FORM 1

THE UNIVERSITY OF MELBOURNE
HUMAN RESEARCH ETHICS COMMITTEE

APPLICATION FOR APPROVAL OF A PROJECT INVOLVING HUMAN PARTICIPANTS

PROJECT REFERENCE DETAILS

Enter the Ethics ID number assigned by Themis Research to this ethics application.	0723086.1
Enter the title of the Project as recorded in Themis Research	Biomarkers in Chronic Fatigue Syndrome
Enter the name of the Responsible Researcher as recorded in Themis Research	Gooley, A/Prof Paul Raymond

1. PROJECT DETAILS

1.1 EXECUTIVE SUMMARY IN PLAIN ENGLISH: *Provide a brief summary of the project outlining the broad aims, background, key questions, research design/approach, the participants in the study and what they will be asked to do, and the importance or relevance of the project.* [This description must be in everyday language, free from jargon, technical terms or discipline-specific phrases. (No more than 300 words).]

In a study of the intestinal microbial flora of patients with chronic fatigue syndrome (CFS), it was found that there was a high count of D-lactic acid producing bacteria in the faecal samples of 108 CFS patients as compared to 177 control individuals. D-lactic acid has been reported to be toxic to human if accumulated, and that humans cannot readily metabolize D-lactic acid. The aim of the study is to determine the concentrations of D-lactic acids in body fluids (urine, blood, faecal samples), the levels of D-lactic acid producing bacteria in faecal samples of CFS patients, and compare with those from control subjects. CFS patients and non-CFS subjects will be examined and recruited by Dr. Ian Buttfield (Clinical Consultant). Samples from patients and control subjects will be analysed for the presence of D-lactic acid and other host and microbial metabolic compounds. Analytical analyses (urine, blood and microbial metabolic samples) will be performed by Mr. Christopher Armstrong (research student) and supervised by A/Prof Paul Gooley and Dr. David Stapleton. All faecal analyses from patients and control subjects will be performed by the microbiology staff (Bioscreen) supervised by Drs.Neil McGregor and Henry Butt. All researchers, except Dr Buttfield, are academic staff or affiliated members of the University of Melbourne in the capacity of providing supervision for Mr. Armstrong postgraduate studies.
The importance of the project is such that it may start research which may change the approach and management of patients with CFS. It is envisaged that the outcome of the project will improve the lifestyle of these patients; but importantly to recognize that this chronic and debilitating disease has an organic basis.

1.2 AIMS OF AND JUSTIFICATION FOR THE RESEARCH: *State the aims and significance of the project. Where relevant, state the specific hypothesis to be tested. Also provide a brief description of current research/literature review, a justification as to why this research should proceed and an explanation of any expected benefits to the community.* [No more than 500 words]

Significance of project and benefits to the community: It has been estimated that 27% of patients seeking medical assistance in a primary care clinic complained of chronic fatigue yearly (Goldenberg, 1995). The current understanding for the causation of CFS is psychiatric particularly when the initial clinical and laboratory evaluation is inconclusive. Understanding the organic basis of the disorder will change management protocol and outcome, significantly improve the lifestyle of the patient, reduce the financial burden to the government, and change the stigma attached to the disease.
Literature Review: CFS is a clinically defined illness that is characterized by unexplained, persistent, and debilitating fatigue that presents in multi-organ symptoms[1,2]. Debilitating neuropsychologic, musculoskeletal, immunologic and gastrointestinal symptoms are frequently associated with the disorder. CFS affects between

0.002% and 2.6% of the general population [3,4], including individuals of both sexes, all ages, and from many regions of the world[5]. Despite substantial research efforts, details of the etiologic and pathophysiologic processes that contribute to CFS have not been forthcoming. In a study of 27 polysymptomatic CFS patients, the intestinal microbial flora of these patients was found to be significantly different from those of non-CFS control subjects (n=4)[6]. This observation was supported by a recent study confirming the disturbances of the intestinal ecology in CFS patients, and that these changes may play a role in the pathogenesis of chronic fatigue syndrome[7]. Changes in the gastrointestinal microbial ecology were significantly associated with mental fatigue, neurological and cognitive functions in CFS patient[8,9]. In a larger study of 108 CFS patients it was found that CFS patients had significantly higher faecal colonization of facultative anaerobic Gram positive D-lactic acid producing organisms than those of non-CFS control subjects (p<0.001)[10] suggesting that D-lactic acid may play a role in the pathogenesis of the disorder. D-lactic acid is neurotoxic to humans[11]and patients with D-lactic acidosis have significant cognitive dysfunction and neurological impairment[12], symptoms very similar to those expressed by patients with CFS.

Hypothesis: Increased concentration of D-lactic acid in blood plasma and urine of patients with CFS is related to increased intestinal colonization of D-lactic acid bacteria

Aim: To determine the concentration of D-lactic acid in CFS patients with increased colonization of D-lactic acid producing bacteria

References:

1. Holmes GP, Kaplan JE, Gantz NM, Komaroff AL, Schonberger LB, Straus SE, Jones JF, Dubois RE, Cunningham-Rundles C, Pahwa S, Tosato G, Zegans LS, Purtilo DT, Brown N, Schooley RT, Brus I. Chronic fatigue syndrome: a working case definition. Ann Intern Med 108:387–389, 1988.
2. Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A. The chronic fatigue syndrome: a comprehensive approach to its definition and study. Ann Intern Med 121:953–959, 1994.
3. Lloyd AR, Hickie I, Boughton CR, Spencer O, Wakefield D. Prevalence of chronic fatigue syndrome in an Australian population. Med J Aust 153:522–528, 1990.
4. Jason LA, Taylor R, Wagner L, Holden J, Ferrari JR, Plioplys AV, Plioplys S, Lipkin D, Papernik M. Estimating rates of chronic fatigue syndrome from a community-based sample: a pilot study. Am J Community Psychol 23:557–568, 1995.
5. Levine PH. Epidemiologic advances in chronic fatigue syndrome. J Psychiatr Res 31:7–18, 1997.
6. Butt HL, Emms TM, Buttfield I, Dunstan RH, McGregor NR, Roberts TR, Spears M. Exploring management protocols for chronic fatigue syndrome: the efficacy of L-serine supplementation. Proceedings of the Nutrition Society of Australia, 1998;22:190
7. Evengård B., Nord C.E., Sullivan Å Patients with chronic fatigue syndrome have higher numbers of anaerobic bacteria in the intestine compared to healthy subjects 17th European Congress of Clinical Microbiology and Infectious Diseases ICC, Munich, Germany, 31 Mar - 04 Apr 2007
8. Butt HL, Dunstan RH, McGregor NR, Roberts TK. 'Bacterial Colonosis' in patients with persistent fatigue. Proceedings of International Clinical and Scientific Meeting, Sydney Australia. p15, 2001
9. Aziz Q, Thompson DG. Brain-gut axis in health and disease. *Gastroenterology.* 1998;114(3):559-78.
10. Sheedy JR, Scanlon D, Wettenhall REH, McGregor N, Lewis DP, Gooley PR, Butt HL, Stapleton D. Increased D-lactic acid intestinal bacteria found in patients with Chronic Fatigue Syndrome. Nature Medicine *(to be submitted for publication)*
11. Stolberg L, Rolfe R, Gitlin N et al. D-Lactic Acidosis due to Abnormal Gut Flora. New England Journal of Medicine **306,** 1344-1348. 1982.
12. Uribarri J, Oh MS, Carroll HJ. D-lactic acidosis. A review of clinical presentation, biochemical features, and pathophysiologic mechanisms. *Medicine (Baltimore).* 1998;77(2):73-82.

1.3 METHOD *Provide an outline of the proposed method, including details of the recruitment strategy and data collection techniques, the tasks participants will be asked to do, the estimated time commitment involved, and how data will be analysed*. [No more than 500 words]

Patient Recruitment:

The Clinical Consultant (Dr. Ian Buttfield) will examine and recruit CFS referred patients from medical practitioners and from existing patients from the South Australian Society of CFS. Currently Dr. Buttfield has a 4-month appointment waiting-list for CFS patients. It is anticipated that Dr. Buttfield will commit 1hr/week over the course of 6months to recruit 20 CFS patients and 20 non-CFS individuals for the study.

Patients will be given a relevant information sheet explaining the purpose of the study. A consent form will be signed by the patient if successfully recruited into the study. Instructions to collect the samples (ie faeces and urine) will also be included. Dr. Buttfield will be responsible for the collection of blood samples and the transfer of all clinical samples to The University of Melbourne. All analyses will be preformed at no cost to the patients

A morning mid-stream urine specimen (ie first urine on rising) and faecal samples will be collected on the agreed day. Each patient is requested to complete an 86 question self-reported symptom checklist, used in a previous study[1], to access symptom severity. Samples, once collected, will be stored at 4^0 - 12^0C and transported by overnight express to the Bio21, University of Melbourne for processing. Sample collection and storage during transit will be according to practices accredited by the National Association of Testing Authorities (NATA). Sample packaging for transport will be packed in compliance with IATA packing instruction 650, 'DIAGNOSTIC SPECIMEN (UN3373). Product of Human Origin for Diagnostic In-vitro testing. Known to be non-infectious'

Patient Inclusion Criteria

- *CFS diagnosis according to the Canadian criteria.*

- *patients not on antidepressants, anti-pyrexials, anti-inflammatories or antibiotics for the 4 weeks prior to recruitment.*

Exclusion Criteria

- *Starting any new treatment for CFS symptom control including: pre- or probiotics or herbal supplements; new dietary regimes; anti-depressant, anti-inflammatory, anti-pyrexial, antibiotics therapies.*
- *Other unrelated medical conditions*
- *Non-compliance*
- *Urine/faecal parameters do not conform to set collection criteria (eg. haematuria, bacteriuria, gastroenteritis)*

Laboratory Studies

- *Quantitative culture of aerobic and anaerobic faecal organisms will be performed by the microbiology staff (Bioscreen) and supervised by Dr. Butt (approx. 2hr/wk)and Dr. McGregor (approx 1hr/wk)*
- *Determination of lactic acid isomers and other microbial metabolites in patients' blood, urine and faecal fluids will be analysed by NMR and HPLC-MS. This section of work will be performed by Mr. Armstrong (10hr/wk) and supervised by A/Prof. Gooley (2hr/wk) and Dr. Stapleton (2hr/wk)*

Data Analyses

Data will be analysed by Mr Armstrong under the supervision of Dr. McGregor (approx 1 hr/wk). Continuous variables will be compared by Analysis of Variance, t-test and Mann-Whitney U test. Prevalence variables will be compared using Chi square and odds ratio analysis.

References

1. McGregor NR. Dunstan RH. Zerbes M. Butt HL. Roberts TK. Klineberg IJ. Preliminary determination of the association between symptom expression and urinary metabolites in subjects with chronic fatigue syndrome. Biochemical & Molecular Medicine. 1996; 58(1):85-92.

1.4 USE OF INDEPENDENT CONTRACTORS *Will parts of this project be carried out by independent contractors? (e.g. interviewing, questionnaire design and analysis, sample testing, etc)*

☐ ***NO***

If YES, confirm that the independent contractor will be engaged on the basis of relevant qualifications and experience and will receive from the Responsible Researcher, a copy of the approved ethics protocol and be made aware of their responsibilities arising from it. [The responsibility for effective oversight and proper conduct of the project remains with the Responsible Researcher]

1.5 MONITORING

(a) *How will researchers monitor the conduct of the project to ensure that it complies with the protocols set out in this application, the University's human ethics guidelines and the National Statement on Ethical Conduct in Research Involving Humans?* [Address, in particular, cases where several people are involved in recruiting, interviewing or administering procedures, or when the research is being carried out at some distance from the Principal Researcher (i.e. interstate or overseas)]

Dr. Buttfield will be recruiting chronic fatigue patients in Adelaide. Dr. Buttfield is a specialist physician with over 30 years clinical experience in the diagnosis and management of patients with chronic diseases including chronic fatigue syndrome.

(b) *For student research projects how will the student be supervised to ensure they comply with the protocols? If the student is working overseas, provide additional details of any local supervision arrangements.*

While operating procedures are available Mr Armstrong will be personally supervised by Gooley and Stapleton in the use and operation of the equipment to be used. Assoc/Prof Gooley and Dr Stapleton are expert in NMR and HPLC-MS, respectively. Gooley and Stapleton share weekly laboratory meetings and Mr Armstrong will present his work on a monthly basis, but this meeting will provide a forum for more frequent discussion of issues and procedures.

2. PARTICIPANT DETAILS

2.1 DOES THE RESEARCH *SPECIFICALLY TARGET*: [Tick as many as applicable]

		YES	NO
a.	students or staff of this University	☐	✓
b.	adults (over the age of 18 years and competent to give consent)	✓	
c.	children/legal minors (anyone under the age of 18 years)	☐	✓
d.	the elderly	☐	✓
e.	people from non-English speaking backgrounds	☐	✓

f.	pensioners or welfare recipients	☐	✓
g.	anyone intellectually or mentally impaired who cannot provide consent	☐	✓
h.	anyone who has a physical disability	☐	✓
i.	patients or clients of professionals	☐	✓
j.	anyone who is a prisoner or parolee	☐	✓
k.	a ward of the state	☐	✓
l.	any other person whose capacity to give informed consent may be compromised	☐	✓
m.	Aboriginal and/or Torres Strait Islander people and/or communities	☐	✓
n.	other collectives where a leader or council of elders may need to give consent	☐	✓

2.2 NUMBER, AGE RANGE AND SOURCE OF PARTICIPANTS
Provide number, age range and source of participants.

The CFS and control subjects should be age and sex matched and should be between the ages of 18 and 50 years of age. These subjects are to be recruited by Dr Buttfield.

2.3 JUSTIFICATION OF PARTICIPANT NUMBERS [The quality and validity of research is an essential condition of its ethical acceptability (refer National Statement page 5)] *Where applicable, provide a justification of sample size (including details of statistical power of the sample, where appropriate), explaining how this sample size will allow the aims of the study to be achieved.*

There are to be two groups in the study: a defined CFS group and a control group. A pilot study showed that the lactic acid producing bacteria had a higher prevalence in CFS patients (107/110; 96.4%) compared with control subjects (96/158; 60.8%) p<0.001 (Odds Ratio 17.2). Using the prevalence data, assuming a 95% and 60% carriage, in the CFS and controls, respectively the sample size required with a power of 0.7 at a P<0.01 would be 29 subjects per group and at P<0.001 would be 42. However using the bacterial colony counts and t-test sample size assessment, assuming a lactic acid producing bacterial count of 2672E6 and 846E6 for CFS and control respectively the sample size required with a power of 0.7 at a P<0.001 would be 5 subjects per group and at a power of 0.9 would be 6 subjects. Thus, a minimum sample size of 10 subjects per arm will provide sufficient power and statistical significance to conduct the study.

2.4 PARTICIPANT RECRUITMENT
(a) *Please indicate the method of recruitment by ticking the appropriate boxes. Tick all that apply.*

Mail out - *see below*	☐	**Email -** *see below*	☐	**Telephone**	☐
Advertisement - *see below*	☐	**Recruitment carried out by third party** (eg. employer, doctor) – *see below*	☐	**Recruitment carried out by researcher/s**	✓
Contact details obtained from public documents (eg. phone book)	☐	**Contact details obtained from private sources** (eg. employee list, membership database) – *see below*	☐	**Personal contacts**	☐
Participants from a previous study	☐	**Snowball** (participants suggest other potential participants)	☐	**Other** *(Please explain in no more than 50 words)*:	☐

- *If using a **mail out** or **email** who will be distributing it?*
  N/A
- *If using an **advertisement**:*
  - *explain where will it be placed?*[e.g. on waiting room wall, in newspaper, in newsletter]
    N/A
  - *have you attached a copy?*

    Yes ☐ No ☐ NA ☐ *If "No" please explain (no more than 50 words):*
- *If recruitment is to be conducted by a **third party**, (eg employer, doctor) have you attached an approval letter?*
  N/A

  - requesting their assistance?[yes, no or not applicable]
  Yes ☐ No ☐ NA ☐ *If "No" please explain (no more than 50 words):*

  - confirming their willingness to assist?
  Yes ☐ No ☐ NA ☐ *If "No" please explain (no more than 50 words):*

  - that has been drafted for the third party to send to potential participants?
  Yes ☐ No ☐ NA ☐ *If "No" please explain (no more than 50 words):*
- *If contact details are to be obtained from **private sources**, have you attached an approval letter?*

Yes ☐ No ☐ *If "No" please explain (no more than 50 words):*

(b) *Describe how, by whom, where potential participants are to be identified or selected for this research.*

Patients will be reviewed by appointment. New patients will be invited to participate by referral only either from the CFS Support Group (Adelaide) or from other medical practitioners. There is no selection (except those listed in item1.3) and hence no bias other than the fact that Dr Buttfield is a specialist physician who treats patients with chronic fatigue syndrome, pain and drug dependence. All patients will be examined at Dr. Buttfield's surgery (Unley, South Australia). The full clinical examination will be performed as per a specialist physician and the well-being of the patients will be evaluated according to normal clinical principles.

(c) *Describe how, by whom, where potential participants are to be approached or invited to take part in this research.*

Participants are invited to take part in the study by the attending physician Dr. Buttfield if the patient satisfies all the inclusion and exclusion criteria stated in item 1.3

2.5 DEPENDENT RELATIONSHIPS

[The issue of research involving persons in dependent or unequal relationships (e.g. teacher/student, doctor/patient, student/lecturer, client/counsellor, warder/prisoner, and employer/employee) is discussed in Section 7 of the National Statement. Such a relationship may compromise a participant's ability to give consent which is free from any form of pressure (real or implied)]. *Are any of the participants in a dependent relationship with any of the researchers, particularly those involved in recruiting for or conducting the project?*

☐ NO *(If YES, explain the dependent relationship and the steps to be taken by the researchers to ensure that participation is purely voluntary and not influenced by the relationship in any way.*

2.6 PAYMENT OR INCENTIVES OFFERED TO PARTICIPANTS

Do you propose to pay, reimburse or reward participants?

☐ NO *(If YES, how, how much and for what purpose? Please justify the approach)*

2.7 DECEPTION OR CONCEALMENT

[Deception and concealment is discussed in Section 17 of the National Statement. Essentially the practice is not considered ethical unless there are compelling reasons given for its use] *Will the true purpose of the research, or the collection of data itself, be concealed from participants or will participants in any way be deceived?*

NO

If you answered YES, provide a clear justification. [You will also need to provide participants with details of the deception in a debriefing (refer 3.4) and give them the opportunity to withdraw their data if they wish to do so.]

3. RISK AND RISK MANAGEMENT

3.1 STUDY PROFILE –DOES THE RESEARCH INVOLVE THE FOLLOWING:

[Tick as many as apply. Provide details in methodology –section 1.5 and attach information where indicated]

	YES	NO
• use of questionnaires designed by the researcher ***(attach a copy)***	✓	☐
• use of standard survey instruments ***(attach a copy)***	☐	✓
• use of on-line surveys ***(attach printout of screen information)***	☐	✓
• use of interviews ***(attach the list of interview questions)***	☐	✓
• use of focus groups ***(attach the list of focus group topics/questions)***	☐	✓
• observation of participants without their knowledge	☐	✓
• covert observation	☐	✓
• audio-taping interviewees or events	☐	✓
• video-taping interviewees or events	☐	✓
• access to personal and/or confidential data (including student, patient or client data) without the participant's specific consent	☐	✓

• administration of any stimuli, tasks, investigations or procedures which may be experienced by participants as physically or mentally painful, stressful or unpleasant during or after the research process	☐	✓
• performance of any acts which might diminish the self-esteem of participants or cause them to experience embarrassment, regret or depression	☐	✓
• research about participants involved in illegal activities	☐	✓
• research conducted in an overseas setting	☐	✓
• administration of any substance or agent	☐	✓
• use of non-treatment or placebo control conditions	☐	✓
• collection of body tissues or fluid samples	✓	☐
• collection and/or testing of DNA samples	☐	✓

3.2 POTENTIAL RISKS TO PARTICIPANTS

Identify, as far as possible, all potential risks to participants (e.g. physical, psychological, social, legal or economic etc.), associated with the project and the setting (e.g. overseas) in which the project is conducted. It may be useful to consider the study profile above and your response to participant details in section 2

Potential risks to participants may include haematoma and patient fainting resulting from veni-punctures. Dr. Buttfield will be the phlebotomist and well qualified to handle these situations.

3.3 MANAGING POTENTIAL RISKS

Describe what measures you have in place to minimize these potential risks to participants and to ensure that support is available if needed. [Depending on risks, participants may need additional support (e.g. external counseling) during or after the study]

Dr. Buttfield is the attending physician and the phlebotomist and will attend to the needs of the patients if arise.

3.4 DEBRIEFING (if applicable)

What debriefing will participants receive following the study and when? (Attach a copy of any written material or statement to be used in such a debriefing, if applicable). [Participants may need to talk about the experience of being involved in the study with the researchers, as well as learn more about the aims of the research]

Results and data collected from the study will be collated for peers reviewed publication and will be made available after the study.

3.5 BENEFITS COMPARED TO POTENTIAL RISKS

Outline the benefits of the study to the community (and participants, if applicable), relative to the potential risks to participants

N/A

3.6 MANAGING ADVERSE / UNEXPECTED OUTCOMES

Describe what measures you have in place in the event that participants experience adverse effects arising from their involvement in the project (e.g. adverse drug reaction, revelation of illegal activity, or unexpected distress due to questioning)

N/A

3.7 POTENTIAL RISKS TO RESEARCHERS

Will there be any significant risks to researchers associated with the project and the setting (e.g. overseas) in which the project is conducted. (e.g. personal safety, health, emotional well being)? [Refer to the University's Environmental Health & Safety Manual for more information]

NO *(If YES, how will such risks be addressed)*

4. INFORMATION FOR PARTICIPANTS AND INFORMED CONSENT

Before research is undertaken, the informed and voluntary consent of participants (and other properly interested parties) is generally required (refer sections 1.7 - 1.12 of the National Statement for more details). Information needs to be provided to participants at their level of comprehension about the purpose, methods, demands, risks, inconveniences, discomforts and possible outcomes of the research. Such information is often provided in a written **Plain Language Statement**. Each participant's consent needs to be clearly established (e.g. by using a signed **Consent Form**, returning an anonymous survey or recording an agreement for interview).

4.1 PROVIDING INFORMATION FOR PARTICIPANTS

(a) *Will you be providing participants with information in a written Plain Language Statement?*

✓ YES ☐ *(If NO, provide details of the protocol you will use to explain the research project to participants and invite their participation?)*

(b) *Will arrangements be made to ensure that participants who have difficulty understanding English can comprehend the information provided about the research project?*

☐ NO *(If YES, what arrangements have been made? If NO, give reasons.*

The patient population involved in the study will consist predominately subjects with English as the first or second language.

4.2 PLAIN LANGUAGE STATEMENT (IF APPLICABLE)

CONFIRM THAT THE PLAIN LANGUAGE STATEMENT WILL:

		YES	NOT APPLICABLE
1.	be printed on University of Melbourne letterhead	✓	
2.	include clear identification of the University, the Department(s) involved, the project title, the Principal and Other Researchers (including contact details), and the study level if it is a student research project.	✓	
3.	provide details of the purpose of the research project	✓	
4.	provide details of what involvement in the project will require (e.g., involvement in interviews, completion of questionnaire, audio/video-taping of events), and estimated time commitment	✓	
5.	provide details of any risks involved and the procedures in place to minimise these.	✓	
6.	advise that the project has received clearance by the HREC	✓	
7.	(if the sample size is small), confirm that this may have implications for protecting the identity of the participants		N/A
8.	include a clear statement that if participants are in a dependent relationship with any of the researchers that involvement in the project will not affect ongoing assessment/grades/management or treatment of health (if relevant)	✓	
9.	state that involvement in the project is voluntary and that participants are free to withdraw consent at any time, and to withdraw any unprocessed data previously supplied	✓	
10.	provide advice as to arrangements to be made to protect confidentiality of data, including that confidentiality of information provided is subject to legal limitations (see ** below)	☐	✓
11.	provide advice as to whether or not data is to be destroyed after a minimum period (if relevant)	☐	✓
12.	provide in the footer, the project HREC number, date and version of the PLS	☐	
13.	provide advice that if participants have any concerns about the conduct of this research project that they can contact the Executive Officer, Human Research Ethics, The University of Melbourne, ph: 8344 2073; fax 9347 6739	✓	

[**Re 10 – it is possible for data to be subject to subpoena, freedom of information request or mandated reporting by some professions. Depending on the research proposal you may need to specifically state these limitations]

PLEASE ATTACH A COPY OF THE PLAIN LANGUAGE STATEMENT TO YOUR APPLICATION

4.3 OBTAINING CONSENT

(a) *How will each participant's consent be established*?

By signing and returning a Consent Form – *see 4.4 below*	✓	**By returning an anonymous survey**	☐
Via a verbal agreement	☐	**Via a person with lawful authority to consent** (eg. parent, doctor) – *see 4.3(b) below*	☐
Via a recorded agreement for interview	☐	**Other** *(Please describe in no more than 50 words)*:	☐

(b) *If participants are unable to give informed consent, explain who will consent on their behalf and how such consent will be obtained.*

N/A

4.4 CONSENT FORM (IF APPLICABLE)

CONFIRM THAT THE CONSENT FORM WILL:

		YES	NOT APPLICABLE
1.	be printed on University of Melbourne letterhead	✓	
2.	include the title of the project and names of researchers	✓	
3.	state that the project is for research purposes	✓	
4.	state that involvement in the project is voluntary and that participants are free to withdraw at any time, and free to withdraw any unprocessed identifiable data previously supplied	✓	
5.	outline particular requirements of participants including, for example, whether interviews are to be audio and/or video-taped		✓
6.	include arrangements to protect the confidentiality of data	✓	
7.	include advice that there are legal limitations to data confidentiality (see below)**		✓
8.	(if the sample size is small) confirm that this may have implications for protecting the identity of the participants		✓
9.	(once signed and returned) be retained by the researcher	✓	

[**Re 7 – it is possible for data to be subject to subpoena, freedom of information request or mandated reporting by some professions. Depending on the research proposal you may need to specifically state and explain these limitations]

PLEASE ATTACH A COPY OF THE CONSENT FORM TO YOUR APPLICATION

5. PRIVACY AND CONFIDENTIALITY

[Section 18 of the National Statement describes 'Privacy' as "…a complex concept that stems from a core idea that individuals have a sphere of life from which they should be able to exclude any intrusion." A major application of the concept of privacy is information privacy: the interest of a person in controlling access to and use of any information personal to that person. 'Confidentiality', a narrower more specific term than 'privacy' refers to the legal and ethical obligation that arises from a relationship in which a person receives information from or about another.

At the Commonwealth level, the collection, storage, use and disclosure of personal information by Commonwealth agencies is regulated by the *Privacy Act 1988*. Sections 95 and 95A of the Act are of particular relevance to researchers. There is regulation at State and Territory level in the form of legislation related to privacy generally or the administration of agencies, or administrative codes of practice. In Victoria, the *Health Records Act 2001* regulates health information handled by the Victorian public sector and private sector, while the Information Privacy Act 2000 regulates the collection and handling of non-health-related personal information. Section 18.1 of the National Statement states that an HREC must be satisfied that a research proposal conforms to all relevant Commonwealth, State or Territory privacy legislation or codes of practice]

5.1 ACCESSING PERSONAL INFORMATION

[Personal Information' includes names, addresses, or information/opinion about an individual whose identity is apparent, or can reasonably be ascertained, from the information/opinion. It also includes Health Information (e.g. health opinions, organ donation or genetic information) and Sensitive Information (e.g. political views, sexual preferences, criminal records)]

Is there a requirement for the researchers to obtain ***Personal Information*** *(either identifiable or potentially identifiable) about individuals* ***without their consent****?*

		YES	NO
a)	from Commonwealth departments or agencies?		✓
b)	from State departments or agencies?		✓
c)	from Other Third Parties, such as non-government organisations?		✓

If you answered YES to (a), (b) or (c), you will need to complete Module P and attach it to this application

5.2 REPORTING PROJECT OUTCOMES

(a) *Will the project outcomes be made public at the end of the project?*

✓ YES *(If YES, give details of how the results will be made public (eg in journal articles book, conference paper, the media, working paper or other). If NO, explain why not.*

Results will be published in peer reviewed journal

(b) *Will a report of the project outcomes be made available to participants at the end of the project?*

☐ YES ☐ NO *(If Yes, give details of the type of report and how it will be made available. If No, explain why not.*

Results of each individual analysis will be made available to the patient

5.3 WILL THE RESEARCH INVOLVE:

	YES	NO
• complete anonymity of participants (i.e., researchers will not know the identity of participants as participants are part of a random sample and are required to return responses with no form of personal identification)?		✓
• de-identified samples or data (i.e., an irreversible process whereby identifiers are removed from data and replaced by a code, with no record retained of how the code relates to the identifiers. It is then impossible to identify the individual to whom the sample of information relates)?		✓
• potentially identifiable samples or data (i.e., a reversible process in which the identifiers are removed and replaced by a code. Those handling the data subsequently do so using the code. If necessary, it is possible to link the code to the original identifiers and identify the individual to whom the sample or information relates)?		✓
• participants having the option of being identified in any publication arising from the research?		✓
• participants being referred to by pseudonym in any publication arising from the research?		✓
• any other method of protecting the privacy of participants? *Please describe:*		

Note that where the sample size is very small, it may be impossible to guarantee anonymity/confidentiality of participant identity. Participants involved in such projects need to be clearly advised of this limitation in the Plain Language Statement.

6. DATA STORAGE, SECURITY AND DISPOSAL

6.1 DATA STORAGE

Does data storage comply with the University policy? [University of Melbourne Policy on the Management of Research Data and Records is available at: **http://www.unimelb.edu.au/records/research.html** The Joint NHMRC/AVCC Statement and Guidelines on Research Practice is available at: **http://www.nhmrc.gov.au/funding/policy/researchprac.htm**]

✓ YES *(If NO, please explain.)*

6.2 DATA SECURITY

(a) *Will the Principal Researcher be responsible for security of data collected?*

✓ YES *(If NO, please provide further details. You may also use this space to explain any differences between arrangements in the field, and on return to campus.)*

(b) *Will data be kept in locked facilities in the Department through which the project is being conducted?*

✓ YES *(If NO, please explain how and where data will be held, including any arrangements for data security during fieldwork.)*

(c) *Which of the following methods will be used to ensure confidentiality of data? (select all options that are relevant)*

- data and codes and all identifying information to be kept in separate locked filing cabinets ☐
- access to computer files to be available by password only ✓
- access by named researcher(s) only ☐
- other *(please describe)* ☐

(d) *Will others besides the researchers associated with this project have access to the raw data?*

✓ NO *(If YES, please explain who and for what purpose? What is their connection to the project?)*

6.3 DATA RETENTION AND DISPOSAL

[Research data and records should be maintained for as long as they are of *continuing value* to the researcher and as long as recordkeeping requirements such as patent requirements, legislative and other regulatory requirements exist. The minimum retention period for research data and records is five years after publication, or public release, of the work of the research as stated in the University of Melbourne *Code of Conduct for Research*. If the project involves clinical trial(s), the data should be kept for a minimum of 15 years (refer to Section 12.1 of the National Statement for further details)]

Specify how long materials (e.g. files, audiotapes, questionnaires, videotapes, photographs) collected during the study will be retained after the study and how they will ultimately be disposed of.

Research files will be disposed of by shredding after 15 years storage.

7. POTENTIAL CONFLICT OF INTEREST

7.1 POTENTIAL CONFLICT OF INTEREST

Is there any affiliation or financial interest for researchers in this research or its outcomes or any circumstances which might represent a perceived, potential or actual conflict of interest?

✓ NO *(If YES, give brief details?)*

[If you have declared a potential conflict of interest, you should include an appropriate comment on the Plain Language Statement and Consent Form]

7.2 COMPLIANCE WITH THE CODE OF CONDUCT FOR RESEARCH

[University researchers must disclose and manage Conflict of Interest in accord with the provisions of the University's *Code of Conduct for Research*. See http://www.unimelb.edu.au/ExecServ/Statutes/r171r8.html]

Is the Conflict of Interest noted above in section 7.1 being managed in accordance with the Code of Conduct?

✓ Not Applicable

8. DECLARATION BY RESEARCHERS

The information contained herein is, to the best of our knowledge and belief, accurate.

We have read the University's current human ethics guidelines, and accept responsibility for the conduct of the procedures set out in the attached application in accordance with the guidelines, the University's Code of Conduct for Research and any other condition laid down by the University of Melbourne's Human Research Ethics Committee or its Sub-Committees. We have attempted to identify all risks related to the research that may arise in conducting this research and acknowledge our obligations and the rights of the participants. We have the appropriate qualifications, experience and facilities to conduct the research set out in the attached application and to deal with any emergencies and contingencies related to the research that may arise.

If approval is granted, the project will be undertaken in strict accordance with the approved protocol and relevant laws, regulations and guidelines.

We, the researcher(s) agree:

- *To only start this research project after obtaining final approval from the Human Research Ethics Committee (HREC);*
- *To only carry out this research project where adequate funding is available to enable the project to be carried out according to good research practice and in an ethical manner;*
- *To provide additional information as requested by the HREC;*
- *To provide progress reports to the HREC as requested, including annual and final reports;*
- *To maintain the confidentiality of all data collected from or about project participants, and maintain security procedures for the protection of privacy;*
- *To notify the HREC in writing immediately if any change to the project is proposed and await approval before proceeding with the proposed change;*
- *To notify the HREC in writing immediately if any adverse event occurs after the approval of the HREC has been obtained;*
- *To agree to an audit if requested by the HREC;*
- *To only use data and any tissue samples collected for the study for which approval has been given;*

We have read the NH&MRC National Statement on Ethical Conduct in Research Involving Humans and agree to comply with its provisions.

All researchers associated with this project must sign

Researchers' Name (please PRINT)	Signature	Date
A/Prof Paul Gooley		
Dr. Henry Butt		
Dr. Ian Buttfield		
Mr. Christopher Armstrong		
Dr. Neil McGregor		
Dr. David Stapleton		

9. DECLARATION BY DEPARTMENTAL HUMAN ETHICS ADVISORY GROUP (HEAG)

DATE APPLICATION RECEIVED: / / *HEAG NO:*

☐ *TECHNICAL REVIEW COMPLETED* ☐ *ETHICAL REVIEW COMPLETED*

The HEAG has reviewed this project and considers the methodological/technical and ethical aspects of the proposal to be appropriate to the tasks proposed and recommends approval of the project. The HEAG considers that the researcher(s) has/have the necessary qualifications, experience and facilities to conduct the research set out in the attached application, and to deal with any emergencies and contingencies that may arise. [Note: If the HEAG Chair is also a principal researcher for this project, the declaration should be signed by another authorised member of the HEAG]

Comments/Provisos:

Name of HEAG Chair (in BLOCK LETTERS)	
Signature	
Date	

10. DECLARATION BY HEAD OF DEPARTMENT

DATE APPLICATION RECEIVED: / / *HEAG NO:*

☐ *TECHNICAL REVIEW COMPLETED* ☐ *ETHICAL REVIEW COMPLETED*

I have reviewed this project and consider the methodological, technical and ethical aspects of the proposal to be appropriate to the tasks proposed and recommend approval of the project. I consider that the researcher(s) has/have the necessary qualifications, experience and facilities to conduct the research set out in the attached application, and to deal with any emergencies and contingencies that may arise. [Note: If the Head of Department is also a principal researcher for this project, the declaration should be signed by another authorised member of the Department]

This project has the approval and support of this Department/School/Centre.

Name of Head (in BLOCK LETTERS)	
Signature	
Date	

11. WHEN COMPLETE

When this form has been completed and finalised it should be attached to the coversheet section of the application completed in Themis Research and then submitted to the nominated Human Ethics Advisory Group for review.