MINISTRY OF BUSINESS, INNOVATION & EMPLOYMENT
HĪKINA WHAKATUTUKI

BRIEFING

Interface between ACC cover and compensation for treatment injuries sustained in clinical trials

Date:	28 April 2017	**Priority:**	Medium
Security classification:	**In confidence**	**Tracking number:**	3108 16-17

Action sought

	Action sought	Deadline
Hon Michael Woodhouse Minister for ACC	**Agree** to raise with the Minister of Health whether aspects of the clinical trials regulatory regime could be addressed through the Therapeutic Products Bill to ensure all participants can receive ACC-equivalent compensation for injury **Discuss** at the next officials' meeting the attached response to Middlemore Clinical Trials and your desired approach to further work in this area.	8 May 2017

Contact for telephone discussion (if required)

Name	Position	Telephone		1st contact
Kathryn MacIver	Manager, Accident Compensation Policy	04 901 3971	s 9(2)(a)	✓
Steve James	Senior Policy Advisor	s 9(2)(a)		

The following departments/agencies have been consulted [double click box & click 'checked']

☐ Treasury	☐ MoJ	☐ NZTE	☐ MSD	☐ TEC	☐ MoE
☐ MFAT	☐ MPI	☐ MfE	☐ DIA	☐ TPK	☒ MoH
		☐ Other:	ACC		

Minister's office to complete:

☐ Approved ☐ Declined
☐ Noted ☐ Needs change
☐ Seen ☐ Overtaken by Events
☐ See Minister's Notes ☐ Withdrawn

Comments:

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Purpose

1. This briefing provides advice on the current exclusion from treatment injury cover under the ACC Scheme for participants injured in commercial clinical trials. It proposes that the exclusion be maintained, and recommends next steps in this area of work.

Executive summary

2. On 7 March 2017, you received a letter from Middlemore Clinical Trials, an Auckland-based site for conducting clinical trials, requesting a meeting with you to discuss the regulatory and legislative regime around participant injuries in clinical trials and how they are assessed under the Accident Compensation Act 2001 (the AC Act).

3. Section 32 of the AC Act excludes clinical trial participants from treatment injury cover for commercial clinical trials (clinical trials that are principally for the benefit of the manufacturer or distributor of the medicine or item being trialled). This applies to the majority of clinical trials in New Zealand, which are largely sponsored by pharmaceutical companies seeking commercial market access for medicines and treatments.

4. In place of ACC cover, sponsors are expected to compensate participants injured in commercial clinical trials. As part of the ethics approval process for clinical trials, which is administered by the Ministry of Health, ethics committees seek an undertaking from sponsors that they carry indemnity insurance to compensate for injuries to the extent that would be provided by ACC if cover were available. Participants can seek redress through the courts if they disagree with the decision on whether to provide compensation, or the amount of compensation offered.

5. Since 2009, around 50,000 people have participated in clinical trials in New Zealand, and 136 adverse events have been reported to Medsafe through its voluntary reporting system. Two serious injuries alleged to have occurred as a result of commercial clinical trials in 2012, that have either not been resolved or experienced significant delays in compensation, have received media attention through s 9(2)(a) s 9(2)(a) other industry stakeholders support amending the AC Act to extend the regime to cover commercial trials.

6. There is limited information relating to injuries in commercial trials, and while there may be unknown cases, instances of further serious injuries have not been identified. Minor to moderate injuries likely addressed by the public health system. Government priorities to increase the market for clinical trials in New Zealand may result in more injuries in future due to increasing overall numbers of trials and participants.

7. The current clinical trials regulatory regime also has a number of gaps that make it challenging to verify that participants injured in trials have adequate access to equivalent compensation. There is a lack of reliable information on instances of serious injuries and whether compensation has been provided and the amount of compensation paid. There are also potential issues with participants' level of understanding that they are ineligible for ACC

cover. The resolution process for compensation also potentially has high transaction costs, as the main recourse for participants who disagree with the amount of compensation offered for injury is through the courts, which can be an expensive and time consuming process. However, commercial trial sponsors and sites have an incentive to settle compensation disputes privately, as serious injuries can carry reputational risks to the industry.

8. We have considered two options put forward by stakeholders to address the issues with the existing regulatory regime – removing the exclusion from the AC Act entirely and ACC moving to provide immediate support to injured participants while compensation is negotiated between trial sponsors or sites.

9. Officials recommend no changes to the AC Act at this time, as there is a lack of information to adequately assess the costs to the Scheme from claims for treatment injury across all clinical trials. The option of providing immediate cover to injured participants, while retaining the exclusion, is incompatible with the Scheme as it would suggest providing support to participants without first making a determination of injury, creating an inequity in assessments for treatment injury.

10. While retaining the current provisions in the AC Act, there is scope for improvements to the regulatory regime around clinical trials to gain better information on injuries and compensation to ensure there is adequate alignment with ACC entitlements. Such measures could include:

    a. strengthening the reporting system around clinical trial injuries

    b. requiring minimum levels of indemnity insurance by sponsors of trials to cover injuries

    c. requiring disclosure of instances and the amount of compensation to participants

    d. expanding the information provided to participants of trials regarding the exclusion of cover under ACC

    e. establishing an independent method to assess claims for injury alleged to have taken place in private clinical trials

    f. encouraging industry stakeholders to update guidelines relating to trial injury compensation to further align with ACC cover assessments and entitlements.

11. In March 2016, Cabinet agreed to strengthen the regulatory regime around clinical trials through the Therapeutic Products Bill, which is currently being drafted by the Parliamentary Counsel Office [SOC-16-MIN-0025 refers]. The Bill could present an opportunity to further explore the proposed regulatory measures in further detail. As the Bill and regulatory regime around clinical trials are administered under the Health portfolio, we recommend you discuss these matters with the Minister of Health.

Recommended action

The Ministry of Business, Innovation and Employment recommends that you:

a **Note** that section 32 of the Accident Compensation Act 2001 excludes participants in commercial clinical trials from treatment injury cover under ACC

Noted

b **Note** that in place of ACC cover, sponsors of such clinical trials are liable for compensating individuals injured due to their participation in a trial, and commit to abiding by industry guidelines for compensation as part of the ethics approval process for trials

Noted

c **Note** that out of around 50,000 trial participants since 2009, there have been two known cases of individuals suffering serious injuries alleged to be the result of participating in such trials, where compensation has not been paid or significantly delayed, leading to calls to remove the ACC exclusion from cover

Noted

d **Note** that it is a Government priority to expand support for health research in New Zealand and that the number of clinical trials taking place could increase, raising the overall likelihood of serious injuries taking place outside of ACC cover provision

Noted

e **Note** that following further analysis on the exclusion from ACC cover, officials consider that there is insufficient evidence to justify removing the exclusion at this time, but that improvements in the approval and monitoring systems for clinical trials may benefit participants and produce further information to re-evaluate this position in future

Noted

f **Agree** to raise with the Minister of Health, whether aspects of the clinical trials regulatory regime could be addressed through the Therapeutic Products Bill to ensure all injured participants receive timely ACC-equivalent compensation for injury

Agree/Disagree

g **Discuss** at the next officials' meeting the attached response to Middlemore Clinical Trials and your desired approach to further work in this area.

Agree/Disagree

Kathryn MacIver
Manager, Accident Compensation Policy

28 / 04 / 17

Hon Michael Woodhouse
Minister for ACC

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Background

Clinical trial injuries and ACC cover

Two cases of injury in clinical trials have recently received media attention

1. On 7 March 2017, Middlemore clinical trials wrote to you seeking a meeting with you to discuss risks to the regulatory and legislative framework around clinical trials. The request follows on from two cases of alleged treatment injuries that occurred in 2012 as a result of participation in clinical trials. A draft response to Middlemore Clinical Trials is attached as Annex 1.

2. The cases received media attention through s 9(2)(a) s 9(2)(a) in January 2017, and have also been previously brought to the attention of the Minister for ACC via the National Ethics Advisory Council (NEAC), which wrote to the Minister in 2015 detailing the cases.

3. The first case involved a participant injured in a phase III trial for gout medicine, who suffered a severe artrial fibrillation that required hospitalisation and was unable to return to work as a builder following the incident. The second case involved a participant who suffered diabetic lumbar plexus neuropathy following treatment for a phase III diabetes medicine trial, which resulted in paralysis and difficulty using his legs. Both cases fall outside of eligibility for cover from ACC due to an exclusion in the Accident Compensation Act 2001 (AC Act) to treatment injury cover for participants in commercial clinical trials.

ACC excludes cover for treatment injury for participants in certain clinical trials

4. In 1992, the AC Act (then the Accident Rehabilitation and Compensation Insurance Act) was amended to place restrictions around the participants in clinical trials. To receive ACC cover for treatment injury as a result of participation in a clinical trial:

   a. the participant must have agreed in writing to participant in the trial

   b. the trial must have been approved by an ethics committee; and

   c. the committee approving the trial was satisfied that it was not to be conducted principally for the benefit of the manufacturer or distributer of the medicine or item being trialled.

5. The amendment was made in response to concerns around rising costs to the Scheme and that, if participants in trials received cover for treatment injuries through the no-fault ACC Scheme, international pharmaceutical companies would be incentivised to conduct trials that could present a higher risk of injury in New Zealand as opposed to other countries.

6. The result the amendment is that participants in trials that are excluded from eligibility for treatment injury cover must seek redress from the trial sites and sponsors directly. Typically this is first through mediation with the company sponsoring the trial, which holds indemnity insurance to provide for compensation. Injured participants have the right to seek redress in the courts if they disagree with the amount of compensation offered.

7. The approach is broadly consistent with arrangements in other comparable jurisdictions such as Australia, the United Kingdom, other countries in Western Europe and the United States.

Clinical trials in New Zealand

8. Clinical trials are investigations in human subjects, designed to verify the safety and effectiveness of medicines, treatments, medical devices or other health interventions.

9. According to data from Medsafe, the regulatory body responsible for medicines safety and control in New Zealand, there were around 900 clinical trials in New Zealand between 2009 and 2017 involving almost 50,000 participants. The most common types of study over this

period were phase III trials, which are typically large studies conducted immediately prior to a drug or treatment being approved for distribution.

10. Data from the Ministry of Health (MoH) breaks down the number of applications to the Health Research Council (HRC) by the category of sponsor, as shown in Table 1. The vast majority of trials are sponsored by pharmaceutical companies conducting trials to gain approval for commercial distribution of a drug or treatment, and suggests that most studies would fall outside of the criteria for treatment injury eligibility under ACC.

11. On average, around 50 phase III studies have been conducted per year since 2009, compared to an average 21 studies per year for phase I studies (which involve testing a drug or treatment on humans for the first time) and an average 30 studies per year for phase II trials. The majority of participants are involved in phase III trials. Phase IV trials, which are conducted following market-approval, appear to be less common, although one large trial in 2016 involved around 1200 participants.

Financial Year	Pharmaceutical Company	Academic Institution	No Sponsor / Investigator Led	Collaborative Research	DH B	Other Govt Agency	N G O	Other
2012	101	4	3	14	1	2		4
2013	129	3	9	9		2		3
2014	144	5	9	7	3	1	1	2
2015	153	13	8	6				

Table 1: Number of approved clinical trials 2012-2015 (Source – Ministry of Health)

12. Medsafe also collects data relating to adverse events reported by trial sponsors. Adverse events cover serious and unexpected drug reactions, along with other events such as a serious departure from trial protocol. Table 2 below shows there have been 132 reported adverse events since 2009, with the majority of these occurring in phase III trials. This is likely due to the larger number of average participants in phase III trials.

Year	Phase I	Phase II	Phase III	Phase IV	Total
2009		1	2		3
2010	4	1	13		20
2011	3	2	5	1	12
2012	2	4	26		35
2013	1	6	9		16
2014	2	1	16		20
2015	1	7	13		21
2016		1	3		5
2017					
Total	**13**	**23**	**87**	**1**	**132**

Table 2: Reported adverse events 2009-2017 (Source - Medsafe)

Regulatory framework for clinical trials

Medicines Act 1981

13. Medicines sold or distributed in New Zealand are regulated under the Medicines Act 1981 (the Medicines Act) and associated regulations, which are implemented by Medsafe.

14. Medicines and medical devices sold, distributed or advertised in New Zealand must be approved under the Medicines Act. However, section 30 of the Medicines Act provides an exemption for medicines used in a clinical trial if the trial and persons conducting it are approved by the Director-General of Health on recommendation from the HRC.

Ethics approval process and compensation arrangements

15. A decision from one of the Health and Disability Ethics Committees[1] (HDECs) forms the basis for whether clinical trial participants would be eligible for treatment injury cover by ACC in the event of an injury from participating in the trial.

16. Typically, trials that are determined principally for the benefit of the manufacturer or distributor of the item being trialled are sponsored by pharmaceutical companies seeking market access to commercially distribute a medicine or treatment. Non-commercial trials that do not receive this determination are usually focused towards medical interventions that aim primarily to directly benefit participants, or are targeted to vulnerable groups such as Māori or Pasifika.

17. HDECs also require trial applicants to confirm in relation to an injury as a result of the trial that:

    a. compensation would be available to an ACC equivalent level, covering rehabilitation, weekly compensation, first-week compensation, lump sum compensation and funeral grants or other compensation for surviving spouses or dependents

    b. participation in the trial does not affect the right of participants to pursue legal remedies that allegedly result from an injury suffered from participation in the trial

    c. sponsors hold sufficient insurance cover to compensate participants injured as a result of the trial.

18. HDECs also seek agreement from trial sponsors that in the event of an injury, the sponsors would follow guidelines written by Medicines New Zealand, the industry association for companies involved in research, development, manufacture and marketing of prescription medicines, on the circumstances in which sponsors should provide compensation for injuries sustained in clinical trials.

19. The guidelines encourage sponsors to pay compensation for more serious injuries of an enduring and disabling character, including exacerbation of an existing condition. The amount of compensation is recommended to be no less than what would be provided by ACC, however this could be abated or excluded based on the risk. Compensation is not recommended in a range of circumstances, such as for phase IV trials, a departure from protocol or wrongful act by a third party (such as a trial site or medical practitioner) or for injuries caused within the trial but not by the trial medicine itself (such as a licenced medical product that is used for comparison in a trial).

Approval process for medical devices and other non-pharmaceutical treatments

20. Currently, the requirement for clinical trials to be approved by the Director-General of Health under the Medicines Act 1981 only applies to medicines. Other types of trials, including those for medical devices, cell and tissue therapeutic products and hybrids are encouraged to go through the formal ethics approval process when seeking to conduct a trial, however it is not currently a legislative requirement. Medsafe maintains guidance on sponsors and sites conducting these types of trials in New Zealand.

21. It is unclear whether trials that are not currently captured by the regulatory approval regime would fall under the exemption from treatment injury cover. As clinical trials are not currently defined in legislation, it may be difficult to determine whether such trials technically constitute a clinical trial, and could unintendedly attract ACC cover.

[1] Health and Disability Ethics Committees are Ministerial committees established under section 11 of the New Zealand Public Health and Disability Act 2000.

Future growth in the clinical trials industry is likely

22. It is a current priority of the Government to increase the number of clinical trials in New Zealand, owing to the economic benefits trials can bring via international sponsors, develop the knowledge and expertise of the domestic health workforce as well as provide benefits to participants in trials through access to new and innovative treatments.

23. Growing scientific research in New Zealand is part of the Building Innovation work stream of the Business Growth Agenda and in 2011, the Health Select Committee held an inquiry to look at ways to support the growth of the clinical trials industry. There are a number of initiatives underway across Government that aim to support additional trials, or expand the nature or scope of trials being conducted in New Zealand. These include:

    a. the first New Zealand Health Research Strategy, which is currently being developed by the Ministry of Business, Innovation and Employment, MoH and the Health Research Council. The proposed strategy aims to improve New Zealand's health research and innovation system, and a draft is being considered by the Cabinet Social Policy Committee on 10 May 2017

    b. the current consultation on the Code of Health and Disability Services Consumers' Rights relating to persons not able to give informed consent to treatment. Changes to the code could see trials and experimental treatment for patients with mental disabilities, in intensive care or emergency situations or with degenerative diseases that affect cognition such as Alzheimer's and dementia, which are not permitted under the current code

    c. greater interest from overseas trial sponsors. China is increasingly seeking partnerships with other countries to conduct medical research, including New Zealand through the free trade agreement between the two countries. Phase I trials are thought to be of particular interest. The Australia – New Zealand Science, Research and Innovation Agreement, which was signed in February 2017, may also make New Zealand a more attractive location for clinical trials.

Issues in the existing regulatory framework

24. Stakeholders in the clinical trials industry have raised a number of potential issues with the compensation system for participants injured without ACC cover. They point to issues in the provision of compensation for injuries, the level of information available to participants, transaction costs in seeking redress and the underlying incentives as potentially damaging to participants and the clinical trials industry.

Provision of cover

25. The ethics approval process through HDECs requires sponsors to have indemnity insurance to cover treatment injuries suffered by trial participants. However, there is no equivalent requirement for trial sites. This has the potential to leave injured participants in a position where there is no immediate compensation pathway if there is dispute between sponsors and sites as to whether an injury was caused by the new medicine or treatment being tested, or through their administration by the trial site or other factors such as mistakes or negligence by site staff.

26. Some aspects of compensation that are features of the ACC Scheme may be difficult to replicate outside of it. Delays in determining who is responsible for compensation may result in claimants not receiving support in a timely manner. In the alleged injury involving diabetes medicine, the claimant has gone four years without a resolution on compensation for injury. Delays in receiving support can impact on rehabilitation outcomes from injury.

27. Part of the undertaking by sponsors to provide injury cover when applications for trials are considered by a HDEC relies on adherence to Medicines New Zealand's industry guidelines on compensation. However, some aspects of these guidelines potentially do not align with

the Scheme and not all sponsors belong to Medicines New Zealand. Potential issues in the guideline's recommendations include:

a. not paying compensation for injuries in phase IV trials

b. abating or excluding compensation depending on the expected risk of a trial

c. providing compensation for injuries of an enduring and disabling character only.

28. As a number of clinical trials, such as those for medical devices, cell and tissue therapeutic products and hybrids, fall outside of the existing regulatory regime, there is a risk that some trials in these areas are not undergoing ethics approval. In this situation there may not be an undertaking by the sponsor to provide ACC equivalent compensation in the event of an injury, or injuries may be unintentionally captured under the Scheme.

Information shortcomings

29. Participants may not understand they are not covered by ACC in the event of an injury caused by participating in a private clinical trial. The wording used in the HDEC's participant information sheet and consent form template states that in the event of an injury caused by the trial "compensation would be available from the study's sponsor [x] in line with industry guidelines." This text has been criticised as implying to participants that the provision of compensation is more certain than in actuality, especially if there are disputes as to who is responsible for the injury.

30. There can also be information asymmetries between trial sponsors and sites, and the bodies responsible for regulating clinical trials. It is difficult for Medsafe and HDECs to assess whether adequate compensation is being paid to injured participants as:

a. Medsafe's adverse event reporting system is voluntary, meaning that injuries could be occurring without the knowledge of the relevant regulators. This makes it difficult to gain a complete picture of treatment injuries taking place in private clinical trials

b. there is anecdotal evidence that rather than claim indemnity insurance, sponsors may privately settle claims for compensation from injured participants. In such cases, the amount agreed in a settlement would likely be confidential, making it difficult for regulators to verify that the agreed amount of compensation would be equivalent to ACC coverage.

Transaction costs

31. If a participant is injured, they have to apply to the sponsor for compensation. If the amount or responsibility for compensation is disputed, the claimants recourse is the court system. Accessing the courts to receive compensation can involve significant additional costs to the claimant in engaging legal advice. This approach can also result in additional burden on the claimant in terms of time and emotional capacity which can distract from rehabilitation from injury.

32. MoH also considers that the legal market to negotiate or challenge the amount of compensation offered by sponsors is underdeveloped in New Zealand due to the presence of ACC cover for most injuries. There are reportedly a lack of legal professionals with the appropriate experience to act on fault-based injury claims, meaning higher costs for participants to engage the few legal professionals who can act in this area.

Incentives

33. There is an argument that it is against the interests of trial sponsors to accept responsibility for treatment injuries that may be caused by participation in a private clinical trial. This could lead to delays in providing compensation to injured participants or a lack of compensation at all.

34. Conversely, trial sponsors may have an incentive to provide compensation quickly, and potentially over and above what ACC would pay, given the risk of reputational damage to a trial site or sponsor if a participant decided to publicise a negative experience of injury compensation. Industry guidelines appear to be cognisant of their social licence to operate, which relies on both the regulatory controls around trials to allow them to proceed, and for the New Zealand public to have sufficient trust in their safety to volunteer to participate in trials.

Proposals for change

35. Stakeholders have put forward two potential options for addressing the issues around compensation in the clinical trials regulatory and legislative framework:

    a. removing the exclusion for treatment injury cover

    b. ACC providing immediate support to injured participants in the period between the injury occurring and compensation being paid by the trial sponsor or site.

36. Both options are discussed below. Officials consider that there may also be options to improve the regulatory system around clinical trial approvals and information collecting that could further align the compensation regime with the Scheme, or produce additional information to consider removing the exclusion in future.

Removal of ACC Exclusion

37. Removing the exclusion would involve amending the AC Act to allow treatment injury cover for participants in all clinical trials. Without the exclusion, all personal injuries as a result of a clinical trial that meet the criteria for treatment injury would be eligible for cover under ACC.

38. Providing treatment injury cover for participants in all clinical trials would have the following impacts:

    a. there would be greater transparency around the amount of compensation and support provided to injured participants

    b. participants would receive cover determinations within the statutory requirements of the AC Act, in which the maximum period for determining a claim is nine months

    c. participants would not be able to pursue tort claims in court for compensation, as claims for compensatory damages for injuries eligible for coverage under ACC are prohibited by the AC Act

    d. costs to the Treatment Injury Account of the Scheme would increase by an indeterminate amount to cover participant injuries, and could grow over time if the clinical trial industry expands.

Analysis

39. The main benefit of removing the exclusion would likely be that participants injured in clinical trials would receive a determination on cover, whether they eventually received cover or not, faster than the two known cases that have been subject to delays. This would likely address much of the transaction cost issues identified by stakeholders.

40. It is not clear, however, whether expanding the Scheme to participants in private clinical trials would result in an accepted cover determination for an injury that would not be compensated by a trial sponsor. In the two cases that have attracted public interest, a key point of contention was whether the injury was caused as a result of participation in the trial, or through underlying health factors. These same considerations are made when ACC assesses treatment injury claims.

41. It is unclear how this option would impact on the Scheme and affect the Outstanding Claims Liability. As removal of the exclusion would constitute an expansion of the Scheme, it is expected that covering injuries from currently excluded clinical trials would increase overall

costs to the Treatment Injury Account, which is the fastest growing account in terms of liabilities to the Scheme.

42. Since the treatment injury provisions took effect in 2005, ACC has recorded only three claims for treatment injuries for clinical trials. Of those, one claim was accepted with a total claim cost of around $37,000. It is unclear whether the claim was related to a commercial clinical trial. Of the remaining claims, one was withdrawn by the claimant while the other was declined on the basis that it was not an injury resulting from treatment.

43. ACC also holds wider data around treatment injuries that result from adverse reactions to approved medicines. Injuries from clinical trials of medicines are likely to be similar in nature. Since 2005, there have been 16,167 claims for adverse reactions, with around 11,000 of these covered by ACC. The majority of accepted claims were for allergic reactions and anaphylactic reactions to medicines. These claims can result in significant costs to the Scheme. The top 10 claims for treatment injury for adverse medication reactions cost between $410,000 and $820,000.

44. Officials have been unable to develop a reliable estimate for how many additional claims removing the exclusion would attract to ACC as the two publicised cases are the only known cases of serious injury from private clinical trials. Medsafe's adverse event reports provide some indication of potential injuries based on past trials, however it is unclear from this data whether the reported adverse events would have been of a significant or serious enough nature to attract a treatment injury claim. Additionally, the voluntary nature of the reporting system means that it may not be a complete representation of injuries that are taking place in clinical trials.

45. Costs for clinical trial treatment injuries could be reclaimed through the introduction of a levy, which would also ensure the allocation of risk of participant injuries remains on the sponsor and/or trial site. This would also have the effect of addressing one of the original justifications for creating the exclusion around allocating risk towards sponsors and sites.

46. The practicalities of imposing a levy are uncertain. ACC does not currently levy treatment providers or registered health professionals for treatment injuries and this would be a significant departure from current practice. Levying sponsors based outside of New Zealand may also be an issue.

Recommendation

47. Officials do not recommend removing the exclusion for treatment injury cover in the AC Act at this time, as there is not sufficient information on the extent of injuries taking place in clinical trials not currently covered under ACC or that participants are being inadequately compensated. This option would present uncertainties in the potential additional costs and liabilities to the Scheme.

Providing immediate compensation from ACC

48. Middlemore Clinical Trials, in their letter to you, support a measure that would involve ACC providing compensation support to injured participants in the period between the injury occurring and compensation being agreed between the participant and the trial sponsor or site. This option is supported by the New Zealand Association of Clinical Research (NZACRes), and was first raised in a meeting with MBIE and ACC officials in July 2016.

49. As with removal of the exclusion from the treatment injury provisions of the AC Act entirely, the main benefit with this option is that injured participants would not be left without compensation while responsibility for the injury and compensation is being determined.

Analysis

50. Theoretically, this could be a lower cost option to a complete removal of the exclusion under the AC Act, as the provision of support from ACC to injured participants would be for a shorter period of time.

51. The option, however, presents uncertainty to the costs to the Scheme as ACC could be liable to provide support to participants until an agreement for compensation is reached between the participant and sponsor or site. Immediate cover by ACC could act as a disincentive on both the participant and sponsor/site to reach an agreement in a timely manner. There is the risk of ACC supporting injured participants indefinitely under this proposal, which impacts on the overall sustainability of the Scheme.

52. There are also inequities in ACC providing immediate cover for clinical trial injuries, as it implies that support would be provided before a determination is made on cover. This would be inequitable with how all other ACC claims are processed. Conversely, if cover determinations were required before support is provided, ACC would be in a similar position to trial sponsors and sites in determining the nature and extent of the injury. It is unlikely there would be any advantages in timeliness of support in this situation.

53. It is likely that this option would also involve operational challenges to ACC in processing and determining assessments for compensation. For comparison, treatment injury claims can take up to nine months to assess for determination. Additionally, assessment of compensation claims for clinical trials outside of the Scheme would involve determining fault on the part of the sponsor or site. As ACC operates on a no-fault basis, there may be limited utility on ACC advising on fault-based compensation claims.

Recommendation

54. Officials do not consider that this option is a practicable solution to the issues around compensation for trial participants not covered by ACC. Providing immediate support to such claimants without first making a determination like any other ACC claim would introduce significant inequities to the Scheme. Conversely, if ACC were required to make a cover determination prior to providing support, it is unlikely this would offer a substantially faster process than the existing arrangements, as both ACC and sponsors or sites would consider similar matters.

Other regulatory measures

55. Noting the above issues around the available information about injuries in private clinical trials, officials consider that there could be merit in further examining the approval and reporting systems around clinical trials, to gain a greater understanding of the extent and frequency of injuries. Such measures might include:

    a. strengthening Medsafe's adverse event reporting system to produce more reliable data on the extent of injuries from private clinical trials. This could involve making the reporting system mandatory

    b. requiring sponsors to insure for a minimum amount to cover indemnity for participant injuries in line with overseas jurisdictions for clinical trials

    c. requiring trial sponsors to provide information to HDECs on compensation they have provided to injured participants, and the amounts of such compensation.

56. Other measures could also have the potential to align the existing compensation regime around private clinical trials more closely to ACC, without exposing the Scheme to unknown additional costs. This could include:

    a. strengthening the HDECs informed consent template to make it clearer that compensation is not available from ACC, and that compensation from sponsors and/or sites requires establishing fault

    b. establishing an independent method to assess claims for injury alleged to have taken place in private clinical trials. There have already been instances of DHBs assessing claims for compensation on behalf of trial sponsors

    c. recommending that Medicines NZ amend their industry guidelines for compensation to recommend that compensation be paid for phase IV trials.

57. Officials recommend working with MoH to determine whether such regulatory changes could be made to strengthen information and reporting around clinical trials, and ensure that the compensation arrangements in these trials align with ACC entitlements. The Therapeutic Products Bill (the Bill), of which an exposure draft is due to be released by MoH to stakeholders for comment, could be an opportunity to progress these measures.

58. In 2014 Cabinet agreed to introduce a new Bill to redesign the regulatory regime for therapeutic products in New Zealand and replace the Medicines Act 1981 and its associated regulations. The policy intent behind the Bill is to modernise the existing regulatory regime to align with comparable overseas jurisdictions and ensure it is fit for purpose for advances in medical technology.

59. In 2016, Cabinet agreed to further policy changes to the Bill relating to clinical trials including:

    a. introducing requirements that, along with medicines, clinical trials for medical devices, cell and tissue therapeutic products and hybrids would require regulatory approval

    b. where appropriate, set greater requirements for regulatory approval of clinical trials and change conditions where appropriate

    c. introduce additional information, reporting and monitoring requirements, including the power to audit trials and revoke approvals.

60. These policy decisions broadly align with the proposed regulatory measures outlined above, and as such are a potential opportunity to support greater information to assess the case for the exclusion from ACC cover for clinical trial injuries, and to ensure there is alignment with ACC entitlements for trials that are captured by the cover exclusion. As the regulatory regime around clinical trial approval is administered by MoH, you may wish to discuss this issue with the Minister of Health.

Next steps

61. A draft response to Middlemore Clinical Trials is attached to this briefing as Annex 1. The response acknowledges the concerns raised by Middlemore Clinical Trials and states that changes to the AC Act do not appear justified at this time. We recommend you discuss the response and your preferred approach to Middlemore Clinical Trial's request for a meeting with you at the next officials' meeting.

62. You may wish to discuss the issue of compensation for participants injured in private clinical trials with the Minister of Health, and gauge his interest in examining in further detail possible changes to the regulatory approval process for clinical trials through the Therapeutic Products Bill.

Annexes

Annex 1: Letter from Michelle Sullivan, Middlemore Clinical Trials and draft response

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Middlemore Clinical Trials

Future of healthcare

Tuesday, 7 March 2017

Minister for ACC
Hon Michael Woodhouse
Wellington

Copy to:
Minister of Health
Hon Dr Jonathan Coleman

Dear Minister Woodhouse

Commercial clinical trials in NZ – treatment injury compensation for patients

Middlemore Clinical Trials is a Charitable Trust with an independent board of trustees that administers commercial clinical trials and major grant-funded research studies on behalf of Counties Manukau Health. We are one of New Zealand's leading clinical trials sites, and we seek a meeting with you to:

- **Brief** you on the risks to NZ participants in clinical trials under the current regulatory & legislative framework;
- **Discuss** options to better support NZ patients participating in clinical trials in NZ; and
- **Update** you on the commercial opportunities for NZ in the global clinical trial sector.

Currently the commercial sponsors of clinical trials (pharmaceutical or biotech company) and the site undertaking the clinical trial are required by law to carry appropriate indemnity insurance to provide compensation and assistance to at least the level provided by ACC. However, disputes between the sponsor's insurer and that of the site, can certainly mean that no assistance at all may be provided in the short term, and not until final acceptance of responsibility is made. This potentially can leave those affected without assistance for possibly several years.

Treatment injury compensation is a barrier to growing commercial clinical trial business. We have one case study (details appended to this letter) that is a red flag for the industry. Fully four years has passed with no resolution. This indicates that the current system is not working, and needs to be changed to minimise harm to the NZ public that participate in clinical trials, and enhance New Zealand's standing as an attractive location to undertake commercial clinical trials.

The issue of treatment injury of individuals taking part in sponsored clinical trials has been previously raised by Dr Richard Stubbs and the NZ Association for Clinical Research (NZACRes). This led to a meeting of officials in Wellington on 25 July 2016 to explore ACC involvement in treatment injury of individuals taking part in sponsored clinical trials. This meeting involved officials from ACC, Ministry of Health and MBIE, as well as representatives from NZACRes.

We would like to revisit the NZACRes initiative and endorse their proposal that ACC provide immediate cover, as would be the case in any other injury, while negotiating with the relevant insurers where ultimate responsibility lies. The numbers of cases will be very small, probably only one

a year or less, but the matter is an important one. Failure to address this gap currently results in extended hardship to the handful of individuals that do suffer treatment harm, it may impact on participation in clinical trials and it deters companies from investing in trials here.

ACC coverage for treatment injury compensation has industry-wide support amongst clinical trial providers and would be a sensible, workable solution to ensure New Zealanders do not suffer as a result of participation in a clinical trial. Such a solution would mean that New Zealand can then focus on growing our thriving clinical trials niche within our health research ecosystem.

Yours sincerely,

Dr Michelle Sullivan
Chair, Middlemore Clinical Trials

Treatment Injury Case Study

In August 2012, one of our participants in a Phase 3 clinical trial of a new insulin analogue suffered a treatment injury. Mr D-B was diagnosed with a diabetic polyradiculopathy causing permanent disability (paralysis of the lower limbs). The principal investigator and local neurologists thought that the neurological condition was likely related to the study drug and/or study protocol (i.e. abrupt improvement in blood glucose control). Because Mr D-B was a participant in a commercial clinical trial, he was not eligible for support under the Accident Compensation and Rehabilitation Act 2003. In March 2013, Mr D-B made a claim for compensation from the study sponsor (Eli Lilly Inc.). This claim was rejected. Eli Lilly maintained that the neurological condition was a pre-existing condition based on opinion of a US academic neurologist. Eli Lilly agreed to mediation in June 2014 and a mediator was appointed. Mr D-B retained his own independent legal counsel, but 4-years later a date for mediation had still not been set. Talking to CM Health staff, we have no doubt Mr D-B would have received compensation and rehabilitation support from ACC long ago if he had not been a clinical trial participant.

We wrote to the chief legal counsel for Eli Lilly in Australia in September 2016 enquiring about the lack of progress. She replied *"As you know, we have been trying for almost two years to progress this matter to mediation. Lilly is still awaiting a response to our most recent expert report which we provided in November 2015. We were promised a response so that we could progress the mediation, and none has been provided. More recently, we made an offer to meet with Mr D-B's lawyer in New Zealand to see if we could find a way of progressing the matter. That offer of a meeting was rejected by Mr D-B. In circumstances where Mr D-B is not able to respond to our expert report, and is unwilling to allow his lawyer to discuss his case with us, there is nothing further that Lilly can do. We have told Mr D-B's lawyer that if he wishes to re-engage on the matter then we would be happy to do so."*

Whatever the rights and wrongs, the impasse reached in this case causes us very great concern. We see this as a very high risk to the entire New Zealand clinical trial industry. We are a high-performing site and we are dependent on the good will of the hundreds of New Zealanders who volunteer to participate in clinical trials for philanthropic reasons with no expectation of self gain. The New Zealand public might be much less willing to participate if the details of this case became known. Some equitable solution to the problem needs to be found.

Benefits from participation in commercial clinical trials

New Zealand has a reputation as an excellent provider of commercial clinical trials. Despite a relatively high cost of business in New Zealand, we are generally regarded as a good place to do business based on our speed to start up (including ethics and Maori approvals). Middlemore Clinical Trials also sees opportunities to grow both the volume and the value of clinical trials we undertake. There are many strategic opportunities to attract new clinical trials to New Zealand that will meet the health needs of New Zealanders.

As you likely aware, commercial clinical trials in NZ deliver enormous benefits to individual patients, the health sector, and the economy. Individual patients benefit from participating in clinical trials through potential access to new medicines (often potentially life-saving) and through increased levels of care from intensive Principal Investigators (SMO-level) and nurses with time dedicated to closely managing and monitoring the patient's condition. The health sector (DHB) benefits through avoided drug costs, avoided personnel costs (as the SMO and nursing time is paid for by the trial sponsor) and

frequently investments in new equipment and/or training. The export value of the commercial clinical trial sector is unknown but this niche industry does generate significant income for New Zealand (some estimates value the industry at $100M+).

Risks from participation in commercial clinical trials

The nature of clinical trials means that there are risks involved - precisely because the medicines being administered are undergoing rigorous testing to the highest international standards. This means that patients consent to involvement knowing that there is a small but real risk of harm. However, participant consent forms clearly state that should harm occur, they will be compensated by the sponsor company as such harm is outside the scope of ACC coverage. Unfortunately, there is no automatic mechanism by which sponsor companies provide said compensation. As a result, there are situations when patients suffer trial-related harm that results in severe health consequences and knock-on financial hardship because there is no access to rehabilitation services and no compensation has been paid. We have one such case, detailed in the Treatment Injury Case Study.

Dr Michelle Sullivan

Chair, Middlemore Clinical Trials

Private Bag 93311

Auckland 1640

Copy to:

Minister of Health

Dr Jonathan Coleman

Dear Michelle,

Thank you for your letter seeking a meeting to brief me on the risks to participants in the New Zealand clinical trials industry, and your support of a proposal for the Accident Compensation Corporation to provide immediate support to injured participants while the details of compensation by sponsors or trial sites is worked out.

I note that the clinical trials industry is an important part of the Government's Business Growth Agenda focus to support the growth of health and scientific research in New Zealand. Clinical trials provide a number of benefits to the New Zealand economy, health system and in cases of patient trials, the participants themselves.

When the exclusion from treatment injury cover for participants in certain clinical trials was implemented in 1992, the key drivers behind the change were to ensure that trial sponsors were not unduly incentivised to conduct higher-risk trials in New Zealand over other countries by not directly bearing the cost of injuries, and to contain costs to the ACC Scheme from the types of injuries that can occur in clinical trials that, while seemingly rare, can be very high-cost claims.

I am aware of the case you mention in your letter regarding the participant of an insulin analogue study, who suffered a treatment injury in 2012 and to date has not received any form of compensation. I understand there is a similar case of a participant in a gout medicine trial in the same year who is in a similar situation.

While these injuries appear serious, and if found to be the result of participation in a clinical trial should be compensated, I do not consider there is sufficient justification to consider amending the Accident Compensation Act 2001 at this time to remove the exclusion. I note that based on data from the Ministry of Health, there have been almost 50,000 participants in clinical trials since 2009.

The proposal for ACC to provide immediate assistance while compensation is negotiated between the participant and the trial sponsor or site has the potential to raise similar issues. I hold concerns

that the proposal would put ACC in a situation where its support to an injured participant would be dependent on a process outside its control. There would also potentially be a disincentive on both the participant and sponsor or site to resolve the compensation claim in a timely manner if the financial burden in the meantime was met by ACC.

Additionally, like trial sponsors and sites, ACC would have to determine the circumstances relating to the injury before providing any assistance. I do not consider it would be within the principles of the Scheme to offer support before the cause of the injury was established due to the inequities this would raise between claimants across the Scheme.

I have raised the issues around the compensation regime for clinical trial participants not covered under ACC with the Minister of Health, with a view to the Ministry of Business, Innovation and Employment and the Ministry of Health working further to identify improvements. For example, there may be ways the existing approval framework around clinical trials might be improved to better align with the ACC Scheme, and produce more reliable data around the instances of injuries and compensation paid. This will help to reassess the current provisions in future if the need arises.

I would encourage you to meet and discuss with MBIE and Ministry of Health officials if you wish to further progress this issue at this stage. The MBIE contact for further discussion is Steve James – s 9(2)(a)

Thank you for taking to time to write to me.

Yours sincerely

Michael Woodhouse

Minister for ACC