pugatchconsilium

BIOPHARMACEUTICAL COMPETITIVENESS & INVESTMENT (BCI) SURVEY 2017 BROCHURE:

Quantifying the Impact of Policy on the Biopharmaceutical Industry, Patients and the Economy

As one of the leading innovative industries today, the multinational biopharmaceutical industry is an integral partner for supplying life-saving medicines, creating high-value jobs and driving sustainable economic growth. The 2017 results of the Biopharmaceutical Competitiveness & Investment (BCI) Survey reveal that the dynamism of the biopharmaceutical industry, its contribution to the U.S. economy and its ability to develop a steady stream of life-saving medicines hinge on a supportive policy environment.

As a preview of the fourth edition of the BCI Survey, a global executive opinion survey of countries' biopharmaceutical competitiveness, this brief presents the 2017 overall results and uses them as a basis for exploring the impact of policies on the economy and biopharmaceutical innovation.

The 2017 BCI results reflect the policy choices in the U.S. and other countries over the past 30 years to promote innovation from the laboratory to the bedside. And investment follows supportive policy conditions. Home to many of the top biopharmaceutical companies worldwide, the U.S. and other biopharmaceutical leaders benefit tremendously from the wider footprint of the industry on trade, jobs and healthy lives.

At the same time, the BCI results also underscore how policies that jettison support for innovation and create uncertainty take a tangible toll on these benefits. Less supportive policies in major countries translate into reduced commercial activity and revenue for biopharmaceutical companies there, and hamper their investment both internationally and at home. As a result, to maintain a steady pace of innovation and economic growth countries like the U.S. have ended up footing more of the bill than they otherwise would have, in the form of higher prices, lower exports, fewer jobs and reduced investment in new medicines.

The solution is not a race to the bottom in policy conditions. In an era when competition is heating up and countries like China are making quick work of closing policy gaps, a deterioration in key policy issues can be a country's undoing – and this includes established leaders. For the U.S., failing to nurture the innovation ecosystem risks losing out to other countries that are working to pull investment their way instead. This bears a higher cost than just losing its number one spot among biopharmaceutical markets.

Using the 2017 BCI Survey results, this brief quantifies exactly how much policies undermining biopharmaceutical innovation in key markets cost the U.S. each year and how much more the U.S. could stand to lose in long-term investment, economic growth, trade and social welfare if it fails to consistently work to foster its own policy environment and stay ahead of the curve.

1. The biopharmaceutical policy ecosystem: The good, the bad and the ugly

The nuts and bolts of biopharmaceutical R&D: What 2017 BCI leaders are getting right

In order to identify and measure the impact of detrimental policies for biopharmaceutical innovation it is important to have a clear picture of which policies enable innovation and investment in the biopharmaceutical sector, and which do not.

Figure 1 outlines major policy conditions necessary for biopharmaceutical innovation globally, all of which are reflected in the BCI Survey questions. Policies should support activities spanning the entire lifecycle of research and development (R&D), from the discovery of new molecules to the launch and availability of cutting edge medicines in different markets, and enable the cycle to begin again. These policies include scientific and clinical capabilities and infrastructure, an effective and efficient regulatory system and market access framework and robust intellectual property (IP) protections.

FIGURE 1 The policy ecosystem supporting biopharmaceutical innovation based on the BCI Survey

Source: Pugatch Consilium, based on the 2017 Biopharmaceutical Competitiveness & Investment (BCI) Survey (Pugatch Consilium, forthcoming)

Countries with strong policy environments are those considered most competitive for biopharmaceutical investment. According to the 2017 BCI Survey results (see Figure 2), the outstanding feature among those rated as most attractive (those scoring at least 75 out of 100 for "newcomer" markets and at least 80 for "mature" markets, measured using different surveys) is a clear, systematic and ongoing commitment to a policy environment that supports biopharmaceutical innovation.

Biopharmaceutical competitiveness directly translates into actual investment. One proxy of high-level and sustained biopharmaceutical investment is the intensity of clinical research. Looking at the rate of clinical trial activity among countries covered in the BCI Survey, the majority of countries that display a relatively high rate of clinical research (100 trials or more registered to date in the NIH registry, Clinicatrials.gov, per million population) are those that achieve 70% of the total possible BCI score in their respective groups or higher.

FIGURE 2 BCI 2017 Overall Results: Some countries are nearing the summit while others are beginning the climb

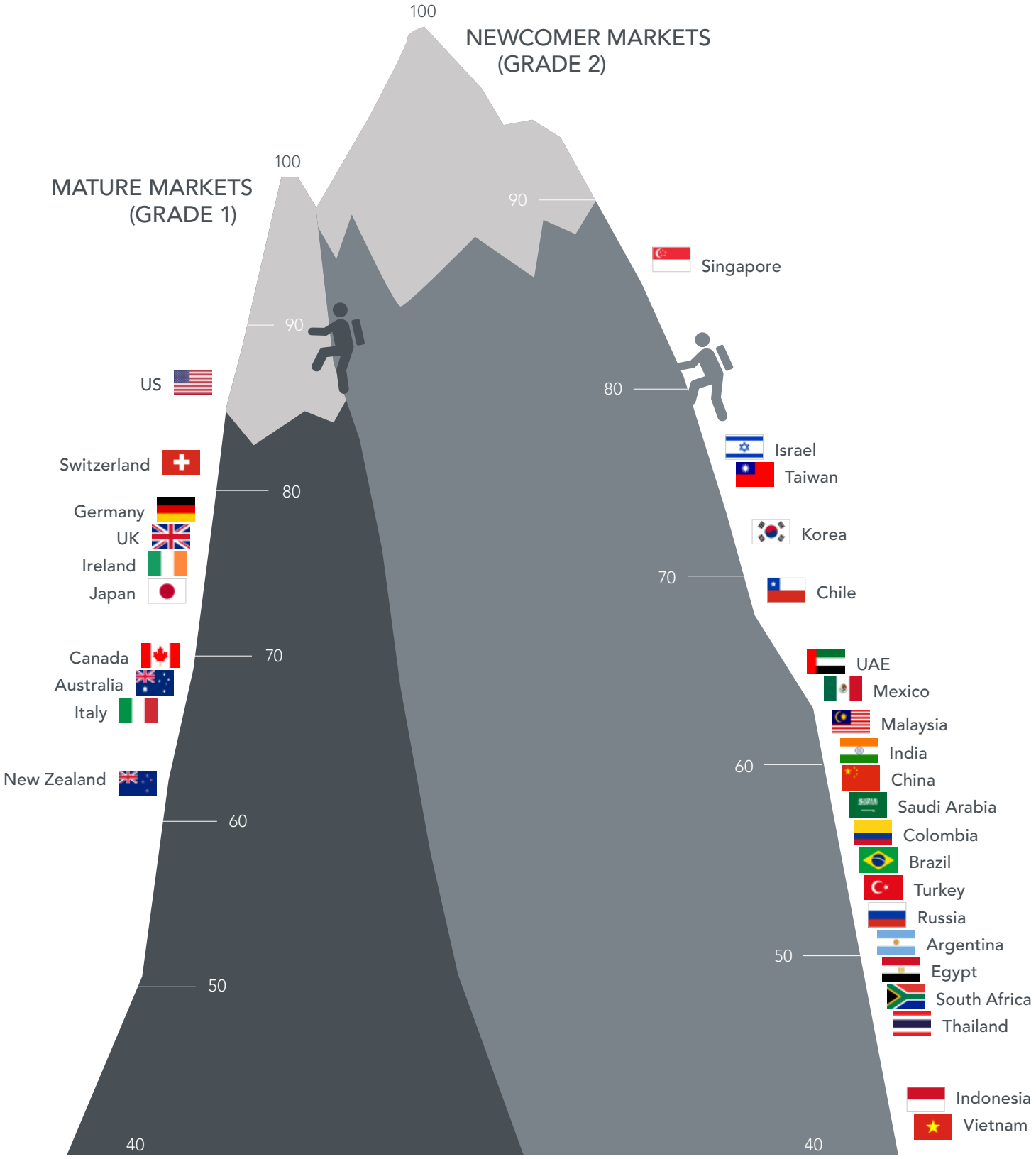


FIGURE 3 Biopharmaceutical policy environment (BCI 2017 score) and rate of investment (clinical trial activity)

Source: Pugatch Consilium (forthcoming); Clinicaltrials.gov (2017)

*NB: Clinical trial activity measured by number of clinical trials to date registered in Clinicaltrials.gov as of May 2017; BCI scores for newcomer and mature markets based on separate surveys and scored separately

Which policies hold back biopharmaceutical investment and innovation the most and where?

At the same time, a number of countries punch below their weight in competitiveness because of detrimental policies for biopharmaceutical innovators. Countries displaying a number of serious challenges tend to score below 65 in the BCI. With just a few exceptions these same countries also experience very low rates of investment in clinical research – less than 50 clinical trials per million population (and in most cases, less than 25). Even countries with a higher BCI score (such as mature markets scoring 65-80) and rate of clinical trial activity are held back from their optimum performance due to specific biopharmaceutical policy challenges.

Which are the biopharmaceutical policies that tend to deter innovators the most? Table 1 outlines a number of what may be considered the most pressing policies affecting biopharmaceutical companies today and where these challenges are most visible. The table illustrates a selection of markets from the BCI Survey that tend to display these challenges (either wholly or partly) within 3 main categories of the BCI, Regulatory System, Market Access & Financing and IP Protections, and are ranked in the bottom tiers of their respective groups. For example, Turkey, Russia, South Africa, Indonesia, Vietnam and Korea are countries that executives ranked in the bottom two quartiles in the Market Access & Financing category of the BCI, and display significant discriminatory pricing, reimbursement and procurement procedures for innovative drugs.

Opting to utilize these and other biopharmaceutical policies that undercut innovation means fewer sales for research-based companies at lower prices and for shorter periods of time, compared to an environment more closely resembling the ecosystem illustrated in Figure 1. This translates into lower revenues for the biopharmaceutical industry and a reduced ability to recoup R&D costs, and ultimately limits investment, trade, jobs and social welfare benefits in countries that fund innovation, notably the U.S.

TABLE 1 Sample of the most damaging policies identified in the BCI's Regulatory Framework, Market Access and IP Protections categories*

Regulatory System	Market Access & Financing	IP Protection
Significant regulatory delays (12-18+ months) and red tape	Direct price cuts and reference pricing	Patenting challenges (patentability criteria beyond international standards and patent office backlogs)
Requirements for new drug registration out of sync with international standards	Arbitrary or inconsistent pricing rules	Compulsory licensing
Major gaps in regulatory capacity (standards for drug approval and their implementation do not adequately ensure safety and quality of medicines)	Discriminatory reimbursement and procurement procedures for innovative drugs	Weak patent enforcement (including ineffective or discriminatory patent linkage)
	Market access conditional on localization (local content, manufacturing and tech transfer requirements)	RDP failures (unfair commercial use and disclosure and inadequate application)
	Import barriers (such as high tariffs and taxes on medicines)	Lack of patent term extension

Newcomer Markets

Countries displaying <65% of the total possible category score and one or more of the above challenges*

BCI countries				BCI countries			
Singapore				Colombia	⊘	⊘	⊘
Israel				Brazil	⊘	⊘	⊘
Taiwan		⊘		Turkey	⊘	⊘	⊘
Korea		⊘		Russia	⊘	⊘	⊘
Chile				Argentina	⊘	⊘	⊘
UAE		⊘		Egypt	⊘	⊘	⊘
Mexico		⊘	⊘	South Africa	⊘	⊘	⊘
Malaysia	⊘	⊘		Thailand	⊘	⊘	⊘
India	⊘	⊘	⊘	Indonesia	⊘	⊘	⊘
China	⊘	⊘	⊘	Vietnam	⊘	⊘	⊘
Saudi Arabia	⊘	⊘	⊘				

Mature Markets

Countries displaying <75% of the total possible score in the Regulatory and Market Access categories and <85% in IP Protections, and one or more of the above challenges*

BCI countries				BCI countries			
US				Japan		⊘	
Switzerland				Canada	⊘	⊘	⊘
Germany		⊘		Australia	⊘	⊘	⊘
UK		⊘		Italy	⊘	⊘	⊘
Ireland		⊘		New Zealand	⊘	⊘	⊘

*Based on BCI results, Pugatch Consilium analysis and PhRMA Special 301 Submission 2017; country order is based on the overall BCI score, from top to bottom

Damaging policies discourage biopharmaceutical investment, trade, jobs and innovation by:

- Denying market access or limiting terms of access
- Eroding IP-derived market exclusivity
- Creating uncertainty and additional expenses
- Hindering ability to recoup R&D costs
- Allowing for substandard drugs
- Diluting patient/consumer confidence
- Diminishing likelihood of new drug launch

2. Modeling the opportunity costs of damaging policies for the biopharmaceutical industry

But how much exactly is the use of damaging policies costing the biopharmaceutical industry and the countries that work to support biopharmaceutical innovation? How much more in biopharmaceutical sales and exports could these countries expect to realize if the most damaging policies for innovation were avoided and major markets globally provided support for innovation in line with their market size and capabilities?

Measuring the relative share of policy challenges in key markets

Using the BCI Survey scores this analysis captures the most damaging policies in place in a given country and quantifies the extent to which they impact companies' current commercial activities and countries' trade in biopharmaceuticals. It does so by assuming that an incremental improvement in a country's BCI score would reflect a reform to one or several of the most damaging policies utilized there (depending on the extent to which such policies are in place).

We constructed three scenarios of incremental improvement to countries' BCI scores: 1) Minimal; 2) Medium; and 3) Substantial improvement. The improvement identified in each scenario is calculated relative to an optimal environment, in this case the score of the countries ranked at the top of the 2017 BCI (Singapore for newcomer markets and the U.S. for mature markets). Both score 87 out of 100 – a score that reflects a high level of competitiveness and support for innovation (at the time the BCI Survey was conducted in Q1-2 2017). The improvements required in each scenario are as follows:

1) Minimal improvement, equal to a rise in score of 10% of the top BCI score (9 points);

2) Medium improvement, equal to a rise in score of 20% of the top BCI score (17 points); and

3) Substantial improvement, equal to a rise in score of 30% of the top BCI score (26 points).

The scenarios are applied to each of the other 29 BCI 2017 countries (20 newcomer markets and 9 mature markets) and the percentage change need to achieve the rise in score in the three scenarios is calculated (and presented in Table 2). The same rise in score is applied to all countries in order to measure the needed changes on a like-for-like basis and adequately capture the relative share of the most damaging policies in place in a given country. Countries that require only a small change in their 2017 BCI score in each scenario are those that display isolated policy challenges, while countries requiring a large change in score are those in which various challenges are visible in key areas of the biopharmaceutical policy ecosystem.

Estimating the impact of damaging policies on the biopharmaceutical industry

The impact of the most damaging policies on the biopharmaceutical industry in each market is measured using the following formula:

(Current biopharmaceutical sales) (% change in sales) = Unrealized sales of the biopharmaceutical industry

Current sales are measured using IMS 2015 estimates of total sales per market (see Table 3). The percentage change in sales is equivalent to the percentage change in policy for each scenario (identified in Table 2). It is worth noting that

empirical studies that have measured the relative effect of policy changes on commercial activities by pharmaceutical companies tend to identify on average a 0.2 to 0.3 multiplier (see for instance, Sood et al, 2009[1]). However in this analysis, the multiplier is viewed as already accounted for in that the percentage change in policy applied to sales only encompasses an incremental share of the total policy environment (between 10 and 30%).

TABLE 2 Measuring the change in BCI score needed to reform the most damaging biopharmaceutical policies in three scenarios

	BCI 2017 Overall Score	% change in BCI 2017 score required for: 1. Minimal improvement (+9)	2. Medium improvement (+17)	3. Substantial improvement (+26)
Newcomer markets				
Vietnam	43.75	20%	40%	60%
Indonesia	43.82	20%	40%	60%
Thailand	49.64	18%	35%	53%
South Africa	53.28	16%	33%	49%
Egypt	53.32	16%	33%	49%
Argentina	53.40	16%	33%	49%
Russia	53.68	16%	33%	49%
Turkey	54.48	16%	32%	48%
Brazil	54.50	16%	32%	48%
Colombia	55.60	16%	31%	47%
Saudi Arabia	57.50	15%	30%	46%
China	58.04	15%	30%	45%
India	58.58	15%	30%	45%
Malaysia	62.44	14%	28%	40%*
Mexico	63.08	14%	28%	38%*
UAE	64.64	14%	27%	35%*
Chile	69.39	13%	25%	26%
Korea	72.00	12%	21%*	21%*
Taiwan	76.76	11%	14%*	14%*
Israel	76.97	11%	13%*	13%*
Mature markets				
New Zealand	63.51	14%	27%	37%*
Italy	67.90	13%	26%	28%*
Australia	68.22	13%	25%	27%*
Canada	70.27	12%	24%*	24%*
Japan	72.42	12%	20%*	20%*
Ireland	75.80	11%	15%*	15%*
UK	75.88	11%*	15%*	15%*
Germany	78.11	11%	11%*	11%*
Switzerland	82.49	5%	5%*	5%*

* % change capped at % needed to reach top BCI score (Singapore for newcomer markets and U.S. for mature markets)

TABLE 3 Biopharmaceutical industry sales per market (2015), newcomer and mature markets

Newcomer Markets				Mature Markets	
Argentina	$6,550,954,546	Malaysia	$1,545,657,181	Australia	$11,006,540,275
Brazil	$25,629,699,537	Mexico	$10,153,226,608	Canada	$19,169,950,979
Chile	$2,356,115,025	Russia	$12,269,303,131	Germany	$42,621,040,947
China	$115,215,452,417	Saudi Arabia	$6,103,768,056	Ireland	$2,079,617,845
Colombia	$3,268,522,477	South Africa	$2,707,715,982	Italy	$27,211,877,419
Egypt	$3,972,635,439	Taiwan	$4,403,843,244	Japan	$81,359,009,965
India	$16,573,364,318	Thailand	$3,761,943,259	New Zealand	$954,104,186
Indonesia	$4,191,490,215	Turkey	$7,057,588,899	Switzerland	$5,562,595,895
Israel	$3,606,431,083	UAE	$2,111,444,106	UK	$28,398,651,895
Korea	$12,547,267,753	Vietnam	$3,142,179,071		

Source: IMS (2015)

FIGURE 4 Total unrealized global sales for the biopharmaceutical industry from the most damaging policies worldwide

The most pressing policy challenges worldwide cost the biopharmaceutical industry up to $149.29 billion in global sales annually

Source: Pugatch Consilium analysis based on IMS (2015) and Pugatch Consilium (forthcoming)

The formula on p.6 is applied to the three scenarios for each market to calculate total unrealized sales of the biopharmaceutical industry worldwide – sales "left on the table", so to speak, due to the most damaging policies in place in key markets. As Figure 4 indicates, the most pressing policy challenges among the markets in the BCI Survey in 2017 are estimated to cost the biopharmaceutical industry between $63.11 billion and $149.29 billion in global sales annually – and this may be regarded as a conservative estimate.

These costs to the biopharmaceutical industry end up being passed on to economies and patients. Countries with weak policy environments lose out on the investment that would have come from a market-based level of commercial activity by the industry. Studies show that higher profitability in the biopharmaceutical industry translates into more R&D activity.[2] For their part, countries with supportive policy environments – and patients and health systems there – may end up absorbing a share of these costs that goes beyond what would be commensurate with their market size. These countries, notably the U.S., also forgo domestic R&D investment that could have taken place had conditions for trade and product launch in other markets been more supportive. In fact, studies find that roughly 80% of productivity gains globally are fed back into domestic R&D investment (both in the primary sector and in other industries).[3]

Estimating the impact of damaging policies on the U.S. trade deficit

In addition to unrealized sales, we estimate the impact of the most damaging biopharmaceutical policies in each BCI market on U.S. exports there using the following formula:

(Current U.S. biopharmaceutical exports) (% change in exports) = Unrealized biopharmaceutical exports

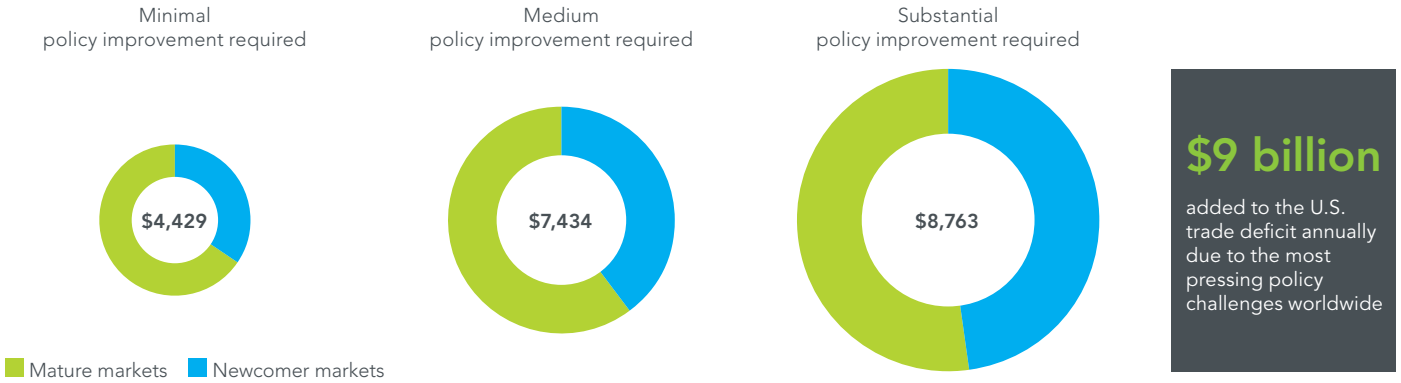
Current U.S. exports to each market are measured using data from the U.S. Department of Commerce and the U.S. International Trade Commission. As with the above sales calculations, the percentage change in exports is equivalent to the percentage change in policy identified in Table 2 and the formula is applied to the three scenarios for each market to calculate total unrealized U.S. biopharmaceutical exports resulting from the most damaging policies worldwide. As Figure 5 indicates, we estimate the most pressing policy challenges among the BCI Survey markets to result in losses to U.S. exports of, in the very least, $4.4 billion to $8.8 billion annually. In other words, damaging policies in major markets abroad not only cost the biopharmaceutical industry itself, but also hurt the U.S. economy and workers by undermining U.S. biopharmaceutical exports to these markets.

TABLE 4 U.S. biopharmaceutical exports (NAICS 3254) in newcomer and mature markets, 2015

Newcomer Markets				Mature Markets	
Argentina	$563,083,000	Malaysia	$120,053,000	Australia	$939,647,000
Brazil	$1,240,464,000	Mexico	$1,675,880,000	Canada	$4,731,657,000
Chile	$172,902,000	Russia	$204,950,000	Germany	$3,650,428,000
China	$2,510,162,000	Saudi Arabia	$348,148,224	Ireland	$2,418,920,000
Colombia	$324,856,000	South Africa	$181,482,965	Italy	$2,944,599,000
Egypt	$69,673,668	Taiwan	$430,476,000	Japan	$3,816,885,000
India	$475,312,000	Thailand	$215,158,000	New Zealand	$73,121,625
Indonesia	$89,826,000	Turkey	$154,590,000	Switzerland	$2,330,637,000
Israel	$216,427,538	UAE	$153,872,196	UK	$4,752,400,000
Korea	$1,130,543,000	Vietnam	$130,058,000		

Note: Data compiled from tariff and trade data from the U.S. Department of Commerce, U.S. Census Bureau and the U.S. International Trade Commission

FIGURE 5 Total unrealized U.S. biopharmaceutical exports (USD million) from the most damaging policies worldwide



Source: Pugatch Consilium analysis based on U.S. Department of Commerce, U.S. Census Bureau and U.S. International Trade Commission; and Pugatch Consilium (forthcoming)

3. Moving in different directions? A cautionary tale for the U.S.

Though the U.S. is considered the world leader in biopharmaceutical innovation, no market's spot in the global competition for investment is a given. As the largest biopharmaceutical market worldwide a deterioration in policy conditions or failure to maintain an environment that nurtures innovation in the U.S. itself bears a serious long-term cost for the economy. Policy choices akin to some of the detrimental policies employed in other countries today could substantially erode the industry's contribution to the U.S. economy, innovation system and social welfare improvements.

Applying a similar step-wise scenario analysis used in section 2, if the U.S. biopharmaceutical policy environment itself were to deteriorate incrementally as reflected in a 1) 10% drop its BCI 2017 score (which would be roughly equal to Germany's score in the BCI); 2) a 20% drop (roughly equal to Canada's score) and 3) a 30% drop (equal to New Zealand's score), the U.S. could expect to see a drop of between $43.35 billion and $130.04 billion in biopharmaceutical sales per year. By some estimates, this equates to nearly a third of its current level of sales.[4]

Crucially, lost sales would translate into substantially higher losses to key areas of the economy and trade, including output, exports, employment and R&D investment – on which the biopharmaceutical sector has a significant multiplying effect.[5] For example, considering the externalities associated with biopharmaceutical sales in terms of additional output from the pharmaceutical supply chain and related sectors, the U.S. could lose up to $280 billion in total (direct and indirect) output from the biopharmaceutical sector (as seen in Table 5). Concurrently, we estimate the U.S. could lose nearly $20 billion in biopharmaceutical exports, further impacting the current trade deficit.

The biopharmaceutical industry is a major contributor to U.S. employment and particularly of high-value and highly skilled jobs. The multiplying effect of biopharmaceutical jobs on other supporting and related sectors is substantial; according to one estimate, for every one job in the biopharmaceutical industry another 4 jobs are created.[6] Were the U.S. to opt for introducing policies that damage biopharmaceutical innovation, it could lose over 1,000,000 jobs, with an estimated 175,000 of these in life sciences fields and over 200,000 in management or financial positions.

TABLE 5 Estimated policy-related losses to the U.S. from a U.S. biopharmaceutical policy U-turn

If the U.S. policy environment itself deteriorated, the U.S. could lose up to an additional $280 billion in total output, nearly $20 billion in exports, over 1,000,000 jobs and over $25 billion in R&D spending per year

Sales and exports impact + externalities (in USD billion) if the U.S.' BCI 2017 score were to drop by:	10%	20%	30%
Total biopharma output (total industry sales) loss	**$43.35**	**$86.70**	**$130.04**
Total output loss with externalities (suppliers + other sectors; multiplier = 2.18)	**$94.50**	**$189.00**	**$283,50**
Loss of U.S. biopharma exports	**$5.80**	**$11.60**	**$17.40**
Loss in employment (approx. 1.53 jobs for every $1 million in sales, as of 2014)	66,323	132,646	198,968
Total employment loss in pharma + other sectors (multiplier = 5.21)	**345,542**	**691,084**	**1,036,626**
Life sciences jobs lost (approx. 17% of U.S. pharma jobs)	58.742	117,484	176,226
Management/financial jobs lost (20% of U.S. pharma jobs)	69,108	138,217	207,325
Loss in associated R&D investment (approx. 24.8% of sales in 2015)	**$10.62**	**$21.24**	**$31.86**

Source: Pugatch Consilium analysis, based on IMS (2015); TEConomy/PhRMA (2016); PhRMA (2016)

The U.S. could also experience a marked drop in the level of investment in R&D domestically, undercutting the industry's long-standing reliance on the U.S. for its "bread and butter" and its contribution to long-term economic growth and global competitiveness there. Specifically, with nearly 20% of sales re-invested in R&D on average worldwide (and likely higher in the U.S.), the U.S. could lose up to around $25 billion in R&D spending per year. This not only means reduced investment but a drop in social welfare improvements that would have resulted from development of new medicines.

The U.S. must consider another scenario: at the same time as it is considering a dilution in policy conditions other competitors are going the opposite direction – seeking to shore up their policy environments. This could mean tthe up to $280 billion in output, over 1,000,000 jobs and $25 billion in R&D investment would be shifted to countries seeking to pull investment away from the U.S.

While not the only country raising the stakes, a prime example is China – with recent moves to speed up regulatory approval and shore up biopharmaceutical IP protection, on top of long-term efforts to create a world-class science base, China is racing ahead in its biopharmaceutical environment and could be a candidate for investment and jobs that would have otherwise stayed in the U.S. In fact, according to our estimates, if proposed reforms are fully implemented China could experience around a 30% increase in its 2017 BCI score (measured prior to reforms), particularly in the categories of Clinical Research, Regulatory Framework and IP Protections (as outlined in the below box).

4. A race to the top, not the bottom

This analysis suggests that for the U.S. and other long-term supporters of biopharmaceutical innovation now is not the time to skimp on support. While it may be tempting to even the playing field through a race to the bottom in policy, in the long run it is more strategic and effective to instead aim for a higher policy ceiling worldwide.

An upward, rather than downward, policy trajectory would enable the U.S. to stay in the global innovation game – and maintain the benefits that patients and the economy secure from the biopharmaceutical industry's activity domestically. At the same time it could allow other countries to absorb a more proportionate share of funding for global biopharmaceutical innovation, while also promoting substantial health and economic gains in these countries.

A selection of recent proposed biopharmaceutical reforms in China

Clinical research

- Simplified review of clinical trial sites
- 60 day ceiling on clinical trial approval
- Streamlined ethics committee review and trial amendment system
- Improved transparency and communication with innovators

Regulatory framework

- Expanded priority review and possibility of conditional approval and early access
- Acceptance of foreign clinical data for market authorization, provided other conditions for approval are met
- Manufacturer accountability for pharmacovigilance and post-marketing surveillance

Intellectual property

- Expanded patent linkage system with a more specific patent notification system and a 24 month stay on market authorization of a potentially infringing follow-on product
- System for securing a 6 year term of RDP with market authorization and an extended term of protection for orphan or pediatric indications (10+3 years) and biologics (10 years)

Source: CFDA Circulars 52, 53, 54 and 55 (2017)

DOCUMENT NOTES:

1 Sood, N. et al (2009), "The effect of regulation on pharmaceutical revenues: experience in nineteen countries", *Health Affairs*, Vol.28, No.1, Exhibit 6

2 Scherer, F. (2001), "The Link Between Gross Profitability and Pharmaceutical R&D Spending", *Health Affairs*, Vol.20, No.5, pp.216-220; Simanjuntak and Tjandrawinata (2011): "Impact of Profitability, R&D Intensity, and Cash Flow on R&D Expenditure in Pharmaceutical Companies", Available at https://ssrn.com/abstract=1824267)

3 Keller, W. (2002), "Trade and the Transmission of Technology", *Journal of Economic Growth*, Vol.7, No.1, pp.5-24)

4 According to IMS data, total biopharmaceutical sales in the U.S. were approximately $433.48 billion in 2015.

5 Though not all of the sales come from U.S. companies it can be assumed that the large majority conduct significant levels of research and commercial activity in the U.S. beyond strictly sales.

6 TEConomy Partners & PhRMA (2016), *The Economic Impact of the U.S. Biopharmaceutical Industry: National and State Estimates*, pp.10-11