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NSW Tribunal approved trial to test drug on COVID-19 patients incapable of giving their own consent

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The NSW Guardianship Act 1987 (the Act) enables the NSW Civil and Administrative Tribunal (the Tribunal) to approve clinical trials that require recruitment of people without capacity to consent. Approval will only be granted if the clinical trial satisfies the requirements under s 45AA of the Act. Such approval does not import consent, which must be obtained under Pt 5 of the Act.

On 24 April 2020, the Tribunal approved a Phase II trial for the drug STC3141 (the Trial), to be administered to COVID-19 patients under mechanical ventilation.[1] As such, the nature of the Trial required recruitment of patients who are unable to consent. The Tribunal adjourned the question of whether consent could be given by the "person responsible"[2] pending the amendment of Personal Responsible Information and Consent Forms to be used in the Trial. This meant that, subject to a further hearing, consent for treatment of patients in this Trial could only be given by the Tribunal.

Introduction

The global pandemic has propelled research into vaccines and treatments for the novel coronavirus with extraordinary urgency.[3] One of the most devastating effects of COVID-19 is its ability to trigger Acute Respiratory Distress Syndrome (ARDS).[4] This is life-threatening. Patients with ARDS may require artificial ventilation, which requires them to be sedated into an induced coma. The intravenous drug STC3141 aims to inhibit the inflammatory response that underlies ARDS.

Professor Anders Aneman (the Applicant) applied to the Tribunal for approval of the Trial under s 45AA of the Act — that is, a clinical trial in which patient participants are unable to consent. The Applicant sought to test the safety and efficacy of STC3141 on 160 ICU patients with confirmed COVID-19 infection and ARDS at Liverpool Hospital in Sydney.[5]

The Trial required continuous infusion of STC3141 for up to 5 days in mechanically ventilated patients from the ages of 18 to 80,[6] to compare its efficacy against standard ICU care.[7] Therefore, the nature of the Trial necessitated recruitment of patients who cannot consent.

The common law provides that a person is not to be given medical treatment without their informed consent. The consent process for clinical trials must be rigorous given the risks and uncertainties they present. As with some other jurisdictions, the NSW Act provides a mechanism for the Tribunal (under s 45AB(1)(b) of the Act) to consent to participation in clinical trials on behalf of patients (aged 16 years and over) who are incapable of consenting to medical treatment.[8]

In triggering this authority, the Tribunal must consider a range of factors under s 45AA of the Act. Provided the relevant ethics committee has approved the Trial, the Tribunal must be satisfied that the drugs or techniques proposed are intended to cure or alleviate a particular condition; that the Trial will not involve any known substantial risk to the patients; and that it is in the best interests of the patients.[9]

Given the significant public interest in this case, the matter was heard less than 24 hours after the Tribunal received all relevant documentation.[10] In particular, at the time of hearing[11] NSW had the highest number of cases in Australia (2976 confirmed cases and 31 deaths) with 47 confirmed cases in hospital, of which 21 cases were in intensive care.[12]

In summary, the Tribunal identified its role in this hearing to consider the following:

1 Whether a clinical trial recruiting human subjects who are unable to give their own consent should be allowed under s 44AA of the Act; and
2 Whether the "person responsible" (as defined by the Act) can provide substitute consent if the subject is unable to give their own consent under s 44AB(1)(a) of the Act.[13]

The Tribunal approved the Trial under s 44AA. However, it left open the question of consent pursuant to s 45AB(1)(a), to allow the Applicant to submit amended Person Responsible Information and Consent Forms. Subject to a determination on this issue, consent to treatment with STC3141 in the context of this Phase II trial could only be given by the Tribunal pursuant to its authority under s 45AB(b).

This article focuses on the Tribunal's application of s 45AA of the Act — that is, how the Tribunal determined the first issue.

Background

STC3141

There is a worldwide flurry of clinical research targeting COVID-19, with multiple Australian studies already having been registered.[14] STC3141 was developed by researchers at the Australian National University to treat patients with virus-associated ARDS.[15] The inflammatory response caused by infections such as COVID-19 can trigger ARDS. The drug STC3141 is expected to inhibit the immune response and ultimately improve oxygenation, reducing the number of days a person requires ventilation.

At the time of hearing, STC3141 had not yet been approved elsewhere in the world. It had however completed its Phase I trial during which it had been administered to 48 healthy human volunteers with no reported deaths or serious adverse effects.[16]

This Phase II trial at Liverpool Hospital was designed as a two-stage study.[17]

Stage 1: Testing the safety of STC3141 in 10 patients, out of the total cohort of 160.

Stage 2: Testing the efficacy of STC3141 in alleviating symptoms associated with COVID-19 in the remaining 150 patients. Half of these patients would be randomised to receive STC3141 for up to 5 days and the other half would receive standard intensive care unit care.

The Act

Part 5 of the Act applies to patients aged 16 years and above who are not capable of giving consent to medical or dental treatment.[18] Significantly, the objects of Pt 5 of the Act are to ensure that:

1 people are not deprived of necessary treatment simply because they lack the capacity to consent to it;[19] and
2 any treatment that is administered to people who do not have capacity to consent is for the purpose of promoting and maintaining their health and well-being.[20]

Section 45AA of the Act authorises the Tribunal to approve a clinical trial which involves patients who are incapable of giving consent (ie patients to whom Pt 5 of the Act applies). However, the Tribunal's approval under s 45AA does not obviate the need for consent obtained under Pt 5.

The issues are separate and distinct:

(i) firstly, approval of the Trial as one in which patients (aged 16 or over) without capacity to consent may participate (s 45AA); and
(ii) secondly, determination as to whether consent to treatment as part of the Trial can be given by the person responsible (s 45AB).

This decision concerned the first issue only and the Tribunal ultimately approved the Phase II trial of STC3141 as one in which patients without capacity can participate. In doing so, it determined the requirements under s 45AA were satisfied.

Application of s 45AA to the STC3141 clinical trial

In determining whether the Trial met the requirements of s 45AA of the Act, the Tribunal noted:

1 STC3141 is intended to improve respiratory function in ARDS patients and alleviate symptoms of COVID-19 in these patients.[21]
2 The Trial would not involve any known substantial risk to patients; there were no serious adverse events reported from the Phase I trial. Further, there is currently no disease-specific treatment for COVID-19-related ARDS, and patients who do not receive the treatment (ie the control group) would still receive standard ICU care.[22]
3 This was a Phase II trial. Phase I of the trial had demonstrated STC3141 was well tolerated by healthy human volunteers.[23] As such, safety and ethical considerations made it appropriate to be available to patients with viral ARDS without their consent.[24] Further, the study *could* only be conducted on critically ill patients who are be unable to consent, since they required mechanical ventilation and continuous sedation.[25]
4 It was in the best interests of COVID-19 patients to participate in the Trial (having regard to the potential benefits and risks) in circumstances where there is currently no disease-specific treatment for COVID-19-related ARDS. Potential benefits include faster recovery times, reduced number and severity of complications arising from ARDS, and improved survival rates. Further, there was no known risk of serious adverse events associated with STC3141.[26]
5 The Trial had received appropriate ethics approval from the South Western Sydney Local Health District Human Research Ethics Committee on 21 April 2020, which further approved amendments to the study on 23 April 2020.

On the basis of these findings, the Tribunal approved Phase II of the STC3141 trial under s 45AA.

Consent for participation in the clinical trial

The Tribunal was not in a position to determine whether the "person responsible" for the patient could give appropriate consent (under Div 3 of Pt 5 of the Act). This was because in order to defer consent to the "person responsible", the Tribunal had to be satisfied that the Consent Forms and Information Sheets for the Trial sufficiently informed the "person responsible" to enable them to consent on behalf of the patient. The Applicant agreed that amendments to the Consent Forms were needed.

As such, the Tribunal adjourned hearing the second issue.[27] It determined in the meantime that consent to medical treatment on behalf of patients to participate in the Trial could only be given by the Tribunal under s 45AB(1)(b) of the Act. Therefore pending the hearing of the second issue, application had to be made for the Tribunal's consent to participation of any individual patient in the Trial.

The process for such application is set out in s 42 of the Act.[28] An application to the Tribunal for consent under s 42 must specify, in respect to the particular patient:

1 the grounds on which it is alleged they are unable to consent themselves;
2 the particular condition that requires treatment;
3 the alternative courses of treatment that are available for that condition;
4 the general nature and effect of those alternative courses of treatment;
5 the nature and degree of significant risks (if any) associated with those alternative courses of treatment; and
6 the reasons for which it is proposed that any particular course of treatment should be carried out.[29]

If the Tribunal considers it is appropriate for the patient to have the treatment, it may consent to it,[30] having regard to the following factors:[31]

1 The views (if any) of:
   (a) the patient;
   (b) the person who is proposing the treatment be carried out on the patient;
   (c) any persons responsible for the patient; and
2 Those matters specified in the application to the Tribunal for consent, as required under s 42; and
3 The objects of Pt 5 of the Act.

The Tribunal is not obliged to consider an application under s 42 if it is not satisfied that the applicant has a "sufficient interest" in the health and well-being of the patient.[32] The term "sufficient interest" is not defined; however, the Tribunal's exercise of this discretion should align with the objects of Pt 5 of the Act — particularly by ensuring that people are not deprived of necessary treatment just because they lack the capacity to consent to it.[33]

Comment

While the Tribunal's decision is a positive step towards one potential treatment for COVID-19, there are number of hurdles in the way. The first is a practical one. Phase II of the STC3141 trial requires recruitment of 160 COVID-19 patients on mechanical ventilation. Of patients hospitalised for COVID-19, the percentage who are admitted to ICU ranges from 17%–35%, with 29%–91% of these patients requiring mechanical ventilation.[34] In addition, the threshold for starting mechanical ventilation is controversial.[35]

Further, as the number of COVID-19 cases came under relative control in NSW (albeit, at the time of writing, cases have been increasing again[36]), so did the number of patients requiring intensive care. Indeed at the time of writing, recruitment for the STC3141 Phase II trial has been withdrawn due to participant recruitment difficulties.[37]

Even if the study were recruiting, there remained the issue of consent. A patient could not be recruited to the Trial unless an application were made to the Tribunal for consent on their behalf. Under the Act, the Tribunal need only hear an application if it is satisfied the applicant has a sufficient interest in the health and well-being of the patient, and must only give consent if it considers the treatment appropriate for that patient.

Conclusion

Statutory frameworks may provide mechanisms for substituted decision-making in certain situations. However, they also protect an individual's autonomy and espouse fundamental principles of consent in common law.

Legislative provisions around consent are found in other jurisdictions across Australia, however they are not uniform. For example Victoria,[38] Queensland,[39] the Northern Territory[40] and the Australian Capital Territory[41] also have legislative regimes for consent to medical research on behalf of people who are unable to consent themselves. On the other hand, South Australia,[42] Western Australia[43] and Tasmania[44] do not make specific reference to consent for medical research or clinical trials on behalf of adults who lack capacity.

Although this article has not studied the different legislative frameworks in detail, the NSW Tribunal's decision exemplifies the role of our legal system in promoting and supporting medical progress in times of crisis, while at the same time safeguarding patient autonomy and fundamental principles of consent.

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Footnotes

1. STC3141 — An Open Label, Multi-Centre Study to Determine the Safety and Efficacy of STC3141 Administered as an Infusion for up to 5 Days in Subjects with COVID-19 Respiratory Distress Syndrome Requiring Intensive Care [2020] NSWCATGD 16.
2. Guardianship Act 1987 (NSW), s 33A.
3. As at 10 July 2020, there were at least 120 vaccines being developed worldwide. See W Joost Wiersinga et al, "Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review", *JAMA,* published online July 10 2020, accessed on 31 July 2020 at https://jamanetwork.com/journals/jama/fullarticle/2768391?guestaccesskey=0bf3c746-6364-4fc8-82e8-bb647de9a10b&utm_source=silverchair&utm_medium=email&utm_campaign=article_alert-jama&utm_term=mostread&utm_content=olf-widget_07292020&alert=article#.
4. This is reported to occur in 15% of patients hospitalised with COVID-19, with pneumonia occurring in 75%. See W Joost Wiersinga et al, "Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review", *JAMA,* published online July 10 2020, accessed on 31 July 2020 at https://jamanetwork.com/journals/jama/fullarticle/2768391?guestaccesskey=0bf3c746-6364-4fc8-82e8-bb647de9a10b&utm_source=silverchair&utm_medium=email&utm_campaign=article_alert-jama&utm_term=mostread&utm_content=olf-widget_07292020&alert=article#.
5. [2020] NSWCATGD 16, at [15].
6. See Australian New Zealand Clinical Trials Registry, https://anzctr.org.au/Trial/Registration/TrialReview.aspx?ACTRN=12620000588998, accessed on 31 July 2020.
7. See Australian New Zealand Clinical Trials Registry, https://anzctr.org.au/Trial/Registration/TrialReview.aspx?ACTRN=12620000588998, accessed on 31 July 2020.
8. That is, patients to whom Pt 5 of the Act applies.
9. Guardianship Amendment Bill 1998 [Act 1998 No 7], Explanatory Note 3.
10. [2020] NSWCATGD 16, at [8].
11. 24 April 2020.
12. [2020] NSWCATGD 16, at [5].
13. [2020] NSWCATGD 16, at [7].
14. See *ASHM COVID-19 Taskforce update on registered COVID-19 studies in Australia and New Zealand*, https://ashm.org.au/covid-19/research-and-data/clinical-trials-in-australia/.
15. [2020] NSWCATGD 16, at [16].
16. [2020] NSWCATGD 16, at [16]. "Participant Information Sheet".
17. [2020] NSWCATGD 16, at [12].
18. Guardianship Act 1987 (NSW), s 34.
19. Guardianship Act 1987 (NSW), s 33(2). For the purposes of Pt 5, a person is incapable of giving consent to treatment if they are not capable of understanding the general nature and effect of the proposes treatment, or not capable of indicating whether or not they consent.
20. Guardianship Act 1987 (NSW), s 32.
21. [2020] NSWCATGD 16, at [32].
22. [2020] NSWCATGD 16, at [36].
23. [2020] NSWCATGD 16, at [38].
24. [2020] NSWCATGD 16, at [41].
25. [2020] NSWCATGD 16, at [40].
26. [2020] NSWCATGD 16, at [45].
27. At the date of writing, this has not yet been heard.
28. Guardianship Act 1987 (NSW), s 42.
29. Guardianship Act 1987 (NSW), s 42(2).
30. Guardianship Act 1987 (NSW), s 44(1).
31. Guardianship Act 1987 (NSW), s 44(2).
32. Guardianship Act 1987 (NSW), s 44(3).
33. Guardianship Act 1987 (NSW), s 32(a).
34. The rate of hospitalisation is unclear, given various thresholds. See W Joost Wiersinga et al, "Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review", *JAMA,* published online July 10 2020, accessed on 31 July 2020 at https://jamanetwork.com/journals/jama/fullarticle/2768391?guestaccesskey=0bf3c746-6364-4fc8-82e8-bb647de9a10b&utm_source=silverchair&utm_medium=email&utm_campaign=article_alert-jama&utm_term=mostread&utm_content=olf-widget_07292020&alert=article#.

35. W Joost Wiersinga et al, "Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review", *JAMA,* published online July 10 2020, accessed on 31 July 2020 at https://jamanetwork.com/journals/jama/fullarticle/2768391?guestaccesskey=0bf3c746-6364-4fc8-82e8-bb647de9a10b&utm_source=silverchair&utm_medium=email&utm_campaign=article_alert-jama&utm_term=mostread&utm_content=olf-widget_07292020&alert=article#.
36. At the time of writing (31 July 2020), there were 91 known cases of COVID-19 in NSW. For updated figures please see www.health.nsw.gov.au/Infectious/covid-19/Pages/stats-nsw.aspx.
37. See Australian New Zealand Clinical Trials Registry (accessed on 31 July 2020), www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=379714&isReview=true.
38. See Medical Treatment Planning and Decisions Act 2016 (Vic), Pt 5 which applies to the administration of a medical research procedure to an adult who does not have decision-making capacity in relation to the procedure.
39. See Guardianship and Administration Act 2000 (Qld), Sch 2, s 13 which sets out the process for obtaining approval from the Queensland Civil and Administrative Tribunal for approval of clinical research. Consent to approved clinical research follows order of priority provisions set out in s 66.
40. See Guardianship of Adults Act 2016 (NT), Advance Personal Planning Act 2013 (NT).
41. See Guardianship and Property Management Act 1991 (ACT), Medical Treatment (Health Directions) Act 2006 (ACT), Powers of Attorney Act 2006 (ACT).
42. General principles pertaining to decision-making for persons with impaired capacity may apply. See Advance Care Directives Act 2013 (SA), Consent to Medical Treatment and Palliative Care Act 1995 (SA) and Guardianship and Administration Act 1993 (SA).
43. General principles pertaining to decision-making for persons with impaired capacity may apply. See Guardianship and Administration Act 1990 (WA), in particular, Pt 9D — Treatment decisions in relation to patients under legal incapacity.
44. General principles pertaining to decision-making for persons with impaired capacity may apply. Guardianship and Administration Act 1995 (Tas).