s 9(2)(a)

6 June 2018

Hon Dr David Clark
Minister of Health
PO Box 18041
Parliament Buildings
Wellington 6160

Hon Iain Lees-Galloway
Minister for ACC
PO Box 18041
Parliament Buildings
Wellington 6160

Dear Hon Dr David Clark and Hon Iain Lees-Galloway,

Compensation for participant injuries in pharmaceutically-sponsored clinical trials

s 9(2)(a)

On 11 May 2017 I wrote to Hon Peter Dunne, Associate Minister of Health and Hon Michael Woodhouse, Minister for ACC, advising of the need for an urgent review of the exclusion from ACC cover for Treatment Injury of participants injured in pharmaceutically-sponsored clinical trials in New Zealand (s 32(6) of the Accident Compensation Act 2001). I enclose a copy of my letter.

By letters dated 15 and 19 June 2017 respectively (copies enclosed), Ministers Dunne and Woodhouse advised that no review would be undertaken, because they did not consider there was sufficient justification at that time to remove the ACC cover-exclusion for commercially funded participants in clinical trials.

The purpose of this letter is to urge you both to reconsider the previous Ministers' decisions in this respect and to instruct your Ministries to undertake such a review on an urgent basis.

An indication of the need urgency is that since that correspondence, I understand that a man has died in a clinical trial of a medical device in Christchurch in 2017, when a catheter slipped during a cardiac procedure. While serious injuries and deaths in clinical trials are uncommon, they do occur. In 2014 two men suffered serious injuries in separate commercially-sponsored Phase III clinical trials, both having been approved by the Multi-Centre Ethics Committee.[1] In 2015, the pharmaceutical company sponsor finally reached a confidential settlement of one man's claim, while the man in the other trial has never received any compensation for his injury. In all three of these cases it is likely that the participants or their dependents would have been covered and compensated by the ACC scheme, had the trials in question been publicly-funded.

As explained in my 11 May 2017 letter, since 1992 participants injured in clinical trials sponsored by a pharmaceutical company have been excluded from ACC Treatment Injury cover and access to legally enforceable, no-fault compensation. Instead they must rely on

[1] See MEC Ref 11/1/092, Multi-region Ethics Committee Minutes 15 November 2011, p 10; MEC Ref 12/02/013, Multi-region Ethics Committee Minutes, 21 February 2012, p 6.

compensation from the sponsor or researcher in the event of injury. The legal arrangements in place for compensating injured participants are seriously legally and ethically deficient and leave injured participants financially vulnerable. The reason is that the sponsor's obligation to pay ACC-equivalent compensation under applicable guidelines[2] is expressly stated to be "without legal commitment." As a result, the sponsor's obligation is morally binding only; it is legally unenforceable by the injured subject. By comparison, participants injured in publicly-funded clinical trials are legally entitled to reasonably generous, no-fault compensation for ACC Treatment Injury, provided they are able to establish the criteria for cover.

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s 9(2)(a) The reason is that the Health and Disability Ethics Committees' (HDEC) template Participant Information Sheet (PIS) incorrectly states that "compensation would be available from the drug sponsor if something should go wrong." Potential participants are not given a copy of and never see the *Guidelines*, which are the only document in which it is stated that the compensation obligation is "without legal commitment." Accordingly, many participants consent to inclusion in commercially sponsored clinical trials without giving fully informed consent to the compensation arrangement in place. On 6 December 2016 the Chairs of the HDECs wrote to me (enclosed, with my reply of 11 May 2017), advising that they agreed that their PIS template needed to be revised to make it more explicit that a sponsor's legal commitment to pay compensation was lacking. Minister Dunne's letter stated that this exercise would be completed by the end of September 2017. This has not happened, and the PIS template wording remains exactly the same. I feel sure that Health Legal would advise you that the failure to correct this misrepresentation, drawn to the Ministry's and HDECs' attention, exposes HDECs to the potential for legal liability, should a participant be injured in a trial, having relied on the information in their PIS template.

The National Ethics Advisory Committee, officials in the Ministry of Health, and the chairs of HDECs collectively have all opposed the exclusion of injuries in commercial trials from ACC cover, and made successive (but unsuccessful) approaches for change. The simplest way to achieve this would be by repeal of s 32(6). Various reasons were given by Ministers Dunne and Woodhouse in support of s 32(6). All are either fallacious or surmountable. (Though tempted to state reasons in support of this rather arrogant-sounding claim, you will no doubt be grateful that I appreciate that this already long letter is not the place to do so!) In particular, extending ACC cover to participants injured in commercial trials could fiscally neutral i.e. achieved without requiring taxpayer funding. Pharmaceutical companies would be required to pay a levy to ACC for cover for injuries in their trials (exchanging the insurance premium they are required now to pay for payment of a levy). That levy can be set to cover ACC's additional costs of compensating these injuries. Indeed, the levy could be set at a higher rate, if that was considered necessary to achieve adequate deterrence of pharmaceutical companies from conducting unsafe clinical research.

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[2] See Medicines New Zealand, *Guidelines on Clinical Trials Compensation for Injury resulting from Participation in an Industry-sponsored Clinical Trial* (2015)

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In closing, in view of the recent death of a participant and the deficiencies in informed consent processes, I emphasise the need for you to give serious consideration to expediting this issue. (I would be pleased to lend any expertise to assist).

I look forward to your reply.

Yours sincerely,

s 9(2)(a)

Office of Hon Peter Dunne

MP for Ōhāriu

Minister of Internal Affairs

Associate Minister of Conservation

Associate Minister of Health

15 JUN 2017

s 9(2)(a)

Ref. 1730141

Dear s 9(2)(a)

Thank you for your letter of 11 May 2017 about ACC compensation for people injured in pharmaceutically-sponsored clinical trials. Responsibility for ACC legislation lies with the Minister for ACC, Hon Michael Woodhouse, and I understand he will be responding to you about this matter.

The Government agrees that it is important that participants in commercial clinical trials are appropriately protected and that researchers are open about their claims and any adverse outcomes that occur during their trials. There has been some progress in this area. Serious adverse events in clinical trials must be reported on in annual progress reports. Since 2016 the Health and Disability Ethics Committees (HDECs) have also specifically requested that a declaration about claims made in commercially sponsored trials be included in annual reports.

Further work is under way. By the end of September, HDECs are proposing to update the guidance in templates for participants in clinical trials to make it clearer for participants what avenues for redress they have and that ACC cover does not apply to commercially sponsored trials. Work on national ethics guidelines formerly undertaken by the National Ethics Advisory Committee will be progressed this year, and updated advice on protection for study participants in commercially sponsored trials will form part of these guidelines.

The Ministry of Health is developing a Therapeutic Products Bill to update the regulatory regime around medicines, medical devices and other therapeutic products in New Zealand. The Bill could be an opportunity to consider these issues further in the interests of protecting trial participants. An Exposure Draft of the Bill and other consultation material is expected to be released before the end of 2017.

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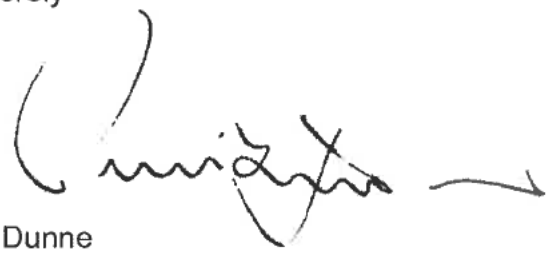
Thank you for raising your concerns with me.

Yours sincerely



Hon Peter Dunne
Associate Minister of Health

cc Hon Michael Woodhouse
Minister for ACC
Parliament Buildings
Wellington

Office of Hon Michael Woodhouse

Minister for ACC
Minister of Immigration
Minister for Workplace Relations and Safety
Deputy Leader of the House

19 JUN 2017

s 9(2)(a)

Copy to:
Hon Peter Dunne
Associate Minister of Health

Dear s 9(2)(a)

Thank you for your 11 May 2017 letter seeking a review of the exclusion from ACC cover for participants injured in commercial clinical trials, for instance, those sponsored by pharmaceutical companies (s 32(6) of the Accident Compensation Act 2001).

You suggest that this would address your concerns regarding injured commercial clinical trial participants being reliant on compensation from sponsors or researchers, which is potentially difficult to enforce. You also suggest that such reform could relieve the clinical trials industry of insurance and claims costs in exchange for payment of ACC levies, and that this would likely be welcomed by the industry.

It is important that participants in commercial clinical trials have appropriate protections, and where people are injured as a result of their participation that they receive appropriate compensation.

I do not consider that there is sufficient justification at this time to remove the ACC cover exclusion for commercial clinical trial participants. The exclusion was introduced to ensure that commercial trial sponsors and researchers would take responsibility for injury costs relating to their trials, to incentivise good risk management and avoid cost pressure on the Accident Compensation Scheme (AC Scheme).

While information regarding clinical trial-related injuries and compensation paid is limited, there is little evidence at this time to indicate that commercial trial sponsors and researchers are not taking responsibility for injuries relating to their trials and that people who are injured are missing out on compensation. I am only aware of two people that have had claims relating to alleged injuries

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resulting from their participation in commercial clinical trials delayed or denied by the companies concerned. I understand that one of those claims has since been resolved.

Additionally, it is not clear that expanding the AC Scheme in this way would necessarily result in injury claims being accepted by ACC that would not be accepted and compensated by sponsors or researchers under current arrangements. Like trial sponsors and sites, ACC would have to determine the circumstances relating to the injury before providing any assistance. For example, ACC would need to determine whether an alleged injury was caused as a result of participation in a trial, or through underlying health factors before accepting a claim.

I acknowledge that if the AC Scheme was expanded to provide cover for participants injured in commercial clinical trials, that the industry could be levied to cover the costs of those injuries. However, challenges would remain in establishing levies that fairly reflect risk and provide good incentives for risk management for the industry given the limited information on the numbers and severity of injuries relating to different types of clinical trials.

I understand that the Ministry of Health is developing a Therapeutic Products Bill (the Bill) to update the regulatory regime around medicines, medical devices and other therapeutic products in New Zealand. The Bill could be an opportunity to consider these issues further in the interests of trial participant protection.

Hon Peter Dunne will respond to you separately on this and other initiatives being progressed by the Ministry of Health and Health and Disability Ethics Committees to better support safe and transparent conduct of commercial clinical trials in New Zealand.

The clinical trials industry is important for New Zealand, providing benefits to the economy, health system and participants themselves. The Government is committed to supporting growth in health and scientific research in New Zealand, and to ensuring that this is done in a safe and responsible way.

Thank you for taking the time to write to me.

Yours sincerely

Hon Michael Woodhouse
Minister for ACC

Health and Disability Ethics Committees

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6 December 2016

s 9(2)(a)

Dear s 9(2)(a)

Thank you for forwarding a copy of your contributory paper s 9(2)(a) s 9(2)(a) s 9(2)(a) which we discussed at a recent HDEC Chairs meeting.

As you are aware, the differential access to injury compensation cover for study participants has not gone unnoticed by the HDECs. Over the years since the 1992 law change to exclude study participants in commercially-sponsored trials from ACC cover, successive approaches have been made by the HDECs, individual ethics committee members, NEAC and the Ministry of Health to engage on this issue and to revisit the risks for ACC to provide compensation - with or without a commercial levy, and what other alternatives we may be able to explore around improving navigation of the process for participants, more detail on compensation fees payable as a comparator, etc. All parties agree on a moral obligation to pay compensation for study related injuries. At times, it is the causal nature of those injuries which is the subject of a difference of opinion, be it claimants, ACC or commercially sponsored insurers, and also the level of compensation cover appropriate to that trial injury. ACC's no-fault system allows for minor, moderate and short term cover whereas industry guidelines focus on severity and long-term injury. There is likely a degree of cost-shifting to the public health system for minor injuries that goes undetected and is not monitored.

The HDECs require evidence of valid and current indemnity or insurance cover and the localities check the level of cover – that it is appropriate to the trial risk and level of participant recruitment. The HDECs are considering whether a minimum level of insurance cover should be required per trial, as in Australia.

It is important to note that ACC also requires a causal link for a treatment injury or a research study injury to be determined before compensation is payable and that process of itself can take anywhere from months to years if subject to review or appeal procedures. Participants in DHB led studies for example, may still find themselves having to demonstrate a causal link between the injury and study drug or procedure, and this may take months to resolve.

We note your criticisms of the PIS template that lacks a statement "without legal commitment" to inform participants that the obligation is voluntary and not enforceable legally and that recourse is via mediation or the Courts. The Medicines NZ Guidelines 2015 do now include a clause for mediation payable by the sponsor although they also state the decision is not binding (as they are a member based organisation of approximately fifteen companies and cannot bind them to such an obligation). As Chairs we welcome external feedback on our templates and resources for researchers to access. We agree that more transparent information for study participants is necessary to inform them that cover is required as part of ethical review but that legal commitment and enforcement powers are limited. We intend updating the PIS/CF templates in the near future.

HDECs have moral sway and do apply this. For instance, the HDECs could a)withdraw ethics approval which is powerful in and of itself in terms of publishing study results and, b) write to all parties involved, or c) ultimately refuse to approve future applications from a company that was neglectful or strongly non-compliant in its obligations. The HDECs check the CI has valid insurance and that the study has cover. The obligation to check back-to-back insurance agreements with the study sites and sponsor is a locality level obligation, not an HDEC one. It is in the sites interests to monitor insurance is in place and the DHBs/universities are proactive about this. The clinical trials environment is a high trust and disaggregated one and for the most part, works very well. There are very few unresolved cases of harm. HDECs now require annual reporting from researchers of claims made by participants in clinical trials.

We continue to engage on these matters and find common ground on our respective positions. ACC has as you have noted, decided not to review the current legislation, partly on the grounds that there is insufficient demand to do so (i.e. so few unresolved cases of note), and that collecting a levy is administratively time consuming and problematic as commercial companies morph and merge routinely, and can also exit the NZ market at short notice for commercial reasons. The concern that the exposure risk for ACC is hard to quantify if a major clinical trial resulted in serious injury to several participants remains, and as you note, drug companies have found the insurance cover they hold can be insufficient on these rare occasions, resulting in liquidation of said [French] company.

As Chairs we have asked for the PIS to be revised and made more explicit in terms of the voluntary nature of the relationship. The Secretariat continues to work with ACC and Medicines NZ on improving the pathway for claimants to access advice.

Thank you for your paper.

Yours sincerely,

Brian Fergus

Helen Walker

Raewyn Idoine

Kate O'Connor

s 9(2)(a)

s 9(2)(a)

11 May 2017

The Chairs
Health and Disability Ethics Committees
Freyberg Building
20 Aitken St
PO Box 5013
Wellington

Attention: Brian Fergus, Raewyn Idoine, Helen Walker, Kate O'Connor

Dear HDEC Chairs,

Compensation for participant injuries in pharmaceutically-sponsored clinical trials

I refer to your letter of 6 December 2017. Thank you for taking the time to write to me.

I enclose a copy of my letter of 11 May 2017 to the Hon Peter Dunne and the Hon Michael Woodhouse, advising of the need for an urgent review of the exclusion from ACC cover for Treatment Injury of participants injured in pharmaceutically-sponsored clinical trials in New Zealand (s 32(6) of the Accident Compensation Act 2001).

I welcome your advice that the HDEC PIS template is being revised to make it completely clear that a sponsor's compensation obligation is purely voluntary. This is a minimum first step to better protect these subjects. If this results in a decrease in recruitment in the meantime, that is the price that must unfortunately be paid for participants giving a fully informed consent to participation, in full knowledge that the sponsor's obligation to compensate them in the event of injury is a moral one only and not legally enforceable.

I appreciate the successive approaches made by the HDECs, individual HDEC members, NEAC and the Ministry of Health to highlight the lack of financial protection of participants injured in commercially-funded clinical trials. I urge you and your committees to continue pressing for what would be a simple and entirely effective reform. I agree that HDECs do have moral sway which they can deploy. In addition to the three options in para 4 of your letter, I have urged in my published articles[1] that HDECs consider seriously the option of declining to approve studies of above minimal risk where legally enforceable, no fault compensation is not put in place by the sponsor. This is within the power and protective remit of the HDECs and is entirely do-able by the companies, as indicated by the fact that ABPI requires sponsors to put in place binding contracts with participants to pay no fault compensation for Phase I studies in the UK, see ABPI's *Clinical Trial Compensation Guidelines: Phase I Clinical Trial Compensation Guidelines* (2014).

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You refer to a concern about ACC's indeterminate exposure in the event of catastrophic injuries to multiple participants should a major clinical trial go wrong, if injuries in commercially funded trials were brought back within ACC cover. While such claims could admittedly be expensive, the extent of potential injury would be no greater than in claims involving serious injury caused by medical treatment generally or for workplace or sporting accidents resulting in similar serious injury, and the number of claims much fewer as research-related injury, particularly serious injury, is rare. ACC's liability in such a situation is not unquantifiable and unlimited, unlike a common law damages claim, but is fixed and quantifiable according to the compensation entitlements established in the statute. At present, the whole financial burden of injuries is borne by subjects, unless and to the extent that the company chooses to compensate them, rather than injury costs being spread across all levy-payers who contribute to the compensation scheme. If s 32(6) was repealed, there would be no possibility of injured participants going un- or under-compensated, as happened in the Northwick Park case.

Thank you again for responding to me. I look forward to seeing the revised PIS and to positive progress on the issue without further delay.

Yours sincerely,

s 9(2)(a)