PRELIMINARY SUBMISSION TO NSW LAW REFORM COMMISSION REVIEW OF THE NSW GUARDIANSHIP ACT 1987

1. The South Eastern Sydney Local Health District Human Research Ethics Committee welcomes the opportunity to make this preliminary submission to the NSW Law Reform Commission review of the *Guardianship Act 1987*, and in particular the provisions of Division 4A of Part 5 of the Act relating to clinical trials.

2. We take this opportunity to inform you of some of the broad issues we consider relevant to the Commission's terms of reference.

3. We firstly set out a brief description of the work we do. Then, by way of case study, we describe an application that came before us (SPICE III) and in which we encountered a number of challenges arising out of the provisions of Division 4A of Part 5 of the Act. Finally, we identify a number of other issues that we consider it would be useful for the Commission to receive submissions on in the subsequent stages of the Commission's review.

The SESLHD HREC

4. The South Eastern Sydney Local Health District (SESLHD) is a Local Health District constituted pursuant to the *Health Services Act 1997* (NSW).

5. The SESLHD extends to the local government areas of Botany Bay, Hurstville, Kogarah, Randwick, Rockdale, Sutherland, Sydney (part), Waverley, and Woollahra. Within its boundaries, it manages a number of public hospitals, including a number of teaching hospitals (Prince of Wales Hospital, Royal Hospital for Women, St George Hospital, Sydney Eye Hospital). Associated with these hospitals are a number of internationally-renowned medical research facilities, including NeuRA, the Black Dog Institute and the University of New South Wales.

6. Health research conducted at the SESLHD hospitals, and their associated research facilities, is governed by various Policy Directives and Guidelines issued by NSW

Health, and in particular:

a. Policy Directive PD2007_035 *Human Research Ethics Committees: Standards for Scientific Review of Clinical Trials;*

b. Policy Directive PD2010_055 *Ethical and scientific review of human research in NSW Public Health Organisations*;

c. Guideline GL2013_009 *Human Research Ethics Committees: Standard Operating Procedures for NSW Public Health Organisations*.

d. Guideline GL2011_001 *Research Governance in NSW Health Organisations*

e. Policy Directive PD2010_056 *Authorisation to Commence Human Research in NSW Public Health Organisations*

7. These Policy Directives and Guidelines provide the detailed requirements for the conduct of medical research in the NSW public health system (including the SESLHD and its associated research facilities). In particular, they require that medical research be conducted in accordance with the National Health and Medical Research Council's *National Statement on Ethical Conduct in Human Research* (2007) updated May 2015.

8. Consistently with these Policy Directives and Guidelines, the SESLHD has established a Scientific Review Committee (SRC) and a Human Research Ethics Committee HREC) to ensure the highest standards of scientific and ethical review of medical research conducted within its boundaries.

9. A consequence of the international recognition of the scientific excellence of the research facilities and clinicians within the SESLHD is that the HREC is frequently called upon to review scientific and ethical merit of multi-centre studies. This includes studies where the research sites (other than those within SESLHD) are located in other LHDs, in other jurisdictions within Australia, and internationally.

10. The SESLHD HREC was accredited by NSW Health as a "Lead HREC" (and has subsequently been certified as a Lead HREC by the NHMRC), that is an HREC

accredited to conduct the single and scientific review of multi-centre research projects on behalf of all sites within the NSW public health system.

11. In 2013, NSW Health in conjunction with the corresponding government health agencies in Queensland, South Australia, and Victoria agreed to implement a scheme of National Mutual Acceptance (NMA) of single ethical review of multi-centre clinical trials conducted in each participating jurisdiction's public health organisations (it is proposed that the remaining jurisdictions will participate in the scheme in due course). The NMA is governed by the *Standard Principles for Operation: National Mutual Acceptance of Single Ethical and Scientific Review of Multi-Centre Human Research Projects*. One aspect of the scheme is that although it provides for a single ethical approval to be provided through the NMA, a human research project cannot commence until authorization is provided by a participating site.

12. One important aspect of ethical approval of human research is the requirement that the research be lawful (see, for example, clause 5.7.3(b) of the NHMRC Statement). It is for this reason that one of the requirements of clause 5.1.30(e) of the NHMRC Statement is that the HREC include at least one legal practitioner.

13. The laws governing matters such as consent to medical treatment and procedures, and in particular in relation to consent to medical research, are different in the various jurisdictions throughout Australia. This is one reason why, despite the best endeavours of the NMA, site-specific approval of human research is still required before the commencement of research at a particular site is authorized.

SPICE III TRIAL

14. What follows is a description of some of the difficulties encountered by the SESLHD HREC in considering an application for ethical approval for the conduct of the SPICE III trial at Prince of Wales Hospital. As a Lead HREC, ethical approval by the SESLHD HREC would have allowed the SPICE III trial to be conducted at various other sites in NSW, including Nepean Hospital, St Vincent's Hospital, Westmead Hospital and Royal North Shore Hospital.

15. The study was part of the SPICE (Sedation Practice in Intensive Care Evaluation) Project, coordinated by the Australian and New Zealand Intensive Care Research Centre at Monash University in Victoria. The study was to be conducted in approximately 35 study intensive care units and recruit 4000 patients worldwide. The study commenced in Victoria in November 2013, in Tasmania and New Zealand in around April 2014 and in Queensland, South Australia and the Northern Territory in May 2014.

16. The primary aim of the study was to compare the comparative efficacy (measured by reference to 90 day mortality in critically ill patients who are expected to require mechanical ventilation for longer than 24 hours) of two different sedative regimens that were widely used in clinical practice throughout Australia. As at the date of the trial the choice of sedative regimen was largely based upon the personal preferences and experiences of the individual clinician. There was no scientific basis for preferring one regimen over the other, and therefore no ethical difficulty posed by the fact of randomization.

17. By virtue of the inclusion criteria for the study, none of the patients who were eligible to participate in the study were competent to provide informed consent for their treatment.

18. It is neither necessary nor appropriate to disclose the details of the HREC's consideration of the SPICE III trial. However, it is a matter of public record that:

    a. The application for approval of the SPICE III trial was first considered by the SESLHD HREC at its meeting on 30 October 2012;

    b. There were concerns on the part of the SESLHD HREC as to the lawfulness of the study being conducted in NSW in the absence of approval from the NSW Guardianship Tribunal (as it then was). Other than that aspect, the HREC was satisfied that the study was ethical and clinically-appropriate;

    c. There was a contention by the Principal Investigator that the SPICE III Trial was not a "clinical trial" within the meaning of the Act at all;

    d. The Tribunal approval process took 12 months from the date of the initial

hearing (17 December 2013) until the date of approval of the study in accordance with section 45AA of the Act (see *Application for approval for adults unable to consent to their own treatment to participate in a clinical trial (SPICE III Trial)* [2014] NSWCATGD 44);

e. There was then a further period of 6 months before the NCAT made further orders enabling the consent to individual participation of a patient in the trial to be provided by a "person responsible" (see *Application for additional orders relating to a clinical trial previously approved by the Tribunal and known as the SPICE III Trial* [2015] NSWCATGD 24).

19. In drawing attention to this case study we do not in any way seek to impugn the decisions of NCAT, nor suggest that the procedures adopted by them were other than were required by the Act.

20. However we do make the observation that because of the requirements of Division 4A of Part 5 of the Act (which impose requirements that are more onerous than those applicable in Victoria) the commencement of the study in NSW was delayed by a period in excess of 18 months.

21. Delays of that magnitude have consequences for the ability of NSW institutions to attract research funding and personnel. They also create the potential for "forum-shopping" in selection of a Lead HREC for ethical approval, and the potential for subconscious bias in HREC consideration of inter-state multi-centre trials.

22. These issues are likely to be encountered more frequently as more research is conducted into intensive care patients, or patients with cognitive or other deficits that render them incapable of providing consent.

23. We also note the somewhat anomalous position created by the definition of "clinical trial" in its application to another study (the TRANSFUSE study). The primary aim of the TRANSFUSE study was to compare the clinical outcomes between critically ill patients who receive transfusions of fresh blood as opposed to stored blood. Again, participants were likely to be incapable of providing consent due to the effects of sedation and their illness. However, because the study was not a trial of drugs or techniques it was not (so NCAT found) a "clinical trial" and therefore not subject to

the same consent requirements as had been found to be applicable to the SPICE III trial (see *Application for approval for adults unable to consent to their own treatment to participate in a clinical trial (TRANSFUSE Trial)* [2015] NSWCATGD 18).

24. It is not readily apparent what is the policy rationale for the consent requirements under the Act differentiating between the SPICE III trial and the TRANSFUSE trial. If experienced members of an HREC are unable to adduce the relevant differences, the research community and general public will be at a disadvantage when designing or considering participation in investigations aligned with the underlying rationale.

Issues for consideration by the NSWLRC

25. We assume that the work of the NSWLRC review into the Guardianship Act will involve an examination of the consent requirements relating to medical treatment more generally (ie the remainder of the provisions of Part 5).

26. No doubt that work will involve consideration of the ethical considerations upon which a regime (or regimes) of alternative forms of consent ought be based (eg, principles of beneficence, non-maleficence, autonomy, or some combination thereof).

27. In the particular context of medical research, an important issue for the NSWLRC to consider is the extent to which these ethical principles are capable of application in the context of a clinical trial, and if so the extent to which they need to be modified in the particular context. For example, principles of beneficence may have a tendency to exclude incapable patients (whether because of a permanent incapacity or a transient incapacity) from clinical research altogether, and it is difficult to see how they could apply to a study such as SPICE III where the very purpose of the study is to determine the comparative efficacy of the alternative treatments. Principles of non-maleficence may be incapable of application, or at least exclude study designs that are placebo-controlled (since every intervention arm is likely to carry *some* risk, however minor). Principles of autonomy may be of limited utility in circumstances (such as emergency care research) where there is simply no opportunity to have regard to or inquire of a patient's expressed wishes (or even their assumed wishes as divined by a person responsible).

28. Whatever ethical principles inform the alternative consent regime, they ought to avoid the unintended consequence of stultifying research with potential benefits for those patients.

29. One issue that arises for consideration in this context is the tension between protecting the vulnerable from exploitation, while at the same time not excluding people from making a valuable contribution to society by participating in medical research on the grounds of disability rendering them incompetent.

30. Apart from the criteria that ought to govern the circumstances in which incompetent patients ought be lawfully allowed to participate in medical research, consideration will also need to be given to the question of who the appropriate consent body should be. Should it be sufficient that an HREC has approved the study and the person responsible has provided consent? Should the approval be provided by an administrative tribunal (such as NCAT) or some other public authority (such as the Public Guardian)? If so, what are the procedures and criteria for approval best suited to balancing the interests of the patient with the interests of medical research (which includes not only medical researchers but also other, future, patients who may benefit from the results of a particular study)? In particular, how do the procedures and criteria for approval accommodate participation in studies involving time-critical interventions? Ought such a body reconsider either the scientific merits or the ethics of the proposed research, or would this be beyond their capacity?

31. One issue that arises from the NHMRC Statement is whether deferred consent (see clause 4.4.6- 4.4.14 of the NHMRC Statement) or waiver of consent (see clause 2.3.9 - 2.3.11 of the NHMRC Statement) ought be allowed? If so, what is the appropriate body to authorise a deferred consent or a waiver of consent? What are the appropriate criteria to be applied? Would it apply in all cases or only a defined subset of medical research (and what are the appropriate criteria for determining that subset)?

32. Other issues include:

    a. To which medical research should the provisions apply (eg is there a proper basis for the SPICE III trial being treated differently to the TRANSFUSE trial? Should it apply to a placebo arm or the standard care arm of the trial, or only to the intervention arm?)

b. Should there be different consent regimes depending upon the nature of the treatment or procedure contemplated, or the degree of risk involved?

c. To what extent should NSW seek to mirror provisions in other jurisdictions, take the lead in producing a national model law, or provide for mutual recognition, in order to minimise the issues arising from inter-state multi-centre research?

d. Does the NHMRC have a role in seeking to harmonise provisions relating to consent to participation in medical research by incapable persons?

e. Should there in fact be *any* provisions specifically directed towards medical research (noting that as we understand it only NSW, Victoria and Queensland have such provisions)?

Moving forward

33. As is apparent, the issues that are raised by the conduct of medical research upon those who are incapable of providing consent are complex.

34. These issues have already been considered by the Victorian Law Reform Commission and are discussed in Chapter 14 of *Guardianship - Final Report 24.* No doubt that report, and the submissions made to the VLRC, will provide a useful starting point for the NSWLRC's consideration of the issues identified above. The recommendations of the VLRC, so far as we are aware, have not been implemented in Victoria.

35. We are, of course, keen to assist the NSWLRC with its review of the Act and the members of the SESLHD HREC would welcome the opportunity to make further submissions, participate in round-table discussions, or otherwise assist the NSWLRC in its consideration of these issues.

1 April 2016