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AKATHISIA CLINIC

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

Prior to addressing the Terms of Reference, I would like to address the quality of the information that apparently is accepted and released by the Therapeutic Goods Administration (TGA) which is information provided by Drug companies. This differs in bulk (number of pages In Product Information) and quality from information produced by the United States Food and Drug Administration (US FDA) and even more that is known from medical literature which has been provided to the TGA by concerned persons such as myself.

It is not a scrap of use if the TGA promotes pharmaceutical industry information and this is what the United States Food and Drug Administration (US FDA) has done and is now trying to undo and the TGA has also done and now needs to undo.

While my interest lies in drugs used in psychiatry, I will use, in this preamble, the example of Chantix (varenicline), one of the 167 drugs, which produce violence, depression, suicidality and other psychiatric side effects in vulnerable persons.

To make the committee aware of both the enormity and magnitude of the problem cased by the TGA not communicating what it knows or should know to the public and to prescribers, I offer these recent publications and invite the reader to extrapolate these statistics to human costs, pressures on doctors, hospitals, jails, ambulances, Emergency rooms, the justice system and of course the taxpayer:

A recent report in PloS analysed reports to the US FDA of violence and homicides, based on their AERS system. This is the paper:

<http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0015337>

It was taken up by TIME Magazine and of course all the pharmacovigilantes, but not the TGA, not yet.

<http://healthland.time.com/2011/01/07/top-ten-legal-drugs-linked-to-violence>

The US FSA has suicide warnings out on a score of drugs.

http://google2.fda.gov/search?q=suicide+warnings&x=0&y=0&client=FDAGov&site=FDAGov&lr=&proxstylesheet=FDAGov&output=xml_no_dtd&getfields=*

The TGA does not.

Chantix, known as Champix in Canada, is prescribed to assist with stopping smoking. There is no reason to suggest that those to whom it was prescribed had a psychiatric disorder. Although there has been a defence of the side effects from certain pharma-funded quarters to the effect that stopping smoking causes these side effects, it certainly does not.

The following paragraph came to my desk, a few days ago, from News on One Click, a health advocacy. I have had many warnings from the US FDA as I am registered to get alerts by emails.

There are numerous such health advocacies, and information about drugs which is not in Product Information (PI) and is sometimes denied by drug companies (through their well remunerated 'experts, known as Key Opinion Leaders) is readily available from any number of sources: decisions made by science courts on suicide epidemiology, (which when science courts are involved, their findings predict successful litigation), good epidemiological studies of side effects, settled Qui Tam cases put forward by whistleblowers and joined by Attorneys General State and Federal. These are often criminal cases for fraudulent promotion and the fines in these cases make no difference to the behaviour of drug companies as, to pay a \$2.2 billion dollar fine for false promotion of a group of drugs which had grossed them \$180 billion is seen as an irritation superimposed on a good business plan.

See

<http://www.bmjjournals.org/content/341/bmj.c5095.full>

CHANTIX Linked to Highest Reports--Hostility-Aggression, Psychosis

FYI The latest January 2011 QuarterWatch (analyzing MedWatch adverse effect reports for Quarter 2 of 2010) found that overall; the FDA received 33,068 domestic reports of serious injury, disability or death associated with drug therapy in this quarter. This was an increase of 12% from the same quarter one year ago and little changed from the previous quarter.

<http://www.ismp.org/QuarterWatch/2010Q2.pdf>

A year after FDA required a prominent boxed warning, a mandatory Medication Guide for every patient and declining use, CHANTIX continued to account for the largest numbers of reported serious psychiatric side effects that pose serious risks of harm. The case reports involving CHANTIX, primarily of hostility-aggression, depression and psychosis, pose serious risks--not only to those who use it--but also to others who may be victimized by consumers of the drug who become psychotic or aggressive.

For this reason, the Federal Aviation Administration has banned varenicline for pilots and air traffic controllers; the Department of Transportation has limited its use among truck drivers; and the Department of Defense has banned it for use by some military personnel, including pilots and missile crews.

QuarterWatch reports:

"In the second quarter OF 2010, CHANTIX accounted for 130 possible cases of clinical depression, 112 possible cases of hostility-aggression, and 70 cases of psychosis or losing touch with reality. "

So, why has the FDA failed to protect the public at large?

The time has come for the FDA use its regulatory authority to withdraw CHANTIX from the market to protect the public at large--including children, families, neighbors--from drug-induced violence.

Read more.... <http://www.ahrp.org/cms/content/blogsection/0/9/>

I am using this drug, not a psychiatric drug, as an example.

It has exactly the same side effects as psychiatric drugs: akathisia, worsening depression or new depression, homicidal and suicidal ideation, behaviours and acts.

The suicide rate (and other forms of violence) in schizophrenia has gone up 20-fold between cohorts of 1875-1924 and 1994-1998.

In epidemiological terms, psychiatry, as practiced with current medications by practitioners misinformed about their side effects (in some people) now makes no inroads into either the prevalence or the cure of mental illness.

This death rate is caused by unmonitored medication. It is a simple as this:

Most psychiatric drugs cause akathisia in some users and some of the people who develop akathisia kill themselves and others. Sub lethal variants fill hospital beds unrecognised.

I reported about 194 cases including a homicide and several suicides to TGA in 2003-4 and had not response other than acknowledgement. This summary is appended, called Reports made to TGA from a rural psychiatric unit.

Suicide attempts associated with akathisia are in the basic psychiatry text DSM from 1994 at 333.9.

The number of people under mental health care continues to increase; with each new akathisia inducer that is added to our prescribers' repertoire. This trend was exacerbated when SSRI antidepressants were introduced in 1990, and prescribed for conditions they could not cure while they produced akathisia in up to 27% of users in some studies. This is now known to be caused by genetic factors. Many of these drugs have gene information in their product information but one has to know a bit to even see it let alone understand it.

It is widely believed that an understanding of pharmacogenetics or genetic pharmacology will reverse this trend, and other side effects in other medical specialities are now known to be related to genetic factors, inability to metabolise drugs or adverse drug reactions and interactions.

The FDA website has genetic information about 43 drugs with CYP450 Pharmacogenetic information in drug labels. There are scores of others.

(<http://www.fda.gov/Drugs/ScienceResearch/ResearchAreas/Pharmacogenetics/ucm083378.htm>)

The TGA has been informed but has not acted in this information.

It really matters.

My reluctant conclusion is that the TGA may be inadequately staffed and in a client relationship with those it regulates.

Documents on which decisions are made not available so this inquiry needs to be extended to what the TGA has been told, where it gets its information from and not only how it promulgates it.

I cannot stress how important this issue is.

JAMA published a paper in 1998, a meta-analysis of a number of meta-analyses, which showed that adverse drug reactions and interactions were between the 4th and 6th highest causes of death in the United States. They did not even look at psychiatric drugs. Psychiatry was not examined.

On this basis, adverse drug reactions and interactions should be given the same level of prominence, the same level of research, the same level of care, the same level of concern as the causes of death that slightly outnumber them them, which are cancer, heart attacks and strokes.

Drugs also contribute to the rate of cancers (prolactin and oestrogens to breast cancer), heart attacks (prolongation of QT interval) and strokes/bleeding disorders (NSAIDs, Proton Pump Inhibitors, (PPIs) and SSRIs).

I have no idea of the responsibilities of the TGA to "classes of people." It should at least indicate that, for example, persons from Vanuatu have a rate of 79% of deficient alleles at 2C19 and Asians have a 50% rate of unstable alleles at 2D6 and 35% of unstable alleles at 2C19. It is well in those communities but TGA has failed to warn that these "classes of people" are prone to adverse drug reactions and interactions.

They do very badly on antidepressants and cannot handle more than one medication safely, so are prone to drug-drug interactions.

TGA has failed to warn about the effects of psychiatric drugs on children and did not tell Australian prescribers the paroxetine had been banned in kids in 2004 because it induced toxic psychosis and behavioural changes.

<http://www.google.com.au/#hl=en&source=hp&biw=1078&bih=914&q=seroxat+banned&aq=f&aqi=g-v1&aql=&oq=&fp=582c89cbfedc80c2>

I could go on.

The irony about Chantix (varenicline) is that the TGA was licensing this drug in Australia just as the first reports of suicides and homicides were coming in to my desktop.

My correspondence with the TGA and indeed Ministers was left unanswered. I was once told that warnings would be issued. To date, my general practitioner has not had one. Nor have I.

Chantix (varenicline) has the same side effects as antidepressants and antipsychotics, where they are recognised as manifestations of akathisia. The TGA has still done nothing about these catastrophic events.

As a preliminary before I address the rest of the Terms of Reference, I would like to link this submission information that I received on FOI from the US FDA concerning the licensing of Risperdal (risperidone) which has today been posted by a friend on the PSYCHRIGHTS website.

http://psychrights.org/Research/Digest/NLPs/Risperdal/19931107FDARisperdalNDA_SafetyReviewSafety_Review.pdf

I got this information (in a garbled form) from my friend who is a False Claims ACT Qui Tam whistleblower in the United States and I sent a successful Freedom of Information request to the US FDA to get this same document.

Please note: I can provide similar information for Zyprexa (olanzapine), Seroquel (quetiapine) and all the antidepressants.

It was announced in TIME MAGAZINE some weeks before these Risperidal (risperidone) and Zyprexa (olanzapine) NDA documents were signed that the atypicals mentioned above were 'nearing approval'. They were, of course, touted as 'wonder drugs'. 66% of users of Risperdal (risperidone) did not complete six-week trials. It was a very poorly tolerated drug. It is now available in depot form. As a result, when patients refuse to take it because they cannot tolerate it, mental health review tribunals sanction its injection.

In trials for risperidone there were 15 deaths in 2067 remaining patients and 9 more deaths by suicide. That is, there were 24 deaths, death rate of about 1 in every 108. The average death rates in clinical trials for Zyprexa (olanzapine), Risperdal (risperidone) and Seroquel (quetiapine) were 1 in 145. That means that one out of every 145 clinical trial subjects who entered these trials died. This is six times the rate expected for schizophrenia on other medications. Curiously, there were no deaths on placebo.

Australian prescribers have not been told.

I doubt the TGA has been told.

Other regulatory agencies were also victims of this fraud.

This brief report comes from 1996. xxxxxxxx who first uncovered this fraud. It has all been published and no one cares. Perhaps no one knows what to do, Pharmacogenetics will solve this problem if doctors are asked to attend to this new knowledge, as it is their obligation as doctors, to keep up to date.

<http://www.ncbi.nlm.nih.gov/pubmed/16804639>

It is not a scrap of use having Terms of Reference concerning how information is going to be communicated to the general community until it has been established that the information that is being communicated is high quality information, not drug company promotional material.

I welcome the new National Prescriber Service website. However, I note that the consumer information is that which is approved by the US FDA.

The US FDA is not a trusted agency and assessors have known conflicts of interest. It is constantly under supervision and evaluation and subject to many adverse reports by other monitoring agencies.

One has to remember that the pharmaceutical industry is very valuable to the USA economy, very powerful and has 2.5 lobbyists in Washington for every Senator and Congressman and spends billions on promotion, and four billion contributing to elections funds of legislators on both sides of aisle. They are very powerful because they fund learned professors, institutes, key opinion leaders, educate through specially coached drug representatives who have no qualms in going around from psychiatrist to psychiatrist spreading adverse information about me, the whistleblower.

As a result, I have problems. In USA I would be in line for huge rewards for being a whistleblower under the False Claims legislation.

http://en.wikipedia.org/wiki/False_Claims_Act

We need a False Claims Act in Australia as penalties of fraud by drug companies are risible here and it is a playground for exploitation of our most vulnerable people and taxpayers.

It is all very well for these bits of consumer information to say "go tell your doctor that you are feeling suicidal." In my experience of literally hundreds of cases is that they tell their doctors and the doctor (even, or especially, the psychiatrist) does not know what to do, and adds more drugs or increases doses of these drugs which are already problematic, gives more drugs demanding the same already used up or impaired metabolic pathways and chronic mental illness, in fact a toxidrome, now called "intractable schizophrenia" by those who do not know of this problem is the outcome and no one recovers.

I have one request:

Please do not pass the buck as others have done. This is someone's responsibility. Everyone else says it is the TGA's responsibility.

I am sick of buck passing as in this footnote.¹ Please suggest that the buck stop at the TGA. If TGA lacks relevant workforce of skills they should use consultants and offer grants for producing useful, readable and understandable academic detailing of drugs as happens in USA. (I will put my hand up for some, in good company)

Terms of Reference

1. The current arrangements for disclosure of information or advice in relation to all therapeutic goods currently on the market in Australia or previously approved for marketing in Australia;
 - 1.1. Compared with the United States Food and Drug Administration (US FDA) (which is not trusted, unsatisfactory, under investigation and has been severely criticised in all reports made about it), the TGA does even less.

- 1.2. I would suggest that the TGA has a website on which all adverse drug reactions are reported and accessible. They should be more accessible than the website produced by the US FDA called AERS.
- 1.3. <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm>
- 1.4. The ARES is translated regularly by the Citizens Commission For Human Rights into a website that can be readily understood.
- 1.5. <http://www.cchrint.org/psychdrugdangers>
- 1.6. This site also lists all warnings about psychiatric drugs that have been formally issued by the most reliable agencies,
- 1.7. Since 2004, I have been getting regular alerts on changed Product Information (PI), new side effects or interactions from the US FDA. I have had nothing like that from the TGA, not even acknowledgement of most of my 500 adverse drug event reports.
- 1.8. In 2004, when the XXXXXXXXXXXXXXXX, a former Health Minister, Professor of Medicine, and, at that time, Chancellor of the Australian National University, wrote for me to the TGA about the already known information, about the doubling to trebling of suicides in antidepressant trials. XXXXXXXXXXX and I both received a letter from Professor XXX XXX to the effect that he would ask the drug companies to put this product insert and warning into Australian Product Information (PI).
- 1.9. They did not. Professor XXXXXXXX also assured us that drug companies would be told to notify prescribers. I assure you that they have not done so.
- 1.10. Notwithstanding the fact that the US FDA had ordered a product insert, to be put into product information for all antidepressants, old and new.
- 1.11. <http://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM173233.pdf>
- 1.12. Nothing was done by the TGA to warn about worsening depression, suicidality, violence, akathisia, mania and hypomania in patients, psychiatric and non-psychiatric. There are many other problems to which American prescribers were alerted. The TGA took no notice of the March 22, 2004 Public Health Advisory from the US FDA which I have footnoted², until 4 September 2005, 18 months later
- 1.13. <http://www.tga.gov.au/adr/aadr/aadr0508.htm#a1>
- 1.14. At that time TGA took advice from a known key opinion leader whose links with the pharmaceutical industry are a matter of public

record and can be found by searching his name, (admittedly he does use two spellings), and the names of drug companies. It mis-cited his paper to the effect that suicide rates fell when antidepressants were introduced although the cited paper said they did not fall.

- 1.15. Australian prescribers and patients got no Black Box warning about the dangers and risks of these drugs for children where later Product Information (PI) admits that they double suicide rates.
- 1.16. At that time, the TGA took advice from the author of one of the papers it has mis-cited and Australian prescribers and patients got no black box warning about the dangers and risks of these drugs for children.
- 1.17. They don't seem to know that each time they write a prescription for an antidepressant for a person under 24, they are using a drug that has not been approved and not been approved for very good reasons.
- 1.18. I don't know very many of my friends who spend much time on the website of the TGA. There needs to be urgently a system of emailing individual doctors with information as important as this.
- 1.19. The TGA should not take advice from anybody who has any connections with the pharmaceutical industry.
- 1.20. Indeed, the TGA should be very cautious about anyone who has had pharmaceutical industry benefits or is likely in the future to have pharmaceutical industry benefits. It is my view that public servants should be free of conflicts of interest.

2. Opportunities for increased provision of public information on therapeutic goods currently on the market in Australia or previously approved for marketing in Australia;
 - 2.1. Opportunities include the welcome website for the National Prescriber Service. There is a need to update information as legal decisions based on science hearings find that drugs cause catastrophic side effects not previously admitted. These were known for a decade before Prozac (fluoxetine) was licensed in Australia and are true of the rest.
 - 2.2. The website of the US FDA provides Product Information (PI) but it is still unsatisfactory.
 - 2.3. For example, Efexor (venlafaxine), a drug that has been associated with much suicide and homicide, included homicidal ideation among the listed side effects but only in 1996 and 1997.
 - 2.4. After this time, homicidal ideation dropped out of side effects lists. Nonetheless, I see it all the time, not only on Efexor (venlafaxine),

2.5. The TGA should take it upon itself to educate or subcontract education about pharmacogenetics to the community. There are many doctors conscientious enough to wish to practice personalised medicine. There is a three-year-old report in place and nothing has been done about it.

[http://www.deloitte.com/assets/Dcom-Australia/Local%20Assets/Documents/Deloitte_PGx%20Report_4%20Dec%202008\(3\).pdf](http://www.deloitte.com/assets/Dcom-Australia/Local%20Assets/Documents/Deloitte_PGx%20Report_4%20Dec%202008(3).pdf)

Is this the duty of the TGA? Or some other agencies or a public private partnership?

3. Opportunities for improved public understanding of the procedures for ongoing monitoring of products already on the market and the evaluation, assessment and testing of new products;
 - 3.1. The public has no idea of the procedures for ongoing monitoring of products. I have an interest in the area and I know only of a couple of studies.
 - 3.2. The point I would like to make here is that the assessment procedures used by the US FDA are entirely unacceptable. A drug can have 998 unsuccessful trials. However, if two trials find it to be better than placebo, the drug is licensed.
 - 3.3. XXXXXXXXXXXXXXX, who has accessed various drug company archives with court ordered approval, gave the following evidence to a House of Commons inquiry:
 - 3.3.1. *First, in order for a drug to be licensed, it has to show superiority to placebo in two controlled trials. Companies however can run ten or more trials in carefully selected samples using instruments carefully designed to pick up any effect in order to demonstrate this, and even if the results show the drug failing to beat placebo in the clear majority of trials, this is not held against them. These other trials are commonly termed failed trials rather than drug failures.¹⁴*
 - 3.4. When the US FDA was made aware of successful litigation based on suicide epidemiology and the bulk of evidence, and having held some public hearings, it ordered that a Black Box warning about their effects in children, part of a “class suicidality labeling language for antidepressants” be incorporated in each drug’s product information, part of which reads as follows:
 - 3.4.1. *WARNINGS – Clinical Worsening and Suicide Risk*

3.4.2. *Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. There has been a long-standing concern that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients.*

3.4.3. *The following symptoms of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric.¹⁵*

3.5. In June 2005, the FDA conceded causation of suicide by antidepressants and later extended suicide warnings to other drugs.¹⁶ Australian prescribers and patients were not advised of this problem by the relevant authority, which I would have thought was the Therapeutic Goods Administration.

3.6. The Therapeutic Goods Administration did not follow or adopt any of the public health advisories produced by the FDA, nor did it demand that drug companies notify prescribers of these major changes or include them in Australian prescribing information. Failing to make clear that these effects are not related to the psychiatric diagnosis causes some Australian prescribers to believe they are seeing an exacerbation of a psychiatric condition rather than a neurotoxic side effect, i.e., a toxidrome.

4. The timeliness of the provision to the public of information regarding the evaluation, assessment and testing of new products;

4.1. Using the example of Chantix (varenicline), the TGA was licensing this drug for stopping smoking just as the first reports of suicides and homicides were coming in on my desktop from various pharmacovigilante groups.

4.2. Nobody has had any information about these side effects. Every emergency department in every hospital should have been immediately notified to watch out for this side effect, as well as every psychiatrist, general practitioner, psychiatric unit, ambulance driver and police station.

4.3. The tragedy that results is the person who cannot metabolise Chantix (varenicline) for genetic reasons is then given a whole lot of antipsychotics or antidepressant drugs. There is an urgent need for the understanding that adverse drug reactions are genetically

5. Any constraints on the release of further information, including possible implications for public health or safety, which might influence future arrangements;
 - 5.1. As antidepressants helped only 2.7% of users in clinical trials and doubled to trebled suicides, there is no great fear of leaving somebody untreated. The people who do benefit are the people who benefitted from old antidepressants. These were the biologically depressed, more seriously depressed or the “hospital depression” cases.
 - 5.2. Even treating biological depression, your patient might be a Poor Metaboliser and commit suicide or get sicker. This was a matter of 1960 textbooks.
 - 5.3. Australian Product Information (PI) fudges it and implies that everybody who is getting these antidepressants is depressed and, of course, they are not.
 - 5.4. The TGA should commission some proper Product Information (PI) to sort out the various distortions. For example, in the labels for antipsychotics the statement is made that suicide is inherent in schizophrenia. It is not. It wasn't until the early 1960s that the suicide rate in schizophrenia and violence rate in schizophrenia started rising and it is now 20-fold what it was before we started treating with drugs that cause akathisia. This is gross misinformation. The TGA needs to be very careful about what they promote.
 - 5.5. Similarly Product information for antidepressants conflates medication induced mania with bipolar, this is catastrophic; medication excludes a diagnosis of bipolar. The correct treatment for one is catastrophic for the other and outcomes for bipolar are now worse than 100 years ago with affected persons having more frequent and longer episodes, and instead of 0.5% carrying that diagnosis and it is being diagnosed in 10% of the population, by doctors educated by drug companies.
6. Arrangements for the public disclosure of information utilised by other comparable international regulators;
 - 6.1. This has been addressed but none is satisfactory to me. The quality of this information is at issue.
7. Opportunities to improve public access to information through enhancements to web-based and other information dissemination mechanisms; and

7.1. And blogs and a help line are needed for discussion and provision of expert advice or failing that advice about where to go for help. There are a lot of angry consumers out there and a lot of totally unresponsive and poorly educated prescribers.

8. The need to improve public awareness of, and access to, information on the arrangements for regulation of therapeutic goods advertising.

8.1. Desperate. The public are information carriers as it is almost impossible to get doctors to listen, over the louder voice of the pharmaceutical industry.

8.2. I sought many times to engage with the TGA by sending reports and asking for contact back to assure me that appropriate warnings were to be given.

8.3. I sent 80+ redacted reports to XXXXXX who called and inquiry into the serious even catastrophic drug drug interactions I was reporting.

8.4. And expert committee reported on Christmas Eve of 2009, and this attracted a paragraph in The Australian.

8.5. My colleagues still have not heard of the report which would save many lives, many have been lost (I do coroners reports) since that time and they were preventable.

8.6. I sent, to XXXXXX, a further 87 redacted reports of similar catastrophic side effects in persons on whom I had conducted pharmacogenetic tests and who had been found to be poor metabolisers or worse. These included people who had committed suicide and homicide. XXXXXX seems to have been advised that the TGA had this issue under control and, if it is aware, TGA does not seem able to do anything about it.

8.7. I confess I gave up trying to form a relationship with relevant people there in 2005, when acutely frustrated about yet another tragedy I told the official at the TGA that they would get sued if they did not issue warnings. The response "We get sued all the time."

8.8. I gave up.

¹ 10218—PSYCHIATRIC DRUGS
XXXXXXX to the Deputy Premier, and Minister for Health—

1. Has the Minister and her predecessors been warned by individuals that suicides committed by patients and clients under mental health care could be caused by psychiatric drugs:
 1. That affect persons who have a genetically determined inability to metabolize them;

2. That such persons should be recognized by their adverse medication responses?
2. How many persons have committed suicide whilst under mental health care in the years 2003 to 2008?
3. How many have committed homicide?
4. Do these figures represent a deterioration or improvement in the numbers of suicides under mental health care:
 1. Before 1990;
 2. Before 2002?

Answer—

I am advised:

1. NSW Health advises me that there has been correspondence to previous Health Ministers in relation to this issue. I have also received such correspondence. The Chief Psychiatrist in consultation with the NSW Mental Health Clinical Advisory Council is currently considering these issues.
2. According to the Mental Health Client Incident Information System, there were 937 notifications of suspected suicides of persons under mental health care that were reported to the NSW Health Department between 1 Jan 2003 and 31 Dec 2008.
3. According to the Mental Health Client Incident Information System, there were 43 notifications of suspected homicides by persons under mental health care that were reported to the NSW Health Department between 1 Jan 2003 and 31 Dec 2008.
4. It is not possible to compare the data over this time period due to the fact that different methodology was used to collate this data.

Question asked on 13 May 2010 (session 54-1) and published in Questions & Answers Paper No. 197 <[http://bulletin/prod/la/lapaper.nsf/V3QnBySN/541~197/\\$file/197-QA-S.pdf](http://bulletin/prod/la/lapaper.nsf/V3QnBySN/541~197/$file/197-QA-S.pdf)> .

10219—SUICIDES CAUSED BY ANTIDEPRESSANTS
XXXXXX to the Deputy Premier, and Minister for Health—

1. How many suicides have been investigated by toxicologists or geneticists, as recommended in The Pharmacogenetics Journal to which a NSW psychiatrist has contributed?
2. Has NSW Health had genetic evaluations for "ability to metabolise drugs" as is done by medical examiners and coroners in the USA and UK to distinguish between suicide caused by mental illness and suicide caused by psychiatric drugs?
3. Can the Minister provide advice from the Department of Health on the issue of antidepressant-induced akathisia suicide and homicide?
4. Is the Minister aware:
 1. of the claim antidepressant drugs increase suicide;
 2. this is the subject of public health advisories in all countries other than Australia and NSW?
5. Is the Minister aware that antidepressants caused about 1 in 500 users to commit suicide in clinical trials presented to the US FDA for the purposes of licensing and follow-up studies?

Answer—

I am advised:

1. Any deaths and suicides of people under the care of public mental health services are investigated by the NSW Coroner. Questions relating to the Coronial process should be directed to the NSW Attorney General.
2. NSW Health has not funded any research into 'genetic evaluations for ability to metabolise drugs'.
3. to (5) The Chief Psychiatrist in consultation with the NSW Mental Health Clinical Advisory Council is currently considering these issues.
4. I invite the Member to submit any studies or material he may have on these issues for further consideration.

Question asked on 13 May 2010 (session 54-1) and published in Questions & Answers Paper No. 197 <[http://bulletin/prod/la/lapaper.nsf/V3QnBySN/541~197/\\$file/197-QA-S.pdf](http://bulletin/prod/la/lapaper.nsf/V3QnBySN/541~197/$file/197-QA-S.pdf)> .

**10220—DEATHS DUE TO ZYPREXA AND RISPERDAL
XXXXXXX to the Deputy Premier, and Minister for Health—**

1. Is the Minister aware that in Zyprexa and Risperdal clinical trials presented to the US FDA to get these drugs licensed, it was revealed that:
 1. 1 in 208 (20) Zyprexa (olanzapine) subjects died;
 2. 1 in 250 (12) risperidone clinical trial subjects died;
 3. most of the deaths (21) were suicides?
2. Is the Minister aware of damages being paid to States and individuals consequent on litigation for fraudulent promotion of medication?
3. Is the Minister aware that by 2003, 288 deaths had been reported to the TGA of persons taking new "Atypical" drugs?
4. What warnings have been issued to patients and prescribers re the above drugs?
5. (a) Have these deaths been thoroughly investigated by coroners as they are in the USA, as described in the editorial provided to which an Australian (NSW) psychiatrist has contributed?
6. (b) Has an inquiry been made into what medications they were taking or had recently taken?

Answer—

I am advised:

(1) and (2) Agreement for drugs to be included for Australian use rests with the Commonwealth Government. The Therapeutic Goods Administration (TGA) regularly evaluates prescription medicines for quality and safety and to ensure that the product is effective for its intended use. NSW Health ensures that any warnings issued by the TGA are included in relevant clinical guidelines.

(3) The TGA's Office of Medicines Safety Monitoring receives reports of suspected adverse reactions to prescribed medicines, vaccines, over-the-counter medicines and complementary medicines.

(4) The TGA provides advice on suspected adverse reactions to prescription medicines to the public and prescribers as required. Information is available to patients and prescribers in the Approved Product Information leaflets on

medicines approved in Australia.

(5) Questions concerning the Coronial Process should be directed to the NSW Attorney General

Question asked on 13 May 2010 (session 54-1) and published in Questions & Answers Paper No. 197
<[http://bulletin/prod/la/lapaper.nsf/V3QnBySN/541~197/\\$file/197-QA-S.pdf](http://bulletin/prod/la/lapaper.nsf/V3QnBySN/541~197/$file/197-QA-S.pdf)> .
Answer received on 17 June 2010 and printed in Questions & Answers Paper No. 211 <

² FDA Public Health Advisory

Worsening Depression and Sociality in Patients

Being Treated With Antidepressant

March 22, 2004

This information is out-of-date. For current information on antidepressant drugs, please see <http://www.fda.gov/cder/drug/antidepressants/default.htm>

Today the Food and Drug Administration (FDA) asked manufacturers of the following antidepressant drugs to include in their labeling a Warning statement that recommends close observation of adult and pediatric patients treated with these agents for worsening depression or the emergence of suicidality. The drugs that are the focus of this new Warning are: Prozac (fluoxetine); Zoloft (sertraline); Paxil (paroxetine); Luvox (fluvoxamine); Celexa (citalopram); Lexapro (escitalopram); Wellbutrin (bupropion); Effexor (venlafaxine); Serzone (nefazodone); and Remeron (mirtazapine).

Warning Information

Health care providers should carefully monitor patients receiving antidepressants for possible worsening of depression or suicidality, especially at the beginning of therapy or when the dose either increases or decreases. Although FDA has not concluded that these drugs cause worsening depression or suicidality, health care providers should be aware that worsening of symptoms could be due to the underlying disease or might be a result of drug therapy.

Health care providers should carefully evaluate patients in whom depression persistently worsens, or emergent suicidality is severe, abrupt in onset, or was not part of the presenting symptoms, to determine what intervention, including discontinuing or modifying the current drug therapy, is indicated.

Anxiety, agitation, panic attacks, insomnia, irritability, hostility, impulsivity, akathisia (severe restlessness), hypomania, and mania have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although FDA has not concluded that these symptoms are a precursor to either worsening of depression or the emergence of suicidal impulses, there is concern that patients who experience one or more of these symptoms may be at increased risk for worsening depression or suicidality. Therefore, therapy should be evaluated, and medications may need to be discontinued, when symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

If a decision is made to discontinue treatment, certain of these medications should be tapered rather than stopped abruptly (see labeling for individual drug products for details).

Because antidepressants are believed to have the potential for inducing manic episodes in patients with bipolar disorder, there is a concern about using antidepressants alone in this population. Therefore, patients should be adequately screened to determine if they are at risk for bipolar disorder before initiating antidepressant treatment so that they can be appropriately monitored during treatment. Such screening should include a detailed psychiatric history,

including a family history of suicide, bipolar disorder, and depression.

Health care providers should instruct patients, their families and their caregivers to be alert for the emergence of agitation, irritability, and the other symptoms described above, as well as the emergence of suicidality and worsening depression, and to report such symptoms immediately to their health care provider.

Background

Among antidepressants, only Prozac (fluoxetine) is approved for the treatment of pediatric major depressive disorder. Prozac (fluoxetine), Zoloft (sertraline), and Luvox (fluvoxamine) are approved for pediatric obsessive compulsive disorder. None of these drugs is approved as monotherapy for use in treating bipolar depression, either in adults or children.

The requested labeling changes are consistent with recommendations made to the Agency at a meeting of the Psychopharmacological Drugs Advisory Committee (PDAC) and the Pediatric Subcommittee of the Anti-Infective Drugs Advisory Committee (Peds AC), held on February 2, 2004. The possibility of suicidality associated with the use of antidepressant drug products in the pediatric population was also the subject of two previous FDA communications (FDA Talk Paper on June 19, 2003, and FDA Public Health Advisory on October 27, 2003).

FDA is continuing to review available clinical trial data for pediatric patients with depression and other psychiatric disorders to try to determine whether there is evidence that some or all antidepressants increase the risk of suicidality. Later this summer, the FDA plans to update the PDAC and Peds AC about the results of this review.

FDA plans to work closely with each of the nine manufacturers of the antidepressants that are the subject of today's request to continue investigating how to optimize the safe use of these drugs and implement the proposed labeling changes and other safety communications in a timely manner.

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