

MINISTRY OF HEALTH RESPONSE TO NORWEGIAN TV DOCUMENTARY TO SCREEN ON NEW ZEALAND'S TVNZ'S SUNDAY PROGRAMME ON NOVEMBER 5 2006

The Ministry of Health, health professionals and health groups are concerned about the impact that this Norwegian television documentary, which is dominated by long-standing critics of New Zealand's Meningococcal B Immunisation Programme, will have here.

The Ministry acknowledges that there is likely to be considerable public concern about any claims regarding possible adverse reactions linked to the MeNZB™ vaccine, and believes New Zealand parents are not getting the full picture from this documentary.

The documentary contains a number of claims which are likely to cause unwarranted alarm. It largely ignores the impact of the meningococcal B epidemic in New Zealand and the effectiveness of the MeNZB™ vaccine in helping to reduce harm to and deaths of young New Zealanders.

The documentary focuses on four individuals with adverse events following vaccination. It features one case of chronic fatigue syndrome and another of a neurological condition, both of which occurred after vaccination in Norway with a Norwegian-produced meningococcal B vaccine. It also shows a case of thrombocytopenia (transient low platelets) and another of pain in the right arm and neck following MeNZB™ vaccination in New Zealand.

When talking about adverse events it is important to remember that just because a condition occurs after vaccination, it does not prove it was caused by the vaccine.

Scientific data gives us confidence that the MeNZB™ vaccine is both safe and effective. The vaccine was appropriately tested before being given to children and young New Zealanders. The New Zealand trials and rigorous ongoing safety monitoring have found that the side effects observed were similar to those recognised in other well-established vaccination programmes.

All medical interventions have side effects and vaccination is no exception. However monitoring showed the most common side effects from MeNZB™ were mild temporary reactions and more serious reactions were extremely rare. This needs to be weighed against the risk of disability, amputation or death from the epidemic strain of meningococcal B.

This response addresses the following

No-one experimented on New Zealand children

The vaccine was not introduced in Norway because the epidemic was disappearing

MeNZB™ safety monitoring in New Zealand is comprehensive

Misleading statistics have been quoted

There is no scientific evidence that chronic fatigue is caused by vaccines

No-one experimented on New Zealand children

Claims that an experiment was carried out on New Zealand children and that New Zealand children were used as guinea pigs are scaremongering and untrue. Many of the issues are a repeat of claims previously made by long-standing critics of the MeNZB™ programme, Ron Law and Barbara Sumner Burstyn who both feature in the documentary.

Licensing of vaccines without phase III trials is not new or unethical

Clinical trials for vaccines usually comprise three phases –

- phase I is carried out in a small number of healthy adults with the primary aim to identify whether the vaccine produces an immune response and to determine if the vaccination is intolerable, that is, causes unacceptable degrees of pain or swelling
- phase II is carried out in a larger (e.g. 1,000 participants) group to see if the vaccine produces an acceptable immune response that is likely to protect against infection and to further quantify the side effects
- phase III trials are larger trials involving hundreds to tens of thousands of participants and are designed to see if the vaccine works in preventing the disease. When the disease the vaccine is protecting against is relatively rare, these trials need large numbers of participants followed up for a long period of time.

In all of these trials, half of the group gets the vaccine while the other half gets a placebo which may be a different vaccine. Participants and the nurses who administer the vaccines, do not know who has got the vaccine and who has not.

Like the United Kingdom and the United States, New Zealand did not undertake phase III trials for its meningococcal vaccine. Instead, increased antibody levels measured in the blood of participants from phase I and phase II trials provided strong evidence that the MeNZB™ vaccine would be effective.

The decision not to carry out phase III trials in New Zealand was made in order to protect our children and young people from a devastating disease as quickly as possible. If we had carried out the additional trials, many more children would have become ill and possibly died or lost limbs. This approach was endorsed by the World Health Organization (WHO) and leading public health experts who judged that there was already sufficient information that showed that vaccines similar to MeNZB™ were effective and safe in large populations.

Professor Donald Evans, Director of Bioethics Research at Dunedin School of Medicine, stated publicly that delaying the vaccination programme would have been unethical, given the seriousness of the disease. This view was supported both nationally and internationally.

MeNZB™ has been properly licensed for use in New Zealand

The MeNZB™ vaccine has been granted provisional consent for use in New Zealand to manage the meningococcal B epidemic. Use of provisional consent does not indicate that the vaccine is experimental. Medsafe granted provisional consent on the advice of its expert advisory committees on the grounds that the vaccine was urgently required. The data provided, though less comprehensive than that required for full consent, demonstrated that the vaccine had acceptable levels of safety,

quality and efficacy, and that the benefit-risk profile was acceptable. This conclusion was reached after the committee considered evidence on the immune response of adults and children vaccinated with MeNZB™ in the phase I and II trials conducted in New Zealand which showed that the vaccine produced a sufficient response to protect against infection with meningococcal B bacteria.

Medsafe also reviewed comprehensive safety data from similar vaccines used extensively overseas, as well as the Norwegian Institute of Public Health-produced vaccine, called MenBvac, upon which the New Zealand vaccine was based. While the MeNZB™ vaccine is similar to MenBvac used in the Norwegian studies it differs in a number of ways. Firstly, it includes the New Zealand epidemic strain instead of the strain that caused the Norwegian epidemic, and secondly the vaccine is made by a different manufacturer.

The Norwegian TV documentary suggests that Norway provided the sole data on which the New Zealand immunisation programme was based. This is not true. New Zealand also drew on data from extensive trials of closely related vaccines from other countries including Cuba, Columbia, Brazil and Argentina, across different age groups. Such information was from phase I, II and III trials as well as ongoing use in the general population. These vaccines have been used for many years and have had over 60 million doses administered with excellent safety records.

International expert advice from the WHO, the Centers for Disease Control and Prevention in the United States and the medicine regulator in the United Kingdom supported the clinical trial programme for MeNZB™. In addition, Medsafe sought advice and technical support from both the medicine regulator and the National Institute for Biological Standards and Control in the United Kingdom to assess the quality and safety of the final formulation of the MeNZB™ vaccine.

Giving a booster vaccine dose to infants is common with childhood vaccines

Overseas studies as well the New Zealand trials showed that the youngest infants (vaccinated at 6 weeks, 3 months and 5 months of age) do not produce as many antibodies as older children after three doses. For this reason New Zealand introduced a booster fourth dose for infants who received their first vaccine under six months of age. This means these infants will ultimately achieve an antibody level similar to other age groups. This approach is common with many childhood schedule vaccines.

The vaccine was not introduced in Norway because the epidemic was disappearing

By the time the appropriate clinical trials had been completed in Norway the epidemic was waning. There was no need to vaccinate children in Norway because the disease was no longer occurring at such an alarming rate.

Meningococcal B vaccines work

The Norwegian vaccine was 57% effective (i.e. it was able to prevent 57% of cases) 29 months after vaccination with two doses. Subsequent trials have shown that three doses provide a higher level of antibody response and hence protection against the disease. For this reason New Zealand used a three dose schedule for under 20 year olds, and a four dose schedule for the youngest infants.

A Victoria University study, which will be published in a scientific peer-reviewed journal, found the effectiveness of New Zealand's MeNZB™ vaccine two years after the start of the immunisation programme was 80%.

Norway was not looking for a market for their vaccine

It is suggested in the documentary that the Norwegians were looking for a market for their vaccine. This is not correct. The New Zealand Government through WHO approached the Norwegian Institute of Public Health and asked them if they could produce a vaccine for us.

Most adverse events in the Norwegian trials were not serious

MenBvac was evaluated in 28 studies in Norway including three large phase III trials. These included trials involving more than 170,000 teenagers. The great majority of adverse events were not serious – for example sore arms or fever.

All of the information that was available from the Norwegian clinical trials was provided to New Zealand and considered by the expert advisory committee at Medsafe that recommended that the vaccine be given consent for use. Information on possible side effects was provided to health professionals and parents through every avenue possible, e.g. letters, consent forms, information pamphlets, web pages, 0800 numbers, public meetings etc. In addition information on rare serious adverse events such as the chronic fatigue case was provided on the vaccine data sheet inserted into every vaccine package. The Norwegian findings were also summarised in a *New Zealand Medical Journal* article.

MeNZB™ safety monitoring in New Zealand is comprehensive

Ensuring and monitoring the safety of the MeNZB™ vaccine has been paramount. In New Zealand we instituted what national and international experts regard as a gold standard in safety monitoring for a new vaccine. An Independent Safety Monitoring Board, made up of national and international experts in the field, oversaw the safety monitoring.

Usually once a vaccine is licensed for use the only safety monitoring that takes place is through voluntary reports of potential adverse events from GPs and other health professionals. In New Zealand this system is operated by the Centre for Adverse Reactions Monitoring (CARM) at Otago University. In addition to this we monitored:

- emergency department consultations and admissions to hospital for the first 100,000 children to be vaccinated aged 5 years and over and the first 100,000 children aged under 5 years
- all GP visits for 6 weeks after vaccination for under 5 year olds at a number of general practices
- all deaths that occurred within 90 days of vaccination.

We particularly monitored for any events that had been linked to other vaccines, including MenBvac, even if they were only “possibly” related.

No safety concerns were found with MeNZB™ in New Zealand

The Independent Safety Monitoring Board reviewed all the data collected during the safety monitoring and found no concerns regarding the vaccine's safety. This does not mean that no serious adverse events occurred during the programme, but that there were **no significant or unexpected cases** - in other words they occurred at

the same rate as would have been expected without the vaccination programme. Serious health conditions occur every year in a small number of children. As expected, these conditions continued to occur during the programme, both in children who received the vaccine and children who did not receive the vaccine.

Hospital monitoring

There was no increase in the incidence of monitored conditions following the implementation of the immunisation programme.

- No increase in the incidence of encephalitis or acute flaccid paralysis was found compared with background levels.
- No increased incidence of seizures was found following MeNZB™ compared with that seen with other vaccines. In particular, no increased risk of febrile seizure was found within seven days following MeNZB™ vaccination.
- No increased incidence of thrombocytopenia¹ was found following MeNZB™ compared with that seen with MMR vaccine. A number of the children who developed thrombocytopenia subsequently received further doses of MeNZB™ without any ill effect.

GP and health professional surveillance

Voluntary reports

A total of 2,212 reports of events following MeNZB™ were received by CARM between July 2004 and June 2006, during which time over 3 million doses were administered. Overall the main pattern of events observed was that of local reactions (injection site pain/inflammation etc), fever, headache and skin reactions. A summary of the reports made to CARM can be found at <http://www.immunise.moh.govt.nz/documents/safetymonitoring-0606.pdf>

The patterns of events observed was similar to that seen with other vaccines in the national immunisation schedule.

Monitoring of GP visits

A large number of children were assessed through this system. The pattern of adverse events was in line with that seen through CARM's voluntary reporting system. The reactions largely comprised of local events such as injection site pain and somatic immune responses such as a fevers or headaches.

Deaths in vaccine recipients

The Independent Safety Monitoring Board and the MeNZB™ Mortality Review Group reviewed all deaths that occurred within 90 days of receipt of MeNZB™ vaccine. MeNZB™ vaccination was not certified by the reporting clinician or coroner as a contributing cause of death in any of the cases that were reviewed.

Adverse events presented in the Norway TV documentary

- Both New Zealand adverse events that feature in the documentary have been reported to CARM and have been included in the statistics reported for this vaccine.

Misleading statistics have been quoted

¹ Thrombocytopenia is a decrease in the number of platelets found in the blood. It is usually mild, and not permanent, often occurring after a viral infection. It has been associated with MMR (a live vaccine), but is unlikely to be associated with and inactivated vaccine such as MeNZB™.

Deaths from meningococcal disease

The documentary states that there have been six deaths this year. What is doesn't mention is that three of these deaths were in adults over 50 years old who were not part of the immunisation programme. There were three deaths in under 20 year olds, two of which were from the particular strain that the vaccine is able to protect against. One child who died from the vaccine strain had received only one dose, so would not have been fully protected, while the other child died after three doses.

These tragic deaths are a reminder of why we developed a vaccine and launched New Zealand's largest immunisation programme. Meningococcal B has already had a devastating effect on society, and while the immunisation programme has done much to reduce the number of cases nationally, no vaccine can provide a 100 per cent guarantee.

Cases of meningococcal disease

Since January 2006 there have been 19 epidemic strain cases in children who were fully vaccinated among more than 1 million children who were fully vaccinated, and 15 epidemic strain cases among about 200,000 children were not vaccinated at all or only partly vaccinated.

Since the vaccination programme began in July 2004, there have been 187 cases of the epidemic strain in children under 20 years - 158 cases were not vaccinated at all or only partly vaccinated and 29 cases had received three doses of vaccine. Two of the 29 were in infants who were overdue for their fourth dose.

MeNZB™-related claims to ACC

There have been 33 MeNZB™-related claims accepted by ACC. Many are not related to the vaccine itself but to receiving an injection. Details of the injuries are as follows:

- 15 musculoskeletal injuries - e.g. contusion, haematoma, tendon & muscle injury
- 10 allergic reactions
- 3 nerve damage
- 2 infections
- 2 haematological reactions
- 1 miscellaneous

The average amount paid was \$79, reflecting the fact that payments were mainly for things such as GP visits and prescriptions.

Payment of a claim does not mean that the vaccination caused the condition – just that it may be possible or cannot be ruled out. ACC takes a conservative approach with regard to payment of claims.

There is no scientific evidence that shows chronic fatigue is caused by vaccines

To date, there is no scientific evidence that chronic fatigue syndrome is caused by vaccines.

We were informed about the single case of chronic fatigue reported from the MenBvac trials before our programme started. This condition was listed on the vaccine data sheet as a rare adverse event reported from the trials with the parent Norwegian vaccine.

The chronic fatigue case received a settlement and was the subject of some media coverage in Norway earlier this year. Following this publicity a further 160 individuals claiming symptoms of chronic fatigue also applied for compensation.

In the documentary Professor Saugstad cites a number of cases of chronic fatigue amongst people vaccinated in the trials, he doesn't provide any information on the number of cases of chronic fatigue who did not get the vaccine. The usual prevalence of chronic fatigue among adults is estimated at 0.18% to 0.42% so cases are likely to occur after vaccination just by chance.

The Ministry of Health takes adverse event claims seriously and is in regular contact with the Norwegian Institute of Public Health which is investigating the claims.

Prior to recent New Zealand media coverage of the one case from the Norwegian MenBvac trials, no cases of chronic fatigue syndrome associated with MeNZB™ had been recorded on the CARM database in New Zealand. In the two weeks since media coverage five enquiries have been made to the Ministry of Health or CARM from individuals who consider they may have had a "fatigue-like illness" since vaccination. New Zealand will continue to monitor this situation closely through its post-marketing surveillance programme operated by Medsafe.

What happens now?

The Ministry will continue to monitor the situation in Norway and provide information to health professionals and the public about any significant developments.

Both the Ministry and the Immunisation Advisory Centre, phone 0800 IMMUNE or 0800 466 863, will have detailed information available. Anyone with health concerns should discuss them with their GP.

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