

## **Pharmaceutical industry behaviour and the Trans Pacific Partnership Agreement**

Erik Monasterio, Deborah Gleeson

Trans Pacific Partnership Agreement (TPPA) is a regional trade agreement involving 12 countries, including New Zealand, which has the potential to significantly alter the domestic environment for health policy-making. One of the key concerns is the future of New Zealand's Pharmaceutical Management Agency (PHARMAC), on which affordable access to medicines for New Zealanders hinges.

Through the TPPA, the United States (US) is seeking to eliminate therapeutic reference pricing, introduce appeals processes for pharmaceutical companies to challenge formulary listing and pricing decisions, and introduce onerous disclosure and "transparency" provisions that facilitate industry involvement in decision-making around coverage and pricing of medicines (and medical devices).

This editorial examines trends in pharmaceutical industry conduct and strategy over the past 15–20 years and argues that if the TPPA (based on the US proposals) is successfully prosecuted, it will contribute to adverse health outcomes by increasing costs and reducing access to affordable medicines for New Zealanders. This in turn can be expected to disproportionately affect disadvantaged population groups, including Māori and Pacific peoples.

### **The Trans Pacific Partnership Agreement**

New Zealand is 1 of 12 countries engaged in the final stages of negotiations for a regional trade agreement, the Trans Pacific Partnership Agreement (TPPA). The TPPA could have wide-ranging ramifications for health policy, however little is known about it amongst medical practitioners in many countries, including New Zealand.

Concerns have been expressed about many aspects of the TPPA which have the potential to significantly alter domestic environments for health policy-making in areas such as pharmaceutical policy, tobacco control, and alcohol and food policy.<sup>1,2</sup> In the New Zealand context, one of the key concerns is the future of PHARMAC, on which affordable access to medicines for New Zealanders hinges.<sup>3</sup>

While the ramifications for health policy and programmes are significant, however, the negotiations are conducted under conditions of confidentiality, and draft texts are not available to the public. What little is known about the TPPA is derived mainly from leaked negotiating documents.

In this editorial, we draw on leaked documents to outline the proposals that have been made for pharmaceuticals in the TPPA and the new privileges they would provide to the pharmaceutical industry. We place these extra privileges in the context of strategies that have been used by the pharmaceutical industry to increase its market share and extend its monopolies.

We argue that there are hidden dangers in allowing the industry any greater influence over New Zealand's pharmaceutical policies, laws and programs.

There are three main avenues through which the TPPA is likely to provide the pharmaceutical industry with extra privileges.

- First, the US has proposed a suite of provisions for the intellectual property (IP) chapter for the TPPA<sup>4,5</sup> that taken together, would expand patent protection and prolong monopolies for pharmaceutical companies. For example, these include proposals to mandate that countries will allow patents for new uses and methods of using a known product, even when there is no evidence of additional therapeutic benefit.

Patents would have to be permitted for diagnostic and treatment methods. Countries would also have to extend the term of patents beyond the current 20 years granted, to compensate for any delays in the process of issuing the patent or approving it for marketing. These and many more provisions proposed by the US would provide additional privileges beyond those provided by current New Zealand patent law, and would work together to delay the availability of generic medicines in New Zealand.<sup>6</sup>

Recently leaked documents<sup>7</sup> have shown that the US has continued to pursue these proposals despite the resistance of many of the other countries, including New Zealand.

- The second way the TPPA would confer additional privileges on the pharmaceutical industry is through mandating procedural changes to pharmaceutical coverage programs, including New Zealand's Pharmaceutical Management Agency (PHARMAC).

PHARMAC's autonomy, its strategies for procurement and price negotiation, and its careful evaluation of value for money make it highly effective in containing costs while maintaining access to essential medicines.<sup>3</sup>

The very features that make PHARMAC effective make it a target for the big transnational pharmaceutical companies based in the US. The 2012 special 301 watch report of the US Trade Representative cites US industry concerns over "the lack of transparency, fairness, and predictability of the PHARMAC pricing and reimbursement regime, as well as the negative aspects of the overall climate for innovative medicines in New Zealand".<sup>8, p21</sup>

The US negotiating objectives listed in the "fast track" (Trade Priorities Act) bill introduced into Congress in January 2014 include "the elimination of government measures such as price controls and reference pricing which deny full market access for US products".<sup>9, p20</sup>

US proposals for an annex to the transparency chapter of the TPPA<sup>10</sup> endanger effective pricing strategies such as therapeutic reference pricing, provide new avenues for industry to appeal decisions and require additional disclosure of information and avenues for consultation and input by the industry.<sup>3,11</sup> Even a less egregious set of provisions such as those in the Australia-US Free Trade Agreement could impinge significantly on PHARMAC's decision-making autonomy and flexibility.

The US transparency chapter annex proposal would also institutionalise direct-to-consumer advertising (DTCA) of pharmaceuticals via the internet. While this practice is currently legal in New Zealand, accepting such a provision would mean that New Zealand would not be able to change its laws in response to mounting evidence that the risks associated with DTCA outweigh the benefits.<sup>11</sup>

- A third avenue for granting additional privileges to industry is via the highly controversial investor-state dispute settlement (ISDS) mechanism in the investment chapter of the TPPA. ISDS allows foreign corporations to sue governments for compensation (for awards that often amount to hundreds of millions of dollars) in international tribunals.

A US pharmaceutical company, Eli Lilly, has launched such action against Canada after it revoked patents for two drugs, seeking \$500 million Canadian dollars in compensation.<sup>12</sup> Leaked text suggests that New Zealand has already agreed to the ISDS mechanism in the TPPA.<sup>13</sup>

The way in which these three different mechanisms could work together in practice to promote the interests of the pharmaceutical industry is highly worrying. Increased IP protection means drugs would cost more for longer periods; changes to PHARMAC's procedures proposed by the US would further erode its capacity to obtain value for money; and an ISDS mechanism applying to the IP and transparency chapters would provide new avenues to the industry to challenge decision making regarding patents, pricing and reimbursement.

The challenge of escalating prescription drug costs at a time of increasing fiscal constraint has become a major concern to health care providers, a critical policy issue and a major focus of political debate. Future significant increase in medication costs, which is a likely outcome of a TPPA agreement based on the US proposals will contribute to significantly adverse health outcomes by reducing access and adherence to important medications; this can be expected to disproportionately affect disadvantaged population groups, including Maori and Pacific peoples.<sup>3</sup>

## **What we have learnt about pharmaceutical industry strategy**

It is salutary to note that in the US drug spending is driven by brand-name drugs, which account for 20% of all prescriptions but 80% of all costs.<sup>14</sup> It is not surprising nor counterintuitive that the business model of the pharmaceutical industry, which seeks to maximise profits and returns to shareholders is often in direct conflict with public health interests and legal safeguards.

Given the current state of affairs and the implications of the TPPA negotiations, we urge close attention to the lessons that have been learnt about pharmaceutical industry conduct over the past 15–20 years.

We provide a (by no means exhaustive) list of concerns in relation to pharmaceutical industry strategy that should caution against allowing greater influence to be exerted by the pharmaceutical industry, a weakening of government drug monitoring and funding programmes, and changes to intellectual property law. These include: promotion of off-label prescribing (i.e. prescribing a drug for an indication outside of that for which it is licensed), reporting bias with unpublished negative findings and

misreported studies,<sup>15</sup> medical ghost-writing (the practice of pharmaceutical companies secretly authoring journal articles published under the by-line of academic researchers)<sup>16</sup> and evidence of increasing expenditure on promotion, to the extent that almost twice as much is spent on advertisement than in research and development.<sup>17</sup>

Dr Peter Gotzsche (a physician and medical researcher with very high numerical literacy, and head of the Nordic Cochrane Centre) has recently published a book that draws on 20 years research to convincingly argue that the drug industry has corrupted the scientific process to play up the benefits and play down the harms of their drugs.<sup>18</sup> His is unfortunately not an outlier's voice, as other books and peer-reviewed articles from eminent academics, including former editors of the *New England Journal of Medicine*, have consistently reached similar conclusions in the past 10 years.<sup>19,20</sup>

Recent landmark legal cases by the US Department of Justice have highlighted the extent to which the largest drug companies have repeatedly and systematically engaged in illegal activities to promote drug sales. Common recent crimes include illegal marketing of medications for off-label uses, misrepresentation of research results, withholding data on harms, and Medicaid and Medicare Fraud.<sup>9</sup> As these crimes are widespread and recurrent, it has been suggested that they are probably committed deliberately and that some of these behaviours may be resistant to external regulatory approaches.<sup>21,22</sup>

In 2012 GlaxoSmithKline (GSK) agreed to plead guilty and pay a record US\$3bn in penalties for unlawful promotion of prescription drugs, failure to report safety data, and false price reporting. It also signed a 123-page corporate integrity agreement with the US Department of Justice that regulates its activity for the next 5 years.<sup>23</sup>

Despite entering into such an agreement and after seeking to reassure the public of its intentions to root out corruption, GSK has again become embroiled in allegations of serious corruption and criminal behaviour in relation to drug sales in China.<sup>24</sup>

Commenting on a recent legal case against AstraZeneca, US Attorney General Eric Holder said that illegal acts by drug companies "...can put the public health at risk, corrupt medical decisions by health care providers, and take billions of dollars directly out of taxpayers' pockets."<sup>25</sup>

Off-label use of medications is costly, potentially harmful and of questionable benefit. Radley et al found that 73% of the off-label use of 160 commonly prescribed drugs lacked evidence of clinical efficacy, and only 27% was supported by strong scientific evidence.<sup>26</sup> A Christchurch based study estimated that the cost for off-label use of the atypical antipsychotic medication, quetiapine was \$9.5 million in New Zealand in 2010.<sup>27</sup>

Pharmaceutical industry marketing appears to have influenced the rapid expansion in off-label prescribing of psychotropic drugs to child and youth populations, often by overstating benefits and hiding known harms.<sup>28</sup>

The success of marketing over reason is perhaps best highlighted in the extraordinary worldwide expansion in the use of atypical antipsychotic medications, designed for the treatment of psychosis and psychotic spectrum disorders, which are rare conditions affecting around 2% of the general population.

Antipsychotic global sales were US\$25.4 billion and the seventh biggest therapeutic group in 2010; Seroquel™ (quetiapine), Zyprexa™ (olanzapine) and Abilify™ (aripiprazole) were the 5<sup>th</sup>, 10<sup>th</sup> and 13<sup>th</sup> biggest selling pharmaceuticals, with sales of US\$6.8; US\$5.7 and US\$5.4 billion respectively.<sup>29</sup> Even the recent record-breaking fines imposed on the industry are unlikely to act as a significant disincentive in the face of such profitable sales.

Beyond illegal practices the pharmaceutical industry has also engaged in other (legal) strategies to extend periods of market monopoly. The term “life-cycle management” (evergreening) refers to this practice, which includes slight changes in formulation without the requirement of showing superiority over existing medicine, which can then be protected by later issue patents,<sup>30</sup> negotiating settlements with generic companies to prevent challenges to potentially weak or invalid patents<sup>31</sup> and legal action against licensing authorities to delay market entry of generic medications.<sup>32</sup>

For example, recent research on eight commonly prescribed drugs subject to evergreening strategies in the public hospital system of the canton of Geneva (which represents about 5% of Switzerland’s total population), estimated an additional cost of 30 million euros between 2000 and 2008, without any proven clinical advantage.<sup>14,33</sup>

## Conclusion

The range of strategies used by the pharmaceutical industry to advance and protect its economic interests and market share is well documented. This calls for patent law that prioritises the public interest, and for public institutions and decision making processes that are independent and free from pharmaceutical industry influence.

In the context of the TPPA negotiations, it is vital that New Zealand does not cede further ground to the pharmaceutical industry, by ‘locking in’ direct-to-consumer advertising, and by providing further intellectual property privileges, opportunities to influence decision making, and new avenues for legal challenges.

The TPPA negotiations are now in the final stages, with the conclusion of a deal predicted in the first half of 2014. It is time for New Zealand’s medical practitioners to join the growing chorus of voices highlighting the hidden costs of “free” trade, before the deal is done.

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## References:

1. Wyber R, Perry W. The Trans-Pacific Partnership: An Analysis of the Impact on Health in New Zealand. Nyes Institute, 2013. <http://www.nyesinstitute.org/reviews/tpp/>



2. Gleeson D, Friel S. Emerging threats to public health from regional trade agreements. *The Lancet* 2013;381(9876):1507–1509.
3. Gleeson D, Lopert R, Reid P. How the Trans Pacific Partnership Agreement could undermine PHARMAC and threaten access to affordable medicines and health equity in New Zealand. *Health Policy* 2013;112(3):227–233.
4. Trans Pacific Partnership. Intellectual Property Rights Chapter Draft – February 10, 2011. Available from: <http://keionline.org/sites/default/files/tpp-10feb2011-us-text-ipr-chapter.pdf>
5. Trans Pacific Partnership. Intellectual Property Rights Chapter (Selected Provisions. Leaked Draft Text, September 2011. <http://www.citizenstrade.org/ctc/wp-content/uploads/2011/10/TransPacificIP1.pdf>
6. Kilic B, Maybarduk P. Dangers for Access to Medicines in the Trans Pacific Partnership Agreement (TPP): Comparative Analysis of the United States' Intellectual Property Proposal and Laws of New Zealand. Public Citizen, 2012. <http://www.citizen.org/documents/ComparativeAnalysisTPPandNZ.pdf>
7. Trans Pacific Partnership. Intellectual Property Rights Chapter: Consolidated Text. Leaked Draft Text, TPP Negotiations IP Group, 30 August 2013. <http://wikileaks.org/tpp/static/pdf/Wikileaks-secret-TPP-treaty-IP-chapter.pdf>
8. United States Trade Representative. (2012) Special 301 Report. USTR, Executive Officer of the President of the United States: Washington D.C. <http://www.ustr.gov/sites/default/files/2012%20Special%20301%20Report.pdf>
9. United States Congress. (2014) Bipartisan Congressional Trade Priorities Act of 2014 Bill <http://www.finance.senate.gov/imo/media/doc/TPA%20bill%20text.pdf>
10. Trans Pacific Partnership. Transparency Chapter – Annex on Transparency and Procedural Fairness for Healthcare Technologies, 2011. <http://www.citizenstrade.org/ctc/wp-content/uploads/2011/10/TransPacificTransparency.pdf>
11. Lopert R Gleeson D. The high price of “free” trade: U.S. trade agreements and access to medicines. *Journal of Law, Medicine and Ethics* 2013;41(1):199–223.
12. Baker BK. Threat of pharmaceutical-related IP investment rights in the Trans-Pacific Partnership Agreement: an Eli Lilly v. Canada case study. *Investment Treaty News*, 20 September 2013. <http://www.iisd.org/itm/2013/09/20/threat-of-pharmaceutical-related-ip-investment-rights-in-the-trans-pacific-partnership-agreement-an-eli-lilly-v-canada-case-study/>
13. Trans Pacific Partnership. (2012) Investment Chapter (Leaked Draft Text). <http://www.citizenstrade.org/ctc/wp-content/uploads/2012/06/tppinvestment.pdf>
14. Kesselheim AS. Rising Health Care Costs and Life-Cycle Management in the Pharmaceutical Market. *PLoS Med* 2013;10(6):e1001461. doi:10.1371/journal.pmed.1001461.
15. Doshi P, Dickersin K, Healy D, et al. Restoring invisible and abandoned trials: a call for people to publish the findings. *BMJ* 2013;346:f2865.
16. Lacasse JR, Leo J. Ghostwriting at elite academic medical centers in the United States. *PLoS Med* 2010;7(2):e1000230.
17. Gagnon, MA, Lexchin J. The cost of pushing pills: a new estimate of pharmaceutical promotion expenditures in the United States. *PLoS Med* 2008;5(1):e1.
18. Gotzsche P. *Deadly Medicines and Organised Crime: How Big Pharma has Corrupted Healthcare*. Radcliffe Publishing, 2013.
19. Kassirer JP. *On the Take: How Medicine's Complicity with Big Business Can Endanger Your Health*. New York, NY: Oxford University Press, 2004.
20. Angell M. Drug companies & doctors: A story of corruption. *The New York Review of Books*, 2009;56(1):8–13.
21. Gøtzsche PC. Corporate crime in the pharmaceutical industry is common, serious and repetitive; 2013. [www.cochrane.dk/research/corporatecrime](http://www.cochrane.dk/research/corporatecrime)
22. Kesselheim AS, Mello MM, Studdert DM. Strategies and practices in off-label marketing of pharmaceuticals: a retrospective analysis of whistleblower complaints. *PLoS Med* 2011;8(4):e1000431.

23. GlaxoSmithKline to plead guilty and pay \$3 billion to resolve fraud allegations and failure to report safety data. The United States Department of Justice <http://www.justice.gov/opa/pr/2012/July/12-civ-842.html>
24. Parry J. Head of GSK in China is replaced as details of fraud scandal emerge. *BMJ* (Clinical Research ed.). 2012;347:f4791–f4791.
25. Tanne JH. AstraZeneca pays \$520m fine for off-label marketing. *BMJ* 2010;340:c2380.
26. Radley DC, Finkelstein SN, Stafford RS. Off-label prescribing among office-based physicians. *Archives of Internal Medicine* 2006;166(9):1021.
27. Monasterio E, McKean A. Off-label use of atypical antipsychotic medications in Canterbury, New Zealand. *N Z Med J* 2011;124(1336):24–29. <http://journal.nzma.org.nz/journal/124-1336/4700/content.pdf>
28. Monasterio E, McKean A. Use of quetiapine in child and adolescent populations—Response to letter from Dr Lambe. *Australian and New Zealand Journal of Psychiatry* 2013;47(11):1084–1085.
29. Anon. Top 20 Global Therapeutic Products 2010, Total audited markets. Available from <http://www.imshealth.com> Accessed 16 August 2011.
30. Hitchings AW, Baker EH, Khong TK. Making medicines evergreen. *BMJ* 2012;345:e7941.
31. Kesselheim A S, Murtagh L, Mello MM. “Pay for delay” settlements of disputes over pharmaceutical patents. *New England Journal of Medicine* 2011;365(15):1439–1445. <http://www.nejm.org/doi/full/10.1056/NEJMhle1102235>
32. Hawkes N. AstraZeneca takes legal action to delay generic quetiapine in US. *BMJ* 2012;344:e2099.
33. Vernaz N, Haller G, Girardin F, et al. Patented drug extension strategies on healthcare spending: a cost-evaluation analysis. *PLoS Med* 2013;10(6):e1001460.