

18 October 2006

Dear Health Professional,

Meningococcal B Immunisation Programme Update

This letter is to update you on some developments since the mass immunisation programme ended on June 30, 2006.

We want to provide information on the following areas that we hope will be useful:

1. MeNZB™ effectiveness, including information on disease trends;
2. Monitoring of adverse events following MeNZB™ immunisation;
3. A reminder to record MeNZB™ vaccinations on the National Immunisation Register.

Please distribute this among your staff.

Your role in the programme has been critical to its success and I thank you for your support and participation.

Yours sincerely,

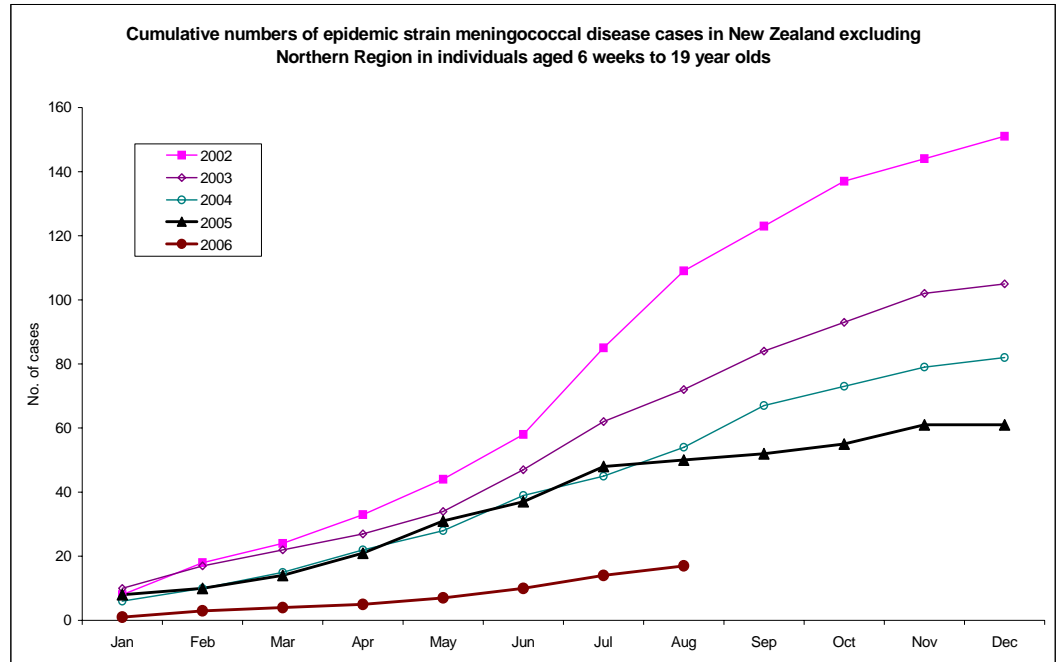
A handwritten signature in black ink, appearing to read 'J O'Hallahan', with a long horizontal flourish extending to the right.

Jane O'Hallahan
Director - Meningococcal B Immunisation Programme

Topic 1	MeNZB™ effectiveness																																																																														
<p>Overview</p>	<ul style="list-style-type: none"> Results of an effectiveness study carried out by Victoria University show that the MeNZB™ vaccine is 80 per cent effective. This study also shows children and young New Zealanders who are not immunised have a five times higher risk of getting the epidemic strain of group B meningococcal disease than those who are fully immunised. The effectiveness study will be published in a scientific peer reviewed journal later this year. 																																																																														
<p>Explanation</p>	<ul style="list-style-type: none"> A number of methods are being used to assess the effectiveness of the MeNZB™ vaccine in New Zealand children. These include monitoring of meningococcal disease notifications and cases in fully vaccinated individuals (vaccine breakthroughs), the study carried out by Victoria University, and seroprevalence and carriage studies. The staggered roll-out meant it was not until mid-2005 that a significant number of New Zealanders were fully immunised, but the initial impact of the vaccine has seen a critical reduction in the number of epidemic strain meningococcal cases since the immunisation programme began. The following graphs show the monthly number of epidemic strain cases aged under 20 years in the northern region (where the programme started) and the rest of New Zealand for 2002-2006. <p>Northern region</p> <ul style="list-style-type: none"> There was no evidence of a decrease in cases in the northern region prior to introduction of the vaccine in mid-late 2004. However a dramatic decrease in cases occurred in 2005 and has continued in 2006. Cases of the epidemic strain fell by 76 per cent between 2003 and 2005. In Maori and Pacific communities, with the highest rates of the disease, cases fell by 90 per cent and 70 per cent respectively. <div data-bbox="475 1366 1516 2016"> <p style="text-align: center;">Cumulative numbers of epidemic strain meningococcal disease cases in the Northern Region among individuals aged 6 weeks to 19 years</p> <table border="1"> <caption>Cumulative cases in Northern Region (Jan-Dec)</caption> <thead> <tr> <th>Year</th> <th>Jan</th> <th>Feb</th> <th>Mar</th> <th>Apr</th> <th>May</th> <th>Jun</th> <th>Jul</th> <th>Aug</th> <th>Sep</th> <th>Oct</th> <th>Nov</th> <th>Dec</th> </tr> </thead> <tbody> <tr> <td>2002</td> <td>5</td> <td>10</td> <td>15</td> <td>20</td> <td>25</td> <td>32</td> <td>38</td> <td>48</td> <td>58</td> <td>62</td> <td>62</td> <td>67</td> </tr> <tr> <td>2003</td> <td>5</td> <td>12</td> <td>18</td> <td>20</td> <td>32</td> <td>34</td> <td>50</td> <td>57</td> <td>68</td> <td>78</td> <td>82</td> <td>84</td> </tr> <tr> <td>2004</td> <td>5</td> <td>8</td> <td>12</td> <td>18</td> <td>22</td> <td>26</td> <td>37</td> <td>43</td> <td>51</td> <td>58</td> <td>60</td> <td>61</td> </tr> <tr> <td>2005</td> <td>2</td> <td>3</td> <td>4</td> <td>6</td> <td>8</td> <td>12</td> <td>15</td> <td>17</td> <td>18</td> <td>18</td> <td>20</td> <td>20</td> </tr> <tr> <td>2006</td> <td>2</td> <td>2</td> <td>4</td> <td>5</td> <td>5</td> <td>7</td> <td>13</td> <td>14</td> <td>14</td> <td>14</td> <td>14</td> <td>14</td> </tr> </tbody> </table> </div>	Year	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	2002	5	10	15	20	25	32	38	48	58	62	62	67	2003	5	12	18	20	32	34	50	57	68	78	82	84	2004	5	8	12	18	22	26	37	43	51	58	60	61	2005	2	3	4	6	8	12	15	17	18	18	20	20	2006	2	2	4	5	5	7	13	14	14	14	14	14
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Rest of New Zealand

- In the remainder of the country there is evidence that the number of cases was decreasing prior to the introduction of the vaccine during the first half of 2005. However this decrease has been much more marked in 2006 suggesting that the vaccine has also had an effect.



- The effectiveness study carried out by Victoria University is able to separate the effects of the vaccine from the effects of the natural progression of the epidemic over time.
- Since the programme began in July 2004, there have been 29 cases of epidemic strain disease in children who have had three doses of MeNZB™ and 158 cases in children who have received less than three doses (including unvaccinated).

Key messages for the public

- This effectiveness study confirms that the vaccine works.
- As time goes on, we will understand more about the impact of the vaccine on the number of Meningococcal B epidemic strain cases.
- It is important that children and young people complete all three doses. For young babies who began their vaccinations before they were six months old, it is critical that they have all four doses.
- It is important to remember that no vaccine provides 100 per cent protection. Most people who are immunised with MeNZB™ vaccine are protected, but the vaccine may not protect every person who receives the full course. The MeNZB™ vaccine will not protect against other strains of meningococcal disease so people need to be vigilant about the signs and symptoms of the disease.

Topic 2	Monitoring of adverse events following MeNZB™ immunisation																																				
Overview	<ul style="list-style-type: none"> With the end of the mass immunisation campaign, the intensive safety surveillance has drawn to a close. The monitoring of adverse events following MeNZB™ is now the same as for other vaccines, i.e. through health professionals reporting adverse events to the Centre for Adverse Reactions Monitoring (CARM). The Independent Safety Monitoring Board (ISMB), established by the Health Research Council of New Zealand, reviewed safety data throughout the programme and advised that it found no evidence for any concern arising from the safety data. The findings from the entire safety monitoring programme will be submitted for publication in peer reviewed scientific journals. Below is a summary of MeNZB™ associated adverse events reported to CARM. More details of the reports can be found on the Meningococcal B Immunisation Programme website: http://www.immunise.moh.govt.nz/safety/safetymonitoringreports.html 																																				
Explanation	<p>From 19 July 2004 to 30 June 2006, over 3 million doses of MeNZB™ vaccine were administered, with almost 1.06 million individuals having received at least one dose of vaccine. For the same period 2,212 spontaneous reports of events following MeNZB™ vaccination were received by CARM. The most frequently reported event terms (irrespective of possible causal association with immunisation) and the proportion of the total reports that these events account for are included in Table 1.</p> <p>Table 1. Most frequent event terms (irrespective of possible causal association) reported to CARM following MeNZB™ vaccination for the period 19 July 2004 to 30 June 2006.</p> <table border="1" data-bbox="491 1196 1501 1671"> <thead> <tr> <th data-bbox="491 1196 842 1290">Events</th> <th data-bbox="842 1196 1166 1290">Number of reports* received to 30 June 2006</th> <th data-bbox="1166 1196 1501 1290">Proportion of total reports* (% n=2212) to 30 June 2006</th> </tr> </thead> <tbody> <tr> <td data-bbox="491 1290 842 1352">Local injection site reactions</td> <td data-bbox="842 1290 1166 1352">925</td> <td data-bbox="1166 1290 1501 1352">41.8</td> </tr> <tr> <td data-bbox="491 1352 842 1384">Skin reactions</td> <td data-bbox="842 1352 1166 1384">804</td> <td data-bbox="1166 1352 1501 1384">36.3</td> </tr> <tr> <td data-bbox="491 1384 842 1415">Fever</td> <td data-bbox="842 1384 1166 1415">705</td> <td data-bbox="1166 1384 1501 1415">31.9</td> </tr> <tr> <td data-bbox="491 1415 842 1447">Gastrointestinal symptoms</td> <td data-bbox="842 1415 1166 1447">577</td> <td data-bbox="1166 1415 1501 1447">26.1</td> </tr> <tr> <td data-bbox="491 1447 842 1478">Headache</td> <td data-bbox="842 1447 1166 1478">250</td> <td data-bbox="1166 1447 1501 1478">11.3</td> </tr> <tr> <td data-bbox="491 1478 842 1509">Musculoskeletal</td> <td data-bbox="842 1478 1166 1509">165</td> <td data-bbox="1166 1478 1501 1509">7.5</td> </tr> <tr> <td data-bbox="491 1509 842 1541">Irritability</td> <td data-bbox="842 1509 1166 1541">122</td> <td data-bbox="1166 1509 1501 1541">5.5</td> </tr> <tr> <td data-bbox="491 1541 842 1572">Syncope/fainting</td> <td data-bbox="842 1541 1166 1572">88</td> <td data-bbox="1166 1541 1501 1572">4.0</td> </tr> <tr> <td data-bbox="491 1572 842 1603">Sleepiness</td> <td data-bbox="842 1572 1166 1603">81</td> <td data-bbox="1166 1572 1501 1603">3.7</td> </tr> <tr> <td data-bbox="491 1603 842 1635">Seizure (non-febrile)</td> <td data-bbox="842 1603 1166 1635">33</td> <td data-bbox="1166 1603 1501 1635">1.5</td> </tr> <tr> <td data-bbox="491 1635 842 1666">Febrile seizure</td> <td data-bbox="842 1635 1166 1666">27</td> <td data-bbox="1166 1635 1501 1666">1.2</td> </tr> </tbody> </table> <p data-bbox="518 1675 1533 1733">* Each report may include more than one event, therefore the proportion of all reports will total to > 100%.</p> <p>Overall, the main pattern of events observed was that of local reactions (injection site pain/limb pain, injection site inflammation, injection site erythema, injection site mass); somatic immune responses (fever, headache, gastrointestinal and musculoskeletal symptoms) and hypersensitivity (skin reactions – most commonly rashes, less frequently urticaria and much less frequently erythema multiforme; peri-orbital oedema and facial swelling and bronchospasm, with occasional anaphylactic-type events). Sleepiness and irritability were also reported accounting for around four and five per cent of reports respectively.</p>	Events	Number of reports* received to 30 June 2006	Proportion of total reports* (% n=2212) to 30 June 2006	Local injection site reactions	925	41.8	Skin reactions	804	36.3	Fever	705	31.9	Gastrointestinal symptoms	577	26.1	Headache	250	11.3	Musculoskeletal	165	7.5	Irritability	122	5.5	Syncope/fainting	88	4.0	Sleepiness	81	3.7	Seizure (non-febrile)	33	1.5	Febrile seizure	27	1.2
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	<p><i>Hypersensitivity-type events of a more significant nature</i></p> <ul style="list-style-type: none"> • Urticaria (n=195); Peri-orbital oedema (n=35); Facial oedema (n=21); Bronchospasm/chest tightness (n=24); Angioedema (n=13); Peripheral (limb) oedema (n=9) • Anaphylactic-type events (n=9) <ul style="list-style-type: none"> o Six anaphylactic-type events were mild reactions. Three anaphylactic-type events were for more significant reactions: one occurred approximately five hours post immunisation and resulted in overnight admission to hospital for observation; two occurred shortly following immunisation, with one also presenting with urticaria. Both were hospitalised for observation. It is difficult to establish whether these events were classic anaphylactic reactions. <p><i>Haematological disorders</i></p> <ul style="list-style-type: none"> • Thrombocytopenia/Ideopathic thrombocytopenic purpura (n=6) In two reports the duration to onset was two and five days and the others ranged from 12-36 days. One occurred following MeNZB™ given concurrently with MMR vaccine. <i>(Note: the hospital-based monitoring found no increased incidence of thrombocytopenia following MeNZB™ vaccination when compared with other routine childhood vaccinations).</i> • Henoch Schönlein Purpura (HSP) (n=2) In one report of HSP the duration to onset was one day and the other 10 days. The latter report documented a coryzal-like illness at about the same time as immunisation. <i>(Note: the Hospital-based monitoring found no increased risk of HSP within 30 days after MeNZB™ vaccination)</i> <p><i>Notable reports received but <u>not</u> considered to be associated with MeNZB™</i></p> <ul style="list-style-type: none"> • Kawasaki Disease (n=2) One child with duration to onset of 34 days went on to receive a second MeNZB™ without exacerbation of symptoms. Onset for the other case was six days after a second MeNZB™ dose but no further information was provided. <i>(Note: the hospital-based monitoring found no increased incidence of Kawasaki Disease following the start of the MeNZB™ vaccination programme)</i> • Wegeners Granulomatosis (n=1) Symptoms began two weeks after a first MeNZB™ dose, and were considered Wegeners Granulomatosis following a positive biopsy. However, some uncertainty around the exact diagnosis exists.
Key messages for the public	<ul style="list-style-type: none"> • The reporting rate of potentially MeNZB™ associated adverse events was low, considering the large volume of MeNZB™ doses given. The pattern of reactions observed was consistent with common or expected patterns of adverse events following immunisation with vaccines typically used around the world. • Few clinically significant safety issues were raised during the surveillance period, with the one exception the slightly elevated number of urticaria reports. • Although, as with all post-marketing surveillance, the possibility of an excess risk of an undetected, rare adverse event cannot be unequivocally ruled out, the ISMB concluded that the combined results of <u>all</u> the safety monitoring activities provide confidence that MeNZB™ is safe.

Topic 2	Other issues
Overview	<ul style="list-style-type: none"> • There has been recent news interest in Norway regarding the meningococcal B vaccine developed by the Norwegian Institute of Public Health (NIPH), upon which New Zealand's MeNZB™ vaccine is based. • A single case of chronic fatigue syndrome, which was reported to Norway's equivalent of New Zealand's CARM from Norway's trials of its meningococcal B vaccine in the late 1980s, received a settlement and was the subject of some media coverage in Norway earlier this year. As a result, a number of participants from the Norwegian trials have recently claimed a link between the vaccine and chronic fatigue. The NIPH is undertaking a study to investigate the claims, with the results expected next year. • To date, no cases of chronic fatigue associated with MeNZB™ are recorded on CARM's database. • To date, studies of other vaccines have not shown an increased risk of chronic fatigue syndrome after vaccination. • New Zealand established a gold standard in safety monitoring for a new vaccine. The introduction of MeNZB™ was supported by research data from a number of countries over many years. As with other vaccines, MeNZB™ was subject to passive safety surveillance - where health professionals voluntarily report possible adverse events to CARM – as well as extra checks which included daily and weekly monitoring in hospitals for adverse events. Any child in the first area of roll out who went into hospital with any condition that could be remotely or possibly related to a vaccine was very carefully assessed. This included monitoring for neurological and immunological conditions. There has been no increase in the incidence of monitored conditions since the immunisation programme started. • The Independent Safety Monitoring Board (ISMB), a panel of international and New Zealand experts established by the Health Research Council of New Zealand, reviewed safety data throughout the programme. The ISMB advised that based on the data it had seen, it found no evidence of any significant adverse health event associated with the vaccine.
Explanation	<ul style="list-style-type: none"> • Chronic fatigue was listed as a possible adverse event on the MeNZB™ data sheet because of the single case originally reported from Norway's clinical trials. • Chronic fatigue syndrome is defined as “self reported, persistent or relapsing fatigue lasting six or more consecutive months”. Clinical investigations would be required to exclude other underlying causes. • For more information please go to the Immunisation Advisory Centre website http://immune.org.nz/?T=930 or the Ministry of Health Meningococcal B website http://www.immunise.moh.govt.nz/resources/healthprofessionals.html
Key messages for the public	<ul style="list-style-type: none"> • To date, no cases of chronic fatigue associated with MeNZB™ are recorded on CARM's database. • To date, studies of other vaccines have not shown an increased risk of chronic fatigue syndrome after vaccination. • New Zealand established a gold standard in safety monitoring for a new vaccine.

	<p>This included monitoring for neurological and immunological conditions. There has been no increase in the incidence of monitored conditions since the immunisation programme started.</p> <ul style="list-style-type: none"> • The key to investigations of events that take a long time to develop is the ability to identify everyone who has received the vaccine. New Zealand is well placed to do this as the NZ Meningococcal B Immunisation Programme requires that all MeNZB™ vaccinations are recorded on the National Immunisation Register.
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Topic 3	A reminder to record MeNZB™ vaccinations on the National Immunisation Register
Overview	<ul style="list-style-type: none"> • Although the mass campaign for MeNZB™ is now completed, there is still a requirement that all MeNZB™ immunisations be recorded on the National Immunisation Register (NIR).
Explanation	<ul style="list-style-type: none"> • A small number of vaccinators may not have recorded immunisations on the register as they incorrectly believe that with the end of the mass campaign the requirement for MeNZB™ to go on the NIR has also ended. • Information regarding the requirement for MeNZB™ vaccinations to be recorded on the NIR can be found on page 100 of the Immunisation Handbook 2006, and is included in immunisation and NIR information pamphlets for parents and caregivers. • The Ministry of Health will continue to monitor the safety and the effectiveness of the vaccine, including identification of vaccine failures. Key to these activities is the ability to identify everyone who is vaccinated. • Vaccine effectiveness information is required to inform decisions regarding how long the vaccine will need to be used in New Zealand to maintain epidemic control.
Key messages for the public	<ul style="list-style-type: none"> • All MeNZB™ vaccinations must be recorded on the National Immunisation Register. There is no opt-off for MeNZB™. • Vaccines given concurrently with MeNZB™ should also be recorded. • The key to safety and effectiveness investigations is the ability to identify everyone who has received the vaccine.