

## **ATAGI Statement: Use of multi-dose vials in vaccination programs**

### ***Why has Australia chosen to use multi-dose vials for the H1N1 program?***

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#### **Summary**

The use of multi-dose vials allows the earliest possible availability of H1N1 vaccine by improving the efficiency of vaccine manufacture and administration. By these means, the maximum number of people, especially those more vulnerable to severe complications of influenza, can receive H1N1 vaccine as early as possible. This is important, especially if there is sustained transmission during the summer months of 2009-10 and/or an early second wave of H1N1 in 2010. A comprehensive support package for immunisation service providers, including guidelines on the use of multi-dose vials, will be supplied with the H1N1 influenza vaccine rollout. Strict adherence to these guidelines will eliminate the small but important risk of contamination and/or transmission of infective agents caused by inappropriate infection control practices.

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#### **Advantages of multi-dose vials**

Multi-dose vials have been used in immunisation programs since the 1930s and have been administered to many millions of people worldwide. For vaccines used in multi-dose formulations, thiomersal offers better protection from potential bacterial and fungal contamination than other preservatives such as 2-phenoxyethanol.<sup>1</sup>

Vaccines presented in multi-dose vials are currently used in many other countries. These include the United States for most annual seasonal influenza vaccines, diphtheria and tetanus toxoids, inactivated poliomyelitis vaccine; measles, mumps and rubella vaccine; quadrivalent meningococcal polysaccharide vaccine and the 23 valent pneumococcal polysaccharide vaccine<sup>2</sup>, and Canada for some annual seasonal influenza vaccine, hepatitis B vaccine and quadrivalent meningococcal polysaccharide vaccines.<sup>3</sup> The WHO Expanded Programme on Immunization uses vaccines presented in multi-dose vials for diphtheria, tetanus, pertussis, hepatitis B, and *Haemophilus influenzae* type b in many countries.<sup>1</sup>

Multi-dose vials are no longer routinely used in the Australian health care setting as single dose preparations are now available for all vaccines delivered under the National Immunisation Program (NIP). However, where a large scale immunisation program needs to be rapidly delivered, a number of factors favour the use of multi-dose vials.<sup>4</sup> These include expedited vaccine manufacture and distribution and reducing vaccine wastage. With respect to manufacture, the presentation of vaccine in MDVs means vaccine is available in a much more timely fashion. Multi-dose vials also have significantly lower filling costs, with less need for the overfill that occurs when preparing either single dose vials or syringes, and a significant reduction in packaging costs.<sup>1, 4, 5</sup> With respect to distribution, the main advantage is more efficient storage.<sup>4, 6</sup> Single dose vials require approximately six times more refrigerator space and single dose syringes a third more space again than multi-dose vials. This can be an issue for many practices or clinics where vaccine storage is already at a premium.

There are particular benefits of multi-dose vials in high-volume clinic settings. In a study conducted in Canada, influenza vaccines presented in pre-filled syringes were directly compared with those presented in multi-dose vials in a large clinic setting.<sup>6</sup> The problems with pre-filled syringes included; the inability to choose needle sizes; difficulties opening packaging; single dose syringes with large air bubbles requiring expulsion; and extra refrigeration required for pre-filled syringes (including purchase of vaccine refrigerators). Although pre-filled syringes required less hands-on time drawing up vaccines, with potentially reduced labour costs and obviated the need to purchase separate syringes and needles, the authors concluded that multi-dose vials offered the best value overall in this setting.<sup>6</sup>

## Precautions with multi-dose vials

The primary risk with use of multi-dose vials is a breach in infection control through user error. Multi-dose vials can be contaminated when, for example:

- an unsterile needle is inserted into the vial;
- a needle is left in the vial for multiple redraws;
- the vial septum is allowed to come into contact with liquids (such as being submerged in ice water in an esky or prepared in a contaminated area); and
- a contaminated syringe is re-used.

These risks are increased if the vial does not contain a preservative, such as thiomersal, to prevent microbial growth.

The potential avenues for contamination of multi-dose vials and/or transmission of infectious agents can be overcome by careful adherence to appropriate infection control protocols. These are well documented in both Australian and international guidelines. Although the Australian Drug Evaluation Committee (ADEC) of the Therapeutic Goods Administration (TGA) has declined registration for pharmaceuticals presented in multi-dose vials on several occasions, it has also stated that there are special circumstances where their use is appropriate and can meet registration requirements.<sup>7</sup> For example, BCG vaccine is currently registered by the TGA for use in a multi-dose vial presentation. Prototype pandemic influenza H5N1 vaccines, (Emerflu, Panvax H5N1 and Prepandemerix), have been registered in multi-dose vial presentations by ADEC and on the 18<sup>th</sup> September 2009, registration approval was given for the 5mL and 10mL multi-dose vial presentations of PANVAX H1N1 vaccine.

Although there have been multiple case reports of instances of transmission of bacteria or blood borne viruses through inappropriate practice in the use of multi-dose vials in well-resourced countries, including Australia, these have almost entirely applied to specific high risk settings, such as haemodialysis, or contamination of anaesthetic vials.<sup>5,8</sup> In contrast, transmission of infective agents or laboratory-confirmed contamination has been rarely documented in relation to vaccines or immunisation programs in recent times. There are historical examples in industrialised countries and more recent examples in poorly resourced settings in non-industrialised countries, (which have prompted recent revision of WHO protocols).<sup>9</sup>

In the context of Australian vaccination programs and with strict adherence to recommended protocols, the risk of contamination or transmission of infection would be negligible.

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## Use of multi-dose vials internationally

The use of multi-dose vials for distribution and administration of seasonal influenza vaccine is well accepted in many comparable countries including the USA and Canada.<sup>10,11</sup> These countries, like Australia, strongly discourage the use of multi-dose vials in other health care settings outside the well-defined and low risk scenario prevailing in immunisation.

In addition, most countries who have committed to providing monovalent pandemic H1N1 vaccine to their populations, including the USA, the United Kingdom, and Canada, will be using vaccine presented in multi-dose vials.<sup>12-14</sup>

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## References

1. World Health Organization. Thiomersal and vaccines: questions and answers [http://www.who.int/vaccine\\_safety/topics/thiomersal/questions/en/index.html](http://www.who.int/vaccine_safety/topics/thiomersal/questions/en/index.html) (Accessed September 2009).
2. United States. CDC. Vaccine management Recommendations for Storage and Handling of Selected Biologicals, April 2009. <http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/C/storage-handling.pdf>
3. National Advisory Committee on Immunization (NACI). Thimerosal: updated statement. *CCDR* 2007;33 (ACS-6): 1-13.

4. Drain. P.K.; Nelson C.M, Lloyd J.S. Single-dose versus multi-dose vaccine vials for immunization programmes in developing countries. *Bulletin of the World Health Organization*. 2003; 81: 726-31.
  5. Hutin Y, Hauri A, Chiarello L, et al. Best infection control practices for intradermal, subcutaneous and intramuscular needle injections. *Bulletin of the World Health Organization*. 2003; 81: 493-500.
  6. Scheifele D.W; Skowronski D; King A et al. Evaluation of ready-to-use and multi-dose influenza vaccine formats in large clinics. *Canadian Journal of Public Health*; Sep/Oct 2000; 91: 329-32.
  7. Australian Drug Evaluations Committee (ADEC) Resolution No.5578. 2005. <http://www.tga.gov.au/docs/html/tganews/news19/inbrief.htm> (Accessed September 2009).
  8. Mattner F, Gastmeier P. Bacterial contamination of multiple-dose vials: a prevalence study. *American Journal of Infection Control*. 2004;32: 12-16.
  9. World Health Organization. Policy Statement (2000). The use of opened multi-dose vials of vaccine in subsequent immunization sessions. (*currently under review*) <http://www.who.int/vaccines-documents/DocsPDF99/www9924.pdf> (accessed September 2009).
  10. National Advisory Committee on Immunization (NACI) Statement on Influenza Vaccination for the 2007-2008 season. *CCDR* 2008;34,ACS3;1-46. <http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/07pdf/acs33-07.pdf> (accessed September 2009).
  11. Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2008 Prevention and Control of Influenza *MMWR* August 8, 2008 / 57(RR07):1-60.
  12. United States CDC.General Questions and Answers on 2009 H1N1 Influenza Vaccine Safety [http://www.cdc.gov/h1n1flu/vaccination/vaccine\\_safety\\_qa.htm](http://www.cdc.gov/h1n1flu/vaccination/vaccine_safety_qa.htm) (Accessed September 2009).
  13. Public Health Agency of Canada Frequently Asked Questions - H1N1 Flu Virus [http://www.phac-aspc.gc.ca/alert-alerte/h1n1/faq\\_rg\\_h1n1-eng.php](http://www.phac-aspc.gc.ca/alert-alerte/h1n1/faq_rg_h1n1-eng.php) (Accessed September 2009).
  14. United Kingdom. Department of Health Statement [http://www.immunisation.nhs.uk/publications/Letter\\_260609\\_SwineFlu.pdf](http://www.immunisation.nhs.uk/publications/Letter_260609_SwineFlu.pdf) (Accessed September 2009).
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