28 April 2020

Attn: Dr Ashley Bloomfield
Director-General of Health and Chief Executive
Ministry of Health
PO Box 5013
Wellington 6140

Dear Dr Bloomfield

Firstly, we want to acknowledge the challenges Ministry of Health staff must have faced in recent months. Thank you for your commitment and hard work.

Please treat this letter as an OIA request.

Given how busy you are, we have tried to make the questions as specific as possible and have split them into four parts: vaccine manufacturing, a New Zealand vaccination strategy, vaccine effectiveness and antibodies. These questions all directly or indirectly relate to a vaccine for SARS-CoV-2 (the virus that can cause the disease COVID-19).

The answers will be used as the basis of a McGuinness Institute think piece. At present, much of the public narrative around the SARS-CoV-2 virus assumes a vaccine will take about 18 months to develop and scale, and then life will return to normal. Our initial research found that two different perspectives exist. Scientists consider a range of options is possible, from 12 months to no vaccine. In contrast, politicians and policy analysts have tended to focus on what is most likely, being 18 months until a vaccine is produced. New Zealand needs to make sure its modelling is sensitive to what scientists think (a range of possibilities) not by what is most likely (the average expected timeframe). The Institute believes it is prudent to explore all possibilities and ideally, engage early with challenges before they become problematic. The answers to the questions below will help us to explore New Zealand's options, and ideally provide some useful public policy solutions for wider consideration.

PART A: Vaccine manufacturing

1. Is there a vaccine manufacturing facility in New Zealand (i.e. assuming a license can be obtained to mass produce a vaccine here)?

2. If there is a vaccine manufacturing facility in New Zealand, can you advise:
   a. Who owns the manufacturing facility?
      Note: We understand Otago University has the ability to contribute to making vaccines but we would like official confirmation that this is the case and that manufacturing at scale is possible.
   b. How long would it take to manufacture 5 million or 10 million (in case we need to vaccinate people twice) vaccines?
      Note: We are only looking for rough estimates; for example if New Zealand does have a manufacturing facility, how many months it would take to manufacture 5 and 10 million respectively.
   c. Does the manufacturing facility have the necessary components to make a vaccine in stock (see list of vaccine components here)? If yes, what expiry date do they have on current stock levels? A copy of a recent stock take would be sufficient. If it does not, are they able to purchase the remaining stock from overseas? Are any essential components in short supply?

d. Has the facility manufactured any human vaccines over the last 20 years (since 2000)? If yes, what vaccines were produced and how much did the licenses cost? Were there resulting logistical or safety issues?

3. Does Australia have a vaccine manufacturing facility?
   a. If yes, what is the size of its production facility? Is it large enough to supply the New Zealand market?
   b. If yes, do New Zealand and Australia have a mutual arrangement where New Zealand would get priority over other countries? If yes, please explain. If no, is this being considered?

4. Does New Zealand have any specific agreements or loose relationships with vaccine suppliers around the world that the country can rely upon or leverage?
   a. If yes, please name the vaccine supplier and the type of agreement (if this is confidential information, a simple 'yes' is sufficient).
   b. If no, do we have any country agreements? If we do not, can you clarify whether New Zealand is simply reliant on aggressively going to the market?

PART B: A New Zealand vaccination strategy

5. Has an inoculation strategy been developed or in development, in preparation for a mass vaccination program against SARS-CoV-2?
   a. Yes, if it has been developed, can you advise name and link to the document?
   b. Yes, if it is in development, can you advise name and timeframe when the document is expected to be released?
   c. If no, is there a previous inoculation strategy document that you will use or might update? Can you provide the link or name of the previous inoculation strategy document?

6. We understand special fridges are required to hold vaccines. How many fridges does New Zealand have available? Has there been any consideration of taking a stock take and purchasing any additional fridges now globally (before they are in short supply)?

7. Have the syringes (listed on the national reserve supply composition here) been checked for quality (we note they expire in 2022)? As the vaccine may take over 18 months to develop, there is a risk the syringes may expire. Has the MoH considered purchasing another 10 million?

8. Has there been consideration of the anti-vaccine lobby in New Zealand?

9. To what extent will vaccination be compulsory or will it be voluntary?
   Note: We expect that the benefits of being vaccinated will be measured against the perceived risk of acquiring the disease.

10. Can inoculation of a vaccine be made mandatory under current New Zealand law?

11. What lessons can be learned from the flu vaccine? Given concerns about the quantity ordered and the public release to GPs not being adequate, has a review been undertaken? If yes, can we please have a link to or soft copy of the written review?

12. In recent years, the government has rolled out the meningococcal vaccine and the HPV vaccine? Was a review undertaken for each of these? If yes, can we please have a link to or soft copy of the written review/s?

13. We expect GPs will be paid for giving the vaccine to eligible patients and pharmacists to customers; however, can you confirm this?

PART C: Vaccine effectiveness

There seems to be some concerning evidence that antibody persistence is not guaranteed in those who have recovered from COVID-19 and that coronavirus vaccines in general may be technically difficult to produce.

On 22 April 2020 we emailed an OIA to the MoH regarding the H5N1 vaccine that is currently listed on the MoH national reserve supply composition (see here). We understand that the vaccine no longer works as the virus mutated very quickly after it was purchase – meaning the vaccine is no longer effective. Our 22 April OIA to MoH sought clarification on this. We are currently waiting for a response, but this insight raises questions over the extent the SARS-CoV-2 virus might mutate, resulting in an early vaccine being ineffective.

14. Who is undertaking viral surveillance for SARS-CoV-2 in New Zealand? (e.g. is it ESR or MoH)?

15. What mutations (or strains) of SARS-CoV-2 has New Zealand found to date?
    a. Does New Zealand have the 'L-type' or 'S-type' strains? If yes, what is the numbers of percentages?
    b. Are there any other strains in New Zealand?
    c. From your experience, do you consider one of the strains is more deadly than another?
    d. What is the MoH advice to officials (e.g. to ministers, Treasury, and the Reserve Bank) as to when a vaccine might be available for sale to the New Zealand Government (e.g. a 5% chance in less than six months, an 80% chance in six to 18 months, a 10% chance in 18–36 months, and 5% beyond 36 months)? We are interested in how this has been positioned with officials.

16. Given the vaccine is being fast-tracked, there is a risk countries might agree to indemnify vaccine makers from legal liability in the event of manufacturing defects?
    a. Has the New Zealand Government ever accepted legal liability for a past vaccine in the last 20 years?
    Note: The US underwrote the risks of H1N1 in 1976/77, which added to the fear of the vaccine itself (see Nate Silver's *The Signal and the Noise,* pp. 209–210). Shortly after the programme started it was halted largely due to an unusually high number of Guillain-Barre syndrome cases occurring in vaccinated people.
    b. Would the New Zealand Government ever accept legal liability for a fast-tracked vaccine? If no, is this because it would be covered by ACC?

PART D: Antibodies

We note that the World Health Organization (WHO) has stated that '[t]here is currently no evidence that people who have recovered from COVID-19 and have antibodies are protected from a second infection' (see the 24 April 2020 scientific brief in the attachment).

17. Have any New Zealand patients been tested to see if they have developed antibodies?
    a. If yes, what number have been tested?
    b. Of those tested, what number of people showed '*very low levels of neutralizing antibodies in their blood*'? [See background below, WHO 24 April]
    c. If yes, what was the level of antibodies and the median found?
    d. If yes, has their immunity been tested more than once to indicate over time whether their immunity has stayed the same, increased or waned?

18. Is the MoH considering an immunity passport system?

19. Does New Zealand have the necessary skills and equipment to create in vats antibodies for COVID-19 patients?

Please note that we have copied in DPMC and ERS, as MoH is clearly working closely together with both organisations.

Kind regards,

Wendy McGuinness
Chief Executive

Attachment 1: Timeline

Attachment 1: Timeline

This very brief timeline has been prepared for the McGuinness Institute's upcoming think piece. Charting the development of the coronavirus vaccinations narrative, this information may help to provide context to the questions above.

1. A 2003 article published in the *British Medical Journal* 'Two strains of the SARS virus sequenced' (see here) notes that:

> The differences between the two strains turn out to be minor. Both comprise about 30000 nucleotides, *making the genome of SARS-CoV the largest of any RNA virus*. It is possible but unlikely that the differences are a result of sequencing errors.
>
> As more strains are sequenced, the degree of difference between them will provide vital clues to the rate of mutation. Although all other known coronaviruses have been allocated to one of three serotypes, *both teams of microbiologists believe the new virus belongs in a fourth category of its own*.
>
> The structural differences from other coronaviruses, and the lack of evidence of recombination, suggest that the SARS virus is not a result of other viruses swapping DNA with a previously benign coronavirus that already lived unnoticed in humans.
>
> Rather, the researchers say, *the evidence indicates that SARS is genuinely new in humans and until recently inhabited an unknown animal species, probably in Guangdong province, China*. [Italics added]

2. A *2009 WHO Bulletin* (see here) interviews Dr Harvey V. Fineberg, the president of the Institute of Medicine, Washington DC, United States of America (USA) in 2009. He shares his insights into why his 1978 study of that public health response to the 1976 swine flu fiasco' is still relevant. His answers emphasise the need to stay flexible and manage of the physical and social risks of vaccinations:

> **Q: A recurring theme in your study is the difficulty of linking scientific evidence and policy. How do you determine policy when you don't have the hard scientific facts and when a public health threat is probable but not certain?**
> A: What we saw back in '76 was that political leaders wanted to do the right thing but lacked technical expertise, and public health experts recognized the uncertainty of the threat yet wanted to convey the seriousness of the risk in a way that would overcome political inertia. The challenge of communication between technical experts and policy-makers is as relevant today as it was in the '70s. Policy-makers and experts cannot rely exclusively on such semiquantitative qualifiers as "usually", "occasionally" and "possibly." An event is "possible" when its chance of occurring is 1 per 10 and remains "possible" when the odds have dropped to 1 per million. A change in likelihood of over five orders of magnitude has policy implications. Words that suffice for everyday discourse are not adequate for tracking and adjusting to a dynamic situation such as a flu outbreak. The responsibility of the technical expert here is to think hard and precisely about what is known and unknown, to portray the uncertainty in a way that is accurate and adjustable over time as circumstances change, and to communicate this to the policy-maker. Both policy-makers and technical experts face an intensified dilemma of communication when it comes to reaching the public, whose understanding, support and participation may become crucial.
>
> **Q: Why was the response to the '76 swine flu outbreak deemed a failure?**
> A: In the decision-making, the fundamental strategic flaw was combining all aspects of response into a single "go or no-go" decision – the decision to proceed with characterizing the virus into a vaccine, to produce the vaccine, to test it and to deliver it to every man, woman and child in the USA – that was all decided and announced in March '76 in one fell

swoop. This big lesson has been absorbed by policy-makers: separate what needs to be done to prepare for future decisions from reaching conclusions and announcing them, before relevant information is at hand. For example, you can proceed to develop a vaccine, but you do not simultaneously need to decide whether to proceed with immunization, what its scope will be and who priority recipients will be.

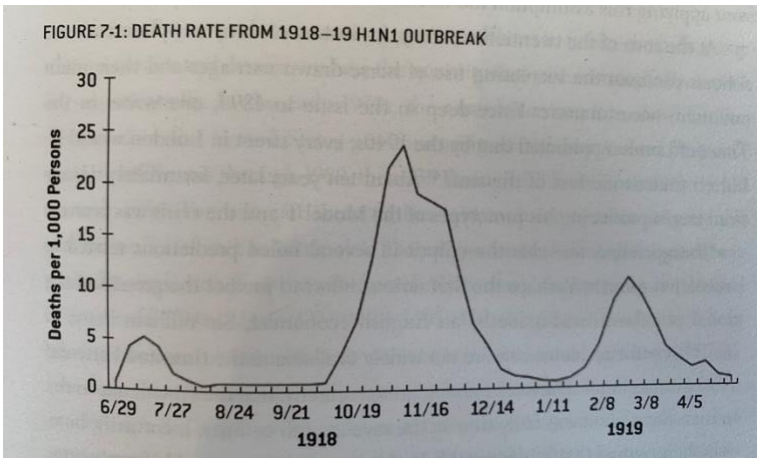
Q: The US Centers for Disease Control and Prevention (CDC) lost credibility over the '76 swine flu affair, not only due to about 30 deaths from adverse vaccine reactions?
A: Once set on its course, CDC did not establish a basis for review and reconsideration of the situation. As facts evolved, such as the absence of further cases, CDC's pursuit of the original strategy to immunize everyone became more and more controversial and costly in terms of long-term credibility. From technical, political and policy points of view, it is very difficult to deal with low probability–high consequence events – events that are relatively unlikely, but that would have catastrophic consequences should they occur. When you have such an event in prospect, the naysayer who argues that you are over-reacting is more likely to be right than wrong. It is just like the person who says, "Don't buy insurance for your house this year; it's not going to burn down." At the end of the year, for most of us in most years, that would have been an economical decision, but its wisdom can be judged only in retrospect. In prospect, it's foolhardy not to have the insurance. This is a fundamental challenge for policy-makers in the face of many threats of this type, including natural pandemic threats.

Q: What other challenges did the '76 response face?
A: Legal liability issues arose when insurers refused to insure vaccine manufacturers against lawsuits. Field trials suggested children would need two shots to gain adequate protection, complicating the logistics. Administrative problems abounded because states varied tremendously in their ability to deliver vaccines. If you immunize very large numbers of elderly people, inevitably some will have a heart attack the next day, so you have to prepare the public for such coincidences. In one city, a few elderly people died of heart attacks soon after being vaccinated and immunizations were temporarily suspended. By the end, there were dozens of cases of Guillain–Barré syndrome. That wouldn't have been a blip on the screen had there been a pandemic but, in the absence of any swine flu disease, these rare events were sufficient to end the programme.

3. Nate Silver, in his 2012 book *The Signal and the Noise*, acknowledges the risk of non-influenza viruses like SARS as a potential threat (alongside risks from other strains of H1N1 or H5N1) (p. 229).

A graph of the death rate of the 1918–19 H1N1 outbreak (see Figure 1 below) shows the level of uncertainty over time; in this case the second and third waves had higher death rates than the first wave (Silver, 2012, p. 211). Silver emphasises the value of 'modelling for insights'.

Figure 1: Graph indicating death rate of the 1918–19 H1N1 outbreak



4. The 2019 WHO publication *The Global Vaccine Action Plan 2011-2020* by Strategic Advisory Group of Experts on Immunization (see here) suggests that a 'post-2020 global immunization strategy' should:

> **Promote long-term planning for the development and implementation of novel vaccine and other preventive innovations, to ensure populations benefit as rapidly as possible**
>
> - Maintain the momentum behind new product/ technology development.
> - Promote dialogue between countries, partners and developers through needs assessments, evaluation, piloting and scale up, to ensure rapid access to safe and effective products that meet national needs.
> - Identify key bottlenecks in new product approval and implementation, and develop new strategies to overcome them.
> - Continue to prioritize capacity building and coordination of national regulatory authorities, including regulatory harmonization to expedite introduction of WHO pre-qualified vaccines.
> - Promote early consideration of the broad implications of novel interventions nearing practical application, to identify possible implementation enablers/barriers and potential acceptability issues.
> - Ensure that the lessons learned from both successful and problematic vaccine introductions are documented and shared to inform future implementation planning.
> - Promote the development of regional and national research capacity to support more locally relevant evidence generation. (pp. 24 & 26)

5. A 30 January 2020 article in *New Scientist* 'Coronavirus: Are there two strains and is one more deadly?' (see here) noted:

> A vaccine that stops people being infected by the new coronavirus would obviously be better than any treatment, but that is some way off. *"A vaccine would take at least a year, if not more,"* says virologist Jonathan Ball at the University of Nottingham, UK.
>
> The good news is that a few existing drugs might help to save lives in the meantime. *And new treatments could be developed in as little as six months.*
>
> There are two ways of treating viral infections. One is to find small molecules that stop viruses replicating by interfering with viral proteins. Antivirals are usually simple to manufacture, and can be taken in pill form, both big advantages.
>
> But 99 per cent of potential small-molecule drugs fail, says Ball. *So developing new antivirals from scratch could take years*.
>
> The second way is to use the same weapons that our bodies use: antibodies. Antibodies are large proteins that bind to viruses and trigger their destruction.
>
> When people are infected with a new virus, it can take two weeks for the body to produce enough antibodies to fight it off. Injecting people with antibodies made by cells growing in a vat can keep viruses in check until a person's immune response kicks in fully. [Italics added]

6. A 5 March 2020 article in *New Scientist* 'Coronavirus: Are there two strains and is one more deadly?' (see here) noted:

When Xiaolu Tang at Peking University in Beijing and colleagues studied the viral genome taken from 103 cases, they found common mutations at two locations on the genome. The team identified two types of the virus based on differences in the genome at these two regions: 72 were considered to be the "L-type" and 29 were classed "S-type".
A separate analysis by the team suggests that the L-type was derived from the older S-type. The first strain is likely to have emerged around the time the virus jumped from animals to humans. The second emerged soon after that, says the team. Both are involved in the current global outbreak. *The fact that the L-type is more prevalent suggests that it is "more aggressive" than the S-type, the team say.*

"There do appear to be two different strains," says Ravinder Kanda at Oxford Brookes University in the UK. "[The L-type] might be more aggressive in transmitting itself, but we have no idea yet how these underlying genetic changes will relate to disease severity," she says.

"I think it's a fact that there are two strains," says Erik Volz at Imperial College London. "It's normal for viruses to undergo evolution when they are transmitted to a new host."

It is vital to know how many strains of the virus exist. Around the world, multiple groups are working on a vaccine for the virus. Any vaccine will need to target features that are found in both strains of the virus in order to be effective. [Italics added]

7. A 19 April 2020 paper (non-peer reviewed) published on *medRxiv* 'Patient-derived mutations impact pathogenicity of SARS-CoV-2' (see here) published by researchers from Zhejiang University found:

SARS-CoV-2 is the seventh member of enveloped RNA beta-coronavirus (Sarbecovirus subgenus) (Zhu et al., 2020); SARS-CoV-2, SARS-CoV and MERS-CoV can lead to devastating diseases, while HKU1, NL63, OC43 and 229E are related with mild symptoms (Corman et al., 2018). So far, no recombination events were detected (Yu, 2020), although this could be at least partially due to the fact that most viral isolates were sequenced with short-reads platform.
[…]
Despite the abundant variability of SARS-CoV-2, *one key question remains as to whether these mutations have any real functional impact on the pathogenicity of SARS-CoV-2*. This is crucial in our understanding of the viral infectious mechanisms and dictates the strategy of drug and vaccine development in preparation for the next stage of the pandemic.
[…]
Our results [being samples of 11 patients] show that the observed mutations can have a direct impact on the viral load and CPE when infecting Vero-E6 cells, *as much as 270-fold differences between the extremities*. This finding suggests that the observed mutations in our study, and possibly in the viral isolates collected around the world, can significantly impact the pathogenicity of SARS-CoV-2.
[…]
In short, our study provides direct evidence that mutations currently occurring in the SARS-CoV-2 genome have the functional potential to impact the viral pathogenicity.
Therefore, *viral surveillance* should be also performed at the cellular level when possible in addition to the accumulating genomic sequencing data. Furthermore, characterizations of all founding mutations in the major geo-based clusters of viruses could be very useful in helping determining if there are actionable pathogenicity differences to aid the current battle against the virus. Finally, similar to flu, drug and vaccine development, while urgent, need to take the impact of these accumulating mutations, especially the founding mutations, into account to avoid potential pitfalls. [Italics added] (pp. 4, 5–6 & 24)

8. A 21 April 2020 article in *NZ Herald* 'Covid 19 coronavirus: Study shows disease has mutated - and some strains hit harder' (see here) on the paper in 7. above noted:

> Professor Li Lanjuan and her colleagues from Zhejiang University found within a small pool of patients many mutations not previously reported. *These mutations included changes so rare that scientists had never considered they might occur.*
>
> The deadliest mutations in the Zhejiang patients had also been found in most patients across Europe, while the milder strains were the predominant varieties found in parts of the United States, such as Washington State, according to their paper. A separate study had found that New York strains had been imported from Europe. The death rate in New York was similar to that in many European countries, if not worse. [Italics added]

9. A 23 April 2020 *Business Insider* article 'As more experimental coronavirus vaccines start human testing, industry leaders and experts doubt they'll be ready before 2022 (see here) noted:

> Geoffrey Porges, an analyst at SVB Leerink, predicted there was a less than 20% chance that a vaccine would be widely available vaccine and proven effective in 2021. Even by 2023, he estimates the likelihood of achieving that is just 50%.

10. A 24 April 2020 scientific brief "'Immunity passports" in the context of COVID-19' from WHO' (see here) notes:

> Some governments have suggested that the detection of antibodies to the SARS-CoV-2, the virus that causes COVID-19, could serve as the basis for an "immunity passport" or "risk-free certificate" that would enable individuals to travel or to return to work assuming that they are protected against re-infection. There is currently no evidence that people who have recovered from COVID-19 and have antibodies are protected from a second infection.
> […]
> WHO continues to review the evidence on antibody responses to SARS-CoV-2 infection.[2-17] Most of these studies show that people who have recovered from infection have antibodies to the virus. However, some of these people have very low levels of neutralizing antibodies in their blood,[4] suggesting that cellular immunity may also be critical for recovery. *As of 24 April 2020, no study has evaluated whether the presence of antibodies to SARS-CoV-2 confers immunity to subsequent infection by this virus in humans.*
>
> Laboratory tests that detect antibodies to SARS-CoV-2 in people, including rapid immunodiagnostic tests, need further validation to determine their accuracy and reliability. Inaccurate immunodiagnostic tests may falsely categorize people in two ways. The first is that they may falsely label people who have been infected as negative, and the second is that people who have not been infected are falsely labelled as positive. Both errors have serious consequences and will affect control efforts. These tests also need to accurately distinguish between past infections from SARS-CoV-2 and those caused by the known set of six human coronaviruses. Four of these viruses cause the common cold and circulate widely. The remaining two are the viruses that cause Middle East Respiratory Syndrome and Severe Acute Respiratory Syndrome. People infected by any one of these viruses may produce antibodies that cross-react with antibodies produced in response to infection with SARS-CoV-2.
>
> Many countries are now testing for SARS-CoV-2 antibodies at the population level or in specific groups, such as health workers, close contacts of known cases, or within households.[21] *WHO supports these studies*, as they are critical for understanding the extent of – and risk factors associated with – infection. These studies will provide data on the percentage of people with detectable COVID-19 antibodies, but most are not designed to determine whether those people are immune to secondary infections. [Italics added]

11. A 25 April 2020 *Business Insider* article 'Scientists fear the hunt for a coronavirus vaccine will fail and we will all have to live with the 'constant threat' of COVID-19' (see here) notes that:

> The UK's Chief Medical Officer, Christopher Whitty, told a Parliamentary committee on Friday that there was "concerning" evidence suggesting that it may not be possible to stimulate immunity to the virus.
> […]
> Doubts about the possibility of a viable vaccine are based largely on the fact that no vaccine has ever been approved for use in the US or UK against other forms of coronavirus.
>
> Whitty told the committee the evidence from other forms of coronavirus was that "immunity [to the virus] wanes relatively quickly."
>
> He said that the world needs "to be careful that we don't assume that we are going to have a vaccine for this disease as we have had for, let's say measles, which once you have it you're protected for life."
>
> "We cannot guarantee success," he added.
>
> "Vaccines are looked for, for every infectious disease, they are not found for all of them."
> […]
> Other scientists have also raised the possibility that a working virus may never emerge to deal with COVID-19.
>
> *In an interview with The Observer David Nabarro, professor of global health at Imperial College, London said the world had to realise that a vaccine may not be possible.*
>
> "You don't necessarily develop a vaccine that is safe and effective against every virus," he told the paper.
>
> "Some viruses are very, very difficult when it comes to vaccine development – so for the foreseeable future, we are going to have to find ways to go about our lives with this virus as a constant threat."
>
> *Even if a fully effective vaccine proves impossible, Whitty believes that a partially effective vaccine would still be worth pursuing.*
>
> "You can have vaccines that are not capable of providing [high levels of] immunity, but they provide enough protection that people don't get severe disease.
>
> "So we might get a vaccine that is rather less effective but is sufficiently effective, that if we vaccinated everyone at a high level of dying from this… we might well be able to massively reduce fatalities even if there was still natural infections." [Italics added]