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Productivity Commission
Level 12, 530 Collins Street
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Dear Dr King,

Draft Mental Health Report

Thank you for the opportunity to contribute in some manner to the Productivity Commissions Mental Health report.

This submission is very intentionally addressed to you, Dr King, as you have expertise in competition economics, regulation and extensive knowledge of the pharmaceutical regulatory environment in Australia.

My key concerns pertain to the draft recommendations made in relation to interventions in early childhood and school. More specifically given our current legislative and regulatory environment I have grave concerns that market forces are such that patient safety will be compromised when it comes to this particular patient group.

The intersection of my professional and personal life over the last decade has afforded me a particularly unique perspective on this matter.

Professionally speaking, whilst I have no mental health training or expertise, I am an economist by training and have been fortunate to work for many years for a global pharmaceutical company alongside a very talented public affairs team.

Personally speaking, my younger sister passed away three years ago; she was 23 years old and died unexpectedly while in the care of a Mental Health Intensive Care Unit in Sydney¹. Of particular note and relevance to your Mental Health Report is that my younger sister commenced on 'early intervention' treatment when she was 12 years old.

It is this particular intersection between my professional and personal life that sparked my curiosity into the **existing legislative and regulatory parameters as pertaining to the registration, marketing and distribution of prescription antipsychotic and mood disorder medicines to adolescents in Australia.**

The following submission aims to provide you with an outline of the key relevant findings I have made to date regarding this matter.

¹ The cause of death was subject to a coronial inquest.

1. A case study in early intervention

As previously mentioned, my sister was 12 years old when a well known and respected clinical psychiatrist expressed to my parents that the 'latest research' showed that if we preventatively medicate children who have a family history of bipolar it can prevent them from developing the illness or prevent them from developing it in a more severe form later on in life. Further, it would help them stay in school; manage their relationships better and when the time comes hold down meaningful employment.

Dr [redacted] outlined that if we were to miss this crucial window of opportunity, life outcomes may not be so optimistic for my sister.

Dr [redacted] commenced the early intervention treatment. My sister was placed on the mood stabiliser (Lithium) and the antipsychotic Olanzapine (Zyprexa).

2. An absence of clinical evidence

In late 2019 in preparation for the coronial inquest into my sister's death² I had the opportunity to spend some time delving into matters concerning my sister's care that had puzzled me for several years.

One of the first things I stumbled upon was a peer reviewed journal article that had been published in late 2017 by Dr Isheetta Zalpuri and Dr Manpreet Singh.

The paper was titled "*Treatment of psychiatric symptoms among offspring of parents with bipolar disorder*"³.

Their paper, published in the Journal of Current Treatment Options in Psychiatry, evaluated recently published literature relevant to the treatment of psychiatric symptoms in high-risk offspring of parents with Bipolar Disorder. I was rather taken by the title as this was what Dr [redacted] had described my sister as, a 'high-risk offspring'.

The abstract summarized the findings as follows:

"Non-pharmacological treatment options including psychotherapy, resilience promotion through good sleep, diet, and exercise hygiene, and omega-3 fatty acid supplementation are important first line interventions for high-risk offspring.

There has been some success in treating this population with open-label trials with mood stabilisers and antipsychotics; however, these results have not been replicated in randomised controlled trials."

It was only after reading this journal article that I realised Dr [redacted] had failed to inform my parents that the medical regime that she had strongly recommended and then prescribed for my sister had never been proven to be effective in a clinical trial⁴.

² The matters outlined in this submission were outside the scope of the coronial inquest.

³ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5831272/>

⁴ Further to this, in examining the TGA's Product Information statement for Olanzapine I discovered that the safety and efficacy of Olanzapine has not been established in patients under 18 years of age. The TGA Product Information statement for Lithium indicated that it had been shown to be safe and effective in children over the age of 12.

While information asymmetry between consumers and providers is to be expected in the delivery of healthcare, I am yet to be convinced the broader Australian community would deem this degree of information asymmetry appropriate.

I am incredibly proud of the work I contributed to while working for the Australian pharmaceutical industry, however reading this journal article puzzled me greatly as to how it was possible for a physician in Australia to prescribe such aggressive preventative treatment to an adolescent in the absence of demonstrated efficacy.

3. The difference between ‘research evidence’ and demonstrated efficacy

The phrase *‘the research has shown’* as used by Dr [redacted], implies the presence of evidence.

To a general member of the public who has limited medical knowledge, the assumption is that this *‘research evidence’*, is evidence that would be deemed vital and necessary for a medical intervention to be administered.

The vast majority of Australians when seeing their GP or any medical specialist assume that the relevant Government agencies have approved the medicine that is being prescribed to them, that this medicine is not only safe but has been proven to be effective in scientifically rigorous clinical trials.

Having worked within the healthcare sector, I am now aware of several nuances that as a general member of the public I had no knowledge of. I now realise that this widely held and very much justified assumption about the safety and efficacy of a medicine is incomplete as health practitioners are able to prescribe ‘off label’, or open label⁵ as referred to in Dr Zalpuri and Dr Singh’s paper which I quoted on the precious page.

It is this practice of ‘off label’ prescribing that concerns me greatly when reading the draft recommendations made in the Mental Health report.

3.1 TGA approval, indications and off label prescribing

In order to adequately express my concerns with the draft recommendations made in relation to interventions in early childhood and school, it is necessary that I first provide a basic understanding of what TGA approval and the practice of off label prescribing mean. I have outlined this for the benefit of those who may be reading this submission who may not be familiar with these terms and systems.

3.1.1. TGA Approval for Prescription Medicines

The Therapeutic Goods Administration (TGA) is a division of the Australian Department of Health and Ageing which was established in 1989 as the main Australian Government entity responsible for ensuring that medicines and medical devices used by Australian consumers are evaluated and regulated before they reach the market and monitored once they are in use.

Prescription medicines are thoroughly evaluated before they are included on the Australian Register of Therapeutic Goods (ARTG). Any application for registration of a new active substance (i.e. medicine), must be supported by extensive information about the synthesis of the substance, the method of manufacture of the dose forms, studies of its pharmacology and toxicology in animals and clinical trials in humans demonstrating the efficacy and safety of the product in its proposed use.

⁵ Open label is the US term for ‘off label’ in the Australian market.

The lawful supply of any therapeutic good in Australia requires that the product is included on the ARTG.

Here however are nuances I, as the average Australian prior to my industry experience was naive to.

Drug manufactures make significant investments not only in the research and development of products but also in running clinical trials in order to get their product registered on the ARTG. Clinical trials are often run for multiple indications⁶ and can be run across multiple age groups.

Clinical trials may fail in one patient population but not another, or they may fail for one indication but not another, in such instances the company would submit the successful clinical trial data to the TGA. For instance say Drug X failed in the adolescent trial but had demonstrated efficacy in the adult population, you would therefore submit for registration on the ARTG for the adult indication of Drug X.

3.1.2 Off label prescribing

Off label prescribing occurs when a drug is prescribed for an indication, a route of administration, or a patient group that is not included in the TGA's Product Information (PI) statement for that drug.

Following on from the example provided above. Drug X is registered on the ARTG and as such is lawfully able to be supplied and prescribed in Australia. While Drug X is registered on the ARTG for a very specific indication, let's say for adults diagnosed with bipolar, our current regulatory and legislative parameters are such that should a prescriber deem it to be in the best interest of their patient, then they are lawfully able to prescribe Drug X to patients outside the registered indication, say adolescents that are considered to be at 'high risk' of developing bipolar.

3.2 'Research evidence' and the role of academics and key opinion leader in prescribing practices

The phrase *'the research has shown'* as used by my sister's treating psychiatrist Dr [redacted] was, I now realise, in reference to academic papers that had been published and presented at conferences in relation to off label trials of mood stabilisers and antipsychotics in an adolescent population.

During my undergraduate studies my perception was that peer reviewed academic papers were pure, untainted, where the research topics were driven by the interests and expertise of the best and brightest minds in society and that their findings were what propelled science, policy and legislations forward. While there is still much truth in that, having worked for one of the largest global pharmaceutical companies I am now acutely aware of how idealistic that understanding was.

In recent years some prominent academic journals have deemed it a requirement of their authors to disclose potential conflicts of interest. While this is very much encouraging to see, there is still a long way to go. More troubling however is that there are large sections of the medical prescribing community that are unaware of the relationship between industry and academic peer reviewed journal articles. As such when prescribers are quoted evidence from a published study they may not be aware, have the time or have been informed to do their due diligence and investigate any potential conflicts of interest about the information they are basing their prescribing practices on.

⁶ An 'indication' for a drug refers to the use of that drug for treating a particular disease. For example, diabetes is an indication for insulin. Another way saying this is that insulin is indicated for the treatment of diabetes.

While working in industry, we referred to academics we worked with as 'Key Opinion Leaders' or KOL's for short. Dr Joseph Biederman, a Harvard world-renowned child psychiatrist known for his advocacy of 'pediatric bipolar disorder' is one such KOL.

I highly recommend you, Dr King and any one else who may be reading this submission become familiar with Dr Joseph Biederman's work with Johnson and Johnson.

My objective with this submission is to provide you with a map, a skeleton outline of the general legislative and regulatory landscape of prescribing practices but more specifically to draw your attention to its present limitations to safeguard patients, particularly the adolescent populations.

The scope and nature of Dr Joseph Biederman's work with Johnson and Johnson will provide you with the nuanced details of how this all plays out in practice.

I strongly urge you to refer to Gardiner Harris's work with The New York Times⁷ but more importantly make the time to dutifully examine the work of lawyer and investigative journalist, Steven Brills⁸, who has written a meticulously researched piece concerning Johnson & Johnson's efforts to market the antipsychotic Risperdal off label, that is, without authorisation from the FDA, to seniors with dementia and children with pediatric bipolar disorder. Of particular note is Chapter 3 in which he details the significance of Dr Biederman's academic contributions.

While this example is of a US based KOL, it is important to keep in mind that Australian prescribers can receive their 'education' about new research and prescribing practices by attending conferences and that these conferences are not just based in Australia with Australian speakers and as such a KOL from a prestigious university in the US has the potential to influence prescribing practices here in Australia.

As you read Gardiner Harris and more importantly Steven Brills work, please have one question in the back of your mind:

Have there been any significant regulatory or legislative changes made to the registration, marketing or distribution of prescription medicines that would prevent similar events from occurring again, both in the US or in the Australian market?

The Australian TGA and the US FDA are very much independent and are able to make their own rulings on what medicines are registered in the market. However the legislated practice of off label prescribing both in the US and Australia creates avenues for collaboration between global marketing divisions within large commercial enterprises and as such it may be naive to assume that the Australian subsidiary of a global enterprise would be engaging in marketing practices that would be drastically different to those of its global headquarters.

For the safety of all Australian children present and future, I can't stress enough how critical it is that you review Steven Brills work prior to finalising the draft recommendations particularly those in relation to interventions in early childhood and school.

4. This is not about 'Big Bad Pharma'

As I have mentioned previously I not only worked alongside a talented team in the public affairs department of a large global pharmaceutical company but I am also incredibly proud of the work I contributed to during that time. While I have stepped out of industry for the present moment I have

⁷ Gardiner Harris, New York Times: Research Centre Tied to Drug Company
<https://www.nytimes.com/2008/11/25/health/25psych.html>

⁸ Steven Brills, Huffington Post: America's Most Admired Lawbreaker
<https://highline.huffingtonpost.com/miracleindustry/americas-most-admired-lawbreaker/chapter-3.html>

not ruled out stepping back into a role where I would be able to once again contribute to an industry who's work and contributions to society I am proud of.

The sentiment that industry is simply "big bad pharma" is not one that I am comfortable with.

I have faith in the people I worked with both within the pharmaceutical company I worked for and those I worked with across the industry. I have faith in their integrity and in the general intent of the sector as a whole.

The industry has understood for a long time that in order to keep moving forward we need to get comfortable with some uncomfortable truths about our actions and as such proactively problem solve a constructive way forward and the industry has done so many times through the continued update of its Code of Conduct⁹.

The industry is full of bright, brilliant and passionate people who want to do good. The pharmaceutical sector plays a vital and necessary role in society, without it's investments and innovations my husband would be blind and would have missed bearing witness to his two children growing up.

Innovation in healthcare requires substantial capital outlay and investment, which comes with great risk. No Government is prepared to spend billions of dollars in research and development without a guaranteed substantial positive outcome for their population. So our best model for innovation in healthcare at present is the commercial enterprise model.

As uncomfortable as that may be, at the end of the day that is what pharmaceutical companies are - commercial enterprises. They do not invest in these medical advances purely because it's a good thing to do, they pick the disease areas they invest in based on the burden of disease on a population, the larger the numbers of people who suffer from this condition the larger the potential market and therefore profit to be made.

Is there something wrong with that? No, I don't believe so. If we could come up with a better model for innovation in healthcare we would, but at present the commercial enterprise model is what we have, so it's what we have to work with.

It may be uncomfortable to admit but it's market forces and profits that have often been the engine room that has driven the most extraordinary advances in healthcare. Bearing this in mind, we need to be cognisant that these market forces are such that profits guide industry's actions and government legislation and regulation is an essential element in augmenting the commercial enterprise model so that patient safety rather than profits drive behavior.

5. The role of Health Consumer Organisations and Professional Prescriber Bodies

The key objective of the role I held within industry was to shape and influence government policy to ensure patients had appropriate access to our medicines.

In addition to the national policy work I contributed to, I also engaged with stakeholders other than government more specifically academics, health consumer organisations¹⁰ and prescriber professional bodies¹¹. While my work with these organisations was very minimal relative to my

⁹ <https://medicinesaustralia.com.au/code-of-conduct/code-of-conduct-current-edition/>

¹⁰ Health Consumer Organisations are not-for-profit organisations that represent the interests and views of consumers of healthcare

¹¹ These are professional bodies that represent health practitioner that are able to prescribe prescription medicines to Australian consumers

other obligations it was substantial enough for me to have a sufficient understanding of what rules and regulations governed the manner of our engagement.

The pharmaceutical industry is, as many would expect incredibly well resourced and mobilised both globally and locally to lobby government in shaping the policy landscape, however in my opinion and experience to date Australian Government agencies like the Therapeutic Goods Administration and the Department of Health are very much aware of this, they hold industry at an appropriate arms-length and very much push back, keeping industry accountable.

However, I cannot say the same of the close relationship between academia and the prescriber professional bodies that the industry strategically engages with. The rules of engagement with these stakeholders are such that there is significant scope for patient safety to be compromised.

Given this industry knowledge, in preparation for the coronial inquiry into my sister's death I was curious to examine The Royal Australian and New Zealand College of Psychiatrist's (RANZCP) Clinical Guidelines for Mood Disorders.

Below are a few of my findings that I urge you Dr King, to keep in mind when finalising the recommendations for the Productivity Commissions Mental Health report.

5.1 RANZCP Clinical Practice Guidelines for Mood Disorders¹²

On page 5-6 of the guidelines there is a fascinating discussion on "*Methodological Considerations*". I recognise that I am not a trained medical professional, however my undergraduate and postgraduate training in pharmacoeconomics have afforded me some understanding of clinical trial design and as such there are several comments made in those paragraphs that concerned me greatly. I would be interested to hear how medical specialists outside the field of psychiatry would interpret such remarks.

For example on page 6 of the guidelines the following statement is made:

"Methodological issues in clinical trials may result in 'failed trials' i.e. trials which do not show a difference between the effects of a drug and placebo despite one existing. This is probably a common reason for evidence not being available despite the fact that there is a general clinical impression that certain medications are effective for particular conditions." Pg 5 RANZCP Clinical Practice Guidelines for Mood Disorders

Please note in particular the last line in that quote, "*a general clinical impression that certain medications are effective*".

In outlining the methodology used to develop the guidelines, the document explains that RANZCP called for expressions of interest from its members and appointed the Chair and the Mood Disorder Committee (MDC). The MDC consisted of Australian and New Zealand specialists from Psychiatry and Psychology with clinical and academic expertise in management of mood disorders. They went on to explain that the guideline makes two types of recommendations, first evidence-based recommendations (EBR's) and secondly consensus based recommendations (CBR's).

Dr King, I have to admit reading the following statement in those guidelines caught me by surprise and given my understanding of statistics and the scientific method I found it deeply disturbing.

"It is important to remember that absence of evidence is not evidence of absence, and so, given our understanding of the nature and optimal management of many

¹² https://www.ranzcp.org/files/resources/college_statements/clinician/cpg/mood-disorders-cpg.aspx

aspects of mood disorders is incomplete, a second type of recommendation was also employed. This was also derived through discussion and agreement within the MDC and termed a consensus-based recommendation (CBR)". Pg 4 RANZCP Clinical Practice Guidelines for Mood Disorders

I'm not sure that's how our Therapeutic Goods Regulator sees it when they are assessing medicines for their safe distribution to the Australian patient population. I know how much tension there was in our organisation as the US stock market and we anxiously waited for the results from a Phase 3 clinical trial. If that trial failed we knew no regulator in any market would approve its use and why should they, a failed trial means our product is no more effective than a placebo.

According to the statement above, a failed clinical trial in an adolescent population for instance, would be classified as an *'absence of evidence'*, however according to RANZCP guidelines that does not constitute *'evidence of absence'*, and so it is completely reasonable for the treatment to be prescribed to patients, because and I quote from page 5 of the guidelines *"there is a general clinical impression that certain medications are effective for particular conditions."*

I may be wrong but it appears to me that the TGA requires one standard of evidence and the RANZCP requires *"a general clinical impression that certain medications are effective for particular conditions"*.

Dr King, I'm not convinced that the broader medical community or the Australian public would deem this appropriate or safe.

Reading through the document I quickly realised that what the guidelines were talking about was off label prescribing. Yes, these medicines have in fact been registered on the ARTG but the MDC has *"a general clinical impression that certain medicines are effective for particular conditions"*, other than the indications registered on the ARTG.

A few paragraphs later, a section appears providing a definition and guidance on off label prescribing:

"In this guideline, some therapies identified as effective for the treatment of mood disorders on the basis of available evidence may have yet to receive approval for such use in Australia and/or New Zealand.

The use of such therapeutic agents outside their approved indication(s) is sometimes referred to as 'off label' use, and in practice this may impact eligibility for third-party payer subsidy. We recommend careful documentation supporting your clinical use of specific therapeutic agents over alternatives which are approved in your country. It is also recommended that this issue is explained to patients, including informing them that they may have to personally meet added costs due to lack of third-party payer subsidy."¹³

Dr King, as a member of the Review panel considering pharmacy remuneration and regulation, your understanding of PBS regulations I'm sure surpass mine. In which case, I'm confident the description the RANZCP mood disorder guidelines provide of off label prescribing would confuse you as much as it does me.

Let me be crystal clear for those who may not have the background knowledge you have. TGA approval and PBS subsidy are two totally different matters.

¹³ Please note this is the entirety of the entire discussion about off label prescribing as contained in the RANZCP mood disorder guidelines

TGA approval has to do with safety and efficacy of a medical product or device.

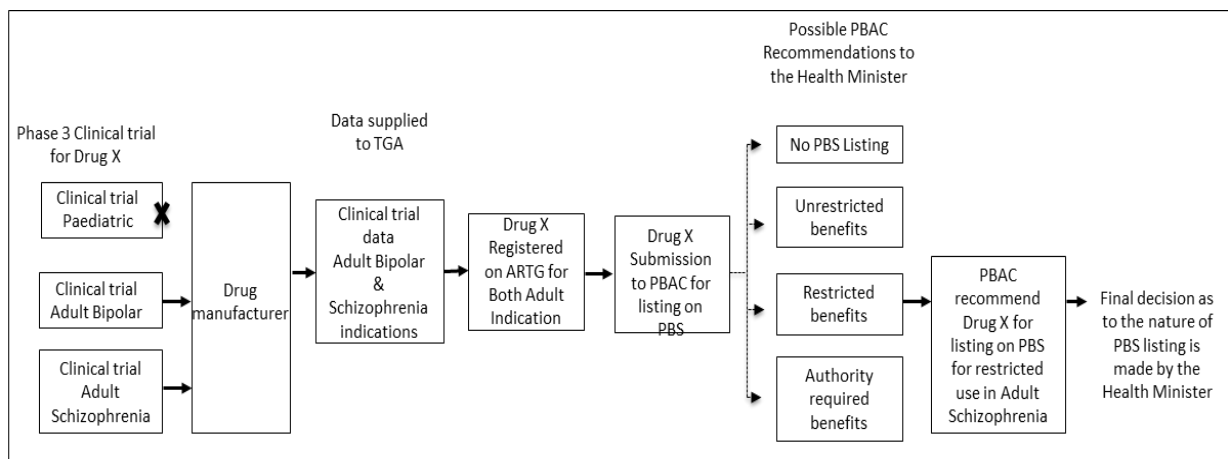
PBS listing has to do with whether the Australian government is prepared to subsidise the already demonstrated to be safe and clinically effective medicine.

The documentation and data pharmaceutical companies are required to submit to the TGA for registration on the ARTG and to the Pharmaceutical Benefits Advisory Committee (PBAC) for PBS listing are completely different in nature.

What I can only assume is that the RANZCP guidelines are referring to is an example where the drug has been listed on the PBS under 'restricted benefit'. That is to say, the drug is available for subsidy under a restricted indication, and the prescriber is prescribing it for an indication which is listed on the ARTG, one that has been deemed to be safe and effective but has not received PBS listing. This however does not constitute off label prescribing as the indication they are prescribing it for is already listed on the ARTG.

The diagram below aims to illustrate the misleading nature of the comments made in the RANZCP guidelines.

Figure 1: TGA approval and PBS process flow for Drug X



In Figure 1 above, Drug X failed in the Pediatric Phase 3 clinical trial, but was successful in both the Bipolar and Schizophrenia adult trials. The drug manufacturer supplies this data to the TGA, both indications are listed on the ARTG. The drug manufacturer then makes a submission to PBAC for PBS listing, however they receive a restricted benefit listing for the schizophrenia indication as PBAC has deemed that the cost-benefit analysis is favorable only in that indication/patients group.

Off label prescribing in this instance, unlike what the RANZCP guidelines attempt to suggest, occurs when the physician prescribes the drug to an adolescent or any other indication that has not been registered on the ARTG.

To be advising an entire body of prescribing professional that the key issue they need to communicate to their patients about off label prescribing is that the medicine may not be available on the PBS and therefore may cost them more out of pocket, is grossly and dangerously misleading both to the patients and the professional integrity and credibility of the prescribers.

Further to the lack of accuracy in their definition of 'off label prescribing', the way in which it is written, the reference to *'in your country'* and the use of the term *'third party payer'*¹⁴ does make one wonder if this definition has been supplied by a party outside our Australian market.

I feel it is necessary for me to repeat myself again here in case you may have missed what I was trying to say earlier.

The legislated practice of off label prescribing both in the US and Australia creates avenues for collaboration between global marketing divisions within large commercial enterprises and as such it may be naive to assume that the Australian subsidiary of a global enterprise would be engaging in marketing practices that would be drastically different to those of its global headquarters.

6. Patient voice and innovation

The public hearings for the Royal Commission into the Violence, Abuse, Neglect and Exploitation of People with Disabilities have made it abundantly clear that patient voice for those suffering with mental illness has historically and continues to be minimised and ignored.

When patient voice is minimized it prolongs the lifespan of ineffective interventions, including medicines, which in turn endangers patient safety and stifles innovation in the market.

The RANZCP position statement titled *'Acknowledging and learning from the past mental health practices'*¹⁵ makes some interesting comments on this matter:

"In order to effectively communicate the nature of modern psychiatry and promote improved mental health, the College has a responsibility to explicitly acknowledge any harm caused by past practices, and to learn from these in order to provide the most effective care now and in the future.

Practices now known to be harmful had a range of causes. They included both systemic approaches to care and individual practices. Some historical treatments may have been well-intentioned but were without an evidence base, ineffective, and distressing to experience.

An entire model of care – the asylum system, which dominated mental health care for the nineteenth and much of the twentieth century – often disregarded the dignity of those it was intended to care for and protect. Until the development of antipsychotic medications in the mid-twentieth century..."

The development of antipsychotic medications in the mid-twentieth century has transformed the delivery and quality of care to those suffering from mental distress, this advancement is one industry should be incredibly proud of. However, I think it's vital that we re-read a segment from that quote:

"Historically treatments may have been well-intended but were without an evidence base, ineffective and distressing to experience".

History can and does repeats itself unless, as RANZCP's policy statement states we learn from past mistakes *"in order to provide the most effective care now and in the future"*. Administering

¹⁴ The term 'third party payer' is one we often used in discussions with global colleagues. In our market the Government functions as a third party payer, in other markets say the US, insurance companies are often referred to as 'third party payers'.

¹⁵ <https://www.ranzcp.org/news-policy/policy-and-advocacy/position-statements/acknowledging-and-learning-from-past-mental-health>

treatments that have failed to be demonstrated as effective under scientifically rigorous settings, have and will continue to cause harm to patients.

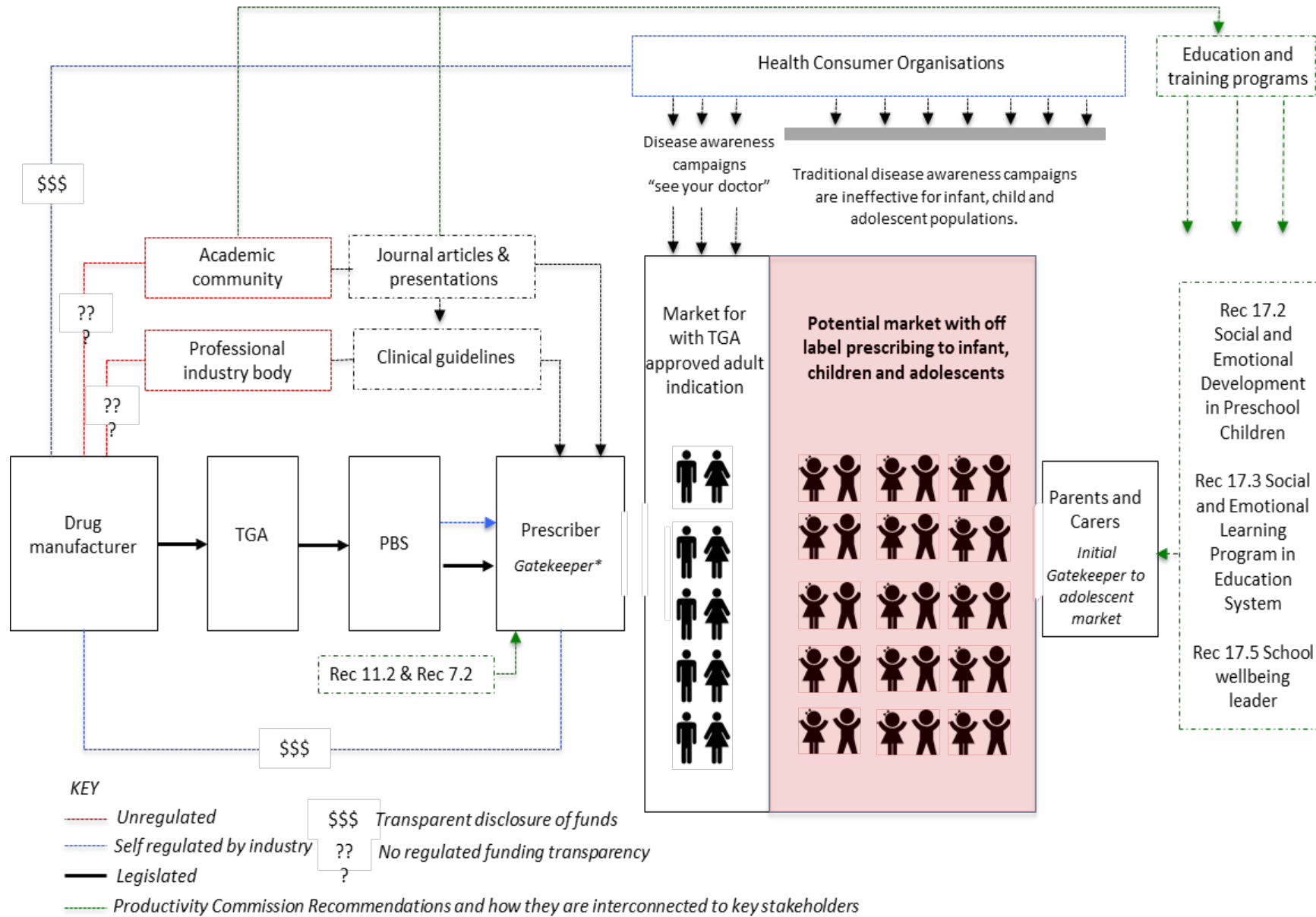
Dr King, I want it to be clear. I do not believe psychiatrists are going out of their way to harm patients. They work with one of the most vulnerable patient populations in our health system, they are desperate to find a means to help their patients but I fear that the current regulatory and legislative parameters are such that in their attempts to help patients there is a very real danger that they may be doing more harm than good.

Given the complex nature of the conditions patients present with, especially in the acute care setting, patient voice is circumstantially almost non-existent and as such, ineffective treatments can remain in the market for longer intervals than they would for other patient populations.

Put another way, the typical post market surveillance mechanisms that would usually serve as a means to circumvent medicines which may be causing harm are hampered significantly given the disease symptom profile mental health patients present with.

Given all these interrelated considerations, tighter regulatory and legislative parameters are essential for this vulnerable patient population and even more so when it comes to the infant, child and adolescent population suffering from mental distress.

The diagram on the following page illustrates the interrelated nature of the issues discussed thus far.



*Prescribers are secondary gatekeepers when it comes to accessing infant and adolescent market. The first gate is getting parents to take their child to a prescriber. The second gate is to convince prescribers that your product is the one that is best suited for the patient.

7. How does all this fit together and what is the relevance of all this to the Productivity Commission?

This diagram on the previous page is a product of my professional exposure to the regulatory and legislative landscape.

I am aware that there may be regulations and legislations that are of relevance that I am may not be aware of and hence I would welcome further public discussions to that end. However in the spirit of transparency and in the interest of public safety, I feel it is critical that I disclose my professional understanding of how each of these key players interrelates.

On the left hand side we see the drug manufacturer.

The dark solid arrows represent a relationship that is governed by legislation:

- The nature of the interactions between drug manufacturers and the TGA is governed by the Therapeutic Goods Act 1989.
- The nature of interactions between drug manufacturers and their ability to be listed on the PBS is governed by the National Health Act 1953 and National Health (Pharmaceutical Benefits) Regulations 1960.

The dotted blue arrows represent self-regulation by industry codes of conduct:

- The way in which a prescriber interacts with PBS regulations is governed both by legislation and by their respective professional code of conduct¹⁶.
- The way in which drug manufacturers interacts with prescribers is governed by the Medicines Australia Code of Conduct (the Code)¹⁷.
- The way in which drug manufacturers interact with Health Consumer Organisations is self-regulated through the Code. Member Companies are required to annually disclose a description of the nature of the support and the monetary value of the financial support¹⁸. For example Janssen (pharmaceutical companies of Johnson and Johnson) disclosed last year their interactions with the Mental Illness Fellowship of Australia (which included the funding of a Parliamentary Friends Of Mental Illness Dinner amongst other things). They also disclosed their interactions with Sane Australia which involved contributions in excess of \$70k that went towards “shared decision making in the management of schizophrenia: a mixed-method study of consumers and carers and funding towards their “Lived Experience Engagement Program: review and redesign of the SANE speakers program, Phase 2”¹⁹.

Having made these discoveries following my sister’s coronial inquest, most concerning to me now is the absence of regulation, be it formalised legislation or industry self-regulated in relation to how industry engages with the academics and professional prescriber industry bodies as highlighted by the red dotted arrows in the diagram.

I can only speak from my own professional experience and while I did not contribute to any work in relation to a mental health products or mental health policy while in industry, I did worked

¹⁶ This relationship, the one between PBS regulation and prescriber choice and actions is one I welcome input and feedback on from prescribers as I have limited professional insights as to how this interaction plays out in practice. I have never been part of an industry marketing sales team and nor am I a qualified prescriber.

¹⁷ <https://medicinesaustralia.com.au/wp-content/uploads/sites/52/2020/01/20200108-PUB-Edition-19-FINAL.pdf>

¹⁸ <https://medicinesaustralia.com.au/code-of-conduct/transparency-reporting/health-consumer-organisation-support-reports/>

¹⁹ <https://medicinesaustralia.com.au/wp-content/uploads/sites/52/2019/06/20190630-HCOSR-R6-Janssen.pdf>

alongside a brand manager for one of our products and on behalf of our business engaged with health consumer organisations, professional prescriber bodies and an academic.

The funding contributions I personally coordinated and administered for the health consumer organisation were less than a seventh in size relative to the financial contribution made to the corresponding professional industry body and a twentieth of the size relative to the contribution that was made to an Australian academic²⁰.

As I've said before I am incredibly proud of the work I contributed to in the industry. I am proud of the partnership and programs I contributed to through our funding of that HCO and the corresponding professional industry body as well as the academic we provided funding to. There is no need for any of that to be hidden and yet the lack of both formalized legislation or industry self-regulation means that the contributions made to the professional industry body and to the academic are not publically disclosed.

It is this lack of transparency and accountability that created the setting for academics such as Dr Joseph Biederman to engage in work with industry in the manner that he did. While retributive justice is being pursued through legal mechanisms in the US in response to the damage done to children and elderly patients, restorative justice measures in the form of legislative or regulatory changes have not been made either here in Australia or in the US to ensure that current and future patients are protected from the clinical guidelines and prescribing practices that have been encouraged by industry and the likes of Dr Biederman.

7.1 Relevance of all this to the Productivity Commission?

This brings us to the green dotted lines in Figure 2. These represent the potential interaction between current stakeholders and the proposed recommendations made by the Productivity Commission's Draft Mental Health report.

On page 141 of the Commission's Draft report, Figure 2.3 highlights that mental illness begins early in life and tends to decline with age, note worthy is that this appears according to the graph provided to be particularly true of attention deficit and bipolar disorder.

Further Figure 2.7 in the Productivity Commissions report highlights that mental illness affects people differently and that that 2% of children and adolescents have conduct disorders. The report goes on to state:

“Childhood behavioural disorders are a group of disorders which typically have their onset in the developmental period. Some examples of neurodevelopmental and behavioural disorders include attention-deficit hyperactive disorder (ADHD), conduct disorder, and oppositional defiant disorder. These disorders are usually characterised by developmental deficits which can affect personal, social, academic, or workplace functioning. People with these disorders typically have problems with self-control of emotions and behaviours, which can manifest as inattention, impulsivity, and a lack of concern for the rights of others” Pg 150 Productivity Commission Draft Mental Health Report.

Given the burden of disease that mental health accounts for not just in Australia but on a global scale, commercially speaking it is very much in industry's interest to dedicate resources to developing medicines to alleviate patient's mental distress, and in turn to dedicate the resources necessary to get those drugs registered by the FDA in the US and the TGA in Australia.

These references above from the Productivity Commission's Draft report highlight that mental illness has a very particular disease profile and trajectory. Given this particular profile and

²⁰ The nature of the research was not disease specific to any of the products distributed by our company but it was a significant financial contribution that we were not required to formally disclose under the Medicines Australia Code of Conduct.

trajectory industry is very much incentivised to develop medicines that will help infant, children and adolescents. If industry can demonstrate that a medicine is safe and effective for the adult population but has not to date been able to demonstrate it's safety and efficacy for the adolescent indication I feel it is very naive or ignorant to assume it's because they haven't tried.

So if they have tried and they still can't demonstrate a statistically significant difference between the drug and placebo why should the Australian taxpayer subsidise that treatment, why should Australian children be subjected to treatments that our regulator has not deemed safe and effective for their age cohort?

The legislated practice of off label prescribing is reckless and dangerous when it comes to the administration of psychiatric drugs to children.

That is not to imply that this is a practice that all psychiatrists or clinical psychologists engage in but it is to say the pharmaceutical industry is a for profit industry. If there are profits to be made they will seek to make them within the existing regulatory and legislative parameters. Knowing what I now know about:

- The legislated practice of off label prescribing;
- The presence of 'consensus-based recommendations' in the RANZCP clinical guidelines which state that "*the absence of evidence is not evidence of absence*" and that as such it is acceptable that "*a general clinical impression that certain medications are effective*" is deemed as an acceptable measure of safety and efficacy;
- The lack of transparency regarding the nature and scope of engagement between the academic community and professional prescriber bodies;

I have grave concerns that market forces are such that patient safety will be compromised when it comes to the adolescent patients.

I have these concerns because we have historic evidence in Dr Biederman's work both on attention deficit disorder and his work with Johnson and Johnson that patient safety has been compromised. And as I said previously, while retributive justice is being pursued through legal mechanisms in the US to rectify the damage done to children and elderly patients, restorative justice measures to protect the current and future infant, children and adolescent populations are yet to be enacted.

I am in full agreement with the Productivity Commission's conclusion that early intervention is absolutely essential when it comes to mental health, it *is* where we should be investing our resources to address the mental health crisis we are witnessing amongst our youth but interventions must be evidence based and it would be ignorant and dangerous to enact the Commission's recommendations prior to the much needed legislative and regulatory changes necessary to ensure children's safety.

7.2 Commentary on the Commissions Draft recommendations

Should there be appropriate regulation and legislation put in place to protect Australia's children I would express my full support for the Commissions draft recommendations.

However in it's absence, as is the present case, there are two groups of recommendations in the Draft report that concern me greatly. Chiefly those that are aimed at what we in industry would referee to as the "gatekeepers" of the adolescent mental health market.

The first group concerns workforce recommendations:

- Recommendation 11.2 - Increasing the number of Psychiatrist
- Recommendation 7.2 - Psychiatrists Consultation by Video Conference.

If I were to view these recommendations through the lens of a drug manufacturer who had a mental health product, the implementation of these recommendations would signal that more patients would have access to a prescriber thereby expanding our potential market.

The second group of recommendations that concern me are those in relation to the education and training of educators who engage with children in both the preschool and school setting. This includes but is not limited to:

- Recommendation 17.2 - Social and Emotional Development in Preschool Children
- Recommendation 17.3 - Social and Emotional Learning Programs in the Education System
- Recommendation 17.5 – Wellbeing Leaders in Schools

Again, if I were to view these recommendations through the lens of industry, the implementation of these recommendations presents the opportunities to apply pressure on parents and carers as they are the primary gatekeepers to the adolescent market. They are the ones that need to take their child to the physician. The most effective way to influence parents is by applying pressure on them through teachers and childcare workers.

I know how vulgar and crude that may all sound, that is not to say that this would in fact take place, but given market forces and current regulatory and legislative parameters it is very much feasible.

In Australia we have legislated against direct to consumer advertising from the pharmaceutical industry. The general Australian consumer is not exposed advertisements for prescription medicines the way that a US consumer would be.

We are however exposed to industry marketing but we don't recognise it as such. Prior to working in industry I hadn't noticed Industry run disease awareness campaigns and had naively assumed they were Government health awareness campaigns. My personal rule of thumb now is that if a campaign ends with "go see your GP" it probably has industry funding behind it.

My concern with Recommendations 17.2, 17.3 and 17.5 is that there is potential for these education and training programs to become 'disease awareness' campaigns aimed at getting parents to take their children to a prescriber but they would be even less obvious than the current disease awareness campaigns as they would be presented to educators by academics and industry KOL's who under those settings would not have to disclose their conflict of interest as these would not be conferences or education seminars with 'prescribers' in attendance but rather school teachers and preschool educators.

Some may argue that it is awfully cynical of me to view the matter in such a way, I think it would also be awfully ignorant and dangerous if we don't at least acknowledge this as a very real possibility.

7.3 Comments on Funding the Employment of Wellbeing Leaders in Schools

The Commission has sought input on the funding mechanism for the employment of wellbeing leaders in schools. More specifically you have asked:

"What existing funding could State and Territory Governments redirect towards employing wellbeing leaders in government schools?"

In keeping with the comments made in this submission, I recommend the practice of off label prescribing of antipsychotics, mood stabilisers and antidepressants to adolescents receiving care in State and Territory run adolescent psychiatric units be band and that the funds that were being spent on these medicines be redirected towards the funding of wellbeing leaders in government schools.

If a drug manufacturer fails to demonstrate the safety and efficacy of their product in the adolescent population, Australian tax dollars should not be used to fund the administration of this treatment to adolescents.

Practices such as frontal lobotomies amongst other psychiatric treatments have been outlawed because as stated by RANZCP²¹ while “well-intentioned” they “were without an evidence base, ineffective and distressing to experience”. It’s important that we ensure we are not unknowingly administering in effect chemical lobotomies to Australian adolescents.

8. A note to parents, carers and prescribers

If by some chance you are a parent, career or prescriber who is reading this submission and you are either reading for the first time about the practice of off label prescribing or realising that the definition you had been given as a prescriber was not entirely accurate, please know that while some of what I have shared may alarm you, existing government regulations are in place that allow for you to protect your children and patients.

However the way those regulations and legislations currently exist, it means there is an onus on you as parents, carers and prescribers to be educated and informed. Below is a question; an action step and a statement you should keep in mind next time you see a physician or patient.

1. As the treating medical professional ask yourself, is this medicine ‘indicated’ for use in children? As a parent, ask the prescriber “Has this medicine been shown to be effective and safe for use in children, is it registered on the ARTG for pediatric use?”

If you as the prescriber are unable to answer that question, or as a parent are not given an answer that satisfies your curiosity then investigate the matter yourself.

2. Go to the TGA website and look up the Product Information Statement and look to see what comments are made under ‘Pediatric Use’.

Below is a screen shot of the TGA website²². I have typed in Olanzapine, the drug that was administered to my sister when she was 12. You’ll notice ZYPREXA, Olanzapine comes up. ZYPREXA is the brand and Olanzapine is the name of the drug.

The screenshot shows the Australian Register of Therapeutic Goods (ARTG) website. The search bar contains 'olanzapine'. The results are filtered by 'safety of medicines & medical devices (1)' and 'prescription medicines (1)'. The search results are displayed in a table with three columns. The first column shows 'ZYPREXA olanzapine 20mg tablet blister pack' with ARTG ID 77390. The second column shows 'ZYPREXA olanzapine 15mg tablet blister pack' with ARTG ID 77388. The third column shows 'ZYPREXA IM olanzapine 10mg powder for injection vial' with ARTG ID 76867. The 'Product Information' link for the first result is circled in red. The website header includes the Australian Government logo and navigation links for Home, Safety information, Consumers, Health professionals, Industry, About the TGA, and News room.

²¹ <https://www.ranzcp.org/news-policy/policy-and-advocacy/position-statements/acknowledging-and-learning-from-past-mental-health>

²² <https://search.tga.gov.au/s/search.html?collection=tga-websites-web&query=olanzapine>

When I open the Product Information statement for Olanzapine I see this on page 7.

elevated ALT and/or AST, in patients with signs and symptoms of hepatic impairment, in patients with pre-existing conditions associated with limited hepatic functional reserve and in patients who are being treated with potentially hepatotoxic drugs.

Use in the elderly

Caution should be used when ZYPREXA is administered to the elderly, especially if there are other factors that may influence drug metabolism and/or pharmacodynamic parameters.

Paediatric use

The safety and efficacy of ZYPREXA have not been established in patients under 18 years of age.

Effects on laboratory tests

No information is available on the effect of ZYPREXA on laboratory tests.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Given the primary central nervous system effects of ZYPREXA, caution should be used when it is taken in combination with other centrally acting drugs and alcohol. As it exhibits *in vitro* dopamine antagonism, ZYPREXA may antagonise the effects of direct and indirect dopamine agonists.

Only now, after knowing the safety and efficacy profile in patients under the age of 18 years are you as a parent and prescriber in a position to make an informed decision regarding what treatment options are you are comfortable with for your child or what is appropriate to be prescribed to your patients.

Now this is not to say that you can't consent to your child receiving a medicine off label but it is important that you are accurately informed about the safety and efficacy of the treatment.

3. If you choose not to go ahead with the treatment and you are in the general community you simply do not fill the script; however if the interaction with the prescriber takes place in a hospital then you formally have to say to your child's doctor that "I withdraw my consent for treatment".

This however may not be possible if your child has been admitted as an involuntary patient in an adolescent psychiatric unit, under those circumstance there are no regulatory or legislative parameters that can protect your child from receiving treatment that to date has not been shown to be clinically safe or effective in children under 18 years of age.

7. Concluding remarks and one request

Dr King, I recently reviewed my postgraduate notes from the health economics course I completed at Monash University several years ago and I came across this statement:

"When the provider as the consumer's agent makes decisions that incorporate their own interests in addition to or over and above the consumer's interests, we refer to an 'imperfect agency relationship'. This arises if the provider, in acting as an agent for the patient, chooses a different type or amount of health care on behalf of the patient than the patient would have done if fully informed.

Because the perfect agency relationship is unlikely to be attained, the asymmetry of information between consumer and provider is a fundamentally source of market failure. It gives rise to potentially high information costs for consumers but, more importantly, it opens up opportunities for exploitation, monopoly pricing and over supply by the providers".

Prescribers don't get the 'kick backs' from industry they once did because we have appropriate regulations and legislation in place, but I'm not sure we can say the same for academics and industry prescriber bodies that generate the literature that informs the clinical guidelines that prescribers base their prescribing practices on.

A few months ago I was explaining some of the discoveries I had made about the legislations and regulations surrounding off label prescribing to a friend of mine who works as a school psychologist. I shared with her my sister's story, how she had received early intervention and I asked her if she had ever seen anything like that before. I was desperate to know if my sister's case was a one off, one prescriber desperate to help a patient but had been misinformed. My friend replied that in all her years she had never heard of the practice of preventatively medicating a 'high risk' child for bipolar.

A few weeks later, while on holiday overseas I received a text message from my friend. She explained how she had had a family meeting with a student's parents earlier that day and the parents explain that on the advice of their daughters psychiatrist they had decided to preemptively medicate her for bipolar.

My gut sank, and so I have found myself spending weeks researching seeking answers to questions and preparing diagrams in an attempt to illustrate to you how and why this is happening.

Thank you for taking the time to read this submission Dr King.

For the safety of all current and future Australian children, I now strongly urge and request you to make the time to dutifully examine Steven Brills'²³ piece concerning Johnson & Johnson's efforts to market the antipsychotic Risperdal off label.

If you would like to have further discussions regarding any of the matters I have raised I am more than willing to do so.

Kind regards,
Hristina Piltz

²³ 'America's Most Admired Lawbreaker'

<https://highline.huffingtonpost.com/miracleindustry/americas-most-admired-lawbreaker/chapter-3.html>

Last minute additional comments in response to the Letter written to Ms Wilkins

In uploading my submission to the Productivity Commissions website I read your letter in response to an article written by Ms Wilkins titled *"1.25 million Australians 0 to 3 years old at risk of dangerous psychiatric drugs"*.

After reading your letter I was curious as to what Ms Wilkins had said in her article and I am now somewhat concerned that you failed to address the following claims made in her article.

"In 2007/08 there were 53 Australian infants under one year old on antidepressants and antipsychotics (306 in total aged 0-3 on a psychiatric drug). By 2015 there were a staggering 7,817 children aged 2-6 years on psychiatric drugs in Australia (including 1,459 children on antidepressants when no antidepressant is approved for use in children under 18 in Australia for depression). These children have been given these drugs despite the Australian government issuing 67 psychiatric drug warnings including to warn of the risk of agitation, increased blood pressure, hallucinations, life-threatening heart problems and suicidal behaviour."

Given the weak regulatory and legislative parameters I have outlined in my submission above, my professional understanding is that the claims Ms Wilkins makes may in fact be true.

Can you please confirm what the national statistics are based on AIHW data in relation to the number of Australian infants on antidepressants and antipsychotics and the number of children aged 2-6 on psychiatric drugs in Australia?

Further Ms Wilkins goes on to state:

"Between 2008 and 2012 alone, his company, Harvey Whiteford Medical PTY LTD, received more than \$1.1 million from the Department of Health for providing planning and services for national mental health reform."

I was deeply disappointed to read this. I have read your letter in response in which you state:

"He has made the necessary disclosures arising from his current and previous work in mental health and the Commission is satisfied as to the independence of his contribution to the Inquiry."

Dr Joseph Biederman, whom I make numerous mentions of in the submission was able to engage in the work he did with Johnson and Johnson and avoid the industry transparency and code requirements in the United States because he had a standalone entity which he received the funds through.

In light of my awareness that Prof. Harvey Whiteford also has his own company, Harvey Whiteford Medical PTY LTD, I think it is only appropriate that there is public disclosure of what funding he has received from the Pharmaceutical industry since the creation of his company.