

## Short reports

# SURVEILLANCE OF ADVERSE EVENTS FOLLOWING IMMUNISATION: THE MODEL OF SAEFVIC, VICTORIA

Hazel J Clothier, Nigel W Crawford, Ann Kempe, Jim P Buttery

## Abstract

State-based adverse events following immunisation (AEFI) reporting systems in Australia demonstrate marked regional differences in surveillance methodologies and reporting rates. To improve AEFI services in Victoria, Surveillance of Adverse Events Following Vaccination in the Community (SAEFVIC) was established in 2007. SAEFVIC comprises a central reporting enhanced passive surveillance system integrated with clinical services. AEFI may be reported by phone, fax or on-line. Immunisation nurse specialists follow up all reports, coupled with physician review as required. Supervised re-vaccination in a hospital environment, when appropriate, helps ensure clinical support for vaccinees, families and health-care providers. The *Brighton Collaboration*, the *Australian Immunisation Handbook* and in-house case definitions are used to categorise AEFI reports. In the first 3 years (2007–2010) of operation 3,265 reports were received, describing 4,293 AEFI. The number of reports received increased annually over the 3-year period. Seventy-six per cent of AEFI met one of 52 established case definitions and the remainder were recorded verbatim; 22% of reported AEFI were considered severe. Of 1,086 persons reporting an AEFI in 2009, 356 (36%) attended for a clinical consultation and 325 (83%) were revaccinated, of which 114 were day stay or overnight patients. Enhanced passive AEFI surveillance using integrated clinical services has been shown to improve adverse event reporting with reporting rates in Victoria increasing from 2.6 per 100,000 in 2003 to 13.5 per 100,000 per annum in 2009. This report describes the SAEFVIC service model and summarises outcomes and lessons learnt in the first 3 years of operation. *Commun Dis Intell* 2011;35(4):294–298.

Keywords: Surveillance, adverse event, immunisation, vaccine safety

## Introduction

The international definition of an adverse event following immunisation (AEFI) is ‘an unwanted or unexpected event following the administration of a vaccine(s). AEFI may be caused by a vaccine(s) or may

occur by coincidence: that is, it would have occurred regardless of vaccination’. AEFIs also include conditions that may occur following the incorrect handling and/or administration of a vaccine.

In Victoria prior to 2007, AEFI surveillance was conducted as a passive system whereby reports were sent directly to the Adverse Drug Reaction Unit (ADRU) in the Therapeutic Goods Administration (TGA) and reviewed by the Adverse Drug Reactions Advisory Committee (ADRAC), now replaced by the Advisory Committee on the Safety of Medicines (ACSOM). This system was known to be insensitive and AEFI events appeared to be significantly under-reported: the overall reporting rate per 100,000 population in 2002 being 2.6 in Victoria, compared with the Australian Capital Territory (22.5 per 100,000) and South Australia (10.8 per 100,000) where enhanced surveillance systems were already in place.<sup>1,2</sup>

In May 2007, under contract with the Victorian Department of Health, an enhanced passive surveillance system known as Surveillance of Adverse Events Following Vaccination in the Community (SAEFVIC) was initiated. SAEFVIC comprised a partnership led by the Murdoch Childrens Research Institute, with the Royal Children’s Hospital, the Victorian Infectious Diseases Service at the Royal Melbourne Hospital and Monash Medical Centre. The service continues to provide Victorian-wide enhanced passive surveillance integrated with a clinical support service. Patients and their families, and immunisation service providers can access advice and support from expert immunisation nurses and physicians. The objectives of the system were to: increase the number of AEFI reports, to maximise confidence in the immunisation program for those who have experienced AEFI, and importantly, to provide clinical feedback directly to vaccinees and the AEFI reporters. Effective clinical communication is paramount for SAEFVIC to function effectively.

## Aims

SAEFVIC aims to provide increased early detection and appropriate rapid response to AEFI in adults and children, integrated with clinical support for reporting health care workers and patients/families.

The intention is to enhance the passive surveillance of all significant or rare AEFI, regardless of causality. The surveillance information is used to detect vaccine safety 'signals', prompt action and maintain confidence in immunisation programs. This collaboration aims to deliver a system with world-leading sensitivity for Victorian health authorities to rapidly detect and research vaccine safety concerns, whether they are new trends or just temporally associated events.

This report describes the Victorian SAEFVIC service model and summarises outcomes in the first 3 years of operation.

## Methods

### Reporting

AEFI may be reported by phone, fax or, as of 2010, on-line. SAEFVIC encourages reporting from health care professionals, including immunisation providers and accepts self or parent reports. Reports sent by the vaccine service-provider directly to the TGA are re-directed back to SAEFVIC. Once assessed by a SAEFVIC immunisation nurse all reports are forwarded to the TGA.

### Follow-up

Accredited immunisation nurses follow up all reports of AEFI and discuss with reporters the nature of the AEFI, any ongoing concerns and strategies for future vaccinations. Informed consent to contact the vaccinee or their guardian is normally provided at the time of the report or at the time of follow-up. The initial contact is by telephone and a minimum of three attempts made, before a letter is sent to the reporter to advise SAEFVIC has been unable to follow-up with the case.

### Clinical review

All persons reporting a serious AEFI (requiring hospitalisation or having ongoing sequelae) or those who have concerns about future vaccinations are offered the option to attend a clinical review with a medical specialist. Clinics are available on a weekly basis at the Royal Children's Hospital and on a fortnightly basis at Monash Children's Hospital. In addition, there are monthly adult vaccine safety clinics in two tertiary centres, the Royal Melbourne Hospital and the Monash Medical Centre. Clinic appointments are on average for 30 minutes and are organised so that revaccination, if indicated, is possible at the time of the appointment. These may be provided in the hospital clinic under medical or nursing supervision if required. Supervised vaccination may be within the clinic, as a day patient or supported by an overnight admission depending on the severity and time of onset of previous AEFI.

For rural areas, SAEFVIC clinicians can liaise with a local clinician to provide a more convenient consultation option.

### Passive surveillance

AEFI are recorded using standard case definitions where available (currently  $n=52$ ), in the following order: the *Brighton Collaboration* ( $n=23$ ),<sup>3</sup> the *Australian Immunisation Handbook* ( $n=22$ )<sup>4</sup> and then the definitions derived by SAEFVIC from published literature ( $n=7$ ). The remaining AEFI are recorded verbatim using standard medical terminology where possible for consistency. Regular analysis for quarterly reporting to the Victorian Department of Health is conducted and case reports of points of interest are published in the Immunisation newsletter.

Additional analysis is conducted as required in response to local, national or international concerns or in response to possible safety signals or unusual trends noticed in the AEFI data. AEFI rates are calculated by the type of vaccine delivered for those vaccines recorded on the Australian Childhood Immunisation Register (ACIR). This means the analysis is limited to children under 7 years of age and will be affected by any under-reporting to ACIR.<sup>5</sup> Additional calculations are possible if appropriate denominator data are available, for example the Department of Health records of vaccine doses distributed.

SAEFVIC contributes to national AEFI surveillance by forwarding reports to the TGA. As an additional vaccine safety review, SAEFVIC also reviews all TGA AEFI summaries forwarded to each state, in collaboration with the Immunisation Section of the Victorian Department of Health.

### Data analysis

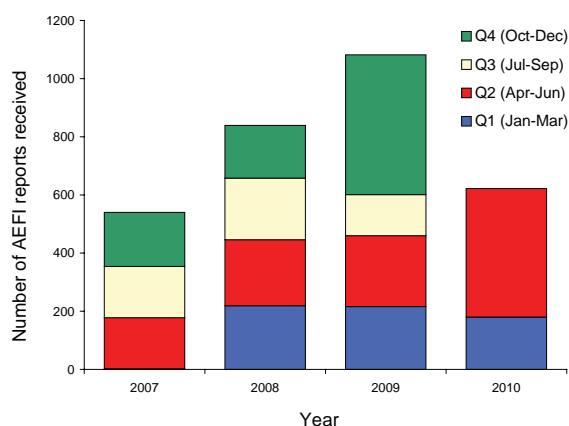
AEFI reported to SAEFVIC from 1 July 2007 to 30 June 2010 were analysed by number, AEFI symptoms reported and population-based reporting rate. Clinical review data were analysed for reports received for the calendar year 2009. Analyses were conducted using Microsoft Excel and STATA 11.0. Australian Bureau of statistics estimated resident population data were used to calculate AEFI rates.

## Results

For the 3-year period July 2007 to June 2010, 3,265 reports describing 4,293 AEFI were received. Between 1 and 6 separate AEFI case definitions were extracted in relation to each report received. A total of 5,648 vaccines were administered to the subjects of AEFI reports in the 3 year period with between 1 and 5 vaccines included in each of the AEFI reports in this period. The number of reports

received increased in each 12-month period, from 804 in 2007–2008 to 1,336 in 2009–2010. There was a notable increase observed in the fourth quarter of 2009 and second quarter of 2010 (Figure 1). The first increase coincided with the release of the H1N1 2009 pandemic influenza vaccine (PANVAX®) and the second increase coincided with the release of the trivalent seasonal influenza vaccine when more febrile seizures in children were noted (Figure 1).<sup>6</sup>

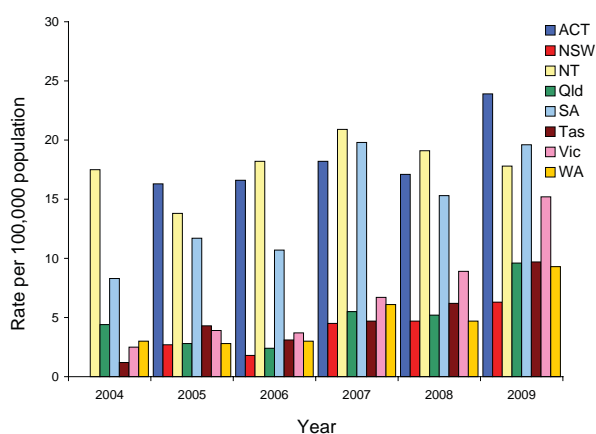
**Figure 1: Number of adverse events following immunisation reports received, SAEFVIC, May 2007 to July 2010, by year and quarter**



AEFI reporting rates per 100,000 population increased from baseline reporting rates of 2.6 per 100,000 in 2003, prior to SAEFVIC commencing operation, to 13.5 per 100,000 per annum in 2009 (Figure 2).<sup>7,8</sup>

Of all 4,293 AEFI reports, 3,262 (76%) were classified according to previously discussed case definitions. The most frequently reported AEFI were: injection site reactions (minor, common or expected) 987

**Figure 2: Adverse events following immunisation reporting rates per 100,000 population, 2003 to 2009, by state or territory<sup>7,8</sup>**



(23%); fever ( $\geq 38^{\circ}\text{C}$ ) 472 (11%); rash 429 (10%); urticaria 300 (7%); and vasovagal episode 215 (5%). Of all 4,293 AEFI reports, 944 (22%) were considered serious (requiring hospitalisation or having ongoing sequelae). Of the serious AEFI reported there were 26 cases of anaphylaxis, 16 intussusception and 32 afebrile seizures. Three deaths were reported following vaccination. The deaths were due to ovarian cancer, sudden infant death syndrome and a car accident. Review by SAEFVIC clinicians of the 3 deaths did not support a likely aetiological association between vaccination and subsequent death.

An increased proportion of reports received by SAEFVIC related to people who required advice prior to vaccination. These types of reports increased from one in 2008 to 75 or 10% of all reports received in the first 6 months of 2010. The main concern raised related to the influenza vaccine for individuals with a past history of egg allergy. These reports are recorded on the database as 'non-events' in order to provide clarity that no adverse event has occurred.

Of the 1,086 people for whom AEFI were reported in 2009, 356 (36%) attended for clinical review. Of the 41 people who presented in 2009 with concerns prior to receiving vaccine, 33 (80%) also attended for clinical review. Of 356 clinic attendees, 325 (83%) continued with vaccination, 95 (26%) were vaccinated in a hospital setting and 19 (6%) were admitted as day or overnight patients for additional monitoring.

In 2010, most of the AEFI reports were sent directly to SAEFVIC from across Victoria, with only 2 reports being redirected back from the TGA. This was a decrease compared with the 85 reports (19% of all reports received) in 2007, which was the first year of the program.

## Discussion

In the 3 years following the establishment of SAEFVIC as a dedicated Victorian passive AEFI surveillance system, the number of AEFI reported increased. The Victorian AEFI reporting rate of 13.8 per 100,000 population, is now closer to that of similar sized states.<sup>8</sup>

Scheduled and ad hoc analyses of data have identified and permitted further investigation of potential immunisation concerns arising during the review period. In 2007, following introduction of the 4-valent human papillomavirus (4vHPV) vaccine, SAEFVIC investigated potential signals such as an event of mass psychogenic illness occurring in school-aged girls following administration of the 4vHPV vaccine<sup>9</sup> and later a review of all cases of syncope and seizures post the 4vHPV vaccine.<sup>10</sup> SAEFVIC has reported on rare AEFI cases such as 4vHPV vac-

cine associated lipotrophy, measles-mumps-rubella vaccine associated orchitis, and prolonged rotavirus vaccine excretion in an infant diagnosed with severe combined immunodeficiency.<sup>11–13</sup> SAEFVIC has also been involved in supporting active surveillance of intussusception following rotavirus vaccine.<sup>14</sup>

Offering vaccination under an appropriate level of supervision permits adequate medical support in the event of a recurrence and appears to improve parental, adult vaccinee and community confidence, in the immunisation program. Stringent clinical review and monitoring for recurrence of AEFI has enabled SAEFVIC to provide evidence-based advice for administration of vaccine to infants experiencing apnoea as an AEFI.<sup>15</sup> Most importantly, it also allows us to document the risk of recurrence of AEFI; an area where current evidence is sparse.

In the absence of a more systematic, centralised, national AEFI surveillance system, we believe SAEFVIC presents a suitable model for enhanced passive surveillance of AEFI. The link between the reporting system and access to individualised clinical advice and possible vaccination or re-vaccination under medical supervision in those with a previous AEFI, provides an incentive for the initial reporting of AEFI. A vaccine safety service was established in Western Australia based on the SAEFVIC model.

SAEFVIC has an advisory board of stakeholders including local government, immunisation nurses, physicians and general practitioners. The board meets annually and assists us to improve the reporting system, the clinical service, and communication strategies. The introduction of new vaccines to the National Immunisation Program such as HPV, rotavirus and monovalent H1N1 vaccine, meant the service has had to adapt rapidly and has been greatly enhanced through the electronic reporting function introduced in 2010. Future enhancements being considered are to improve the compatibility with other state reporting systems, reporting AEFI rates by vaccines administered and maximising reporting from immunisation providers.

## Conclusion

Enhanced passive AEFI surveillance linked to an integrated clinical immunisation service has been shown to improve AEFI reporting within Victoria and has contributed to the detection and investigation of both potential and actual AEFI signals.

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## Conflict of interest

NWC and JPB have acted as chief investigators for epidemiological studies sponsored by vaccine manufacturers (CSL) and serological testing (Merck). Industry sourced honoraria for sitting on advisory boards (NWC), data safety monitoring boards (JPB), lecturing (NWC) and travel expenses for attendance at scientific meetings, are paid directly to an administrative fund held by Murdoch Childrens Research Institute.

## Author details

Ms Hazel J Clothier, Surveillance Manager<sup>1</sup>  
Nigel W Crawford, Paediatrician<sup>1</sup>  
Ann Kempe, Lecturer<sup>2</sup>  
Jim P Buttery, Director and paediatrician<sup>1,3</sup>

1. SAEFVIC, Murdoch Childrens Research Institute, Flemington Road, Parkville, Victoria
2. School of Nursing and Midwifery, Monash University, Melbourne, Victoria
3. Department of Paediatrics, Monash University, Melbourne

Corresponding author: Ms Hazel J Clothier, Surveillance Manager, SAEFVIC, Murdoch Childrens Research Institute, Flemington Road, PARKVILLE VIC 3052. Telephone: +61 3 9345 4143. Facsimile: +61 9345 4163. Email: Hazel.clothier@mcri.edu.au

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