GlaxoSmithKline
Vaccines

**Via email: puliyel@gmail.com**

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Wavre, 14 January 2015

Dear Dr. Puliyel,

Your email dated 12 January 2015 addressed to Sir Andrew Witty in which you make reference to GlaxoSmithKline's *Infanrix-hexa* Periodic Safety Update Report (PSUR) for the period 23 October 2009 to 22 October 2011 has been forwarded to me in my capacity as the GlaxoSmithKline (GSK) Vaccines Chief Medical Officer.

At the outset, on behalf of GSK, please accept my thanks for reaching out to us and for sharing your analysis of the data in the PSUR relating to the cases of Sudden Infant Death reportedly occurring in children who previously were vaccinated with *Infanrix-hexa*. At GSK, patient safety is of paramount importance to us and we take the safety of those who place their trust in our medicines and vaccines very seriously. We have robust systems and process in place that enable us to carefully monitor and continuously evaluate the safety of all of our products. We appreciate your sharing your analysis with us to give us an opportunity to evaluate it.

Before specifically addressing your analysis, it's important to note that the issue of whether there is an increased risk of Sudden Infant Death following vaccination generally and following vaccination with DTP-containing vaccines more specifically is one that has been considered and thoroughly evaluated not only by GSK but also by a number of world-renowned regulatory agencies and public health authorities, including the European Medicines Agency, the US Centers for Disease Control and Prevention and the World Health Organization. The clear consensus amongst such agencies and authorities is that one cannot reasonably conclude, based on available data and information, that there is a causal relationship between vaccination generally or vaccination with *Infanrix hexa* and Sudden Infant Death.

Regarding the a analysis you were kind enough to send to us and which we have since learned you have submitted to PubMed, we note that you have used the period of 10-19 days post-vaccination as a control for the period of 0-9 days post-vaccination to determine whether there is an excess of Sudden Infant Deaths in the first nine days following administration of *Infanrix-hexa*.

Based on the figures presented in Table 36 of the GSK PSUR referred to above and a second table that you prepared entitled "Daily increment in Sudden Death following Infanrix hexa in children in their first and second year of life," you have suggested that if the reported sudden death rates had been "coincidental SIDS deaths," there should not have been a a difference in the number of reported sudden deaths between the two periods of time (0-9 days v. 10-19 days). Such an assumption (that there should be no difference in the number of cases reported during the two time periods) could be valid only if the reporting of sudden death cases were to occur independently of the time from vaccination to death. In other words, the underlying premise of your analysis would thus be valid **only if** a sudden death case were to have equal probability of

being spontaneously reported regardless of whether it occurred on the day of vaccination or 2 weeks later.

Such an equal probability is highly unlikely. We know from the extensive spontaneous report data available to us that reporting of cases does not occur independently of the time from vaccination to event. On the contrary, available data show that potential reporters are much more likely to think about a potential causal association and thus report an event when the event occurs shortly after vaccination than when it occurs weeks later.

In light of the above, we remain confident in the conclusions previously reached by GSK and shared with regulatory agencies and public health authorities worldwide that the currently available data do not suggest an increased risk of Sudden Infant Death following vaccination with *Infanrix-hexa*. Nevertheless, as part of our ongoing monitoring and evaluation of the safety of all of medicines and vaccines, we will continue to monitor and evaluate all cases of Sudden Infant Death reported and share the results of those analyses with authorities in those countries where *Infanrix hexa* is licensed. Should the available data and information change to suggest that there is such an increased risk, we remain committed to promptly notifying the authorities and to taking the necessary actions to communicate such data and information to healthcare professionals.
I note that the email that you sent to Sir Andrew Witty was addressed to "undisclosed-recipients." As we have no way of knowing to whom the email was directed other than Sir Andrew, we ask that you share this response with the other recipients of your email.
In the meantime, we thank you again for taking the time to share your analysis with us.

Sincerely,

Dr Norman Begg
Chief Medical Officer, GSK Vaccines