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## **FORENSIC & MEDICO-LEGAL PSYCHIATRY**

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### **Review to Improve Transparency of the Therapeutic Goods Administration (TGA).**

#### **Supplementary Submission**

1. Having attended the meeting at Parramatta on 23 February and been invited to do a supplementary or perhaps clarifying submission, I offer the following.
2. The TGA appears to be in a client relationship with drug makers. It is widely seen as too close to the industry and not representative of the interests of Australian patients, who deserve better. So does the taxpayer.
3. The issue that needs to be transparent is: Does TGA has conflicts of interest? Is it serving two masters? Or does it simply lack relevant skills??
4. Patients and prescribers have a right to know about side effects to give informed consent. They have a right to know about genetic pathways of metabolism so they can compare their drugs to there own genotypes and teach recalcitrant doctors to so that.
5. They have a right to know about drug-drug and drug-gene interactions.
6. If XXXXXX is correct in saying that this is all under consideration, it should be a transparent "work in progress" and one where the public can make a contribution.
7. Even the US FDA held public hearings into child and adult suicide on antidepressants and their videos and/or transcripts are available to the public.

8. Why does TGA ignore reports of fatalities on drugs? (Especially when the genetic basis of such fatalities is known and had been provided for TGA)
9. The issue that needs to be transparent is: Does TGA has conflicts of interest? Is it serving two masters? Or does it simply lack relevant skills??
10. The TGA is not responsive and its machinations remain secretive. US FDA changes its warnings, but TGA is secretive and non responsive to the public outrage.
11. The issue that needs to be transparent is: Does TGA has conflicts of interest? Is it serving two masters? Or does it simply lack relevant skills?
12. Even rare side effects become a public health problem if a drug is given to is given to a large number of people so with a million Australians on antidepressants, which cause suicide at a rate of 189-240/100,000 in clinical trials and follow up studies causes suicide attempts and violence at some 20-40 times that rate, yet TGA manages to turn a blind eye on the effects to the side effects of these drugs in the community.
13. The issue that needs to be transparent is: Does TGA have conflicts of interest? Is it serving two masters? Or does it simply lack relevant skills??
14. TGA has been is non responsive to the sleep walking fatalities and other tragic events causes by Zolpidem
15. Re Zolpidem/Zopliclone
16. XXXXXX has reported to TGA a case series of 545 ADRs to the Adverse Drug Reactions Advisory Committee (ADRAC), where zolpidem was the suspected drug; it was the sole suspected drug in about 60% of the cases.<sup>1</sup> Sleepwalking, amnesia and other parasomnia-related behaviours were features in approximately 85%. In the remaining 15%, ADRs occurred when the person was conscious; effects included dependence and toxicity-related phenomena, both idiosyncratic and those predictable from the drug's pharmacology. Zolpidem was associated with triggering both isolated and repeated episodes, involving multiple different sleep-related behaviours.
17. The most significant ADRs of zolpidem cases included:
  - 17.1.1. Death from suicide or accident (n=13)
  - 17.1.2. Attempted murder (n=4)
  - 17.1.3. Suicide attempt (n=12)
  - 17.1.4. Suicidal ideation (n=14)
  - 17.1.5. Unintentional overdose (n=20)
  - 17.1.6. Sleep driving (n=32): 60% resulting in motor vehicle accident
  - 17.1.7. Sleep-eating (n=36): most causing weight gain
  - 17.1.8. Sleep-smoking (n =5)
  - 17.1.9. Sleep-drinking of alcohol (n=9)
  - 17.1.10. Disinhibited behaviour on an aeroplane (n=5)

- 17.1.11. Withdrawal anxiety and panic (n=34)
  - 17.1.12. Psychotic behaviour and severe self harm (n=7)
  - 17.1.13. Hallucinations (n=19)
  - 17.1.14. Anterograde amnesia (n=30)
  - 17.1.15. Addiction and dependence. (n=17)
  - 17.1.16. Lucire has reported 15 cases of zolpidem-induced sleep activities to Sanofi Aventis, over 50 to ADRAC, including 3 fatalities. Zolpidem use on its own was rare, (n = 2). In most, an antidepressant had caused an ADR involving insomnia, suicidal and homicidal thoughts and behaviours and bowel symptoms, which adding zolpidem complicated with hallucinatory delirium and the sleep behaviours. Zolpidem was often added to proton pump inhibitors, the "PPIs," whose Product information (PI) warns against their use in conjunction with drugs metabolized by CYP450 2C19. Over the counter purchases may cause serious problems.
18. The issue that needs to be transparent is: Does TGA has conflicts of interest? Is it serving two masters? Or does it simply lack the relevant skills to see that this drug is a public health disaster?
  19. "Atypical" anti psychotics (some of which are marketed as antidepressants in USA were even worse with so death rate of 1 in every 145 clinical trial subjects and 288 deaths reported on these drugs by 2003, the TGA cannot put to and two together (why) and solve this problems.
  20. The issue that needs to be transparent is: Does TGA has conflicts of interest? Is it serving two masters? Or does it simply lack relevant skills?
  21. I would like to see the information on which decisions to approve a drug is made. I once asked what information they used to license a drug and they said there were whole pallets of documents. I would be happy to come in and look at whole pallets of documents, which cannot be sent out on FOI.
  22. TGA appears to accept information from drug companies and license drugs on company summaries without any attempt to access primary data from clinical trials.
  23. The decisions not to be influenced or to ignore new information should be open to scrutiny. The pharmaceutical industry has deceived TGA, and TGA has been advised of this deceit published all over the world in medical journals and law journals
  24. Does the TGA have a process for following the emergent literature and issues??
  25. I would like to see transparency in their decision in regard to antidepressants and antipsychotics. That is, these decisions are in the past but I would like to see even now how they were made.

26. I want to know on what basis over 10,000 reports from the community about antidepressant side effects including suicide and homicide have been ignored.
27. I personally made 500 serious ADR reports and 193 reports of admissions to hospital for suicidal and homicidal behaviours and a homicide from one rural (pop. 150,000) psychiatric unit in 2003-2004. These are serious adverse reactions and included multiple admissions. If I include what happened to the same patients in 2005, there were 7 suicides, an SSRI plus atypical bleeding death and a homicide.
28. Who looks at these reports or are they just binned? The issue that needs to be transparent is: Does TGA has conflicts of interest? Is it serving two masters? Or does it simply lack the relevant skills to see that these drugs have caused a public health disaster?
29. The rate of hospitalized suicide attempts was rocketing. In 1997, when Zyprexa and Risperdal were introduced and prescribed in combination with SSRIs the rate rose to 17/100,000 in NSW. And the rise in suicide numbers under mental health care accounted entirely for that rise in NSW South Australia, Western Australia and ACT.
30. When the TGA continued to ignore my letters and submissions, I referred the matter to XXXXXX at that time Chief Medical Officer, who confirmed to me in writing that he had again referred the matter to the TGA.
31. I would like to know how they made this decision.
32. The issue that needs to be transparent is: Does TGA has conflicts of interest? Is it serving two masters? Or does it simply lack the relevant skills to see that these drugs and the way they are being prescribed, in high doses and combined inappropriately have created a public health disaster?
33. I would like to know why post marketing studies and analyses, for instance, XXXXXXXX and various others which I have handed to the TGA, and which have all have been ignored.
34. On 1, 8 and 9 November I sent 87 redacted reports of persons who had committed suicide and homicide to XXXXXX. These were genetically tested people. I would like to know, as a matter of transparency, why XXXXXX wrote the following sentence:
  - 34.1.1. "I believe the specific issues you have raised in these and your previous communications have been thoroughly addressed by the panel's report, and by the ongoing work of the TGA in this area."
35. I had never previously reported on genetically tested patients.
36. XXXXXX tells me that this is ongoing work of the TGA; I would like to see it.

37. I see this as a matter of transparency.
38. I would like to see how XXXXXX, who had already established in *Hall and al.* that he believed that antidepressants did more good than harm, which was not a pharmacist or a pharmacologist, was put on the expert panel.
39. I would like to know, as a matter of transparency, how the expert panel, whose work in the main was excellent, which looked at 90 redacted reports of persons who had become suicidal and homicidal on antidepressants and had committed homicide, came to the conclusion, on the basis of the information put in front of them, that these drugs did more good than harm.
40. This is not consistent with the literature.
41. It is not consistent with the fact that mental health presentations doubled in the decade after Prozac (fluoxetine) and have gone up by 4% a year along with costs and the number of mentally ill people treated and increasing numbers of suicides and homicides under mental health care. There is no transparency in this decision. I would like to see the reason for it.
42. I would like to know why XXXXXX was advising the TGA after March 24, 2004. On March 24, 2004 the United States Food and Drug Administration (US FDA) issued a Public Health (THIS IS A PUBLIC HEALTH ISSUE) Advisory on Worsening Depression, Suicidality and other problems in adults taking antidepressants for conditions, "psychiatric and other" (that is caused by personal factors not by psychological condition were simply not delivered in Australia to our doctors or citizens.
43. I would like to know who made the decision not to follow the advisory put out by the US FDA and how come Australian prescribers and parents were not warned that they double suicidality in kids, and why the TGA did not check this data by accessing reports to FDA and clinical trials, withheld from FDA where children did commit suicide on these drugs.
44. I would like to know who made the decision to issue a **watered down** advisory 15 months later. I would like to know the connection to the industry of everybody who was involved in that decision and that advice. This is an issue of transparency.
45. The issue that needs to be transparent is: Does TGA have conflicts of interest? Is it serving two masters? Or does it simply lack the relevant skills to see that these drugs have created a PUBLIC HEALTH disaster?
46. I would like to see the curriculum vitae of all the decision makers and those who advise them and declarations of possible conflicts of interest.
47. I would like to know if the decision makers have any past or present contacts with the pharmaceutical industry.
48. In view of the increasing rates of diagnosis of mental illness and increasing costs under mental health care, I would like to know why the TGA has not

investigated the following propositions, which it has permitted to enter into Product Information (PI).

- 48.1. That suicide attempts are inherent in schizophrenia. They certainly were not before we started treating it with akathisia inducing drugs.
  - 48.2. Product Information (PI) for antidepressants conflates bipolar disorder, which affects 0.5% of the population, with medication-induced mania.
  - 48.3. Why the TGA permits the Product Information (PI) not to put black box warnings on all antidepressants, especially in regard to children, suicide and homicide.
  - 48.4. Why does the TGA not include information about gene-based reactions to every drug?
  - 48.5. I would like to know why the TGA has decided not to follow US FDA Advisories, which are three times the size of Australian.
49. In brief, I would like to know all the links that the TGA has to the pharmaceutical industry and if anybody there has a conflict of interest.
50. The issue that needs to be transparent is: Does TGA have conflicts of interest? Is it serving two masters? Or does it simply lack the relevant skills to see that this drug is a public health disaster?

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<sup>1</sup> XXXXXX "Sleep-Driving, Sleep-Eating and Sleep-Smoking Associated with Zolpidem: Consumers Demonstrating their Valuable Role in Pharmacovigilance". Conference proceedings. (poster) Drug Safety 2007: 30(10); 984.