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## **Delving into the Fog of Ambiguity**

An Analysis of the Trans-Pacific Partnership's Data Exclusivity  
Provisions and their Implications for Access to Medicines in  
New Zealand

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## **Abstract**

The Trans-Pacific Partnership is a multilateral free-trade agreement, which New Zealand became a party to in 2016. The focus of this paper is to examine the inconsistencies that arise between the language of the TPP and New Zealand law, with respect to data exclusivity regimes. Compliance with the TPP seems to entail an extension to the terms of data exclusivity for both biologics and small-molecule pharmaceuticals. This may have the effect of impeding access to medicines by delaying the entry of competition into the market. In particular the underlying rationale behind the biologic data exclusivity provisions appears to be the protection of American corporate profits, rather than the stimulation of innovation or the long-term improvement on access to healthcare. As a result, these provisions are not in New Zealand's interest and if implemented into law they may be economically detrimental.

Key words: Trans-Pacific Partnership, Data Exclusivity, Biologics, Public Health, New Zealand

## I Introduction

The Trans-Pacific Partnership (TPP) was signed on 4 February 2016, following 6 years of negotiations.<sup>1</sup> Its twelve member nations from the Asia-Pacific region collectively produce 40% of global economic output, with a combined population of 800 million.<sup>2</sup> As a member New Zealand stands to benefit economically from this arrangement. Estimates by the Foreign Affairs, Defence and Trade Committee predict that by 2030 the TPP will add an additional \$2.7 billion a year to New Zealand's GDP.<sup>3</sup> New Zealand's entry into this free trade agreement has been further rationalised on the basis that opting out would put the country at a significant competitive disadvantage, particularly given the large quantity of exports New Zealand makes to TPP members.<sup>4</sup> The TPP however, has attracted substantial criticism. The negotiations have been shrouded in a veil of secrecy, providing limited opportunity for public input.<sup>5</sup> Moreover, the extensive involvement of multinational corporations has raised serious concerns, particularly in light of this secrecy and lack of public involvement.<sup>6</sup> These issues aside, the focus of this paper is to provide a close analysis of the TPP's data exclusivity provisions, and examine their implications within the New Zealand context.

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<sup>1</sup> Foreign Affairs, Defence and Trade Committee *International Treaty Examination of the Trans-Pacific Partnership Agreement* (4 May 2016) at 2.

<sup>2</sup> At 2.

<sup>3</sup> At 2.

<sup>4</sup> At 2.

<sup>5</sup> Trevor Timm "The TTIP and the TPP trade deals: enough of the secrecy" (4 May 2016) The Guardian <<https://www.theguardian.com/commentisfree/2016/may/04/ttip-tpp-trade-deals-secrecy-greenpeace-leak>>.

<sup>6</sup> Deborah Gleeson, Pat Neuwelt, Erik Monasterio and Ruth Lopert "How the Transnational Pharmaceutical Industry Pursues its Interests Through International Trade and Investment Agreements: A Case Study of the Trans Pacific Partnership" in Alice De Jonge and Roman Tomasic (eds) *Handbook of Research on Transnational Corporations* (Edward Elgar Publishing Ltd., 2015). (Forthcoming)

This paper will begin by outlining the role of data exclusivity and patents within the pharmaceutical industry. The next part will provide a breakdown on the relevant sections of the TPP, followed by an analysis of their potential implications on innovation and access to medicines in New Zealand. This will include a discussion on the interplay between intellectual property and the protein-based class of drugs known as biologics. The paper will then examine the consequences of the TPP's data exclusivity requirements in the biologics context. Lastly, there will be an analysis of the scope of the discretion conferred upon TPP members to relax intellectual property safeguards in order to protect public health.

In conclusion, it is submitted that the TPP requires increased data exclusivity periods. Moreover, these changes could have detrimental effects on access to medicines. Whether this is the case depends entirely on the interpretation taken by the New Zealand Government.

## **II Patents, Data Exclusivity and Regulatory Approval within the Pharmaceutical Industry**

It is common practice for pharmaceutical manufacturers to protect their inventions with patents. A patent allows its holder to exclude others from making or selling the patented pharmaceutical during the protected period,<sup>7</sup> which is 20 years in New Zealand.<sup>8</sup> The monopoly granted to patent holders can be described as providing an incentive for innovation.<sup>9</sup> Additionally, patent registration requires pharmaceutical companies to disclose information concerning the development of the relevant pharmaceutical.<sup>10</sup> This requirement

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<sup>7</sup> Patents Act 2013, s18.

<sup>8</sup> Section 20.

<sup>9</sup> Susy Frankel *Intellectual Property in New Zealand* (2nd ed, LexisNexis, 2011) at 391.

<sup>10</sup> Patents Act 2013, s39.

to disclose scientific information stimulates the dissemination of knowledge, from which the public can ultimately benefit.

Once the patent term has expired, competitors may enter the market and offer generic versions of the drug, which tend to be cheaper. A fundamental premise of our economic system is that “all elements of a bargain-quality, service, safety, and durability - and not just the immediate cost, are favourably affected by the free opportunity to select among alternative offers”.<sup>11</sup> In the New Zealand context, cheaper drug prices means that Pharmac, the government agency responsible for the funding of medicines, may be able to subsidise or fund new types of treatment, which were previously too expensive.

Before anyone can market a pharmaceutical however, regulatory approval is required to confirm that the product is safe and effective. In New Zealand, the regulatory body responsible for this function is Medsafe. For pioneer compounds a comprehensive analysis of drug safety and efficacy is required. The necessary clinical trials typically involve 3-4 phases of clinical testing. Phase I trials are usually carried out on a small sample of healthy volunteers to investigate the fundamental pharmacodynamic and pharmacokinetic parameters.<sup>12</sup> Phase II trials typically involve moderately sized sample groups, with tests aimed at generating preliminary efficacy and safety data.<sup>13</sup> Phase III trials involve a test of efficacy relative to a control or placebo drug on a large population.<sup>14</sup> Phase IV trials are generally of the nature of post-marketing monitoring and surveillance programmes.<sup>15</sup>

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<sup>11</sup> *National Society of Professional Engineers v United States* 435 US 679 (1978) at 695-696.

<sup>12</sup> Chris Frampton and Shaun Holt “Clinical Trials - An Overview” (27 June 2016) Health Quality and Safety Commission New Zealand <<https://www.hqsc.govt.nz/assets/Consumer-Engagement/Publications/Training-guide/019-clinical-trials-research-review.pdf>> at 2.

<sup>13</sup> At 2.

<sup>14</sup> At 2.

<sup>15</sup> At 2.

Conducting a full set of clinical trials can be extremely expensive.<sup>16</sup> However, where regulatory approval is sought for a generic form of an off-patent drug an abbreviated approval process is often available. In New Zealand the requirement for lengthy clinical trials can be bypassed if it is established that the generic drug is bioequivalent to a pioneer drug, which has been previously approved by Medsafe.<sup>17</sup> According to Medsafe two products are bioequivalent “when the bioavailabilities of two different formulations of the same pharmaceutical form and containing the same active ingredient are shown to be comparable after administration of the same dose.”<sup>18</sup> Bioavailability may be defined as “the rate and extent of absorption of the active ingredient in a medicine into systemic circulation.”<sup>19</sup> Under this approach, bioequivalence studies may be conducted instead of comprehensive clinical trials, allowing for cost savings.

Data exclusivity regulations prevent generic manufacturers from relying on the clinical data submitted by pioneer drug manufacturers, in order to obtain regulatory approval for their generic versions of the drug.<sup>20</sup> The current term of data exclusivity in New Zealand lasts five years from the date that the application for regulatory approval of the pioneer pharmaceutical was received.<sup>21</sup> During this period generic producers must conduct their own

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<sup>16</sup> Aylin Sertkaya, Hui-Hsing Wong, Amber Jessup and Trinidad Beleche “Key cost drivers of pharmaceutical clinical trials in the United States” 13 (2016) Clin Trials 137.

<sup>17</sup> Medsafe “Generic Medicines and Bioequivalence” (March 2013)  
<<http://www.medsafe.govt.nz/profs/PUArticles/Mar2013GenericMedBioequivalence.htm>>.

<sup>18</sup> Medsafe, New Zealand Ministry of Health “Guideline on the Regulation of Therapeutic Products in New Zealand, Bioequivalence of Medicines, Edition 2.0” (June 2015)  
<<http://www.medsafe.govt.nz/regulatory/Guideline/GRTPNZ/bioequivalence-of-medicines.pdf>> at 1.1.

<sup>19</sup> At 1.1.

<sup>20</sup> Jerome Reichman “Rethinking the Role of Clinical Trial Data in the International Intellectual Property Law: The Case for a Public Goods Approach” (2009) 13 Marq Intell Prop L Rev 1 at 4-5.

<sup>21</sup> Medicines Act 1981, s23B and s23A.

clinical trials in full if they wish to obtain regulatory approval. Since conducting clinical trials may not be economically feasible, data exclusivity can delay the entry of competition into the market.<sup>22</sup>

In some cases data exclusivity will have no practical effect. This because the data exclusivity period may run concurrently with the patent term, and thus generic versions of the patented drug cannot be marketed without infringing the patent. However, data exclusivity provides high commercial value where an inventor's patent becomes invalidated. Since data exclusivity is not affected by patent invalidation, it can still be an effective means of deterring the onset of competition in these situations.<sup>23</sup>

### **III Article 18.50 of The Trans-Pacific Partnership**

According to Article 18.50.1 (a) of the TPP:<sup>24</sup>

If a Party requires, as a condition for granting marketing approval for a new pharmaceutical product, the submission of undisclosed test or other data concerning the safety and efficacy of the product, that Party shall not permit third persons, without the consent of the person that previously submitted such information, to market the same or a similar product on the basis of: (i) that information; or (ii) the marketing approval granted to the person that submitted such information, *for at least five years from the date of marketing approval* of the new pharmaceutical product in the territory of the Party.

This restriction on the use of undisclosed test data in the regulatory approval process amounts to a requirement of five years' data exclusivity. In New Zealand the period of data exclusivity expires "on the date 5 years after the

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<sup>22</sup> Jerome Reichman, above n 20, at 4-5.

<sup>23</sup> At 5.

<sup>24</sup> Trans-Pacific Partnership Agreement (signed 4 February 2016). (emphasis added)

innovative medicine application to which that information relates is or was, as the case may be, received by the Minister.”<sup>25</sup> To ensure conformity with this article the Medicines Act may require amendment so that the data exclusivity period ends five years from the date that marketing approval is granted rather than five years from the date on which the application was received. This may result in a small extension to the data exclusivity period. For example, if three months lapsed between the date that the application was received and the date that approval was granted, then the five-year period of exclusivity would be longer by three months.

Article 18.50.1 (b) of the TPP ensures that a five-year term of data exclusivity would apply in respect of the use of overseas clinical data.<sup>26</sup> Medsafe allows an analysis of bioequivalence to be performed between a generic pharmaceutical and an innovator product obtained from an overseas market.<sup>27</sup> The proviso is that “the overseas sourced innovator product must be shown, using a series of in vitro tests, to be the same as the innovator product approved in New Zealand.”<sup>28</sup> In such cases, a five-year term of data exclusivity would have to apply from the date of marketing approval.

Article 18.50.2 (a) requires parties to:<sup>29</sup>

Apply paragraph 1, *mutatis mutandis*, for a period of at least three years with respect to new clinical information submitted as required in support of a marketing approval of a previously approved pharmaceutical product covering a new indication, new formulation or new method of administration...

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<sup>25</sup> The Medicines Act 1981, s23A.

<sup>26</sup> Trans-Pacific Partnership Agreement (signed 4 February 2016).

<sup>27</sup> Medsafe, above n 18, at 1.3.

<sup>28</sup> At 1.3.

<sup>29</sup> Trans-Pacific Partnership Agreement.

The Medicines Act limits the application of data exclusivity to “innovative medicine applications”.<sup>30</sup> This is defined as an application that refers to an active ingredient that has not previously been referred to in any other application.<sup>31</sup> In order to comply with its TPP obligations New Zealand would have to introduce three years’ data exclusivity in order to restrict the unauthorised use of undisclosed clinical information, which had previously been submitted in applications concerning new indications, formulations, or methods of administration of previously approved products. This three-year period would have to begin on the date that the marketing approval was granted.

The New Zealand market for pharmaceuticals is very small on the global scale.<sup>32</sup> Realistically, the length of data exclusivity in New Zealand is unlikely to affect investment in research overseas, and thus the availability of innovative pharmaceuticals in the future. However, extended terms of data exclusivity may delay or deter generics manufacturers from obtaining regulatory approval in New Zealand for their products. This could genuinely slow down the onset of competition within the New Zealand market, hindering the availability of cheaper drugs. The United States, with a substantial comparative advantage in

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<sup>30</sup> Medicines Act 1981, s23B.

<sup>31</sup> Section 23A.

<sup>32</sup> In 2012, the US, EU/EEA and Japan accounted for 85% of sales for the top 100 pharmaceuticals - see Evaluate Pharma “Pharmaceutical and Biotech Sales Analysis by Country - Top Drugs, Top Regions” (May, 2014) <<http://info.evaluategroup.com/rs/evaluatepharmaltd/images/EvaluatePharma%20-%20Pharmaceutical%20%26%20Biotech%20Sales%20Analysis%20by%20Country%20-%20Report.pdf>>. As of 1 Jan 2016 New Zealand had an estimated population of 4.51 million in 2014 compared with a global population of 7.3 billion in mid-2015 - see Statistics New Zealand “National Population Projections: 2014-2068” (28 November 2014) <[http://www.stats.govt.nz/browse\\_for\\_stats/population/estimates\\_and\\_projections/NationalPopulationProjections\\_HOTP2014.aspx](http://www.stats.govt.nz/browse_for_stats/population/estimates_and_projections/NationalPopulationProjections_HOTP2014.aspx)>. Also see - *World Population Prospects: The 2015 Revision, Key Findings and Advance Tables* (United Nations, Department of Economic and Social Affairs, Population Division, Working Paper No. ESA/P/WP.241, 2015) at 1.

pharmaceutical manufacture stands to benefit from protecting the profits of its pharmaceutical sector. However, as a country with a small pharmaceutical industry, which largely relies on overseas imports, it is not in New Zealand's interest to increase the term of data exclusivity.

Interestingly, the Select Committee on Foreign Affairs, Defence and Trade reports that ratification of the TPP will not require any changes to New Zealand laws in respect of the provisions discussed.<sup>33</sup> Their view is that the TPP data exclusivity obligations "can be met without changes to policy settings or practice".<sup>34</sup> However, it is difficult to see how this can be so when the TPP text is inconsistent with the Medicines Act and imposes new requirements. The Select Committee also reports that:<sup>35</sup>

The TPP would also require New Zealand to provide five years' data protection to new small molecule (but not biologic) pharmaceutical products that contain a both new and a previously approved active ingredient. This would not require a change to New Zealand law but entails a loss of policy flexibility in the future for small molecule pharmaceuticals.

This statement requires correction. In the case of applications for previously approved active ingredients, in other words applications for new uses or formulations, the term of data exclusivity imposed by the TPP is three, not five years. Moreover, a change in New Zealand law would be required to provide for this.

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<sup>33</sup> Foreign Affairs, Defence and Trade Committee, above n 1, at 79-80.

<sup>34</sup> At 79-80.

<sup>35</sup> At 79-80.

In the case of biologics, which will be discussed later, the Committee notes that TPP obligations can be “met by current New Zealand policy settings and practice.”<sup>36</sup> Again, there are issues with this.

The Select Committee’s views appear to be represented in the Trans-Pacific Partnership Agreement Amendment Bill - under which there are no proposed changes to New Zealand’s data exclusivity regime.<sup>37</sup> Again, this is surprising since the TPP’s data exclusivity provisions are inconsistent with New Zealand law, and the very purpose of this Bill is “to align New Zealand’s domestic law with certain obligations in the [TPP]”.<sup>38</sup> While this response, or lack thereof, may seem to nullify some of the concerns regarding enhanced intellectual property protection, it is somewhat baffling that the New Zealand Government would disregard its international commitments.

#### **IV Article 18.51 of The Trans-Pacific Partnership**

According to article 18.51, in the case of biologic medicines, members must comply with one of two options. The first option is to provide a term of data exclusivity of “at least eight years from the date of first marketing approval of that product”. The second option is to provide protection of clinical trial data for at least five years, along with other measures to “provide effective market protection” and “deliver a comparable outcome in the market”.<sup>39</sup>

Under the Medicines Act no distinction is drawn between the term of data exclusivity afforded to drugs based on whether they contain a biologic entity or not.<sup>40</sup> In order to determine whether the TPP provisions are consistent with

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<sup>36</sup> At 79-80.

<sup>37</sup> Trans-Pacific Partnership Agreement Amendment Bill 2016.

<sup>38</sup> Trans-Pacific Partnership Agreement Amendment Bill 2016.

<sup>39</sup> Trans-Pacific Partnership Agreement, art 18.51.

<sup>40</sup> An active ingredient is defined as including “chemical and biological entities”. Medicines Act 1981, s23A.

New Zealand law it is first necessary to identify the meaning of the second option.

*A The Meaning of the Language of Article 18.51*

While the language of the first option is clear, the language used in the second option is inherently vague. This ambiguity suggests that the text is accommodating two contrary points of view. In other words it seems likely that the matter was intentionally left ambiguous in order for the parties to conclude their negotiations despite having an unresolved conflict of opinion. This conclusion is supported by the fact that the United States has been clearly advocating for extended terms of data exclusivity for biologics.<sup>41</sup> In contrast, other parties have staunchly defended their views on the need for shorter terms, doing so even as the treaty negotiations approached their final stages.<sup>42</sup>

In interpreting the meaning of this language the New Zealand Select Committee on Foreign Affairs, Trade and Defence emphasised that the second option “must deliver a comparable outcome to the eight-year option.”<sup>43</sup> This seems consistent with the ordinary meaning of the language of the provision.<sup>44</sup> However, they then conclude that:<sup>45</sup>

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<sup>41</sup> “In TPP, U.S. Floats 12-year Data Period for Biologics, Flexibilities for Developing Countries” (27 November 2013) Inside U.S. Trade.

<sup>42</sup> The Australian Minister of Trade and Investment was reported on the 7th Nov 2015 as insisting that Australia had not moved “one iota” on the issue of data exclusivity for biologics and had protected the five-year rule. See “US senator’s claims Australia is being greedy over trade deal rejected” *The Guardian* (Online ed, 7 November 2015).

<sup>43</sup> Foreign Affairs, Defence and Trade Committee, above n 1, at 10.

<sup>44</sup> Such an interpretation is consistent with the rules of treaty interpretation under the Vienna Convention. See Vienna Convention on the Law of Treaties 1155 UNTS 331 (entered in force 27 January 1980), art 31.

<sup>45</sup> Foreign Affairs, Defence and Trade Committee, above n 1, at 79.

The second option can be met by current New Zealand policy settings and practice. New Zealand already provides five years' data protection for biologics. This, together with measures like patent protection for biologics and the time for Medsafe's regulatory approval process, as well as other market circumstances, provide effective market protection for biologics in New Zealand.

Although the data protection obligations in TPP would be new obligations for New Zealand, as they can be met without changes to policy settings or practice they will not result in any additional costs for consumers or the medicines budget.

In examining the meaning of the second option, the words "comparable outcome" read in light of the provision as a whole can be understood as a reference to the protection offered by the eight-year term. Thus, the language of the second option indicates that some form of action with the effect of preventing, or deterring biosimilar market entry for a period of eight years is required. This could be achieved for example by having five years of data exclusivity, with the addition of three years of market exclusivity. However it is unrealistic to say that biologics will not require any further protection than that provided by the current five-year term.

In response to the Select Committee's points, patents will not suffice as an additional protective measure if there is no valid patent in place. Likewise, where Medsafe's regulatory approval period is less than three years, the associated delays alone will not constitute comparable protection. For example, take a biologic drug that is not patented, where the regulatory approval process takes one year. If the term of data exclusivity lasted five years from the date that the drug was approved, then this would all add up to six years of protection, but not eight. So the measures proposed by the Select Committee would not be sufficient to ensure a comparable outcome in such a situation.

It may be that other member nations will accept New Zealand's interpretation of the TPP. However, one commentator has raised concerns that:<sup>46</sup>

The legal language provides room for the United States to continue to pressure the other TPP countries to ensure that they keep biosimilars... off the market for eight years, in order to provide equivalent "effective market protection" and a "comparable outcome" to eight years of data protection.

### *B Other Relevant TPP Clauses*

A biologic is defined in the TPP as "a product that is, or, alternatively, contains, a protein produced using biotechnology processes, for use in human beings for the prevention, treatment, or cure of a disease or condition."<sup>47</sup> This wide definition has been described as constraining Government discretion.<sup>48</sup> However, the language also provides some degree of flexibility since parties are not obliged to apply this provision to biologic products which are not protein based, or to protein based drugs that are created strictly via chemical synthesis.

Article 18.51.3 also provides that the "parties shall consult after 10 years from the date of entry into force of this Agreement, or as otherwise decided by the Commission, to review the period of exclusivity." Concerns have been raised that "this could result in countries being pressured to provide market exclusivity for more products, or to lengthen the period of protection."<sup>49</sup>

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<sup>46</sup> Deborah Gleeson "Submission to the Productivity Commission Inquiry into Australia's Intellectual Property Arrangements, The Trans Pacific Partnership Agreement, Intellectual Property and Access to Affordable Medicines" at 7.

<sup>47</sup> Trans-Pacific Partnership, art 18.51.2.

<sup>48</sup> Deborah Gleeson, above n 46, at 7.

<sup>49</sup> At 7.

## V Should Biologics Have a Longer Data Exclusivity Term?

### A *Small-Molecule Pharmaceuticals versus Biologics*

Traditional chemical drugs consist of a homogeneous array of small-molecules, with well-defined physical structures, usually manufactured in the laboratory.<sup>50</sup> Such products embody the stereotypical representation of pharmaceuticals. In comparison, biologic drugs are generally composed of larger molecules, usually complex proteins, which are produced via biotechnological processes.<sup>51</sup> They may consist of a heterogeneous mixture of proteins. This is typically the case if they have been derived from rDNA.<sup>52</sup> Although the degree of complexity and size may vary substantially, biologics, as their name suggests, can be differentiated by their biologic origin.<sup>53</sup> Such drugs are produced within cells, often through the use of rDNA methods, and then extracted and purified.<sup>54</sup> The figure below provides a comparison of size and complexity between caffeine, a small-molecule drug with 24 atoms, and human growth hormone, a relatively small biologic protein hormone, but still one with over 3000 atoms.<sup>55</sup>

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<sup>50</sup> Vincent Roth “Will FDA Data Exclusivity Make Biologic Patents Passé?” (2013) 29 Santa Clara Computer & High Tech L J 249 at 255.

<sup>51</sup> Carolyn Castagna “Therapeutic Monoclonal Antibodies: The Dilemma of Delivering Affordable Biologics to Patients While Delivering Continuing to Incentivise Innovation” (2009) 82 Temple L Rev 1071 at 1072-1073.

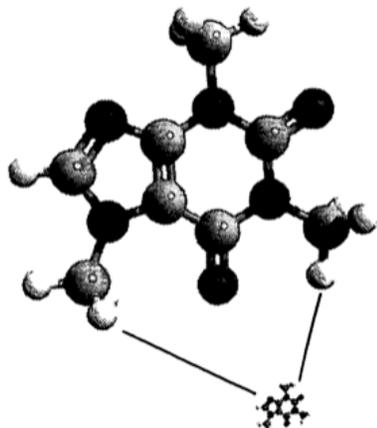
<sup>52</sup> BIO, “The Trans-Pacific Partnership and Innovation in the Bioeconomy: The Need for 12 Years of Data Protection for Biologics”  
<[https://www.bio.org/sites/default/files/files/TPP%20White%20Paper%20\\_2\\_.pdf](https://www.bio.org/sites/default/files/files/TPP%20White%20Paper%20_2_.pdf)> at 8.

<sup>53</sup> Carolyn Castagna, above n 51, at 1072.

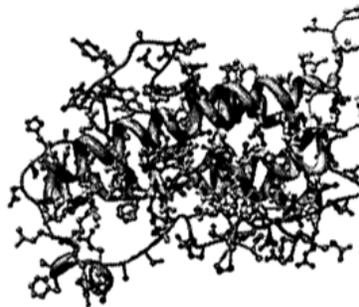
<sup>54</sup> At 1072.

<sup>55</sup> Image sourced from - Vincent Roth, above n 50, at 255.

**Figure 1. Caffeine (generic)**



**Figure 2. Human Growth Hormone (biologic)**



Biologic production techniques tend to be vastly more expensive than those used to produce small-molecule chemical drugs.<sup>56</sup> These expenses are reflected in the higher prices of biologics. Treatment costs in some cases can soar as high as \$500,000 USD per year.<sup>57</sup> Despite these sometimes staggering prices, the biologic market is experiencing massive growth. The industry began with the discovery of rDNA techniques in 1973, with the first biologic drug, recombinant human insulin gaining FDA approval in 1982.<sup>58</sup> By 2012 biologics represented 20% of all drugs on the US market and in 2011 alone the US drug development pipeline contained around 900 new biologics.<sup>59</sup> Early biologics were used to treat protein deficiencies and included proteins such as insulin for the treatment of diabetes and clotting factors for the treatment of

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<sup>56</sup> At 255.

<sup>57</sup> One of the most expensive small-molecule drugs for arthritis costs around \$300, while treatment for arthritis with the biologic Enbrel costs around \$20,000 a year. Avastin a treatment for colon cancer costs around \$100,000 a year while Cerezyme a biologic treatment for Gaucher disease costs between \$200,000 and \$500,000 a year. (All prices in USD). See Karen Tumulty & Michael Scherer “How Drug-Industry Lobbyists Won on Health Care” (Oct. 22, 2009) <<http://www.time.com/time/magazine/article/0,9171,1931729,00.html>>.

<sup>58</sup> Vincent Roth, above n 50, at 254.

<sup>59</sup> At 254.

haemophilia.<sup>60</sup> Monoclonal antibodies are a particularly new and innovative class of biologics. These are man-made antibodies, which are designed to target bacteria, viruses and cancerous cells.<sup>61</sup> Monoclonal antibodies present exciting possibilities to treat a wide range of conditions.<sup>62</sup> As has been illustrated, biologic treatments bring us right to the frontiers of modern medicine, but this comes at often exorbitant prices.<sup>63</sup>

### *B Generics versus Biosimilars*

In the case of small-molecule pharmaceuticals, the entry of generic manufacturers into the market after patent expiry increases competition, which drives prices down.<sup>64</sup> These generics are identical copies of the pioneer pharmaceuticals.<sup>65</sup> They can be produced by competitors through chemical synthesis, and analytical tests can be conducted to verify that the active ingredients are identical to those in the pioneer drug.<sup>66</sup> In terms of regulatory

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<sup>60</sup> Linfong Tzeng “Follow-On Biologics, Data Exclusivity, and the FDA” (2010) 25 Berkeley Tech L J 135 at 136.

<sup>61</sup> Key functions of antibodies include the neutralisation of bacterial toxins, the opsonisation of pathogens which thereby facilitates their ingestion and destruction by macrophages, and the activation of complement, a key response of the immune system. See Kenneth M. Murphy *Janeway’s Immunobiology* (8th ed, Garland Science, Taylor & Francis Group, LLC, New York, 2012) at figure 1.25.

<sup>62</sup> Carolyn Castagna, above n 51, at 1076.

<sup>63</sup> Karen Tumulty & Michael Scherer, above n 57.

<sup>64</sup> Competition within small-molecule pharmaceutical markets has been reported as driving down prices by as much as 80% in the 24 months following patent expiry. See Ernst Berndt and Murray Aitken “Brand Loyalty, Generic Entry and Price Competition in Pharmaceuticals in the Quarter Century After the 1984 Waxman-Hatch Legislation” (October 2010) NBER Working Papers <<http://www.nber.org/papers/w16431.pdf>> at 19.

<sup>65</sup> This is essentially a requirement for regulatory approval under the generics pathway. “A generic medicine contains the same active ingredient (including different salts), in the same quantity as an innovator medicine.” See Medsafe, above n 17.

<sup>66</sup> Benjamin Deadman, Mark Hopkin, Ian Baxendale and Steven Ley “The synthesis of Bcr-Abl inhibiting anticancer pharmaceutical agents imatinib, nilotinib and dasatinib” (2013) 11

approval, once it has been established that both drugs contain identical active ingredients it can be assumed that they will have the same pharmacological effect.<sup>67</sup> In such a situation, after data exclusivity periods expire, generic manufacturers can take advantage of an abbreviated regulatory approval process and need only establish bioequivalence between the generic and the pioneer drug.<sup>68</sup>

Biosimilars can be thought of as generic versions of biologic drugs. However, there are key differences. Biologic production leads to unpredictability in the final structure of the biologic.<sup>69</sup> This is because biologics are highly sensitive to their manufacturing process.<sup>70</sup> Indeed, proteins produced via biotechnological methods are so sensitive to changes in the manufacturing process that the FDA will often require new evidence of safety whenever a biologics manufacturer changes an aspect of their manufacture process.<sup>71</sup> Moreover, due to the size and complexity of biologics it may be impossible to fully elucidate all the discrete structural differences between the biologic and the biosimilar.<sup>72</sup> Modern scientific techniques allow for the determination of recombinant protein amino acid sequences.<sup>73</sup> However it is much more difficult to analyse other aspects of a protein's structure - the process "is fraught with uncertainties that increase with the size and complexity of the

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Org Biomol Chem 1766. The authors discuss the various synthetic pathways, which have been developed for synthesising a selection of Bcr-Abl tyrosine kinase inhibitors used in the treatment of chronic myelogenous leukemia.

<sup>67</sup> BIO, above n 52, at 8.

<sup>68</sup> Medsafe, above n 17.

<sup>69</sup> Linfong Tzeng, above 60, at 138.

<sup>70</sup> Vincent Roth, above 50, at 275.

<sup>71</sup> BIO, above n 52, at 9.

<sup>72</sup> Linfong Tzeng, above n 60, at 139.

<sup>73</sup> Medsafe, New Zealand Ministry of Health "Medsafe position on biosimilar medicines" <<http://www.medsafe.govt.nz/profs/RIss/Medsafe%20position%20on%20biosimilars.pdf>> at 1.

protein itself.”<sup>74</sup> This means that biosimilar manufacturers may not know whether their product is identical to the reference biologic.

This presents serious issues from a regulatory perspective. Even the most subtle differences between biologics can lead to variations in safety and efficacy parameters. For example, biologic drugs have the potential to elicit immune responses, where the body generates anti-drug antibodies (ADA) against the biologic drug.<sup>75</sup> This can result in serious clinical consequences.<sup>76</sup> Sometimes the ADA will neutralise biologic drugs by binding to specific sites, thus making the treatment less effective.<sup>77</sup> Grave concerns also arise where the body’s ADA neutralise endogenous counterparts of the biologic.<sup>78</sup> Such “neutralizing ADA that are cross-reactive with the endogenous protein can cause significant safety concerns because they inhibit the inherent physiological pathway and can lead to a deficiency syndrome.”<sup>79</sup>

For example when Johnson & Johnson commenced a new manufacture process for erythropoietin it did not expect to alter the biologic’s clinical performance. However, Johnson & Johnson’s Eprex triggered adverse immunological responses in some patients, and ultimately several died after developing pure red cell aplasia.<sup>80</sup>

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<sup>74</sup> At 1.

<sup>75</sup> Gopi Shankar, Elizabeth Shores, Carrie Wagner and Anthony Mire-Sluis “Scientific and regulatory considerations on the immunogenicity of biologics” (2006) 24 Trends Biotechnol 274 at 274.

<sup>76</sup> At 274.

<sup>77</sup> At 274.

<sup>78</sup> At 274.

<sup>79</sup> At 274.

<sup>80</sup> Bryan Liang, Timothy Mackey “Emerging patient safety issues under health care reform: follow-on biologics and immunogenicity” (2011) 7 Ther Clin Risk Manag 489 at 490. BIO “Why Is Patient Safety a Concern in the Biosimilars Debate?” (27 June 2016) <<http://www.bio.org/articles/why-patient-safety-concern-biosimilars-debate>>.

The very premise of generic approval is that products with the same active ingredients are the same, so there is no need to replicate clinical data.<sup>81</sup> This theory starts to break down where the biosimilar is merely similar, or cannot be proved to be the same. In light of this Medsafe has stated that a mere demonstration of bioequivalence will not suffice for the regulatory approval of a biosimilar.<sup>82</sup> Instead Medsafe applies an approach based on the clinical comparability of the two pharmaceuticals, which requires clinical and non-clinical studies.<sup>83</sup> In particular the immunogenicity of a biosimilar must be thoroughly investigated and applicants must submit risk management plans, which may include post-marketing safety monitoring.<sup>84</sup> An abridged evaluation procedure is still offered, but evidently the regulatory approval process will be more costly and time consuming.<sup>85</sup> As an example of a comparative approach taken overseas, the FDA explains that: “a biological product may be demonstrated to be ‘biosimilar’ if data shows that the product is ‘highly similar’ to the reference product notwithstanding minor differences in clinically inactive components and there are no clinically meaningful differences between the biological product and the reference product in terms of safety, purity and potency.”<sup>86</sup> Interestingly, despite the availability of this approval pathway, biosimilar manufacturers have encountered roadblocks in bringing their products to the United States market. As of 23 July 2016, the

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<sup>81</sup> BIO, above n 52, at 9.

<sup>82</sup> Medsafe, above n 73, at 1.

<sup>83</sup> At 1.

<sup>84</sup> At 3.

<sup>85</sup> At 1-4.

<sup>86</sup> Food and Drug Administration, U.S. Department of Health and Human Services

“Implementation of the Biologics Price Competition and Innovation Act of 2009”

<<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/ucm215089.htm>>.

FDA had only approved two drugs under the biosimilar pathway, only one of them being commercially available.<sup>87</sup>

### *C Do Biologic Pioneers Need More Intellectual Property Protection?*

In light of the changes outlined in the TPP, it is worth considering the underlying rationale behind the provisions. Firstly, it can be argued that biologic patents are more difficult to enforce and thus are weaker. Therefore increased data exclusivity terms may be necessary to compensate for this deficiency. Let's assume that a pharmaceutical company is trying to enforce their patent. If the patented compound is a small-molecule it may be easier to show that a competitor's drug contains the identical compound and thus establish infringement of the patent.<sup>88</sup> However, two functionally similar biologics may vary structurally and exhibit different properties solely due to differences in the manufacturing processes.<sup>89</sup> In such cases a patent may not extend to cover structural variants of the protein, and can be designed around.<sup>90</sup> As the Biotechnology Industry Organisation points out:<sup>91</sup>

An inventor may have generated experimental evidence showing a protein with a particular sequence exhibits properties that make the protein useful. However, the inventor may not have tested variants of that protein. Without experimental data proving those variants also share the

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<sup>87</sup> Emma Court "These drugs could cut American health costs by \$250 billion (if only we could take them)" (25 July 2016) MarketWatch <<http://www.marketwatch.com/story/these-new-drugs-might-never-get-a-chance-to-save-the-us-250-billion-2016-07-20>>.

<sup>88</sup> When the active ingredient of a drug is a small-molecule tests can be conducted to conclusively establish that the two compounds are identical. For example, basic spectroscopic analysis by NMR (nuclear magnetic resonance spectroscopy) or IR (infra-red spectroscopy) should allow the two compounds to be differentiated within the lab.

<sup>89</sup> Vincent Roth, above 50, at 275.

<sup>90</sup> BIO, above n 52, at 17.

<sup>91</sup> At 17.

essential properties as the tested protein, a patent examiner usually will not grant the inventor rights extending to those variants.

For these reasons small-molecule drug patents might offer better protection, simply because they are easier to enforce. It has also been suggested that a biosimilar could be sufficiently similar to the pioneer biologic that their manufacturers could exploit the benefits of accelerated approval pathways but still avoid patent infringement due to structural differences.<sup>92</sup>

However, these claims do not go uncontested. The United States Federal Trade Commission holds the view that patent protection for biologics is adequate, particularly given the multitude of patents that may be in force at any given time:<sup>93</sup>

Pioneer biologics are capable of being covered by numerous and varied patents, including manufacturing and technology platform patents. There is no evidence that patents claiming a biologic drug product have been, or are likely to be, designed around more frequently than those claiming small-molecule products.

A second argument which has been run is that the majority of biotech companies, in the United States market at least, are small start-ups which are dependent on private capital.<sup>94</sup> On this basis, the prospect of strong intellectual property protection is necessary to stimulate private investment in these

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<sup>92</sup> Vincent Roth, above n 50, at 276.

<sup>93</sup> Pamela Jones Harbour, “Follow-On Biologic Drug Competition: A Report by the Federal Trade Commission” (11 June 2009) United States of America Federal Trade Commission <[https://www.ftc.gov/sites/default/files/documents/public\\_statements/follow-biologic-drug-competition-report-federal-trade-commission/090611fobspeech.pdf](https://www.ftc.gov/sites/default/files/documents/public_statements/follow-biologic-drug-competition-report-federal-trade-commission/090611fobspeech.pdf)> at 8.

<sup>94</sup> Vincent Roth, above n 50, at 285. BIO, above n 52, at 12.

companies.<sup>95</sup> In contrast traditional pharmaceutical companies have been described as “large, publicly traded companies that are capable of financing their own research and development without resorting to outside sources of capital.”<sup>96</sup> However, the position is not quite so clear-cut. In reality, many of the big players which dominate the pharmaceutical industry also manufacture and invest in biologics. In 2012 for example, it was reported that “40% of all biotech products in clinical development were being developed by big pharma”.<sup>97</sup> It is misleading to consider the two markets in isolation.

A third line of argument is that increased protection is necessary due to the particularly high development costs and risks of failure associated with biologics.<sup>98</sup> Moreover, the few successful products created need to be sufficiently protected so that the developers can make enough profits to off-set the losses from their less successful endeavours.<sup>99</sup> The central premise of these arguments is that there are insufficient incentives for innovation within this field.

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<sup>95</sup> Stuart Graham & Ted Sichelman “Patenting by High Technology Entrepreneurs” Shubha Ghosh and Robin Malloy (eds) *Creativity, Law and Entrepreneurship* (Edward Elgar, 2011) at 170-172.

<sup>96</sup> BIO, above n 52, at 12.

<sup>97</sup> Emily Waltz “It's official: biologics are pharma's darlings” (2014) 32 *Nature Biotechnol* 117.

<sup>98</sup> One study estimated the pre-approval costs of developing a biologic to be around \$1.2 billion USD. See Joseph DiMasi & Henry Grabowski, “The Costs of Biopharmaceutical R&D: Is Biotech Different?” (2007) 28 *Manage Decis Econ* 469.

Another study put the cost at \$1.9 billion USD. See Erik Palmer “Conquering the complexities of biologics to get to biosimilars” (26 March 2013) *Fierce Pharma Manufacturing* <<http://www.fiercepharma.com/regulatory/conquering-complexities-of-biologics-to-get-to-biosimilars>>. Biologics have also been estimated to have a higher risk of failure in phase 3 clinical trials than their small-molecule counterparts. See Henry Grabowski “Data Exclusivity for New Biological Entities” (June 2007)

<<http://www.econ.duke.edu/Paper/PDF/DataExclusivityWorkingPapers.pdf>> (working paper, on file with Duke Univ. Dept. Econ.).

<sup>99</sup> BIO, above n 52, at 12.

However, this proposition does not seem well founded. The biologics market is highly lucrative and is experiencing massive growth. As of February 2015 two of the market leaders PDL BioPharma Inc. and Gilead Sciences Inc. had net income margins over the last 12 months of 55.44% and 48.62% respectively, and Gilead Sciences' revenue, increased by 222% in 2014 alone to reach a mammoth \$24.89 billion USD.<sup>100</sup> In 2011 alone, global sales for the biologics Remicade and Avastin totalled \$7.19 billion and \$5.98 billion USD respectively.<sup>101</sup> In 2010, in the United States, combined sales of the top 12 biologic products was around \$30 billion.<sup>102</sup> In the same year global sales of biologics amounted to \$157 billion.<sup>103</sup> The Nasdaq Biotechnology Index has risen 227% from the end of 2011 until Feb 2015, compared with a 91% rise in the Nasdaq Composite Index.<sup>104</sup> This indicates substantial growth in biotechnology relative to other industries. Moreover, "while global spending on all medicines grew 24 percent from 2007 to 2012, spending on biologics grew 367 percent during the same period."<sup>105</sup> If there is anyone we should be concerned about, it is the patients themselves. While the market is flourishing, healthcare systems are burdened with massive costs. In 2013, the average daily cost of a biologic in the United States was \$45 compared with \$2 for small-molecule drugs.<sup>106</sup>

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<sup>100</sup> Philip van Doorn "These are the most profitable Nasdaq biotech companies" MarketWatch (2 March 2015) <<http://www.marketwatch.com/story/these-are-the-most-profitable-nasdaq-biotech-companies-2015-02-27>>.

<sup>101</sup> Erwin Blackstone and Joseph Fuhr "The Economics of Biosimilars" (2013) 6 Am Health Drug Benefits 469 at 469.

<sup>102</sup> Andrew Bourgojn "What You Need to Know About the Follow-On Biologic Market in the U.S.: Implications, Strategies, and Impact" (January 2011) <<http://thomsonreuters.com/content/dam/openweb/documents/pdf/pharma-life-sciences/white-paper/newport-biologics.pdf>>.

<sup>103</sup> Erwin Blackstone and Joseph Fuhr, above n 101, at 473.

<sup>104</sup> Philip van Doorn, above n 100.

<sup>105</sup> Foreign Affairs, Defence and Trade Committee, above n 1, at 10.

<sup>106</sup> Erwin Blackstone and Joseph Fuhr, above n 101, at 469.

In any case it is hard to see how a mere five year term of data exclusivity for biologics in New Zealand would chill innovation in biotechnology overseas, particularly given the growth of the biologics market, its lucrative nature and the fact that the New Zealand market is relatively small.

Another point is that the more complex biosimilar regulatory approval process means that manufacturers will probably incur relatively greater upfront costs in bringing their products to the market.<sup>107</sup> Patients suffering from serious diseases may also be reluctant to participate in clinical trials when there is a chance that the biosimilar will not be effective. Rather, it is in their interest to opt for a course of treatment with the approved pioneer biologic.<sup>108</sup> These factors collectively constitute a significant barrier to market entry for competitors in the biologics arena.

Additionally, where biologic manufacturers do not disclose their manufacturing process, this presents a strong impediment to biosimilar market entry. As one commentator has noted:<sup>109</sup>

[The non-disclosure of manufacturing process information] has not been an issue in the small-molecule, chemical world. Because of the simplicity of their molecular structures, different manufacturing processes can still arrive at an identical compound, thus achieving structural identity. However, because of the size and complexity involved with biologics, not knowing how the product is made is an impediment in developing a biosimilar.

The presence of these market barriers dilutes the strength of the arguments made for extending biologic data exclusivity periods.

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<sup>107</sup> BIO, above n 52, at 9.

<sup>108</sup> Erwin Blackstone and Joseph Fuhr, above n 101, at 472.

<sup>109</sup> Vincent Roth, above n 50, at 289.

Furthermore, data exclusivity has been described as providing an incentive for pharmaceutical companies to invest in the research required to establish the safety and efficacy of a drug.<sup>110</sup> The argument here seems to be that without such protection firms would lack the incentives to seek regulatory approval, since they could instead use the data obtained by competitors and cut costs in the development process. This reasoning seems somewhat flawed since pharmaceutical companies have no choice but to obtain regulatory approval if they want to market their drugs and make any kind of profit at all. Every kind of incentive exists for manufacturers to get their drugs approved as quickly as possible. At any rate, biosimilar manufacturers, even under an accelerated approval pathway, will probably have to generate large amounts of safety and efficacy data. They should still derive some benefit from having access to existing clinical data. However, the argument that longer data exclusivity periods are required for biologics than for small-molecule drugs does not seem persuasive, since generics manufacturers should be able to “free-ride” to a much greater extent on existing clinical data than biosimilar manufacturers.

One might even go further and suggest that biologics manufacturers should have less protection, since this would facilitate the entry of competition into the market. This argument is particularly relevant in the New Zealand context, where biologic drugs can be very expensive.<sup>111</sup>

Additionally, intellectual property protections for pharmaceutical products have been becoming increasingly comprehensive over the years, as the United States secures various TRIPS plus agreements.<sup>112</sup> “With each new success, the

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<sup>110</sup> Kristina Lybecker “When Patents Aren’t Enough: Why Biologics Necessitate Data Exclusivity Protection” (2013-14) 40 Wm Mitchell L Rev 1427 at 1428. BIO, above n 52, at 3.

<sup>111</sup> In 2014, the biologic Humira was the most expensive drug funded by Pharmac, at \$62.2 million. See Radio New Zealand “Massive savings claimed by drugs agency” (12 December 2014) <<http://www.radionz.co.nz/news/national/261585/massive-savings-claimed-by-drugs-agency>>.

<sup>112</sup> Carsten Fink & Patrick Reichenmiller “Tightening TRIPS: The Intellectual Property Provisions of Recent US Free Trade Agreements” (7 February 2005) The World Bank Group

pharmaceutical companies' demands have become more audacious.”<sup>113</sup> Therefore we must consider the arguments mounted by pharmaceutical companies and industry lobby groups with some scepticism, since they have an incentive to protect the profits of their industry. In light of the arguments presented for both sides it does not seem that the case for extended periods of exclusivity for biologics has been made out.

*D In Any Case is Data Exclusivity an Appropriate Means of Compensating for the Alleged Deficiencies in the Patent System?*

Data exclusivity automatically applies upon regulatory approval. No application is required.<sup>114</sup> Patents however, require their holder to make an application and engage in costly litigation to safeguard their rights.<sup>115</sup> A system where data exclusivity provides a substitute for some forms of intellectual property protection may reduce wasted expenditure on litigation and applications. If biologics manufacturers come to rely on extended terms of data exclusivity rather than patents they will not have to incur these expenses. Such savings could theoretically be re-diverted towards innovation.

Unfortunately, these benefits come at a price. Data exclusivity forces competitors wishing to obtain regulatory approval during the relevant period to carry out all their own clinical trials, rather than follow an abbreviated approval pathway. This is a gross waste of resources. Moreover, serious ethical concerns are raised by unnecessarily experimenting on humans and animals.<sup>116</sup> Clinical testing involves using a control group of sick patients, some of whom will

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<<http://documents.worldbank.org/curated/en/173901468140377145/pdf/321110TradeNote20.pdf>>.

<sup>113</sup> Jerome Reichman, above n 20, at 7-8.

<sup>114</sup> Vincent Roth, above n 50, at 281.

<sup>115</sup> In 2000, \$4 billion alone was spent on patent litigation in the US - at 281.

<sup>116</sup> Clinical trials involve the ascertainment of drug therapeutic indexes and immunogenicity properties. Patients may be exposed to some risk while these parameters are being investigated.

receive a control instead of vital lifesaving treatment.<sup>117</sup> While these ethical concerns could be reduced by using a proven treatment as the control for the clinical stages, this adds further cost.

There is an argument that data exclusivity encourages pharmaceutical companies to “conduct more and better trials than they otherwise would be inclined to do.”<sup>118</sup> However, it seems questionable whether repeating clinical trials would yield a higher probability of new discoveries, compared with the probability of innovation resulting from diverting those same resources towards a project of one’s choice.

Patent law on the other hand has the advantage of incentivising the disclosure of information, which enhances the public domain and allows competitors to build on the efforts of others to design even better innovations.<sup>119</sup> Data exclusivity has the opposite effect, hindering the dissemination of knowledge during the period of exclusivity.<sup>120</sup> Thus, as a matter of principle the extension of data exclusivity regimes should not be encouraged to compensate for deficiencies in the patent system where and when they arise. A system of data exclusivity replaces patents with secrets and undermines the social contract

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<sup>117</sup> Chris Frampton and Shaun Holt, above n 12.

<sup>118</sup> Rebecca Eisenberg “The Role Of The FDA In Innovation Policy” 13 (2007) *Mich Telecomm & Tech L Rev* 345 at 366-87.

<sup>119</sup> See the judgment of Justice Story in *Pennock v Dialogue* 27 US 1 (1829): “While one great object [of patents is], by holding out a reasonable reward to inventors and giving them an exclusive right to their inventions for a limited period, to stimulate the efforts of genius, the main object was ‘to promote the progress of Science and useful Arts,’ and this could be done best, by giving the public at large a right to make, construct, use, and vend the thing invented, at as early a period as possible, having a due regard to the rights of the inventor.”

<sup>120</sup> In order to take advantage of data exclusivity the test data must be undisclosed. If the data has been publicly disclosed then the protection conferred by data exclusivity becomes redundant.

foundation for patent law.<sup>121</sup> If the protection offered by patents is deemed insufficient for whatever reason, it is better to strengthen that protection.

*E Will an Increased Term of Data Exclusivity for Biologics Impact Patients?*

It has been argued that “the generic drug business model is largely inapplicable to biosimilars.”<sup>122</sup> This is because while generic small-molecule pharmaceuticals are relatively easy to manufacture, biosimilar manufacturers face massive barriers to market entry, which will deter the onset of competition, resulting in higher prices.<sup>123</sup> The biosimilar regulatory approval process is also much more complex, and the cost of biosimilar manufacturing facilities, can be in the order of several hundred million dollars.<sup>124</sup> One analyst has predicted the development of a typical biosimilar product to take 8-10 years at a cost of \$100-\$200 million USD.<sup>125</sup> In stark contrast the development of a small-molecule generic may only take 3-5 years, at a mere cost of \$1-5 million.<sup>126</sup> As a result when competitors enter the biologics market the cost savings to patients should be lower relative to those experienced in the small-molecule pharmaceutical market. Competitors simply cannot offer huge cost savings if they need to recoup the enormous expenses incurred in bringing their products to the market.

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<sup>121</sup> This point was developed in discussion with Professor Susy Frankel, Victoria University of Wellington, Faculty of Law.

<sup>122</sup> BIO, above n 52, at 10.

<sup>123</sup> At 9-10.

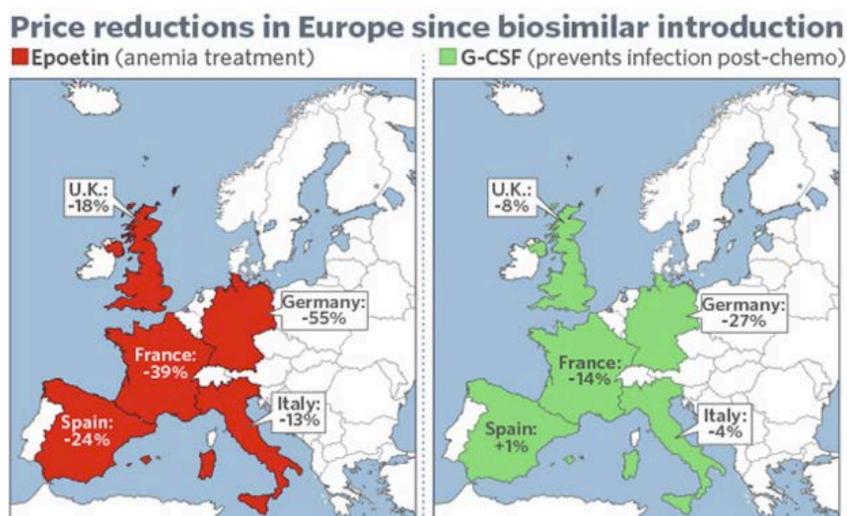
<sup>124</sup> At 9-10.

<sup>125</sup> Sumanth Kambhammettu “The European Biosimilars Market: Trends and Key Success Factors” (27 October 2008), <at <http://www.obbec.com/specialreports/20-biopharmaceuticals/2152-the-european-biosimilars-market-trends-and-key-success-factors>>.

<sup>126</sup> Senate Committee on Health, Education, Labor, and Pensions “Congressional Budget Office Cost Estimate, Biologics Price Competition and Innovation Act of 2007” (25 June 2008) <<http://www.cbo.gov/ftpdocs/94xx/doc9496/s1695.pdf>>.

Despite this negative outlook, significant cost reductions have resulted from the approval of some biosimilars in Europe. The onset of biosimilar competition for erythropoietin, used to regulate the production of red blood cells, saw prices fall by 36% in Austria, 81% in Croatia, 55% in Germany and 13% in Sweden.<sup>127</sup> Likewise, biosimilar production of granulocyte colony-stimulating factor, used to accelerate recovery from neutropenia in some cancer patients, resulted in price decreases of 79% in Bulgaria, 22% in France, 50% in Norway and 40% in Sweden.<sup>128</sup> The figure below illustrates some of the price reductions resulting from biosimilar market entry in Europe.

**Figure 3. Biosimilar Price Reductions in Europe<sup>129</sup>**



<sup>127</sup> IMS Institute for Healthcare Informatics “Assessing Biosimilar Uptake and Competition in European Markets” (October 2014)

[http://www.imshealth.com:90/files/web/IMSH%20Institute/Healthcare%20Briefs/Assessing\\_biosimilar\\_uptake\\_and\\_competition\\_in\\_European\\_markets.pdf](http://www.imshealth.com:90/files/web/IMSH%20Institute/Healthcare%20Briefs/Assessing_biosimilar_uptake_and_competition_in_European_markets.pdf) at 19.

<sup>128</sup> At 19.

<sup>129</sup> Sourced from Emma Court, above n 87.

An overall analysis of the literature shows that estimates of cost savings from competition in the American and European biologic markets range from 10-50%.<sup>130</sup> Another estimate comes from Professor Grabowski, who states that biosimiliars have offered discounts of 25 percent or more in Europe.”<sup>131</sup> In general however, these price reductions are not as significant as those observed in small-molecule markets.<sup>132</sup> However, when a medication costs millions per year to fund, even a small percent decrease in its price is substantial.

Additionally, even when biosimilars do reach the market, doctors may be reluctant to accept them as substitutes.<sup>133</sup> The risks of adverse immunological consequences probably play a part in these decisions.<sup>134</sup> Thus, biosimilars may take time to gain acceptance, further delaying the onset of effective competition.

This said, the availability of biosimilars has had a positive effect on increasing access to medicines in New Zealand. The first biosimilar to be accepted in New Zealand was Zarzio, in 2012. This is a medication designed to boost leukocyte

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<sup>130</sup> Andrew Mulcahy, Zachary Predmore and Soeren Mattke “The Cost Savings Potential of Biosimilars in the United States” (2014) Rand Corporation  
<[https://www.rand.org/content/dam/rand/pubs/perspectives/PE100/PE127/RAND\\_PE127.pdf](https://www.rand.org/content/dam/rand/pubs/perspectives/PE100/PE127/RAND_PE127.pdf)>  
at 4.

<sup>131</sup> Henry Grabowski, Rahul Guha and Maria Salgado “Biosimilar Competition: Lessons from Europe” (2014) 13 Nat Rev Drug Discov 99 at 99-100.

<sup>132</sup> Competition within small-molecule pharmaceutical markets has been reported as driving down prices by as much as 80% in the 24 months following patent expiry. See Ernst Berndt and Murray Aitken, above n 64, at 19.

<sup>133</sup> “Pharmaceuticals, Going Large” The Economist (3 January 2015)  
<<http://www.economist.com/news/business/21637387-wave-new-medicines-known-biologics-will-be-good-drugmakers-may-not-be-so-good>>.

<sup>134</sup> Federal Trade Commission “Emerging Healthcare Issues: Follow-On Biologic Drug Competition” (June 2009)  
<<https://www.ftc.gov/sites/default/files/documents/reports/emerging-health-care-issues-follow-biologic-drug-competition-federal-trade-commission-report/p083901biologicsreport.pdf>>.

cell counts in patients undergoing chemotherapy. According to Pharmac, the effect of competition was obvious. Pharmac was able to take advantage of cost savings and provide wider access to the drug.<sup>135</sup> Likewise, in 2014, once biosimilar versions of infliximab became available overseas, Pharmac was able to use its enhanced bargaining power to negotiate a 30% price reduction with the supplier of the original biologic.<sup>136</sup> This is significant given that current spending on this drug is \$15 million a year and growing rapidly.<sup>137</sup>

Against this background we can see how extending the period of data exclusivity for biologics could help delay the onset of competition. These costs would be passed on to Pharmac, and the New Zealand taxpayer. Ultimately, delaying the onset of competition will compromise Pharmac's ability to fund medicines for the treatment of those in need.

Enhanced intellectual property protections for biologics is beneficial to the United States economy since they have a strong comparative advantage in this field.<sup>138</sup> There is also substantial biologics innovation taking place in the European Union, and to a lesser extent in Japan.<sup>139</sup> However, since New

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<sup>135</sup> Pharmac "Biosimilar filgrastim, More for less– the biosimilar filgrastim story" (10 December 2015) <<https://www.pharmac.govt.nz/about/annual-review/2014/biosimilar-filgrastim/>>.

<sup>136</sup> Infliximab is used to treat rheumatoid arthritis, inflammatory bowel diseases, and psoriasis. See Pharmac "Pharmac secures significant savings for DHBs on biologic drug" (4 December 2014) <<https://www.pharmac.govt.nz/news/media-2014-12-04-infliximab-savings/>>.

<sup>137</sup> Pharmac, above n 136.

<sup>138</sup> China Association of Enterprises with Foreign Investment R&D-based Pharmaceutical Association Committee in coordination with the Biotechnology Industry Organisation and the support of the Boston Consulting Group "Building a World-Class Innovative Therapeutic Biologics Industry in China" <[https://www.bio.org/sites/default/files/files/BIO\\_RDAC\\_Biologics\\_White\\_Paper\\_Jan\\_2013.pdf](https://www.bio.org/sites/default/files/files/BIO_RDAC_Biologics_White_Paper_Jan_2013.pdf)> at 8-9.

<sup>139</sup> In 2010 all 31 top biologic products with sales over \$1 billion were developed in the US and Europe. At 8.

Zealand is dependent on the imports of biologics from overseas this means that the harmful effects on access to medicines cannot be rationalised under the guise of protecting New Zealand innovators. The real reason for the TPP's data exclusivity provisions is to extend and protect the profits of United States pharmaceutical companies.

## **VI Article 18.50.3 of The Trans-Pacific Partnership**

### *A Interpretation of Article 18.50.3*

Article 18.50.3 holds that notwithstanding articles 18.50.1, 18.50.2 and 18.51 (Biologics) "a Party may take measures to protect public health in accordance" with the Doha Declaration.<sup>140</sup> This prompts the question, what can TPP members actually do to protect public health? In answering this question we can examine whether New Zealand's current exemptions to regulatory data protection under section 23C of the Medicines Act are consistent with the TPP. The two key issues that arise in this interpretation process are the meaning of "measures" and the meaning of "public health".

In interpreting any international treaty, it is appropriate to have reference to the customary rules of interpretation of international law as codified in the Vienna Convention on the Law of Treaties.<sup>141</sup> This treaty holds that:<sup>142</sup>

A treaty shall be interpreted in good faith in accordance with the ordinary meaning to be given to the terms of the treaty in their context and in light of its object and purpose.

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<sup>140</sup> Trans-Pacific Partnership Agreement (signed 4 February 2016), art 18.50.3.

<sup>141</sup> Susy Frankel and Daniel Gervais "Plain Packaging and the Interpretation of the TRIPS Agreement" 46 (2013) Vand J Transnatl L 1149 at 1166.

<sup>142</sup> Vienna Convention on the Law of Treaties, above n 44, art 31.1.

## *B The Meaning of “Public Health”*

The process of interpretation in accordance with the Vienna Convention logically begins with the plain meaning in its context.<sup>143</sup> In order to ascertain the plain or ordinary meaning of “public health” reference can be made to the dictionary.<sup>144</sup> Public health is defined by the Oxford English Dictionary as “the health of the population as a whole, especially as monitored, regulated, and promoted by the state.”<sup>145</sup> It is also defined the World Health Organisation as “all organized measures (whether public or private) to prevent disease, promote health, and prolong life among the population as a whole.”<sup>146</sup>

These definitions are silent on the issue of how serious a matter must be before it concerns the health of the “population as a whole” as opposed to that of the individual or a group of individuals. At this stage it is appropriate to refer to the context and purpose of the treaty. As Frankel and Gervais note: “The structure of Article 31.1 [of the Vienna Convention] is precisely that the context and object and purpose of the treaty are part of the ordinary meaning exercise.” Rather than changing the ordinary meaning, context and purpose “are tools to locate or discern the ordinary meaning and inform proper interpretation.”<sup>147</sup>

Looking at the TPP, we can find a further reference to public health in article 18.6.1, which holds, *inter alia*, that:<sup>148</sup>

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<sup>143</sup> Susy Frankel “WTO Application of “the Customary Rules of Interpretation of Public International Law” to Intellectual Property” 46 (2006) Va J Int’l L 365 at 386.

<sup>144</sup> Susy Frankel and Daniel Gervais, above n 141, at 1172. The authors refer to the dictionary as part of the process of ascertaining the ordinary meaning of the text.

<sup>145</sup> Oxford English Dictionary (3rd Edition)

<<http://www.oed.com/view/Entry/239546?redirectedFrom=public+health#eid>>.

<sup>146</sup> Capital Area Public Health Network “What is Public Health”

<<http://www.capitalareaphn.org/about/what-is-public-health>>.

<sup>147</sup> Susy Frankel and Daniel Gervais, above n 141, at 1169-1170.

<sup>148</sup> Trans-Pacific Partnership Agreement (signed 4 February 2016).

[T]he Parties affirm that this Chapter can and should be interpreted and implemented in a manner supportive of each Party's right to protect public health and, in particular, to promote access to medicines for all. Each Party has the right to determine what constitutes a national emergency or other circumstances of extreme urgency, it being understood that public health crises, including those relating to HIV/AIDS, tuberculosis, malaria and other epidemics, can represent a national emergency or other circumstances of extreme urgency.

The language of this provision seems to indicate that it was intended to offer interpretive guidance in interpreting subsequent "public health provisions". It is at the start of the chapter, and it provides interpretive guidance. Thus it is appropriate to refer to this section as part of the wider context.<sup>149</sup> Within this section the words "public health" are followed by references to "national emergencies" and "circumstances of extreme urgency". The use of these words colours the meaning of "public health" in a restrictive fashion, such that it may be understood to refer to situations of widespread and serious public health issues, such as epidemics, but perhaps not serious obscure diseases or conditions, and certainly not common ailments.

In terms of the object and purpose of the provisions at issue, the references within articles 18.6.1 and 18.50.3 make it clear that consistency with the Doha Declaration on TRIPS and Public Health is one of the underlying purposes behind article 18.50.3. Thus the Doha Declaration itself should form an integral part of the interpretive background, against which the words "public health" must be understood. The Doha Declaration begins with the words:<sup>150</sup>

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<sup>149</sup> This approach is in accordance with the Vienna Convention. See Vienna Convention on the Law of Treaties, above n 44, art 31.1.

<sup>150</sup> Doha WTO Ministerial 2001: Declaration on the TRIPS Agreement and Public Health, WT/MIN(01)/DEC/2 (adopted 14 November 2001), art 1.

We recognize the gravity of the public health problems afflicting many developing and least developed countries, especially those resulting from HIV/AIDS, tuberculosis, malaria and other epidemics.

Here “public health” is used in the context of references to epidemics affecting developing countries. This suggests that one purpose of the provision at issue is to allow developing countries to facilitate access to medicines in order to manage epidemics. To ensure consistency with this purpose “public health” should certainly include health issues that affect a large portion of the public, such that they could be classified as a matter of widespread concern.

However, while “public health” should be read as including epidemics, it should also be open to member nations to define public health issues more widely, if their governments see it fit to do so. This is because the Doha Declaration also provides that “each member has the right to determine what constitutes a national emergency or other circumstances of extreme urgency.”<sup>151</sup>

What this suggests is that a purpose of the Doha Declaration is to ensure that TRIPS members have the individual autonomy to determine what health matters are sufficiently serious that measures can be taken to protect public health, at the expense of intellectual property rights.<sup>152</sup>

The only way to give effect to this purpose would be to interpret the meaning of “public health” widely and generously so that members have the discretion to take measures to protect “public health” where appropriate. This conclusion is supported by reference to the TRIPS document itself.

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<sup>151</sup> Article 5(c).

<sup>152</sup> Such measures could include granting compulsory licenses, even though this would undermine intellectual property rights.

The reason we can refer to TRIPS itself is because the TPP provides that members “may take measures to protect public health in accordance with: (a) the Declaration on TRIPS and Public Health”.<sup>153</sup>

The Doha Declaration in turn provides that:

In applying the customary rules of interpretation of public international law, each provision of the TRIPS Agreement shall be read in the light of the object and purpose of the Agreement as expressed, in particular, in its objectives and principles.<sup>154</sup>

Accordingly, the interpreter can refer directly to the principles and objectives of TRIPS in interpreting the words “public health” since these references make it clear that the principles and objectives of TRIPS form part of the wider interpretive context.

The principles of TRIPS are referred to in article 8, which provides that:

“Members may, in formulating or amending their laws and regulations, adopt measures necessary to protect public health and nutrition...”<sup>155</sup>

“Public health” read in this context is not coloured in any restrictive manner. In fact, the open-textured nature of this provision confers a wide discretion upon members in their interpretation of the language. This reasoning supports the conclusion reached above.

### *C The Meaning of “Measures”*

If we begin this analysis by reading the word “measures” in its wider context, the words “a Party may take measures to protect public health in accordance

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<sup>153</sup> Trans-Pacific Partnership Agreement, art 18.50.3.

<sup>154</sup> Doha Declaration, above n 150, art 5(a).

<sup>155</sup> Agreement on Trade-Related Aspects of Intellectual Property Rights 1869 UNTS 299 (signed 15 April 1994, entered in force 1 January 1995), art 8.

with the Doha Declaration” immediately prompt one to include the text of the Doha Declaration as part of the interpretive background.<sup>156</sup>

The Doha Declaration in turn provides that “each member has the right to grant compulsory licences and the freedom to determine the grounds upon which such licences are granted.”<sup>157</sup> If we read the word “measures” in light of this background it can be logically understood as referring to actions with a similar effect, in terms of their ability to alleviate any public health issues which are exacerbated by the protection of intellectual property rights. On this basis, measures with a similar effect to compulsory licenses should be available in the context of data exclusivity regimes.

Compulsory licenses may be granted by governments to allow generic manufacturers to produce on-patent drugs without being in breach of patent.<sup>158</sup> An equivalent measure in the data exclusivity context would be for governments to give specific competitors a license to use regulatory approval data. This would have the effect of encouraging the onset of competition. This interpretation does not necessarily mean that the measures available are limited to the issuance of licenses. This is just one option that would seem to be available.

#### *D Section 23C of the Medicines Act and Article 18.50.3*

Overall, it seems that the New Zealand Government would have the discretion to provide competitors with a license to use the inventor’s regulatory approval data in order to more easily obtain marketing approval for their generic or biosimilar versions of a drug. The New Zealand Government should also be

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<sup>156</sup> Trans-Pacific Partnership Agreement, art 18.50.3.

<sup>157</sup> Doha Declaration, above n 150, art 5(b).

<sup>158</sup> World Trade Organisation “Compulsory licensing of pharmaceuticals and TRIPS” (2006)

<[https://www.wto.org/english/tratop\\_e/trips\\_e/public\\_health\\_faq\\_e.htm](https://www.wto.org/english/tratop_e/trips_e/public_health_faq_e.htm)>.

afforded a certain degree of discretion in determining when article 18.50.3 is engaged.

Under the Medicines Act confidential supporting information may be used without consent, for the purpose of determining whether to grant an application for a pharmaceutical “if that disclosure or use is, in the opinion of the Minister, necessary to protect the health or safety of members of the public”.<sup>159</sup> This discretion granted under the Medicines Act is consistent with the requirements imposed by the TPP, provided that the discretion is exercised reasonably.

## **VII Article 18.54 of The Trans-Pacific Partnership**

This article provides that data exclusivity provisions will still have effect if they continue to be in force after the term of the patent has expired.<sup>160</sup> This provision simply ensures that the practical purpose of data exclusivity is not circumvented, since it is in such cases where the relevant patent has expired that data exclusivity has its true commercial value.

## **VIII Conclusion**

The continued supply of new generic and biosimilar pharmaceuticals into the New Zealand market should allow Pharmac to facilitate wider access to life savings treatments. However, the language of the TPP imposes an extension on the terms of data exclusivity for both biologics and small-molecule pharmaceuticals. These provisions have the potential to impede access to medicines by delaying the entry of competition into the market. In particular, the true rationale behind the biologics provisions appears to be the protection of American corporate profits, rather than the stimulation of innovation.

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<sup>159</sup> Medicines Act 1981, s23C(1)(a)(ii).

<sup>160</sup> Trans-Pacific Partnership Agreement, art 18.54.

Clearly, these provisions are not in New Zealand's interest as a net importer of pharmaceuticals. However, the extent of the harm is somewhat mitigated by article 18.50.3 which would allow the Minister of Health some discretion to issue compulsory licenses for the use of protected clinical trial data. Moreover, despite the stark inconsistencies between the language of the TPP and New Zealand law, the Select Committee on Foreign Affairs, Defence and Trade, has underplayed the significance of the imminent changes. Thus, it remains to be seen whether the TPP provisions will actually become incorporated into New Zealand law, or whether they will stand as a relic of American corporate interests.

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