GlaxoSmithKline Research
& Development Limited
980 Great West Road
Brentford
Middlesex
TW8 9GS

Tel. +44 (0)20 8047 5000
www.gsk.com

Jon Jureidini
Clinical Professor
Discipline of Psychiatry
The University of Adelaide
Department of Psychological Medicine
Women's and Children's Hospital
North Adelaide
5006
Australia

29 May 2014

Dear Professor Jureidini

Thank you for your letter of April 21 2014.

I am pleased that Case Report Forms for Study 329 that we committed to providing are now available and you have access to the anonymised patient level data, following approval of your research proposal by the independent review panel.

With regard to the points raised in your letter, I think you perhaps misunderstood my position with regard to the use of randomised controlled trials (RCTs) as a method of detecting safety signals with a medicine.

I hope that you agree that well designed randomised controlled trials provide the most reliable evidence to determine the efficacy and safety of a treatment. I also agree with you that individual trials can, for a variety of reasons, not always give the full picture and so it is important to look at the consistency of the data coming from other trials as well. Statistical significance is an accepted method by which to assess consistency in both individual studies and pooled datasets.

In our research investigating paroxetine's safety and efficacy in paediatrics the individual trials had shown an inconsistent and variable pattern of both safety and efficacy. Study 329 showed an imbalance in possibly suicide-related events which was not consistent with other data emerging around the same time. As I have detailed previously, it was only after pooling all the data together from individual randomised controlled trials that we saw a statistically significant association.

Registered in England & Wales
No. 835139

Registered office
980 Great West Road
Brentford, Middlesex. TW8 9GS

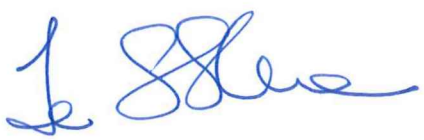
Once we had analysed all the data together, and saw a statistically significant association with an increased risk of possibly suicide-related adverse events among adolescent patients taking paroxetine, we took the information to regulatory authorities, communicated the information to the medical community and published the information in the peer reviewed literature (Apter et al as referenced in my letter from 12 December 2013). Some regulatory authorities agreed with our analysis immediately and product labels were amended on the basis of the findings while others requested more detailed and wider analysis of trials in this area and public discussion. FDA's own review of over 20 trials of various SSRIs published by Hammad et al (also referenced in my letter from 12 December 2013) concluded that the use of these medicines in paediatric patients is associated with 'a modestly increased risk of suicidality'. Subsequent actions by GSK and regulatory authorities ensured that paroxetine product information detailed the association between all antidepressants including paroxetine and an increased risk of suicide-related events in this patient group. This information was widely communicated to prescribing physicians likely to use paroxetine and not only to investigators.

The safety and well-being of the patients who take part in our trials is of paramount importance to me personally as well as to GSK as a company. With respect, I cannot agree with your comment that our approach is "in keeping with GSK's commercial interests".

As I have mentioned in my earlier letters, it is standard in clinical trials carried out according to good clinical practice guidelines for our trial investigators and treating physicians to be responsible for patients' medical care during and after a trial. This would include the management of any adverse experiences that arise during the trial. Being closest to patients' medical histories, they are best placed to do this and we are confident of their commitment to provide the care patients need.

In terms of next steps in your analysis of the data from study 329, I trust you are in the process of conducting your analysis. I would reiterate my earlier offer of support to your team if they require advice on how to navigate the datasets or they have questions related to the access system itself. Please do not hesitate to get in touch on either aspect. And obviously I remain available to discuss the conclusions of your analysis, following its completion and publication in a scientific journal.

Yours sincerely



James Shannon
Chief Medical Officer