

Inquiry into the COVID pandemic

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In line with the Inquiry Terms of Reference, we would like to forward our appreciation and thanks for the opportunity to make comments on the "Australian Government's response to the COVID-19 pandemic and other issues relevant to the health and medical research and innovation sectors, such as the effect of COVID-19 on research and the Government's response".

We collectively are biomedical scientists, physicians and managers with a national and International standing as well as extensive experience in research prioritization management and commercialization. We have been active in clinical design for a treating the host response to the current COVID-19 pandemic.

Summary:

Overall it is clear that the response to the COVID pandemic was a test of the National resilience, responsiveness and strategic depth of the Australian health and research enterprise, in a manner not dissimilar to the bushfire challenges in December 2019-Jan 2020. In that context, we believe Australia made excellent public health decisions to protect the public and the Nation as a whole. The results speak for themselves. Likewise, across many research areas such as modelling, epidemiology and testing the response is outstanding.

To us, one of the few areas of disappointment is the therapeutic research arena. It is this important domain that would have enabled us to have or have approaches to an armamentarium of safe, effective, cheap, and already available therapies for host treatment in this pandemic. We believe this area requires attention. Attention to prevent fragmentation of effort and to implement strategic principles matched to the needs of a pandemic like those enacted so well in allied response areas.

What is evident in the current course of the pandemic:

- The public health and advice-giving response from the Chief Medical Officer (CMO) and State Chief Health Officers (CHOs) was analogous to the exceptional leadership with Chief Fire Commissioners in the bushfire crisis. Likewise, the role of politicians in letting the CMO and staff have the space to act in leadership was outstanding as it was also in a similar way in the bushfire crisis. Additionally, the CMO/CHOs and staff in engaging physicians and GPs and other groups on the front line and getting realistic feedback is an excellent example of strategic management at its best.
- The epidemiological and modelling teams and those that implemented early and targeted testing and tracing have been truly exemplary. Our view is that the immunological /vaccine development research community are well globally connected and thoroughly organized.
- From a strategic management perspective, the formation of the National COVID-19 Coordination Commission (NCCC) to anticipate and mitigate the economic and social effects

of the global coronavirus pandemic was a laudable development. We believe that approach has a place in addressing the therapeutic area of disappointment we have highlighted.

- Broadly the role of the community in accepting a high stringency in isolation was something we should be nationally proud of.
- For us one of the few areas of disappointment resides with the therapeutic research arena. The area that enables us to have or to have approaches to an armamentarium of safe, effective, cheap, and already available therapies for treatment in this pandemic. We believe this area requires attention.

What were we expecting in the area of therapeutic research area with COVID-19?

An understanding that the machinery that supports therapeutic research funding year in year out in a bottom up grant in aid process while very important, differs from that needed in response to a crisis. A top down process utilizing a single national panel lead by strategists is needed. This panel may consist of biomedical discipline and technical experts if they have demonstrated leadership skills and authoritative behaviors in the national interest, but should also include those not within specific biomedical disciplines but with outstanding skills and reputations as leaders – that is, in serving unmet need with critical decision making on a regular basis (Australia had a brilliant example with the Essington Lewis leadership in the biggest crisis in our history)

From a strategic management perspective, a similar approach to that established with the National COVID-19 Coordination Commission (NCCC), that describes how Australia's biomedical research capacity could deliver the needed therapeutic armamentarium should have been developed, and in a top down managerial fashion implement the necessary research for implementation. Why this approach is critical is because it is self-evident that the suite of solutions needed to reduce the morbidity and mortality from COVID cuts across fixed interests and previously effective methods of succeeding in grant funding rounds, including silos of 'ology disciplines in Universities, news cycles and campaigns for untested policies.

In summary, we believe the best approach for therapeutic solutions draws on the success of the NCCC and should achieve an identification of the top 5 to 10 drugs this country would focus its research on in the current and future pandemics.

What would the therapeutic Armamentarium look like in Australia a pandemic?

In any pandemic the ideal position to be in is one in which an effective vaccine or antiviral drug is available to the population. Australian biomedical research is contributing importantly to this effort. Both goals are being globally pursued and both require time to achieve fruition. There are however therapeutic measures that enable societies to bridge time chasm that involve the principle of treating the host with existing (repurposed) approved drugs. The concept of treating the host is entirely complementary to opportunities arising in the area of drug repurposing that our team has highlighted recently (1,2). In the case of COVID-19 disease this would mean identifying drugs that are focused, not on the elimination of the virus, but upon the survival of the patient with severe COVID-19 disease. This includes drugs approved for other indications that have the beneficial phenotype for treating severe COVID-19 disease. The fundamental advantages of this approach are; firstly, to buy needed time for the concurrent development of anti-viral or vaccines, secondly to provide health authorities a treatment insurance as they begin to release the public from social isolation.

With the emergence of the virus that causes COVID-19 the sites of viral attack were quickly ascertained. From that information it is possible to short list known therapeutics that could be tested not only to buy time for vaccine and anti-viral development but to provide the necessary therapeutic insurance as social isolation is eased. Because of the evolutionary nature of any virus in a pandemic a knowledge of what therapeutics were or were not effective also impacts upon treating these host approaches.

In summary based on these principles, we would expect to have an identification of the top 5 to 10 drugs in an Australian therapeutic Armamentarium to be explored in response to this and future pandemics.

What strengths would Australia bring to bear on the creation of a treating the host armamentarium?

In looking at the many areas of success to date in Australia's response to COVID-19 the one standout feature is a cultural pragmatism. We would argue that the treating the host concept in therapeutics described above fits well with an Australian cultural pragmatism. For example, it is identical in principal to the saving of life and assets strategy employed in the recent Australian bushfire crisis. In that case treat the host, ***not*** immediately the fire. In addition to building on pragmatism the following to our mind underutilizes skills in the context of COVID-19 could be employed:

- Our internationally recognized skill base in pharmacology, clinical pharmacology and pharmacy that could form a cornerstone of a national pandemic response in treating the host.
- Our data handling capacity. One of the key inputs to identifying candidate repurposing drugs is analysis of existing administrative data sets relating to existing non pandemic drug treatments. Australia has invested heavily in health records and we have outstanding ICT and statistical graduates in this country all of which is ideally harnessed in responding to this pandemic by unitizing data-based selection of drugs to treat the host.
- Australia has been one of the global leaders in prevention particularly as it relates to nutrition. We know recognize the profound link between immune function and response and the gastrointestinal system. There is no reason why Australia should not lead in drug diet interactions in a pragmatic treating the host response to COVID-19 disease.

What were our observations and impressions on the existing response?

At the risk of dwelling too intensely on the negatives we gained the following key impressions:

- The absence of an Australian cohesive vision and strategy for implementation in the therapeutics area.
- The absence of a National set of therapeutic drug targets for COVID-19.
- The absence of a single national authority coordinating the therapeutic approach and implementation in the response to COVID-19 (We acknowledge that there were

calls from funding agencies however for research proposals in the COVID-19 area but as mentioned in our view a top down process is needed in a crisis.)

- As seasoned investigators we saw fragmentation. Fragmentation of a national focus, fragmentation of strategy, fragmentation of effort and fragmentation resources. There was significant fragmentation in the duplication of committees – LHDs, state committees, federal committees, specialty groups etc, often with technically skilled successful experts but because of that very point, collectively at risk of lacking the exposure at a national level to crisis strategy and management that is needed in a pandemic.
- Lack of involvement of leading therapeutics/clinical pharmacology/toxicology teams (vaccine and antiviral input was however sought), or opportunities for leadership.

Conclusions and recommendations.

As we indicated at the start of this submission, we are extremely impressed with so much of the biomedical activity that has gone on in Australia in response to COVID-19 disease. We are all indebted to that professionalism. On reflection the success has been due to consultative top down leadership, clarity of purpose and message, effective translation and an absence of fragmentation and duplication.

For us one of the few areas of disappointment is the therapeutic research arena which we believe can be remedied. The area that enables us to have or to have approaches to an armamentarium of safe, effective, cheap, and already available therapies for treatment in this pandemic. In the absence of vaccine or antiviral for CoV-SARs-2 and all of us still within its presence we would suggest:

- this area requires attention if for no other reason it stands in contradistinction to the allied high level COVID-19 coordinated responses.
- An overarching strategy group analogous to the NCCC be established to ensure Australia has as soon as possible a path to having a therapeutic armamentarium with this and any subsequent pandemics. Tasked with delivering the top 5 to 10 drugs in an such a repository to be evaluated in a treating the host response to COVID-19 and future pandemics.
- Longer term non-pandemic aspects of what we have raised on therapeutic research needs we believe further discussion. What learnings can we take to create new commercial opportunities for Australia particularly in the area of repurposing existing drugs for new indications.

We would like to thank you again for the opportunity to respond and of course would be happy to elaborate further on what we have raised if you wish us to do so.

Potential conflicts of interest.

Two of us (JM, RH) were on a NHMRC application for trialing two candidate treating the host candidate drugs in response to COVID-119. As of writing this response we are unaware of the outcome of that application.

Two of us submitted a comprehensive proposal for Australia to establish a Repurposing Center to the MRFF funding program, which included within its methodology an opportunity for such a national therapeutics solution for national benefit. This program was put on hold immediately after submission due to the COVID-19pandemic.

These are the private views of the authors and do not necessarily represent the views of our host or affiliated organizations.

REFERENCES

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