the Australia and New Zealand School of Government

CASE PROGRAM 2006.18.1

New Zealand's Meningococcal Vaccine Strategy (A)

On 11 May 2004, Meningococcal Vaccine Strategy (MVS[1]) Director Jane O'Hallahan had to decide whether she could continue to confirm 31 May as the day on which the new MeNZB™ vaccine would be rolled out. Earlier roll outs of the vaccine, urgently needed to combat New Zealand's extraordinarily high levels of Group B meningococcal disease, had been delayed by production problems. Now, two shipments of MeNZB™ vaccine, sufficient to deliver doses to 150,000 children, were in storage. Clinical trial results, the first of which had been forwarded to the independent licensing authority Medsafe[2] months earlier, were all positive. Consent to proceed seemed likely, but recent requests for additional data and overseas expertise cast new doubt on when it might be granted.

The Counties Manukau District Health Board, piloting New Zealand's largest-ever immunisation programme, had implementation contracts poised to sign, and additional vaccinators trained and ready. Schools were waiting to send out forms for parental consent; but the National Immunisation Register (NIR), designed to assist in monitoring vaccine safety and coverage, was still in development. A date too early could damage carefully nurtured confidence; too late, might waste thousands of

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This case was written by Janet Tyson, Australia and New Zealand School of Government, under the supervision of Dr Richard Norman, and with assistance from Professor Claudia Scott and Dr Karen Baehler, Victoria University of Wellington. It has been prepared as a basis for class discussion rather than to illustrate either effective or ineffective handling of a managerial situation. The assistance of Jane O'Hallahan, Christine Roseveare and Robbie Lane is gratefully acknowledged.

[1] A glossary of terms and list of organisations and individuals is included at the end of this case.
[2] The Medicines and Medical Devices Safety Authority, which licences new medicines for use in New Zealand.

dollars, as well as precious vaccine. With every day's delay another child risked lifetime disability or death. Jane O'Hallahan reflected: "The MVS was all about second-guessing outcomes and making knife-edge decisions. These compounded in the final decision we had to make about delivery."

A particular strain of meningococcal disease

Between 1991 and 2004, New Zealand, with a population of four million, had had over 5600 cases of meningococcal disease, with 224 deaths. In 1991, a particular sub-strain of the meningococcal B bacterium was identified as the cause of the majority of cases in the epidemic.[3] In 2001, 650 cases and 26 deaths were reported, or 17.4 cases per 100,000,[4] eleven times the normal rate of infection. Meningococcal disease became a prominent notifiable disease, and efforts to get a vaccine to combat it gained pace.

Meningococcal disease presents most commonly as meningitis [swelling of the meninges around the brain] or meningococcal septicaemia [severe blood poisoning]. Early symptoms can be fever, vomiting and headache, which can progress rapidly to shock and death.[5] As a Medical Officer of Health in the Wellington/Wairarapa area for ten years, Jane O'Hallahan had seen many cases, sometimes two or three in one high-risk family. She knew: "There is a huge amount of fear about the disease. It literally steals children away in the night."

Vaccination is the most powerful public health tool to combat epidemics of infectious disease. But, although meningococcal disease had been a focus of international efforts for the past decade, with advances in vaccines against some strains, there was no vaccine available for the particular strain of meningococcus B that accounted for almost 80 percent of New Zealand cases. Further, it was known that developing a vaccine against meningococcus B posed particular challenges. [6]

In the absence of a vaccine, initiatives to prevent and control meningococcal disease included intensified epidemiological surveillance, promoting public awareness to encourage early medical intervention, and promoting professional awareness to encourage early diagnosis and treatment. When a case occurred, much effort went into tracing all possible contacts and offering them prophylactic antibiotics.

As the epidemic prolonged, medical personnel had become extremely skilled at identifying and treating the disease. Most parents, especially in high-risk areas, were alert to danger signs. But sometimes the disease struck with such speed there was nothing doctors could do. A promising young woman cricket player who became ill and died within 24 hours, had been a high-profile victim in 2003. More common, but usually less publicised, were the cases of young children and babies who lost parts or

[3] Martin, D.R., R. McDowell, E Sneyd, M Baker (2003) The Epidemiology of Meningoccal Disease in New Zealand in 2002. Report prepared for the Ministry of Health by the Institute of Environmental Health and Research Ltd (ESR). Wellington: Ministry of Health. "The Epidemiology."
[4] The World Health Organisation defines an epidemic as three cases per 100,000.
[5] The Epidemiology, page 5, quoting MOH Communicable Disease Control Manual.
[6] The main strains of meningococcal disease are A, B, C, Y and W135. For most strains, vaccines can be made using the relatively straightforward polysaccharide technique. For the B strain this is not possible and more complex protein-based procedures are called for.

all of their limbs to remove dead tissue, and faced a lifetime of rehabilitation and plastic surgery.
By international standards, the New Zealand death rate, just over two percent, was among the lowest in the western world. The major public health problem was the morbidity - the high level of disability resulting from the disease, anything from multiple amputations to brain damage. A 2003 study[7] calculated a 16 percent morbidity rate, with direct health care costs at $400,000[8] a year and an ongoing cost of $1 billion to society.[9]

Those most at risk were the youngest and most vulnerable, with up to 50 percent of all cases occurring in under-five year olds. Within the under-five age group, 50 percent of cases were in babies under twelve months of age;[10] the risk increased in winter-time, multiplied where children lived in overcrowded housing, and peaked for children of Pacific ethnicity. There was marked geographic variation in the occurrence of the disease *(Exhibit 1)*, with cases most common in areas measured as most deprived on the New Zealand Deprivation Index.[11]

Mass immunisation

By 1993, New Zealand had begun an international search for possible vaccines against group B meningococcal disease, in 1995 holding a workshop, attended by international experts including one from the World Health Organization (WHO), to discuss options. The WHO was keen for New Zealand to launch a mass immunisation of everyone under 20 years old. But first a vaccine was needed, and cumulative experience of recent years pointed to the fact that it should specifically target New Zealand's epidemic strain of bacteria. Such an "orphan" vaccine, with a very small production run and no potential future use, had limited appeal to manufacturers, and early attempts tried to incorporate the New Zealand strain into a more comprehensive (multivalent) vaccine formulation.

In March 1997 the New Zealand Government approved an allocation of up to $6 million towards prevention of meningococcal disease. In an unusual step, the Ministry of Health took a lead in negotiating research contracts.

By September 1998, with WHO assistance, the first steps were taken towards realising a strain-specific vaccine for New Zealand, with what proved to be an abortive attempt to involve four competing manufacturers in preparing vaccine for clinical trials, from which one could be selected to continue the development. The clinical trial process is essential in proving the safety and efficiency of a vaccine for use in humans.

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[7] Proceedings of the Meningococcal Vaccine Strategy World Health Organisation Satellite Meeting, 10 March 2004, Auckland New Zealand, reported in NZ Medical Journal, Volume 117 No 1200.
[8] All figures in New Zealand dollars, at that time approx .53 US dollars.
[9] O'Hallahan, J, Lennon, D, Oster, P, Lane, R. et al (2005) From secondary prevention to primary prevention – a unique strategy that gives hope to a country ravaged by meningococcal disease. *Vaccine* 23 (2005); 2197-2201.
[10] Ibid.
[11] The New Zealand Deprivation Index rates 10 as most deprived, one as least.

Without intervention the epidemic would eventually wane, as it had in Norway after twenty years. Predictions were that New Zealand still had six or eight more years to run. One expert had said 30 years.[12] Ten more years could mean 5000 more cases and 200 more deaths. Norwegian scientists had developed a strain-specific vaccine (MenBVac™) against their meningococcal B epidemic, but by the time all three phases of clinical trials were completed in 1990 – showing the vaccine to be safe and effective - the epidemic had ended. For New Zealand to get benefit from a vaccine, it would have to be developed in a fraction of the 12 or more years normally needed.

Profitable vaccine manufacture depends on large production volume and wide application. International investigations had been proceeding for some time, without significant progress, for a more generic vaccine against group B meningococcal disease. New Zealand was asking for accelerated development of a strain-specific vaccine of which minimal quantities, from an international view, would be needed.

In 2000, research findings[13] highlighted the link between poverty and overcrowding, and added to the debate in medical circles over the value of giving priority to developing a vaccine. Although some strong arguments were made that alternative interventions such as improvements in housing should be tried first, the view prevailed that immunisation was the only way of directly controlling the epidemic.

In response to a further request for international assistance, potential suppliers, each of them a research institute teamed with a manufacturing partner, came to New Zealand to present their case. Formal requests for proposal went to three of these in December 2000.

The Meningococcal Vaccine Strategy

In 2001 a dedicated team was established to progress the Meningococcal Vaccine Strategy (MVS). Jane O'Hallahan was chosen to lead what was initially a part-time position with two policy analysts.

Around the same time, a small group of IT specialists began development of a long-planned national immunisation recall database, intended to record the general schedule of nine childhood immunisations as they were given to each birth cohort. Available information (of questionable accuracy) showed New Zealand to have very low levels of immunisation by international standards, particularly for Māori and Pacific peoples.

The small MVS team had large targets, notably to have a vaccine ready for first roll out in April 2003, and the disease virtually eliminated by 2006. To achieve this, a vaccine would have to be developed, tested, proved and produced within three years. There was no precedent to assess if this would be possible; very little was "set in concrete" according to O'Hallahan:

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[12] The epidemic in Norway was caused by a strain closely related to the New Zealand one. Towards its end, the MenBVac™ was developed, but only in clinical lot quantities.

[13] Household crowding a major risk factor for epidemic meningococcal disease in Auckland children. Baker M, McNicholas A et al, Institute of Environmental Science and Research, Wellington. *Journal of Pediatric Infectious Disease*, October 2000.

"For the first year, 2001-02, we were uncertain if we would get funds and how much we would need. At the outset, we didn't have a vaccine manufacturer. We didn't know what it would cost [a recent example in Canada had cost a prohibitive $75 a dose[14]], how many doses would be needed, and what the cost-benefit ratio would look like."

In February 2001, as O'Hallahan was taking up her new role, an independent panel, with international membership, selected the US-based multinational company Chiron Corporation, which had within its divisions the world's sixth largest vaccine manufacturer,[15] as provider. Chiron was working with the Norwegian Institute of Public Health (NIPH), which had developed the MenBVac for a similar strain of disease.

In a public/private partnership that was a first for each side, the multinational corporate Chiron and the government department the Ministry of Health jointly sponsored the Meningococcal Vaccine Strategy. The partnership also included Auckland University and ESR.[16] All were represented in the Meningococcal Management Team (MMT), the scientific grouping established in July 2001 to oversee the progress of the clinical trials. Initial work was carried out under a separate contract, funded from the earlier vote for meningococcal disease prevention.

"We had to go through the process of building a relationship with Chiron without any guarantee that we would get money at the end – and before it was realised the scale of funding that would be needed," Jane O'Hallahan said.

"Once we established the relationship with Chiron, we had to keep the company's confidence while we got a decision from Cabinet. As we were putting our Cabinet paper out for consultation[17] we were trying to set up contracts, with both Chiron and the University of Auckland, without a specific figure or many other necessary details.… I was not at all certain that our approach to Cabinet for funding would be successful."

The paper to Cabinet

Throughout 2001, in tandem with other work, members of the MVS worked to build support for what would be New Zealand's biggest ever single expenditure on public health. The team mounted a major education campaign for key stakeholders, including politicians on both sides of the house, always "putting a human face on the disease" with the assistance of some very powerful pictures showing the damage it could do.

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[14] The Memorandum to Cabinet Health and Education Committee: Request for Group B Meningococcal Vaccination Campaign Funding Proposal. Version for publication provided 23-2-05. (Cabinet Paper).

[15] At Siena in Italy.

[16] Institute of Environmental Science and Research Ltd, which had identified the particular group B substrain.

[17] Eleven different government agencies, from the Office of the Commissioner for Children to the Ministry of Foreign Affairs and Trade, were consulted on the paper. The Ministry for Pacific Island Affairs, and the Ministry for Māori Development, asked for more detail on the clinical trials.

The MOH's Memorandum to Cabinet Health and Education Committee: Request for Group B Meningococcal Vaccination Campaign Funding Proposal went out for consultation with other agencies in August 2001.

In the paper, the MOH pointed out that the continuing group B meningococcal disease epidemic was a "national public health emergency". The disease had "extraordinary rates in Pacific and Māori communities, but is extremely high for all New Zealanders."[18]

It estimated current treatment and rehabilitative costs and future costs of $300 million, with corresponding costs to society of $630 million. On top of this was the human cost of deaths and loss of quality of life. It also noted "a high degree of media and public expectation exists that a vaccine will be available to stop the epidemic."[19]

Three possible scenarios were costed: nationwide immunisation for all under-20s; vaccinating every under-five year old nationally, plus high risk older groups from the Bay of Plenty northwards;[20] or nationwide immunisation for under-fives only.

The MVS team recommended the first, and most expensive option, to deliver a vaccine to all under 20 year olds, citing WHO expert opinion that mass immunisation of a broader age band was the only way to significantly reduce the impact of the disease. They used both QALY – cost per quality adjusted life years and NPV (net present value) for their costings. Jane O'Hallahan said:

"We also used the argument around the rule of rescue.[21] As a developed country, if there is the possibility of a preventative for a devastating epidemic, it does behove a government to do something. Not totally despite the cost, but even if it is a high cost, it should be carefully considered."

The proposed group B meningococcal vaccine scored highly on a range of decision criteria other than the strictly clinical, the paper pointed out. "These include equity, contribution to reducing health inequalities, obligation to Māori under the Treaty[22] (the greatest beneficiaries would be children, particularly Māori and Pacific children) and public acceptability (there is a high level of community concern over the epidemic, with some families concerned to send their children to school because of the risk of the disease.)"

Treasury challenged the MOH arguments (as well as congratulating the team on setting a new benchmark for a health Cabinet Paper), saying that, on the basis of economic criteria required for other health spending such as that used by the drug agency Pharmac, funding would be better spent on other social interventions. It said if any option was to proceed, it should be the third and least expensive targeting only under-five year olds. It also commended the rigor of the paper's risk/benefit analysis.

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[18] Cabinet paper, p1.
[19] Cabinet paper, p1
[20] Targetting areas with disease rates over 30/100,000 and dealing with an estimated 70 percent of cases.
[21] Cabinet Paper, p3.
[22] Treaty of Waitangi, signed between New Zealand Māori and the British Crown in 1840. Much current New Zealand legislation includes a requirement to acknowledge the Treaty.

In Parliament, the paper gained considerable cross-party support. During the consultation phase two cases occurred in Southland, one involving a 12-year-old, who would have been excluded from vaccine eligibility in scenarios two and three.

Cabinet approved in principle funding for the MVS in December 2001, and in April 2002, $200 million was appropriated to the MVS over five years. The funds were to cover all development and administration costs for a strictly limited quantity of vaccine. Agreeing that this was a public health emergency, Government made a special allocation outside Vote: Health.[23]

The variables of vaccine

With certainty over the funding, progress could be made on the main contract with Chiron. The scientific work done in 2001 had given encouraging initial results about the likely effectiveness of the vaccine. At the same time, statistics showing a new peak in cases of the disease[24] underscored the need for haste.

And there were still fundamental uncertainties about the vaccine, not least because its manufacture is a biological process and inherently more challenging to replicate with the perfect consistency needed for medical use. Jane O'Hallahan:

> "Could it be developed (upscaled) in commercial lots at Chiron's plant in Siena, when the related Norwegian version had been developed in laboratory quantities only? Could New Zealand conduct clinical trials on a scale much vaster than previously experienced – and would it be possible to recruit children for these trials? We had to make significant investments to answer these questions, without having the experience to make qualified judgements."

Problems did in fact emerge early on. While Chiron now owned the rights to the Norwegian MenBVac process, the technology still had to be transferred from the NIPH laboratory in Oslo to Chiron's production department in Siena, and from there to the manufacturing department for bulk production. Because of unexpected difficulties replicating the Norwegian process in Italy, the first batches of MeNZB vaccine, for use in clinical trials, were produced in Norway, and the original roll out date of November 2003 was changed to April 2004.

Licensure, logistics and other limiting factors

In September 2001 Jane O'Hallahan had set out a list of limiting factors and risks.[25] Licensure was at the top - if, and when it would be granted, and to what age groups.

As a new medicine, the MeNZB vaccine would have to be approved by the independent licensing authority MedSafe, which would require a number of proofs of safety and efficacy before granting consent, including a series of clinical trials.

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[23] Vote:Health, (the annual Budget allocation for the Health portfolio) was $7.9 billion in 2002-03.
[24] 650 cases were notified in 2001.
[25] Meningococcal Disease in New Zealand: Proposed Epidemic Control Strategy Using Meningococcal B:4:P1.7b,4 Outer Membrane Vesicle Vaccine. February 2002.

Normally, three phases of trials were conducted, the first with a small group of volunteers, the second with a slightly larger group that had given informed consent, and the third phase, on a much larger scale (in Norway involving 170,000 young people) where control group would receive a placebo instead of immunisation over a period of two or three years.

The comprehensive Norwegian results, and subsequent experience in the UK, gave the MVS team confidence that, given satisfactory results in the first two phases of trials, it would then be possible to use the vaccine in a mass immunisation campaign, accompanied by stringent real-time safety monitoring that could call a halt at the sign of potential problems. There were also ethical questions about using placebos at the height of an epidemic; the decision meant a new vaccine could be ready for use within three years.

Vaccine availability would be the second significant limiting factor. The Norwegian trails had demonstrated that, to achieve immunity, each child should have three doses of vaccine, ideally over a period of three months. This alone multiplied logistical issues, as would the decision to deliver to school-age children through schools, with the interruption of holidays, especially over Christmas. Orders and shipping would have to be carefully scheduled to ensure there was continuity of supply to support whatever roll out option was decided.

Also, as the paper to Cabinet had argued, "the fewer people who are vaccinated, the lower the chance to effectively control the epidemic in New Zealand."[26] To control the epidemic, the sequence of three doses should be delivered to at least 90 percent of the under-20 population. This coverage far exceeded any recorded in New Zealand, even for single-dose immunisations.

The National Immunisation Register (NIR)

"There is a need to be able to accurately track 95 percent of the population to ensure that sufficient coverage is attained to achieve epidemic control," Jane O'Hallahan noted in her list of limiting factors. She put a priority on having the national immunisation recall database – soon to be known as the National Immunisation Register (NIR) - up and running. This was predicted for the end of 2002.

In her view the most immediately important use of a register would be for the MeNZB vaccine roll out, to track who had been immunised, where and by whom, as well as providing data within 48 hours for the stringent safety monitoring requirements for a new vaccine.

To meet the needs of the MVS, the register would have to retrospectively enrol all under-fives. However, the focus of current development was to have the NIR recording the immunisation status of each new birth cohort.

O'Hallahan already had concerns about how the small immunisation database development team would meet its deadline with the resources available, but felt there was little direct action she could take.

[26] Cabinet paper, p 26.

In 2001 and 2002 one of the MVS team members worked half-time with the NIR developers, attempting to ensure that specifications included MVS needs. MVS also held the first meeting around developing a separate, school-based immunisation recording system to feed data into the NIR.[27]

A further logistics limitation would be the workforce to deliver the vaccine. Unlike some other countries, New Zealand did not have a dedicated immunisation workforce, and there had not been a mass vaccination of under-fives on this scale before. General Practitioners and their practice nurses, and Public Health Nurses, would be the core of the workforce, with others such as the Well Child Nurses working in areas with high Māori populations being brought in. Whether this existing workforce would be enough, and what training and equipment might be required, would only be known when vaccine availability and quantity was confirmed.

District Health Boards and other new health structures

As the MVS was being planned, the organisational structures of the New Zealand health sector were being redrawn, and the MOH itself significantly reshaped. In January 2001, the MOH absorbed the former Health Funding Authority, increasing significantly in size. It added a regional presence and established a separate Māori directorate, Te Kete Hauora.[28]

The major effect of the health sector restructure was to create a single central authority responsible for both policy and for funding (see *Exhibit 2*). Twenty-one District Health Boards (DHBs) were established,[29] a move that put health funding and decision-making in the hands of local communities. The DHBs were responsible for delivery of primary, secondary and tertiary health care (hospital services, personal health, mental health and disability services).

Public health, charged with "promoting well-being, and preventing ill health before it happens," retained a central identity and a direct funding relationship with the Ministry of Health. Fifty percent of public health funding went to the twelve dedicated Public Health Units, while the remainder was contestable by a range of providers including DHBs.

For a mass immunisation programme there could be a strong argument for centralised delivery through the 12 regions of the Public Health Service. But this option would centralise a major health initiative at a time when the Ministry, and its Public Health Directorate, were working hard to build relationships with the new District Health Boards.

For the MVS team, it was a foregone conclusion that vaccine delivery would be through the DHBs. This meant establishing fresh working relationships with 21 entities, "all, we are discovering, very different beasts," Jane O'Hallahan said.

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[27] The School-Based Vaccine System (SBVS) would be developed by external consultants and delivered on time in early 2004.
[28] The Basket of Health.
[29] In place of four Regional Health Authorities.

Relationships with schools, primary care and other providers would be filtered through DHBs, which were themselves still finding their feet in many respects.

The Counties Manukau pilot

Another decision was always clear. South Auckland was "a given." If and when a vaccine was developed, children living in the Counties Manukau District Health Board area would be the first to be immunised.

The Counties Manukau DHB area had accounted for 21 percent of all New Zealand cases of meningococcal disease between 1998 and 2001, an average of 91 cases a year. Twenty-five percent of the 400,000 under-20s in Counties Manukau were of Pacific ethnicity, and 23 percent Māori.[30]

Kidz First, Counties Manukau's children's hospital, was positioned near the northern boundary of the DHB. Many of its patients came from the low-decile, high-risk eastern suburbs in the adjoining Auckland DHB. These "eastern corridor" children, the MVS team had decided after some difficult debate, to include with the pilot, as an exception to the "delivery by DHB" rule.

At the height of the epidemic, two or three children a day were coming in with the disease; Kidz First clinicians had become expert at detection and treatment, and there was a high level of community awareness. Counties Manukau DHB had worked closely with Auckland University and was running the clinical trials on behalf of the MOH. It was the only DHB to have developed a computerised immunisation register, Kidslink, which was already recording information for each birth cohort.

The pilot role made Counties Manukau DHB, from 2002 onwards, the testing ground for every aspect of the Meningococcal B Immunisation Programme from the logistics of the roll out to contract negotiation to workforce training. As the scope of the project grew, it grew in complexity. There were a lot of goal posts on the MVS's GANTT charts, and most of them kept moving. Jane O'Hallahan said:

> "We wanted to remain flexible, to manage changing circumstances, while working to certain key principles. It would be fair to say that Counties Manukau felt rather impeded in their planning process by lack of definite decisions we were able to make."

Reducing inequalities

In the wider political environment, some apparent certainties were shifting. Reducing inequalities, in particular in recognition of Treaty obligations, had been a powerful argument in the original paper to Cabinet, and "Closing the Gaps" a prominent Government policy.

In July 2002 the Labour Government was again campaigning (successfully) for re-election, but this time there was no mention of "Closing the Gaps". There had been sustained criticism from the Opposition of any "race-based" funding or services.

[30] Source rollout paper March.

However, the MVS planners continued to factor in the statistics of meningococcal disease: Pacific and Māori children had the highest rates, but in some years half the total number of its victims were Pākehā.[31]

For Jane O'Hallahan, the most crucial decision, the one by which the whole Programme would be publicly judged and remembered, was the priority in which the vaccine would be rolled out, after the first-stage pilot had been successfully completed.

In April 2003, she tabled a paper[32] suggesting four roll out options, already workshopped with an internal MOH group, to a range of external stakeholders including Māori, DHB, Public Health and University medical representatives.

The options were presented [33] "against five criteria: burden of disease; reducing inequalities, logistics, ease of communication, and monitoring and evaluation"; and with a number of "best assumptions from information available at the time." These included that the vaccine would be available – and licensed – for children from six months of age upwards, although trials with this group were still to begin. Planning was on the assumption that earlier upscale issues had been overcome, and that sufficient doses for the pilot population of 150,000 children would be ready.

A key principle was to have enough vaccine to complete the three-dose course for any group targeted, before allocating any vaccine to other groups. If vaccine was "allocated" to six month to four year olds in Northland, enough should be set aside to vaccinate the entire six months-four year population of Northland before vaccine was made available to another group.

The ideal roll out

"The ideal roll out option is one that gives priority to the age-groups and regions where there is a high burden of disease for Māori and Pacific children and young people, as this has the greatest potential to reduce health inequalities," the paper said.

"The rationale for the priority must be easy to communicate and clearly understood by the public, especially the 'boundaries' between higher and lower priorities."

The ideal roll out would see the National Immunisation Register operative in a DHB three months before the Meningococcal B Immunisation Programme began, the paper added. The NIR development team was by this time working with IT experts from Counties Manukau, attempting to use the district health board's Kidslink software to accelerate progress with the national register.

The four options (see *Exhibit 3)* were labelled "High Five", "North to South" "Grouped DHBs" and "All Together". Each of the first three were variations on priority for the under-fives, the fourth delivery to all age groups within a DHB or region.

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[31] Commonly used term for non-Māori of European origin.
[32] Prepared by Senior Analyst Christine Roseveare.
[33] National Roll Out Options Paper, March 20, Draft 3 p5.

Workshop participants were challenged to identify the strongest option to achieve the project's goals of eliminating 90 percent of the epidemic in two year. They put forward three other options: a variation on the all together approach; and taking the "top six" DHBs by case numbers all together, then age-staggered by DHB risk. A Māori adviser argued strongly for immunising Māori and Pacific peoples first throughout the country. While this was not successful it would later be agreed to establish a National Rollout Advisory Group (NRAG) with a predominantly Māori and Pacific membership.

Implementation

At its June 2003 meeting, the Meningococcal Management Team endorsed an option that incorporated many of the suggestions from the workshops, and was seen as most closely matching desired outcomes.

This was the All Together, North to South and South to North roll out. Immunisation would start in the far north of the North Island, moving south by DHB as everyone under 20 had been immunised, and vaccine became available. Once the North Island was virtually covered, immunisation would begin in the south of the South Island, starting with the Otago and Southland DHBs where the greatest disease burden was. A year after the first North Island immunisations, children in the Nelson Marlborough DHB would have their first dose. As long as the pilot started by May 2004, the "top three" DHBs, Auckland, Waitemata and Northland, would all have completed immunisation by Christmas and the long school holidays, during which up to 40 percent of children in some areas would relocate to a new home, school and health care provider.

Although the MMT endorsed the recommendation, Jane O'Hallahan said:

> "We agonised about …the fact that while we desired to give it [first] to the high-risk communities, we weren't going to be able to achieve that in all cases. We were trying to get a system in place that was fairest. But even the [chosen] rollout strategy is going to mean that some low-risk children will get it ahead of some high-risk children. It took us a while to come to terms with that."

The blackest month

In August 2003, the reassuring results of the first completed series of clinical trials, in adults, were announced at the annual conference of the Paediatric Society of New Zealand. The indications were that the vaccine was safe, and produced protective antibodies.

The MVS now moved into another phase, with planning for the roll out proper, in the three northern DHBs. Work began on development of national guidelines for delivery of the roll out; however new decisions about the NIR brought further delays.

Another cloud on the horizon was Chiron's continuing difficulties in adapting its vaccine production to manufacturing quantities, with some worrying delays; at meetings in London, and then in California, Jane O'Hallahan reiterated how important the vaccine was to the children of New Zealand, again showing graphic pictures of victims.

In July 2003, hearing of further delays in upscaling, O'Hallahan and MOH lawyer Adina Halpern had made a dash to the Chiron plant in Siena. They intended to "give Chiron as much encouragement as we could to persist with the upscale" knowing that by now it was only a moral obligation and to be weighed against far more lucrative commercial possibilities. Their visit, involving New Zealand's High Commissioner to Italy, and WHO vaccine experts, "was a delicate balance, which almost backfired on us. There were some very tense times around the table." She was by now determined that, whatever vaccine was available, New Zealand children would be getting it. As they left, production seemed to be back on track.

But then in October 2003, O'Hallahan learned that Chiron had come across new and puzzling problems in its attempt to upscale production of the MeNZB vaccine to manufacturing quantity lots. With the company's product development schedule booked for years ahead, there was only a two-month window of opportunity to get it right.

O'Hallahan had to decide whether the DHBs, in particular Counties Manukau DHB, should be put fully in the picture, or allowed to continue planning while a last-ditch effort was made for another upscale attempt. An increasing number of agreements and contracts were ready to be signed; within three months, Counties Manukau expected to activate the roll out; sending permission slips through schools and bringing in 50 extra nurses for vaccination training.

> "We were looking at a contingency plan of …getting vaccine from Norway where they had only been able to produce small volumes. We were facing a scenario when we might have only 100,000 doses, or maybe only 30,000; it might take a whole year to roll out just in the pilot DHB. That wasn't viable. [The only possible way to roll out] would be by partial DHB. That had considerable logistical problems because the programming would have been extraordinarily long and had a huge impact on the workforce for a very lengthy time.
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> "October was the blackest month. It was the only time when I wondered whether we were really going to have the programme."

Chiron agreed to make one more attempt, then a whole valuable week was lost when the company's only centrifuge went out of action. At last, a midnight phone call from Italy to New Zealand, brought O'Hallahan the news she most wanted to hear.

One of the key technical personnel, who had been particularly touched by the ravages of the disease on New Zealand children, had spent hours, including an all-night session observing the fermenter. He had discovered and was able to resolve the technical problem that was preventing the upscaling.

Production went smoothly from that point, with each batch passing the requisite international quality tests, increasing confidence that the vaccine would gain the provisional consent from Medsafe to be delivered in the mass campaign.

Breakthroughs and frustrations

By January 2004, the MVS team knew it would have as much vaccine as it could use to commence the Meningococcal B Immunisation Programme if provisional consent to use the vaccine was granted. Provisional consent, under the Medicines Act 1981, is used as a means of allowing use under strict safety supervision in situations such as an epidemic, where the steps in the approval process must be accelerated.

Now, what would ultimately determine the roll out was the need to provide certainty around the NIR, and the possible timing of the consent. With the roll out deadline now 31 May 2004, O'Hallahan again made her frustrations about the NIR clear in a paper to the Deputy Director-General. At last she felt that the "birth cohort recording" focus would be abandoned and top priority given to what the MVS needed.

But the delay had already meant a missed opportunity to introduce NIR along with new Accident Compensation changes and the requirements of the Primary Health Organisation (PHO) management grouping, effective from 1 January.[34]

To manage the increasingly complex challenge of keeping stakeholders appropriately informed, a stakeholder manager had been appointed, while relationship managers had started to work with each DHB.

By the time of the World Health Organization's immunisation group meeting in Auckland on 10 March 2004, attended by Medsafe representatives as well as MVS, Meningococcal Management Team and public health specialists, the MVS had further positive data, this time the results of the clinical trials involving the older infant 16-24 month old group.

Medsafe's Vaccine Safety Committee held a meeting on 5 April, at which it made the recommendation that provisional consent should be granted for the MeNZB vaccine to be given to children six months and over – subject to further information and data being received from Chiron. In its first experience of handling a licensure application for a vaccine not previously tested in the market, Medsafe was proceeding with caution. There was no indication how long it might take for its outstanding queries to be answered; it was impossible for the MVS team to know under what conditions consent might be granted.

Yet by this point much of the implementation depended on having the provisional consent. For example, schools could not send out parental approval forms before consent was granted. If school immunisations started after the middle of the year, additional vaccinators would be needed to complete the course before the long school holidays.

By 11 May, Jane O'Hallahan knew that Medsafe's additional consultation was threatening the planned roll out deadline, less than three weeks away. There had not yet been a satisfactory field trial for the NIR. But she was reluctant to ease the

[34] The NIR would have to interface with the PMS (patient management system) software, which was not standardised. Six different vendors provided a version of PMS software to general practices and other primary health care.

pressure on any party to deliver as soon as possible, and she worried that further revisions of the roll out date would undermine confidence. “The DHBs were saying to us, how can we plan if you keep changing your mind? We needed to put a stake in the sand for them.” Should she stick with 31 May?

Glossary

Auckland University	Ran New Zealand-based clinical trials on behalf of MOH; member of MMT.
Chiron	US-based multinational corporation which includes a vaccine manufacturing division with a plant in Siena, Italy. Also a member of the MMT.
DHB	District Health Board
ESR	Institute of Environmental Science and Research Limited; advisor to the MMT.
GP	General Practitioner
KidzFirst	Main children's hospital in Counties Manukau DHB.
Medsafe	Independent licensing authority for medications in New Zealand
MenBvac™	Vaccine developed against Norwegian epidemic of group B Meningococcal disease.
MeNZB™	The trade name of the vaccine developed to control New Zealand's Group B meningococcal epidemic.
MMT	Meningococcal Management Team; scientific-based advisory group.
MOH, the Ministry	The New Zealand Ministry of Health
MVS	Meningococcal Vaccine Strategy
NIR	National Immunisation Register
NPV	Net present value
NRAG	National Rollout Advisory Group
O'Hallahan, Jane	Director of MVS
OMV	Outer membrane vesicle, a type of vaccine
Pharmac	New Zealand agency that funds and approves medications.
PHO	Primary Health Organisation, a new management entity introduced in 2004.
PMS	Patient Management System – a computerised information system used by primary health care providers.
Public Health Directorate.	One of the Directorates within the Ministry of Health
QALY	Quality Adjusted Life Years, a measure for calculating the benefit of an intervention.
SBVS	School-Based Vaccination System
Te Kete Hauora	Māori Directorate of the Ministry of Health
Treasury	The New Zealand Treasury
WHO	The World Health Organization

Exhibit 1
Map of Meningococcal disease rates by Health District (source: The Epidemiology).

Exhibit 2: Diagram of relationships under new MOH structure (courtesy of Dr Peter Crampton, Otago School of Medicine).

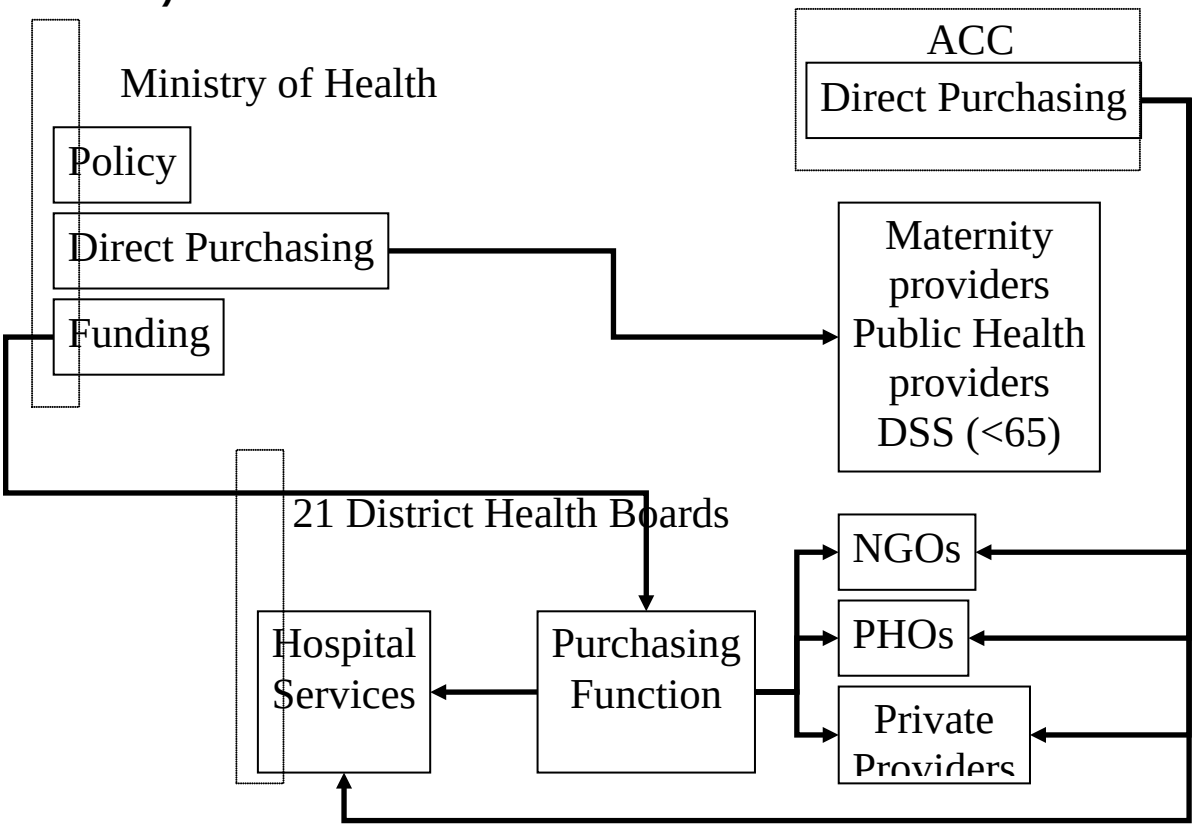

Exhibit 3 – Options proposed for Roll Out

- "High Five" would allocate vaccine to DHBs according to the rates of the disease in their under-fives over the past five years. Once this had been achieved nationwide, vaccination of school-age children would proceed in the same order, then the out-of-school population.

- "North to South" would do this allocation by region.

- "Grouped DHBs" would allow for situations like the Wellington and Hutt DHBs where there was a lot of interboundary flow.

- The "All Together" option would see the full three-dose series of vaccinations given to every age group in one DHB before any vaccine was made available to another DHB.

Source: National Roll Out Paper, March 2003.

The all together North to South/South to North Option

- Vaccine to be allocated to DHBs in the North Island "North to South" and then the South Island "South to North"

This option is favoured for the following reasons:

- Burden of disease
- Reducing inequalities/impact on Māori and Pacific children
- Logistics and practicality
- Acceptability and ease of communication
- Monitoring and evaluation

District Health Board disease rates 1998-2002 per 100,000		Yearly average Number of cases 1998-2002	
Lakes (Rotorua area)	72.7	Counties-Manukau	91.8
Counties-Manukau	71.3	Waikato	36.2
Northland	60.4	Waitemata	31.6

DHB under 20 population numbers by ethnicity		% of population by ethnicity	
Pacific	Counties Manukau 31,725	Counties Manukau	25%
Māori	Waikato 30,588	Tairawhiti (East Coast and Gisborne)	57%
European and Other	Canterbury 99,570	South Canterbury	89%

Data extracted from National Roll Out Summary for MMT, June 2003