

# Clinical trial research regulation in Victoria

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# Introduction

Streamlining research in Victoria was initiated in 2009 with single ethics review for multi-site clinical trials.

This involved considerable consultation to develop a framework:

- A limited number of ethics committees providing ethics review (one only)
- A process for acceptance of that review at research sites – site specific assessment or often referred to as research governance (or alternatively used to broadly encompass governance of all processes)
- Standardisation of forms, processes and procedures
- Introduction of an information platform for work flow, connectivity between hospital administrators, and to provide a means for data collection on Victoria's research activity
- Benchmarking time taken for the ethics process

# Implementation of streamlining research

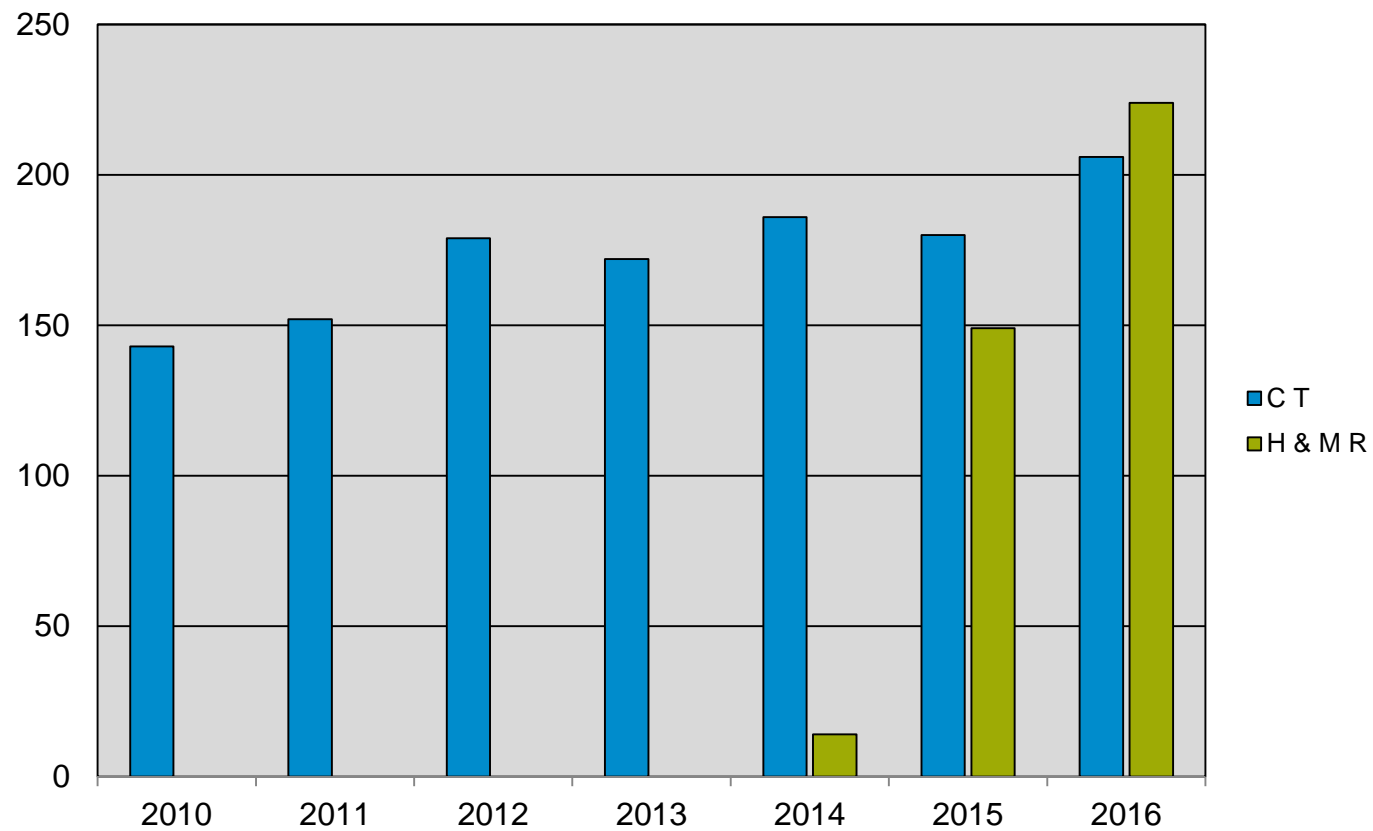
- Initially multi-site clinical trials only, due to the funding agreement of Government as clinical trials have significant industry involvement
- Communications include comprehensive website guidance for investigators/applicants, companies and research offices:
  - clinical trials
  - health & medical research
- Regular Streamlining E-bulletin, May Workshop, Forums (targeted topics) and e-mail communications
- Regular meetings with the sector: reviewing ethics committee research manager's meetings and working through Biomedical Research Victoria to engage the broader hospital sector

## Outcomes to date

- **Benchmarking** of the reviewing ethics committees for review time:  
30 working days, with clock-time taken out when an application is with the applicant/investigator
- **Reduce duplication** of ethics reviews: **saved 1,970 ethics reviews** from **2009 to 2016**. This represents a large saving of time and resources  
**Total number of ethics reviews= 1,377; total SSAs= 3,347**  
*\*\*Ask where would we be now if single review was not implemented?*
- **Growth in clinical trials** has occurred, despite increased global competitiveness for trials in AsiaPac, South America, Eastern Europe and elsewhere

# Growth of research activity

## Victorian Multi-Site Clinical Trials and Health & Medical Research By Calendar Year



# Driving improved performance:

## Shorter time for ethics review completion and site assessment

- All participating hospital CEOs and research offices receive benchmark reports 6 monthly. Reports provide information on any data quality issues and is a means of taking corrective action [data is only as good as its quality]
- Improved overall timeliness:
  - **87%** of multi-site trials meet the 30 working day benchmark
  - **117** days without clock - average regulatory approval time for commercially sponsored multi-site trials(start of ethics to first SSA authorised)
- Delays identified:
  - Time for applicants/investigators to respond to ethics committee request for information - 30 to 40 days on average
  - SSA process is not commenced early – approx. 50% of applicants /administrators wait until ethics approval before starting SSA

# National Mutual Acceptance (NMA)

NMA – single ethical review between jurisdictions operating single ethics review

For applications in Victoria only:

Research Type	Start Date
Clinical trials	November 2009
Clinical trials and health/medical research	February 2015

For applications in Victoria and other states/territories

Streamlined System	Research Type	States/Territories	Start Date
IMA	Clinical trials	QLD, VIC	October 2011
		NSW, QLD, VIC	February 2012
NMA	Clinical trials	NSW, QLD, SA, VIC	November 2013
	All human research	NSW, QLD, SA, VIC	December 2015
		ACT, NSW, QLD, SA, VIC	August 2016

## Site specific assessment/governance at research sites

There are numerous sign-offs, compliance and local policy requirements, but one of the identified holdups is the research agreement and budget for a clinical trial or clinical research



# Enablers

The Southern Eastern Border States (SEBS) panel plays a role with Medicines Australia and Medical Technology Association Australia negotiating changes to research contracts and standardised schedules of Special Conditions.

Participating jurisdictions:

New South Wales, Queensland, South Australia and Victoria

# Standard Clinical Trial Research Agreements (CTRA)

## **Medicines – commercially sponsored CTRAs have been revised**

*Website: [medicinesaustralia.com.au/policy/clinical-trials/clinical-trials-research-agreements/](http://medicinesaustralia.com.au/policy/clinical-trials/clinical-trials-research-agreements/)*

- Standard sponsor agreement – standard CTRA
- Contract Research Organisation (Local-sponsor) - CRO CTRA
- Collaborative or Cooperative Research Group – CRG CTRA
- Phase IV clinical trial (Medicines) CTRA
- Phase IV (medicines) CRO CTRA

## Transition arrangements

The updated CTRA templates for use from 1 May 2017

There is no need to revise previously agreed CTRAs currently in use

Between 1 May 2017 and 31 July 2017 either use the current (November 2012/March 2013) versions of the CTRA templates or the March 2017 versions for new clinical trial projects. Both are acceptable.

On or after 1 August 2017, the March 2017 CTRA templates must be used

# Standard Research Agreements

## Medicines Australia

SEBS is currently reviewing an Investigator Initiated company supported research agreement with Medicines Australia

## Medical Technology Association Australia (MTAA)

A revised agreement has been developed and will be available on the MTAA website soon

Further revisions will be made to align wording with the MA CTRA's for consistency

The MTAA Clinical Investigator Research Agreement is acceptable in Victoria and endorsed by DHHS

SEBS will soon have public endorsement of this agreement

# Non commercial Research Agreements

The VMIA **Investigator Initiated clinical trial** research agreement is available on the DHHS website at: [www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research](http://www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research)

Other research agreements for Investigator-Initiated research (no company involvement)

There are 2 agreements in-part based on the VMIA, CTRA with adaptations for:

- Non-interventional/non trial
- Non-CTN clinical trials that may involve an intervention

These will be negotiated through the National Mutual Acceptance Jurisdictional Working Group. Member jurisdictions will undertake legal review and provide comments on the current documents and then final versions will be provided on jurisdiction websites. Expected by second half 2017.

## What next?

Much progress has been made in implementing a consolidated approach to the regulatory complexities around clinical trials and other research with significant timeliness improvement and efficiency gains.

However

2017 is promising to be a year of significant advancements

# New developments

Implementation of the National Health & Medical Research Council (NHMRC),  
*Safety monitoring and reporting in clinical trials involving therapeutic goods*  
(September 2016)

The key change is that the sponsor has responsibility for reporting safety events to the ethics committee for clinical trials

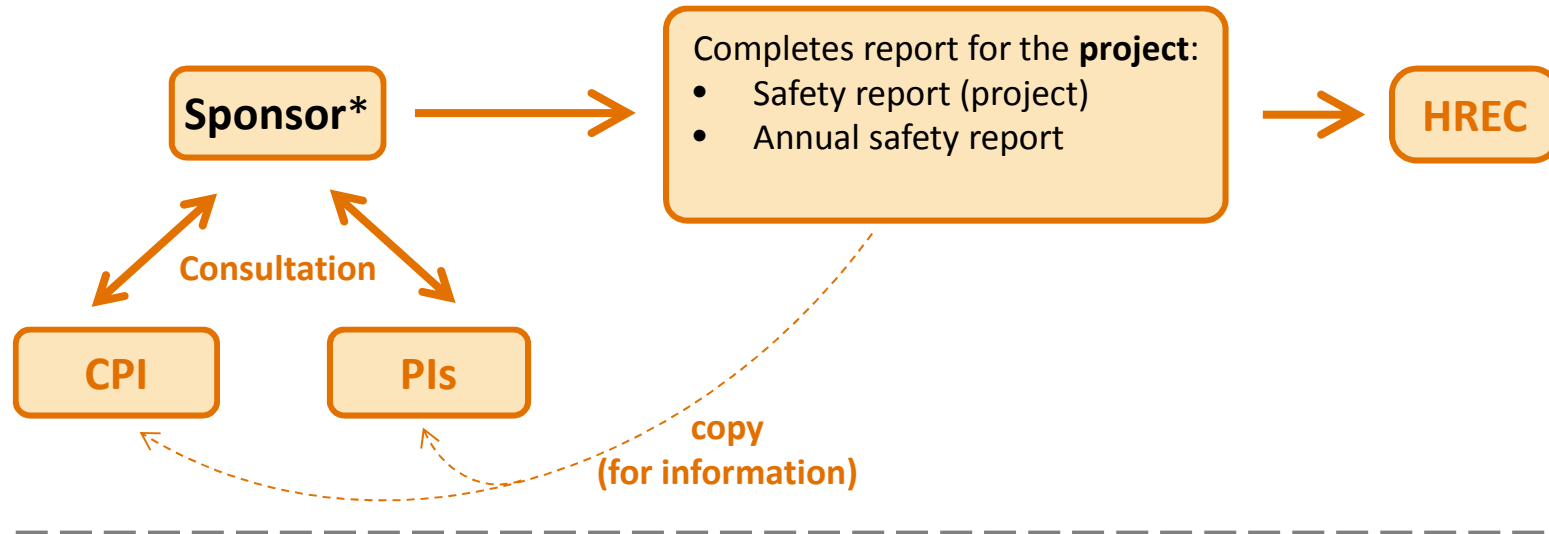
There are changes in nomenclature and terminology

Timelines may be changed for reporting, depending on the risk of the event

Frequency of reporting is different

Due to the degree of changes, NHMRC plans to release 3 guidance documents for the clinical trials sector

## Safety Reporting Responsibilities – Multi-site Project



**Sponsor = Commercial, collaborative research group, investigator, institution or other**

**CPI = Coordinating Principal Investigator**

**PI = Principal Investigator**

**HREC = Human Research Ethics Committee**

**RGO = Research Governance Officer**

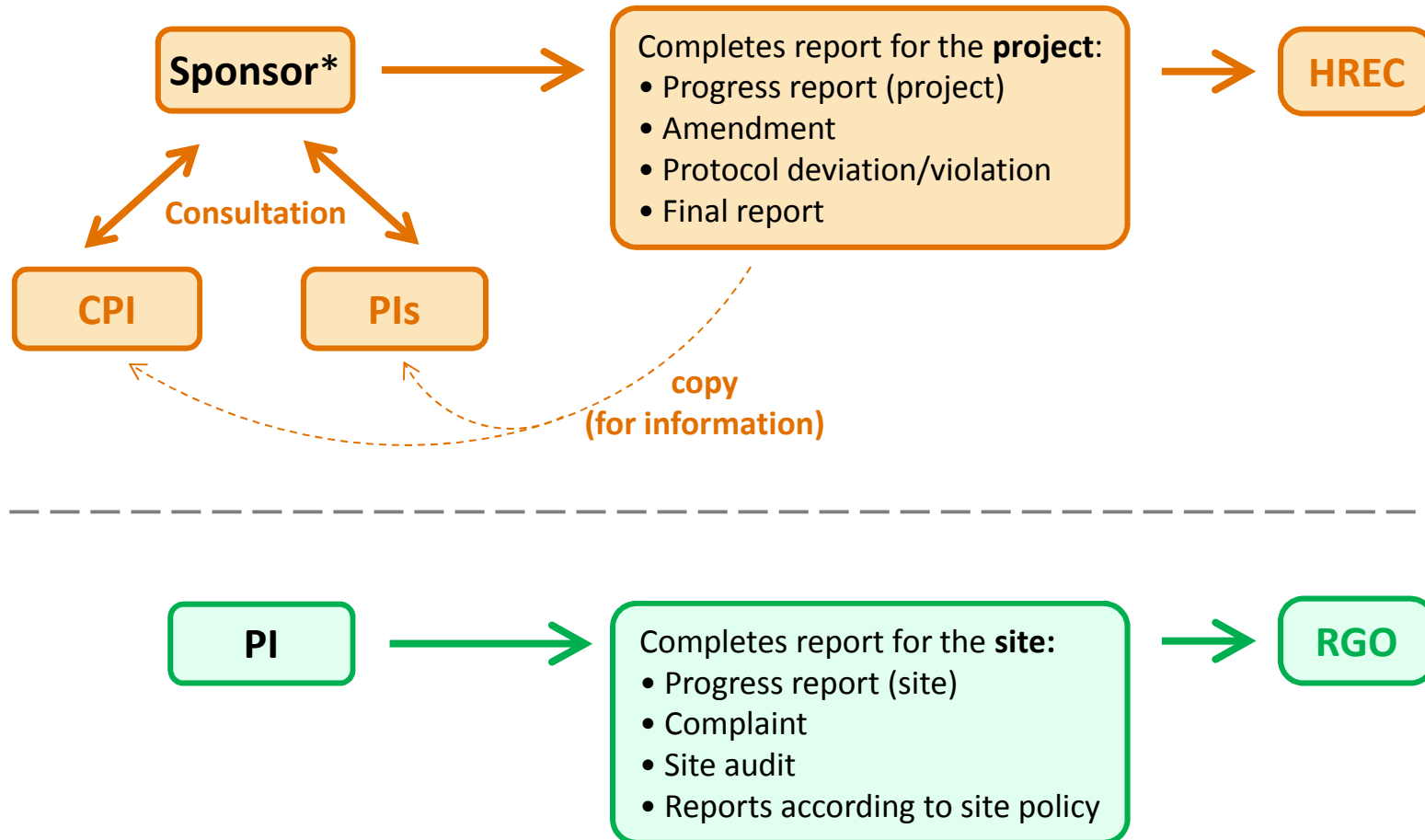
# Reporting Responsibilities – Multi-site Project

(excluding safety reporting)

Other reporting responsibilities have been brought in to line with that of safety reporting to ethics committee and the site RGO



## Reporting Responsibilities – Multi-site Project (excluding safety reporting)



# Reporting forms for research projects

- One implication of this changed process is that the Coordinating Principal Investigator (lead site) will not have responsibility for submitting safety events to the ethics committee.
- For e-submission it will be necessary for the project sponsor to “own” or have the NEAF “transferred” to them to submit relevant reports
- The reporting forms are on a dedicated Reporting Page on the Clinical Trials website: [www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research](http://www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research)
- **IMPORTANT:** Revised versions are on the website. It is important to bookmark the website and not use downloaded/saved template versions

# Reporting forms

## HREC reporting templates

Sponsor	Safety report (HREC)
	Annual safety report
	Amendment request form
	Progress report- Project report
	Project final report/Site closure
	Protocol deviation or violation

## RGO/Site reporting templates

PI/CPI	Complaint report
	Progress report – Site form (RGO)
	Site audit report for research

## Victorian Specific Module

Recently the VSM has been legally reviewed by the Department following policy changes and request from the sector to review this form.

Problem: the VSM is not well adopted across jurisdictions by investigators and interstate ethics committees.

## Victorian Specific Module – review outcomes

**Section 1** - Intended as information for ethics reviewers, key fields have been integrated in to the new Human Research Ethics Application form developed by NHMRC (not yet implemented by jurisdictions) – **section will be removed**

**Section 2** - Guardianship matters relating to persons not competent to provide consent for research - **section will be re-drafted and retained entirely**

**Section 3** – Privacy, in part addressed by the Human Research Ethics Application (HREA) form - **section will be re-drafted and retained**

## Victorian Specific Module – review outcomes

**Section 4** - Radiation Safety at DHHS has agreed that submission to ethics is no longer required

Compliance with the ARPANZA *Code of Practice for Radiation Protection in the Medical Applications of Ionizing Radiation (2008)* a Medical Physicists Report is required for research projects as specified, in the Code

*The Section 4 form will be used locally by the Medical Physicist to assess research projects at sites and will advise on wording for the Participant Information and Consent Form*

**Section 5** - Use of human tissue and blood (adult and children) - **this section will be retained and undergo revision with assistance of the legal team within the Department**

## Victorian Specific Module – review outcomes

We aim to provide the revision as either one shorter form or as individual documents to be used according to the requirements of the research project. This is yet to be decided with legal advice.

Implementation of new VSM document/s: when the HREA is programmed in to Online Forms – Q3 2017

# NHMRC National Ethics Application Form (NEAF) current

## Ethics and research governance/site specific assessment (SSA) application forms

- The Online Forms website (<https://au.ethicsform.org>) must be used for any applications to a public health organisation (hospital) in Victoria.
- Online Forms must be used for ethics applications and research governance/SSA applications.
- The National Ethics Application Form (NEAF) must be used for ethics applications to Victorian HRECs at public health organisations, and for all National Mutual Acceptance (NMA) applications.



# NHMRC Human Research Ethics Application Form (HREA) - transition

When can I use the HREA?

- The HREA will not be used for applications to Victorian human research ethics committees (HRECs) at public health organisations, or for NMA applications, until the Online Forms website (<https://au.ethicsform.org>) has transitioned to the HREA
- HREA use is anticipated for the third quarter of 2017
- Detailed information and advice about the transition will be provided in advance
- All jurisdictions in NMA will implement at the same time and notice will be given of the transition

# Research and involvement of participants that do not have competence to consent

Currently the *Guardianship and Administration Act 1986 (Vic)*

The Act applies to medical research procedures and addresses consent and other processes to conduct research when consent may not be immediately available.

# Research and involvement of participants that do not have competence to consent

There will be a transition of the legislation regarding medical research procedures and incompetence to consent from the *Guardianship and Administration Act 1986* in February 2018 to the ***Medical Treatment Planning and Decisions Act 2016***

Essentially there is little change for medical research procedures regarding consent but there are some new elements to consider.

## How will the Act effect research?

The Act only applies to medical research procedures performed on people who do not have decision-making capacity.

Previously governed by the *Guardianship and Administration Act 1986*.

Changes are minimal, about recognising new instruments.

The process for obtaining consent or approval for a medical research procedure for a person without decision-making capacity has not changed substantially.

## Key aims of the Act

**Shift away from 'best interests' decision making to focus on what the person actually wants**

**To allow a person with capacity to:**

Make an advance care directive that includes binding instructions and preferences and values for future medical treatment

Appoint a medical treatment decision maker

Appoint a support person

**Provide a scheme for decision making about medical research procedures for people without capacity**

## Advance care directives

An **instructional directive** that allows people to consent to or refuse a particular medical treatment or medical research procedure in the future.

A **values directive** that allows someone to make a statement about their preferences and values as the basis on which medical treatment decisions are made on their behalf, and can include statements of treatment outcomes that they would want.

## Medical treatment decision makers

New single role of medical treatment decision makers

This will replace all the previous roles (eg enduring attorneys and persons responsible).

Make decisions about medical research procedures on behalf of a person who does not have decision-making capacity.

A person may appoint a medical treatment decision maker, otherwise there is a default list.

# Medical treatment decision maker hierarchy

An appointed medical treatment decision maker who is willing and available

An adult who is the first person who has a close and continuing relationship and is willing and available:

- Spouse or domestic partner;
- Primary carer;
- Adult child;
- Parent;
- Adult sibling.

A medical treatment decision maker for a person under 18 years is the child's parent or guardian.



## New decision-making test

The 'best interests' test has been replaced.

The decision of the medical treatment decision maker must be the decision they reasonably believe the person would have made, if they had decision-making capacity.

There is a staged process for determining this:

- **first consider any relevant values directive;**
- **next consider any relevant preferences expressed by the person;**
- **next consider the person's values, whether expressed or implied;**
- **If none of the above, must make a decision to promote the person's personal and social wellbeing.**

# Obligations of medical research practitioners - emergencies

**Emergency medical treatment or medical research procedure can be administered without consent or authorisation to**

- Save the person's life
- Prevent serious damage
- Prevent suffering from significant pain and distress

A medical research practitioners cannot administer a medical research procedure if aware the person has refused the procedure in an ACD or otherwise

Does not have to search for an Advanced Care Directive if not readily available

# Consent for a person without capacity

Have relevant human research ethics committee approval; and

Either:

- the person's consent in an instructional directive; or
- consent from the person's medical treatment decision maker.

Medical research practitioner must record in medical record that the person did not have capacity and was not likely to regain capacity.

# Administering medical research procedures without consent

If reasonable steps have been taken to locate a person's **instructional directive** and to identify and contact the medical treatment decision maker but have been unable to do so.

Medical research practitioner may administer a medical research procedure without consent if they believe that the inclusion of the person in the medical research would not be contrary to **the person's preferences, values or personal and social wellbeing.**

# Administering medical research procedures without consent

Remaining provisions consistent with existing obligations in the *GAA Act* that the medical research practitioner believes the medical research procedure:

- is approved by relevant human research ethics committee;
- has a purpose of assessing the effectiveness of the procedure;
- poses no more risk than the inherent risk of the person's condition; and
- based on valid hypotheses and reasonable possibility of benefit compared to standard treatment.

**Must provide a certificate to the Public Advocate, certifying that all the requirements have been complied with.**

## Other existing obligations for ongoing procedures remain

Medical research practitioner must continue to take reasonable steps to identify and contact a medical treatment decision maker.

Continue to provide a medical research practitioner's certificate to the Public Advocate and the relevant ethics committee.

Inform the medical treatment decision maker (if identified) or the person (if they regain capacity) and provide the option of refusing the continuation of the research procedure.

# Protections

A medical research practitioner who administers a medical research procedure in good faith believing they have complied with the requirements set out in the Act will not be liable.

# VCAT

Continues to be able to make orders about medical research procedures.

VCAT will also be required to make orders considering the persons **preferences, values and personal and social wellbeing.**

Provide advice to a medical treatment decision maker.



# Summary

There are some new terms and the provisions have been re-ordered, but the substantive changes are limited.

Two key changes:

- you must identify and consider an advance care directive; and
- decisions must be made based on the person's preferences, values and personal and social wellbeing.

# Contacts

- » Coordinating Office for Clinical Trial Research, DHHS
- » Website: [www2.health.vic.gov.au/about/clinical-trials-and-research](http://www2.health.vic.gov.au/about/clinical-trials-and-research)
- » Coordinating Office Tel: 03 9096 7394
- » Email: [multisite.ethics@dhhs.vic.gov.au](mailto:multisite.ethics@dhhs.vic.gov.au)
- » Online Forms Helpdesk
- » Helpdesk Tel: 02 9037 8404
- » Helpdesk Email: [helpdesk@infonetica.net](mailto:helpdesk@infonetica.net)
- » Your organisation's research office