Submission 265 — Professor John Rasko

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Dear Secretariat

I am writing on my own behalf to address some of the questions posed as part of the public consultation for the McKeon Review. For thirty years I have been involved in biomedical research and have established a large clinical and basic research program comprising the Department of Cell and Molecular Therapies at Royal Prince Alfred Hospital and the Gene and Stem Cell Therapy program at the Centenary Institute. I have an international profile in biomedical research specifically related to genetic therapies, molecular biology and stem cells. I am very familiar with the Australian biomedical research environment having received dozens of grants from the NHMRC, ARC, philanthropy and industry. I am responsible for one of only a handful of public good manufacturing practice, physical containment level 2 laboratories for human cell manufacture in Australia. I feel privileged to undertake biomedical research in Australia and recognise our strengths in basic medical research up to the proof of concept stage. Having worked in the United States during a post doctoral fellowship for three years, I am very mindful of the substantial weakness that Australia suffers in taking advantage of medical therapeutics that would lead to the success of small and medium biotechnology enterprises and consequent clinical outcomes.

First, I wish to emphasise the critical importance of Australia in maintaining its productivity as a leading contributor to international biomedical research. I cannot emphasise enough the fact that for our nation to take advantage of new developments in clinical therapeutics, we need to begin our own development programs at the ground floor. It is inappropriate to wait until other countries have matured “winners” to the point where they are clinically proven while we wait on the sidelines in anticipation of catching up. Time and again, it is clear that the familiarity and skills born out of drug development both in clinical therapeutic, laboratory monitoring, diagnostics and pathology provide profound benefits in the medium and long term. There may be perceived short-term financial gains obtained by not participating in early-phase studies but these are greatly outweighed by the disadvantage created in the long term. Early familiarity with technologies and therapeutics is essential if we are to maintain the highest level of clinical care for our citizens. Thus, it is without doubt in Australia’s greatest interest to maintain a viable and international competitive health and medical research sector. The means by which this may be achieved is addressed below.

Perhaps the greatest weakness that I perceive in the Australian system compared to many other comparable countries is the failure to provide adequate infrastructure

support and funding for the full costs of research including salaries. The disparity and competition between small and medium-sized biomedical research Institutes and Universities translates into direct and often-fierce competition for public philanthropy. Many Institutes and universities are now spending enormous time and money in attempting to chase funds that are applied for maintaining services and essential infrastructure such as administrative support, maintenance of essential services and core facilities. This “wasted effort” and internal competition within the sector translates into diversion of time and money and should be immediately addressed by the Federal government. This is not anew problem and has been ignored for far too long. The current infrastructure support typically provided by the states and federal government is grossly inadequate to maintain services and infrastructure required for leading biomedical research. Most members of the public I speak with are shocked to hear that only less than 1% of the total health budget is spend on health and medical research – they usually guess it might be ten times that amount. So there appears to be a disconnection between what is perceived as the appropriate proportion spent on medical research and what is actually spent. An immediate doubling of this investment in the health of our nation would be a good start.

In terms of the management of health and medical research, the provision of adequate infrastructure funding linked to competitive, peer-review grant schemes should be seen as the carrot in bringing greater accountability of all research enterprises. My perception is that the silos created by independent biomedical research institutes and university departments have led to relatively inconsistent governance and a lack of rigour in providing the public with transparency. Philanthropic fund raising is poorly regulated in general and there appears to be a plethora of small foundations, which are variably successful in raising large amounts of money. The practice of some independent foundations in funnelling their grant application review processes through the NHMRC and other government bodies is preferable to the wide disparity that currently exists.

The expert review panel should also make note of the shambles that implementation of the RGMS online grant system created. Biomedical researchers have over the last few years been subjected to appalling impositions on their private time because of the failure to properly test and validate the ability of the online system to cope with routine annual grant applications. Although the system is improving, it remains counter-intuitive, difficult to navigate, repetitious and poorly integrated. The RGMS system is ‘user-unfriendly’. This situation is not the case for the ARC, nor is it the case for grant systems available in many other countries. The direct and uncounted consequence is that most Institutions have had to take on considerable additional staff in order to accommodate the demands of this poorly-conceived and implemented system. For a country of our size and with the amounts of money involved, this is simply unacceptable and perhaps a separate inquiry should be established.

The likelihood of truly personalised medicine and the availability of individual genomes in patients with cancer and rare genetic diseases will become a reality in the next decade for those who can afford it. The changes mean that we will all soon face an entirely new world in the way that biomedical research engages directly with clinical care. The Royal Australasian College of Pathologists has a role in this area as diagnostic molecular medicine and monitoring has been gradually introduced in some instances, particularly those associated with successful new drugs such as Herceptin and tyrosine kinase

inhibitors such as Imatinib. Molecular monitoring and genetic testing will continue to burgeon in the coming years. I see little way of avoiding this dramatic change but our population will demand nothing less than the ready availability of information and therapeutic opportunities. It is clear that in the case of various cancers, there is often a small subset that may be treated with existing drugs that would otherwise not be used because of molecular mutations that have not been identified. The opportunities for small subsets within various cancer types to be treated with existing therapies are real, but our patients are missing out because the information is not readily available in each tumour type. There must be new money invested in seeing that these molecular subtypes of disease are readily indentified to offer patients the highest chance of clinical benefit.

In the area in which I am most familiar, cellular therapies with or without genetic manipulation, our patients are demanding access to novel often-times-unproven cellular treatments that are widely advertised overseas and on the internet. I have published in this area concerning “medical tourism” and the number of Australian citizens travelling to clinics in Europe, South East Asia and South America is surprisingly high. The government must play a role in not only strict regulation of appropriate, cost-effective therapies in Australia but also in educating the public in a more direct manner about what is proven versus that which is only in clinical development or experimental. However, it seems to me that the majority of so-called “stem cell therapies” are nothing more than bogus claims using one-size-fits-all cells of dubious origin. These issues are being directly raised in the courts in many states in the United States of America. The current regulatory environment in Australia regarding cellular therapies is very strict and the new biological framework implemented with “full cost recovery” as its mandate will inhibit the early introduction of cell therapies in Australia. The TGA needs to receive adequate funding for careful regulation but at the same time public lobbying and medical tourism will create an environment in Australia where many patients will travel overseas for treatments and thereby lose their protection from an outstanding Australian healthcare system.

It is my opinion that we can do much better to encourage early phase clinical trials in cellular therapies in Australia by providing tax incentives and opportunities for philanthropy to leverage venture capital investment in clinical centres of excellence located in public institutions. This should address our weakness in translating early-phase discoveries into clinical outcomes. We need to be participating in the earliest-phase clinical studies in order to expand the clinical familiarity with these new modalities of therapy. I firmly believe that a new component of medicine will be based on a greater understanding of molecular genetics and implementation of cellular and genetic therapies. Specifically in relation to genetics, Australia has failed to adequately anticipate the dramatic increase in genetic sequence-based information and its analysis. Whilst the technical aspects of gene and genome sequencing can be outsourced or performed in centralised laboratories, the analysis and clinical interpretation of this vast amount of information cannot be adequately addressed. The availability of online sequencing services offshore means that patients are now able to bring their entire genome to clinical practitioners. We need an urgent increase in funding to expand the training of computational scientists, experts in bioinformatics and biostatistics, clinical genetic counsellors and geneticists who can interpret the complexity of this information and provide risk stratification. The public interest and demand is very high and already much of this testing is being performed offshore with little or no regulation.

Historically it would be fair to say that Australia's greatest strengths have been in early biomedical research discoveries. Our weakness has been in translating these basic discoveries into clinical therapeutics. In my opinion this has been due to a lack of adequately trained and experienced middle management and a failure to embrace the concept of investing in high-risk, high-return ideas. The phenomenal success of biomedical and biopharmaceutical industries in California and other parts of the world is due to partnerships between investors who are familiar with high risk venture-capital concepts and managers who can take an idea from discovery to clinical trial. Our hospitals and universities are currently poorly-positioned to take advantage of such opportunities even if they were presented. Biomedical research institutes may have greater agility in facilitating translational research but I am concerned at the cronyism, and even nepotism, that can easily occur without strict independent governance and oversight. The failure of Health Departments to properly incentivise the creation of intellectual property by individuals is just one example of where improvements may be made. Currently there is little or no incentive for clinicians or hospital scientists to pursue the protection of new ideas. I accept that these problems cannot be solved without substantial consultation and negotiation, but little progress appears to have been made over many years.

I am most familiar with developments in the NSW Health system, but with changing funding models it would appear that our system is now inhibiting the encouragement of clinician-scientists. For me, the cornerstone of biomedical research is the clinician-scientist who may stand between the basic research laboratory, translational medicine and clinical trials. Not every physician at the front line needs to be a clinician-scientist, but there appears to be a shift towards de-incentivising these crucial individuals. The Royal Australasian College of Physicians and other Colleges have sought to provide funds to encourage trainees and early-career fellows into making a commitment to biomedical research of clinical relevance, but the sustainability of such a career seem increasingly difficult. Again, part of the solution is to provide new money if we are to be in a position to provide the best possible health care in the future—particularly as our population ages and obvious shifts in disease demographics follow.

In addition to the comments regarding small philanthropic funding agencies above I would also like to highlight the inconsistencies that such well-meaning incentives create. The fundraising success of large foundations that address common diseases such as those of the cardiovascular system, diabetes as well as breast and prostate cancer to name a few does not make sense to my way of thinking. Time and again it has been the case that real breakthrough discoveries have been made in areas not entirely anticipated within a given field. In particular, is obvious to anyone working on the genetics of cancer that new drugs and new genetic information may be relevant to a wide array of different cancers and that fund raising for a specific sub-type of cancer may not necessarily be the best way to achieve clinical outcomes in the future. Of course philanthropy is very important to biomedical research and I would never seek to discourage this activity, but the focus on common diseases does lead to a relative disadvantage for those patients who suffer rare diseases. To this end, I would ask the review committee to take note of international initiatives for about 7000 so-called "rare diseases" which when grouped together actually comprise a substantial percentage of health care needs. The Orphan Drug Act and organisations like the National Organization for Rare Disorders and equivalents in Europe should be examined. As has been highlighted, the new information available from genetics means that substantial

advances in rare diseases may be more easily obtained than the effort required to improve understanding and outcomes for more intractable but common diseases.

One problem that is relatively unique to Australia is our geographic isolation and differences in time zones specifically with Europe and the USA. Anyone who has attempted to participate in spoken communications between Europe, the USA and Australia is confronted with the realisation that very short windows of opportunity are present during the working day for discussion. This problem is long standing of course but new technologies mean that we are increasingly engaging with collaborators throughout the world on a regular basis. This can only be a good thing for Australian biomedical research and healthcare. However, much more can be done to facilitate the ease with which researches and clinicians can communicate with colleagues overseas. The government can play an important role in facilitating the infrastructure acquired to encourage these communications and take advantage of investments in a national broadband network or equivalent. In addition, a more realistic funding model should be implemented to actively encourage Australians to travel internationally to important meetings and to report their findings in an accountable manner.

I recognise the massive problems confronting Australia in “closing the gap” between indigenous and non indigenous Australians as well as our international responsibilities to the developing world, but have little professional insight to offer sadly. My own personal focus on future technologies and our obligations to seeing that they be carefully, wisely and responsibly introduced with fiscal responsibility are critical to the future health of our nation. I wish the panel well in its important deliberations and would be happy to provide further clarifications or advice as required.

Yours sincerely

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