

CORPORATE OFFICE

Level 1
32 Oxford Tce
CHRISTCHURCH

Telephone: 0064 3 364 41
Fax: 0064 3 364 4165

carolyn.gullery@cdhb.health.nz

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[REDACTED]

[REDACTED]

[REDACTED]

Regarding your follow up questions to Official Information Act request/response CDHB 10061(a)

I refer your email dated 12 June 2019 requesting information regarding the recent measles outbreak in Canterbury (copy attached).

In collaboration with Dr Nikki Turner, Head of the Immunisation Advisory Centre (IMAC), Dr Tony Walls (Paediatrician, Infectious Disease) and Dr Ramon Pink, Public Health Physician, we are now able to provide you with a complete response to your request.

- 1. Cases of measles, were found to be caused by vaccine strains, yet there was no clarification of what those vaccine strains were. What were those strains? 38 case were wild strains. What were the additional wild strains, apart from B3?**

Vaccine strain is genotype A. Wild type strains that were identified in the outbreak include genotype B3 and genotype D8.

Genotype B3 is part of the measles outbreak in the Philippines. Genotype D8 is part of a measles outbreak in the United Kingdom.

- 2. Am I to understand that the 13 vaccine strains were from the GSK Priorix MMR vaccine? As these developed symptoms recently, I would presume that to be the case. Given the numbers that vaccine strain were detected in, have resulted in measles infection, will there be any recalls of the batches involved? Were they considered to be potentially hot batches? Were those cases all from the same batch and where do those 13 cases of vaccine strain fit in, to the data on the ESR website? I am somewhat confused, as the CDHB site states, these are not included in the outbreak... yet surely need to be stated on the ESR site somewhere and more detail provided? That would be interpreted as an act of transparency, would it not?
NB: There is evidence in the scientific community that measles vaccine strain, can be transmitted to others from someone who was twice vaccinated with the MMR vaccine. The index case i.e. the fully vaccinated person, transmitted to other partially and fully MMR vaccinated individuals. Therefore the potential for transmission is not theoretical.**

The GSK Priorix MMR vaccine, is the vaccine used in the National Immunisation Schedule. No batches of vaccine are recalled if a rash does develop post MMR vaccination. Post vaccination rash occurs in approximately 5% of children, 6-12 days post vaccination. These children are not infectious to others (Immunisation Handbook 2017, Pg. 322). There is no requirement to recall MMR vaccine batches, due to a post vaccination rash developing. There is no requirement to follow up post vaccination rash cases, and as such, there is no linking of batches to this event. These events are not recorded on the ESR database. They are not regarded as wild virus measles cases, and therefore they are not regarded as part of a measles outbreak.

- 3. What assurances will you be offering to the public who have received the GSK vaccine, who also may experience vaccine strain measles? Could more people be experiencing symptoms, but having had the vaccine, not notify anyone, believing that they were protected? If so, could these also be potentially vaccine strain cases, therefore your number of 13, be higher in fact?**

The side effect profile of the MMR vaccine is well documented (Immunisation Handbook 2017, Pg. 322). This is discussed in the informed consent process pre vaccination. This is not regarded as a case of wild virus measles, and so, it is not recorded as such.

- 4. Given that there is evidence of the vaccine virus being capable of being transmitted to others, in the scientific literature, what public notification will the CDHB be offering, if at all, to inform about this, as this has ramifications for Community Immunity, as well as the process of Informed consent, under risks and benefits, does it not?**

“No transmission of measles vaccine virus from a vaccinee to a contact has ever been documented” (Plotkin’s Vaccine 7th edition 2018 p 607 and p 593). Considering the extensive international use of this vaccine, while there is a theoretical possibility, in practice despite being used widely for over 50 years including extensive use with close contacts of high risk immunosuppressed individuals with no cases of transmission ever recorded, the likelihood of transmission of the vaccine strain to others is extremely unlikely.

- 5. By excluding the 13 cases from the outbreak, this may confuse the public and result in a lack of confidence in the vaccine itself and given that the Mayo Clinic’s own vaccine scientist, Dr Gregory Poland has himself stated in Pub Med papers, that measles is becoming a disease of the vaccinated and that a new vaccine is needed, does this not raise some concerns for the CDHB?**

The side effect profile of the MMR vaccine, including development of a rash in up to 5 percent of children post vaccination, is well documented (Immunisation Handbook 2017, Pg. 322). This is discussed in the informed consent process pre vaccination with parents, caregivers. This is not regarded as a case of wild virus measles, and is therefore not recorded as such.

Since the notification of the first measles wild virus case on February 21st, 2019 nearly 27, 000 MMR vaccines have been delivered in the Canterbury community. Adequate vaccine supply to meet demand posed a logistical challenge for General Practice teams across the region, reflecting public confidence in the vaccine.

Dr Gregory Poland, Editor in Chief of the Vaccine Journal, continues to lead work into improving vaccine efficacy and reduced side effects. In his seminal paper “The Re-Emergence of Measles in Developed Countries: Time to Develop the Next-Generation Measles Vaccines?” (2012) he notes that “... while an excellent vaccine... it remains ... an open question as to whether the current vaccine is sufficiently immunogenic and efficacious to allow eradication – even though measles can be controlled, and even eliminated in some regions for defined periods of time...” The current MMR vaccine will be retained in

the New Zealand National Immunisation Schedule, until a new more effective vaccine supersedes this current “excellent vaccine”. This is reassuring for the Canterbury DHB and for the community.

- 6. How many of the cases that are listed on the ESR website who were under 15 months of age and also above 15 months of age and under 4 years old, were in fact NOT being breastfed, which may have afforded them maternal transfer of antibodies and therefore protection? How many of those mothers had been vaccinated in the past, with the MMR vaccine, whose infants contracted measles?**

Of the 38 confirmed cases of measles, six cases were aged 15 months or less. One case was aged greater than 15 months and less than five years of age. We have no record of the breastfeeding history of these cases. Three of the mothers of these cases were fully vaccinated, three were unsure of vaccination status and one was unvaccinated.

- 7. If 236 people who notified the authorities were investigated, what specific investigations were undertaken, as I was informed by ESR, that not all cases were investigated by lab testing, and some were confirmed by association only? I note that Hospitalisations are listed on ESR database. This would not presumably indicate how many were actually 'admitted,' to a ward, with a proportion of those spending about 3 hours on average in the Accident and Emergency Department, before being sent home. Some people attend the hospital in order to avoid the expense of the After Hours of course, or incurring a charge for attending their GP clinic.**

Of 236 suspect cases that were notified, only three of those cases were not tested. The decision not to test was based on the clinical signs and symptoms and whether or not there was a history of exposure to a confirmed case of wild virus measles.

Of the 38 cases that comprised the Canterbury measles outbreak this year, 15 (39%) of the cases were assessed in ED. Of these, seven cases (18%), were admitted to hospital for 24 hours or more (one to nine days). Three of these seven cases developed respiratory complications; one required support in ICU. The other four cases were unwell with all the clinical features of acute measles infection. Close clinical support was needed. Infants and children under five were either assessed or not admitted, or their admissions were shorter stay than adults.

- 8. If those who were confirmed as having measles by reliable lab testing and to have 'vaccine strain measles' which will not be included in the outbreak, how many of their contacts who also developed measles, were tested by the RT-PCR test, to determine if they also had vaccine strain measles?**

No contacts of those with vaccine strain measles were tested, since “no transmission of measles vaccine virus from a vaccinee to a contact has ever been documented” (Plotkin, 2018). Only contacts of a confirmed wild virus measles case, that showed clinical signs of acute measles infection, were PCR tested.

- 9. Why has GSK not been mentioned in the CDHB information, in regard to the 13 vaccine strain cases? That was one of my questions in the OIA. Are they notified about these cases?**

The MMR vaccine that is used, is Priorix, produced by GSK. It was introduced into the national schedule in 2017.

GSK are not informed of notifications that are identified as due to vaccine strain. There is no requirement for District Health Boards to do this.

10. Will the vaccine strain cases be reported to NZ CARM and reported on both databases? Do you consider this to be a vaccine failure, measles, or an adverse reaction?

Vaccine strains are not cases of wild measles. Symptoms that fit the known profile occurring after vaccination are recognised adverse events following vaccination. This does not in any way correlate with vaccine failure, in fact quite the opposite in that a recognised reaction is highly suggestive of a good immune response to that component of the vaccine.

The side effect profile following the use of the MMR vaccine is well documented. Refer pg. 322 of the NZ Immunisation Handbook 2017. If these reactions are mild and the family are not concerned, then no further action is taken. If the individual or family is concerned, the next step is to have a review by the general practice or after hour's medical service. If there is concern that the reaction is severe or has any unusual features then the healthcare provider notifies CARM (The Centre for Adverse Reaction Monitoring) at the University of Otago, Dunedin. Note that families themselves are also able to directly notify CARM.

CARM collects, reviews and reports on all adverse events reported to them and are funded to report to the MARC (Medicines Adverse Reaction Committee) committee of Medsafe, Ministry of Health.

11. When will the media and the wider public be informed about the genotype results? They are not found easily when one goes to the site.

The public were informed of the outbreak genotype, on the Canterbury DHB website. Media were informed of the link that the Canterbury outbreak genotype was linked to measles outbreaks overseas. Measles is not endemic in New Zealand, and outbreaks occur in New Zealand due to travellers visiting or returning from nations where outbreaks are occurring or where measles is endemic.

12. What are those who had vaccine strains actually told? Will the fact that they have experienced a milder form of measles, result in any type of 'cell mediated immunity' and what strains will they be immune to? Is there any likelihood that there could be a problem with mutations for those people?

The Immunisation Handbook 2017 pages 322- 323, summarises the information for providers to give to parents or vaccinees. Key aspects include: Expected outcomes from the vaccination event; Adverse Events Following Immunisation (AEFI), including MMR vaccine viruses being non-transmissible from vaccinees; elevated risk of Immune Thrombocytopenia; Adverse outcomes not linked to MMR.

The vaccine strain is protective for all measles strains. There are no reports of any significant differences in side effects of vaccine effectiveness across different commercial vaccines. There is no evidence of strain mutation.

As part of their protective action, the vaccine does induce cell-mediated immune responses which are similar to natural infection, but less pronounced (Ward BJ, Griffin DE. Changes in cytokine production after measles virus vaccination: predominant production of IL-4 suggests induction of a Th2 response. Clin Immunol Immunopathol. 1993; 67:171-177).

The vaccine can also have some temporary cell-mediated immune suppression but this has not led to any increased risk to any vaccinee, even when given to high risk patients such as those with unrecognised Tuberculosis (Karp CL, Wysocka M, Wahl LM, et al. Mechanism of suppression of cell-mediated immunity by measles virus. Science. 1996; 273:228-231)

13. Given that the numbers of cases who have been infected is just 38 wild strain and 13 vaccine strain cases and a significant number of those would not have been of an age, when they would be administered the vaccine due to their age, whilst others were either partially or fully vaccinated with the MMR vaccine, yet still contracted measles, what do you see this latest information suggests, about Community Immunity and how this vaccine is perceived, regarding its efficacy and the science that is evolving, around Adversomics and Genomics, both being integral parts of immune response and best health outcomes?

Since the notification of the first measles wild virus case on February 21st, 2019 nearly 27, 000 MMR vaccines have been delivered in the Canterbury community. Adequate vaccine supply to meet demand posed a logistical challenge for General Practice teams across the region, reflecting public confidence in the vaccine.

The perception is that it is safe and effective.

The current MMR vaccine will be retained in the New Zealand National Immunisation Schedule, until a new more effective vaccine supersedes this current “excellent vaccine”. This is reassuring for the CDHB and for the community.

14. Will all other DHBs be providing the same type of information on genotyping of cases on their websites, as that collated information becomes available?

The Canterbury District Health Board provided the genotypes identified in the February/March 2019 measles outbreak on its website, believing this to be in the public interest. These included genotype B3, and genotype D8.

The MMR vaccine strain is genotype A (as noted in the response to Question 1). It is at the discretion of each District Health Board, as to whether this information is posted in their respective websites.

I trust that this satisfies your interest in this matter.

Please note that this response, or an edited version of this response, may be published on the Canterbury DHB Official Information Act responses website page and our Measles Information website page after your receipt of this response.

Yours sincerely



Carolyn Gullery
Executive Director
Planning, Funding & Decision Support