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Representative, U.S. The Honorable Mr. Joe Barton,
United States House of Representatives.
Washington DC.

Representative, U.S.. The Honorable Mr. James Greenwood,
United States House of Representatives,
Washington DC.

Number of US citizens at risk to SSRIs

This letter is to advise you that there is a new and accurate method for calculating the number of patients that have taken SSRIs in the US since introduction of these drugs. Neither the FDA, nor Pharma have been able to make this calculation. This method enables the extent of the harm, induced suicide and dependency caused by SSRIs in the US since 1988 to be quantified in both human and financial terms.

Dear Mr. Barton and Mr. Greenwood,

I have read your public letter to the FDA (24 March 2004) regarding your concerns over the regulation of SSRIs with great interest. I am encouraged that serious questions are now being asked by the US Govt. about the adequacy of FDA's process of safety regulation of SSRIs and the FDA's long intimacy with Pharma and its extended network of funding and influence.

I have an important contribution to make to the investigation of SSRI induced harm caused by the massive prescription of Prozac, Paxil, Zoloft and the other SSRIs to both adults and children without any explicit warnings of the known potential of these drugs to induce suicide or dependency.

The FDA, MHRA *(UK equiv.of FDA)* and PI admit that they have no idea how many patients are taking or have taken SSRIs. I have designed a computer model or simulation that provides a very accurate method for converting the known medication consumed (pills) into the actual number of patients who took them. The method relies on published clinical usage profiles and eliminates all the guesswork and ambiguity involving prescriptions, visits to doctor etc. It is a logical process that does not use statistics and so it can be easily understood without special mathematical skills. The model runs from the year of introduction of the drug, it quantifies and accumulates the growing cohort of long term and new patients from the annual quantity of pills consumed. Some more details are given in Appendix1.

The model logic, arithmetic, assumptions and implementation have been challenged in an extensive series of stress and sensitivity tests, designed to expose errors, to detect benign assumptions, and to measure model response to variation of all input parameters. Independent assessments have been made at two UK Universities and it has been presented twice to the MHRA for critical review. No flaws in the logic and methodology of the IMR patient flow model system have been found.

It has been known by Pharma since1985 and now sadly by many thousands of victims, that every person, healthy or depressed, adult or child, who starts an SSRI, faces a finite risk of drug induced suicide and other harm in the first weeks of use. (Teicher and Cole, 1993)

Since 1988, 68 million Americans have used Paxil, Prozac and Zoloft. Using a most conservative excess suicide rate, at least 21 thousand avoidable suicides may have been induced, without any warnings to the victims or their families.

Table 1 (below): Use of Paroxetine (Paxil) in USA 1993 –2002 showing patient growth.

Paroxetine (Paxil) in USA 1993--2002.

Year	New Patients starting in current year	Long Term Patients at start of current year	Total patients treated in current year	Patients dropping out in current year
1993	850,205	0	850,205	536,447
1994	1,467,859	170,041	1,781,617	1,080,082
1995	1,289,065	453,410	1,990,600	1,098,270
1996	1,653,982	674,428	2,546,312	1,326,963
1997	2,106,261	939,762	3,325,610	1,701,480
1998	2,037,645	1,268,091	3,661,774	1,768,610
1999	1,861,142	1,548,724	3,754,306	1,680,144
2000	2,330,549	1,759,557	4,404,711	1,973,904
2001	1,887,306	2,036,854	4,318,112	1,801,226
2002	3,046,058	2,197,859	5,562,945	2,482,068
Totals	18,530,071			15,449,195

Total of Paxil medication for each year has been used to produce this image of patient growth. A total of 5.8 thousand million Paxil tablets (of all dose values) have been consumed in various quantities by 18.5 million US citizens during the last 10 years. Table 2 (below) gives the number of suicides that may have been induced in this population of 18.5 million Americans at risk after Paxil was introduced. It does not include the additional suicides that may have been induced when patients attempted to withdraw after long use A range of net rates between 32 and 104 induced suicides per100K patients starting Paxil has been used to calculate a range of total deaths. These rates have been derived from clinical data recently released by GSK.(*Glaxo Smith Klein)* These rates are very conservative and are far lower than the net rates measured in earlier randomsed clinical trials *(RCTs),* (1990, 1991) and in epidemiological studies, typically 180-200/100K in excess of placebo.

From table 2, in 2002 over 3 million Americans became new users of Paxil and therefore faced a net risk of induced suicide that is unlikely to be lower than 32/100K and quite probably is higher than 104/100K. Thus somewhere between 987 and 3168 excess suicides may have occurred due to Paxil. But whatever the total, it was not zero,

several hundred Americans died who were not warned of the possible outcome that has been known and denied by the manufacturer for so long.

Table 2 (below): Induced Suicides in USA 1993 –2002 at different possible rates

		Net Induced Suicides (Starting On Drug),					
Year	New Patients	Rate/100K	Rate/100K	Rate/100K	Rate/100K	Rate/100K	Rate/100K
		104	90	75	61	47	32
1993	850,205	884	762	641	519	397	275
1994	1,467,859	1527	1316	1106	896	686	476
1995	1,289,065	1341	1156	971	787	602	418
1996	1,653,982	1720	1483	1246	1010	773	536
1997	2,106,261	2191	1889	1587	1286	984	682
1998	2,037,645	2119	1827	1536	1244	952	660
1999	1,861,142	1936	1669	1403	1136	870	603
2000	2,330,549	2424	2090	1756	1423	1089	755
2001	1,887,306	1963	1693	1422	1152	882	611
2002	3,046,058	3168	2732	2296	1859	1423	987
Totals	18,530,071	19271	16618	13964	11311	8657	6004

There is a simple analogy with another industry that demands two questions. Assuming the lowest rate (32/100K) would the FAA support an airworthiness certificate for a certain aircraft type, that for 10 years consistently crashed and killed 300 to 1000 passengers per year and injured many others? How would the FAA react if the aircraft manufacturer consistently blamed the crashes on the passengers but not the aircraft?

The Crisis in Medical Regulation

The movement to expose these same fundamental regulatory failures in the UK is ahead of that in the US and is now beginning to show results. During 2003 the MHRA has been progressively shamed and forced into a succession of most serious admissions of their failure to protect patients. These failures include cover up of evidence of harm since 1991, failure to challenge pharma, failure to seek out reports of harm from the use of SSRIs, ignorance of the numbers of patients at risk etc, and general denial of any possibility that these drugs can induce suicide, attempted suicide or long term dependency, despite overwhelming evidence to the contrary.

The evidence comes not only from the Industry's hidden Healthy Volunteer trials 1988 (Ref. Tobin v GSK 2001, Wyoming) and from RCTs with manipulated results (SKB, UK Licence Application.1990, 91) but also from the abundant and growing evidence from the victims themselves and the bereaved families. (e.g. Panorama investigations in the UK and Washington, Feb 2004)

There are many parallels between the Pharma biased behaviour of both regulatory bodies (FDA and MHRA) during the last 15 years that are themselves very significant. What is required now in both countries is a full, open and independent enquiry, focussed

on SSRIs, mandated to discover whether Medical Regulation is fundamentally flawed, and, if it is, to measure what harm has been done and who is responsible.

The fundamental requirement for such an enquiry is a detailed and accurate analysis of the total number of patients involved and their period of unwarned risk on these drugs if they survived.

In the UK, US, Canada, Australia etc. there are many who now believe that the greatest medical scandal of all time is about to be exposed, the proper outcome of which must fundamentally change all national processes of drug regulation in favour of the safety and wellbeing of patients not massive commercial profit regardless of harm done.

This tragedy has many causes, here are three of the most fundamental:-

1) All Governments have delegated the responsibility for medical regulation and funding to various agencies without close oversight. This has resulted in the equivalent of the Police Dept. being funded and part staffed by the Mafia.

2) Culture in Pharma consistently values commercial profit above patient safety. FDA and MHRA meekly allow assertions of market vulnerability and commercial confidentiality by Pharma to justify all manner of secrecy, non-disclosure and inaction. Drug safety is not a continuous process of investigation and validation, one dubious licence issued 15 years ago lasts indefinitely without review whilst the drug applicability is continually extended in addition to the lucretive unvalidated uncontrolled off label use (eg Paxil for the under fives)

3) Doctors claim the independence and freedom to override/ignore any FDA regulation and are not compelled to report any suspected adverse drug effects to the FDA, thus the most vital safety feed back is continually lost. By comparison, in Aviation, human safety is paramount. Pilots, of similar status to doctors, must obey air traffic control instructions implicitly and must report all suspected defects that could affect safety. There is no place in modern hi tech aviation for uncontrolled barn storming pilots, so why should modern hi tech medicine be any different especially when there are many more patients at risk from complex ill validated drugs than passengers in complex well validated aircraft?

Robust investigation of medical regulation is inevitable. The purpose of this letter is to inform that there is a viable and accurate method for quantifying the harm done by SSRIs that will assist any enquiry. In addition to offer to explain the function and implementation of the IMR Model in sufficient detail to demonstrate that the results are scientifically credible and worthy of serious consideration by the US Government.

Yours sincerely,

Graham Aldred

A**ppendix 1**

Principle of the IMR Model System.

The clinical study of SSRI use indicates characteristic patterns of usage or tolerance, from the early weeks through to several years. The total quantity of medication that has been issued from the pharmacies is known in annual or quarterly increments. A very accurate method has been devised for converting consumption of medication, moderated by characteristic patient usage, into actual numbers of patients.

The phasing of patients in starting or leaving the drug in the short term or finding themselves dependant for many years, is handled with flexibility and without artificial constraint in the model. The model starts running from the year of introduction of the drug. It generates an image of the patient flow that is progressively updated, giving all the accumulating totals of those joining or leaving the drug as the years go by for the entire and growing national cohort.

Annual cohorts can be characterised individually within the model, with a different usage profile, drop out rate and suicide rate, (e.g. patients in 2001 did behave differently to those in 1994). The IMR model will also calculate the number of long term patients (LTP) dependant at any time and will give breakdowns of how many patients have been on drug for a given number of years, including costs.

There is considerable evidence that the danger of induced suicide or suicidal acts occurs at any dose transition with SSRIs, particularly in the first weeks of starting the drug, when changing dose mid treatment, or when trying to stop after long use. The IMR model uses a range of suicide rates from clinical data to calculate the total suicides induced in various combinations of depressed and anxious patients both when they start the drug and when they attempt to withdraw.

In summary, IMR will calculate any subtotals for any year and for the whole term: new patients, total patients treated, current long term patients, drop out patients (both short and long term), new long term patients, start drug suicides, withdrawal suicides, total and specific costs etc.

IMR has been used to model the patient flow resulting from the use of paroxetine (Paxil), fluoxetine (Prozac) and sertraline (Zoloft) since introduction in several countries including the US. The IMR patient flow model has general applicability beyond SSRIs and could be used to investigate any drug for which there is a known usage profile.

Graham Aldred