for vaccines and pre- and post-approval vaccine supply processes, including the current national testing requirement, should be streamlined and harmonized with global standards in order to supply innovative vaccines in a timely manner.

- While stable supply of vaccines is critical for immunization programs, disruptions can occur given that vaccines are biological products and the production processes are complex and take a long time. As such it is critical to establish

stockpile programs based on foreign best practices, to ensure reliable vaccine supplies during any disruptions.

Intellectual Property

Patent Term Restoration

Japan's patent term restoration system permits term extensions for subsequent approvals for a product, such as for a new use of a previously approved product. PhRMA members appreciate Japan's patent term restoration laws, as they acknowledge the value that additional approvals can provide to patients. However, PhRMA urges the JPO to review its practices in granting patent term restoration for subsequent approvals, to take into account the full regulatory review period in determining the length of any extensions. In particular, the current JPO practice, which provides an extension period based only on what is considered "necessary testing" for the subsequent approval, often results in extension periods for subsequent approvals that are shorter than the extension period of the first approval. As a result, the current practice can act as a disincentive to conduct research on additional medical uses and indications for an approved product.

KOREA

PhRMA and its member companies remain highly concerned with several intellectual property (IP) issues and market access in Korea. Korea's drug pricing policies severely devalue U.S. IP and favor Korea's own pharmaceutical industry at the expense of U.S. companies. As a result, America's cutting-edge R&D and manufacturing sectors are losing out. The upshot is fewer U.S. jobs, fewer U.S. exports, and fewer new medicines for patients worldwide. Korea's pricing practices are inconsistent with its commitments under the U.S.-Korea Free Trade Agreement (KORUS).

Recognizing these deficiencies, PhRMA and its member companies commended the U.S. Government for securing a commitment from Korea to amend its premium pricing policy for global innovative drugs to ensure non-discriminatory and fair treatment for U.S. pharmaceutical exports. While it was hoped that Korea would use this opportunity to demonstrate its broader pledge to appropriately value innovative medicines, Korea has implemented this commitment in a manner that eviscerates the ability of any company to qualify for premium pricing and is in contradiction with the spirit of their 2018 commitment. PhRMA stands ready to work with the U.S. and Korean Governments to secure amendments to Korea's pricing and reimbursement policies consistent with Korea's broader KORUS obligations.

Key Issues of Concern:

- **Impermissible government pricing and reimbursement policies**: On multiple levels, Korea's pricing practices contravene its KORUS commitments and negatively impact the rights of U.S. innovators. First, Korea restricts the prices of innovative medicines by valuing them according to the prices of older medicines. Given the vast amount of medical research that occurs in the United States, Korea seeks to benefit from this research without paying its fair share. This incredibly short-sighted approach, however, harms not just the U.S. industry but patients overall. It is also inconsistent with Korea's commitments under KORUS to value U.S. innovation appropriately, to ensure that patent owners can recognize economic return for its investments, and to guarantee market access free from price distortions. In addition, Korea's pricing policies are formulated without the degree of stakeholder input required by KORUS.

- **Patent term restoration**: As required by KORUS, Korean law provides for patent term restoration (PTR) to compensate for unreasonable delays in granting marketing approval for new medicines. However, Korean court decisions effectively undermined the purpose and value of PTR in Korea by impermissibly narrowing the subject matter eligible for PTR. By limiting the restoration only to the innovative product approved, rather than to the patented invention related to the product, the decisions would have allowed competitors to seek marketing approval for variations of the product during the restored period that would otherwise infringe the innovator's patent. In a positive development, the Supreme Court has reversed

those decisions and remanded the case for reconsideration. Given the number of other cases related to the provision of PTR in Korea, it will be important to continue to monitor these cases to ensure that PTR in Korea is provided in the manner anticipated by KORUS.

- **Patent enforcement concerns**: While Korea has implemented a patent linkage mechanism pursuant to its KORUS commitment, certain key issues of concern remain. These issues include the discretion afforded to the Ministry of Food and Drug Safety (MFDS) as to whether to list a patent in the Green List or to permit a change to the patent listing and the limited period of only nine months for a sales stay.

For these reasons, PhRMA requests that Korea be designated a **Priority Foreign Country** in the 2019 Special 301 Report, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protection and Pricing of Patented Pharmaceuticals

Discriminatory Pricing and Reimbursement Policies

Korea's current P&R system has its origins in a controversial, sweeping regulatory reform that took effect in December 2006. Under this reform, known as the Drug Expenditure Rationalization Plan (DERP), drug prices are determined in a two-step process based primarily on cost reduction rather than a holistic assessment of a drug's value. *First*, the Health Insurance Review & Assessment Service (HIRA), through its Drug Reimbursement Evaluation Committee (DREC), recommends drugs for listing on the basis of a "pharmaco-economic" or PE analysis, which takes into account clinical usefulness and cost-effectiveness. *Second*, the National Health Insurance Service (NHIS) makes pricing recommendations following negotiations with pharmaceutical manufacturers, using HIRA's price as a ceiling. The Ministry of Health and Welfare (MOHW) has the ultimate authority for approving all P&R decisions.

This two-step process inappropriately depresses the price of innovative medicines in several significant ways. First, HIRA's PE analysis recommends reimbursement prices for patented drugs by referencing comparator groups based on therapeutic class, which include off-patent and generic drugs. Off-patent and generic drugs are already subject to drastic price reduction measures in Korea. Linking prices of new patented drugs to prices of already heavily-discounted prices of off-patent and generic drugs results in unsustainably low prices for innovative drugs. In 2012 alone, existing off-patent and generic drugs experienced an average price reduction of 14%. During the period from 2011 to 2013, all existing off-patent and generic drugs saw an overall 20% price reduction. Second, after the HIRA process, the NHIS exploits its superior bargaining power as a single payer to secure an even lower negotiated price and volume cap from the manufacturer of the innovative medicine. These problems are exacerbated by Korea's failure to provide an independent mechanism to review these pricing determinations (as discussed above).

Over the last decade, the Korean Government has used other *ad hoc* measures to further reduce prices of patented drugs. Beginning in 2009, Price-Volume (PV) Agreements were negotiated and implemented under the theory that increased volume of drug consumption should improve efficiency and result in lower prices. Other aspects of Korea's pricing system have created incentives for larger hospitals to force pharmaceutical companies to supply drugs at lower prices. The direct result is that patented pharmaceuticals are subject to repetitive and excessive price decrease mechanisms.

The deleterious impact of DERP and other pricing measures on Korea's market for innovative medicines has been striking. One study found that during the 2007-2014 period, new drug prices in Korea were less than half of the average in Organization for Economic Co-operation and Development (OECD) countries.[148] The impact of price cuts is compounded because existing drug prices are then referenced in setting new drug prices. It is difficult for a new drug to be listed under the Korea's pharmaco-economic (PE) evaluation given the current comparator selection criteria, which inappropriately reference generics. In sum, while these policies have been driven by goals of cost-savings and cost-containment, the end result has been reduced access to innovative medicines for Korean patients and doctors.

Korea's numerous price controls constitute a failure to "appropriately recognize the value of the patented pharmaceutical product," in violation of KORUS Article 5.2(b). Korea's PE system inappropriately links patented drug prices to off-patent and generic drug prices. This unavoidably and automatically devalues patents and undermines incentives for innovation. These effects are amplified by a second round of price reductions following negotiations with NHIS – which, as a single payer, is necessarily driven by budget concerns – as well as *ad hoc* price cuts that further lower reference prices for new drugs. As a result of this two-step price reduction process, and other *ad hoc* price cuts, Korea is failing to recognize the value of patented drugs. In so doing, Korea's P&R system has severely restricted Korean patients' access to patented medicines – as demonstrated, for example, by the exceptionally low rate of rare disease drugs listed for reimbursement. This outcome is precisely what KORUS Article 5.2(b) seeks to prevent.

Moreover, Korea's P&R regime goes far beyond a "limited exception" to the patent holder's exclusive rights, and thus is inconsistent with KORUS Article 18.8(3) and Korea's broader TRIPS obligations. TRIPS Article 28 provides that a patent "shall confer" on its owner the exclusive rights to prevent third parties without the owner's consent from "the acts of: making, using, offering for sale, selling, or importing for these purposes that product."[149] In turn, TRIPS Article 30 permits WTO members to grant only "limited" exceptions to these exclusive rights, provided that such exceptions do not conflict with the "normal exploitation" of the patent and do not prejudice the legitimate interests of the

[148] EK Lee, "Price Comparison Among OECD Countries" (2014).

[149] TRIPS Article 28.

patent owner.[150] The *Canada—Pharmaceuticals* panel appropriately recognized that the "normal exploitation" of a patent includes the realization of anticipated "economic returns" during a defined period of exclusivity "as an inducement to innovation."[151] This TRIPS jurisprudence supports a parallel reading of KORUS Article 18.8(3).

These factors demonstrate the extent to which Korea's P&R measures have gone beyond their purported goal of reasonably controlling health care costs. As the U.S. Department of Commerce has noted, when countries rely on "government fiat rather than competition to set prices" for new drugs, their price controls "reduce company compensation to levels closer to direct production costs," and leave less revenue for research and development "that would provide substantial health benefits to all."[152] Korea's onerous and multiple layers of price cuts are depriving U.S. pharmaceutical manufacturers of the right to sell pharmaceutical products at prices that would permit recoupment of investments and are undermining the incentive to develop innovative products.

Of particular concern to industry was the 7.7 Pricing Policy, which favored Korean pharmaceutical patent holders by according price and other preferences to locally-developed new medicines, while withholding such benefits from imported innovative medicines. Recognizing that this policy was inconsistent with Korea's national treatment commitments under KORUS Article 5.2(a) and 18.1(6). The 7.7 Pricing Policy, the U.S. Government secured a hard-earned commitment from Korea to amend this policy to ensure non-discriminatory and fair treatment for U.S. pharmaceutical exports. Recognizing these deficiencies, PhRMA and its member companies commended the U.S. Government for securing a commitment from Korea to amend its premium pricing policy

[150] TRIPS Article 30.

[151] *Id.* ¶¶ 7.54-55. Similarly, the TRIPS Agreement negotiating history indicates that the "rights conferred" by a patent within the meaning of TRIPS Article 28 include the right to sell pharmaceutical products at prices that would permit recoupment of investments and provide an incentive to develop innovative products. In a 1987 statement, the United States set forth this view, stating that "price control" was not a legitimate reason to deny intellectual property protection or to "impose conditions that preclude reasonable compensation for use of an invention or creation." *See* Statement by the United States at Meeting of 25 March 1987, MTN.GNG/NG11/W/2 (Apr. 3, 1987), at 3. As the United States expressed at that time, "[s]uch policies interfere with obtaining and maintaining intellectual property rights and thus reinforce the direct distortion of trade that results from such policies." *Id.* Others involved in the TRIPS negotiations made similar statements. At a September 1989 meeting, a participant discussed providing patentees "the right to exclude others from making, using or selling the patent or invention for a specified time" and asserted that "[t]hese rights were necessary to provide patentees with the necessary economic incentive to justify investment in innovation." Negotiating Group on Trade-Related Aspects of Intellectual Property Rights, Meeting of the Negotiating Group of 12-14 July 1989: Note by the Secretariat, MTN.GNG/NG11/14 (Sept. 12, 1989), ¶ 75. In a previous meeting, another TRIPS negotiator noted that "the recovery of an investment [of a patented product] depended not only on the duration of patent[] rights[s] but also on a number of other factors, for example whether there was price control." Negotiating Group on Trade-Related Aspects of Intellectual Property Rights, Meeting of Negotiating Group of 16-19 May 1988: Note by the Secretariat, MTN/GNG/NG11/7 (June 21, 1988), ¶ 11.

[152] U.S. Department of Commerce, International Trade Administration, Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Consumers, Pricing, Research and Development and Innovation (Dec. 2004), at vii.

for global innovative drugs by the end of 2018 to ensure non-discriminatory and fair treatment for U.S. pharmaceutical exports. While it was hoped that Korea would use this opportunity to demonstrate its broader pledge to appropriately value innovative medicines, Korea has implemented this commitment in a manner that eviscerates the ability of any company to qualify for premium pricing and is contrary to the spirit of the commitment it made to the U.S. Government. PhRMA stands ready to work with the U.S. and Korean Governments to secure amendments to Korea's pricing and reimbursement policies consistent with Korea's broader KORUS obligations.

Patent Term Restoration

At the request of the patent owner, KORUS Article 18.8(6)(b) requires Korea to restore the term of a patent on a new medicine to compensate for unreasonable marketing approval delays. That Article specifies that any extension "shall confer all of the exclusive rights … of the patent claims." However, decisions by the Korean Intellectual Property Trial and Appeal Board[153] that were later affirmed by the Korean Patent Court[154] appeared to violate Korea's commitment to the United States by impermissibly limiting the extension only to the product actually approved for marketing, rather than to the patented invention related to the product. Left unchallenged, these decisions would have essentially rendered PTR in Korea meaningless.

In a positive development, on January 17, 2019, the Supreme Court reversed the lower Court decisions and remanded the case for reconsideration. Given the number of other cases related to the provision of PTR in Korea, it will be important to continue to monitor these cases to ensure that PTR in Korea is provided in the manner anticipated by KORUS.

Patent Enforcement

Consistent with its IP obligations under KORUS,[155] effective March 15, 2015, Korea implemented the framework of an effective patent enforcement system. Key issues that PhRMA continues to monitor include:

- The discretion afforded to MFDS to determine whether to list a patent in the Green List or to permit a change to the patent listing.

- Korean law only provides for a nine-month sales stay. It is unclear whether this will be an adequate period of time to resolve a patent dispute (consistent with Article 18.9(5)(b) of KORUS) before an infringing product is allowed to enter a market.

[153] *See* Intellectual Property Trial Appeal Board decisions in Case No. 2015Dang3931, rendered in September 2016 and Case No. 2016Dang547, rendered in October 2016.

[154] *See* Patent Court decision in Case Nos. 2016Heo8636 and 2016Heo9189 (consolidated), and Case No. 2016Na1929, all rendered in June 2017.

[155] *See* U.S.-Korea Free Trade Agreement, Art. 18.9, para. 5.

- The sales stay system under Korean law is problematic in that the patentee cannot request a sales stay against an infringing generic product unless a sales stay is also sought against non-infringing generic products.

Market Access Barriers

Lack of Transparency and Predictability in Government Policy-making

Since 2010, MOHW has repeatedly changed its pharmaceutical pricing and reimbursement policies without considering the long-term implications for innovation and market predictability, resulting in an uncertain business environment for innovative pharmaceutical companies in a manner that is inconsistent with Korea's transparency and due process obligations under KORUS.

Also, there are still repetitive and excessive price cut mechanisms working in the market after reimbursement listing, such as biannual ATP investigations, Price-Volume Agreements (PVAs), listing of first generic and expanding reimbursement scope with new indications or change of treatment guidelines.

Separately, the Risk Sharing Agreement (RSA) system should be expanded to provide an alternative pathway for reimbursement listing to enhance patient access to innovative medicines regardless of disease area and alternatives. The RSA is permitted only for rare diseases and anti-cancer products and is dependent on mandatory submission of pharmacoeconomic data not only at the time of initial agreement but for the renewal every three years. In order to provide greater predictability for pharmaceutical companies, companies should be able to negotiate fixed contract terms until all IP protections have expired.

Independent Review Mechanism (IRM)

Under Article 5.3(5)(e) of the U.S.-Korea Free Trade Agreement and the side letter thereto, Korea agreed to "make available an independent review process that may be invoked at the request of an applicant directly affected by a [pricing/reimbursement] recommendation or determination." Korea has taken the position, however, that reimbursed prices negotiated with pharmaceutical companies should not be subject to the IRM because the NHIS does not make "determinations" and merely negotiates the final price at which a company will be reimbursed. However, this interpretation completely negates the original purpose of the IRM, which should apply to the negotiation process for prices of all reimbursed drugs, particularly patented medicines.

MALAYSIA

PhRMA and its member companies operating in Malaysia are alarmed by recent Government of Malaysia actions which undermine intellectual property (IP) protection and, if unaddressed, could inspire other countries to take similarly damaging actions. Addressing serious IP and market access concerns in Malaysia will help narrow America's $22B trade deficit with Malaysia.

Key Issues of Concern:

- **Compulsory Licensing**: Through a flawed and non-transparent process, the Malaysian government issued an unjustified compulsory license (CL) for a breakthrough innovative medicine developed in America that provides a cure for patients suffering from hepatitis C. This action was taken despite the fact that the U.S. manufacturer was engaged at the time in ongoing negotiations with the Government of Malaysia on a voluntary license. If not met with a forceful U.S. Government response, this action carries significant risks of contagion to other markets, which would significantly undermine the current R&D model for innovative medicines on which the U.S. pharmaceutical industry and patients around the world rely.

- **Inadequate IP protection and enforcement**: Malaysia does not have an effective patent enforcement system that provides for the early resolution of patent disputes before marketing approval is granted to infringing follow-on products during the patent term. In addition, its regulatory data protection (RDP) system fails to provide (1) any protection for biologics; and (2) effective protection for a sufficient period of time for chemically synthesized drugs from the date of marketing approval in Malaysia.

- **Listing pharmaceuticals on the national formulary**: Effective 2016, Malaysia adopted a new process for listing products on the Ministry of Health (MOH) Medicines Formulary. While this is a welcome development, PhRMA and its members are concerned that the final guidelines require one year of post-marketing surveillance data prior to listing and that there is no mechanism to ensure that patients who benefited from the medicines during local clinical trials maintain access during this period. In addition, if a product is not approved for listing on the Formulary, the applicant should be provided a detailed explanation for that decision so that it can better understand the criteria for listing and to determine if it may negotiate an alternative access scheme with the government. MOH listing decisions, both by the body responsible for conducting Health Technology Assessment (HTA) analysis and making listing recommendations, and by the panel responsible for the ultimate listing decision currently lack transparency and appear to be based on ambiguous criteria.

- **Halal Pharmaceuticals**: In December 2017, the MOH published a guideline on prescribing and administration of non-halal pharmaceuticals. PhRMA's member companies are strongly supportive of religious and cultural sensitivities, but do not believe that the government should provide preferential treatment to such products in government procurement. Furthermore, it is important to ensure that patients, in partnership with their health care providers, are prescribed the appropriate medicine for their conditions.

- **Preferential treatment of local manufacturers**: The Government of Malaysia indirectly discourages an open and competitive marketplace for international pharmaceutical compounds through procurement preferences for locally manufactured products. For example, the Government of Malaysia has recently announced that it will grant three-year procurement contracts to companies who move production of imported products to Malaysia (with the potential for a two-year extension if those locally produced products are exported).

For these reasons, PhRMA requests that Malaysia be designated a **Priority Foreign Country** in the 2019 Special 301 Report, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protection

Compulsory Licensing

In September 2017, the Malaysian government utilized a non-transparent process to issue a CL on a patent-protected innovative U.S. medicine. This unnecessary and unjustified measure was taken in a unilateral and non-transparent fashion, even as the manufacturer was engaged in good faith negotiations with the government on a voluntary licensing regime. The CL has sent a devastating signal to America's biopharmaceutical innovators that their patents are not safe in Malaysia. If this action is not met by a strong response, the Government of Malaysia may use CLs on other innovative medicines, or inspire other countries to unilaterally determine that it is exempt from its obligations with respect to IP protections under well-established and binding international agreements.

While imposing a license is rarely, if ever, an appropriate mechanism to improve patient access, that is particularly true in this instance where the innovative company has already announced plans to voluntarily license the patent. The manufacturer in this instance was in the process of an in-depth negotiation for a mutually beneficial voluntary licensing scheme when the Government of Malaysia issued its decision on a compulsory path. Following the announcement of the CL, Malaysia continued negotiating with the manufacturer for a voluntary license for use throughout the country, and despite coming to an agreement on price with the manufacturer, moved forward with a CL for use in state-owned hospitals.

The non-transparent manner in which this decision was made raises serious questions around whether appropriate consideration was given as to how it may impact Malaysia's access to innovative medicines in the future. The sudden and unexpected announcement of a CL was made immediately following a meeting between President Donald Trump and then-Prime Minister Najib Razak, without any indication during the visit that such a provocative step would be taken. Furthermore, at no point prior to the announcement did the MOH or any other government ministry or agency offer to meet with relevant industry stakeholders, consider their concerns, or evaluate their input. This is surprising given the Government of Malaysia's historical support for open, transparent, and fair market practices. The sudden nature of this decision denies U.S. manufacturers any sense of predictability around Malaysia's regulatory decision-making in the future. The lack of industry stakeholder input is also troubling given the immediate significance of such a decision to the global market for medicines, and to the potential long-term ramifications for U.S. producers of innovative medicines and other cutting-edge inventions.

Regulatory Data Protection (RDP)

Biopharmaceutical innovators work with hospitals, universities and other partners to rigorously test potential new medicines and demonstrate they are safe and effective for patients who need them. Less than 12% of medicines that enter clinical trials ever result in approved treatments.[156]

To support the significant investment of time and resources needed to develop test data showing a potential new medicine is safe and effective, governments around the world protect that data submitted for regulatory approval from unfair commercial use for a period of time. TRIPS Article 39.3 requires WTO members, including Malaysia, to protect proprietary test data submitted to market authorizing bodies, including the MOH, "against unfair commercial use" and against "disclosure."

The stated objective of Malaysia's Directive (11) dlm. BPFK/PPP/01/03 Jilid 1 is "to protect the undisclosed, unpublished and non-public domain pharmaceutical test data … for the purpose of scientific assessment in consideration of the quality, safety, and efficacy of any new drug product...."[157]

Further, paragraph 4.2 of that Directive provides:

> An application for Data Exclusivity shall only be considered if the application in Malaysia for:

[156] DiMasi JA, Grabowski HG, Hansen RW; Tufts Center for the Study of Drug Development. Innovation in the pharmaceutical industry: new estimates of R&D costs. In: Briefing: Cost of Developing a New Drug, available at https://static1.squarespace.com/static/5a9eb0c8e2ccd1158288d8dc/t/5ac66afc6d2a732e83aae6bf/1522952963800/Tufts_CSDD_briefing_on_RD_cost_study_-_Nov_18%2C_2014..pdf (last visited Feb. 7, 2019).

[157] *See* paragraph 1.2 of Directive BPFK/PPP/01/037.

> (i) New drug product containing a New Chemical Entity is made within eighteen (18) months from the date the product is first registered or granted marketing authorization; AND granted Data Exclusivity / Test Data Protection in the country of origin or in any country, recognized and deemed appropriate by the Director of Pharmaceutical Services….[158]

As such, Malaysia requires the marketing authorization application of the new medicine to be filed within 18 months from the first worldwide regulatory approval in order to be considered as a "new chemical entity" and, thus, eligible for RDP in Malaysia. If the 18-month deadline is not met, the product loses data protection, allowing a follow-on molecule to be approved based on the originator's regulatory data during what should have been the RDP period. It is challenging – if not impossible – to meet the 18-month application requirement if the first worldwide registration was not in the EU or the United States (both are relied upon for the Certificate of Pharmaceutical Product application).

In addition to this inappropriate restriction on products eligible for RDP in Malaysia, the actual term of the protection in Malaysia is measured from the date of first approval in the world. Thus, if a new chemical entity is registered in Malaysia one year after first approval in the world, Malaysia only provides four years of RDP. Indeed, the only instance in which an innovator can receive the full five years of RDP in Malaysia is if they seek marketing approval in Malaysia first.

Malaysia's flawed Directive improperly penalizes innovators for first seeking marketing approval in other countries. As in other markets that seek to promote research and development into innovative medicines, Malaysia should measure the term of the RDP protection from the time that the new molecule is approved in Malaysia.

Finally, Malaysia fails to provide any RDP for biologics. Made from living organisms, biologics are complex and challenging to manufacture and may not be protected adequately by patents alone. Without the certainty of a substantial period of exclusivity, innovators may not have the incentives needed to conduct the expensive, risky and time-consuming work to discover and bring new biologics to market.

Effective Patent Enforcement

PhRMA members encourage Malaysia to efficiently and effectively enforce its Patent Act. A competent and practical enforcement mechanism provides redress and solutions to infringements of IP rights and deters future infringement. Timely and efficient patent enforcement gives owners an appropriate period over which to recoup the value of their significant efforts and investment. For example, patent protection and enforcement would be enhanced by structured enforcement guidelines and a mechanism to curb unfair promotion and sale of generic drugs either prior to patent expiry of innovator drugs, or, in the event of a patent dispute, prior to a court decision on patent disputes.

[158] *Id.*

PhRMA's member companies strongly encourage the improvement and adoption of mechanisms that strengthen patent enforcement and the ability to resolve outstanding patent concerns prior to marketing approval and launch of follow-on products, such as generics. These mechanisms could greatly enhance Malaysia's business environment by: (1) providing transparency and predictability to the process for both innovative and the generic pharmaceutical companies; (2) creating a more predictable environment for investment decisions; and (3) ensuring timely redress of genuine disputes.

Patent and Trademark Laws

Proposed amendments to Malaysia's patent and trademark laws that include provisions for disclosure of traditional knowledge and genetic resources, as well as compulsory licensing, raise concerns for the research-based pharmaceutical industry, and PhRMA encourages a continued consultative process with stakeholders before such amendments are implemented in order to avoid policies that deter or discourage innovation across fields of technology. These proposed amendments also include provisions for effective patent enforcement and patent term restoration. PhRMA member companies are eager to engage in meaningful dialogue with Malaysian Regulatory Authorities to build a system that reflects international best practices.

Market Access Barriers

Listing Pharmaceuticals on the National Formulary

Industry welcomes advances from the Malaysian Government for companies to directly request inclusion on the national formulary through guidelines introduced in January 2016. However, industry is disappointed that the process lacks transparency and appear to be based on ambiguous criteria. In addition, the final guidelines require one year of post-marketing surveillance data prior to listing. If local clinical trials have been completed for a product, it should be automatically listed on the national formulary to enable patients who were on the treatment to continue receiving the product after the clinical trial is complete. A policy is needed to bridge the gap for patients from the end of a clinical trial to the listing in the formulary.

Further, as the government pursues reforms aimed at improving access of medicines to its population, member companies hope that sufficient financing is provided to ensure that more patients can receive innovative medicines in as timely a manner as possible to achieve better health outcomes. We hope that short term measures, such as cost containment policies, do not become a barrier to access and the government considers fair mechanisms to value innovations that are proven to raise the standards of care in Malaysia.

Halal Pharmaceuticals

In December 2017, the MOH published a guideline on prescribing and administration of non-halal pharmaceuticals.[159] PhRMA's member companies are strongly supportive of religious and cultural sensitivities, but strongly believe that it is important to ensure that patients, in partnership with their health care providers, are prescribed the appropriate medicine for their conditions.

Preferential Treatment of Local Manufacturers

Malaysia's National Medicines Policy (MNMP/DUNas), which prioritizes the medium and long-term goals set by the Government for the pharmaceutical sector, endorses potential price controls, generic drugs substitution, and preferences for generics and local manufacturers by promoting national self-reliance for drugs listed on the National Essential Medicines List (NEML). PhRMA member companies submit that the Government of Malaysia should eliminate discriminatory preferences for locally manufactured pharmaceuticals. This preferential treatment discourages an open and competitive marketplace in Malaysia.

[159] Guideline on the Use of Medicines with Non-halal Ingredients, available at https://www.pharmacy.gov.my/v2/ms/dokumen/panduan-penggunaan-ubat-ubatan-mengandungi-unsur-tidak-halal.html (last visited Feb. 7, 2019).

SECTION 306 MONITORING

THE PEOPLE'S REPUBLIC OF CHINA

PhRMA and its member companies operating in the People's Republic of China are committed to supporting the government's efforts to build a patient-centered and pro-innovation health care system. China is taking very important and positive steps on regulatory framework and intellectual property (IP) protection, enforcement system as well as strengthening government reimbursement for innovative medicines. However, we remain concerned about the lack of effective regulatory data protection (RDP) and patent enforcement, inconsistent patent examination guidelines, the non-transparent and unpredictable government pricing and reimbursement policies, the lengthy regulatory approval process, burdensome biological sample exportation policies, areas of divergence from international registration standards, rampant counterfeiting of medicines, and under-regulated active pharmaceutical ingredients.

PhRMA is encouraged by China's ongoing work to strengthen its drug regulatory framework and IP protection and enforcement system, including through the proposed Patent Law amendments (January 2019), which includes language to provide patent term restoration (PTR) to compensate for a portion of the lengthy regulatory review process; draft National People's Congress (NPC) amendment to the Drug Administration Law (DAL) (November 2018), which includes a 60-day clinical trial application (CTA) approval process; the draft National Medical Products Administration (NMPA)[160] measure on the Implementation of Drug Clinical Trial Data Protection in April 2018; NMPA's issuance of Technical Guidelines for Acceptance of Overseas Drug Clinical Trial Data in July 2018; draft NMPA amendments to the Drug Administration Law (DAL) and Drug Registration Regulation (DRR) in October 2017; the Central Committee of the Communist Party / State Council Opinion (CCP/State Council Opinion) on Deepening the Reform of the Review and Approval System and Encouraging the Innovation of Drugs and Medical Devices issued in October 2017; and the draft NMPA Circulars (Nos. 52-55) issued in May 2017. NMPA's May 2017 accession to the International Council on Harmonization (ICH) and June 2018 accession to the ICH Management Committee further exemplifies China's reform efforts. In addition, we are encouraged by the 2017 update to the National Reimbursement Drug List (NRDL) as well as the recent addition of 17 oncology medicines to the NRDL in 2018. These proposals and reforms provide a critical opportunity to enhance patient access to innovative medicines and to address many of the following issues of concern.

PhRMA is eager to continue supporting China in this reform effort to strengthen RDP, patent enforcement and patent examination guidelines, and to accelerate and simplify the regulatory approval process. We are disappointed that the November 2018 NPC draft DAL amendment, as well as the draft Patent Law amendments (issued in

[160] In August 2018, the China Food and Drug Administration (CFDA) changed its name to the National Medical Products Administration (NMPA). Although many of the policies and draft proposals referenced in this submission were issued under the name of CFDA, we have used NMPA consistently throughout this document.

January 2019 for public comments), do not include provisions to advance these IP reforms. PhRMA strongly encourages China to move swiftly to implement proposed reforms in a manner that enables biopharmaceutical innovators both in China and abroad to meet the growing needs of China's patient population. In particular, we welcome the proposed RDP terms of six and 12 years for chemically synthesized drugs and biologics in the recent draft RDP measure, however, the proposed location- and time-based conditions and limitations placed on the terms for innovative drugs and biologics are not consistent with China's international commitments, are not practical, and could well undermine the very goals that are driving these proposed reforms. Moreover, there remains significant uncertainty regarding the scope of the data protected and the criteria for protected categories, and we are very troubled by the broad post-approval data disclosure requirements.

We also remain concerned that the 2017 draft DRR amendment undercuts the laudable goals of the CCP/State Council Opinion and China's long-term innovation plans generally by reintroducing the concept of a globally new drug or biologic. This globally new standard is very likely to be counterproductive for China, making it more difficult for both foreign and domestic innovative manufacturers to benefit from the proposed policy reforms and engage in the type of meaningful development and collaboration with partners in China and around the world that promotes innovation. As such we urge NMPA to clarify the definition of new as it applies to drug and biologic registration applications and define "new" to mean never marketed in China, as opposed to new to the world.

In addition, PhRMA is eager to continue supporting China in its reform effort to develop a regular mechanism for government reimbursement and a value assessment system. PhRMA urges China to establish a comprehensive and sustainable policy framework for government pricing and reimbursement that would include predictable and timely reimbursement decisions for new drugs, systematic and transparent mechanisms for price negotiation linked to reimbursement, adoption of evidence-based methodologies for drug value assessment and an enhanced role for commercial health insurance.

A fair and transparent regulatory and legal process is another priority element for a sound and sustainable drug regulatory regime in China. PhRMA is concerned about China's inconsistency in meeting its domestic legal requirements and bilateral U.S.-China commitments in this regard. In particular, China frequently does not provide reasonable periods for public comment on draft laws, rules, regulations and other binding measures, despite these obligations.[161] As China moves forward in its next phase of reform, PhRMA urges China to publish draft measures and provide ample time for stakeholders to provide meaningful comments.

[161] *See, e.g.*, Fact Sheet: 25th U.S.-China Joint Commission on Commerce and Trade (Dec. 2014), available at https://ustr.gov/about-us/policy-offices/press-office/fact-sheets/2014/december/us-fact-sheet-25th-us-china-joint (last visited Feb. 7, 2019) (stating that "China and the United States agree that for all draft pharmaceutical and medical device rules and regulations where notifications are required under the relevant WTO rules, a comment period will be provided that will be no less than 60 days.").

Key Issues of Concern:

- **Regulatory data protection failures**: China committed as part of its accession to the World Trade Organization (WTO) to provide a 6-year period of RDP against unfair commercial use for clinical test and other data submitted to secure approval of products containing a new chemical ingredient. In practice, however, China's RDP system is not effective. In this regard, we strongly welcome the draft NMPA measures on the Implementation of Drug Clinical Trial Data Protection, which propose up to 6 and 12 years of RDP for chemically synthesized drugs and therapeutic biologics respectively. This draft measure represents a strong first step toward reform in this area.

- **Weak patent enforcement**: Transparent mechanisms and legal standing to sue are needed in China to ensure parties are afforded the opportunity to resolve patent disputes before potentially infringing pharmaceutical products are launched in the market. Neither China's DAL or DRR nor the Patent Law provide an effective mechanism for enforcing an innovator's patent rights vis-à-vis regulatory approval of follow-on products before those products are launched. In this light, we are greatly encouraged by the NMPA's draft Circular 55 (Relevant Policies on Protecting Innovators' Rights to Encourage New Drug and Medical Device Innovation), which proposes a patent enforcement system with the critical components of: a) notice to innovators of potentially infringing subsequent applications referencing the original application prior to approval of such subsequent applications; and b) a stay of marketing approval pending the resolution of disputes concerning those patents.

- **Loss of Patent Term Due to Regulatory Delay**: Lengthy regulatory approval processes for pharmaceutical products results in a significant loss of effective patent term for such products. Though China has indicated it will address this problem by implementing PTR to account for the lengthy regulatory approval process, this continues to be a problem that undermines the incentives intended to be created by the patent system. We commend the inclusion of PTR provisions in the proposed Patent Law amendments, and have proposed revised language to ensure that the resulting mechanism achieves its objectives of encouraging the development of medicines.

- **Restrictive patentability criteria**: In late 2016, the China National Intellectual Property Administration (CNIPA)[162] issued an amendment to its Patent Examination Guidelines that would require examiners to take into account post-filing experimental data submitted by an applicant. This amendment appears to be intended to implement China's commitment, made during the 2013 Joint

[162] In August 2018, the State Intellectual Property Office (SIPO) changed its name to the China National Intellectual Property Administration (CNIPA). Although many of the policies and draft proposals referenced in this submission were issued under the name of SIPO, we have used CNIPA consistently throughout this document.

Commission on Commerce and Trade (JCCT), to permit patent applicants to file additional data after the application filing date. PhRMA recognizes and welcomes this positive step, but concerns remain regarding CNIPA implementation and interpretation of the proposed amendment, especially at the PRB (Patent Reexamination Board) level. In addition, certain therapeutic methods, referred to as "specific therapeutic methods," essentially cannot be protected by patents in China. New specific therapeutic methods are new methods of treatment of a known indication with a known product (such as new dosage regimens, treatment of new subgroups of patients or new routes of administration). Inventions in such methods very often bring important patient benefits, and the inability to obtain patents on these inventions undermines the incentives to invest in them, particularly to the extent they are targeted at particular medical and health problems in China.

- **Delays and lack of transparency in government pricing and reimbursement**: PhRMA welcomes the 2017 update to the NRDL – the first update since 2009 – as well as the recent addition of 17 oncology medicines to the NRDL in 2018. We encourage the Chinese government to shift towards a more timely, transparent and predictable reimbursement system, in which manufacturers may apply for reimbursement at any time, drug clinical assessment is completed within a pre-defined period following the application (*e.g.*, within 90 days), and negotiations between manufacturers and the responsible government agency take place periodically (*e.g.*, semi-annually). While the manner in which the first national reimbursement negotiation was conducted in July 2017 diverges from a sound pricing and reimbursement system, PhRMA is pleased to see the newly established National Healthcare Security Administration (NHSA) moving forward with a negotiation process and the establishment of a regular reimbursement mechanism.

- **Lengthy regulatory approval process**: The overall drug development and approval process in China still takes much longer than international practice and is particularly lengthy and cumbersome for biologics and vaccines. This lengthy regulatory approval process results in a significant loss of effective patent term for biopharmaceutical products. However, the NMPA is undertaking significant reform efforts to accelerate the drug review and approval process and align its regulatory framework with international standards (*e.g.*, inclusion of the 60-day CTA approval period in NPC's draft DAL amendment and NMPA's guidance on the following: conditional approval process for drugs to treat life threatening, serious diseases; acceptance of foreign clinical trial data for registration; expedited approval for drugs treating orphan diseases). PhRMA is encouraged by many recent proposals, including in the draft NMPA amendments to the DAL and DRR, the CCP/State Council Opinion, and the draft NMPA Circulars (Nos. 52-54), to improve the efficiency of global drug development and reduce the time it takes for all innovative new medicines to reach Chinese patients. Moreover, PhRMA is equally encouraged by NMPA approving a number of drugs in 2018 under timelines consistent with FDA and European standards.

- **Counterfeit medicines**: China has been implementing national plans to improve drug safety and severely crack down on the production and sale of counterfeit medicines, resulting in several positive and tangible actions on the enforcement front. However, the production, distribution and sale of counterfeit medicines and unregulated APIs remain rampant in China and continue to pose a threat to China and its trading partners. PhRMA looks forward to meaningful implementation of China's commitment made during the sixth meeting of the U.S.-China Strategic and Economic Dialogue (S&ED) in July 2014 related to effective regulatory control of APIs and anti-counterfeiting.

For these reasons, PhRMA requests that China remain on the **Priority Watch List** and be subject to **Section 306 Monitoring** for the 2019 Special 301 Report, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protection

Over the past 18 months, China has released a series of proposed policies that could strengthen its regulatory framework for innovative medicines in a way that may address long-standing industry concerns about the lack of RDP, loss of patent term due to lengthy regulatory approval processes, ineffective patent enforcement, and inconsistent patent examination guidelines. For example, the April 2018 draft NMPA measures on the Implementation of Drug Clinical Trial Data Protection, propose up to six and 12 years of RDP for chemically synthesized drugs and therapeutic biologics, respectively. The CCP/State Council Opinion, which was issued in October 2017, is the first time that this level of the Chinese government has openly endorsed RDP and patent linkage in a meaningful way. In addition, the NMPA draft Circulars, which were issued in May 2017, propose the establishment of a patent linkage system and specific RDP terms. We also see progress on these issues in the October 2017 NMPA draft DRR amendment, which is a significant improvement over the draft DRR issued in 2016. The establishment of a Supreme Court IP division to hear all appeals stemming from IP disputes is also a welcome development that should help to bring greater consistency to the resolution of these disputes in China.

At the same time, we are disappointed that the proposed amendments to the Patent Law do not include any provisions to advance patent linkage. We urge NMPA and CNIPA to include in the draft DAL amendment, draft DRR amendment and draft Patent Law amendment, the patent linkage, PTR and RDP provisions to ensure that they serve their intended purpose of encouraging stakeholder innovation.

PhRMA looks forward to working with the Chinese and U.S. governments through all available pathways to see these proposed reforms finalized quickly and fully grounded in best practices. The input U.S. stakeholders have already submitted offers important guidance in this regard. It is equally critical to ensure that these reforms are implemented fully in a manner that advances innovation and patient access, is consistent with China's bilateral commitments and international obligations, and ensures that U.S.

biopharmaceutical companies can compete on a level playing field with China's domestic industry.

Regulatory Data Protection Failures

As part of its accession to the WTO in 2001, China committed to provide a six-year period of RDP for undisclosed test or other data submitted to obtain marketing approval for pharmaceuticals in accordance with Article 39.3 of the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS).[163] Indeed, China's DAL and DRR, administered by the NMPA, establish a six-year period of protection for test data of products containing a new chemical ingredient against unfair commercial use.[164] In practice, however, China's regulatory environment allows for unfair commercial use of safety and efficacy data generated by PhRMA member companies.

China's current RDP system in practice is inconsistent with TRIPS Article 39.3 in several ways. First, certain key concepts such as "new chemical ingredient" (sometimes referred to as "new chemical entity") and "unfair commercial use" are undefined or are not in line with international standards. This leads to the inconsistent and arbitrary application of the law by NMPA, in addition to confusion and uncertainty for sponsors of marketing approval applications. The term "new chemical ingredient" should be clearly defined in the DAL, DRR, and other relevant laws and regulations in line with international standards and include biologic and chemically synthesized drugs, recognizing the considerable investment by innovative pharmaceutical companies in developing and proving safety and efficacy of a new product.

Second, RDP should be granted to any product that is "new" to China, *i.e.*, has not been approved by NMPA. In practice, however, China grants RDP only to pharmaceutical products that are "new" to the world – in other words, products that make their international debut in China. That is at odds with the approach of other regulatory systems and even at odds with the approach taken in China for RDP for agricultural chemicals.

During the December 2012 JCCT, China "agreed to define new chemical entity in a manner consistent with international research and development practices in order to ensure regulatory data of pharmaceutical products are protected against unfair commercial use and unauthorized disclosure."[165] Following many years of discussion in the JCCT and other venues, this commitment was a positive development. Unfortunately,

[163] Report of the Working Party on the Accession of China to the World Trade Organization, WT/MIN(01)/3 (Nov. 10, 2001), at para. 284. Article 39.3 provides that a country must protect data submitted in the context of a drug registration application from unfair commercial use.

[164] *See* Regulations for Implementation of the Drug Administration Law of the People's Republic of China, Art. 35; Provisions for Drug Registration (SFDA Order No. 28), Art. 20.

[165] *See* Fact Sheet: 23rd U.S.-China Joint Commission on Commerce and Trade (Dec. 19, 2012, available at https://ustr.gov/about-us/policy-offices/press-office/fact-sheets/2012/december/23rd-JCCT (last visited Feb. 7, 2019).

this commitment remains unfulfilled. Effective implementation of this commitment is necessary. Although the U.S. Government has actively engaged NMPA to revise the definition of new chemical entity, little progress has been made.

The February 2016 NMPA "Chemical Drug Registration Category Work Plan," defines a "new drug" as a chemical entity that is "new to the world." PhRMA is concerned that this revised definition of "new drug" may signal a similar narrowing of thinking with respect to the definition of new chemical ingredient, and therefore, creates a risk that a drug approved or marketed first outside of China may receive weaker or no exclusivity in China. In addition, this revised definition of "new drug" could potentially impact China's JCCT RDP commitment.

Third, China's regulatory procedures permit non-originator, or follow-on, applicants to rely on the data submitted to NMPA or a foreign regulatory agency's approval of the originator product in another market during the RDP term in China. This practice gives an unfair commercial advantage to the follow-on manufacturer by permitting it to rely on the full clinical data submitted by an innovator – which the follow-on manufacturer did not incur the costs to produce – while having to submit only a small amount of China-specific supplemental data to NMPA. NMPA should not approve follow-on drugs during the RDP period unless the follow-on applicant submits full clinical trial data that it has independently developed or received a license to cross-reference from the innovative drug manufacturer. This approach would be consistent with the goals of encouraging innovation in China by protecting innovators' investment in clinical trials. To meet these goals, China will need to ensure that it has regulatory and legal systems that are compatible with other major markets. While the systems need not be identical, implementation of a meaningful RDP mechanism can promote harmonization and enable companies to function more easily in multiple markets. PhRMA notes that it has been 17 years since China's WTO commitment to provide RDP. Thus, prompt and meaningful RDP reform should be a high priority.

In light of these deficiencies, we strongly welcome the draft NMPA measures on the Implementation of Drug Clinical Trial Data Protection, which propose up to 6 and 12 years of RDP for chemically synthesized drugs and therapeutic biologics respectively. However, the proposed location- and time-based conditions and limitations placed on the terms for innovative drugs are not consistent with China's international commitments, are not practical, and could well undermine the very goals that are driving these proposed reforms. In this respect, the Draft Measures would make it difficult – if not impossible – to obtain the benefits of RDP by forcing innovators into arbitrary choices concerning the location of development and timing of submissions. In some cases, the costs of these choices for the overall development program could exceed the benefits of RDP. Moreover, there remains significant uncertainty regarding the scope of the data protected and the criteria for protected categories, and we are very troubled by the broad post-approval data disclosure requirements.

Weak Patent Enforcement

Transparent mechanisms and a legal standing to sue are needed in China to ensure parties are afforded the opportunity to resolve patent disputes before potentially infringing pharmaceutical products are launched on the market. If a follow-on company actually begins to market a drug that infringes the innovator's patents, the damage to the innovator may be irreparable even if the innovator later wins its patent litigation. This could undermine the goal of encouraging innovation in China. In fact, NMPA has approved infringing follow-on products, and research-based pharmaceutical companies have no legal means to resolve patent disputes prior to the marketing of those infringing drugs. Further, although China's laws and regulations provide for injunctive relief, in practice injunctions are rarely, if ever, granted in the context of preventing premature follow-on product market entry, due to high procedural barriers.

In this light, we are greatly encouraged by NMPA's draft Circular 55, which proposes a patent enforcement system with the critical components of: a) notice to innovators of potentially infringing subsequent applications referencing the original application prior to approval of such subsequent applications; and b) a stay of marketing approval pending the resolution of disputes concerning those patents. We also welcome the October 2017 draft DRR amendment, which is a significant improvement over the 2016 DRR amendment. At the same time, this draft does not include the level of detail and specificity required to establish an effective patent enforcement system. For example, we strongly suggest that NMPA make it clear in the DRR that it will not approve potentially infringing follow-on application during the pendency of timely filed patent litigation or for a designated period of time, whichever is shorter. NMPA should also apply linkage to "relevant" patents, *i.e.*, formulation, composition, and method of use patents, as well as process patents for biologics.

Further, PhRMA and its member companies are encouraged by the preliminary steps taken by the Center for Drug Evaluation to establish an Approved Drug List, akin to the Orange Book maintained by the U.S. Food and Drug Administration, that would provide greater certainty to innovators and generic manufacturers alike regarding the patent status of approved medicines and facilitate effective patent enforcement and implementation of regulatory data protection. We are hopeful that NMPA and CNIPA will provide more guidance on the listing process and mechanics of the stay described in Circular 55, and we look forward to working with the Chinese and U.S. governments to ensure that China implements an effective patent enforcement system.

In addition, parallel patent enforcement proceedings through China's judiciary and CNIPA's Patent Reexamination Board (PRB) further frustrate biopharmaceutical innovator's ability to effectively and efficiently resolve patent disputes. Patent owners are often faced with unnecessary and burdensome procedural hurdles to seek the timely resolution of patent disputes because invalidity decisions issued by CNIPA's PRB during an ongoing judicial proceeding are grounds for automatic dismissal of relevant infringement litigations. In that situation, patent owners are required to appeal the PRB decision through the judiciary, and if successful, seek a court to compel PRB to confirm

the judgment. Due to PRB's extremely strict inventive step and supplemental data requirements, and fast docket times, patent infringement defendants can use the PRB proceedings as a tactic to circumvent the judicial process.

Lack of Patent Term Restoration

Pharmaceutical companies must adhere to a drug registration process before marketing drugs in China, as they must in other countries, which causes delays in marketing that reduce the effective term of patent protection for products once they reach the market. Many other countries respond to this problem by restoring the term of patents to compensate for regulatory delay. Such PTR is not available under China's current Patent Law. PhRMA members are encouraged by the proposed amendments to the Patent Law (January 2019), which include the provision of PTR in Article 43. We look forward to continued discussion on the draft Patent Law amendments and implementing regulations on PTR to ensure that it achieves its intended objective of encouraging the development of medicines.

Restrictive Patentability Criteria

Reforms need to continue in China to provide clear and coherent standards, consistent with other major drug markets, for obtaining biopharmaceutical patents. It is critical that such standards reflect the realities of the drug development lifecycle. For example, unlike patent offices in the United States, Europe, Japan, Korea and other major markets, CNIPA does not consistently accept data generated after a patent is filed to describe inventions or satisfy inventive step requirements, pursuant to Articles 26.3 and 22.3 of China's Patent Law, respectively. This practice has caused uncertainty about the ability to obtain and maintain biopharmaceutical patents in China, and has caused denials of patents on new medicines in China that received patents in other jurisdictions.

In late 2016, CNIPA issued an amendment to its Patent Examination Guidelines that requires examiners to consider post-filing experimental data submitted by the applicant. This amendment appears to be intended to implement China's commitment, made during the 2013 JCCT, to permit patent applicants to file additional data after the application filing date. PhRMA recognizes and welcomes this positive step, and is committed to working collaboratively with the appropriate government authorities to facilitate practical implementation of the amendment in a manner that provides greater certainty and protection for U.S. biopharmaceutical innovators.

PhRMA views the 2016 CNIPA revision to Section 3.5 of the Patent Examination Guidelines as an important step toward implementing a clear and consistent standard that permits pharmaceutical manufacturers to submit additional data to confirm that the invention is novel, useful and contains an inventive step. The submission of supplemental data will also support and confirm statements that have already been disclosed in the patent application. We assume that by requiring the examiner to examine supplemental experimental data, this new provision will be implemented in such a way that the

supplemental data can be relied upon to successfully respond to an examiner's rejection for lack of inventive step or insufficient disclosure provided in the patent application.

While PhRMA recognizes and welcomes this positive step, we have two concerns with the data supplementation amendment. First, the amendment to Section 3.5 makes the data supplementation approach applicable only to "Sufficiency of Disclosure of Chemical Inventions." We believe the same approach should be taken to the examination of other patentability issues, such as inventive step, and therefore should be incorporated into Section 6, Chapter 10 of Part II as well. Second, we are concerned that certain language in the proposed amendment may be interpreted too narrowly by CNIPA examiners, resulting in less patent incentives for new medicines in China and thereby harming Chinese patients. Specifically, the amendment permits data supplementation only where "the technical effect to be proved by the supplemented experimental data shall be one which can be derived by a person skilled in the art from the disclosure of the patent application." If this is interpreted so as to require the application to already disclose or demonstrate the precise technical effect to be proven by the offered supplemental data, which seemingly continues to be the case even after the amendment to the Patent Examination Guidelines came into effect, the result would be that supplemental data is rarely accepted. This result can be avoided by incorporating more detailed guidance in the Guidelines to make it explicit that the requirements are in line with those commonly used in other countries. For example, the European Patentability Examination Guidelines (Section 11) provide that supplemental data will be accepted if it proves effects that "are implied by or at least related to the technical problem initially suggested in the originally filed application."[166] In implementing this provision, we urge CNIPA to keep these considerations, goals and benefits in mind and provide additional guidance consistent with them.

Specific therapeutic methods essentially cannot be protected by patents in China. New "specific therapeutic methods" are new methods of treatment of a known indication with a known product (such as new dosage regimens, treatment of new subgroups of patients or new routes of administration). They are distinguished from new product forms (such as dosage forms and formulations), manufacturing processes and treatment of new indications, which can be protected by patents in China either directly or through use of the Swiss-type claim format. Most countries with strong IP laws provide patent protection for specific therapeutic methods either directly (by permitting methods of treatment to be patented) or indirectly (by permitting alternative claim formats that, in effect, can provide patent protection for such inventions). Incentives to develop such new specific therapeutic methods should be provided by the patent system because such new uses of existing medicines can bring important patient benefits, including methods of treatment specific to the Chinese population that may not be developed in the absence of a local incentive to do so. However, Article 25(3) of China's Patent Law does not allow for direct patenting of methods of treatment. The courts, including the Supreme Court (see, *e.g.*, in the decision

[166] Available at http://documents.epo.org/projects/babylon/eponet.nsf/0/0791474853510FFFC125805A004C9571/$File/guidelines_for_examination_part_g_en.pdf (last visited Feb. 7, 2019).

on *Genentech v. PRB* against validity of patent No. ZL 00814590.3) and CNIPA (as stipulated in the Guidelines for Patent Examination), do not permit alternative claim formats that could protect specific therapeutic methods, including either Swiss-type claims where the point of novelty is a specific therapeutic method or other alternative formats that are accepted by patent offices in other countries, including the European Patent Office). We urge CNIPA to revisit this gap in China's patent system and conform China's practice to that of many other countries.

Loss of Patent Rights

Overly rigid requirements to prove patent ownership for subsidiary patents, a lack of clarity about what constitutes adequate proof of patent ownership, and short response timeframes have resulted in the loss of patent rights in Chinese Patent Office invalidation proceedings, without the possibility of appeal.

Mandatory intellectual property sharing related to certain biological material

The Ministry of Science and Technology ("MOST") originally issued the Interim Measures for the Administration of Human Genetic Resources in 1998 to restrict the exploitation and exportation of human biological samples accessed in China. In relevant part, that interim measure required that any research conducted by foreign companies using Chinese human biological samples must be undertaken in collaboration with Chinese partners. These measures remain in effect. Practical guidelines had made unclear for some time what use of human biological samples triggered the requirement for prior approval under these measures.

In 2015, MOST published the Guidelines on Administrative Approvals of Collection, Trade and Exportation of Human Genetic Resources ("2015 Guidelines"), which requires unique clinical trial procedures for research and development that utilizes Chinese human biological samples. According to the 2015 Guidelines, collection and/or exportation of human biological samples from all Sino-foreign collaborations (including clinical studies) are subject to strict review and approval of China Human Genetic Resources Administration Office (HGRAO). Specifically, HGRAO requires that the intellectual property rights arising from the utilization of such samples in exploratory research must be shared with the Chinese and foreign parties.

In 2017, MOST further released the Guidelines on Optimizing the Approval Process of Human Genetic Resources to streamline the approval process and allow for parallel reviews of CTAs and genetic testing (HGRAC). However, under the new process, foreign sponsors and vendors are required to sign an "undertaking letter," which certifies that that they will comply with Chinese regulations that govern clinical studies and the Chinese Administrative Permit Law. They are also accountable for the validity and accuracy of the application in its entirety, based on the official instructions on the application form. The intellectual property sharing requirement and the undertaking letter together form a significant hurdle for foreign companies conducting clinical research in China.

Sample collection during a clinical trial should be left out of the approval process. More clarity with respect to the intellectual property sharing requirement is also needed. We look forward to working with the Chinese and U.S. governments to ensure that these proposed policy revisions are transparently and expeditiously implemented in a manner that provides for effective protection for U.S. biopharmaceutical companies and is consistent with China's international obligations and commitments.

Market Access Barriers

Government Pricing and Reimbursement

To appropriately address the Chinese patient access and affordability challenges, PhRMA urges China to establish a comprehensive and sustainable policy framework for government pricing and reimbursement that would include predictable and timely reimbursement decisions for new drugs, systematic and transparent mechanisms for price negotiation linked to reimbursement, adoption of evidence-based methodologies for drug value assessment, and an enhanced role for commercial health insurance. PhRMA and its members are committed to working with the appropriate government authorities in China to assist in the timely and transparent development of this policy framework.

Government Reimbursement List

PhRMA welcomes the 2017 update to the NRDL – the first update since 2009 – as well as the recent addition of 17 oncology medicines to the NRDL in 2018. These two important steps will significantly improve the access and affordability of innovative medicines for patients in China. While any additions to the NRDL are a positive development, it appears that the negotiation process for these new medicines lacked transparency and diverges from a sound government pricing and reimbursement system. By early 2018, all 31 provinces had included the negotiated drugs into their PRDLs. Still, there remain major implementation challenges, such as low reimbursement percentages and hospital listing restrictions, and cost control regulations, which will continue to restrict patient access to innovative and life-saving medicines.

PhRMA recommends that the Chinese government shift towards a more timely, transparent and predictable reimbursement system, in which manufacturers may apply for reimbursement at any time, drug clinical assessment is completed within a pre-defined period following the application (*e.g.*, within 90 days), and negotiations between manufacturers and the responsible government agency take place periodically (*e.g.*, semi-annually). The drug clinical assessment should be transparent, evidence-based, focused on clinical benefits and independent of economic considerations. Following the clinical assessment, a fair negotiation based on clear conditions and open communication should be conducted between the national reimbursement authority and the manufacturer. These reimbursement system reforms would provide U.S. companies increased market access and improve patient access to innovative medicines.

Government Pricing and Procurement Policies

China, as part of its WTO accession, committed to apply price controls in a WTO-consistent fashion, taking into account the interests of exporting WTO members, and without having the effect of limiting or impairing China's market access commitments on goods and services.[167] Notwithstanding that commitment, PhRMA is concerned that reforms to China's government pricing and procurement mechanisms could exacerbate the already uncertain business environment and further reduce reward for innovation, restrict patient access to high-quality medicines and undermine China's health care reform and innovation policy objectives.

PhRMA is committed to working collaboratively and expeditiously with the appropriate government authorities to implement a transparent and appropriate government pricing policy that recognizes quality-systems, innovation, and the value that our member companies' products bring to patients and China.

Regulatory Approval Process

China is making significant strides in reforming and strengthening its regulatory framework, including shorter review times for CTAs and policies to expedite review of drugs that treat serious and life-threatening diseases. Although there were a number of examples where NMPA granted expedited regulatory approval consistent with timelines in the U.S. and EU, China remains an outlier in the biologic and vaccine drug development and approval process compared to other regulatory authorities. This contributes to low availability of innovative medicines in China, with just eight percent of the new medicines launched between 2011 and 2017 being available in China.[168] Due to China's unique regulatory requirements and testing procedures, a "drug lag" remains in China.

PhRMA is greatly encouraged by China's recent regulatory proposals included in the draft NPC and NMPA amendments to the DAL, the draft NMPA amendment to the DRR, the CCP/State Council Opinion, and the NMPA draft Circulars (Nos. 52-54), which are all intended to accelerate the drug review and approval process and facilitate China's participation in simultaneous global drug development. Regarding the 2018 draft of the DAL and 2017 draft of the DRR, PhRMA is encouraged to see greater flexibility in the drug development process, including a considerably shortened timeline for the approval of clinical trials, new channels for stakeholder-NMPA communications, procedures for amending CTAs and conditional approval of drugs that fill unmet medical needs and treat orphan diseases. Furthermore, we support NMPA's December 2017 draft guidance on Conditional Marketing Approval of Drugs for Urgent Clinical Use, which provides some direction to sponsors, but still lacks full clarity on the application of a conditional

[167] Report of the Working Party on the Accession of China to the World Trade Organization, WT/MIN(01)/3 (Nov. 10, 2001), at para. 64.

[168] PhRMA analysis of IQVIA Analytics Link. *See* https://www.iqvia.com/solutions/commercialization/market-analysis/analytics-link (last visited Feb. 7, 2019).

registration pathway in China. We also support the issuance of guidance in July 2018 on the acceptance of overseas clinical trial data and the August 2018 notice on Soliciting Opinions on List of New Drugs in Urgent Clinical Need Marketed Overseas. Additionally, NMPA's May 2017 accession to the ICH and successful election to the ICH Management Committee further exemplifies China's reform efforts. Being an ICH Member will further encourage NMPA's harmonization with international regulatory standards, including but not limited to the China Pharmacopeia 2020, enforcement of GXP, and further implementation of standardized electronic submission for new drug applications (eCTD) and safety reporting, which will enable companies to pursue global simultaneous drug development and accelerate Chinese patient access to innovative medicines. Industry and other ICH stakeholders have high expectations for NMPA to implement all of ICH's technical guidelines in the coming years.

Clinical Trials Applications

To help China further integrate into the global innovation network and reduce the time it takes for innovative medicines to reach patients, it is critical for China to shorten the CTA review and approval time. We are very encouraged to see a provision in the November 2018 draft NPC DAL amendment that would officially permit a clinical trial to move forward if NMPA has not raised objections within 60 business days. Implementation of the 60-day CTA approval (combined with parallel reviews of HGR submissions as discussed above) will significantly reduce the drug lag as China's CTA review time has represented the largest regulatory barrier for multinational companies in China. Therefore, PhRMA recognizes and applauds the important steps the NMPA is taking to enhance agency capacity and capability by encouraging investment in additional resources and trained evaluators.

Based on PhRMA member company experience in other major markets, it is critically important for the NMPA to maintain consistent and specific timelines for reviewing and approving applications. In addition, applications should be evaluated based on a clear set of standardized criteria coupled with science-based and risk-based decision making (principles embedded in ICH guidelines) that applies equally to both local and foreign manufacturers.

Specifically, we are encouraged that the draft amendment to the DRR indicates an intent to abolish unnecessary distinctions between foreign and domestic applicants and the use of MRCT versus a purely local trial in China to support marketing applications. Furthermore, the State Council Opinion on drug and device reform (October 2017) stipulates that clinical trial data obtained from overseas multi-center trials may be used for registration in China. The NMPA's final guidance on the acceptance of overseas clinical trial data in July 2018 and the notice on Soliciting Opinions on List of New Drugs in Urgent Clinical Need Marketed Overseas in August 2018 will further support a simultaneous global development paradigm shift in China. However, implementation and further clarity on whether ethnic differences require additional clinical studies in China will greatly avoid any uncertainty in China's overall registration process.

Another aspect of complication around clinical trials in China for multinational pharmaceutical companies relate to the approval for genetic testing by Human Genetic Resources Administration Office of China (HGRAO), under the Ministry of Science and Technology (MOST) based on a policy published in 2015. In particular, in early phase studies multinational pharmaceutical companies face a high rejection rate, and inconsistent and complex document requirements. This situation presents a hurdle for China to participate in global development and counters the State Council's reform plan. To improve the process overall, clear and detailed guidelines on document requirements, standardized assessment and approval criteria and a systematic communication channel between HGRAO and sponsor are needed.

PhRMA's view on intellectual property sharing related to certain biological material in connection with the HGRAO process is noted below.

Drug Approvals Process

PhRMA welcomes a number of other key regulatory proposals in draft Circulars 52-54, because they would represent positive movement in China's regulatory reform toward supporting a simultaneous global development / registration framework in China. The proposed changes are consistent with industry's primary recommendations, including streamlined processes for multi-regional clinical trial (MRCT) registrations, expedited pathway for drugs that treat serious and life-threatening illnesses, acceptance of foreign clinical data to satisfy registration in China, structured agency consultation, and establishing an orphan disease list.

To ensure Chinese patients receive timely access to new therapies, PhRMA recommends that the NMPA bring its regulatory framework into compliance with accepted international standards and adopt science-based, transparent, consistent and predictable policies for evaluating and approving drugs and biologics. PhRMA recommends revisions to the DAL and DRR consistent with the proposals stated in NMPA draft Circulars in order to accelerate and simplify the drug regulatory approval process, provide the same requirements for locally manufactured and imported products and clearly outline the criteria and timeline for reviewing and approving clinical trial and marketing application processes. PhRMA and its members stand ready and look forward to working closely with the U.S. and Chinese governments to support China's regulatory reform efforts.

Counterfeit Medicines

Pharmaceutical counterfeiting poses global public health risks, exacerbated by rapid growth of online sales of counterfeit medicines and the production and sale of unregulated active pharmaceutical ingredients (API) used to manufacture counterfeit products. China has been stepping up enforcement efforts against counterfeited drugs in recent years, both through legislative reforms and increased police activity. However, online distribution of counterfeit medicines and unregulated API remain the most serious challenges in China.

Under current pharmaceutical regulations, there is no effective regulatory control over the manufacture and distribution of API, which creates a major regulatory loop-hole that impacts negatively on the security of China's upstream drug supply chain. During the Sixth Meeting of the U.S.-China S&ED in July 2014, China committed to develop and seriously consider amendments to the DAL requiring regulatory control of API. To effectively reduce the risks caused by unregulated API to patient health, a multi-prong approach or "road map" is needed. Targeted measures may include:

- amending the Criminal Code to ease the burden of proof to prosecute brokers or API suppliers who knowingly deal with illegal APIs;
- empowering NMPA or another authority to regulate any party that manufactures API even if that party has not declared an intent to do so;
- empowering NMPA to penalize API manufacturers based on *prima facie* evidence of a product having medicinal use or being an "API" or a "chemical drug substance" without cGMP certification;
- amending the DAL to require adherence to ICH Q7A (*Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients*) with meaningful penalties for failure to do so; and
- deepening cooperation with major Internet Service Providers, portal sites, and search engines for earlier identification and tracking of illegitimate API suppliers through B2B websites.

While NMPA plays a critical role in developing future solutions, any significant reform plan will require coordination and consultation among all relevant ministries within the central government. These efforts to crack down on unregulated API must go hand-in-hand with China's current campaign against counterfeit drugs in order to enhance the effectiveness of China's national drug safety plan objectives.

China has continued to coordinate joint special enforcement campaigns targeting counterfeit drug crimes.[169] It also appears that China is beginning to spend more efforts tackling the sale of counterfeits on the Internet. In 2013, NMPA and the State Information Office jointly led a 5-month crackdown campaign with collaboration of several ministries and offices against illegal online sales of drugs. Reportedly, the government also demands major search engines to filter out fake drug posts, which is a significant partnership with the private sector aimed at protecting Chinese patients.[170] PhRMA hopes

[169] *See, e.g.*, "2,000 Arrested in China in Counterfeit Drug Crackdown," Aug. 5, 2012, available at: http://www.nytimes.com/2012/08/06/world/asia/2000-arrested-in-china-in-crackdown-on-counterfeit-drugs.html?_r=0 (last visited Feb. 7, 2019); "China Detains 1,300 People Suspected of Making and Selling Counterfeit Drugs," Dec. 15, 2013, available at http://www.huffingtonpost.com/2013/12/16/counterfeit-drugs-china-medicine_n_4447483.html (last visited Feb. 7, 2019).

[170] Reportedly, search engines have been required to ensure that qualified websites are listed earlier in the search results, to conduct active searches for illegal online drug sales, to delete false and illegal medical advertising, and to report unqualified websites to the National Internet Information Office and the

that the U.S. Government will work with China to increase transparency of such campaigns, including enhancing information sharing with drug manufacturers to help evaluate the effectiveness of online actions, and supporting enforcement efforts, given the importance of protecting patients. China's actions in this area could serve as a model for other countries facing similar challenges online.

PhRMA encourages China and the U.S. Government to continue and increase further their cooperation related to counterfeit medicines sold on the Internet, given the role of the Internet in the global counterfeit drug trade. This notably requires a holistic approach since not only finished counterfeit medicines are sold on the major online platforms in China but also separate materials (*i.e.*, API, secondary packaging, primary packaging, labels) especially on business to business platforms for these to be assembled in and outside China.

Finally, while we commend China for improvements in customs regulations, which include monitoring and seizure of imports and exports, Chinese Customs authorities rarely exercise their authority to monitor pharmaceutical exports. PhRMA believes that more and better trained resources and support should be targeted to monitoring pharmaceutical and chemical exports to ramp up efforts against counterfeiting and unregulated API producers. This could include, for example, encouraging greater cooperation between Chinese Customs and the Public Security Bureau to ensure the identification and prosecution of those manufacturing and exporting counterfeit medicines. In addition, Chinese Customs could consider working with the World Customs Organization to exchange information and potentially align activities. Close cooperation and intense risk analysis with key intermediaries such as online ecommerce platforms and postal courier companies is critical to effectively monitor and detect small parcels with counterfeit medicines.

NMPA. In response, several Internet companies have stepped in to support the fight against counterfeit drugs. One of the most prominent companies, 360, introduced several products to provide users with accurate information on medicines and block false medical information websites, claiming that such sites accounted for 7.9% of all blocked websites or approximately 40,606 websites.

PRIORITY WATCH LIST

ASIA – PACIFIC

INDIA

We support the Indian Government's efforts to create a stronger business, innovation, and health care environment through the "Make in India" initiative, the National Intellectual Property Rights (IPR) Policy, the National Health Policy 2017, and the National Health Protection Scheme (NHPS) announced in February 2018 to provide health insurance coverage up to INR 500,000 (~7,150 USD) to 500 million Indians and opening of health and wellness centers under the Ayushman Bharat Mission. These efforts can advance improved access to health care for Indian patients, while driving economic growth by enhancing India's global competitiveness and improving ease of doing business. However, despite some positive signs, PhRMA's members remain concerned about the challenging policy and regulatory environment in India.

Market access challenges persist and despite important announcements to expand health care programs, the Indian Government has not increased investment in this critical area, leaving public health care spending at a very low level of approximately 1.4% of GDP during the year 2017-18,[171] and with only 36% of the population covered under any health insurance in 2016-17.[172] Moreover, there are cumbersome procedures related to compensation which prevent India from becoming a part of global clinical trial programs and thereby limit patient access to innovative medicines in India.

Pharmaceutical innovators again saw positive signs from the Indian Government in 2018; however, these signals have not yet been translated into real policy and practical change. To research, develop, and deliver new treatments and cures to patients, biopharmaceutical innovators must be able to secure and effectively enforce intellectual property (IP) rights. With the right policies put in place, India could become a globally-competitive leader in life sciences and biomedical development. The new National IPR Policy puts forward an important framework for strengthening India's innovation ecosystem; still, greater predictability and reliability is needed and implementation of the policy offers an opportunity to advance concrete policy improvements and could serve as a basis for revisiting India's designation in the future.

The innovative biopharmaceutical industry greatly appreciates the efforts to address these concerns at the highest levels of the U.S. and Indian Governments. We welcome the opportunity to continue working with both Governments to improve access to medicines for patients and advancing a "Healthy India" by removing market access barriers and fostering legal and regulatory certainty for the protection of IP in India.

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[171] IndiaSpend, Budget 2018: India's Healthcare Crisis Is Holding back National Potential (Jan. 30, 2018), available at http://www.indiaspend.com/budget-2018-indias-healthcare-crisis-is-holding-back-national-potential-29517/ (last visited Feb. 7, 2019).

[172] See Ministry of Finance response to Lok Sabha Question (Mar. 9, 2018), available at http://164.100.47.194/Loksabha/Questions/QResult15.aspx?qref=64078&lsno=16 (last visited Feb. 7, 2019).

Key Issues of Concern:

- **Lack of Patent Enforcement**: One of the most significant challenges facing biopharmaceutical applicants seeking marketing approval in India is that marketing and manufacturing approvals are not transparent or coordinated between federal and state agencies. Indian law allows Central Drugs Standard Control Organization (CDSCO) to approve third-party manufacturers to commercialize copies of innovator products, regardless of whether those products infringe on an innovator's patent(s). After four years of the medicine's first approval in India, a mere license to manufacture from any of the state drug regulators to manufacture and market the product in India suffices – resulting in irreparable harm to patients, innovators, and other follow-on producers. Coincident with recent changes to Indian customs procedures that eliminated patent enforcement at the border, biopharmaceutical innovators are seeing an increased incidence of infringing products manufactured outside India in neighboring territories being illegally imported into India. Not only do such products violate patents granted in India, they may also potentially threaten patient safety.

- **Unpredictable Patent environment**: India's legal and regulatory systems pose procedural and substantive barriers at every step of the patent process, ranging from impermissible hurdles to patentability posed by narrow patentability standards as set out in Section 3(d) of India's Patents Act, 1970, patent grant delays due to cyclic filings of pre-grant oppositions followed by rampant post-grant opposition proceedings, to onerous patent application disclosure requirements that disproportionately affect foreign patent applicants. Not only is this a concern in the Indian market, but also in other emerging markets that may see India as a model to be emulated. Patent applicants continue to face rejections under Section 3(d), infringement due to state-level marketing authorization for generic versions of on-patented drugs, and the threat of compulsory licenses (CLs), all of which demonstrate that much work needs to be done to improve the patent environment in India.

- **Regulatory data protection failures**: The Indian Regulatory Authority misinterprets Article 39.3 of the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) and relies on test data submitted by originators to seek approval in India and/or another country when granting marketing approval to follow-on pharmaceutical products. This reliance results in unfair commercial use prohibited by the TRIPS Agreement and discourages the development and introduction into India of new medicines for unmet medical needs.

- **High tariffs and taxes on medicines**: Medicines in India face high effective import duties for active ingredients and finished products with the basic import duties averaging around 10%. When combined with the Integrated Goods and Service

Tax, the effective import duty can exceed 20%. Additionally, the Goods and Service Tax (Central GST & State GST) on medicines ranges from 5-12%.[173]

- **Discriminatory and non-transparent market access policies**: The recent price control orders on coronary stents and knee implants, and the threat of an existing recommendation to implement price controls on patented medicines, significantly reduce the benefits of patent protection and create an unviable business environment for the innovative industry. We appreciate the Department of Pharmaceuticals (DoP) January 2019 amendments to Paragraph 32 of The Drug Price Control Order (DPCO) 2013. Specifically, the government rescinded a discriminatory provision against foreign companies which had previously exempted only patented medicines developed in India from price controls for five years from the commencement of marketing in India. The amendments also exempt patented medicines developed outside of India. This was a welcome pro-innovation policy, however, the broad authority granted to the National Pharmaceutical Pricing Authority (NPPA) and continued lack of transparency, predictability, and trust in the decision-making process hinders further investment in India.

- **Unpredictable environment for clinical research**: While the Government is keen to reinvigorate clinical research in India, ambiguities in the Indian regulatory space prevail. In particular, the definition of "trial related injury" is not well defined, and the determination of local clinical trials requirements is highly subjective. These along with the proposal to make innovators pay non-recoverable interim compensation irrespective of the final determination as to the cause of injury/death perpetuate a burdensome environment for clinical research that undermines the availability of new treatments and vaccines for Indian patients.

For these reasons, PhRMA requests that India remain on the **Priority Watch List** in the 2019 Special 301 Report, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protection

India announced the new National IPR Policy in May 2016.[174] India's National IPR Policy recognizes the tremendous economic and socio-cultural benefits that a strong IP regime could bring to India through economic growth, employment, and a vibrant R&D environment. While the Government has established the Cell for IPR Promotion and Management under the National IPR Policy to conduct an IPR awareness campaign

[173] *See* Central Board of Indirect Taxes and Customs, Tariffs on Chapter 30 (Pharmaceuticals), available at http://www.cbic.gov.in/resources//htdocs-cbec/customs/cst1718-020218/Chap-30-01052018.pdf;jsessionid=B8490083D262DD476149822F19D8A442 (last visited Feb. 7, 2019).

[174] Department of Industrial Policy and Promotion, "National Intellectual Property Rights Policy," May 12, 2016, available at http://dipp.nic.in/sites/default/files/National_IPR_Policy_English.pdf (last visited Feb. 7, 2019).

across the country in educational institutions, no concrete measures have been taken to improve the IP regime, *i.e.*, to promote innovation.

The policy also puts forward important administrative and procedural improvements. However, it should be strengthened to accelerate the reforms needed to foster medical innovation and enhance India's global competitiveness. For example, while the policy focuses on government, open source R&D, Corporate Social Responsibility credits, tax breaks, loan guarantees for start-ups, support systems for Micro-, Small- and Medium-sized Enterprises and other mechanisms to encourage innovation in India, it is also important to incentivize the private sector and scientific institutions by providing effective and meaningful IP protection and enforcement mechanisms. Implementation of the National IPR Policy should include a consultative process with relevant stakeholders and meaningful reforms to India's IP policies that lead to improvements in IP protection and enforcement for medicines.

Restrictive Patentability Criteria

PhRMA members continue to face considerable barriers at every step of the patent application process, including restrictive patentability criteria posed by Section 3(d) of India's Patents Act, outdated patent application disclosure requirements, and narrow patentability standards applied during pre- and post- grant opposition proceedings.

TRIPS Article 27 requires that patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that an invention is new, involves an inventive step, and is capable of industrial application. Section 3(d) of the Indian Patents Act as amended by the Patents (Amendment) Act 2005 adds an impermissible hurdle to patentability by adding a fourth substantive criterion of "enhanced efficacy" to the TRIPS requirements. Moreover, this additional hurdle appears to be applied only to pharmaceuticals. Under this provision, salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substances are presumed to be the same substance as the original chemical entity and thus not patentable, unless it can be shown that they differ significantly in properties with regard to efficacy. Further, indiscriminate and routine use of Section 3(d) by the Indian Patent Office during prosecution of patent applications by the Indian Patent Office even for a novel compound or a derivative with onus of proof on the applicant to prove otherwise poses an unreasonable and unnecessary burden on the innovators.

Additional substantive requirements for patentability beyond those enumerated in the TRIPS Agreement are inconsistent with India's international obligations. For example, Article 27 of the TRIPS Agreement provides an exclusive list of the types of subject matter that can be precluded from patent coverage, and this list does not include "new forms of known substances lacking enhanced efficacy," as excluded by Section 3(d) of the Indian law. Therefore, Section 3(d) is inconsistent with the framework provided by the TRIPS Agreement. Moreover, Section 3(d) represents an additional hurdle for patents on inventions specifically relating to chemical compounds and, therefore, the Indian law is in

conflict with the non-discrimination principles provided by TRIPS Article 27 and WTO rules.[175]

From a policy perspective, Section 3(d) undermines incentives for biopharmaceutical innovation by preventing patentability for improvements that do not relate to efficacy, for example an invention relating to the improved safety of a product. Further, Section 3(i) of the Indian Patents Act excludes method of treatment claims, effectively preventing U.S. biotechnology companies with needed treatment methods from entering the Indian market and providing life-saving products.

India's pre- and post-grant patent opposition system is another source of unreasonable restrictive standards for patentability. Patent revocations using "hindsight" analyses made during pre- and post-grant oppositions have cited a lack of inventiveness concluding that inventions were based on "old science" or failed to demonstrate an inventive step. In addition, the lack of clear rules guiding pleading and evidentiary standards during pre-grant opposition proceedings create further uncertainty relating to the patentability of inventions. Further, pre-grant opposition procedures under Section 25 of India's Patents Act have created significant uncertainty and delayed the introduction of new inventions by undermining patent office efficiency and delaying patent prosecution – exacerbating India's already significant patent examination backlog of approximately 6 years.

Weak Patent Enforcement

Indian law permits CDSCO to approve third-party manufacturers to commercialize copies of innovator products, regardless of whether those products infringe on an innovator's patent(s). After four years of the medicine's first approval in India[176] when the medicine ceases to be a new drug, approval from CDSCO is not required and a mere license to manufacture from any of the state drug regulators to manufacture and market the product in India suffices. State regulatory authorities are not required to verify or consider the remaining term of the patent protection on the original product. Therefore, an infringer can obtain marketing/ manufacturing authorization from the state government for a generic version of an on-patent drug, forcing the patent holder to seek redress in

[175] The additional patentability hurdle imposed by section 3(d) was recently reinforced by the Pharmaceutical Patent Examination Guidelines issued in October 2014.

[176] Rule 122E of the Drugs and Cosmetics Rules states that a new drug shall continue to be considered as new drug for a period of four years from the date of its first approval or its inclusion in the Indian Pharmacopoeia, whichever is earlier. The Drugs and Cosmetics Act goes on to specify that "Where an application under this Rule is for the manufacture of drug formulations falling under the purview of new drug as defined in rule 122-E, such application shall also be accompanied with approval, in writing in favor of the applicant, from the licensing authority." Thus, to obtain a manufacturing license for a new drug, the Central Drug Regulatory must provide written approval. In the case of drugs which do not meet the definition of a new drug, an "Application for grant and renewal of license to manufacture for sale or distribution of drugs shall be made to the licensing authority appointed by the State Government." *See* Ministry of Health and Family Welfare, "The Drugs and Cosmetics Rules, 1945 (As amended up to the 30th June, 2005)," available at http://www.cdsco.nic.in/writereaddata/Drugs&CosmeticAct.pdf (last visited Feb. 7, 2019).

India's court system, which often results in irreparable harm to the patent holder. India's National IPR Policy calls for identification of important areas of potential policy development related to ambiguities between IP laws and other laws or authorities whose jurisdictions impact administration or enforcement of patents.[177] India should amend the definition of a "new drug," as well as adopt measures to ensure innovators have timely notice of marketing approval applications and are able to seek injunctive relief before potentially infringing products enter the market.

Moreover, India does not provide mechanisms for notification or resolution of patent disputes prior to marketing approval of generic products. Such mechanisms are needed to prevent the marketing of patent infringing products and resolve disputes in a timely manner. Further, the Sugam initiative launched in November 2015 to implement e-Governance with respect to the licensing system within India's CDSCO lacks transparency and does not facilitate timely notification to a patentee of a possible infringement. In April 2017, India amended Form 44 of the Drugs and Cosmetics Rules[178] to omit Item 8 which previously required new drug applicants to disclose the "patent status of the drug."[179] This action further eroded the ability of patent owners to effectively and timely notify generic manufacturers and state drug regulatory authorities of existing patents related to medicines approved by CDSCO. CDSCO's recent effort to reform the SUGAM initiative under draft Notification GSR 629(E) provides an opportunity to facilitate the notification of manufacturing applications between government agencies and patent holders. On August 10, 2018, industry submitted formal comments to this SUGAM notification and urged the Ministry of Health and Family Welfare (MOHFW) to take immediate steps to increase transparency and cooperation between central and state medicines regulatory authorities. At a minimum, MOHFW should ensure all biopharmaceutical manufacturers, the relevant Indian authorities and the broader public have timely notice of marketing and manufacturing applications filed with central and state regulators.

In at least one specific case, the patent holder was forced to wait seven years before receiving a court decision upholding its patent. In that case, the court ultimately did not grant an injunction because by the time the decision was issued the patent was close to expiration.[180] In another case, a company waited two years for a Court to grant an injunction. During that time the infringing product was marketed and sold.[181] The Commercial Courts, Commercial Division and Commercial Appellate Division of High Courts Act, 2015 provides for the creation of commercial and commercial appellate divisions in high courts, and commercial courts at the district level to assist in addressing disputes in a timely manner. While this is a promising development, these courts are now overburdened with cases and will require a significant amount of technical expertise and

[177] *See* Secs. 3.8 and 3.8.3 of the National IPR Policy.

[178] Form 44, Schedule A, Drugs and Cosmetics Rules, 1945.

[179] *Id.*

[180] *F. Hoffman-La Roche Ltd v. Cipla*, RFA(OS) 92/2012, Delhi High Ct., (Nov. 27, 2015), available at http://delhihighcourt.nic.in/dhcqrydisp_o.asp?pn=258821&yr=2015 (last visited Feb. 7, 2019)

[181] *Merck Sharp & Dohme Corp. v. Glenmark Pharms*, Delhi High Ct., 2015 (64) PTC417(Del).

commitment of resources to be properly implemented. While the draft National IPR Policy proposed to establish specialized patent benches at the High Court level and designate an IP court at the district level, the final National IPR Policy did not include this provision.[182]

Compulsory Licensing

The grounds for issuing a CL in India are broad, vague and appear to include criteria that are not clearly related to legitimate health emergencies. While the Indian Government continues to take a more measured and cautious approach in responding to recent CL cases, the MOHFW continues to entertain potential recommendations to impose CLs on certain anti-cancer medicines under the special provisions of Section 92 of India's Patents Act, which would cause further difficulty for patent owners to defend their patents. Moreover, Indian pharmaceutical companies continue to initiate requests for voluntary licenses under Section 84(6)(iv) of the Patents Act as a strategy and subsequently seek a CL by using it as a commercial tool under the guise of better access to medicines, rather than a measure of last resort. Internationally, in various multilateral forums, India has advocated for the broad adoption and implementation of legislation that facilitates the use of CLs, contrary to the spirit of the TRIPS Agreement. A market with ongoing threats of CLs perpetuates an unreliable environment for patent protection and investment.

In addition, Section 146 of the India Patents Act further exacerbates the uncertainty and scope of India's CL provisions. Rules promulgated under that section require all patent holders to file an annual statement summarizing "the extent to which the patented invention has been worked on a commercial scale in India."[183] Notwithstanding the commercially sensitive nature of information required to satisfy Section 146, it also provides an impermissible basis for local companies to seek compulsory licenses, as occurred in 2012. Moreover, the rationale for requesting this information is unclear, and appears merely to be a disguise for facilitating questionable administrative challenges to existing patents.

We believe that resort to CLs is not a sustainable or effective way to address health care needs. Voluntary arrangements independently undertaken by our member companies can better ensure that current and future patients have access to innovative medicines. Statements from the Government incorrectly imply that CLs are widely used

[182] Department of Industrial Policy and Promotion, Press Release, Oct. 22, 2014, available at http://dipp.nic.in/sites/default/files/ipr_PressRelease_24October2014_0.pdf (last visited Feb. 7, 2019); "National Intellectual Property Rights Policy," May 12, 2016, available at http://dipp.nic.in/sites/default/files/National_IPR_Policy_English.pdf (last visited Feb. 7, 2019).

[183] India Patents Act, Section 146(2).

by other governments, both developed and developing.[184] These are misunderstandings and do not justify widespread use of compulsory licensing.

At a minimum, India should ensure that CLs are exercised with extreme caution and as a measure of last resort. India should also clarify that importation satisfies the "working" requirement, pursuant to TRIPS Article 27.1.

Administrative Burdens

PhRMA welcomes the Indian Government's ongoing work to address India's patent examination backlog including the commitment to reduce examination periods from up to seven years to 18 months from initial submission. Currently, the patent applications that are being examined were filed in 2011-2013. Backlogs undermine incentives to innovate and hinder timely patient access to valuable new treatments and cures. Because the term of a patent begins on the date an application is filed, unreasonable delays can directly reduce the value of granted patents and undermine investment in future research activity. For biopharmaceutical companies, patent examination backlogs can postpone clinical trial activity and ultimately the introduction of new medicines in India. Generic manufacturers are also affected by patent examination backlogs. So long as a patent application is unreasonably delayed, generic manufacturers cannot assess whether they will have freedom to operate. That lack of certainty could discourage the launch of generic medicines or expose generic companies to damages once the patent is granted. In addition to increasing the number of patent examiners, it is equally important to assess administrative procedures that unduly extend patent examination timelines.

Section 8 of the Patents Act sets forth requirements that have been interpreted in a manner that creates heightened and unduly burdensome procedures that mainly impact foreign patent applicants – those most likely to have patent applications pending in other jurisdictions. Section 8(1) requires patent applicants to notify the Controller and "keep the Controller informed in writing" of the "detailed particulars" of patent applications for the "same or substantially the same invention" filed outside of India. Section 8(2) requires a patent applicant in India to furnish details to the Indian Controller about the processing of those corresponding foreign patent applications if that information is requested. These additional patent application processing requirements have been interpreted in a manner that creates heightened and unduly burdensome patent application procedures that mainly impact foreign patent applicants – those most likely to have patent applications pending in other jurisdictions. Further, Section 8 was enacted in 1970 when the information was only available from the applicant; much of the information sought is now publicly available on patent office websites in most major jurisdictions. For example, through the Global Dossier Initiative of five major patent offices (the U.S. Patent and Trademark Office, the European Patent Office, the State Intellectual Property Office of

[184] *See, e.g.*, http://thehill.com/blogs/congress-blog/campaign/316883-india-honors--not-dishonors--patent-laws (last visited Feb. 7, 2019). These misstatements of wide-spread use of CLs in the U.S. and the premise that CLs can resolve access problems in India have been refuted by OPPI and PhRMA.

China, the Japanese Patent Office, and the Korean Intellectual Property Office), the current file histories from each of these offices are accessible at one website. Thus, accurate information about counterpart foreign applications is readily available to the India Patent Office examiners. Recent court decisions provide greater clarity on the applicability and scope of Section 8. In particular, current jurisprudence limits Section 8 to information that is material to patentability and to deliberate failures to disclose this information.[185]

In June 2017, India became a receiving office of information accessible via the World Intellectual Property Organization Centralized Access to Search and Examination (WIPO CASE) system. However, the practical effect of India's participation as a WIPO CASE receiving country remains unclear. Despite signaling the need for clarification, the Indian Patent Office has yet to issue guidance on the scope of Section 8 or how information accessible on the WIPO CASE system affects disclosure under that section.

In view of the expressed goals to ensure consistency at the Indian Patent Office, the IP5 Patent Prosecution Highway (PPH) program may also be of interest to India. India's inclusion in this initiative will help facilitate removing anomalies in Indian patent examination process, as well as advancing India's goals of enhancing quality and consistency in Indian-issued patents. Such participation would also help to alleviate further administrative burdens on patent applicants, while also providing the relevant information to facilitate more efficient and consistent examination of patent applications in the Indian Patent Office. It would also be consistent with a key proposed amendment in the Draft Patent Amendment Rules (4 December 2018), which would provide expedited examination for: "Applicants who are eligible under an arrangement for processing an international application pursuant to an agreement between the Indian Patent Office (IPO) and any other participating Patent Office." We believe this provision should be enacted, in order to facilitate efficient and high quality patent prosecution in India under a PPH arrangement with one of the IP5 participants.

Additionally, recent requests pursuant to Section 8(2) for the translation of foreign search and/or examination reports are not only unduly burdensome but costly as well. In practice, attorneys routinely receive informal translations of foreign search and/or examination reports intermingled with local attorney advice and counsel (information subject to attorney-client privilege). Moreover, translations of the search and/or examination reports may not yet be available at the time of the Section 8(2) request.

Further, the remedy for failure to comply with Sections 8(1) and 8(2) is extreme compared to other countries with similar (but less onerous) administrative requirements. In India, the failure to disclose under Section 8 can be treated as a strict liability offense that by itself can invalidate a patent (although a recent court decision indicates some

[185] *See Telefonaktiebolaget Lm Ericsson v. Intex Technologies (India) Ltd.*, Delhi High Court Judgment dated Mar. 13, 2015 in CS (OS) No. 1045 of 2014, available at http://lobis.nic.in/ddir/dhc/MAN/judgement/16-03-2015/MAN13032015S10452014.pdf (last visited Feb. 7, 2019); *Sukesh Behl & Anr. v. Koninklijke Phillips Electronics*, Delhi High Court, 2015(61) PTC183(Del); *Merck Sharp & Dohme Corp. v. Glenmark Pharms*, Delhi High Court, 2015 (64) PTC417(Del).

flexibility for mere clerical errors). This is in contrast to a requirement that the failure to disclose be material and/or intentional as in the U.S. or Israel. Thus, India's disclosure requirement and remedy are each more burdensome as compared to other jurisdictions, thereby creating a barrier to patentability that has an unfairly greater effect on foreign patent applicants, and, in some instances resulted in India revoking patents on the grounds of non-compliance with this particular provision.[186]

Regulatory Data Protection Failures

Contrary to its TRIPS Article 39.3 obligation, India fails to ensure that there is no unfair commercial use of the regulatory data submitted by another party in securing marketing approval in India or in a third country. Rather, when a pharmaceutical product has been previously approved by a Regulatory Authority in India or in another country, India requires only limited clinical data (in some cases involving as few as 16 Indian patients). This is *in lieu* of requiring submission of the entire dossier for review by India's Regulatory Authority. Moreover, in some instances when an applicant seeks approval for a generic or biosimilar product that has already been approved abroad, Indian authorities waive the requirement to submit even this data.[187] In those circumstances, any subsequent approval of the drug in India is based entirely on the prior approval of the drug in a third country.

By linking approval in other countries that require the submission of confidential test and other data to its own drug approval process, India, in effect, uses those countries as its agents. Approval by the Indian regulatory authorities based on third-country approvals amounts to indirect reliance on the clinical trial and other test data that underlie the third-country approvals. This indirect reliance results in unfair commercial use prohibited by TRIPS Article 39.3.

Market Access Barriers

High Tariffs and Taxes on Medicines

PhRMA member companies operating in India face high effective import duties for active ingredients and finished products. Though the basic import duties for pharmaceutical products average about 10%, due to the integrated GST imposed on imports, the effective import duty can exceed 20%. Moreover, excessive duties on the reagents and equipment imported for use in research and development and manufacture of biotech products make biotech operations difficult to sustain. Compared to other Asian countries in similar stages of development, import duties in India are very high. And while

[186] *See, e.g.*, *Ajantha Pharma Ltd. v. Allergan*, Intellectual Property Appellate Board (2013).

[187] *See* Rules 122A and B of the Ministry of Health and Family Welfare, "The Drugs and Cosmetics Rules, 1945 (as amended up to the 30th June, 2005)," available at http://www.cdsco.nic.in/writereaddata/Drugs&CosmeticAct.pdf (last visited Feb. 7, 2019).

certain essential and life-saving medicines may be granted exemptions from some of the taxes, the eligibility criteria are vague and subject to constant revision and debate.[188]

GST was implemented in July 2017 and, while it is expected to significantly reduce layers and complexity in the indirect tax system, it levies an additional 5-12% tax on medicines.[189] Proposals to exempt certain life-saving drugs from GST and customs duties should be expanded to all medicines.[190]

Insufficient Financing and Low Access to Care

PhRMA's members are concerned about the general lack of access to health care in India. The Indian government released the National Health Policy in March 2017[191] and the NHPS in February 2018, which calls for greater access to health care for low-income patients. The policy denotes expanding comprehensive primary health care through "Health and Wellness Centres," including care for major non-communicable diseases (NCDs), mental health, geriatric health care, palliative care and rehabilitative care services. The policy also calls for increasing public health expenditure to 2.5% of GDP by 2025.

India has insufficient numbers of qualified health care personnel, inadequate and poorly equipped health care facilities, and most importantly lacks a comprehensive system of health care financing that would pool financial risk through insurance and help to share the cost burdens.[192] Despite the encouraging and ambitious goals in the new National Health Policy, government spending on health care remains at about 1.4% of GDP, one of the lowest levels of expenditure in the world.[193] Without increased resources (both in terms of government spending and through reducing barriers for commercial health insurance) and a full implementation of the reform, high out-of-pocket spending on health care and pressure on the cost of medicines will persist.

Discriminatory and Non-Transparent Pharmaceutical Pricing Policies

Despite decades of government price controls in India, the objective of which has been to improve access to medicines, essential medicines are still not easily accessible.

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[188] *See, e.g.*, Business Standard, "Puzzle in Wednesday order on duty exemption," Feb. 19, 2016, available at http://www.business-standard.com/article/companies/puzzle-in-wednesday-order-on-duty-exemption-116021800993_1.html (last visited Feb. 7, 2019).

[189] *See*, Ernst & Young, GST Implementation in India, http://www.ey.com/in/en/services/ey-goods-and-services-tax-gst (last visited Feb. 7, 2019)

[190] Hindu Business Line, "GST: The right prescription," Aug. 5, 2016, available at http://www.thehindubusinessline.com/specials/pulse/gst-the-right-prescription/article8949378.ece (last visited Feb. 7, 2019).

[191] Available at http://cdsco.nic.in/writereaddata/National-Health-Policy.pdf (last visited Feb. 7, 2019).

[192] "Health Systems Financing: The Path to Universal Coverage," *The World Health Report*, World Health Organization, 2010.

[193] *Supra* n. 17171.

Still, India has thousands of manufacturers of pharmaceuticals who operate in a very competitive environment, and as a result, India has some of the lowest prices of medicines in the world.[194] Focusing on the key barriers to access in India – insufficient financing, infrastructure, and quality – would significantly improve access to medicines for patients.

In 2014, an Inter-Ministerial Committee was constituted to suggest a methodology to be applied to pricing of patented medicines before their marketing in India.[195] Earlier, a DoP Committee on Price Negotiation for Patented Drugs report in February 2013 recommended an international reference pricing scheme with a purchasing power parity adjustment for government procured patented medicines, with those patented medicines to be provided through health insurance. A final decision based on the recommendations of the 2014 Inter-Ministerial Committee has yet to be made. However, PhRMA members are highly concerned that the threat of the 2013 or follow-on recommendations represent a potential effort to significantly reduce the benefits of patent protection, which will *de facto* discriminate against importers in order to pacify the domestic industry, and will create an unviable and unbalanced government pricing framework and business environment for innovative pharmaceutical companies.

The recent price control orders on coronary stents and knee implants, and the threat of an existing recommendation to implement price controls on patented medicines, significantly reduce the benefits of patent protection and create an unviable business environment for the innovative industry. We appreciate the DOP January 2019 amendments to Paragraph 32 of the DPCO 2013. Specifically, the government rescinded a discriminatory provision against foreign companies which had previously exempted only patented medicines developed in India from price controls for five years from the commencement of marketing in India. The amendments also exempt patented medicines developed outside of India. This was a welcome pro-innovation policy, however, the broad authority granted to the NPPA and continued lack of transparency, predictability, and trust in the decision-making process hinders further investment in India.

Furthermore, expansion of price controls to a larger range of medicines will not substantially improve access to medicines in India because lack of access is more a function of insufficient health care financing, poor access to physicians, and inadequate health care facilities.[196] For example, even medicines and vaccines that are offered free of charge often do not reach the patients who need these medicines.[197] A 2015 study by

[194] Analysis based on IMS MIDAS Data.

[195] Government of India Speed Post No. 31011/5/2009/PI-II(pt), Ministry of Chemicals & Fertilizers, Department of Pharmaceuticals, Subject: Inter-Ministerial Committee on Prices of Patented Drugs. New Delhi, Feb. 17, 2014.

[196] "A Study of Healthcare Accessibility," Dr. DY Patil Medical College, Pune, India, prepared for India Health Progress, Mar. 2011. Wagstaff, Adam, "Health System Innovation in India Part I: India's health system challenges," available at http://blogs.worldbank.org/developmenttalk/health-system-innovation-in-india-part-i-india-s-health-system-challenges (last visited Feb. 7, 2019).

[197] "India Turns to Mobile Phones in Bid to Improve Vaccination Rate," *India Real Time/Wall Street Journal*, Aug. 4, 2011. Patra, Nilanjan, "'When Will They Ever Learn?': The Great Indian Experience of

IMS – "Analyzing the Impact of Price Controls on Access to Medicines" – found that price controls are neither an effective nor a sustainable strategy for improving access to medicines. The study further found that the primary beneficiaries of price controls have been high-income patients, rather than the intended low-income population.[198] A considerable body of evidence demonstrates that price controls contribute to lower investment in pharmaceutical research and development, ultimately harming patients who are in need of improved therapies.[199]

PhRMA members believe that competitive market conditions are the most efficient way of allocating resources and rewarding innovation; however, the research-based pharmaceutical industry recognizes the unique circumstances in India and is committed to engaging with the Government to discuss pragmatic public policy approaches through industry and public consultations that will enable the development of simple and transparent government pricing and reimbursement mechanisms that provide access to medicines, reward R&D and innovation, encourage clinical trials, include the patient perspective, and encourage continued investment into unmet medical needs.

Unpredictable Environment for Clinical Research & Drug Approval

India has many of the components of an effective regulatory system, such as institutional capacity across central and state regulators and a robust technical framework. India also has several components to support a broader ecosystem for clinical research and drug development, such as the presence of a highly skilled workforce of qualified scientists, hundreds of medical colleges, and a large and diverse patient pool. Still, India faces the consequences of an unpredictable regulatory environment as clinical trials falter[200] and new medicines face significant launch delays.[201]

We welcome the fact that the MOHFW and the Central Drugs Standard Control Organization (CDSCO) have undertaken regulatory reform efforts with the goal of strengthening the regulatory regime and reinvigorating clinical research. Strong, transparent and predictable regulatory frameworks are essential to protecting patients as well as to promoting globally-competitive innovative and generic pharmaceutical industries. In 2016, the Indian Government announced its intention to revise the Drugs &

Universal Immunisation Programme," Dec. 2009, available at http://www.isid.ac.in/~pu/conference/dec_09_conf/Papers/NilanjanPatra.pdf (last visited Feb. 7, 2019).

[198] IMS, "Assessing the Impact of Price Control Measures on Access to Medicines in India." June 2015.

[199] "Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Consumers, Pricing, Research and Development, and Innovation," U.S. Dept. of Commerce, Int'l Trade Administration, Dec. 2004. Vernon, John, "Drug Research and Price Controls," *Regulation*, Winder 2002-2003.

[200] Scrip, "Industry Sponsored Trials Fall Sharply In Challenging Indian Environment," Sept. 8, 2016, available at https://scrip.pharmamedtechbi.com/SC097232/Industry-Sponsored-Trials-Fall-Sharply-In-Challenging-Indian-Environment (last visited Feb. 7, 2019); Asia Sentinel "Southeast Asia Steals Indian Pharma," July 14, 2014, available at http://www.asiasentinel.com/econ-business/southeast-asia-steals-indian-pharma/ (last visited Feb. 7, 2019).

[201] Ernst R. Berndt and Iain M. Cockburn. The Hidden Cost of Low Prices: Limited Access to New Drugs in India. *Health Affairs*, 33, no.9 (2014): 1567-1575.

Cosmetics Act and Rules "to make it easier for companies to do business while ensuring the safety and efficacy of medicines."[202] However, MOHFW has yet to issue the final New Drugs & Clinical Trials Rules. In the meantime, inconsistencies and ambiguities continue to prevail in the Indian regulatory space, resulting in lack of clarity and a cumbersome approval process for trial sponsors. In particular, the Indian regulatory system exhibits slow approval times, ambiguities in the interpretation of compensation rules, and a lack of an appeals mechanism in decisions about causation. The piecemeal approach to reform continues to reinforce the unpredictability of the clinical trials regime and the slow resurgence of trials, especially in the presence of global multiregional trials. Such uncertainty in the regulatory process for clinical trials threatens the overall clinical research environment in India, as well as the availability of new treatments and vaccines for Indian patents.

The Indian Government, as per the notice issued on August 4, 2016, has taken several measures to improve the clinical trial environment, such as removal of restrictions on the number of trials that may be conducted by an investigator at a given point of time, the minimum number of beds at the clinical trial site, and the need to obtain an objection certificate from the DCGI in case of addition or deletion of new clinical trial site or investigator.[203]

Still, challenges remain. Rule 122 DAB of the Drugs & Cosmetics Rules (1945) originally dated January 30, 2013, and subsequently amended on December 12, 2014, is overly broad and lacks a legally or scientifically sound process for determining causality of injury. Definitions for "trial related injury," "standard of care," and "medical management" remain uncertain. Further, clinical trial waiver decisions related to cases of national emergency, extreme urgency, epidemics and for orphan drugs for rare diseases can be considered but are often highly subjective. The shared recommendation of the Drug Technical Advisory Board (DTAB) on February 16, 2015, and the Apex Committee on July 26, 2016, to amend the Drugs and Cosmetics Rules (1945), permitting waiver of local clinical trial for approval of new drugs if already approved and marketed in a well-regulated country, has not been acted upon.

As a result, there is great uncertainty relating to future costs and liabilities associated with conducting trials in India, resulting in many sponsors not launching trials in India until these uncertainties have been resolved. Research shows that if India were to address outstanding concerns with clinical trials regulations, India could see an increase in the number of new clinical trials per year to above 800, adding over $600 million in economic gains.[204] Greater clarity and predictability are needed for

[202] Reuters, "India to revise drugs law, draft new rules for medical devices," June 22, 2016, available at http://in.reuters.com/article/us-india-drug-lawmaking-idINKCN0Z819O (last visited Feb. 7, 2019).

[203] CDSCO Notice, Aug. 4, 2016, available at http://www.cdsco.nic.in/writereaddata/NOTICE%20DATED%204th%20August%202016.pdf (last visited Feb. 7, 2019).

[204] Pugatch Consilium, "Quantifying the Economic Gains of Strengthening India's Clinical Research Policy Environment." Sept. 2015, available at http://www.pugatch-

administrative procedures of drug registration applications and drug review standards and procedures in order to make the latest research products available in India.

consilium.com/reports/Quantifying%20the%20Economic%20Gains%20from%20Strengthening%20the%20Clinical%20Research%20Policy%20Environment%20in%20India.pdf (last visited Feb. 7, 2019).

INDONESIA

PhRMA and its member companies operating in Indonesia remain concerned with the country's discriminatory intellectual property (IP) policies, the market access barriers as well as limited anti-counterfeiting enforcement efforts. These barriers stem from the lack of legislative and regulatory transparency and advance consultation. As a result, PhRMA's member companies continue to face significant market access constraints.

Key Issues of Concern:

- **Restrictive patentability criteria**: 2017 amendments to the Patent Law preclude patents on new uses (indications) and establish an additional patentability criterion of "increased meaningful benefit" for certain forms of innovation, such as new salts or new dosage forms. These restrictions are overly broad and will undermine support for important innovations and appear to conflict with existing international obligations by imposing additional or heightened patentability criteria that discriminate against particular classes of technology. We are also concerned by amendments to the Patent Law that would impose new patent disclosure requirements regarding the source and origin of genetic resources. Such requirements introduce uncertainties into the patent system that inhibit innovation in relevant technologies and undermine the potential of benefit-sharing.

- **Compulsory licensing**: Indonesia has issued compulsory licenses (CLs) on nine patented pharmaceutical products (in 2004, 2007 and 2012), despite concerns raised by the affected PhRMA member companies. PhRMA is troubled by Indonesia's decision to issue these licenses, which were granted without attempts to engage with the affected PhRMA member companies to find more sustainable and long-term solutions and in a manner that appears inconsistent with Indonesia's international obligations. PhRMA is also concerned by 2017 amendments to the Patent Law and implementing regulations, which include provisions that discourage voluntary licensing between private parties and promote compulsory licensing on grounds that are vague or appear to be inconsistent with Indonesia's international obligations. PhRMA member companies are prepared to work collaboratively with Indonesian authorities to find solutions that benefit patients in Indonesia while maintaining adequate and effective IP protection.

- **Registration delays**: PhRMA member companies continue to face burdensome regulatory delays in the registration process of new products, in contravention of Indonesia's own regulations. We understand that efforts to achieve stronger conformance with international best practices are being made with respect to regulatory timelines and processes as part of the ASEAN Pharmaceutical Regulatory Harmonization. We encourage the Indonesian Government to also make efforts to achieve stronger conformance with international best practices with respect to regulatory data protection and bioequivalence requirements.

- **Forced localization requirements**: Government policies driving forced localization requirements have been increasing. The local manufacturing and technology transfer requirements of Decree 1010, and the apparent requirement in the recent Patent Law that patented products be made in Indonesia, are discriminatory, difficult to implement, or implemented inconsistently. Indonesia's positions contravene its obligations under the World Trade Organization (WTO) rules, which prohibit members from discriminating based on whether products are imported or locally produced. Specifically, Article 27.1 of the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) states that "patents shall be available and patent rights enjoyable without discrimination as to the place of invention, the field of technology and whether products are imported or locally produced." These requirements will have lasting implications for market access and patient health in Indonesia. To prevent import restrictions on innovative medicines, it is imperative that a solution is reached to allow all legitimate high-quality pharmaceuticals to be traded, sold and distributed in Indonesia, regardless of origin.

- **Cost-Focused Formulary Decisions**: While Indonesia is to be commended for developing guidelines and an online portal (eFORNAS) for listing new molecules on the Indonesian National Formulary, actual listing decisions appear to be primarily based on price and the overall Social Insurance Administration Organization (BPJS) budget. Consistent with the guidelines, listing decisions should better reflect all of the evidence submitted, including scientific data demonstrating the drug's safety and efficacy. To this end, PhRMA's member companies are encouraged by the fact that the government procurement agency is considering implementation of Multiple Criteria Decision Analysis (MCDA) for procuring pharmaceuticals.

- **Mandatory Halal certification**: On September 25, 2014, the Indonesian Parliament passed the Halal Products Law. The Law has broad application to all consumables, including pharmaceuticals, and requires that producers label their products as "halal" or as "non-halal," based on whether the products are halal certified. PhRMA's member companies are strongly supportive of religious and cultural sensitivities, but are concerned that this mandatory labeling requirement could have unexpected negative implications on patient health.

For these reasons, PhRMA requests that Indonesia remain on the **Priority Watch List** in the 2019 Special 301 Report, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protection

Restrictive Patentability Criteria

The recently revised Patent Law would preclude patents on new uses (indications) and establish an additional patentability criterion of "increased meaningful benefit" for

certain forms of innovation, such as new salts or new dosage forms. These restrictions undermine support for important innovations and are contrary to existing international obligations by imposing additional or heightened patentability criteria in a manner that discriminates against particular classes of technology.

Additional substantive requirements for patentability beyond that the invention be new, involve an inventive step and capable of industrial application, are inconsistent with the TRIPS Agreement. Article 27 of the TRIPS Agreement provides a non-extendable list of the types of subject matter that can be excluded from patent coverage, and this list does not include new uses of existing compounds. Therefore, the new Patent Law appears to be inconsistent with the framework provided by the TRIPS Agreement. Moreover, the new Patent Law imposes an additional hurdle for patents on inventions specifically relating to chemical compounds and, therefore, is in conflict with the non-discrimination principle provided by TRIPS Article 27.

To bring valuable new medicines to patients, biopharmaceutical innovators must be able to secure patents on *all* inventions that are new, involve an inventive step and are capable of industrial application. Restrictions that narrow patentability prevent innovators from building on prior knowledge to develop valuable new and improved treatments that can improve health outcomes and reduce costs by making it easier for patients to take medicines and improving patient adherence to prescribed therapies.

Burdensome and Vague Disclosure Obligations

The amended Patent Law also requires disclosure of the origin of genetic resources or traditional knowledge "related" to inventions. We support the objectives of the Convention on Biological Diversity ("CBD") and recognize the national sovereignty of States over biological resources. However, such requirements introduce uncertainties into the patent system that inhibit innovation in relevant technologies and undermine the potential of benefit-sharing. We therefore recommend eliminating this vague requirement, which is likely to cause uncertainty for innovators and undermine the sustainable use of technology related to biological resources.

Compulsory Licensing

Between 2004 and 2012, Indonesia issued CLs on nine patented pharmaceutical products. PhRMA is troubled by Indonesia's decision to issue government use permits without attempts to engage the affected PhRMA member companies in discussions to find more sustainable and long-term solutions. We are further concerned that a number of patents on different products were aggregated together and dealt with as a group rather than considering each on its merits as required by Article 31(a) of TRIPS. In addition, other than the stipulated remuneration, there is no ability to appeal the CL or otherwise obtain judicial or other independent body review, as required by TRIPS Article 31(i).

The amended Patent Law and implementing regulations create further uncertainty in this area by discouraging voluntary licensing agreements between private parties and

by promoting compulsory licensing on grounds that are vague or appear to be inconsistent with Indonesia's international obligations. In particular, the Patent Law unnecessarily requires disclosure of private licensing agreements and allows compulsory licensing if a patented product is not being manufactured in Indonesia within 36 months of receiving a patent grant. Requiring disclosure of private agreement terms would discourage entry into such agreements to the detriment of Indonesia. The local manufacturing requirement would also appear to contravene Indonesia's national treatment obligations (including TRIPS Article 27.1), pursuant to which manufacturers should be able to meet the "local working" requirements through importation.

Indonesia should make clear in its law that any compulsory licensing action needs to be taken on a patent-by-patent basis with full consideration of particular circumstances in each case. CLs should only be used in extraordinary circumstances as a last resort rather than standard government practice. As a general matter, CLs are not a sustainable or effective way to address health care needs. Voluntary arrangements independently undertaken by member companies better ensure that current and future patients have access to innovative medicines.

Market Access Barriers

Registration Delays

PhRMA member companies continue to face burdensome regulatory delays in the registration process of new products. There are a variety of causes for the unpredictable delays, which ultimately result in new products being temporarily or permanently blocked from entering the market. It is uncertain whether the lack of attention to new product applications is due to insufficient personnel capacity or other regulatory reasons. In addition to regulatory delays, PhRMA member companies would like to see Indonesia take steps to bring the National Agency for Food and Drug Control (BPOM) further in line with international best practices, namely in regard to regulatory data protection and bioequivalence requirements.

PhRMA members are encouraged to note that BPOM hired 20 additional registration staff in 2015 and plans to hire more staff in 2019; however, that increase in staffing is not nearly sufficient to meet BPOM's current need. Both BPOM and the industry have agreed to improve the know-how and skills of their registration staff in order to improve the timeliness of the regulatory review process. PhRMA and its members recommend that BPOM evaluate the registration fees to ensure that it has sufficient resources and personnel to review marketing approval applications in a timely manner.

Forced Localization Requirements

Ministry of Health (MOH) Decree 1010/MENKES/PER/XI/2008 ("Decree 1010"), formally implemented in November 2010, prevents multinational research-based pharmaceutical companies from obtaining marketing authorization for their products. Under Decree 1010, only companies registered as "local pharmaceutical industry" are

granted marketing approval. As several of PhRMA's member companies do not manufacture products in Indonesia, they are instead classified as distributors, or "PBF" enterprises. They are so classified despite following globally recognized good manufacturing practices in the same manner as other high quality pharmaceutical firms manufacturing in Indonesia. Product of multinational research-based pharmaceutical companies and other foreign companies are barred from the Indonesian market unless (1) a local manufacturing facility is established; or (2) sensitive IP is transferred to another pharmaceutical firm with local manufacturing facilities in Indonesia. The first condition is not possible for many PhRMA member companies, given the structure of their global pharmaceutical supply chains. The second condition poses a serious threat to IP protection and patient safety.

Another key concern of PhRMA member companies with Decree 1010 is the requirement to locally manufacture imported products within five years after the first importation with some exceptions, *e.g.*, products under patent protection. Even for companies with local manufacturing facilities in Indonesia, this is not always possible for several reasons, including the structure of their global pharmaceutical supply chains and lack of required technology within their local facilities to produce innovative products.

Rather than amend Decree 1010 to mitigate damaging provisions, the MOH created Decree 1799 on December 16, 2010, altering the definition of local manufacturing and introducing the concept of partial manufacture. PhRMA's member companies have sought clarification on several vague and conflicting provisions of Decree 1799 since its release. The guidelines for Drug Registration (popularly known as the Brown Book), issued in July 2011 and revised in 2013 and 2016, were comprehensively renewed in November 2017; some of the provisions in this latest Brown Book provided leeway for PhRMA's member companies to comply with the requirement to locally manufacture imported products within five years of patent expiration. However, under the new Patent Law, the requirements have been made more restrictive and appear to require a patent holder to manufacture or use the relevant patented product or process in Indonesia. Patent holders are required to seek an exception from fulfilling the local manufacturing requirement. While PhRMA's member companies acknowledge the initial steps taken by BPOM to engage in consultations, key concerns remain unresolved and several provisions of Decree 1010, 1799, and the new Patent Law and its implementation regulations still require further clarification.

As a result of the Presidential Instruction No. 6/2016 to accelerate the development of the pharmaceutical and medical device industry in Indonesia, the Minister of Industry is planning to impose a local content requirement as one of the criteria for government procurement for biopharmaceutical and medical device products. The method to calculate the threshold lacks clarity such that it may be impossible to implement or to monitor, and might create another barrier to access to medicines and health care for patients.

In short, PhRMA's member companies are concerned about the localization requirements as well as the lasting implications to market access, IP protection, and patient health if unresolved.

Cost-Focused Formulary Decisions

While Indonesia is to be commended for developing guidelines and an online portal (eFORNAS) for listing new molecules on the Indonesian National Formulary, actual listing decisions appear to be primarily based on price and the overall BPJS budget. Consistent with the guidelines, listing decisions should better reflect all of the evidence submitted, including scientific data demonstrating the drug's safety and efficacy. PhRMA's member companies are encouraged by the fact that the government procurement agency is considering implementation of MCDA in their procurement system.

Mandatory Halal Certification

Indonesia's Mandatory Halal Certification Bill, enacted in September 2014, mandates Halal certification and labeling for food and beverages, medicines, cosmetics, chemical products, biological products, and genetically-engineered products. The legislation establishes a new Halal certification authority, and requires pharmaceutical firms to hire a Halal specialist and disclose sensitive product formulas to the new Halal authority.

Despite public opposition to the Law, including the objection of the Ministry of Health, the most recent draft of the government regulation on the implementation of the Halal Law unfortunately still includes drugs and cosmetics in the regulation. As yet, the President has not signed the proposed regulations. PhRMA's member companies recognize and support the religious and cultural sensitivities of all Indonesians, but are concerned that these measures may have negative implications for patient health. In particular, significant questions remain regarding the process for securing halal certification and how the government will ensure that the new requirements do not impact patient access to the medicines they need.

Counterfeit Medicines

Although PhRMA's member companies welcome Indonesia's ongoing efforts to promote the use of safe medicines, there is an urgent need to expand national enforcement efforts. Although new leadership at BPOM have focused their efforts on combatting counterfeit food and medicine products, the budget and resources for this effort remain inadequate. Increasing and enforcing the penalties for criminals caught manufacturing, supplying, or selling counterfeit pharmaceuticals as well as unsafe medicines will greatly assist Indonesia's efforts to reduce the harmful impact of counterfeit medicines.

Research conducted by Masyarakat Indonesia Anti-Pemalsuan (MIAP), Indonesia's anti-counterfeiting society, suggests that losses incurred by the state as a result of counterfeiting continue to rise each year. Greater collaboration and government initiatives, such as a nationwide campaign and devoted budget to combat counterfeit products, should be intensified to ensure the health and safety of Indonesian patients.

THAILAND

PhRMA's member companies face significant intellectual property (IP) and market access concerns in Thailand. Thailand does not provide equitable and reasonable market access to new medicines developed and manufactured in the United States. Furthermore, many of the reforms proposed by the Government of Thailand are out of step with international or regional best practices.

Key Issues of Concern:

- **Inequitable Access to the Thai Market due to Deficient IP Protections and Enforcement**: The Government of Thailand's failure to provide appropriate and predictable IP protections and enforcement hinders the ability of U.S. innovators – in particular, biopharmaceutical innovators – to equitably and reasonably access the Thai market. Key IP concerns in Thailand include significant patent backlogs, failure to provide meaningful regulatory data protection (RDP) and broad, vague, and non-transparent standards for compulsory licenses (CLs). Despite some indications that the Royal Thai Government might improve its environment for innovative pharmaceuticals, limited steps have been taken to address these longstanding challenges.

- **Discriminatory and Non-Transparent Government Procurement Policies**: The Thai Government continues to implement policies that favor the domestic Thai industry at the expense of medicines imported from the United States. These policies have created discriminatory and unpredictable procurement practices that drastically and arbitrarily cut prices of U.S. products and harm the ability of U.S. companies to compete in Thailand.

For these reasons, PhRMA requests that Thailand be placed on the **Priority Watch List** in the 2019 Special 301 Report, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protections

Significant Patent Backlogs

In 2013, the Department of Intellectual Property (DIP) finalized the Patent Examination Guidelines to complement the Thai Patent Act. The innovative biopharmaceutical industry was invited to provide its input during the drafting, which was appreciated. The Patent Examination Guidelines were intended to set clear benchmarking and examination rationale which would enhance transparency in patent registration as well as help ensure balance and fairness with respect to innovative products.

While the DIP has taken some important initial steps to help clear the patent backlog – including hiring more patent examiners – the waiting-period for a patent review

and grant in Thailand remains unpredictable and averages ten years after application submission. Further, these long patent grant delays create uncertainty regarding investment protection and increase the risk that a third party will use a patentable invention that is the subject of a pending patent application during the pending/review periods. Indeed, at least one PhRMA member has experienced a third-party launch of a product that was the subject of a pending patent application. In that instance it took over 18 years for the patent to be granted, and even then the member was unable to obtain meaningful enforcement of the patent. Patent term adjustments are not available in Thailand to compensate for unreasonable patent office delays, thereby reducing the effective patent term and further exacerbating the uncertainty caused by its patent grant delays.

Additionally, though some of the recent draft amendments to the Patent Act seek to streamline some procedures during the patent application process, other draft provisions could undermine efforts to support innovation and further exacerbate Thailand's backlog. For example, one draft amendment seeks to introduce a pre-grant opposition mechanism allowing third-parties to oppose a patent application up to the date of patent grant.

Regulatory Data Protection Failures

Ministerial regulations issued by the TFDA regarding the Trade Secrets Act of 2002 do not provide RDP that would prevent generic or biosimilar drug applicants, for a fixed period of time, from relying on the innovator's regulatory data to gain approval for generic versions of the innovator's product. The Act aims only to protect against the "physical disclosure" of confidential information.

PhRMA's member companies strongly encourage the Royal Thai Government to institute meaningful RDP. Specifically, Thailand should: (1) implement new regulations that do not permit generic or biosimilars producers to rely directly or indirectly on the originators' data, unless consent has been provided by the originator, for the approval of generic or biosimilar pharmaceutical products during the designated period of protection; (2) bring the country's regulations in line with international standards by making clear that data protection is provided to test or other data submitted by an innovator to obtain marketing approval; (3) provide protection to new indications; and (4) require TFDA officials to protect information provided by the originator by ensuring it is not improperly made public or relied upon by a subsequent producer of a generic or biosimilar pharmaceutical product.

Compulsory Licensing

Despite assurances that Thailand would be judicious in its use of CLs and consult with affected parties as required by the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), Thailand continues to threaten the use of CLs. Further, royalty payments have not been made on products for which CLs have been issued. Thailand's compulsory licensing regime lacks sufficient due

process and dialogue with affected companies, and suffers from a lack of transparency in the reasoning behind CL decisions.

Market Access Barriers

Inconsistent and Unpredictable Median Procurement Price

The Thai Ministry of Public Health (MoPH) and the National Drug System Development Committee are authorized to establish a "median procurement price" for pharmaceuticals. In practice, this price is not calculated as a median, but rather used as a "maximum procurement price" (MPP) for each medicine, and the current methodology and implementation lacks transparency, predictability, and consistency resulting in inequitable market access for research based pharmaceutical companies. In fact, a recent MPP Impact Analysis (MIA) reviewed the MPP process from November 2016 through October 2017, and determined that across the fifteen product categories subject to MPP, there was no discernible rationale or order for how the MPP was set. Moreover, although the MPP system was originally established for products identified in the National List of Essential Medicines (primarily generic products), more than 75% of medicines now subject to the MPP process are in fact innovative medicines.

Moreover, the current methodology and implementation of the MPP policy lacks transparency, predictability, and fairness. For example, companies are still required to "negotiate" a price, but in reality very little negotiation occurs. Although the MoPH has made some adjustments to the notification period surrounding MPP announcement, products are nevertheless subject to price cuts at irregular intervals, disrupting the business plans of U.S. companies and, additionally, there is no independent appeals process. The MoPH utilizes several methods to determine the MPP including by reference to prices in other countries, even though there is no consistently defined basket of reference countries and even when such countries are not comparable in terms of their patient populations and health care systems. In other cases, the Thai Government may also selectively set price of patented medicines based on prices of generic medicines, which undermines intellectual property rights and the value of innovation. Overall, these actions have resulted in price cuts of 50-90% for U.S. products, contributing to an increase in the trade deficit and a loss of market share.

The MPP policy is inconsistent with Thai Government efforts to foster a positive business environment based on good governance, ease of doing business, and rule of law. The MPP process combined with Thailand's recent preference for domestic companies harms U.S. innovators and could delay or prevent the introduction of new medicines. Promisingly, the recent Public Procurement Act introduced in August 2017, mandates the creation of a Reference Price Subcommittee for Pharmaceutical and Medical Supplies, which would be responsible for handling the reference price issues and standardizing the procedure. The innovative biopharmaceutical industry seeks the expedited formation of this subcommittee as well as the inclusion of members from the private sector so that a balance of stakeholders may collaborate on fair and equitable

policies that address the fiscal concerns of the Thai government in the procurement of pharmaceuticals in a fair and equitable manner.

Discriminatory Thai "Innovation" List

In 2016, the Thai Government established the Thai Innovation List, an initiative to develop domestic industrial capacity in several innovation sectors, including pharmaceuticals. Only Thai majority owned companies qualify to be listed. Once listed, Thai companies receive special government procurement privileges including an earmark for at least 30% of orders by Thai government agencies. As of October 2018, 121 Thai pharmaceutical products have been included on the "Innovation" List, even though all are generic versions of existing products. It appears that as long as the Thai company has demonstrated that their generic copy is bioequivalent, it is eligible to be included on the List. As such, the so-called Innovation List exists solely to favor local companies to the exclusion of U.S. and other foreign owned research-based biopharmaceutical companies.

Inconsistent and Non-Transparent Oncology Pre-authorization System (OCPA)

The OCPA was established in 2006 as a direct reimbursement system to hospitals for "high-cost cancer drugs" administered to patients under the Civil Servants Medical Benefit Scheme (CSMBS). The system was intended to reduce out-of-pocket disbursements for its beneficiaries, by identifying those products for which hospitals would be directly reimbursed through prior authorization and approval based upon a pre-defined protocol of individual cancer drugs in the list.

Unfortunately, the process and criteria involved in the OCPA lack predictability and are applied inconsistently between different companies and different products. Further, recent revisions to the OCPA will result in "non-direct reimbursement" for certain innovator products, based on unclear selection criteria.

Specifically, while many innovative medicines, including cancer drugs, had been directly reimbursable by the CSMBS immediately upon being granted marketing authorization, revisions to OCPA procedures in February 2018 structured reimbursements on a tiering or "Group" system: drugs in Group 1 or Group 2 will continue to be directly reimbursable, while those in Groups 3 will require patients to provide advance payment for their medicines and then apply to OCPA for reimbursement, and the cost of drugs in Group 4 will be fully paid by the patient. These revisions, which were due to government budget constraints, will create a barrier to access for patients who cannot afford to pay for their drugs. The criteria for how drugs will be placed into each of these Groups is unclear, and potentially revolve around which drugs have the lowest net procurement price. Only one product per indication will be allowed in Group 1, meaning that patients on other drugs will be forced to pay for their drugs or switch to the product placed in Group 1.

Discriminatory Privileges for the Government Pharmaceutical Organization (GPO)

The GPO – a Thai State enterprise that manufactures pharmaceutical products in Thailand – enjoys discriminatory privileges. Per Ministerial Regulation B.E.2560 (2017), MoPH must procure at least 80% of NLEM medicines from the GPO or the Thai Red Cross and other central government and regional government offices must procure no less than 60 percent from these entities. In addition to these procurement preferences, under the Drug Act B.E. 2510 (1967), the GPO is not required to obtain FDA approval prior to launching medicines on the Thai market. There is no such exemption for private sector manufacturers or sellers, all of whom must obtain market authorization from the Thai FDA prior to selling their products in the Thai market.

Amendments to the Drug Act (Drug Bill)

The current legislation that regulates the pharmaceutical industry is the Drug Act, and it has not been materially amended for more than 25 years. In 2014, the MoPH attempted to amend the Drug Act through a non-transparent process that resulted in a draft Drug Bill that included provision that would have impacted only patented pharmaceuticals. The current version of the Drug Bill takes a similar approach by requiring all innovative applicants seeking marketing approval from the Thai FDA to disclose relevant patents. However, generic applicants are not required submit or make any statements on the patent status of innovative reference products. As Thailand does not have a patent linkage system, generic marketing authorization submissions can be approved for products that would infringe relevant innovator patents.

EUROPE

RUSSIA

PhRMA and its member companies operating in Russia are concerned with a number of market access barriers, especially those linked to intellectual property protection and import substitution efforts, all of which decrease the value awarded to innovation in Russia and the benefits it brings to Russian patients.

Key Issues of Concern:

- **Compulsory licensing and restrictive patentability criteria**: The Russian Government is pursuing draft legislation and other measures that appear to improperly limit certain types of patents for innovative medicines and create vague and arbitrary criteria enabling Russia to seek compulsory licensing actions of patented medicines. In addition, Russian courts have granted (June 2018) and upheld (September 2018), a compulsory license (CL) for an innovative cancer medicine developed in the United States. The parties voluntarily settled the dispute during the appeals period. However, Russian courts are considering additional compulsory license cases.

- **Weak patent enforcement**: There is no mechanism for preliminary injunction in place in Russia to provide patent holders with the opportunity to resolve patent disputes prior to the launch of a follow-on product. Russian courts rarely grant preliminary injunctions in patent infringement cases related to biopharmaceuticals and have ruled previously that marketing authorization of competing follow-on products does not, by itself, constitute patent infringement. This has led to the approval and marketing of follow-on products during the period of patent protection. Russian regulations compound this injury by permitting prematurely launched follow-on products to participate in state procurement tenders. It is also generally not possible to obtain sufficient damages in Russia to compensate for the harm caused by premature launches.

- **Localization and restrictions for state procurement**: Despite being in the process of acceding to the World Trade Organization (WTO) Agreement on Government Procurement (GPA), Russia continues to impose pressure to locally produce finished dosage forms through its government procurement system (*e.g.*, restrictions on public procurement of imported drugs where there are at least two pharmaceuticals with locally produced finished dosage forms (so-called “three’s a crowd”), and a 15% price preference for pharmaceuticals having locally produced finished dosage forms in government procurement tenders, if “three’s a crowd” is not applicable). In addition, in June 2018 the “three’s a crowd” regulation was amended and specific preferences for local full cycle products were introduced with the aim to be implemented in 2019.

- **Pricing environment**: On October 18, 2018, a new pricing methodology for the products included on the Essential Drug List (EDL) came into force. The revisions

to the pricing methodology may discourage local investment and hinder the launch of new medicines, promoting a downward spiral for pharmaceutical prices in Russia. In addition, Ministry of Health (MoH) Order No. 871n, which sets forth the procedure for determining the initial auction prices for medicines (based, *inter alia*, on average-weighted historical prices of state tenders) entered into force in December 2017. However, automatic price referencing under the scheme for state tenders was postponed until 2019.

For these reasons, PhRMA requests that Russia remain on the **Priority Watch List** in the 2019 Special 301 Report, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protection

Compulsory Licensing

PhRMA and its member companies are deeply concerned by recent court decisions in Russia granting and upholding a CL and legislative and regulatory initiatives to expand the use of this drastic measure in the future. In its decision dated June 8, 2018, the Moscow Arbitration Court (1st Instance) granted a compulsory license (CL) under the Patent Statute for an innovative cancer medicine developed in the United States to a local generic drug company.[205] This decision was based on an extremely low evidence test and standard of proof. That decision was upheld in September 2018.[206] The innovator appealed that decision, but the parties have since settled the dispute. However, there remains the risk that this case may influence future court practice and decisions in compulsory licensing cases currently pending before Russian courts.

These court decisions are ominously consistent with Russia's broader policy goals. For example, on December 21, 2017, the Russian President signed Order No. 618 "On Key Areas for the Development of Competition Policy," which approved the National Plan for the Development of Competition in the Russian Federation in 2018-2020. According to this Competition Development Plan, the Russian Government plans to submit a draft law to the State Duma by January 1, 2019, that would allow compulsory licensing wherever it is determined to be in the interests of national security and health protection. While the Order does provide that due notification and reasonable compensation must be provided to the affected patent holder, the multinational biopharmaceutical industry is highly concerned that this would further allow the Russian Government unduly broad discretion to issue CLs.

[205] Available at http://kad.arbitr.ru/Card/322413fa-38a7-4085-9cc7-3c8ff9fd7d92 (last visited Feb. 7, 2019).

[206] Available at https://kad.arbitr.ru/PdfDocument/322413fa-38a7-4085-9cc7-3c8ff9fd7d92/288fda7f-09c8-4b3b-b1c3-9812e278cf96/A40-71471-2017_20180925_Postanovlenie_apelljacionnoj_instancii.pdf (last visited Feb. 7, 2019).

Building on the Competition Development Plan, on January 12, 2018, the Russian Government issued Decree No. 9-r, which approves the Roadmap for Development of Competition in Healthcare (the Roadmap). As one of its priorities, the Roadmap calls for amendments to Article 1360 of the Russian Civil Code by the end of 2018 that would enable the Russian Government to authorize compulsory licensing in order to lower the price of patented medicines.

Restrictive Patentability Criteria

On May 27, 2016, FAS published on its official web-site, the draft Roadmap for Development of Competition in the Healthcare Sector. As noted above, the Roadmap was approved by the Russian Government on January 12, 2018, via Decree No. 9-r. The Roadmap, *inter alia*, proposes amendments to patentability criteria, for any new property or new application of a known active ingredient of a medicinal product (including new indications, new treatment methods, new combinations, and new pharmaceutical forms and manufacturing methods).

Relevant Russian Government agencies are proceeding to implement the Roadmap. On September 14, 2018, the Federal IP Service (Rospatent) issued a draft Order to implement certain procedural changes during patent prosecution to restrict the patentability of such inventions. Furthermore, in December 2018, Rospatent issued Order No. 527 on “double patenting” of pharmaceutical compositions and their uses. PhRMA and its members are concerned that these amendments, if implemented, could restrict the availability of patents for innovative medicines in Russia, violating key provisions of the Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement.

Weak Patent Enforcement

Russia does not maintain an effective mechanism for early resolution of patent disputes before potentially infringing products enter the market. Follow-on drug manufacturers can apply for and receive marketing approval for a generic product even though a patent for the original drug is still in force. The Law on the Circulation of Medicines does not include provisions for patent status review when a company applies for marketing authorization or for price registration on the Essential Drugs List (EDL). Furthermore, Russian courts very rarely grant injunctive relief. As a result, pharmaceutical innovators face significant legal challenges in seeking to effectively protect their innovative products against infringement, resulting in significant damages that are rarely compensable.

Such practices are contrary to Russia’s obligations under TRIPS and the assurances Russia made to the WTO Working Party on the Accession of the Russian Federation to the WTO. In particular, they appear to violate TRIPS Article 41, which requires Members to provide “expeditious remedies to *prevent* infringements” (emphasis added) and provisions of Article 50 with respect to provisional measures. Russia assured the WTO Working Party that it would “counteract ... infringements of intellectual property through improvements in enforcement.”

In order to avoid unnecessary costs and time when litigating damages in patent litigation, and to increase market predictability, Russia should enable patent holders to seek and receive preliminary injunctions before marketing authorization is granted for follow-on products and afford sufficient time for such disputes to be resolved before marketing occurs. This might include a form of automatic postponement of drug registration approval, pending resolution of the patent dispute, or for a set period of time during which it could be expected that most patent disputes in Russia could be litigated.

Predictable and effective patent enforcement procedures are especially important as it relates to the establishment of the common Eurasian Economic Union (EAEU) market for medicines. In this regard, PhRMA and its member companies welcome the draft law issued by the MoH at the end of October 2018 "On Amendments to the Federal Law On Drugs' Circulation". These draft amendments require applicants seeking marketing approvals to provide the MoH information on relevant or associated intellectual property rights within the application for state registration of medicine. Industry stands ready to work with the MoH to ensure that these proposed amendments are drafted and implemented in a manner that provides robust patent protection for innovative medicines and provides business certainty for innovators and follow-on manufacturers alike. PhRMA and its member companies also welcome the proposed development of a patent register by Rospatent.

Regulatory Data Protection Failures

As part of its accession to the WTO, Russia agreed to provide six years of regulatory data protection (RDP).[207] While the Law on Circulation of Medicines[208] provides for this protection, Russia's weak judicial system is particularly concerning to PhRMA members in light of amendments to Russia's Law on the Circulation of Medicines passed in 2014. Specifically, beginning in 2016, the amendments allowed competitors to apply for marketing approval of follow-on medicines as early as four years after marketing authorization for a reference small molecule drug and three years after marketing authorization of a reference biologic medicine. While, on paper, marketing is restricted until after the six-year RDP term has expired, the lack of injunctive relief in Russia (discussed above) raises serious questions about the ability of patent owners to ensure that infringing follow-on products are not launched during the RDP term.

Parallel Imports

Currently, parallel imports are prohibited from countries outside the EAEU, based on the regional principle of exhaustion of trademark rights. However, the EAEU has discretion to allow parallel imports and recent Russian court decisions are already eroding trademark rights. In April 2017 the Board of the Eurasian Economic Commission (EEC)

[207] Report of the Working Party on the Accession of the Russian Federation to the World Trade Organization, WT/ACC/RUS/70, WT/MIN(11)/2 (Nov. 17, 2011), at para. 1295, incorporated in Protocol on the Accession of the Russian Federation, WT/MIN(11)/24, WT/L/839 (Dec. 17, 2011), at para. 2.

[208] Federal Law No. 61-FZ, dated Apr. 12, 2010, "On the Circulation of Medicines."

approved the draft Protocol on Amendments to the Treaty on the Eurasian Economic Union of May 29, 2014. If approved by all EAEU member states the Protocol would grant the Eurasian Intergovernmental Council the authority to use the international principle of exhaustion of trademark rights in respect to certain products (pharmaceuticals are one of the product groups under discussion). PhRMA and its member companies remain concerned that such exemptions could cause medicine shortages in exporting countries and compromise the security of medicine supply chains.

In the meantime, the ability of trademark owners to protect their rights against parallel imports is already being limited by the courts. On February 13, 2018 the Russian Constitutional Court published its position on parallel imports. The Court ruled that it is not allowed to apply similar sanctions against the parallel importer of an original product and the parallel importer of a counterfeit product, except in cases when the original product may cause harm similar to a counterfeit product. This Constitutional Court interpretation may affect the existing court practice on parallel imports and increase the number of cases when the trademark owner is not able to prevent parallel imports or obtain compensation from parallel importer.

Moreover, at the end of October 2018, the Federal Antimonopoly Service drafted a law (without consultation and outside the established legislative process) to amend Part IV of the Russian Civil Code to enable the Russian Government to authorize parallel imports of certain products which are: in deficit on the Russian market, or sold for excessive prices, or if their quality significantly differs from quality of analogues products circulating on the markets of foreign countries. Despite concern voiced by some member states, the EAEU Commission recently reaffirmed its activities on amending the EAEU Treaty to allow temporary application of the parallel importation regime for certain types of goods at the EAEU level. This initiative directly contradicts the EAEU Treaty and mentioned Constitutional Court decision.

PhRMA and its member companies are concerned that the Federal Antimonopoly Service announced this initiative despite the international regulations.

Market Access Barriers

Localization Barriers

Russia is in the process of acceding to the GPA, has provisions regarding accession to the GPA in its protocol of accession to the WTO, and participates in the GPA Committee as an observer.[209] Notwithstanding the GPA accession process, Russia continues discriminatory practices in its government procurement system.

On November 30, 2015, the Russian Government adopted Resolution No. 1289 “On Restrictions and Conditions of Access of Foreign Essential Medicines to State and

[209] *See* https://www.wto.org/english/news_e/news16_e/gpro_22jun16_e.htm (last visited Feb. 7, 2019) and https://www.wto.org/english/tratop_e/gproc_e/memobs_e.htm (last visited Feb. 7, 2019).

Municipal Tenders," which codifies the so-called "three's a crowd" approach in relation to medicines included on the EDL. According to Resolution No. 1289, if two or more EAEU pharmaceutical manufacturers bid on a tender for an EDL product, then any foreign bid for that same tender must be rejected. Medicines not covered by Resolution No. 1289 remain subject to the tender preferences established by the Ministry of Economic Development (MoED), where local companies receive a 15 percent price preference.

On May 12, 2018, the Russian Government adopted Resolution No. 572 "On Amendments to the Resolution of the Russian Government No. 1289," amending the so called "three's a crowd" regulation and introducing the regulatory framework for additional preferences in state procurement of essential medicines for products made using locally manufactured active pharmaceutical substances.

On November 5, 2018, Order No 126n of the Ministry of Finance (dated June 4, 2018) entered into force and introduced additional price preferences (up to 25%) for local (EAEU) finished dosage forms and full-cycle medicines.

The Russian Government has also taken a number of steps to isolate certain segments of the pharmaceutical market for sole-supply contracts given to Russian companies. For example, in March 2018, the Russian Government signed Decree No. 520-r appointing the National Immunobiological Company (NIB) as the sole supplier of certain blood products subject to procurement in 2018-2019 by a number of state purchasers. Furthermore, in April 2018, the Russian Government signed Decree No. 744-r appointing NIB as the sole supplier of certain local full-cycle immunobiological products in 2018-2019 purchased by the MoH under the National Immunization Schedule. In August 2017, the Russian Government signed Decree No. 1721-r also appointing NIB as the sole supplier of certain medicines and medical devices for the Federal Service for the Execution of Sentences in 2017-2018.

A number of other measures aimed at supporting local manufacturers are under development and implementation in Russia. For instance, on June 17, 2016, the Russian Government signed Resolution No. 548 and approved the Rules for Provision of Federal Subsidies for Partial Reimbursement of Costs Related to Patenting of Russian Inventions Abroad. The Russian Government, in its continuation of the "Pharma 2020" strategy, plans to provide additional government support and financial incentives for locally produced drugs. PhRMA and its member companies are concerned that these measures may further discriminate against foreign manufacturers, and hinder patient access to certain medicines.

Deteriorating Pricing Environment

On October 18, new Pricing Registration Rules and Pricing Methodology came into force. These measures change the methodology for calculating maximum ceiling prices for EDL medicines and skews the reference basket used to set prices towards the lowest-price in lower-income countries. It could result in a downward price spiral.

Furthermore, on November 22, 2018, the Russian Government submitted to the State Duma the draft Federal Law “On Amendments to the Federal Law "On Circulation of Medicines" in relation to the provisions governing EDL pricing”.[210] The draft law proposes re-registration of all maximum selling prices for essential medicines in 2019-2020. The draft also proposes the obligation of the foreign manufacturers to lower the prices in Russia if the prices in foreign countries go down. The State Duma submitted the draft to the relevant committees for analysis.

In addition, MoH Order No. 871n (Oct. 26, 2017), which sets forth the procedure for determining the initial auction prices for medicines (based, *inter alia*, on average-weighted historical prices of state tenders), entered into force in December 2017, but the automatic price referencing under the scheme for state tenders was postponed until January 1, 2019.[211]

Good Manufacturing Practice

Since January 2016, Russia has required local Good Manufacturing Practice (GMP) certificates for foreign producers as part of the drug registration application. Due to the timelines for GMP inspections and capacity constraints, this may hinder access to the market for U.S. and other foreign producers. PhRMA’s members welcome adoption of the Federal Law dated June 4, 2018, No. 140-FZ “On Amendments to the Federal Law On Circulation of Medicines,” which if implemented appropriately could mitigate these concerns. PhRMA’s members are also concerned with the existing discriminatory approaches exercised by the Ministry of Industry and Trade (MIT) related to GMP inspections of foreign sites. Foreign manufacturers are finding it increasingly difficult to obtain GMP certificates (the refusal rate increased from 21.8% in 2017 to 30.7% in 2018)

Additionally, in July 2018, MIT announced its intention to change the existing methodology for calculation of fees for GMP inspections and to specifically increase the fees for GMP inspections of foreign production sites.[212] Meanwhile, no fee is charged for local GMP inspections. However, PhRMA’s members hope that these constraints may be addressed through constructive dialogue between the inspectorate, MIT and the industry.

Eurasian Economic Union

The EAEU, comprised of Russia, Belarus, Kazakhstan, Armenia, and Kyrgyzstan entered into force on January 1, 2015. The treaties establishing the Eurasian Customs Union and the Single Economic Space were terminated by the agreement establishing the EAEU, which incorporated both into its legal framework. The EAEU envisages the gradual integration of the former Soviet countries’ economies, establishing a free trade

[210] Available at http://sozd.parliament.gov.ru/bill/592388-7 (last visited Feb. 7, 2019).

[211] *See* MoH Order No. 386n “On Amendemnts to the Procedure for Determining the Initinal (Maximum) Price of a Contract, Price of a Cole Supplier Contract, during State Procurement of Medicines, Approved by the MoH Order dated 26 October 2017 No. 871n” (June 26, 2018).

[212] Project ID 02/08/07-18/00082058.

area, unbarred financial interaction and unhindered labor migration. One of the first sectors to be integrated is the pharmaceutical sector through the creation of a single pharmaceutical market. To this end, the EAEU Agreement on Common Principles and Rules of Drug Circulation in the EAEU was executed in the city of Minsk on December 23, 2014, and the EAEU Intergovernmental Council approved the necessary regulations to establish a common pharmaceutical market in the EAEU entered into force on May 6, 2017.

Although the innovative pharmaceutical industry has some concerns regarding how the single pharmaceutical market is being implemented (discussed further below), we stand ready to work with the Government and Eurasian Economic Commission to ensure that there is a robust regulatory review system and continued patient access throughout the EAEU.

Orphan Drugs Legislation

The Law on the Circulation of Medicines includes a definition and an accelerated registration procedure for orphan drugs that eliminates the need for otherwise obligatory local trials. Although the industry, as a general matter, supports accelerated pathways for orphan drugs, the procedure lacks sufficient detail to fully evaluate its effectiveness. PhRMA's members are hopeful that these issues may be resolved under the EAEU regulatory framework.

Biologic and Biosimilar products in Russia

The Law on the Circulation of Medicines sets forth the basic regulations for biologics and biosimilars. Although PhRMA's members welcome Russia's actions to better regulate biologics and biosimilars, there remain some concerns regarding implementation of the relevant regulations (including assessment guidelines for biosimilar drugs, determining the interchangeability of biologic drugs, mutual recognition of inspections and import testing*, etc.*). PhRMA's members are hopeful that these issues may be resolved under the EAEU regulatory framework.

TURKEY

PhRMA and its member companies face market access barriers in Turkey due to forced localization policies, unpredictable registration timelines and reimbursement processes, strict and unpredictable government pricing and deficiencies in Turkey's intellectual property (IP) framework. Ongoing currency issues and high inflation are causing–severe pressure on prices of pharmaceuticals and threatening both supply continuity and the sustainability of the industry.

During the last decade, Turkey has undertaken reforms to modernize its economy and expand its health care system in many positive ways for Turkish patients. However, a general lack of transparency and inconsistency in decision-making has contributed to unclear policies that undermine Turkey's investment climate and damage market access for PhRMA member companies.

While PhRMA and its member companies appreciate the increased dialogue that exists between the Turkish Government and the innovative pharmaceutical industry in Turkey, and welcomes the recently passed Industrial Property Law that better aligned Turkey with the European Patent Convention, still more attention needs to be paid to the impact of Turkish government policies on the innovative pharmaceutical industries' research and development process, including the potential of PhRMA member companies to invest in Turkey.

Key Issues of Concern:

- **Weak patent enforcement and regulatory data protection failures**: While patents and regulatory test data have received IP protection in Turkey since 1995 and 2005, respectively, significant improvements are still needed. For instance, while Turkey's new Industrial Property Law, which was passed by the Turkish Parliament in 2016 better aligns Turkey with the European Patent Convention, certain provisions in the new law inappropriately expand the possibility of granting compulsory licenses (CLs) in Turkey. In addition, Turkey does not provide an effective mechanism for resolving patent disputes before the marketing of follow-on products. Further, Turkey inappropriately ties the regulatory data protection period (RDP) to the patent term and the lack of RDP for combination products is still an unresolved issue. Finally, the RDP term begins with first marketing authorization in the European Union (EU) and thus, as a result of significant regulatory approval delays in Turkey, the effective RDP term is reduced significantly. Consistent with Turkey's international obligations, the RDP term should begin when a product receives marketing authorization in Turkey.

- **Fixed Exchange Rate and Inflation**: The Turkish Government continues to set sub-optimal levels for the overall pharmaceutical budget that disregard exchange rate fluctuations. The practice Turkey uses of an international reference pricing system that employs a fixed FX rate instead of market value to convert the value

of the Euro into local currency is problematic. Though Turkish regulations specify that the exchange rate be updated at the beginning of the year to reflect 70% of the average exchange rate the preceding year, the Turkish Government set the exchange rate for 2018 below this mark. Such actions create uncertainty in the Turkish marketplace. This practice coupled with the current currency issues and high inflation (20.3 percent in 2018) is causing severe pressure on pharmaceutical prices and is threatening both supply continuity and the sustainability of the industry. Industry is asking for immediate resolution of the issue.

- **Localization policies**: Following the implementation of the 10th Development Program and provisions in Article 46 of the 64th Government Action Plan (released on December 10, 2015), the Turkish government has initiated a localization program which calls for the delisting of imported products from the reimbursement list if they are not produced locally and provides preferential reimbursement arrangements for health care products produced domestically. PhRMA member companies began receiving notices in February 2017 that their products would be delisted within 12 months unless localization plans were in place. Subsequently, new waves of product delistments were announced in May and November 2018.

- **Local inspection requirements**: PhRMA and its member companies welcome efforts by the Turkish Drug and Medical Device Agency (TITCK) to improve the regulatory approval procedures of highly innovative and/or life-saving products with no or limited therapeutic alternatives in Turkey. Specifically, prioritizing the Good Manufacturing Practices (GMP) audit procedures and allowing a parallel marketing application process for those products has decreased the delays in approving those products. However, while products deemed highly innovative are receiving preferential reviews, products without this designation face increased delays due to the lack of resources and the absence of efficient procedures for conducting GMP inspections. PhRMA and its member companies commend Turkey for becoming a PIC/S (Pharmaceutical Inspection Convention and Co-operation Scheme) member to better align its GMP inspections practices with the other members of the scheme. GMP inspection delays continue to add to registration delays, hindering patient access to innovative medicines and negating the benefits of the patent and data protection periods for many products.

For these reasons, PhRMA requests that Turkey be placed on the **Priority Watch List** in the 2019 Special 301 Report, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protection

Weak Patent Enforcement

In January 2017, Turkey enacted a new Industrial Property Law (No. 6769) to support and strengthen IP rights, including patent rights. However, the IP Court judges lack relevant training and capacity to effectively resolve disputes. Consequently, the

quality of IP trials has substantively decreased, and the IP Court judges refer and defer cases to court- appointed expert panels, which often consist of a single patent attorney and lecturers from universities. Despite the new law on court appointed experts, the expert examination system also lacks appropriate procedural safeguards. While relevant case law provides that the IP Court judge can deviate from the expert panel's opinion where he provides a reasoned opinion to the contrary, in practice, decisions in the majority of cases mirror the opinions of the panel.

Compulsory Licensing

In addition, PhRMA and our member companies are concerned about the compulsory license provisions of Industrial Property Law No. 6769. That law inappropriately expands the discretion to consider compulsory licenses in cases of *non-use* of the patent and in cases where a third-party claims that *domestic demands* are not being met. The vagueness of that provision creates tremendous uncertainty for patent holders, and may be abused by competitor third parties.

Furthermore, compulsory licensing is included as a provision in the draft registration regulation. According to the draft regulation, a guideline will be published for execution. The scope and content of this guideline is not yet known.

Regulatory Data Protection Failures

In 2005, the Turkish Government took positive steps toward establishing protection for the commercially valuable regulatory data generated by innovative pharmaceutical companies, and now provides RDP for a period of six years for products starting from the first MA registration in any of the EU-Turkey Customs Union member states. However, if a product is patented in Turkey, RDP ends when that patent expires, even if this is prior to the end of the six-year RDP term. RDP is a form of protection that serves a different purpose than patent protection and is thus independent and separate from patent protection. Therefore, it should not be limited to the period of patent protection.

Another significant concern for the innovative industry is that the period of RDP currently begins on the earliest marketing authorization in any country of the EU-Turkey Customs Union. Considering the extended regulatory approval times and delays stemming from the GMP certification approval period, current estimates are that it could take one to three years to register a new medicine in Turkey and result in approval in Turkey long after approval in the EU. Under these adverse circumstances, new products receive, in practice, no more than one to two years of RDP in Turkey, undermining incentives needed for innovators to undertake risky and expensive research and testing.

RDP in Turkey was further undermined by the Regulation to Amend the Registration Regulation of Medicinal Products for Human Use,[213] This Regulation, contrary to EU standards, eliminates RDP for combination products, unless the

[213] Official Gazette No. 27208 (Apr. 22, 2009).

combination product introduces a new indication. Innovative companies invest considerable amounts of time and effort to develop products that provide increased efficacy and safety, as well as new indications, from new combinations of separate molecules.

In addition, Turkey does not provide RDP for biologics. RDP is essential for all medicines, and particularly critical for biologic therapies. Made using living organisms, biologics are complex and challenging to manufacture and may not be protected adequately by patents alone. Unlike generic versions of traditional chemical compounds, biosimilars are not identical to the original innovative medicine and there is greater uncertainty about whether an innovator's patent right will cover a biosimilar version. Without the certainty of RDP, innovators will not have the incentive needed to conduct the expensive, risky and time-consuming work to discover and launch new biologics.

Market Access Barriers

Localization Policies

PhRMA and its members have serious concerns about the Turkish government's implementation of its forced localization efforts for medicines. In 2018, the Turkish Government began to implement policies[214] announced in December 2015, calling for the delisting of certain products manufactured outside of Turkey from the reimbursement list. Initial announcements indicated that there would be five waves of delisting, and so far the first two phases have been implemented. However, additional products, including from the third wave, continue to be included in the list as they meet the defined criteria.

As part of the first wave of delisting notices, which impacted 71 products in total with the addition of new products in 2018, PhRMA members began receiving notices in February 2017 that their products would be delisted within 12 months unless they submitted plans to "localize" these products in Turkey. Critically, "localize" has never been defined. The second phase of product delisting notifications, impacting 176 products, was announced in May 2017, of which 119 products were delisted as of July 31, 2018. Further action under the third and subsequent waves has halted as of this submission, and no formal announcements have been made regarding subsequent phases.

PhRMA and its members believe that these measures are inconsistent with Turkey's national treatment obligations under several World Trade Organization Agreements and constitute a significant restriction on trade.[215] The vast majority of

[214] *See*, *e.g.*, Article 46 of the 64th Government Immediate Action Plan.

[215] *See*, *e.g.*, the General Agreement on Tariffs and Trade (GATT), Art. III:4 (requiring that imported products "shall be accorded treatment no less favourable than that accorded to like products of national origin in respect of all laws, regulations and requirements"), as incorporated into Article 2.1 of the WTO Agreement on Trade-Related Investment Measures. Compelling manufacturers of patented pharmaceuticals to produce locally in order to remain or be added to the reimbursement list as part of the fifth phase of implementation of this policy would also be inconsistent with Article 27.1 of the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) (requiring that "patents shall

medicines sold in Turkey are distributed through the Social Security Institution (SSI) reimbursement list, and exclusion from this list effectively bars market access for these products. This forced localization in Turkey could have significant long-term consequences for the ability of U.S. biopharmaceutical companies to operate in Turkey and for patient access to certain medicines in the country.

Pricing and Non-Transparent Reimbursement

In Turkey, pharmaceutical pricing is regulated by TITCK. The reimbursement system is based on a positive list and reimbursement decisions are carried out by the inter-ministerial Reimbursement Commissions, led by the SSI under the Ministry of Family, Labor and Social Services (MoFLSS). The reimbursement decision process lacks transparency and is not subject to clearly defined decision criteria.

Pharmaceutical companies are still burdened with a substantial price discount from the lowest price in a basket of five European countries (France, Portugal, Spain, Italy and Greece). Over the last couple of years, TITCK has begun to annually adjust the fixed Euro/Turkish Lira exchange rate used to set prices under the Pricing Decree. However, per that decree, the annual exchange rate is set at 70% of the preceding year's average real exchange rate, automatically building in further discounts for the Government.

Setting aside the inappropriateness of fixing the exchange rate in this manner, the exchange rate for 2018 should have increased 23% increase under the Pricing Decree to 2.87 TL/EUR. And yet, citing inflation and budget concerns, the Government capped the adjustment at 15% and only increased the exchange rate to 2.69 TL/EUR. While the Turkish Government has suggested that this is a temporary measure for 2018 only, overriding the regulation exacerbates the business environment and hinders sustainability and predictability for pharmaceutical companies. It is particularly troubling that TITCK is not adjusting the exchange rate to reflect the 70% standard required by the regulation, when rampant inflation and economic vulnerabilities in Turkey throughout 2018 has led to an actual TL/EUR exchange rate of 6.06 as of January 7, 2019 (with a high in 2018 of 7.82 and a yearly average of 5.67).

By definition, Turkey's fixed exchange rate discriminates not only against pharmaceuticals – the only sector subject to this fixed exchange rate – but also against imported pharmaceuticals contrary to Turkey's national treatment obligations. Whereas prices for imported products are determined based on the fixed exchange rate, domestic manufacturers of innovative products that are only available in Turkey may negotiate prices directly with the MOH based on cost and pharmaco-economic data. It also appears to be inconsistent with Article II:3 of the Bilateral Investment Treaty (BIT) between U.S. and Turkey, which requires that investments "shall at all times be accorded fair and equitable treatment and shall enjoy full protection and security in a manner consistent with international law." Failure to update the exchange rate to reflect the actual exchange

be available and *patent rights enjoyable without discrimination as to* the place of invention, the field of technology and *whether products are imported or locally produced*" (emphasis added)).

rate has undermined the U.S. pharmaceutical industry's "legitimate expectations" as to the manner in which prices would be calculated. It is also "tantamount to expropriation," in that it substantially deprives the U.S. pharmaceutical industry of the reasonably-to-be-expected economic benefits of its investments in Turkey to the obvious benefit of the Turkish Government, contrary to Article III:1 of the U.S.-Turkey BIT.

Pharmaceutical Product Registration

Marketing of new drugs in Turkey is governed by the regulatory procedures prescribed by TITCK and the Ministry of Health (MOH) for the approval of medicinal products. The data and documents required to register medicinal products are listed in the MOH's Registration Regulation of Medicinal Products for Human Use (Registration Regulation).[216] Although this regulation requires TITCK to assess and authorize the registration of medicinal products within 210 days of the product's dossier being submitted and efforts have been taken to improve the regulatory process, a 2017 survey by AIFD indicate that the average regulatory approval period is 261 days for high priority products, 289 days for prioritized products, 449 days for normal prioritized products, and 439 days for the products without prioritization category.[217] Furthermore, without additional resources to complete product registrations, expediting certain applications over others only further delays the review time for those applications not receiving prioritized attention.

In May 2016, TITCK published a "Guideline for the Operating Procedures and Principles of the Priority Evaluation Committee of Medicinal Products for Human Use" and PhRMA's member companies appreciate TITCK's efforts to create an expedited pathway for product registration. While not included in the May 2016 TITCK document, the agency is inappropriately requiring companies to commit to a specific retail and public sale price and to estimate the number of SKUs that will be sold at the time the company submits its prioritization application.

TITCK is also in the process of updating the Registration Regulation to achieve harmonization with the relevant legislation of the EU. While the initial draft was promising, subsequent amendments raise a number of concerns:

- No provisions to bring Turkey's RDP mechanism into line with EU practices;
- Vague definition of manufacturing sites;
- Inadequate clinical trial data requirements for combination products;
- Redefines "generics" as "equivalent", blurring the lines between these two distinct terms; and
- Deviates from global best practices to reduce the standards for biosimilars.

[216] Official Gazette No. 25705 (Jan. 19, 2005) (Registration Regulation).

[217] Based on AIFD Survey 2017.

TITCK became an observer in the International Council for Harmonisation (ICH) in 2017, and aims to become a full ICH member by 2021. The ICH provides valuable work toward harmonizing international drug development and regulatory standards. In light of TITCK's intent to gain full ICH membership, it is important that this Regulation meets international standards.

Local Inspection Requirements

The MOH's revisions to the Registration Regulation have compounded the country's registration delays.[218] Effective March 1, 2010, a GMP certificate that is issued by the Turkish MOH must be submitted with each application to register a medicinal product for each of the facilities at which the product is manufactured. The GMP certificate can only be issued by the MOH following an on-site inspection by Ministry staff, or by the competent authority of a country that recognizes the GMP certificates issued by the Turkish MOH. However, for the reasons explained further below, neither option can be completed in a timely manner.

Despite increasing the number of inspectors at the end of 2013, the MOH still does not have adequate resources to complete these GMP inspections in a timely manner, with a median inspection period of 381 days for highly prioritized products (GMP 1). The inspection period for GMP 2 (prioritized) and GMP 3 (normal) products without priority is 739 days, although when they are added to an existing inspection the period is 307 days for GMP 2 products.[219]

PhRMA views it as a positive development that the TITCK's 2018-2022 Strategic Plan stipulates that the Agency is responsible for accelerating the GMP inspection and certification processes of priority medicines which are needed on the market within 1 year. However, the absence of strategic performance indicators for products prioritized by TITCK may give rise to uncertainty in the GMP inspection processes of these products.

Furthermore, although the Amended Registration Regulation permits applicants to submit GMP certificates issued by competent authorities in other countries, it does so only to the extent that the pertinent country recognizes the GMP certificates issued by Turkey. While PhRMA members commend Turkey for joining PIC/S, this is but the first of many steps that will be required before Turkey could enter into mutual recognition agreements with the United States and other trading partners.

[218] Regulation to Amend the Registration Regulation of Medicinal Products for Human Use, Official Gazette No. 27208 (Apr. 22, 2009) (Amended Registration Regulation); MOH, *Important Announcement Regarding GMP Certificates*, (Dec. 31, 2009) (establishing an implementation date for the GMP certification requirement).

[219] Based on AIFD Survey 2017.

Orphan Drug Guidelines

Since 2009, the MOH has been developing a pathway for orphan medicines in Turkey. Although there have been some successful workshops to progress the issue, there still remains no published pathway.

In August 2015, the Ministry of Science, Industry and Technology (MoSIT) published an in-depth analysis of the impact of rare diseases on Turkey's population in its "Pharmaceutical Sector Strategy and Action Plan of 2015". This study called for the creation of a national orphan drug policy. The innovative pharmaceutical industry looks forward to working with key stakeholders, including the MOH, SSI, MoSIT, Ministry of Economy, Ministry of Development, Ministry of Finance, Treasury and civil society organizations, to establish a market access pathway and appropriate incentives to facilitate the development and commercialization of medicines to treat rare diseases. As part of this process, it will be critical for Turkey to define orphan drugs based on international best practices, including EU prevalence standards, and thereby better ensure that Turkish citizens have access to the medicines they need.

UKRAINE

PhRMA and its members are highly troubled by the reintroduction of proposed intellectual property legislation that would impose impermissible exclusions on patent-eligible subject matter as well as restrictive patentability criteria. As the government of Ukraine begins to roll-out national health care insurance and drug reimbursement to its population, PhRMA's member companies believe that expanding limited reimbursement lists, bolstering poorly funded medicines budgets, and reforming its discriminatory, and non-transparent procurement practices are essential.

Key Issues of Concern:

- **Proposed Intellectual Property Law**: Intellectual property policies and laws in Ukraine are not certain or predictable. The Verkhovna Rada recently rejected a Draft Law 7538 that would have significantly limited biopharmaceutical inventors from patenting new inventions and enforcing existing intellectual property. Despite rejecting that law in September 2018, a new bill is already under consideration promoting the same provisions as the 2017 draft law – including impermissible patentable subject matter exclusions, restrictive patentability criteria, and vague compulsory licensing provisions.

- **Limited reimbursement list and inadequately funded medicines budget**: Patients in Ukraine largely pay out-of-pocket for most medicines due to inadequate hospital funding and an extremely limited out-patient reimbursement list that is not set to expand beyond basic conditions until at least 2020.

- **Defunct procurement system**: Public procurement of medicines has long been a major challenge in Ukraine as State procurements are riddled with duplication, corruption, inefficiency, and conflicts of interests due to multiple, non-harmonized lists that favor local producers and are non-transparent in nature. Recent reform efforts promise to restructure and modernize the system, though considerable work lies ahead.

For these reasons, PhRMA requests that Ukraine remain on the **Priority Watch List** in the 2019 Special 301 Report, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protection

Proposed Intellectual Property Law

PhRMA members are concerned with the unpredictability and uncertainty created by recently proposed amendments to Ukraine's intellectual property law. In late 2017, Ukraine's Ministry of Economic Development and Trade published for legislative consideration Draft Law 7538. Provisions of that draft law appeared inconsistent with

Ukraine's obligations to the World Trade Organization (WTO) and its commitments under the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) – including impermissible exclusions on patent-eligible subject matter, restrictive patentability criteria, and ambiguous and vague compulsory licensing provisions.

Draft Law 7538 was rejected by Ukraine's legislature in September 2018. However, in October 2018, a nearly identical draft law was introduced for consideration by the Verkhovna Rada. The current draft law creates significant uncertainty and unpredictability for biopharmaceutical inventors operating in Ukraine.

Market Access Barriers

Limited Reimbursement List and Inadequately Funded Medicines Budget

PhRMA Members are enthusiastic about Ukraine's pivotal new national health care reform bill signed in January 2018, 2018-VIII, "On state financial guarantees of medical care of the population," which established the National Health Service of Ukraine (NSZU) to provide mandatory national health care insurance and reimbursable medicines for its population.

Although the law requires the State to pay for drugs used during in-patient care, due to the State's failure to provide appropriate funding for public-sector hospitals, many patients are nevertheless forced to pay for these treatments out-of-pocket. Moreover, the vast majority of citizens with national health care currently pay out-of-pocket for outpatient medicines, though a pilot reimbursement scheme was rolled out in April 2017 for essential medicines for cardiovascular conditions, type 2 diabetes, and asthma. Though it was initially anticipated that this pilot would soon be expanded to other therapeutic areas, it was announced in June 2018 that such expansions will not take place until at least 2020.[220]

Ukraine is the only European country where patients largely pay out-of-pocket for most medicines, particularly as outpatients. While PhRMA members understand the budgetary pressures Ukraine faces as it rolls out national health care insurance, we encourage the government to both expand its reimbursement list and make appropriate allocations to support the modernized health system it seeks to create.

Procurement System Reform

Public procurement of medicines has long been a major challenge in Ukraine as State procurements are riddled with duplication, corruption, inefficiency, and conflicts of interests due to multiple, non-harmonized lists that favor local producers and are non-transparent in nature.

[220] IHS (June 2018). Ukrainian MoH publishes updated Affordable Medicines price list, postpones expansion to 2020.

The Ministry of Health (MoH) of Ukraine started work on reforming this sphere back in 2015, creating a working group on reforming the system of procurement of medicines and medical products and in late August of 2018, the Cabinet of Ministers approved establishment of the Central Procurement Organization (CPO), which will procure medicines and medical products at national, local and international levels using long-term framework agreements and e-procurement tools.

PhRMA is encouraged by this work and urges the MoH to continuously monitor the roll-out and performance to ensure that the country's renewed approach to procurement sufficiently eliminates corruption risks, minimizes inefficiency, facilitates transparent criteria and decision-making, reflects patient needs, and encourages a level playing field among local and foreign producers.

LATIN AMERICA

ARGENTINA

PhRMA and its member companies operating in Argentina recognize the important economic reforms the Government of Argentina has implemented since 2016. We welcomed the resumption of bilateral dialogue through the Trade and Investment Framework Agreement concluded in March 2016. Recent reforms have the potential to drive future economic growth in Argentina, and constructive dialogue that delivers real results could transform an important bilateral trade and investment relationship. Regulatory reforms by the sanitary authority that brought Argentina closer to international standards and reduced clinical trials approval times are already attracting investment in early phase trials. Nevertheless, registration and evaluation regulations for biopharmaceutical products have not yet been released, thus generating legal uncertainty for companies.

Biopharmaceutical innovators in the United States continue to face serious intellectual property (IP) issues and longstanding market access barriers put in place by the previous Argentine Government. While the current administration has signaled willingness to address significant IP concerns related to patentability and regulatory data protection (RDP), the government has not initiated any reforms. Despite positive engagement by our local sister association La Cámara Argentina de Especialidades Medicinales (CAEMe) and American Chamber of Commerce in Argentina (AmCham) at various levels of the Argentine Government over the last three years, these IP issues remain.

Key Issues of Concern:

- **Restrictive patentability criteria**: The Argentine Government amended its criteria for granting pharmaceutical patents in 2012. A joint regulation issued by the Ministries of Health and Industry and the Argentina Patent Office (Instituto Nacional de la Propiedad Industrial or INPI) established guidelines that significantly limit the type of pharmaceutical inventions that can be patented. These guidelines are contrary to Argentina's obligations under the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) and have led to the rejection of many pharmaceutical patent applications. In addition, there have been reported instances of courts invalidating patents granted under the previous rules by applying the new guidelines retroactively.[221]

- **Regulatory data protection failures**: Argentina does not provide protection for regulatory test data, as required under TRIPS. Specifically, Law 24,766 permits Argentine officials to rely on data submitted by originators to approve requests by competitors to market similar products.

[221] *See, e.g.,* Argentina: Polymorph patents under fire, available at http://aippi.org/no-show/argentina-polymorph-patents-under-fire/ (last visited Feb. 7, 2019).

- **Discriminatory Reimbursement Policies**: On October 1, 2015, the Ministry of Health and the Secretary of Commerce issued a Joint Resolution establishing a "preferential" reimbursement system for national generics and biosimilar products, to the potential detriment of manufacturers producing medicines outside Argentina.

For these reasons, PhRMA requests that Argentina remain on the **Priority Watch List** in the 2019 Special 301 Report, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protection

Restrictive Patentability Criteria

In 2012, the Argentine Government published a regulation that significantly narrowed the scope of chemical compounds and compositions that can be patented, leading to the rejection of many pharmaceutical patent applications. The regulation contemplates that similar limitations could be added in the future for "pharmaceutical biological inventions."

The regulation (N^{os} 118/2012, 546/2012 and 107/2012), issued jointly by the Ministries of Health, Industry and INPI sets out Guidelines for Patentability Examination of Patent Applications on Chemical and Pharmaceutical Inventions. It expressly states that pharmaceutical patents are not available for compositions, dosages, salts, esters and ethers, polymorphs, analogous processes, active metabolites and pro-drugs, enantiomers, and selection patents. Also the ability to describe and claim an invention using Markush-type claims is severely limited.

The imposition of additional patentability criteria for pharmaceutical patents beyond those of demonstrating novelty, inventive step and industrial application is inconsistent with Articles 1 and 27.1 of TRIPS, as well as Argentina's obligations under its bilateral investment treaty with the United States. While the Argentine Government recognizes that the guidelines and resolution are problematic, it has yet to reform its approach.[222]

In 2015, the INPI passed Resolution 283/2015 which narrows the patentability of certain biotechnological inventions, including inventions based on nucleotide or amino acid sequences. The resolution also expands the scope of subject matter that is not patentable to include genetically modified organelles. These and other restrictions in Resolution 2083/2015 potentially create an unprecedented class of inventions that are excluded from patentability.

[222] On June 6, 2012, CAEMe, joined by over 40 innovative biopharmaceutical companies, filed an administrative petition seeking to invalidate the Joint Resolution. That administrative review petition was dismissed on April 5, 2013. On August 30, 2013, CAEMe filed a civil complaint in federal court challenging the Joint Resolution, the administrative review dismissal, and application of the Guidelines to pharmaceutical patent applications. That complaint is currently pending.

Regulatory Data Protection Failures

Biopharmaceutical innovators work with hospitals, universities and other partners to rigorously test potential new medicines and demonstrate they are safe and effective for patients who need them. Less than 12% of medicines that enter clinical trials ever result in approved treatments.[223]

To support the significant investment of time and resources needed to develop test data showing a potential new medicine is safe and effective, governments around the world protect that data submitted for regulatory approval from unfair commercial use for a period of time. WTO members considered such protection so important to incentivize biopharmaceutical innovation that they established a TRIPS provision (Article 39.3) requiring each country to safeguard regulatory test data for a period of time after the approval of a new medicine in that country.

Argentina was among the countries that crafted that provision, but has so far failed to provide protection of test and other data in a manner consistent with its international obligations. Indeed, Law No. 24,766 allows Argentine officials to rely on data submitted by innovators in other markets to approve requests by competitors to market similar products in Argentina. The Law provides no period of protection against reliance and does not define “dishonest” use.

Weak Patent Enforcement

A critical tool to protect against irreparable harm from the loss of IP is the ability to seek a preliminary injunction to prevent the sale of an infringing product during litigation. Preliminary injunctions become all the more important when there are no other effective mechanisms to facilitate early resolution of patent disputes.

Articles 83 and 87 of Law No. 24,481 on Patents and Utility Models provide for the grant of preliminary injunctions. These Articles were amended in 2003 by Law 25,859 to fulfill the terms in the agreement to settle a dispute between the United States and Argentina (WT/DS171/13). The agreed-upon terms were intended to provide, under certain conditions, effective and expeditious means for patent owners in Argentina to obtain relief from infringement before the conclusion of an infringement trial. Unfortunately, these terms, as implemented in the Argentine legal system, have not had the intended effect. Member companies have reported that the process of obtaining injunctive relief has become very lengthy and burdensome, thereby denying the relief that they were intended to provide.

[223] DiMasi JA, Grabowski HG, Hansen RW; Tufts Center for the Study of Drug Development. Innovation in the pharmaceutical industry: new estimates of R&D costs. In: Briefing: Cost of Developing a New Drug, available at https://static1.squarespace.com/static/5a9eb0c8e2ccd1158288d8dc/t/5ac66afc6d2a732e83aae6bf/1522952963800/Tufts_CSDD_briefing_on_RD_cost_study_-_Nov_18%2C_2014..pdf (last visited Feb. 7, 2019).

Patent Backlogs

The ability to secure a patent in a reasonable period of time is critical to attracting investment in the research and development needed to create new medicines and bring them to patients who need them. Patent backlogs hinder innovation by creating uncertainty and significantly raising investment risk.

Patent application delays can be lengthy in Argentina, where life science innovators wait an average of 6.6 years for patents to be granted.[224] According to some estimates, the overall patent backlog is approximately 21,000 applications. Argentina's patent law does not provide for patent term adjustments to compensate for unwarranted delays in the examination of patent applications.

To address this challenge, Argentina should hire additional qualified examiners and consider participating in work sharing arrangements, such as Patent Prosecution Highway programs, with other major patent offices. Argentina should also accede to the Patent Cooperation Treaty (PCT), a step that would facilitate the filing and examination of patent applications in Argentina as it does now in more than 140 Contracting Parties. Accession to the PCT could allow Argentina to reduce its current patent application backlog and use the PCT system to reduce the review period for future patent applications.

The Argentine Senate approved accession to the PCT in 1998. However, it was never discussed in the Lower House. In 2011, the Lower House resumed consideration at committee level, but with no results. Promisingly, Argentina signed a Memorandum of Understanding with the World Intellectual Property Office on May 6, 2016, related to establishing a Patent Prosecution Highway, offering hope that Argentina will move forward with acceding to the PCT.

Market Access Barriers

Discriminatory Reimbursement Policies

On October 1, 2015, the Ministry of Health and the Secretary of Commerce issued Joint Resolutions 1710 and 406, which establish a "preferential" reimbursement system for national generics and biosimilar products. These resolutions provide that Health Insurance Agents must give preference to Argentine products available in the market that have the same active ingredient or that are biosimilar to those originating abroad. This resolution is subject to the condition that the final selling price of the Argentine products must be significantly lower than the average price of similar products of foreign origin.

[224] Schultz M. and Madigan K, The Long Wait for Innovation: The Global Patent Pendency Problem, CPIP (2016), available at https://sls.gmu.edu/cpip/wp-content/uploads/sites/31/2016/10/Schultz-Madigan-The-Long-Wait-for-Innovation-The-Global-Patent-Pendency-Problem.pdf (last visited Feb. 7, 2019).

Key terms are undefined, but on its face the new reimbursement system appears to be inconsistent with international biosimilar guidelines (providing that biosimilars cannot be automatically substituted for the original biologic) and Argentina's national treatment obligations under the WTO General Agreement on Tariffs and Trade.

In addition, provisions of the "Buy Argentine and Development of Suppliers (27.437)" policy further condition market participation in Argentina for foreign innovators. Foreign companies are required to enter "Productive Cooperation Agreement Proposals" (ACPs) with local firms in order to participate in the development policy – including mandatory levels of direct investment, technology transfer, or other capacity building programs.

BRAZIL

PhRMA and its member companies operating in Brazil remain concerned regarding restrictive patentability criteria and procedures, weak patent enforcement, the lack of regulatory data protection (RDP) and government pricing policies.

Key Issues of Concern:

Restrictive patentability criteria and procedures: Since 1999, Article 229-C of Brazil's Patent Law has been interpreted to permit the health regulatory agency, the Brazilian National Health Surveillance Agency (ANVISA), to review all patent applications for pharmaceutical compound and/or process inventions. That article created a dual patent examination process for pharmaceutical inventions, resulting in both: contradictory and/or additive patentability requirements to those established by Brazilian Patent Law and adopted by the Brazilian Patent Authority (INPI); and duplicative, prolonged patent review processes that contribute to the already existing patent backlog. Under the terms of regulatory changes adopted in 2017, ANVISA's opinion on the patentability of new biopharmaceutical inventions are no longer binding on INPI. This is a welcome step, but does not end Brazil's "dual examination" system. ANVISA remains able to reject patents based on vague and undefined public health grounds. In addition, the Brazilian Federal Prosecutor's Office has challenged the 2017 ANVISA amendments. That challenge is pending review and further creates uncertainty on ANVISA's role in patent examination. Most recently (September 2018), a Federal Court ordered INPI to reexam an issued patent on an innovative medicine to take into account ANVISA's review. That case is still pending.

- **Patent backlogs**: With around 190,000 patent applications pending at INPI, Brazil's patent backlog still exceeds 11 years (and is even longer for pharmaceuticals), hindering innovation and significantly raising investment risk. The last Government proposal to address the patent backlog excluded pharmaceutical patents, due to the dual patent examination process for pharmaceutical inventions.

- **Patent term adjustment for mailbox patents**: Under Patent Law 9,279/96, Brazil provides 20 years of patent protection from the date of filing or a minimum of ten years from the date of patent grant. However, in September 2013, INPI issued a binding opinion followed by the filing of related lawsuits to entirely invalidate or limit the term of approximately 240 so-called "mailbox patents," *i.e.*, patents related to biopharmaceutical products or agrochemical compounds that were filed after Brazil acceded to the World Trade Organization (WTO) on January 1, 1995, but before the Patent Law went into effect on May 14, 1997. These lawsuits, primarily affecting pharmaceutical patents, are currently proceeding through the legal system including the Court of Appeals, but most decisions have upheld INPI's

retrospective decision to no longer provide a minimum ten years of post-grant patent protection.

- **Regulatory data protection failures**: Although Brazil applies RDP for veterinary, fertilizer, and agrochemical products, the same protection is not given to biopharmaceutical products.

- **Regressive taxes on medicines**: Combined federal and state taxes add up to 34% to the cost of medicines in Brazil – one of the highest tax burden on medicines in the world.[225] The innovative pharmaceutical industry supports the proposals to eliminate taxes on certain products including medicines, including PEC 491/11, under consideration by the Special Committee in the House.

- **Product Development Partnerships (PDPs) and government purchasing**: Brazil has developed a regulatory framework for the establishment of PDPs. While this framework provides improved transparency around PDPs, Brazil still lacks clear rules regarding the purchasing preferences offered to PDPs. In addition, while the Ministry of Health (MoH) is tasked with reviewing and approving PDPs, it does not take into account the patent status of products that are the object of a PDP proposal submitted by third parties.

For these reasons, PhRMA requests that Brazil be placed on the **Priority Watch List** in the 2019 Special 301 Report, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protection

Restrictive Patentability Criteria and Procedures

One of the most serious problems facing the pharmaceutical industry today in Brazil was created by Article 229-C, the 1999 amendment to the Brazilian Patent Law that authorizes ANVISA to review patent applications claiming pharmaceutical products and/or processes that may present a "health risk." This review has been an additional procedure to, and been given equal weight as, the examination conducted by INPI.

This "dual examination" is incompatible with Brazil's obligations under the "anti-discrimination" provisions of Article 27.1 of the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). Until recently, ANVISA did not limit its role to the review of the potential sanitary risk aspects of the subject matter of the patent application but also reviewed the patentability requirements. ANVISA lacks sufficient

[225] Globally, on average, taxes account for 6.3% of the retail price of medicines. *See* EMIS, "Pharmaceutical Sector in Brazil," December 2013, available at https://www.emis.com/sites/default/files/EMIS%20Insight%20-%20Brazil%20Pharmaceutical%20Sector%20Report.pdf (last visited Feb. 7, 2019).

technical expertise on patentability and its role in reviewing patentability has generated uncertainty for patent applicants and undermined incentives for innovation.

Under the terms of a Joint Ordinance signed in April 2017, and new rules published by INPI in May 2017 and by ANVISA in August 2017, ANVISA may issue opinions on the patentability of new biopharmaceutical inventions, although those opinions are no longer binding on INPI. However, ANVISA opinions are binding for patent applications for biopharmaceutical products and processes it believes present a "health risk". While communications between INPI and ANVISA may have improved, PhRMA continues to believe that Brazil must end its "dual examination" system and bring its patent system in line with global rules and norms.

In addition, the Brazilian Federal Prosecutor's Office has challenged the 2017 ANVISA amendments. That challenge is pending review and further creates uncertainty on ANVISA's role in patent examination. In September 2018 a Federal Court ordered INPI to reexam an issued patent on an innovative medicine to take into account ANVISA's review. That case is still pending.

Patent Backlogs

While PhRMA recognizes efforts underway at INPI to reduce the patent backlog, delays in patent grants have continued to worsen, undermining otherwise valid patent rights and incentives for companies to bring innovative products to Brazil.

The latest data foresee that INPI will close 2018 with around 190.000 patent applications pending. The average review time exceeded 11 years. For pharmaceuticals the delays are even longer – around 13 years for traditional medicines and 12 years for biologics.[226] Unfortunately, this is a significant increase from the average time for all patent applications of 5.4 years in 2011. Although the former Government authorized new examiner positions (including in the pharmaceutical and biotech fields) to reduce the backlog, more needs to be done to mitigate the backlog.

In 2017, INPI announced plans to automatically grant certain patent applications under simplified procedures. However, the proposal expressly states that pharmaceutical patents will not benefit from these procedures due to the dual patent examination process for pharmaceutical inventions.

Patent Term Adjustment for Mailbox Patents

In September 2013, INPI issued a binding opinion regarding the term for patents relating to biopharmaceutical or agrochemical compounds that were filed between

[226] R. Nunes and R. Salomão Romano, "Brazilian PTO Considers Automatically Granting 231,000 Patents to Get Rid of Backlog," IP Watchdog (Jan. 11, 2018), available at www.ipwatchdog.com/2018/01/11/brazilian-pto-considers-automatically-granting-patents/id=91787/ (last visited Feb. 7, 2019).

January 1, 1995 and May 14, 1997 (known as "mailbox patents"). Brazilian Patent Law 9,279/96 Article 40 provides that "Patents will be given a 20-year protection from the date of filing" (caput) and "A minimum of ten-year protection will be given from the date of grant".[227] Per the binding opinion, however, in the event that a company's patent was filed in Brazil after the country acceded to the WTO on January 1, 1995, but before the Patent Law came into force on May 14, 1997, the application should not have received the minimum ten years of protection from the date that the patent was granted, considering that de Patent Law specified that for such patents were provided 20 years of patent protection from the date of filing.

Under Brazil's Patent Law, approximately 250 mailbox patent applications (the majority on pharmaceuticals) were granted a minimum of ten years patent protection under Article 40. INPI's September 2013 opinion has the effect of revoking the granted ten-year minimum terms for those mailbox patents. The opinion, however, is not self-executing. As a result, INPI has filed multiple lawsuits in Federal District Courts against the impacted mailbox patent holders seeking to invalidate their patents. Many of those cases are now before the Court of Appeals, which has upheld INPI's retrospective decision to no longer provide a minimum ten years of post-grant patent protection.

INPI is seeking to invalidate the patents entirely or, in the alternative, to adjust the patent term expiration dates for the impacted patents to 20 years from the date of filing. In either case, pharmaceutical patents are being targeted and the patent terms which were originally granted by the Brazilian Government and upon which innovators have relied are now being challenged *ex post facto* by the same Government. The elimination of the ten-year minimum term for these mailbox patents is particularly unfair when the only reason for this minimum level of protection is that it took INPI more than ten years to review the patent application. This is another example of Brazil's deteriorating and unpredictable IP environment for pharmaceutical innovators.

Regulatory Data Protection Failures

Brazilian law (Law 10.603/02) provides data protection for veterinary, fertilizer, and agrochemical products, but still does not provide similar protection for pharmaceutical products for human use, resulting in discriminatory treatment. Contrary to TRIPS Article 39, Brazil continues to allow Government officials to grant marketing approval for pharmaceuticals to competitors relying on test and other data submitted by innovators to prove the safety and efficacy of their products. Additional efforts are needed to provide certainty that test and other data will be fully protected against unauthorized use to secure marketing approval for a fixed period of time.

[227] It should be noted that there are two constitutional challenges pending before the Brazilian Supreme Court requesting that article 40, sole paragraph, of the Brazilian IP Law be declared unconstitutional. The first constitutional challenge was filed by ABIFINA, a Brazilian association representing national companies with chemical interests including many generics companies. The second one was filed by the Brazilian Federal Public Prosecutor Office. Interfarma, among others, has successfully petitioned to participate in these cases as *amicus curiae*.

PhRMA members continue to seek protection for their data through the judicial system. Although there have been lawsuits seeking to secure a period of data protection for specific products, so far the cases are still pending in the Brazilian courts, leaving innovators without reliable RDP.

Market Access Barriers

Regressive Taxes on Medicines

In Brazil, federal and state taxes on medicines can add nearly 34 percent to the retail price of medicines – among the highest tax burdens on medicines in the world.[228] Recognizing the significant burden that this imposes on Brazilian patients, the innovative pharmaceutical industry supports the proposals to eliminate taxes on certain products including medicines, such as PEC 491/11, under consideration by the Special Committee in the House.

High tariffs and taxes can prevent access to new treatments for patient that need them. Under the WTO Pharmaceutical Agreement, 34 countries agreed to eliminate import duties on a wide range of medicines and other health products.[229] However, the majority of Latin American economies, including Brazil, are not parties to the WTO Pharmaceutical Agreement. Between 2006 and 2013, the value of worldwide biopharmaceutical trade in countries that are not parties to that Agreement increased at a compound annual growth rate of more than 20 percent. This means that a larger proportion of medicines distributed around the world are potentially subject to tariffs.[230] To help remedy this trend, Brazil should accede to the WTO Pharmaceutical Agreement.

Government Purchasing and PDPs

The Brazilian Government issued Federal Law 12.349/10 granting preferences for locally manufactured products and services in public tenders. Locally produced medicines automatically have on average a 25% price preference in government tenders. More recently, an amendment to Portaria MDIC 279/11 provided a list of pharmaceutical products eligible for preference margins and defined the parameters for its application in public purchases. While the issuance of Portaria MDIC 279/11 brought more transparency to the purchase process, it still does not adequately define the compensation to be offered by those companies that benefit from this mechanism.

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[228] *Id.*

[229] General Agreement on Tariffs and Trade, "Trade in Pharmaceutical Products" (L/7430), Mar. 1994, available at https://ustr.gov/sites/default/files/WTO%20Pharmaceutical%20Agreement%20March%201994.pdf (last visited Feb. 7, 2019).

[230] Banik, N. and P. Stevens, "Pharmaceutical tariffs, trade flows and emerging economies," Geneva Network, Sep. 2015, available at http://geneva-network.com/wp-content/uploads/2015/09/GN-Tariffs-on-medicines.pdf (last visited Feb. 7, 2019).

More recently, in July 2017, Brazil's MoH announced it was investigating the introduction of new price criteria for public purchases of certain types of drugs in order to further cut spending. The MoH plans to begin with drugs for the treatment of rheumatoid arthritis, and has already contacted the industry to discuss the new measure. According to the MoH, six of the eight drugs currently included in the treatment protocol for the disease would be dropped as a consequence of the new price criterion (although industry was able to convince MoH that patients already using drugs under the former treatment protocol should not be required to change their treatments). No official statements about a new cost-cutting mechanism have been published by the MoH as of yet, and it is unknown which and how many other therapeutic areas are being considered for cost-cutting.

Meanwhile, a new PDP regulation (Portaria 2531/14) was issued in 2014 with participation of the private sector, which on its face appears to provide greater transparency and predictability. Recently, the Brazilian Government announced several PDPs under the new regulation. Even still, it remains unclear what criteria were evaluated in assessing and approving these PDPs and the purchasing preferences that will be extended to an approved PDP. In addition, the MoH does not take into account or assess relevant intellectual property rights of products that are the object of a PDP application. As a result, the MoH has approved several third-party PDP applications for innovative and patent protected products. Recognizing these shortcomings, Brazil is currently conducting a public consultation that intends to improve the transparency and predictability of the PDP process.

Regulatory Burden

All participants in the pharmaceutical industry, innovative and generic alike, face numerous challenges stemming from the deadlines currently enforced by ANVISA. While Brazilian legislation adequately addresses ethics, safety and efficacy standards, it does not provide a mechanism to ensure that ANVISA has adequate capacity to execute its assigned responsibilities. PhRMA and its members commend ANVISA for implementing fast-track approval process for certain products, including those to treat rare diseases, and hopes that this will help the agency to reduce review timelines. Other improvements ANVISA should consider include:

- Reduce approval timelines by hiring additional marketing approval technicians;
- More predictable processes, allowing companies to be prepared in advance, resulting in shorter "clock stops" and faster approvals; and
- Introduction of an expedited process for line extensions (at least similar to the deadline for new products) providing faster access to post-approval innovations.

CHILE

PhRMA members are very concerned about recent actions by the National Congress that are pressuring Chile's new government to issue compulsory licenses (CLs) for certain innovative medicines. These developments add to longstanding intellectual property (IP) problems, including Chile's failure to fully implement its patent enforcement and regulatory data protection (RDP) obligations under the U.S.-Chile Free Trade Agreement.

Key Issues of Concern:

- **Compulsory Licensing**: Action is needed to protect American innovation in Chile. Following a series of politically-driven Congressional resolutions (Nos. 798, 1014 and 68) calling for the compulsory licensing of innovative medicines that provide a cure for many patients suffering from hepatitis C. The Ministry of Health issued Resolution 399 in March 2018 and rejected a reconsideration writ filed by the patentee. That Resolution declares these medicines to be in the public interest for health reasons – a procedural step necessary under Chilean law to proceed with a CL. The MOH Resolution 399 and the earlier Congressional resolutions dramatically increase the risk of a CL in Chile.

- **Weak Patent Enforcement**: PhRMA member companies believe that the Chilean Government's draft legislative and regulatory proposals would, if approved by the Chilean National Congress and implemented, represent a step toward compliance with Chile's treaty obligations. Unfortunately, this legislation, introduced in 2012, is unlikely to move forward in the near term.

- **Regulatory Data Protection**: The Chilean Government's enactment in December 2010 of Supreme Decree 107 corrected several deficiencies in Chile's existing system for protecting proprietary pharmaceutical test data against unfair commercial use and disclosure. The correction of remaining weaknesses, however, will depend upon whether the government makes certain necessary changes to Chile's Industrial Property Law.

- **Proposed Trademark Limitations**: Chile's Congress is currently considering a bill to significantly limit the use of trademarks in biopharmaceutical product packaging through proposed amendments to the Medicines II Law. That bill also restrictions health care providers to prescribe medicines using trademarked names.

For these reasons, PhRMA requests that Chile remain on the **Priority Watch List** in the 2019 Special 301 Report. Further, we urge USTR to provide an opportunity for an assessment of Chile's IP regime through an **Out-of-Cycle Review**, so that the U.S. Government can evaluate progress on these important issues and dedicate the required

bilateral attention necessary to make progress on the barriers confronted by U.S. businesses in Chile.

Intellectual Property Protections

Compulsory Licensing

On January 11, 2017, the Chilean Chamber of Deputies of the National Congress passed Resolution No. 798.[231] That resolution calls on the Minister of Health "to incorporate and use the compulsory licensing mechanism provided for in Article 51(2) of the Industrial Property Law N° 19.039 to facilitate [medicines] acquisition at *competitive prices*."[232] It also calls for the prioritization of certain classes of medicines to be considered for compulsory licensing and highlights the alleged price reductions realized by certain countries after issuing CLs on biopharmaceutical products.

In January 2018, the Chilean Senate approved the Medicines II Bill, which is now pending final approval from the Chamber of Deputies. That bill seeks to amend Article 99 of the Sanitary Code to establish that access to medicines is not adequate "when there are economic, financial, geographic or opportunity barriers that prevent access to a medication." Furthermore, the Health Committee of the Lower Chamber has introduced several amendments that broaden the grounds upon which a CL could be issued.

In addition, the Chamber of Deputies approved Resolution No. 1014 in January 2018 seeking to establish that access to certain hepatitis C medicines is not consistent with the constitutional right to health, thus warranting, they assert, a CL. Further, on March 9, 2018, the former Minister of Health issued Resolution 399 declaring that the compulsory licensing of hepatitis C treatments would be justified on public health grounds. On August 28, 2018, new Minister of Health issued Resolution 1165 rejecting the patentee's challenge to Resolution 399/2018. As a result of this latest resolution, there remains a heightened risk of a CL being issued in Chile.

The research-based pharmaceutical industry is very concerned that these actions inappropriately expand the scope of the government's compulsory licensing authority to pursue objectives that are not clearly related to legitimate health emergencies.

Weak Patent Enforcement

Notwithstanding the requirement contained in Article 17.10.2 of the U.S.-Chile FTA, Chile has thus far failed to establish a satisfactory mechanism to enable effective patent enforcement before marketing approval decisions are made and implemented. Article 17.10.2 requires Chile to "make available to the patent owner the identity of any third party requesting marketing approval effective during the term of the patent" and "not

[231] Resolution No. 798, Chamber of Deputies, available in Spanish at https://www.camara.cl/pdf.aspx?prmid=6893&prmtipo=SOBRETABLA (last visited Feb. 7, 2019).

[232] *Id.* (emphasis added) (unofficial translation).

grant marketing approval to any third party prior to the expiration of the patent term, unless by consent or acquiescence of the patent owner."

During 2011, the Chilean Government indicated to USTR and the innovative pharmaceutical industry its recognition of the need to enact new legislation aimed at establishing an effective patent enforcement mechanism that would bring Chile closer to compliance with its FTA obligations. PhRMA would support a final proposal that:

- Provides sufficient time prior to the grant of sanitary registration of a follow-on product to obtain a final decision regarding the validity or non-infringement of the relevant patents;

- Ensures that the patent holder will have access to the courts to assert its patent rights prior to the grant of sanitary registration for a potentially patent-infringing medicine; and

- Excludes the imposition of additional requirements or conditions that might prove unreasonable or unduly burdensome, and that might discourage reasonable patent enforcement efforts (*e.g.*, excessive bond requirements and disproportionately high fines for declarations subsequently judged to be inaccurate).

PhRMA welcomed the government's work to introduce relevant draft legislation in January 2012. Unfortunately, that legislation has not received any attention since its introduction, and the impact of a lack of effective patent enforcement continues to worsen.

Delays in Granting Pharmaceutical Patents

For many years, applicants for pharmaceutical patents in Chile have had to wait a significant amount of time to obtain final action on their applications by the Chilean patent office. In 2009, the Chilean Government established the Intellectual Property Institute (INAPI) as the successor agency to the DPI, in part, to remedy these unacceptably long delays. One of INAPI's stated objectives is to streamline the patent application review process by limiting the number of substantive office actions and facilitating rapid communication between applicants and examiners, thereby enabling it to rule more expeditiously on patent applications.

The administrative and procedural reforms implemented by INAPI to date have decreased waiting times, with most patent applications filed after 2007 receiving a definitive decision within 4 to 5 years. Therefore, while PhRMA supports the Chilean Government's work to improve patent application processing times, it believes that some further work must be done to expedite a bit more patent application reviews in Chile.

Trademarks

In January 2018, Chile's Senate approved the "Medicines II Bill," which is now pending final approval from the Chamber of Deputies. That Bill, if enacted, would significantly limit the use of trademarks or other "fanciful" designations for any prescribed medicine. This measure appears to deny another important IP protection that is critical to ensure that innovator companies can distinguish their products from others. A trademark for a medicine designates its source and helps doctors and patients identify the quality, safety, and intrinsic effectiveness of a given product – reputational capital that manufacturers strive to build over time.

The Bill proposes a considerable departure from the current trademark protection guaranteed in Article 19 of Chile's Constitution and its international (*e.g.*, WTO TRIPS) and bilateral (*e.g.*, U.S.-Chile FTA) obligations.

Finally, recently an amendment was proved in the Health Committee of the Lower House that severely limits, if not outright excludes, the possibility for doctors to use trademarks in their prescriptions; requiring the International Non-Proprietary Name (INN) be used instead. This will have to be voted and approved by the Plenary of the Lower House.

Regulatory Data Protection

Final enactment in December 2010 of Supreme Decree 107 resolved several longstanding concerns of the U.S. Government and PhRMA regarding deficiencies in Chile's RDP system. Nevertheless, Chile's RDP system still contains the following weaknesses, correction of which will likely require amendment of the Industrial Property Law. Specifically:

- RDP is unavailable for certain pharmaceutical innovations (*e.g.*, new uses, formulations, compositions, dosage forms, *etc*.) that require the presentation of additional clinical test data as a condition of sanitary registration, but that do not involve a new chemical entity not previously registered in Chile;

- Prior voluntary disclosures by the data owner made in the interest of transparency can still justify incomplete recognition or denial of RDP;

- An applicant for sanitary registration must explicitly request RDP and provide a copy of the data for which protection is sought (Art. 4);

- RDP applicants are required to submit sworn statements and other formalities that could conceivably justify denial of RDP if judged to contain technical or procedural errors (Art. 4);

- RDP is only provided to data specifically identified (by title or name) in the sanitary registration application (Art. 6);

- It is not clearly stated that the ISP's obligation not to disclose protected data does not expire after 5 years; and

- S.D. 107 (Art. 10) repeats the IP Law's enumeration of various grounds for revocation or denial of the right to exclusive use that are not stated in the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) or Chile's bilateral trade agreements with the United States and the EU; these conditions significantly weaken the applicability and usefulness of the available data protection.

Although PhRMA recognizes that enactment of Supreme Decree 107 constituted an advance toward implementation of Chile's obligations regarding data protection under the U.S.-Chile FTA, TRIPS, and other multilateral agreements, it believes that full compliance with these obligations will require additional action by Chile to correct the aforementioned deficiencies.

COLOMBIA

PhRMA member companies face urgent intellectual property (IP) challenges and market access barriers in Colombia, including a pending declaration of public interest (DPI) process that could lead to the compulsory licensing of an entire class of innovative medicines that provide a cure for Colombian patients suffering from a serious infectious disease. Other critical barriers include Decree 1782 of 2014, which establishes an unprecedented "third pathway" for approval of non-comparable biologics contrary to World Health Organization (WHO) guidelines and accepted standards of the United States and other countries to ensure the safety and efficacy of biosimilar products. These barriers are in addition to *ad hoc* and non-transparent market access policies and other weaknesses in Colombia's IP regime.

Key Issues of Concern:

- **Compulsory licensing**: Urgent action is needed to protect American inventions in Colombia. In December 2017, Colombia's Ministry of Health and Social Protection (MOH) accepted a Declaration of Public Interest (DPI) petition for review that could lead to the compulsory licensing of the entire class of innovative treatments for hepatitis C. The petition was accepted contrary to Colombia's own procedures and appears to provide no justification for such an extreme and drastic action. The petition follows a similar petition granted against an innovative cancer medicine in 2016, and remains a looming threat to manufacturers of innovative medicines in the United States.

- **Regulatory data protection failures**: Colombia fails to respect existing legislation that would otherwise provide regulatory data protection upon approval of novel pharmaceutical products.

- **Restrictive patentability criteria**: Contrary to its obligations under the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), Colombia does not grant patents for second uses.

- **Weak patent enforcement**: There is no mechanism in place to provide patent holders with the opportunity to resolve patent disputes prior to the launch of a follow-on product. This has led to the approval and marketing of follow-on products, despite the fact that a patent for the original drug is still in force.

- **Increased regulatory barriers under the National Development Plan (NDP)**: Colombia's NDP, which passed into law on May 7, 2015, undermines recent gains Colombia has made to encourage innovation, delays access for Colombians to cutting edge technologies, and is inconsistent with Colombia's international commitments on IP and trade. Particular concerns include Article 72, which makes price and health technology assessment (HTA) criteria in the regulatory approval process). As yet, implementing regulations (including pricing methodologies) have

not been released (albeit that a draft pricing methodology was issued in August 2018), but PhRMA's members are working to ensure that implementation of these Articles does not impede patient access to innovative medicines. PhRMA supports the creation of sustainable health care systems, and believes this can be achieved without creating delays to new medicines and in a manner consistent with Colombia's international obligations. It is our understanding that the Colombian Government is drafting a revised NDP law that will eliminate Article 72 (among other changes).

- **Substandard biologics regulation**: On September 18, 2014, Colombia issued Decree 1782, which establishes marketing approval evaluation requirements for all biologic medicines. As part of the Decree, Colombia has established an unprecedented "abbreviated" pathway for the registration of non-comparable products, which is inconsistent with sanitary and WHO standards and practices in the United States and other countries and which could result in the approval of medicines that are not safe and/or effective. Industry urged the Colombian Government to remove this third pathway from the Decree, to no avail. Since issuing the Decree, the MOH has issued implementing guidelines, but that process has lacked transparency and due process and has not served to resolve the fundamental deficiencies of the third pathway.

- **Arbitrary and non-transparent market access policies**: Colombia's international reference pricing methodology and other cost containment measures are being used to set the same price for both the public and private segments of the market. Such a practice does not account for different supply chain costs in the reference countries, and does not reflect the realities of the Colombian market *vis-à-vis* other jurisdictions.

For these reasons, PhRMA requests that Colombia remain on the **Priority Watch List** in the 2019 Special 301 Report. Further, we urge USTR to provide an opportunity for an assessment of Colombia's IP and market access environment through an **Out-of-Cycle Review**, so that the U.S. Government can evaluate progress on these important issues and dedicate the required bilateral attention necessary to make progress on the barriers confronted by U.S. businesses in Colombia.

Intellectual Property Protection

Compulsory Licensing

On December 20, 2017, the MOH issued Resolution 5246 accepting for review a DPI petition filed by Fundación IFARMA. The petition calls for the compulsory licensing of the entire class of innovative medicines for the treatment of hepatitis C, following a similar petition granted against an innovative cancer medicine in 2016.

Resolution 5246 is both legally and procedurally deficient. It appears to be inconsistent with Colombia's international obligations and aspirations. First, Resolution

5246 is based on a petition that failed to identify the patents for which the DPI is being requested, clearly falling short of the standard set forth in Decree 1074 of 2015 ("Decree"). There is no provision in the Decree that allows for the MOH to unilaterally correct omissions in the petition. On the contrary, Article 2.2.2.24.4 of the Decree expressly places the burden of proof on the petitioner to identify the patented technologies that are supposedly affecting the public interest.

Second, a DPI on a broad category of medicines, namely "antivirals for treatment of hepatitis C" would be baseless for a number of reasons, including that: a) the petition itself identifies an entire class of medicines, which demonstrates that significant competition already exists in this market segment; b) hepatitis C drugs were just recently the subject of significant price reductions in Colombia, and the Ministry itself has publicly asserted over the course of months that this price reduction was between 80 and 90 percent; and c) there is no indication that a health-related emergency regarding hepatitis C exists in Colombia. To the contrary, the incidence of hepatitis C is quite low in Colombia.

The MOH could act on this deeply flawed petition at any time, potentially destroying an entire market for a class of innovative medicines developed in the United States. PhRMA urges USTR and other federal agencies to address this serious threat to American innovation through ongoing discussions under the U.S.-Colombia Trade Promotion Agreement.

Regulatory Data Protection Failures

Existing Colombian legislation Decree 2085 of 2002 (and its subsequent interpretation through a March 2003 joint act signed by the Ministers of Trade and Health) requires that new chemical entities receive a 5-year period of regulatory data protection upon approval. Nevertheless, the Colombian regulatory authority INVIMA recently has begun denying regulatory data protection upon approval of some new chemical entities, simply because they share a minor portion of their chemical structure with previously approved products.

This sudden and drastic change in procedure is inconsistent with the requirements of Decree 2085 of 2002 and contrary to the practice in other countries that provide regulatory data protection for such products. Such disregard of existing legislation undermines incentives to conduct clinical trials and develop new biopharmaceutical products in Colombia.

Restrictive Patentability Criteria

The Andean Court of Justice (ACJ) has issued several legal opinions (89-AI-2000, 01-AI-2001 and 34-AI-2001) holding that Andean Community members should not recognize patents for second uses. These decisions are contrary to long-standing precedents and inconsistent with TRIPS Article 27.1. Andean member countries, including Colombia, have chosen to honor their Andean Community obligations, while ignoring their TRIPS obligations.

The failure to provide patents for second uses harms patients by undermining incentives for biopharmaceutical innovators to invest in evaluating additional therapeutic benefits of known molecules (second uses) and provide more effective solutions for unsatisfied medical needs. The ACJ position is dispositive on the issue and no further domestic appeals or remedies are possible.

Weak Patent Enforcement

There is no mechanism in place to provide patent holders with the opportunity to resolve patent disputes prior to the launch of a follow-on product. This has led to the approval and marketing of follow-on products, despite the fact that a patent for the original drug is still in force.

Market Access Barriers

Substandard Biologics Regulation

On September 18, 2014, Colombia issued Decree 1782, which establishes the marketing approval evaluation requirements for all biologic medicines. As part of the Decree, Colombia has established an unprecedented abbreviated pathway for registration of non-comparable products, which is inconsistent with both WHO and FDA standards and could result in the approval of medicines that are not safe and/or not effective.

PhRMA members participated actively in the public consultations and engaged extensively with MOH and their technical experts, specifically highlighting that the abbreviated “third pathway” created by the Decree is not in line with the WHO guidelines for approval of biologics. In contrast to the Full Dossier Route (for originators) and the Comparability pathway (pathway for Biosimilars) found in WHO guidelines, the “Abbreviated Comparability Pathway” as described in the Decree allows for summary approval of non-comparable products and does not provide adequate controls or any clarity regarding how the safety or efficacy of a product approved via this pathway will be evaluated and assured.

PhRMA members urged the Colombian government to remove this third pathway from the Decree, to no avail. This route has been justified by the MOH, and ratified by the President, as a necessary tool to lower prices of medicines by promoting the swift entry into the market of competitors. However, shaping competition policy is not the appropriate role for a sanitary regulation, which should be strictly focused on ensuring the safety and efficacy of products.

Furthermore, per the Decree, a product approved via the “Abbreviated Comparability Pathway” will use the same non-proprietary name as the innovator, despite the fact that any similar biologic product would be a distinct biologic product from that of the originator or other biosimilar products. Assigning identical non-proprietary names to

products that are not the same could result in inadvertent substitution of the products, and would make it difficult to quickly trace and attribute adverse events to the correct product.

Arbitrary and Non-Transparent Market Access Policies

Colombia sets a maximum price for both the private and institutional markets by setting the price at the level of the distributor. These markets are dissimilar in most characteristics, in that they service different patient populations via different business models.

Moreover, the pricing system is highly subjective. For example, it provides that certain price control exceptions may be made for products providing a significant technical benefit over medicines containing the same active ingredient (*i.e.*, regular versus modified release tablets), yet it does not clearly establish the criteria required to grant such exceptions. Furthermore, in August 2018, the MOH published a new list of drugs to come under direct price control, with a record number of 150 presentations that including products such as contraceptives, anti-hypertensives, and psychiatric drugs. These products are facing an average price reduction of 50% since January 2019.

MIDDLE EAST / AFRICA

ALGERIA

Algeria's policies and actions pose significant intellectual property and market access challenges for PhRMA members. PhRMA and its member companies believe, however, that Algeria has the potential to foster investment in pharmaceutical innovation and address the unmet medical needs of the country.

PhRMA noted some success in collaborating with the prior government in place until mid-2012, with that government stating publicly its support for a new strategy that better integrates the innovative pharmaceutical sector into Algeria's economy and health care system. Subsequent Ministers have reaffirmed their commitment to boosting Algeria's competitiveness in the innovative biopharmaceutical sector, but dozens of proposed reforms have not been implemented. Despite deterioration in the overall business and investment environment, PhRMA's member companies are hopeful for a similarly cooperative dialogue with the government in 2019 to address the key challenges they face in Algeria.

Key Issues of Concern:

- **Weak patent enforcement and regulatory data protection failures**: Algeria has inadequate patent protection, ineffective mechanisms to enforce patents, and does not grant regulatory data protection (RDP). Trademark counterfeiting is a growing problem.

- **Import restrictions and forced localization**: Algeria prohibits imports of almost all pharmaceutical products that compete with similar products that are manufactured domestically. Pharmaceutical products and active pharmaceutical ingredients (API) that are not locally manufactured are subject to annual import quotas.

- **Pricing procedures**: Algeria's pricing and reimbursement mechanisms are cumbersome and delayed. Historically, some patented medicines with no generic equivalent on the market have been referenced against generic products deemed to be in the same therapeutic class. In addition, the new drug pricing procedure issued in August 2015 has key weaknesses related to its reference pricing system and the frequency of updates. As a result, prices in Algeria do not recognize the value of innovative products, nor do they reward the significant investment involved in developing new medicines, or encourage the development of tomorrow's new cures.

- **Cumbersome and Slow Regulatory System**: Despite significant improvements in the Ministry of Health's (MOH's) registration process in 2013, the registration process remains slow and burdensome. As a result, patient access to innovative medicines in Algeria lags significantly behind peer countries.

- **Failure to renew representative office licenses**: Many pharmaceutical companies operating in Algeria have established representative offices. Licenses for such offices must be renewed every two years, and yet in 2018 the Ministry of Commerce has suspended renewing these licenses. In addition to creating significant uncertainty as to the ability of these companies to continue operating in Algeria, it has resulted in local banks threatening to block access to member accounts until their office licenses are renewed.

For these reasons, PhRMA requests that Algeria remain on the **Priority Watch List** in the 2019 Special 301 Report, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protection

Weak Patent Enforcement

Marketing approval authorities in Algeria improperly interpret current laws and regulations by granting marketing approval to copies of patent protected products while the original patent is still in effect. In some cases, this is happening many years in advance of the original product patent expiration despite the owners repeated attempts to alert the authorities and present documentation confirming that the product is under patent in Algeria.

The absence of effective judicial remedies for preventing the infringement of basic patent rights, including the lack of injunctive relief that could prevent 1irreparable harm prior to the resolution of the patent dispute, puts the originator in an untenable position with no possibility to defend its rights. Violations of Algerian patents that have occurred in recent years have still not been corrected.

Regulatory Data Protection Failures

Algeria does not protect pharmaceutical test and other data from unfair commercial use and disclosure. Algeria should correct this deficiency through implementation of meaningful RDP.

Market Access Barriers

Import Restrictions

On October 21, 2008, the Algerian Government issued a decision[233] stipulating that, effective January 2009, the importation of pharmaceutical products that compete with similar products that are being manufactured locally is prohibited. This decision was

[233] The decision was published in November 2008 under the name “Arrêté du 30 novembre 2008 relatif àl’interdiction des produits pharmaceutiques et dispositifs médicaux destinés à la médicine humaine fabriqué en Algérie.

essentially a reinstatement of a previous ministerial decree[234] that was suspended as part of the WTO accession process. Subsequently, the MOH published lists of such products comprising hundreds of branded medicines, and this import policy continues to be implemented in a non-transparent and arbitrary manner. Repealing this decision should be a prerequisite before Algeria can join the WTO.

In August 2015, the MOH issued a Procedure for the inclusion of products on a list of pharmaceutical products prohibited for import. The innovative pharmaceutical industry is highly concerned about the proposed procedures to ban imports of certain products to promote local manufacturing. This proposal contradicts the government's aspirations to attract more investment by the innovative biopharmaceutical industry and for Algeria to accede to the WTO. As the procedures themselves recognize, such restrictions could have major consequences on patient access to innovative products as well as on the operations and sustainability of our member companies in Algeria.

In 2017, the Algerian Government arbitrarily imposed volume restrictions on imports of pharmaceutical products that compete with similar products produced domestically and/or imported generic products.

Algeria's restrictions on the importation of pharmaceuticals severely restrict patient access to innovative medicines, discriminate unfairly against PhRMA members, and are a significant barrier to trade. They have resulted in shortages of some drugs, further harming Algerian patients. During numerous discussions over the last few years between the Algerian government and industry, officials signaled their intent to reform the system to improve access and minimize stock disruptions. As of today, however, the system remains unchanged.

Investments and Commercial Laws

In December 2008, the Algerian Government declared that any company engaged in foreign trade should have a minimum of 51 percent of local Algerian shareholders. This decision applies prospectively, not to companies engaged in foreign trade prior to December 2008. Despite the lack of success in attracting significant new investment, the new government has recently confirmed that this law will continue to be enforced for the foreseeable future.

Since 2009, importers have been required to secure letters of credit and set aside a percentage of the import value as a deposit on their purchase.

In May 2010, the MOH issued a circular that prohibits local manufacturers from selling products to wholesalers, and requires them to sell such products directly to pharmacies. Therefore, PhRMA members who invested in local manufacturing will now also have to invest in distribution infrastructure. While this circular has never been applied, the uncertainty of the regulation continues to concern PhRMA members.

[234] Instruction #5 for the Generalization of Generics (Sept. 2003).

Volume Control

Algeria continues to impose an annual import quota for medicines and active pharmaceutical ingredients with the "requirement that each shipment receives prior clearance from the MOH."

The Government routinely blocks imports as a temporary cost-containment tool. The unintended consequence, however, is that it leads to shortages in the market, to the detriment of Algerian patients. The narrow focus on cost means that it cannot capture the underlying value of promising new medicines for patients or reduce other costs in the health care system, such as avoiding expensive hospitalizations, surgery, rehabilitative or long-term care.

Pricing Procedures

The Algerian Government utilizes international reference pricing (IRP) to determine the government price level of medicines. As a general matter, IRP is a sub-optimal tool for setting drug prices because it doesn't take into consideration the local health and economic interests. Instead of recognizing the value that innovative medicines can provide for patients in a specific country, IRP imports prices from other countries that typically have different disease burdens, indications, willingness (preferences) and ability (income) to pay, industrial goals or market structures. In short, IRP as a policy is not consistent with Algeria's goal of promoting a local innovative biopharmaceutical industry.

In August 2015, the Algerian Government issued a new procedure for determining drug prices. Key weaknesses in Algeria's new pricing procedure and the IRP model include:

- The new pricing procedure references a list of countries including Greece and Turkey. Neither Greece nor Turkey are appropriate reference countries. Prices in Turkey are based on deflated prices in Europe as a result of a discriminatory fixed Euro-Turkish Lira exchange rate and prices in Greece have been set based on the ongoing economic crisis in that country. In short, the artificially low prices in both of these countries do not reflect the true value of innovative medicines and certainly are not consistent with a country seeking to encourage local R&D. This measure ignores the damage that such policies have had on the innovative biopharmaceutical industry in those countries, where investment has stagnated and the industry is in a state of contraction. As such, Turkey and Greece should be removed from Algeria's basket of reference countries.

- To ensure predictability and fairness, the IRP calculation should be based on the average or median price in the basket of countries, not the lowest price in the basket (or even worse, the lowest European price less 10 percent).

- Re-referencing should be predictable, objective (*i.e.*, follow the same procedures for both price increases and decreases in the reference countries) and limited to

reasonable intervals, such as every five years during the marketing approval (MA) renewal process. While the industry commends Algeria for providing a process for allowing manufacturers to seek adjustments during the MA renewal process to account for changes in the reference countries, it is not reasonable or fair to require manufacturers to continually monitor prices in all of the reference countries (a significant administrative burden) and report on relevant alterations.

- Greater clarity is needed in the procedures around the exchange rates to be used to determine prices in the reference countries and how Algeria defines "the country of origin."

- While the innovative pharmaceutical industry commends the Algerian Government for providing an appeal mechanism, ten days is an insufficient period for a company to prepare the appropriate supporting documents for the appeal, particularly given that this will likely require coordination with regional offices and headquarters in other countries. Instead, we would propose that the appeal deadline should be extended to 30 days after the date of the notification of the price established by the Economic Committee.

Cumbersome and Slow Regulatory System

Despite some improvements in the MOH's registration process since 2013, the registration process remains slow and is now falling further behind regulatory reform trends observed in the region, namely in the largest pharmaceutical markets Egypt and Saudi Arabia. In those countries, new review procedures are expected to significantly reduce the time it takes to register new medicines by 90%. This will accelerate marketing authorizations and enable patients to access promising new treatments in as little as 30-60 days after those new medicines are approved for use in Europe or the United States. Algeria should adopt similar review procedures to achieve the same results.

Additional burdensome requirements for obtaining registration to market pharmaceutical products, especially innovative products, have been implemented. As a result, patient access to innovative medicines in Algeria lags significantly behind peer countries. For example, all registration dossiers must be pre-authorized prior to acceptance for review, but there is no transparent process or timeline for completing this preliminary step of the process. After submission to the MOH, registration dossiers are on hold pending National Laboratory results, which causes further delay and complexity in the registration process. Despite the implementation of a new registration process in 2017, no progress or improvement has been achieved.

In addition, the innovative industry continues to face significant and growing access challenges within the reimbursement committee (CRM) process led by the Ministry of Labor (MOL):

- The MOH via the price committee (MOL is a member of this committee) approves a price for the new medicine as part of the marketing approval process. But the

CRM reimbursement process is entirely separate, and the MOH marketing approval price is rarely accepted in the CRM (MOH is member of the CRM) process. As a result, manufacturers are required to enter into separate reimbursement negotiations with the CRM, and the new lower price must then be re-approved by the MOH. These combined procedures are inefficient, redundant, and unfair to innovative pharmaceutical manufacturers.

- There is no clarity or fixed timeline between the first submission to the CRM of the dossier for reimbursement and the application at the pharmacy level. While the intent of the MOL is to reduce the maximum number of products on the list of reimbursable products, this particularly affects imported products so that a new (innovative) product has a very low chance of being reimbursed. And recently even locally produced medicines are affected.

Finally, since June 2010, pharmaceutical companies have noticed lengthy delays of many months in approving variations for imported products already available on the market. The previous government had begun to recognize the negative impact that unnecessary delays have on patients and the business climate, but the backlog continues.

A new health code was recently published in the July 29, 2018 edition of the Algerian Official Gazette. While the new code will seek to modernize and potentially bring significant changes to Algerian health policy, the full effect of the new code will not be known until its implementing legislation has been released.

Failure to Renew Representative Office Licenses

Many pharmaceutical companies operating in Algeria have established representative offices. Licenses for such offices must be renewed annually, and yet in 2018 the Ministry of Commerce has suspended renewing these licenses. In addition to creating significant uncertainty as to the ability of these companies to continue operating in Algeria, it has resulted in local banks threatening to block access to member accounts until their office licenses are renewed.

Industry Association License

PhRMA's member companies have been trying for many years to establish a local pharmaceutical association to engage in public policy advocacy on behalf of the innovative medicines sector. Although the Algerian Government has communicated that the proposed industry association is approved, the formal and official license is still pending.

Establishing an association is a critical step for industry to be able to work with the Algerian Government on realizing the goals set forth in the Vision 2020 report and the various undertakings that the industry and government have agreed to in recent years.

SAUDI ARABIA

Over the last several years, PhRMA and its member companies operating in the Kingdom of Saudi Arabia have observed many improvements in the policy environment. These reforms are consistent with Saudi Arabia's effort to encourage biopharmaceutical innovation, employment, and investment. However, recent actions by the Saudi Food and Drug Administration (SFDA) are undermining these positive developments and the investment climate in Saudi Arabia. We look forward to a constructive dialogue with the relevant Saudi authorities to resolve these concerns.

Key Issues of Concern:

- **Ineffective Patent Enforcement and Regulatory Data Protection (RDP)**: In mid-2017, the SFDA granted marketing approval to a generic version of an innovative medicine during the patent term of that product. SFDA's approval and related price listing of a generic product corresponding to a patented innovator medicine undermines the integrity of Saudi Arabia's patent linkage system. PhRMA member companies are also concerned by Saudi Arabia's failure to provide a sufficient period of RDP from the date of marketing authorization of innovator products in Saudi Arabia, contradicting the country's own regulations and World Trade Organization (WTO) commitments.

For these reasons, PhRMA requests that Saudi Arabia be placed on the **Priority Watch List** in the 2019 Special 301 Report, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protections

Ineffective Patent Enforcement and Regulatory Data Protection

Despite creating a mechanism to provide for effective patent enforcement in 2013, in mid-2017 the SFDA granted marketing authorization to a domestic company to produce a generic version of a U.S. innovative product prior to the expiration of the patent term on that product. Furthermore, the Ministry of Health proceeded to procure the infringing product despite multiple appeals from the relevant innovator company. The local company is now distributing these copies to the Ministry of Health and selected hospitals.

This action appears to be part of a broader pattern of abuse of American innovation, following SFDA's earlier decision to grant marketing approval to copies of another innovative medicine during the period of RDP provided by Saudi law. Indeed, while Saudi Arabian law provides for RDP, in practice it is not applied effectively.

Specifically, Article 5 of a Council of Ministers' Trade Secrets Protection Regulation (decision No. 3218, dated 25/03/1426 H, May 4, 2005), as amended by Ministerial Decision No. 431 of 1.5.1426H (June 8, 2005) states that the submission of confidential

tests or other data, obtained as a result of substantial efforts, for the approval of the marketing of drugs or agricultural products which utilize a new chemical entity, shall be protected by the competent authority against unfair commercial use for at least five years from the approval date. Unfortunately, the Kingdom of Saudi Arabia has not complied with its own regulation and WTO commitments which gave rise to the regulations. Specifically, Saudi Arabia confirmed during its accession to the WTO that:

> [Its] Regulations provided for protection of undisclosed tests and other data submitted to obtain approval of a pharmaceutical or agricultural chemical against unfair commercial use for a minimum period of five years from the date of obtaining the approval including the establishment of the base price. No person other than the person who submitted such data could, without the explicit consent of the person who submitted the data, rely on such data in support of an application for product approval. Any subsequent application for marketing approval would not be granted a market authorization unless the applicant submitted its own data, meeting the same requirements applied to the initial applicant, or had the permission of the person initially submitting the data to rely on such data.[235]

Member companies have approached Saudi authorities concerning the need to enforce their RDP regulations, yet authorities continue to deflect from the substance of these complaints and insist they are not sharing the content of the drug registration file of the innovator product.

The WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), however, imposes more than a non-disclosure obligation. Rather, TRIPS Article 39.3 additionally requires WTO member states to implement an effective system of pharmaceutical drug registration, which prevents "unfair commercial use" of data generated by others. This is fulfilled by preventing reliance on regulatory test data and approvals based on such data for a fixed period of time. In other words, protected data may not be used to support marketing approval for follow-on products for a set amount of time unless authorized by the original submitter of the data.

In short, these actions appear designed to benefit Saudi Arabia's local industry at the expense of U.S. innovators. These actions harm U.S. manufacturing workers, infringe proprietary technology and damage U.S. exports. Contrary to the country's aspirations to promote local investment, intellectual property (IP) infringement, and the lack of effective enforcement sends a hostile message to U.S. inventors and investors that their valuable IP rights are not secure in Saudi Arabia.

We stand ready to work with the Saudi and U.S. governments to ensure that U.S. innovators can rightfully protect and enforce their IP rights in Saudi Arabia, consistent with Saudi Arabia's international obligations.

[235] Report of the Working Party on the Accession of the Kingdom of Saudi Arabia to the World Trade Organization, WT/ACC/SAU/61 (Nov. 1, 2005) ¶ 261.

WATCH LIST

ASIA - PACIFIC

AUSTRALIA

PhRMA and its member companies support the U.S.-Australia Free Trade Agreement (AUSFTA) ratified by both countries in 2004. The Agreement has contributed to expanded patient access to new medicines in Australia, a key priority for PhRMA. However, we believe there is much more that could be done to further protect and strengthen Australia's intellectual property (IP) regime and improve market access for new and innovative medicines, which will also serve to foster innovation in Australia's pharmaceutical and biotechnology sectors domestically and abroad – a key priority of the Australian Government.

In the Pharmaceuticals Annex to the AUSFTA, Australia and the United States agreed to provisions for increased transparency and accountability, and enhanced consultation between the United States Government, industry and the Australian Government to improve the operation of Australia's Pharmaceutical Benefits Scheme (PBS). Annex 2-C of the AUSFTA at [1] commits the Parties to four principles to facilitate high quality health care and continued improvements in public health. These principles include: "(a) the important role played by innovative pharmaceutical products in delivering high quality health care; (b) the importance of research and development in the pharmaceutical industry …; (c) the need to promote timely and affordable access to innovative pharmaceuticals through transparent, expeditious and accountable procedures …; and (d) the need to recognize the value of innovative pharmaceuticals through the operation of competitive markets or by adopting or maintaining procedures that appropriately value the objectively demonstrated therapeutic significance of a pharmaceutical." Annex 2-C of the AUSFTA at [3] also establishes a Medicines Working Group (MWG) to promote discussion and mutual understanding of the importance of pharmaceutical research and development to continued improvement of health care outcomes.

While progress has been made in implementing these agreed principles, on-going collaboration is required to ensure that the full potential of the pharmaceutical industry can be realized. We look forward to constructive outcomes from the locally-established, recently re-invigorated, bilateral (Government-Industry) Access to Medicines Working Group (AMWG), first established in 2006 as part of reforms to the PBS. Industry has also welcomed the implementation of a tranche of reforms to the regulations for the registration and market approval of medicines and medical devices in Australia. These reforms are expected to streamline processes and regulations and make life-saving medicines and medical devices available to Australian patients in a timelier manner.

PhRMA recommends that, as set out in the AUSFTA, regular meetings under the MWG (which is distinct from AWMG) resume as a matter of urgency; it has been approximately ten years since this MWG last met. While intervening negotiations may have provided sufficient opportunity for our officials to remain in contact, those regular contacts are no longer occurring.

Key Issues of Concern:

- **Uncompetitive intellectual property environment**: There are several weaknesses in Australia's IP regime that harm both domestic and multinational firms:

  - Market-size Damages: The Australian Government continues to seek damages from innovators in cases where duly-issued patents on PBS-listed medicines have ultimately been held invalid or not infringed following an initial granting of a preliminary injunction. This action creates significant uncertainty for pharmaceutical patent owners, who need to be able to rely on the rights conferred by granted patents unless and until they are finally invalidated to support the large investments needed to develop new medicines. It also undermines the rights of patent holders in Australia by introducing a strong disincentive to exercise their core right to enforce their IP protections.

  - Weak Patent Law Enforcement: This uncertainty is exacerbated by the difficulty in resolving patent challenges prior to competitor market entry, due to lack of adequate patent holder notification. Contrary to its obligations under art 17.10(4) of the AUSFTA, Australia has not implemented a system by which patent holders, as a matter of practice, receive advance notice of third party applications for marketing approval of potentially patent-infringing pharmaceutical products. In the rare circumstances where any such advance notice is actually provided, the amount of notice is inadequate to enable the final resolution of any patent infringement claims *before* the relevant third party product obtains regulatory approval for market entry during the term of the relevant patent/s.

  - Compulsory Licensing: In 2016, the Australian Government launched a Productivity Commission (Commission) inquiry into Australia's "Intellectual Property Arrangements."[236] The Commission's report was publicly released on December 20, 2016, and contained a number of findings that were not appropriate, reasonable or supported by evidence. In its August 2017 and November 2018 responses to the report, the Australian Government indicated that some damaging recommendations would not be accepted. However, industry is very troubled and will be harmed by changes to national patent law based on the Commission's recommendations. These changes would present a higher standard for what could be considered a patentable invention in Australia and would promote the use of compulsory licensing.

  - Regulatory Data Protection (RDP) Failures: Australia should strengthen its regulatory data protection (RDP) to align with international best practice, to improve the country's attractiveness as a destination for foreign investment by

[236] *See* http://www.pc.gov.au/inquiries/completed/intellectual-property#report (last visited Feb. 7, 2019).

global pharmaceutical companies, and to encourage companies to bring new medicines to Australia sooner.

Beyond the relative adequacy of the RDP term that Australia provides in respect of therapeutic goods containing active components which have not previously obtained market approval, it is highly unsatisfactory that Australia does not provide any RDP protection relating to the registration of new formulations, combinations, indications, populations or dosage forms of currently registered therapeutic goods. Indeed, the absence of any such protection is in direct contravention of Australia's obligations under art 17.10(2) of the AUSFTA, which mandates that the Parties provide at least three years of RDP protection from the date of marketing approval in circumstances where new clinical information must be submitted to obtain regulatory approval of the relevant new therapeutic good (other than information relating to bioequivalence).

- **Market access**

  - Proposed increases to PBAC submission fees (PBAC Cost Recovery): In February 2018, the Department of Health announced that it would be increasing cost recovery for evaluation of applications for PBS listing to ensure that 100% cost recovery is achieved, effective July 1, 2019. Under current submission structures this would mean an increase in PBS evaluation fees from approximately $134k to over $220k (indicative) for a major submission. While industry understands the need for submission fees to reflect the real costs of PBS processes, proposed increases to Pharmaceutical Benefits Advisory Committee (PBAC) submission fees must be balanced with increased efficiencies within the reimbursement process. Industry will continue to work with the Australian Government to ensure the proposed increases are fair and reasonable.

  - Difficulties in listing new medicines on the PBS: Companies continue to face challenges and uncertainty in the listing of new medicines on the PBS. For new medicines, navigating the regulatory framework of market authorization and reimbursement remains complex and, particularly for reimbursement, iterative. This is compounded by an “offset” policy that requires every new dollar spent on new medicines to be counterbalanced by an equivalent offset, determined in advance, from within the existing health budget. This policy is not sustainable alongside a policy of investment in innovation and delays access to innovative and important medicines for Australian patients.

  - Biosimilars: There have been significant developments regarding the introduction of biosimilar medicines into the Australian market. We welcome the commitment and ongoing efforts of the Australian Government, through the Strategic Agreement with Medicines Australia, to ensure appropriate and broad consultation with the sector and help deliver a coordinated and balanced policy.

- Government-initiated post-market reviews of PBS listed medicines: While important steps have been taken by the Australian industry and Government to implement an improved process for post-market reviews, the focus of post-market reviews on cost containment continues to be a concern for industry.

For these reasons, PhRMA requests that Australia be placed on the **Watch List** in the 2019 Special 301 Report, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protection

Market-Size Damages

Biopharmaceutical innovators must be able to rely on and enforce patents issued by competent government authorities. Laws or policies that allow governments or other non-parties to a patent dispute to collect "market-size damages" after the fact from innovators that pursue unsuccessful patent claims unfairly penalize and discourage the use of provisional enforcement measures as part of well-functioning early resolution mechanisms. These policies undermine legal certainty, predictability and the incentive provided by patents to invest in new treatments and cures.

Australia's Therapeutic Goods Act, as amended by the legislation implementing the AUSFTA, provides for the award of damages in limited specific circumstances, where a court determines that the patent holder has engaged in improper conduct specifically identified in that legislation in commencing proceedings or seeking a preliminary injunction.[237] Damages under this scheme have not been sought since its introduction. However, outside of that scheme, and pursuant to the usual undertaking as to damages provided by patent holders as a requirement for obtaining a preliminary injunction, since around 2012 the Australian Government has stated its intent to seek – and has sought – market-size damages from biopharmaceutical innovators that have legitimately but ultimately unsuccessfully pursued patent claims. It has done so even where the preliminary injunction was granted (and replaced by a permanent injunction) several years before the Australian Government first stated its intention to seek such damages. Those claims are purported to compensate the PBS for the effect of any delays in price reductions for patented medicine during the period of a preliminary injunction. The PBS imposes automatic price cuts on medicines as soon as competing versions are listed on the PBS, but the policy does not include any corresponding mechanism to compensate innovators for losses if an infringing product is launched prematurely.

By pursuing market-size damages, the Australian Government is unfairly tipping the scales in pharmaceutical patent disputes –and discouraging innovators from enforcing their granted patents. This policy creates an inappropriate conflict of interest for the

[237] *See* Schedule 7 of the US Free Trade Agreement Implementation Act 2004, available at https://www.legislation.gov.au/Details/C2004A01355/ (last visited Feb. 7, 2019).

Australian Government, by permitting the same government that examined and granted a patent to seek damages if that patent is later held to be invalid or not infringed. It exposes innovators to significant additional compensation claims that may be difficult to quantify and were not agreed to or contemplated at the time the preliminary injunction was granted. The punitive size of these additional claims effectively equates legitimate patent enforcement, in circumstances where the market effects of infringing generic entry are difficult to quantify, with patent abuse. Allowing governments or other non-parties to a patent dispute to collect market-size damages undermines legal certainty, predictability and the incentives that patents provide for investment in new treatments and cures. Australia's practice appears to be inconsistent with the AUSFTA and with World Trade Organization (WTO) intellectual property rules, including with respect to provisional measures.

Indeed, in the course of claiming market-size damages, representatives of the Australian Government have stated that the Australian Government will grant an application to list a competing generic product on the PBS (the effect of which is an automatic price cut), even when:

- the patentee has lodged a certificate, required as a result of the amendments to the Therapeutic Goods Act as a result of the legislation implementing the AUSFTA as a precondition for commencing patent infringement proceedings, stating that infringement proceedings in respect of that product have been commenced in good faith, have reasonable prospects of success, and will be conducted without unreasonable delay; and/or

- a preliminary injunction has been granted by a court which prohibits the supply of that product by the generic company.

Such comments typify the Australian Government's abovementioned conflict of interest, as well as the disregard paid by the Australian Government to the legitimate interests of innovators in enforcing their granted patent rights.

PhRMA members urge USTR and other federal agencies to prioritize actions to address Australia's pursuit of market-size damages.

The Australian Government should immediately and publicly abandon its policy of seeking market size damages, or any damages, when a patent holder has legitimately sought to enforce its patent rights.

Weak Patent Law Enforcement

Mechanisms that provide for the early resolution of patent disputes before a potentially infringing product is allowed to enter the market are critical to ensuring adequate and effective protection of IP rights for the research-based pharmaceutical sector. Such mechanisms prevent marketing of a product potentially covered by a patent until expiration of the patent or until any dispute relating to infringement or validity of such

a patent is resolved. An effective early resolution mechanism provides a procedural gate or safeguard. It ensures drug regulatory entities do not enable the launch of a product which potentially infringes patent rights granted by another entity of the same government, by providing marketing authorization to a product, or granting PBS listing which must be accompanied by an assurance by the generic company that it will supply its product. In this regard, the abovementioned statements by representatives of the Australian Government to the effect that they will grant an application to list a competing generic product on the PBS, even when it has received a certificate submitted by the patent holder that patent infringement proceedings in respect of that product have been commenced in good faith, have reasonable prospects of success, and will be conducted without unreasonable delay, and even when a court has granted a preliminary injunction preventing the generic company supplying that generic product, are highly concerning to PhRMA members.

As indicated above, the AUSFTA provides that when marketing approval is sought by an applicant for a generic product or "product for an approved use," where the product or approved use is claimed by a patent, the Party (here, Australia) should "provide measures in its marketing approval process to prevent" marketing of the generic product or use during the patent term without consent or acquiescence of the patent owner. Further, if Australia permits a third party to request marketing approval for a product or approved use claimed by a patent identified as claiming that product or approved use, it "shall provide for the patent owner to be notified of such request and the identity of any such other person."[238] This should include a database or other mechanism by which a third party may determine whether there are patents that may be infringed by the product or use for which the third party is seeking approval.

However, originator pharmaceutical companies in Australia generally do not receive any notice of a third party's intention to enter the market with a product that may infringe a valid and enforceable patent prior to its listing on the Australian Register of Therapeutic Goods (ARTG). Originator companies are only able to access this information once the generic has already been registered on the ARTG, and even then, the originator company itself has to actively seek that information on the ARTG website – originators are not notified by the generic company or the TGA. As a result, originator pharmaceutical companies in Australia are routinely unaware of a potential infringing product until after the product has received marketing approval (and has been registered on the ARTG). While in recent years the Australian Government has been quicker to identify and publish newly approved generics on the ARTG website, this is not what was envisaged in the AUSFTA. Publishing information on the ARTG that a generic has already been granted marketing approval for its product is not sufficient notification of the *request* by a third party for marketing approval under the AUSFTA.

Originator companies are significantly impacted when generic medicines enter the market prior to the expiry of the originator patent, in part through mandatory and irreversible price cuts for innovator products listed on the PBS, and through market share

[238] *See* Article 17.10(4) of AUSFTA.

erosion. The only legal option available to the innovator patentee is to obtain preliminary injunctive relief (or equivalent relief) to prevent the generic company from launching, which in the case of PBS listing must be obtained in the few months between the time marketing approval of the generic product is published on the ARTG and the next possible PBS listing date, in order to prevent the irreversible price reduction. The preliminary injunction process also comes with risk of market-sized damages as discussed earlier.

This lack of effective mandatory notification, the absence of an effective mechanism for the early resolution of patent disputes before an infringing product is launched in Australia, and the unduly prejudicial penalties being sought by the Australian Government from patent holders for seeking to defend their IP (including liability for market-sized damages as discussed in detail above) significantly weakens the level of IP protection for pharmaceutical innovation in Australia, serving to deprive patent holders of expected benefits under international agreements including the AUSFTA. The Australian Government should implement a means for an innovator patentee to publicly identify each patent that covers its innovator product and the approved uses for that product and an effective notification system, which would make it mandatory for generic companies seeking marketing approval to notify a patentee, at the time of filing their application, that it has applied for approval to market a generic product during the life of a patent that the patentee has identified as covering that product or its approved use. Such a system would allow patentees the opportunity to legitimately assert their IP rights prior to generic launch.

Compulsory Licensing

In 2016, the Australian Government launched a Productivity Commission (Commission) inquiry into Australia's "Intellectual Property Arrangements."[239] The Commission's report was publicly released on December 20, 2016, and contained a number of findings that biopharmaceutical innovators did not consider appropriate or reasonable, such as calls to restrict patent term restoration in Australia, to allow manufacture for export during the restored patent term, and to raise the threshold for a patentable inventive step.[240]

In its August 2017 and November 2018 responses to the report, the Australian Government indicated that some of the report's most damaging recommendations would not be accepted. However, IP Australia now appears poised to recommend amendments to national law based on the Commission recommendations that would create uncertainty by raising the standard by which an invention would be considered patentable, and would promote the use of compulsory licensing. The standard by which inventions are considered patentable in Australia was raised in 2013, and that standard has yet to be considered by any Australian court. Until that standard has been interpreted by Australian

[239] *See* http://www.pc.gov.au/inquiries/completed/intellectual-property#report (last visited Feb. 7, 2019).

[240] In June 2016, PhRMA and a number of its international sister associations submitted comments to the Productivity Commission on these and other concerns with the Commission's draft findings, available at http://www.pc.gov.au/__data/assets/pdf_file/0010/194770/sub087-intellectual-property.pdf (last visited Feb. 7, 2019).

courts, any attempt to further raise the standard is unnecessary, premature, and will create more uncertainty for innovators.

Regulatory Data Protection (RDP) Failures

Biopharmaceutical innovators work with hospitals, universities and other partners to rigorously test potential new medicines and demonstrate that they are safe and effective for patients who need them. Less than 12% of medicines that enter clinical trials ever result in approved treatments.[241]

To support the significant investment of time and resources needed to develop test data showing that a potential new medicine is safe and effective, governments around the world protect such data submitted for regulatory approval from unfair commercial use for a period of time. Indeed, TRIPS Article 39.3 requires each WTO member to protect undisclosed test and other data submitted for marketing approval in that country against disclosure and unfair commercial use.

RDP is essential for all medicines, and particularly critical for biologic therapies. Made from living organisms, biologics are complex and challenging to manufacture and may not be protected adequately by patents alone. Unlike generic versions of traditional chemical compounds, biosimilars are not identical to the original innovative medicine and there is greater uncertainty about whether an innovator's patent right will cover a biosimilar version. Without the certainty of some substantial period of market exclusivity, innovators may not have the incentives needed to conduct the expensive, risky and time-consuming work to discover and bring new biologics to market.

Strengthening RDP protections and terms in Australia so they are aligned with global best practice would further enhance Australia's ability to compete for foreign investments in the knowledge- and innovation-intensive biomedical sector that can drive future economic growth. Australia should extend the term of RDP for new formulations, new combinations, new indications, new populations (*e.g.*, pediatrics) and new dosage forms. Indeed, the absence of such protection is in direct contravention of Australia's obligations under art 17.10(2) of the AUSFTA, which mandates that Parties provide at least three years of RDP protection from the date of marketing approval in circumstances where new clinical information must be submitted to obtain regulatory approval of the relevant new therapeutic good (other than information relating to bioequivalence).

[241] DiMasi JA, Grabowski HG, Hansen RW; Tufts Center for the Study of Drug Development. Innovation in the pharmaceutical industry: new estimates of R&D costs. In: Briefing: Cost of Developing a New Drug, available at https://static1.squarespace.com/static/5a9eb0c8e2ccd1158288d8dc/t/5ac66afc6d2a732e83aae6bf/1522952963800/Tufts_CSDD_briefing_on_RD_cost_study_-_Nov_18%2C_2014..pdf (last visited Feb. 7, 2019).

Market Access

Beginning with legislative changes implemented in June 2017, significant progress has been made with the implementation of the Medicines and Medical Devices Review; this progress highlights the benefits of regulatory review involving industry consultation. Measures such as the "Priority Review" and "Provisional Approval" pathways that deliver expedited access for some medicines in areas of high unmet need are welcome. However, unlike other jurisdictions, there is currently no corresponding change in the health technology assessment system to accommodate these fast-track approvals, especially in the case of the Provisional Approval pathway. It is also noted that the Australian Government has requested that PBAC consider alternative options for listing PD-1 and PD-L1 checkpoint inhibitors for the treatment of multiple cancer indications (pan-tumor).[242] Industry looks forward to working with the Australian Government to implement a fit for purpose reimbursement system to ensure that Australians have timely access to life-saving immuno-oncology medicines.

Difficulties in Listing New Medicines on the PBS

Prescription medicines accessed via the PBS constitute the vast majority of prescription medicines dispensed in Australia.[243] Accordingly, the reimbursement process to obtain PBS-listing, as well as PBAC guidelines and decision making, effectively dictate access to the Australian pharmaceutical market. Predictable and equitable outcomes and processes in PBS listings are therefore critical to securing market access to ensure Australian patients have access to innovative medicines. The purpose of the PBS is to provide timely, reliable and affordable access to medicines for all Australians.

In 2017, Medicines Australia signed a Strategic Agreement with the Australian Government to secure predictability and stability in the PBS and policy environment and to support business planning. This Agreement was not without significant cost to the industry by cementing the application of structured, predictable price reductions for on-patent medicines during their term in the single brand (F1) formulary at 5, 10 and 15 years post listing. Additionally, the Agreement resolves issues with the interpretation of section 99ACB of the National Health Act, and commits to no new determination of any Therapeutic Groups during the term of the Agreement.

It is now particularly important that the PBS remains fit for purpose as new and more advanced health technologies become available. To this end, we look forward to the delivery of the Australian Government's commitment in the Agreement to improve and streamline PBS processes to achieve faster access to new medicines.

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[242] *See* http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/agenda/august-2018-pbac-special-meeting (last visited Feb. 7, 2019).

[243] *See Australian Statistics on Medicines 2014,* available at http://www.pbs.gov.au/statistics/asm/2014/australian-statistics-on-medicines-2014.pdf (last visited Feb. 7, 2019).

The PBAC's approach of comparing new products to the "lowest cost" comparator creates an increasingly difficult barrier to patient access, due to these comparisons being made to cheaper, off-patent medicines that have undergone several rounds of competitive price reductions through price disclosure. As the price-disclosure measure has expanded and matured, creating downward pressure on prices in the multi-brand, competitive market for off-patent medicines, comparators are increasingly being drawn from very low-cost drugs. This approach undermines the intent of Australia's split formulary system – which was designed to recognize the value of innovation by excluding patented products from statutory price reductions applied to off-patent products subject to market competition – and is an additional disincentive to bringing innovative medicines to Australia. Recent activities to provide clarity on this issue have not led to widespread selection of the most appropriate comparator. There is ongoing work to be done in this area and we welcome the Australian Government's commitment to consider the issue of comparator selection as part of the AMWG discussions.

Biosimilars

The continued inclusion of Medicines Australia as a key stakeholder in the development and monitoring of the implementation of biosimilars policy through the Agreement remains a positive element. The application of stakeholder-agreed biosimilar uptake drivers is in its early stages, but offers the potential to encourage competition. It remains critical that measures be taken to improve prescriber and patient understanding in order to build confidence in the appropriate use of biologics and biosimilars medicines. The impact of the Australian Government's policy of allowing decisions regarding substitution (*i.e.*, enabling a patient's medicine to be switched) between biologic and biosimilar products at the pharmacy level, particularly in a system that does not support unique naming conventions for biological medicines, has not yet been assessed. It will be important to ensure that policies seeking to increase the use of biosimilars do not inadvertently disincentivize or hamper competition and discourage innovative manufacturers of original biologics to enter and remain in the Australian market.

Contrary to Australia's goal of fostering a biotechnology industry, the Government elected in early 2018 not to implement a unique naming convention for biologic medicines. It is regrettable that the Government did not recognize the benefit to clinical confidence that such a system would provide, as its absence has the potential to weaken pharmacovigilance, post market monitoring, and confidence in the introduction of biosimilar medicines.

Australia needs to develop a considered, consistent and comprehensive biosimilars policy in consultation with Medicines Australia that supports safe introduction and balanced uptake of biosimilars.

Government-Initiated Post-Market Reviews of PBS Listed Medicines

Recently completed and ongoing post-market reviews include Chronic Obstructive Pulmonary Disease (COPD) Medicines and Ezetimibe in 2015; Post-Market Review of

Pulmonary Arterial Hypertension (PAH) Medicine in 2016; and Post-Market Review of Biological Disease Modifying Anti-Rheumatic Drugs (bDMARDs) to treat Severe Chronic Plaque Psoriasis in 2016.[244]

PhRMA has previously expressed strong concerns about the cost-focus of post-market reviews of medicines listed on the PBS. While the stated objective of the reviews has been to improve Quality Use of Medicine (QUM), in reality, most reviews have narrowly focused on cost. Industry hopes that considering the statutory price reductions included in the Agreement, the focus of future post-market reviews will be to improve QUM.

[244] *See* http://www.pbs.gov.au/info/browse/reviews (last visited Feb. 7, 2019).

EUROPE

EUROPEAN UNION

PhRMA member companies face a variety of government restrictions across Europe that undervalue and diminish patient access to innovative medicines. As a result of Europe's on-going economic challenges, several European Union (EU) Member States continue to seek additional cost savings at the expense of the innovative biopharmaceutical sector, thereby imposing a disproportionate burden on the United States to support R&D for new medicines.

In addition, while the EU generally maintains intellectual property (IP) protections that enable the research and development of innovative biopharmaceuticals, PhRMA and its member companies are very troubled by the potential future direction of an ongoing European Commission (EC) review of protections and incentives for innovative biopharmaceuticals that could result in actions to weaken IP in one of the world's largest markets.

Key Issues of Concern:

- **Intellectual property incentives review**: The European Union is contemplating potentially sweeping changes that could weaken intellectual property protections for biopharmaceuticals and create an unlevel playing field for transatlantic medicines trade and investment. PhRMA and its member companies are concerned that this review will result in the weakening of existing incentive mechanisms for innovation. Of immediate concern are the legislative proposals issued on May 28, 2018, to amend the EU's patent term restoration mechanism (Regulation EC 469/2009 concerning Supplementary Protection Certificates (SPCs)) with the objective of introducing an SPC manufacturing and/or stockpiling waiver. The waiver would allow companies to manufacture generic and biosimilar products in Europe during the effective SPC period for export purposes to third (non-EU) countries or stockpiling for the domestic market. The proposal reduces IP rights and we are concerned that this sends a signal to the world that Europe is weakening its commitment to IP incentives and innovation.

- **Government price controls and patient access to innovative medicines**: Among numerous other government price controls in effect, many EU/EFTA Member States set prices of patent-protected innovative medicines based on prices in less wealthy countries and/or based on older products deemed to be within the same therapeutic class, including generics. Moreover, several countries in Europe are pursing initiatives to jointly procure innovative medicines, or jointly negotiate their price. Such government practices – coupled with rigid and stricter health technology assessment (HTA) interpretations of value – undermine biopharmaceutical innovation and harm patient access to needed medicines. Furthermore, although EU legislation requires transparent and timely processes (*e.g.*, within 180 days) for national pricing and reimbursement (P&R) decisions,

these requirements need to be enforced more rigorously and with broader oversight of national practices.

For these reasons, PhRMA requests that European Union be placed on the **Watch List** in the 2019 Special 301 Report, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved in all available fora, including as part of the recently initiated trade agreement negotiations.

Intellectual Property Protection

EU Incentives Review

In June 2016, the European Member State Health Ministers asked the European Commission, with assistance from Member States, to undertake a review of existing intellectual property-related incentives for the biopharmaceutical industry to gauge their effectiveness and impact on innovation and the availability, accessibility and affordability of medicines. The review involves a number of studies that are likely to be completed later this year. As part of this review the Commission has been working to build a case (by issuing survey's with highly biased RFPs) for the reopening of the following pieces of legislation: SPCs (Regulation EC 469/2009), Medicinal products for human use (Directive 2001/83/EC and Regulation EC 726/2004), Orphan medicinal products (Regulation EC 141/2000) and Paediatrics (Regulation EC 1901/2006).

While the review is still underway, PhRMA and its member companies are very concerned that it could result in proposals to reopen critical parts of Europe's IP framework and potentially weaken existing incentive mechanisms that support biopharmaceutical innovation. Failure to effectively safeguard these incentives in one of the world's largest markets for innovative medicines would harm American exports and jobs and reduce investment in new treatments and cures for patients in Europe and around the world.

Supplementary Protection Certificates

As part of the broader incentives review, PhRMA is very concerned about proposals to "recalibrate the existing [SPC] rules"[245] in a manner that may weaken the scope of the exclusive rights conferred under an SPC. The EU Commission launched a Public Consultation in October 2017, which included a number of questions related to a proposed "SPC manufacturing waiver" that would eliminate the right to exclude others from manufacturing the invention during the exclusivity period granted by an SPC for purposes of export and/or stockpiling.[246] The Commission believes such a waiver would

[245] *See* "Call for tenders: Study on the legal aspects of the supplementary protection certificates in the EU" (June 9, 2016), available at http://ec.europa.eu/growth/tools-databases/newsroom/cf/itemdetail.cfm?item_id=8847 (last visited Jan. 7, 2019).

[246] *See* https://ec.europa.eu/info/consultations/public-consultation-supplementary-protection-certificates-spcs-and-patent-research-exemptions_en (last visited Jan. 7, 2019).

"level the playing field" for EU-based generic manufacturers on global markets. This belief appears to be based on a single study that has been challenged by subsequent analysis showing that, far from creating additional jobs and exports for the EU, the implementation of such an SPC manufacturing waiver would have significant detrimental economic impact on research-based companies both in Europe and around the globe.[247]

Despite such conflicting evidence, on May 28, the EC published a legislative proposal amending the SPC Regulation (469/2009) with the objective to introduce an SPC manufacturing waiver. The waiver would allow companies to manufacture generic and biosimilar products in Europe during the effective SPC period for export purposes to third (non-EU) countries. We are concerned that the proposal reduces IP rights and sends a signal to the world that Europe is weakening its commitment to IP incentives and innovation.

SPC's are a critical part of the European IP system. They partially restore the effective patent term and thereby help to compensate for a portion of the time incurred during the testing and regulatory review period that may "make the period of effective protection under the patent insufficient to cover the investment put into that research."[248] The SPC Regulation itself declares that: "[p]harmaceutical research plays a decisive role in the continuing improvement in public health."[249] It states that "[m]edicinal products, especially those that are the result of long, costly research will not continue to be developed in the Community and in Europe unless they are covered by favourable rules that provide for sufficient protection to encourage such research."[250] Further, as a result of "the period that elapses between the filing of an application for a patent for a new medicinal product and authorisation to place the medicinal product on the market," the Regulation explains that "the period of effective protection under the patent [is] insufficient to cover the investment put into the research," concluding that "[t]his situation leads to a lack of protection which penalises pharmaceutical research."[251]

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[247] *See* Pugatch Consilium, "Unintended Consequences," Oct. 2017, available at http://www.pugatch-consilium.com/reports/Unintended_Consequences_October_%202017.pdf (last visited Jan. 7, 2019); QuintilesIMS, "Assessing the impact of proposals for a Supplementary Protection Certificate Manufacturing Exemption in the EU," 2017, available at https://www.politico.eu/wp-content/uploads/2017/09/EFPIA-SPC-report_120917_v3.pdf (last visited Jan. 7, 2019); Europe Economics, "Impacts of Reducing Patent and Extended Protections against Manufacturing for Stockpiling and Export," Jan. 2018, available at http://www.europabio.org/sites/default/files/Europe%20Economics%20report%20-%20Review%20CRA%20study%20SPC%20waiver.pdf (last visited Jan. 7, 2019); Office of Health Economics, "Review of the CRA's Report 'Assessing the Economic Impacts of Changing Exemption Provisions During Patent and SPC Protection in Europe'," Jan. 2018, available at https://www.ohe.org/publications/review-cra%E2%80%99s-report-%E2%80%9Cassessing-economic-impacts-changing-exemption-provisions-during (last visited Jan. 7, 2019).

[248] See EC Regulation No. 469/2009 concerning the supplementary protection certificate for medicinal products (May 6, 2009) at Recital 4.

[249] Regulation No. 469/2009; *see also* Council Regulation (EEC) No. 1768/92 of 18 June 1992 concerning the creation of a supplementary protection certificate for medicinal products (no longer in force).

[250] Regulation No. 469/2009.

[251] *Id.*

The role SPCs play in biopharmaceutical innovation is even more important today than when Europe adopted these protections in the early 1990s. Over the years, the science of new medicines development has become more difficult, and the scope, complexity and cost of conducting clinical trials has increased dramatically. In large part to meet growing regulatory demands, the number of individual data points that must be collected through such trials has nearly doubled to just under 930,000 between 2001-2005 and 2011-2015.[252] A typical Phase III clinical trial protocol now entails an average of 167 procedures – 60% more than at the start of the last decade.[253] All of this has contributed to an upward trend in the average period for clinical testing required to secure marketing approval for new treatments and to a shorter effective patent term. Indeed, it now takes an average of 15 years to develop and win approval for a new drug.[254] Without the ability to at least partially restore patent life lost to clinical testing in Europe, innovators would find it increasingly difficult to continue to invest in new research and development for the benefit of patients worldwide.

Further, we note that preventing potential abuses of a "manufacturing for export" exemption would be very difficult. Such abuses could consist of illegal diversion of medicines produced pursuant to the exception within Europe, or in foreign markets where the relevant patent term has not expired. Safeguards that would be necessary include effective labelling, notification requirements, inspecting, regulating, and tracking every lot to ensure it is exported as intended. In the end, it may well be impossible to limit the exemption to its intended purpose, further reducing the protections SPCs are intended to provide.

Some stakeholders are calling for the immediate applicability of the SPC manufacturing waiver. Such an application of the waiver, however, would constitute a deprivation of property, taking away rights already granted and reasonably expected under the existing SPC regime.

There are further calls to extend the scope of the proposed manufacturing waiver to stockpiling for sale in the EU Member States. The EU Parliament amended recently the proposal by introducing provisions to allow follow-on manufacturers to produce and

[252] Getz, K.A. and R.A. Campo, "New Benchmarks Characterizing Growth in Protocol Design Complexity," *SAGE Journals*, June 2017, available at http://journals.sagepub.com/doi/10.1177/2168479017713039 (last visited Jan. 7, 2019).

[253] Tufts Center for the Study of Drug Development, *Outlook 2016*, Tufts University, Jan. 2016, available at https://static1.squarespace.com/static/5a9eb0c8e2ccd1158288d8dc/t/5aa2fc9d0852297555747051/1520630944033/Outlook-2016.pdf (last visited Jan. 7, 2019).

[254] *Id*. Even a study requested by the EC found that "the average development time of a medicinal product … has increased from 10 years to 15 years" and that "the effective protection period for the medicinal products in our dataset has declined from an average of 15 years to 13 years during the period 1996 to 2016". *See* EC, "Study on the economic impact of supplementary protection certificates, pharmaceutical incentives and rewards in Europe", prepared by Copenhagen Economics, May 2018, available at https://www.copenhageneconomics.com/dyn/resources/Publication/publicationPDF/5/445/1527517171/copenhagen-economics-2018-study-on-the-economic-impact-of-spcs-pharmaceutical-incentives-and-rewards-in-europe.pdf (last visited Jan. 7, 2019).

stockpile products subject to an SPC. This would create a significantly concerning and contradictory precedent in IP law in the EU. It would weaken IP protection for innovative medicines overall and most importantly, undermine the EU's position and credibility as a trading partner throughout the world.

In addition, any "manufacturing for export" or "stockpiling" waiver will almost certainly be copied by other economies – possibly in an exaggerated form that is even more damaging to biopharmaceutical innovators in the United States, Europe and elsewhere around the world. Already, lawmakers in one Asian country have proposed to permit "manufacturing for export" during the 20-year patent term, which would be inconsistent with World Trade Organization rules.[255] If a leading developed economy like Europe bends the rules, others are sure to break them.

Market Access

Government Price Controls and Patient Access to Innovative Medicines

As detailed further below, many EU Member States engage in practices that restrict availability, limit patient access, and fail to reward the value of state-of-the-art medicines. Moreover, since the U.S. research-based industry is the world leader in the development of new medicines, PhRMA members and their innovative products disproportionately bear the brunt of these measures as they undermine the financial incentive for privately sponsored research and development. Furthermore, even though EU legislation requires transparent and timely processes (*e.g.*, within 180 days) in making such national P&R decisions, these requirements need to be enforced more rigorously and broader oversight of national practices should be in place.

France

Until recently, France had adopted increasingly punitive policies toward innovators through layered mechanisms such as taxes, price-volume clauses that trigger price cuts or clawbacks, and an industry-wide clawback when national spending growth on reimbursed medicines exceeded 0% for retail medicines or 3% for hospital medicines. Clawbacks were up to 70% of net sales revenue. Additionally, there are serious challenges with France's HTA system, which rates the clinical added value of a product as major (ASMR I), important, (ASMR II), moderate (ASMR III), minor (ASMR IV) or no clinical improvement (ASMR V), with corresponding impacts on both pricing and speed of patient access. In practice, only one-third of new medicines were assigned ASMR ratings of I, II or III. Such products were guaranteed prices no lower than the lowest price applied in Germany, Italy, Spain and the United Kingdom for five years, after which prices were commonly cut.[256]

[255] E. Solovy and D. Raju, "A Manufacturing-for-Export Exception to Patent Protection: A Proposal for Exporting Violations of the TRIPS Agreement and Beyond," *Journal of Intellectual Property Law & Practice*, Sept. 2017, available at https://doi.org/10.1093/jiplp/jpx161 (last visited Jan. 7, 2019).

[256] IHS Global Insights (2015).

However, in July 2018, France announced several positive reforms to improve market access and boost the life sciences sector. These reforms have not yet been implemented but would include reducing market access delays, accelerating patient access to medicines that are being developed for new indications (by extending the current Early Access Program), and improving how new medicines are evaluated for P&R decisions. In addition, medicines expenditure would be permitted to grow by at least 0.5% annually for the upcoming 3 years and 3% annually for innovative medicines.

Germany

Germany's Pharmaceutical Market Restructuring Act (AMNOG) of 2011 restructured its pharmaceutical market away from market-based pricing toward a payer-dominated approach. AMNOG subjects new medicines to a rigid early clinical benefit assessment followed by negotiations of a rebate with the umbrella organization of the German sick funds, mainly based on the outcome of the assessment. Those products, deemed not to provide additional clinical benefits, are limited to the lower price of a therapeutic reference price. Lowest-cost comparators and generics are often considered appropriate comparators.[257]

The AMNOG process makes it so difficult to prove additional clinical benefit that by 2016, only 43% of innovative medicines assessed by Germany were determined to provide additional clinical benefit.[258] As a result, some pharmaceutical producers are openly avoiding the German market, as confirmed by the German Pharmaceutical Industry Association (BPI) report revealing that 23% of medicines (40 medicines) that received EMA approval between 2010-2015 were not launched in Germany, compared to just 5% (8 medicines) prior to AMNOG, between 2006-2010. Similarly, a report by the Association of Research-based Pharmaceutical Companies (VFA) reported the system is so unfavorable that 26 new medicines had been withdrawn from the market during the same period.[259]

Ongoing concerns regarding AMNOG are further exacerbated by concerns over the confidentiality of required discounts. Additionally, in March 2017 the Pharmaceutical Care Strengthening Act was approved, extending a price freeze that began in 2009 on non-reference priced drugs from taking a (realized) price increase until the end of 2022.

[257] IQVIA. (2017). P&R Concise Guide: Germany.

[258] Analysis carried out by the Association of Small and Medium-Sized Pharmaceutical Manufacturers (Bundesverband der Pharmazeutischen Industrie, BPI) as reported by IQVIA. (2017). P&R Concise Guide: Germany.

[259] IHS Global Insights (2015). German innovative drug makers association highlights considerable reduction in centrally approved drugs launched after AMNOG.

Greece

Greece's pharmaceutical environment remains one of the worst in Europe as PhRMA member companies face onerous price controls and other market access barriers that undermine innovation, such as mandatory clawbacks and rebates, as well as incremental rebates specifically for new medicines. For example, the government's expenditure on outpatient medicines declined by 62% between 2009-2017, with the 2017 clawback reaching €800 million, more than 30% of the total public pharmaceutical spending (€2.5 billion). This amount is expected to rise further in 2018 to €1 billion in constant public pharmaceutical spending. While declining, arrears to the industry as of August 2018 were still valued at approximately €500 million.

Hungary

Government P&R of medicines in Hungary have been under substantial pressure since the Pharma Economic Act of 2007 and the two Széll Kálmán austerity plans. Hungary erodes the price of innovative medicines by relying on a rigid international reference price calculation that prohibits new products from exceeding the lowest price at launch in any EU countries. Hungary also engages in a "blind bidding system" for therapeutic reference price groups which can be comprised of both patented medicines that have been marketed for at least one year and off-patent medicines. The system requires manufactures to submit "blind" price reductions to the National Health Insurance Fund of Hungary (NEAK) every six months.[260]

Italy

Government P&R policies in Italy have historically resulted in some of the worst patient access to innovative medicines among the major EU countries. For example, the industry payback scheme (including challenges associated with data collection, calculation methodology and ceiling price revisions) has created an uncertain business environment and forces manufacturers to either pay back at least 20% of spending on an innovative medicine over a fixed budget ceiling or accept a 5% price cut.[261] Moreover, Italy fails to adequately recognize the value of innovative medicines through use of therapeutic tenders that can force patented medicines to compete against generic medicines, where price is the only selection criteria. These harmful market access policies have been magnified by the underfunding of the pharmaceutical system.

More recently, Italy has allocated two dedicated funds for oncology (€500 million) and other therapeutic areas (€500 million), and is further developing registries that allow for novel approaches to reimbursement that facilitate greater patient access compared to in the past.

[260] IQVIA. (2018). P&R Concise Guide: Hungary.

[261] IQVIA (2017). P&R Concise Guide: Italy.

Netherlands

In 2015, the Netherlands began placing new high-value medicines into a reimbursement "lock" system that denies patient access until an HTA and subsequent negotiations to force discounts take place. Initially implemented on a case-by-case basis, the Netherlands announced in May 2018 that all new medicines with an annual cost of EUR 50,000 per patient or a combined cost of EUR 40 million would be subject to the reimbursement lock system.[262] Additionally, products deemed by the Ministry of Health, Welfare and Sport to be therapeutically-interchangeable are reimbursed based on the average price of the therapeutic group which can include patented medicines, off-patent medicines and generics.[263]

Poland

Total health care spending in Poland was 6.4% of GDP in 2016 (69% of which was from public sources, which is equivalent to 4.5% of GDP) and well below the OECD average of 9.0%, with Poland ranking 31st among the 35 OECD countries.[264] In this context, the share of public spending on pharmaceuticals has remained stable and under the 17% ceiling at which point industry clawbacks are mandated. Despite the introduction of several new medicines in recent years, the government has constricted this share growth through a combination of therapeutic reference pricing that can tie the price of patented medicines to the lowest price generics, price cuts, fixed margins, high co-pays and other measures.[265] Poland's government pricing and reimbursement system is discriminatory, non-transparent, and significantly backlogged – taking more than 630 days on average from regulatory approval to patient access.[266] As a result, Poland lags far behind most other EU countries in availability of innovative medicines.[267] More recently, the government announced in February 2018 that public health care spending would continue to be increased to reach 6.0% of GDP by 2024, and issued proposed amendments to the 2012 Pharmaceutical Reimbursement Act, including increasing reimbursement budget, engaging in risk-sharing agreements, and allocating unused funds from previous years.[268]

[262] IHS Global Insights (May 2018). Netherlands expands criteria for inclusion of high-cost drugs in "reimbursement lock", renegotiates price of Tecentriq and Soliris.

[263] IQVIA. (2018). P&R Concise Guide: Netherlands.

[264] OECD Health Statistics (Accessed Oct. 29, 2018).

[265] IQVIA. (2018). P&R Concise Guide: Poland.

[266] EFPIA: Market Access Delays (2018).

[267] PhRMA analysis of IQVIA and regulatory data, updated Sept. 2018.

[268] IHS Global Insights (Jul. 2018). Poland's long-awaited National Pharmaceutical Policy issued for public consultation.

Romania

Romania uses international reference pricing to set prices of medicines below the lowest price in a basket of twelve countries (including Lithuania and Bulgaria). This onerous system results in some of the lowest prices in Europe and encourages thriving parallel export trade which has generated considerable domestic shortages.[269] The budget for reimbursed medicines has remained flat at the 2011 level, not taking into consideration the annual consumption growth, which has led to an increase of the clawback tax. The tax requires manufacturers to cover the entire reimbursed medicines budget deficit, including wholesale and retail margins, and amounted 24% in 2018, due to the annual growth of the consumption of medicines.[270]

Spain

Between 2010 and 2012, Spain imposed price and volume control measures that have reduced significantly pharmaceutical spending in the retail sector. The effect of these measures is still noticeable in Spain; public pharmaceutical expenditure in the retail sector in Spain in 2017 was 20% lower than its historical maximum (registered in May 2010). Specific measures include the reimbursement delisting of more than 400 medicines, frequent direct and indirect price cuts, the imposition of mandatory discounts on reimbursed patented medicines, and a change in pharmaceutical copayment policy (pensioners started to contribute with a copayment rate of 10% of the price, subject to some caps and other limits). However, since July 2013, retail pharmaceutical spending has increased, with prices below the EU average.[271]

Despite signs that Spain's economy is recovering from the European fiscal crisis, Spain's 2018 draft national budget foresees only 5.8% of GDP allocated to health care compared with 6.1% in 2016 and 6.0% in 2017.[272] This continues a trend of reductions in public health care expenditure as a proportion of GDP, and is also the lowest level since 2007.

[269] IHS Global Insights country report: Romania. Accessed Sept. 27, 2018.

[270] Romanian National Health Insurance House (CNAS 2018 official data).

[271] IQVIA. (2018). P&R Concise Guide: Spain.

[272] IHS Global Insights (Mar. 2018). Spain's draft federal budget includes reduction of health expenditure to 5.8% of GDP.

UNITED KINGDOM

PhRMA and its member companies operating in the United Kingdom continue to work with the UK Government, NICE, NHS England and National Health Service (NHS) partners to support implementation of policies to strengthen the innovative pharmaceutical industry and address long-standing market access and pricing issues. Of particular concern are the continued lack of patient access to innovative medicines, intellectual property (IP) threats from Brexit and the need for continued support for the government's life sciences strategy.

Key Issues of Concern:

- **Government price controls and patient access to innovative medicines**: Because of long-standing market access barriers such as rigid health technology assessment (HTA), government price controls and insufficient health care budgets, the ability of UK patients to access the latest, innovative medicines remains problematic. In comparison to many EU countries, adoption of the newest medicines remains low in comparison.

- **Intellectual property threats from Brexit:** The UK is seen to have one of the strongest IP frameworks globally. As the UK prepares to exit from the European Union (EU), it is important that the UK maintain IP protections at least at current levels – including effective periods of regulatory data protection and patent term restoration. Future US-UK trade negotiations provide an opportunity to cement these and other high IP standards.

- **Need for UK government life sciences industrial strategy**: The UK government published its Life Sciences Industrial Strategy (LSIS) report in 2017, outlining policy changes aimed at strengthening the life sciences sector in the UK. PhRMA members welcome the proposed changes, and are working to ensure adoption and successful implementation of LSIS policies in the NHS and elsewhere that would foster adoption of new life sciences technologies in the UK.

For these reasons, PhRMA requests that the United Kingdom be placed on the **Watch List** in the 2019 Special 301 Report, and that the U.S. Government continue to support the successful implementation of policies by the UK Government which aim to support the uptake of pharmaceutical innovation, particularly in light of the recent development of a long-term NHS strategy service in England.

Intellectual Property Protection

Effective intellectual property protection and enforcement is essential to develop new medicines for patients who need them. The UK in general is seen to have one of the strongest IP frameworks globally. However, as the UK prepares to exit the EU, it is important to maintain IP protection at least at a level aligned with the current levels of

protection of the EU and UK IP systems as is a vital component of the future EU-UK relationship to ensure business continuity and certainty for PhRMA member companies.

IP rights already obtained or available in the UK under EU law or applications thereof, should continue to be in force as a matter of UK law. In addition, such rights should be available to be granted immediately upon Brexit for new products. Furthermore, the life sciences industry would strongly advocate for finding possible ways for the UK to remain in the scope of the Unitary Patent Agreement to provide the life sciences industry predictability and stability when faced with the uncertainty of Brexit and scope for the UK government to align other aspects of the IP framework in partner countries, such as the U.S., with global gold standards.

In a scenario where the UK leaves the EU without a withdrawal agreement (a hard Brexit), the UK government has determined that the start of data or market exclusivity will be the date of authorization in the EU or UK, whichever is earlier.

This means that:

- Should a company be granted a marketing authorization in the EU prior to the UK, the 10-year RDP term in the UK would begin before the company can start selling in the UK, thereby eroding the period of effective protection from generic competition by the period equal to the delay between EU and UK authorizations.

- For SPCs, a similar approach is being taken i*.e.* basing the commercially significant SPC term on the earlier of UK or EEA authorization. If implemented, this proposal will reduce periods of actual exclusivity in the UK, the value of patents for innovators.

PhRMA members strongly urge that in a hard Brexit scenario, the key dates for RDP, orphan and SPC protection should be the date of UK marketing authorization so that the commercial exclusivity they afford will run from the time of UK marketing authorization.

Moreover, there are some aspects of the UK IP framework that are out of step with other European countries and global practices. It is important to address these aspects to ensure appropriate incentives are in-place for a thriving life sciences industry post-*Brexit*. Notably, UK courts are inappropriately extending their jurisdiction to adjudicate patentability or patent-worthiness of pending patent applications or subject matters that have not been claimed in an issued patent. For example, the UK High Court held that it had a discretionary power to grant a declaration that a pharmaceutical product was known or obvious at the priority date of divisional patent applications without reference to the claims in any granted patent.[273] This essentially declares that any patent that would be infringed by the generic product to be necessarily invalid without regard to examination of its claims.

[273] See *Arrow Generics Ltd v Merck & Co Inc,* [2007] EWHC 1900 (Pat).

This practice seriously undermines the ability to protect innovation, particularly those inventions beyond the initial chemical compound, such as novel therapies, formulations, and dosages that provide enormous benefit to patients and require significant investment. Moreover, because this practice permits the UK courts to adjudicate on the inventiveness or novelty of something that is not the subject matter of a granted patent claim, it creates confusion regarding applicability or enforceability of relevant patents.

This practice has also been applied even where there were no, and will never be, any relevant UK patent rights.[274] Thus, innovators may be compelled to litigate in relation to subject matter relevant to third country patents at the discretion of a UK court where no UK rights are at issue – despite the fact that claims may be still pending at the European Patent Office (EPO), other national patent offices or at appropriate venues in other jurisdictions where litigation may occur under the relevant law. This potentially has an unwarranted extraterritorial impact on other jurisdictions despite the lack of controversy in the UK, contrary to the territorial nature of patents as recognized in the Paris Convention.[275]

Market Access Barriers

Government Price Controls and Patient Access to Innovative Medicines

New products in the UK can be launched upon regulatory approval, potentially making it one of the world's fastest countries for market access. However, UK patients experience materially longer delays in accessing new medicines than patients elsewhere because of rigid national HTA processes, sub-national assessment or commissioning processes, and prescribing policies and incentives aimed at containing costs to meet unreasonable budgets.[276] For every 100 patients in comparable countries who get access to a new medicine in its first year of launch, just 18 patients in the UK receive the same.[277] Moreover, during the first 5 years after the launch of a new medicine, UK patients are significantly less likely to have access than are patients living in other countries.[278]

Another key cause for the UK's low and slow patient access to new medicines is the high rate of rejections by NICE which operates using a cost-effectiveness threshold of between £20,000 and £30,000 per QALY. This threshold has not been revised – even in line with inflation – since NICE's inception in 1999, which means that the threshold has declined in real terms by 30%. Innovative medicines exceeding a cost per QALY threshold of £30,000 (or £50,000 for end-of-life interventions) are generally viewed as not cost-effective, leaving clinically superior products that carry high development costs and/or

[274] *Fujifilm Kyowa Kirin Biologics Co, Ltd v AbbVie Biotechnology Ltd & Another [2017] EWCA Civ 1.*

[275] *See* Paris Convention, Article 4bis(1): "Patents … shall be independent of patents obtained for the same invention in other countries."

[276] IQVIA. (2017). P&R Concise Guide: United Kingdom.

[277] OHE analysis of 61 medicines launched in the UK since 2007 compared to 16 countries (2014).

[278] Office for Life Sciences, "Life sciences competitiveness indicators," Apr. 2017.

small populations from which to recoup expenses without access. In addition, as companies develop new medicines, often in areas where there are many older off-patent medicines that are much lower in cost, demonstration of "cost-effectiveness" becomes exceedingly difficult by design.

Using QALYs to rigidly measure cost-effectiveness in this way fails to recognize the full value of innovative medicines and has turned the UK's HTA into a blunt cost containment tool. In this context, between March 2000 and December 2017, just 57% of all technology appraisals were recommended by NICE in line with marketing authorization; while 23% were recommended in a restricted subset of patients, 1% under the Cancer Drug Fund (CDF), and 4% in research only – and 15% were rejected altogether. Recommendations for cancer medicines were even more restrictive with just 37% of cancer appraisals recommended in-line with marketing authorization; while 32% were recommended in a restricted subset of patients, 4% under the CDF, 3% in research only – and 27% rejected altogether.[279]

PhRMA members recognize the UK government's interest in controlling drug spending in the NHS, but spending on medicines is not currently a driver of health care inflation. On the contrary, over the course of the last five years, NHS spending on medicines has declined by 0.4% after inflation while overall NHS spending has risen at 3.3% over the same period. Innovations in prevention and treatment will be vital to delivering further enhanced efficiencies in the UK health system, as well as improving health outcomes and providing high-quality care.

Need for UK Government Life Sciences Industrial Strategy

During 2017, the Association of the British Pharmaceutical Industry (ABPI) and its industry partners collaborated with the LSIS Board led by Professor Sir John Bell to produce the LSIS. This publication followed the UK Government's industrial strategy green paper from January 2017. The LSIS is a roadmap to building a thriving life sciences sector in the UK. The UK Government has published its response in the form of the Life Sciences Sector Deal, which marks the first phase of implementing the recommendations of the LSIS. As such, ABPI continues to call for implementation of all the recommendations in the LSIS.

An industrial strategy approach is particularly well suited to biopharmaceuticals since the sector is highly impacted by UK Government policy at every stage of the product lifecycle. A holistic approach and comprehensive delivery across the Government, in partnership with the NHS, is a powerful way to support the sector's economic contribution to the UK. To realize the ambition of the LSIS, the UK Government should:

[279] National Institute for Health and Care Excellence (NICE), available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/summary-of-decisions (last visited Feb. 7, 2019).

- Continue to invest in the UK's strong science base;

- Build foundations and infrastructure for the research, development and production of innovative therapies in the UK;

- Transform the NHS into an early adopter of new cost-effective medicines and technologies which are adopted at pace and scale;

- Enable the NHS to make best use of data and digital tools to support research and improve patient care;

- Recognize the potential challenges for the industry as a result of Brexit and prioritize regulatory cooperation on medicines and the ability to trade medicines in the second phase of Brexit negotiations; and

- Continue to work with the ABPI on a new voluntary medicines pricing scheme to succeed the current PPRS, which will reward innovation, improve patient access to medicines, and support NHS sustainability.

LATIN AMERICA

MEXICO

PhRMA and its member companies operating in Mexico remain concerned with weak patent enforcement and significant intellectual property (IP) issues as well as market access barriers including challenges in accessing Mexico's different formularies.

Recognizing these challenges, PhRMA and its members commend the U.S. Government for its conclusion of the U.S.-Mexico-Canada Agreement (USMCA), which marks a historic point for U.S. trade policy and cements critical IP and other standards that will pave the way for the next generation of treatments and cures. PhRMA stands ready to work with the U.S. Government to secure full and faithful implementation of the USMCA and thereby address several of the issues raised below.

Key Issues of Concern:

- **Weak patent enforcement and regulatory data protection failures**: Mexico's health regulatory agency (the Federal National Commission for Protection against Health Risks or COFEPRIS) and the Mexican Patent Office (IMPI) have committed to improve the application of Mexico's 2003 Linkage Decree and to provide protection for data generated to obtain marketing approval for pharmaceutical products. Despite these commitments, PhRMA member companies are unable to obtain accurate and timely information from COFEPRIS prior to marketing authorization being granted on a generic or biosimilar drug where the innovator product is used as a reference. As a result, PHRMA members have little to no notice that a potentially patent infringing product is entering the market. Further, obtaining effective preliminary injunctions or final decisions on cases regarding IP infringement within a reasonable time (as well as collecting adequate damages when appropriate) remains the exception rather than the norm. Further, implementation of substantive regulatory data protection (RDP), including provision of RDP for biologics, is still pending.

- **Market access delays**: Despite recent improvements to the marketing approval process for pharmaceutical products by COFEPRIS, significant barriers to the public market for medicines remain due to the lengthy, non-transparent, and unpredictable reimbursement process.

For these reasons, PhRMA requests that Mexico remain on the **Watch List** in the 2019 Special 301 Report, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protections

Weak Patent Enforcement

To ensure adequate and effective protection of IP rights for the research-based biopharmaceutical sector, mechanisms that provide for the early resolution of patent disputes before an infringing product is allowed to enter the market are critical. Mexico has taken some positive steps to improve patent enforcement, including adopting the Linkage Decree of 2003. However, the continued lack of regulatory guidance requires innovators to redirect significant resources to seek judicial orders compelling Mexico's relevant agencies to follow their own rules and regulations.

Mexico's Linkage Decree (2003) constituted important progress toward an early resolution mechanism and the full recognition of pharmaceutical patent rights in Mexico. However, the decree has not been implemented in a comprehensive and consistent manner. For example, the publication in the Official Gazette of medicine-related patents is a positive step toward the goal of eliminating unnecessary, costly and time-consuming court actions to obtain appropriate legal protection for biopharmaceutical patents. However, COFEPRIS appears to apply linkage inconsistently and possibly in a discriminatory manner. In some cases, marketing authorizations have been issued despite patents listed in the Official Gazette. As a result, there have been concerning instances (at least three in April 2017) where COFEPRIS has granted marketing authorization for entry of products for which a valid patent exists. This undermines company confidence in the IP system in Mexico and impedes companies' ability to do business in Mexico.

Both of Mexico's NAFTA partners provide patent enforcement systems for product, formulation and method of use patents. It is therefore inappropriate for Mexico to not provide effective patent enforcement for method of use patents. Furthermore, effective patent enforcement mechanisms are necessary to protect innovator products from patent infringement by premature commercialization of follow-on products.

A critical tool to protect against irreparable harm from the loss of IP rights is the availability of preliminary injunctions to prevent the sale of an infringing product during litigation. Preliminary injunctions become all the more important when there are no other effective mechanisms to facilitate early resolution of patent disputes.

In Mexico, PhRMA member companies are unable to obtain accurate and timely information from COFEPRIS prior to marketing authorization being granted on a generic or biosimilar drug where the innovator product is used as a reference. As a result, PHRMA members have little to no notice that a potentially patent infringing product is entering the market. Further, obtaining effective preliminary injunctions or final decisions on cases regarding IP infringement within a reasonable time (as well as collecting adequate damages when appropriate) remains the exception rather than the norm. Although injunctions may be initially granted subject to the payment of a bond, counter-bonds, or

in some proceedings mere applications, may be submitted by the alleged infringer to lift the injunction.

In the event that an innovator successfully enforces its intellectual property rights in Mexico, seeking monetary damages is extremely burdensome. In order to claim damages from patent infringers in Mexico, litigants are required to first obtain a final administrative action and then seek damages through a civil action. It is not uncommon for this process to last longer than ten years because these actions must be adjudicated in two separate legal venues.

Mexico has repeatedly committed to provide effective patent enforcement mechanisms in NAFTA, the recently concluded USMCA, and the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS).

PhRMA's members encourage Mexican authorities to establish uniform criteria consistent with court precedents ordering the listing of use patents in the Official Gazette. In addition, PhRMA and its member companies encourage the Mexican Government to hasten patent infringement proceedings; use all available legal mechanisms to enforce Mexican Supreme Court decisions and implement procedures necessary to provide timely and effective preliminary injunctions.

Regulatory Data Protection Failures

Biopharmaceutical innovators work with hospitals, universities and other partners to rigorously test potential new medicines and demonstrate they are safe and effective for patients who need them. Less than 12% of medicines that enter clinical trials ever result in approved treatments.[280]

To support the significant investment of time and resources needed to develop test data to prove that a new medicine is safe and effective, the international community has developed a mechanism recognized as essential to biopharmaceutical innovation whereby the data submitted for regulatory approval is protected from unfair commercial use for a period of time. The mechanism is ensconced in TRIPS Article 39.3 which requires WTO members to protect undisclosed test and other data submitted for marketing approval in that country against disclosure and unfair commercial use.

RDP is essential for all medicines, and particularly critical for biologic therapies. Produced using living organisms, biologics are complex and challenging to manufacture and may not be protected adequately by patents alone. Unlike generic versions of

[280] DiMasi JA, Grabowski HG, Hansen RW; Tufts Center for the Study of Drug Development. Innovation in the pharmaceutical industry: new estimates of R&D costs. In: Briefing: Cost of Developing a New Drug, available at https://static1.squarespace.com/static/5a9eb0c8e2ccd1158288d8dc/t/5ac66afc6d2a732e83aae6bf/1522952963800/Tufts_CSDD_briefing_on_RD_cost_study_-_Nov_18%2C_2014..pdf (last visited Feb. 7, 2019).

traditional chemical compounds, biosimilars are not identical to the original innovative medicine and there is greater uncertainty about whether an innovator's patent right will cover a biosimilar version. Without the certainty of some substantial period of market exclusivity, innovators will not have the incentives needed to conduct the expensive, risky and time-consuming work to discover and bring new biologics to market.

The leaders of COFEPRIS and the IMPI have committed to provide protection for data generated to obtain marketing approval for all pharmaceutical products, including biologics. However, PhRMA and its members remain concerned with the apparent distinction made by the regulatory authorities between the provision of RDP to chemically synthesized (small molecule) and biologic drugs. Consistent with TRIPS, RDP should be provided regardless of the manner in which the medicine is synthesized. Implementation of substantive RDP reform is still pending.

In June 2012, COFEPRIS issued guidelines to implement RDP for a maximum period of five years – an important step toward fulfilling Mexico's obligations under TRIPS and NAFTA. PhRMA members initially welcomed this decision as an important confirmation of Mexico's obligations and its intention to fully implement the NAFTA provisions.

As guidelines, however, their validity may be questioned when applied to a concrete case. Further, they could be hard to enforce and may be revoked at any time. Therefore, PhRMA members strongly urge the passage of binding regulations on RDP to provide greater certainty regarding the extent and durability of Mexico's commitment to strong IP protection, consistent with Mexico's commitments in Articles 20.48 and 49 of the USMCA.

Potential Abuse of the "Bolar" Exemption

Mexico allows generic manufacturers to import active pharmaceutical ingredients and other raw materials contained in a patented pharmaceutical for "experimental use" during the last three years of the patent term, per the *Bolar* exemption. Mexico fails, however, to impose any limits on the amount of raw materials that can be imported under this exception.

Given some of the import volumes reported, PhRMA's members are very concerned that some importers may be abusing the *Bolar* exemption by stockpiling and/or selling patent-infringing and potentially substandard medicines in Mexico or elsewhere. PhRMA members encourage Mexican authorities to establish clear criteria for the issuance of import permits that respect patent rights and appropriately limit imports to quantities required for testing bioequivalence.

Market Access Barriers

Market Access Delays

PhRMA's local sister association (AMIIF) estimates that on average it takes 1,500 days for Mexican patients to access innovative medicines. Key market access issues in Mexico concern the excessive times taken for formulary inclusion and the 5-year registration renewal process. Both significantly exceed stated time frames. COFEPRIS, has made important improvements in the approval process despite limited resources and cost-containment pressures. The New Molecules Committee could undermine the positive improvements COFEPRIS has made.

Following COFEPRIS approval, there remain significant barriers for patients, primarily those covered by public institutions, in accessing life-saving and enhancing interventions. This additional delay is caused by the lengthy, non-transparent, and uncertain reimbursement system used in Mexico, which adds on average two years to the access process (if made available at all in the public sector).

After COFEPRIS grants marketing authorization to a new medicine, the national Committee of Health decides which drugs should be included on the national formulary. Recommended prices for patented and unique drugs (or those with exclusive distributors) for all public institutions are negotiated with the Coordinating Commission for the Negotiation of Prices of Medicines and Other Medical Supplies. Following this recommendation, the public health institutions at federal and local levels, such as the Mexican Institute for Social Security (IMSS) and Institute of Security and Social Services for State Workers (ISSSTE), *etc.*, procure the medicine at the negotiated price. At each step, clinical and pharmaco-economic dossiers, which take manufacturers significant time and expense to create, are required. Further, the institutional approval process is an inefficient process, whereby products with regulatory approval and wide reimbursement throughout the world are often denied listing in Mexico based on alleged inadequate efficacy or safety defined through non-transparent criteria. As a result, there has been a dramatic reduction in public formulary listings for innovative medicines that have been approved by COFEPRIS for inclusion in the national formulary. The two largest public formularies, IMSS and ISSSTE, currently include only 25% of innovative medicines that have received regulatory approval. Decisions denying institutional approval are not subject to any effective method of appeal.

PERU

PhRMA and its member companies operating in Peru are alarmed by legislation pending in the Peruvian Congress that would remove patent protection from a valuable American invention that is benefitting many local patients. This potentially devastating measure adds to serious concerns about other aspects of Peru's intellectual property (IP) regime. PhRMA members are also concerned about market access barriers that appear to discriminate in favor of local producers in Peru at the expense of manufacturers in the United States and elsewhere.

The U.S.-Peru Trade Promotion Agreement (USPTPA), which was signed in 2006 and amended in 2007, obligates Peru to protect pharmaceutical products' safety and efficacy data, provide a pre-launch legal system that will provide patent holders with sufficient time and opportunity to resolve patent disputes prior to the marketing of an infringing product, and establish a stronger IP framework. Peru has failed to adequately comply with these obligations. Although PhRMA and its member companies do not consider the USPTPA a model for future trade agreements, PhRMA has monitored implementation of the USPTPA, and has been closely monitoring the enforcement of the implementation regulations since its entry into force in February 2009.

Key Issues of Concern:

- **Compulsory licensing**: Action is needed to protect American inventions in Peru. In January 2014, the Ministry of Health (MOH) received a petition to issue a compulsory license (CL) on a patented medicine. The MOH did not permit the manufacturer or the local innovative industry association to participate in the petition review process, raising significant due process concerns. Although the petition was not granted, some in the Peruvian Congress have sought to renew the petition through legislation (Bill 275/2016). As in the original petition, the Bill fails to provide any compelling reasons to issue a CL. Nevertheless, the bill has been approved by the Health Committee and pending procedural evaluation to determine whether other committee reviews are required or whether it can proceed to Congress for consideration.

- **Weak patent enforcement**: Peru does not provide patent holders with sufficient time and opportunity to seek injunctive relief prior to the marketing of an infringing product. This is contrary to Peru's trade agreement obligations and creates significant uncertainty for innovators, their competitors and patients alike.

- **Regulatory data protection (RDP) failures**: Peru does not sufficiently support and value the rigorous testing and evaluation biopharmaceutical innovators and their partners around the world undertake to demonstrate potential new medicines are safe and effective for patients who need them. Contrary to Peru's commitments in bilateral and global trade negotiations, Peru provides an insufficient period of RDP and has failed entirely to provide RDP for biologic products.

- **Regulatory barriers, processing delays and duplicative testing requirements**: Peru has introduced a number of measures to help ensure the quality, safety and efficacy of pharmaceuticals, including Interchangeability Regulations (DS 024-2018-SA), which takes important first steps in ensuring the therapeutic equivalence of generics, as well as Decrees 011-2016-SA and 013-2016-SA, which regulate biologic originators and biosimilars, respectively. However, a number of these regulations are applied by the Health Authority in an impractical way in that they request additional documents that may not be issued in the country of manufacture, or impose excessive administrative burdens that serve no purpose other than delaying the marketing approval process and patient access to medicines. In general, the capabilities of the National Authority for Pharmaceutical Products, Medical Devices and Sanitary Products (DIGEMID) should be increased as a way to reduce current uncertainty and unpredictability.

- **Lack of transparency in procedures to include new drugs in national formularies**: Peru has among the lowest levels of access to innovative medicines, mainly in the MOH-subsidized system which provides care to more than 50% of the population. Further, the Institute for the Evaluation of Health Technologies and Research (IETSI), which is in charge of the formulary used by Peru's Social Security program (EsSalud), is increasingly rejecting access to innovative medicines (the rate of rejection has increased to an alarming 70%). The process for seeking inclusion on Peru's formularies should be transparent and recognize the benefits of innovative medicines, in order to avoid the routine rejection of products that improve treatment of a patient's disease.

For these reasons, PhRMA requests that Peru remain on the **Watch List** in the 2019 Special 301 Report. Further, we urge USTR to provide an opportunity for an assessment of Peru's IP and market access environment through an **Out-of-Cycle Review**, so that the U.S. Government can evaluate progress on these important issues and dedicate the required bilateral attention necessary to make progress on the barriers confronted by U.S. businesses in Peru.

Intellectual Property Protection

Compulsory Licensing

PhRMA and its member companies are alarmed by increased legislative activity that would remove patent protection from innovative medicines developed in the United States. In January 2014, the MOH received a petition to issue a CL on a patented medicine. Although MOH initiated a process to review the petition, neither the manufacturer nor the local innovative pharmaceutical industry association were permitted to participate in that review. Moreover, neither MOH nor the Ministry of Commerce responded to correspondence from the manufacturer or local industry association. Although the petition was not granted, the technical analysis being undertaken was done without consulting the manufacturer, raising significant due process concerns. In August 2016, some in the Peruvian Congress sought to renew the CL petition through legislation

(Bill 275/2016), once again failing to demonstrate a legitimate public interest in issuing a CL. This bill has been approved by the Health Committee and is pending procedural evaluations to determine whether other committee reviews are required, or if it can proceed to Congress for consideration. Already, the same CL petitioners are now publicly calling for CLs on other patented medicines.

Weak Patent Enforcement

To ensure adequate and effective protection of IP for the research-based biopharmaceutical sector, mechanisms that provide for the early resolution of patent disputes before an infringing product is allowed to enter the market are critical. Such mechanisms prevent the grant of marketing approval for any product known by regulatory entities to be covered by a patent until expiration of the patent. An effective early resolution mechanism provides a procedural gate or safeguard. It ensures drug regulatory entities do not inadvertently contribute to infringement of patent rights granted by another government entity by providing marketing authorization to a competitor of the innovative firm.

Another critical tool to protect against irreparable harm from the loss of IP is the ability to seek injunctive relief (or equivalent procedural measures) to prevent the sale of an infringing product during expeditious adjudication of patent disputes.

Article 16.10.3 of the USPTPA requires Peru to provide patent holders with sufficient time and opportunity to resolve patent disputes prior to the marketing of an allegedly infringing product if a sanitary registration is requested by an unauthorized manufacturer of a patented product. In response, the Peruvian Government indicated that it would provide notice of sanitary registration applications on the DIGEMID website so that patent holders have notice of an intention to commercialize a potentially infringing product. In reality, the DIGEMID web page is never updated, and this notice alone is not adequate to provide the ability to seek and obtain a remedy before the marketing of the infringing product.

Further, the Peruvian patent enforcement system is ineffective in that it does not provide for timely resolution of patent disputes. The Peruvian system for enforcing patents is a two-step, sequential process: (1) an administrative process for determining infringement by the Institute for Defense of Competition and Intellectual Property (INDECOPI) that takes two years on average; and (2) a judicial action in a civil court to recover damages, which can commence only after the administrative process is exhausted. This judicial action takes four years on average, a duration which discourages patent owners from enforcing their patents.

Regulatory Data Protection Failures

Biopharmaceutical innovators work with hospitals, universities and other partners to rigorously test potential new medicines and demonstrate they are safe and effective

for patients who need them. Less than 12 percent of medicines that enter clinical trials ever result in approved treatments.[281]

To support the significant investment of time and resources needed to develop test data showing a potential new medicine is safe and effective, governments around the world protect such data submitted for regulatory approval from unfair commercial use for a period of time. TRIPS Article 39.3 requires each WTO member to protect undisclosed test and other data submitted for marketing approval in that country against both disclosure and unfair commercial use.

A sufficient period of RDP is essential for all medicines, and particularly critical for biologic therapies. Made using living organisms, biologics are complex and challenging to manufacture and may not be protected adequately by patents alone. Unlike generic versions of traditional chemical compounds, biosimilars are not identical to the original innovative medicine and there is greater uncertainty about whether an innovator's patent right will cover a biosimilar version. Without the certainty of some substantial period of market exclusivity, innovators will not have the incentives needed to conduct the expensive, risky and time-consuming work to discover and bring new biologics to market.

Since 2009, Peru has granted RDP for a very limited period of time (40 months, on average). Further, Peru refuses to grant RDP to biologic products. This action is inconsistent with Peru's obligations under TRIPS, the USPTPA, and national law.

To appropriately support and value the rigorous testing and evaluation of potential new medicines, the Government of Peru should refrain from granting sanitary registrations to third party follow-on versions of any kind of innovative pharmaceutical products for a sufficient period of time, unless the applicants for such versions base their applications on their own clinical data.

Restrictive Patentability Criteria

The Andean Court of Justice (ACJ) has issued several legal opinions (89-AI-2000, 01-AI-2001 and 34-AI-2001) holding that Andean Community members should not recognize patents for second uses. These decisions are contrary to long-standing precedents and inconsistent with TRIPS Article 27.1. Andean member countries, including Peru, have chosen to honor their Andean Community obligations, while ignoring their TRIPS obligations.

The failure to provide patents for second uses adversely affects PhRMA members who dedicate many of their research investments to evaluating additional therapeutic

[281] DiMasi JA, Grabowski HG, Hansen RW; Tufts Center for the Study of Drug Development. Innovation in the pharmaceutical industry: new estimates of R&D costs. In: Briefing: Cost of Developing a New Drug, available at https://static1.squarespace.com/static/5a9eb0c8e2ccd1158288d8dc/t/5ac66afc6d2a732e83aae6bf/1522952963800/Tufts_CSDD_briefing_on_RD_cost_study_-_Nov_18%2C_2014..pdf (last visited Feb. 7, 2019).

benefits of known molecules in order to provide more effective solutions for unsatisfied medical needs. The ACJ position is dispositive on the issue and no further domestic appeals or remedies are possible.

Market Access Barriers

Regulatory Barriers

Peru has introduced a number of measures to help ensure the quality, safety and efficacy of pharmaceuticals, including Interchangeability Regulations (DS 024-2018-SA), making it mandatory for seven generic products to prove they are therapeutically equivalent to the innovator. Although this is an important first step towards ensuring the safety and efficacy of generic drugs, the Interchangeability Regulations should be extended to all generic drugs as soon as possible. Other welcome Decrees include 011-2016-SA and 013-2016-SA, which regulate biologic originators and biosimilars, respectively. However, these regulations are applied by DIGEMID in an impractical way, such as requesting additional documents that may not be issued in the country of manufacture, or imposing excessive and unnecessary administrative burdens that ultimately delay the marketing approval process and patient access to medicines.

Processing Delays

To date, the PHA's implementation of regulations still unduly focuses on administrative details and formatting, with less emphasis on the substance of the application, *i.e.*, whether science supports granting a product marketing approval. For example, failure to provide documentation in the exact format required by DIGEMID is a basis for delaying or even refusing marketing approval. These regulatory measures and delays present unnecessary trade barriers and may have a negative impact on individual companies' plans to bring products to market in Peru. In general, the capabilities of DIGEMID should be increased in order to reduce current uncertainty and unpredictability.

Duplicative Testing

DIGEMID's regulations include numerous provisions that create unnecessary confusion and market access barriers. For instance, Article 45 of Law 29459 provides that: (1) the first batch of any pharmaceutical product after registration or renewal must undergo complete quality testing in Peru even if quality testing has already been performed at the manufacturing facility overseas; and (2) subsequent quality testing on further batches may be performed outside of Peru as long as the laboratory conducting that testing has been certified by DIGEMID. Exceptions for products manufactured in "High Sanitary Vigilance Countries" are provided. However, these certifications are commonly delayed and both the processing time and backlog for these certifications are projected to be lengthy when these regulations are implemented.

Lack of Access for Innovative Medicines

Peru has among the lowest levels of access to innovative medicines, mainly in the MOH-subsidized system which provides care to more than 50% of the population. Further, IETSI, which is in charge of the formulary used by EsSalud, is increasingly rejecting access to innovative medicines (the rate of rejection has increased to an alarming 70%). Innovative biopharmaceutical companies should be able to seek inclusion in Peru's formularies through transparent process that recognizes the value of new medicines, in order to avoid the routine rejection of products that improve treatment of a patient's disease. Currently, innovative medicines are rejected because they have a higher price than older medicines, without considering their added clinical benefits or health system savings (such as lower incidence of relapses and complications, and less intense use of medical personal and resources). Restrictive commercial conditions, such as the lack of longer-term or multi-product agreements, also result in decreased access.

MIDDLE EAST / AFRICA

EGYPT

PhRMA and its member companies remain concerned about the intellectual property (IP) environment and market access in Egypt.

Egypt is one of the most populous countries in the Middle East-Africa region. There is tremendous unmet medical need in the country. Conditions prevailing in the regulatory and IP areas today make it increasingly difficult for PhRMA member companies to operate and invest, though there are encouraging signs that the government may be willing to implement key reforms.

During the past several very challenging years, PhRMA and its member companies have tried to work in good faith with Egyptian officials to address health and industrial issues. Specifically, in 2017, PhRMA and its member companies faced major challenges in meeting the Health Minister to address the government pricing challenges facing the industry. These challenges were a consequence of the Egyptian Government's decision in November 2016 to liberate the foreign exchange rate. That decision triggered a precipitous decline in the value of the Egyptian Pound, jeopardizing the largest, most established pharmaceutical sector in the Middle East region.

Despite the Health Ministry's pledge to implement the second phase of price adjustments in August 2017, to date the Egyptian Government has failed to implement this pledge resulting in significant financial losses for member companies and widely-reported shortages of medicines.

PhRMA notes, however, that other Egyptian officials, particularly the Minister of Investment and International Cooperation have shown a willingness to meet and discuss issues of concern. Those officials recognize the threat to the industry and have expressed interest in supporting the innovative biopharmaceutical industry and encouraging investment in the country. They understand that the industry faces stagnation and contraction if immediate steps are not taken to redress the combined impact of fixed prices and a devaluing Egyptian Pound.

Key Issues of Concern:

- **Weak patent enforcement**: Egypt lacks effective patent enforcement, enabling manufacturers to obtain marketing licenses for follow-on products prior to the expiration of the patent on the original product.

- **Market access policies**: The innovative pharmaceutical industry remains concerned that Egypt has not fully implemented its pledge to adjust prices of medicines in the wake of the Egyptian pound devaluation by more than 100% in November 2016. Industry is also concerned about the lack of a transparent and equitable pricing system that would systematically address such currency devaluations.

For these reasons, PhRMA requests that Egypt remain on the **Watch List** in the 2019 Special 301 Report, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protection

Weak Patent Enforcement

Egypt does not provide an effective mechanism to ensure that marketing licenses are not granted to companies making products that infringe an originator's patent. Some officials have opposed putting in place an effective patent enforcement system similar to the process used by the United States or in other neighboring countries.

In those countries, health officials receiving applications from generics companies are required to check for the existence of a valid patent. If the originator can demonstrate a valid patent, there should be a procedure in place whereby the MOH can either defer the file to a date for examination period closer to the date of the patent expiration and/or specify that the license is valid only after the expiration of the innovator's patent, or after a sufficient period to resolve the patent dispute.

As Egypt is a WTO member, has enacted patent laws, and issues patents through the Patent Bureau, it follows that the MOH should have in place an effective mechanism whereby it can defer market entry of newly licensed medicines until after the expiration of any applicable patents or at least until after a sufficient period for resolving patent disputes.

Market Access Barriers

Market Access Policies

In November 2016, the government of Egypt liberated the foreign exchange rate, resulting in a devaluation (approximately 100%) of the Egyptian Pound. Because the prices of medicines are fixed, biopharmaceutical companies suffered significant financial losses. After engagement by PhRMA and its member companies, the Egyptian government granted a first phase of price adjustments in January 2017 with the commitment to grant a second phase in August 2017. To date, the Egyptian government has failed to implement this pledged second phase of price increases. Implementing this second phase will be of critical importance to the operations of member companies, and will demonstrate the Egyptian government's commitment to build an ecosystem that fosters innovation and investment.

On a positive note, industry is engaged in constructive discussions with the new Minister of Health on the gaps in the current pricing decree 499 with regard to pricing of new innovative products.

UNITED ARAB EMIRATES

The United Arab Emirates (UAE) has made great progress in recent years to provide an increasingly competitive environment for investment in the pharmaceutical sector and life sciences. This effort has resulted in attracting the regional headquarters for many international companies, increased investment in clinical research, and expanding manufacturing operations. Transparency of policies, predictability of the business environment and intellectual property protection have served as mainstay policies for attracting growth. Nevertheless, an issue of growing concern has emerged in this otherwise promising country related to the protection of patents of innovative pharmaceutical products based on the country of origin and the reciprocal patent recognition within the Gulf Cooperation Council (GCC).

Key Issues of Concern:

- **Recognition of GCC patent registration**: As a member of the GCC, the UAE is required by law to recognize patents submitted to the GCC Patent Office as of the date they are filed, as though they were filed in the UAE. However, recent announcements suggest that the UAE will not recognize GCC-filed patents.

- **IP Protection based on Ministerial Decree No. 404 of April 30, 2000**: Contrary to Decree 404, the Ministry of Health (MOH) has registered generic pharmaceutical products for sale in the UAE that appear to infringe the patents on innovative medicines produced by our member companies. At that time, the patents in the countries of origin remained in force and thus should have been honored in the UAE as required by Decree 404.

The innovative biopharmaceutical industry has been in regular consultations with the UAE Government throughout 2018, and there are signals that the Ministry of Health and Prevention and Ministry of Economy are open to solutions that would meet the UAE's obligations. In December 2017, the industry submitted a series of proposals to address the concerns of innovator companies. As of this writing, we have not received a formal response to those proposals.

For these reasons, PhRMA requests that the United Arab Emirates remain on the **Watch List** in the 2019 Special 301 Report, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protection

GCC Patent Recognition

As a member of the GCC, the UAE is required to recognize patents submitted to the GCC Patent Office as of the date they are filed, as though they were directly filed in the UAE. PhRMA member companies are highly concerned by recent generic approvals

in the UAE for patented products within their GCC patent term. As such, we seek affirmation from the MOH and Ministry of Economy that all patents registered in the GCC Patents Office will be granted protection in the UAE.

IP Protection based on Ministerial Decree No. 404 of April 30, 2000

The UAE's commitment to protect IP started in earnest with the MOH's issuance of Ministerial Decree No. 404 on 30 April 2000, which prohibits the registration of any pharmaceutical product until the expiry of the patent term of the original product. Furthermore, the UAE clarified its commitments in Decree 404 via a letter to the U.S. Ambassador (Memorandum of Understanding or MOU) which specifically clarifies that for any drug registration application filed after January 1, 2000, the "protection period shall be extended and remain valid during the validity period of protection related to patent in the Country of Origin of the original drug."

In light of the Decree and the MOU, PhRMA and its member companies are very concerned by the recent MOH decision to register generic pharmaceutical products for sale in the UAE that appear to infringe on the patents of innovative medicines produced by our member companies. At the time of the registration, the patents in the country of origin remained in force and thus should have been honored in the UAE as required by Decree 404 and the MOU.