

**Australian Technical Advisory Group on Immunisation (ATAGI) and
Therapeutic Goods Administration (TGA) Joint Working Group**

**Report of an Analysis of Febrile Convulsions Following Immunisation in Children
Following Monovalent Pandemic H1N1 Vaccine (Panvax[®]/Panvax Junior[®], CSL)**

28 September 2010

In April 2010, an ATAGI – TGA joint working group was established to provide advice to the Chief Medical Officer on adverse events following the 2010 trivalent seasonal influenza vaccine (TIV). In September 2010, this group was reconvened to re-examine the rate of febrile convulsions following administration of the monovalent pandemic H1N1 influenza vaccine, Panvax/Panvax Junior (CSL) in young children, and in particular, to address the following questions:

- 1. Is the rate of early onset systemic adverse reactions (ie fever, febrile convulsions) in Panvax/Panvax Jnr recipients aged less than 5 years, and particularly in those less than 3 years, higher than expected?*
- 2. If the rate of adverse events following immunisation (AEFI) post-Panvax/Panvax Jnr is higher than expected, is this sufficient to alter the overall risk/benefit profile of the use of Panvax/Panvax Jnr?*
- 3. If the risk/benefit profile of Panvax/Panvax Jnr is unfavourable, do the findings alter the recommendations for use of Panvax in this age group and if so how?*

Febrile convulsions in young children are well recognised in the setting of various viral infections, with rates estimated to be as high as at between 10 to 20% in children hospitalised with influenza.^{1,2} Febrile convulsions are also a rare but recognised adverse event following immunisation (AEFI), and have been reported in influenza vaccine post-marketing data at a rate between 1/10,000 and 1/1000 doses, as well as in association with DTPa, Hib and poliomyelitis vaccines.

Detailed investigations in Australia from April to July 2010 determined that the 2010 trivalent influenza vaccine Fluvax/Fluvax Junior (CSL) was associated with febrile convulsions in children < 5 years of age at a rate of 500-700 per 100,000 doses. A report of these investigations is on the TGA website (<http://www.tga.gov.au/alerts/medicines/flu vaccine-report100702.htm>). While data available at that time did not suggest a similarly high rate of febrile convulsions in Panvax/Panvax Jnr recipients, subsequently the question of whether Panvax/Panvax Jnr is also associated with a lesser, but still significant, increased risk of febrile reactions and febrile convulsions arose.

As at 17 September 2010 the TGA had received a total of 48 unique reports of febrile convulsions in children aged less than 5 years who had received Panvax or Panvax Jnr. Each of these cases (the numerator) were carefully reviewed to ensure that a consistent case definition was applied and that the timeframe and age range of the cases (numerator) used in the analysis were consistent with those used in determining the number of doses administered (the denominator).

Of the 48 reports, 19 were excluded from the analysis because:

- 5 occurred in children aged ≥ 4 years; these were excluded from the rate calculation because the available denominator data were in children < 4 years of age;
- 6 reports were of febrile convulsions occurring more than 24 hours post-vaccination; cases occurring more than 24 hours post-vaccination are considered unlikely to be the result of a reaction to the influenza vaccine;
- 6 were considered not to be febrile convulsions on detailed clinical review; and
- 2 cases occurred after 1 June 2010; these were excluded from the rate calculation because the available denominator data used were based on doses administered up to and including 31 May 2010.

However among these 29 cases it was also noted that 9 children had received one or more other vaccines at the same time, and a further 5 had a concurrent illness or infection that could have given rise to a fever or febrile convulsion.

While it is not possible to ascertain the precise number of doses of Panvax that have been administered in children, using data from a number of sources (Australian Institute for Health and Welfare,

Australian Childhood Immunisation Register, NSW Health, QLD Health, and CSL) this has been estimated at between 168,000 and 270,000.

Using these figures, the overall rate of febrile convulsions post Panvax/Panvax Jnr is estimated to lie between 7 and 18 per 100,000 doses nationally. However if the raw figure of 48 cases were utilised (the worst case scenario) the rate would be 29 per 100,000.

The estimate of between 7 and 18 febrile convulsions per 100,000 vaccine doses (or even the less plausible 29 per 100,000 doses) remains within the specified range stated within the Panvax Product Information, which identifies febrile convulsions as a rare adverse event following immunisation (AEFI) based on post-marketing surveillance data. Rare side effects are generally regarded as those that occur at a rate between 1/1,000 and 1/10,000 doses (between 10–100/100,000 doses).

This rate is substantially less (at least 25-fold lower) than the estimated rate of 700 per 100,000 febrile convulsions seen with Fluvax/Fluvax Junior. It is considered that this rate is acceptable, in light of the overall benefits anticipated by vaccination against pandemic H1N1 influenza.

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- 1) Chiu SS, Tse CYC, Lau YL, Peiris M. Influenza A infection is an important cause of febrile seizures. *Pediatrics*. 2001;108(4).
 - 2) Newland JG et al. (2007) Neurologic complications in children hospitalized with influenza: characteristics, incidence, and risk factors. *J Pediatr* 150:306–310.