To whom it may concern:

I am a molecular biologist with expertise in messenger RNA technologies and next-generation sequencing, and a broad interest in biological risk management and the power of emerging life sciences technologies to shape the world. I am writing this submission from the perspective of an educated and interested citizen; these opinions are my own, and this submission does not represent my employer.

Firstly, I would like to strongly agree with the case raised by other submissions to this inquiry that Australia should focus on primary pandemic prevention, rather than merely pandemic response. An alternative way to conceptualise this is a stronger focus on preparedness to respond to diseases with pandemic potential at the earliest possible stage, before they become widespread and disrupt social structures as happened in 2020-22. During COVID-19, we all became familiar with the 'Swiss cheese' metaphor, as applied to pandemic mitigation[1]: each measure (such as vaccination, test-and-trace, masks, sanitation, movement restrictions) prevented some transmission events, and together these measures collectively reduced the disease burden on the community. Similarly, the 'Swiss cheese' model can be applied to primary pandemic prevention and early mitigation: measures such as biosecurity improvements for animal agriculture[2,3], separation of livestock from wildlife[4], surveillance for novel pathogens[5-7], and enhancements to indoor air quality in places where many people gather or pass through[8-11] could collectively reduce the likelihood that a pathogen with pandemic potential will emerge or spread. I endorse the submissions made on this topic by Good Ancestors Policy and Australians for Pandemic Prevention, and I deeply hope that you will consider the strength of both their scientific and economic arguments for a stronger focus on pandemic prevention as we try to learn from COVID-19.

Secondly, I would like to highlight the remarkable potential of messenger RNA technologies for coping with future pandemics. The genome sequence for SARS-CoV-2 was first made publicly available by Chinese scientists on January 11, 2020[12]. Within merely 2-4 months, multiple vaccines were beginning emergency Phase I clinical trials[13,14]. The rapid pace of vaccine development in response to the COVID-19 pandemic was of course dependent on unprecedented international collaboration and funding for research, and the nature of the emergency warranted greater haste and more information sharing than is typical during early vaccine development. However, the defining feature of the unprecedented speed of the vaccine response was the application of messenger RNA (mRNA) technologies. Vaccines based on mRNA have multiple advantages that make them uniquely powerful in a rapidly-changing pandemic situation. Other vaccine technologies (including the use of purified protein, assembled protein complexes, killed pathogen, or live-attenuated pathogen) all require the sequential optimisation of several challenging laboratory steps, even in the earliest preclinical stages. Protein production and purification must typically be optimised for each individual protein[15,16], which means that high-throughput screening of multiple antigens from the pathogen of interest may take months to years to accomplish. By contrast, production of synthetic mRNA is a straightforward process which is methodologically extremely similar regardless of what the mRNA encodes[17]. High-throughput screening of different antigens (eg, different proteins encoded by the pathogen, plus isolated domains or fragments of these proteins) is feasible and can be conducted by any suitably-equipped laboratory with access to the pathogen's genome sequence; there is no requirement for access to the pathogen itself or suitable biosafety facilities and PPE with which to work on it. When mRNA vaccine candidates are ready for clinical trials or even for production and emergency usage as happened during COVID-19, we can once again benefit from the relative simplicity of large-scale mRNA manufacture, as well as the fact that mass deployment of ANY mRNA vaccine has virtually identical infrastructure, personnel and distribution requirements. This stands in powerful contrast to the specialised facilities and expertise which are required to scale up production of many vaccines using a more traditional protein-based or whole-pathogen-based formula. The speed and adaptability of mRNA-based vaccine

development was demonstrated multiple times during the pandemic, with the release of updated booster vaccines based on the sequences of COVID-19 variants that emerged later; the importance of these developments to the ultimate control of the pandemic is still an area of active research and debate[18].

When considering the potential benefits of mRNA technologies for future pandemic prevention and response, we should also take into account other advances in mRNA technology besides the development of new vaccines. For instance, Australian researchers are working on quality control measures for mRNA vaccines[19] and ways to enhance the stability of mRNA vaccines so they are easier to ship and store. As a scientist working in this field, it is difficult to overstate the amount of international interest in this technology and the hope and enthusiasm that we feel towards its potential. I strongly believe that maintaining and increasing Australia's investment in mRNA research and mRNA production and testing facilities will both enhance the likelihood that we can rapidly respond to emerging pandemics, and provide Australia with self-sufficiency for vaccine manufacture in the event of another global pandemic like COVID-19. Enhancing our understanding of and ability to apply this emerging technology should be considered a critical infrastructure investment for Australia's future.

This brings me to my third point: Australia's future pandemic strategy must include a strong focus on emerging technologies, and periodic review of technological advancements that can improve our ability to both prevent and respond to pandemics in the future. The COVID-19 pandemic has given rise to a wave of technological innovations that could prevent or mitigate future pandemics, but many have not yet reached full maturity and a fair assessment of their cost, feasibility and effectiveness cannot yet be carried out because research and development is ongoing. Some examples are widespread metagenomic surveillance[5,6], enhanced air cleaning for indoor spaces[9], far-UVC sterilisation[11], and even baking disposable respirators to allow them to be reused in an emergency situation[20]. In addition to this, the rapid pace of emerging artificial intelligence technologies poses both risks and opportunities in the pandemic response and pandemic prevention space. For example, artificial intelligence has made overwhelming advances in the past 2-3 years in the prediction of protein function from protein structure[21,22]; this could be combined with environmental or wastewater metagenomic data to identify novel pathogens with far greater sensitivity and specificity than is currently possible, and would significantly shift the cost-benefit analysis for implementing an expensive prevention measure like widespread metagenomic surveillance. Ongoing advancements in GPU technology are both driving and being driven by the AI revolution[23-25] and these are also highly relevant because of the likelihood that workflows currently limited by availability of compute resources (again, metagenomics) will become significantly more feasible to implement. I strongly suggest that Australia's pandemic strategy should include a direction to periodically reconsider measures which are scientifically plausible but not currently proven, feasible or cost-effective, because of the likelihood that ongoing technological development changes the evaluation of their usefulness to the community.

I hope that the content of this submission is of interest and value to the inquiry. Thank you for the opportunity to provide comment.

Dr Laura Leighton.

References

[1] Mackay, Emily. "How Swiss Cheese May Be a Solution to Coronavirus." (2020) *The New York Times*, 5 December 2020, https://www.nytimes.com/2020/12/05/health/coronavirus-swiss-cheese-infection-mackay.html.

[2] Bartlett H, Holmes MA, Petrovan SO, Williams DR, Wood JLN, Balmford A (2022) "Understanding the relative risks of zoonosis emergence under contrasting approaches to meeting livestock product demand," *Royal Society Open Science*, vol. 9, no. 6, Jun. 2022. https://doi.org/10.1098/rsos.211573

[3] W. Gilbert, L.F. Thomas, L. Coyne, J. Rushton (2021) "Review: Mitigating the risks posed by intensification in livestock production: the examples of antimicrobial resistance and zoonoses" Animal, Volume 15, Issue 2, 2021. https://doi.org/10.1016/j.animal.2020.100123

[4] Meurens F, Dunoyer C, Fourichon C, Gerdts V, Haddad N, Kortekaas J, Lewandowska M, Monchatre-Leroy E, Summerfield A, Wichgers Schreur PJ, van der Poel WHM, Zhu J (2021) "Animal board invited review: Risks of zoonotic disease emergence at the interface of wildlife and livestock systems" Animal, Volume 15, Issue 6, 2021 https://doi.org/10.1016/j.animal.2021.100241

[5] Mohsin H, Asif A, Fatima M, Rehman Y (2021) "Potential role of viral metagenomics as a surveillance tool for the early detection of emerging novel pathogens." *Arch Microbiol* **203**, 865–872, 2021 https://doi.org/10.1007/s00203-020-02105-5

[6] Chiu KHY, Sridhar S, Yuen KY (2023) "Preparation for the next pandemic: challenges in strengthening surveillance." Emerging Microbes & Infections, 12:2 2023 https://doi.org/10.1080/22221751.2023.2240441

[7] Oeschger TM, McCloskey DS, Buchmann RM, Choubal AM, Boza JM, Mehta S, Erickson D (2021) "Early warning diagnostics for emerging infectious diseases in developing into late-stage pandemics" *Accounts of Chemical Research* **2021** *54* (19), 3656-3666 https://doi.org/10.1021/acs.accounts.1c00383

[8] Duffield G, Bunn S. (2023). "Indoor air quality." Parliamentary Office of Science and Technology, UK Parliament. https://doi.org/10.58248/PB54

[9] Haines CA, Olsiewski P, Bruns R, Gronvall GK (2022). "National Strategy for Improving Indoor Air Quality." Johns Hopkins Center for Health Security. https://centerforhealthsecurity.org/sites/default/files/2023-02/20221026-nsi-iaq-report.pdf

[10] The Lancet COVID-19 Commission Task Force on Safe Work, Safe School, and Safe Travel (2022) "Proposed Non-infectious Air Delivery Rates (NADR) for Reducing Exposure to Airborne Respiratory Infectious Diseases." https://static1.squarespace.com/static/5ef3652ab722df11fcb2ba5d/t/637740d40f35a9699a7fb05f/1668759764821/Lancet+Covid+Commission+TF+Report+Nov+2022.pdf (accessed December 2023)

[11] Welch D, Buonanno M, Grilj V, Shuryak I, Crickmore C, Bigelow AW, Randers-Perhson G, Johnson GW, Brenner DJ (2018). "Far-UVC light: A new tool to control the spread of airborne-mediated microbial diseases." Scientific Reports, 8(1), Article 1. https://doi.org/10.1038/s41598-018-21058-w

[12] Cohen, Jon (2020) “Chinese Researchers Reveal Draft Genome of Virus Implicated in Wuhan Pneumonia Outbreak.” *Science.org*, (Jan 11, 2020) https://www.science.org/content/article/chinese-researchers-reveal-draft-genome-virus-implicated-wuhan-pneumonia-outbreak.

[13] "NIH Clinical Trial of Investigational Vaccine for COVID-19 Begins." *NIH News Releases*, (March 16, 2020) https://www.nih.gov/news-events/news-releases/nih-clinical-trial-investigational-vaccine-covid-19-begins.

[14] Mulligan MJ, Lyke KE, Kitchin N, […], Jansen KU (2020) “Phase I/II study of COVID-19 RNA vaccine BNT162b1 in adults.” *Nature* **586**, 589–593 (2020). https://doi.org/10.1038/s41586-020-2639-4

[15] Stern PL (2020) “Key steps in vaccine development” Annals of Allergy, Asthma & Immunology, Volume 125, Issue 1, 2020, Pages 17-27, ISSN 1081-1206, https://doi.org/10.1016/j.anai.2020.01.025.

[16] Structural Genomics Consortium, Architecture et Fonction des Macromolécules Biologiques., Berkeley Structural Genomics Center. *et al.* (2008) “Protein production and purification.” *Nat Methods* **5**, 135–146 (2008). https://doi.org/10.1038/nmeth.f.202

[17] McKenzie RE, Minnell JJ, Ganley M, Painter GF, Draper SL (2023) “mRNA Synthesis and Encapsulation in Ionizable Lipid Nanoparticles.” *Current Protocols*, *3*(9), e898. https://doi.org/10.1002/cpz1.898

[18] Khoury DS, Docken SS, Subbarao K, Kent SJ, Davenport MP, Cromer D (2023) “Predicting the efficacy of variant-modified COVID-19 vaccine boosters.” *Nat Med* **29**, 574–578 (2023). https://doi.org/10.1038/s41591-023-02228-4

[19] Gunter HM, Idrisoglu S, Singh S, Han DJ, Ariens E, Peters JR, Wong T, Cheetham SW, Xu J, Rai SK, Feldman R, Herbert A, Marcellin E, Tropee R, Munro T, Mercer TR (2023) “mRNA vaccine quality analysis using RNA sequencing.” *Nat Commun* **14**, 5663 (2023). https://doi.org/10.1038/s41467-023-41354-y

[20] Oh C, Araud E, Puthussery JV, Bai H, Clark GG, Verma V, Nguyen TH (2020) “Dry Heat as a Decontamination Method for N95 Respirator Reuse.” ChemRxiv. Cambridge: Cambridge Open Engage; 2020; This content is a preprint and has not been peer-reviewed. https://doi.org/ 10.26434/chemrxiv.12290621.v2

[21] Mufassirin, M.M.M., Newton, M.A.H. & Sattar, A. “Artificial intelligence for template-free protein structure prediction: a comprehensive review.” *Artif Intell Rev* **56**, 7665–7732 (2023). https://doi.org/10.1007/s10462-022-10350-x

[22] Wong F, De La Fuente-Nunez C, Collins JJ (2023) “Leveraging artificial intelligence in the fight against infectious diseases.” *Science***381**,164-170(2023). https://doi.org/10.1126/science.adh1114

[23] *LoginVSI.* "2023 Insights: The Evolution of AI and Its Impact on GPU." (2023) https://www.loginvsi.com/resources/blog/2023-insights-the-evolution-of-ai-and-its-impact-on-gpu/.

[24] Wodecki, Ben. "AMD vs Nvidia: The Battle for AI GPU Supremacy Begins." *AI Business* (2023) https://aibusiness.com/verticals/amd-vs-nvidia-the-battle-for-ai-gpu-supremacy-begins

[25] Morgan, Timothy. “The tidal wave of rising of GPU TAM raises all boats” *The Next Platform* (2023) https://www.nextplatform.com/2023/12/07/the-tidal-wave-of-rising-gpu-tam-raises-all-boats/