STANDARD APPLICATION FORM –

FOR THE ETHICAL REVIEW OF HEALTH-RELATED RESEARCH STUDIES WHICH ARE NOT CLINICAL TRIALS OF MEDICINAL PRODUCTS FOR HUMAN USE AS DEFINED IN STATUTORY INSTRUMENT 190/2004

GUIDANCE MANUAL

PREPARED BY:

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SEPTEMBER 2014

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FOREWORD

Biomedical research, whether by means of a physical intervention on patients or healthy volunteers, use of stored biological material, or data obtained by questionnaires, seeks to diminish existing uncertainties and improve our understanding of health and disease. Ultimately, the results obtained in such research, contribute to appropriate and improved healthcare directed at meeting the needs of patients.

Research Ethics Committees (RECs) play a central role in the research process. The task of RECs has become increasingly demanding and complex over the last decade. As well as upholding the rights of research participants, RECs are tasked with assessing the risks and benefits of research, ensuring consent is valid, protecting confidentiality and privacy, and more recently with the monitoring and auditing of ongoing and completed research. Increasingly, biomedical research is being conducted at multiple research sites both nationally and internationally and because of the volume and varied nature of the research reviewed, members of local RECs have a demanding task maintaining a coherent approach.

It has been recognised that the efficiency of ethical review and the diversity of practice amongst committees has posed a challenge for the research community. The ethical review process had become regarded by some as an obstacle to research rather than a facilitator of it. In response, RECs have adopted a pro-active approach in dispelling this view. By September 2008, RECs recognised for the review of clinical trials of medicines were all utilising a single application form devised by the Irish Council for Bioethics, at the request of the Department of Health & Children. Also in 2008, a group of REC administrators launched an initiative to draft a common application form for research proposals which fall outside the remit of the regulations for clinical trials for medicinal products. A comprehensive series of consultations among the Research Ethics Committees and with the broader research community and State agencies was undertaken and a common form was piloted from January 2010 by four RECs. A formal evaluation of the pilot phase accompanies the final draft of the common application form and guidance manual.

This initiative originated from the RECs themselves and without the energy, enthusiasm and dedication of, in particular, REC administrators and members, this project would not have succeeded. The significant contribution of the Dublin Centre for Clinical Research, Molecular Medicine Ireland,

the Office of the Data Protection Commissioner, the State Claims Agency, the Irish Medicines Board and A&L Goodbody Solicitors should also be acknowledged.

Research ethics committee members dedicate significant time and effort, on a voluntary basis, to undertake their duties, often without adequate financial support, and in so doing, provide an invaluable public service. Undoubtedly, the introduction of a common application form, will significantly contribute to a more streamlined approach that should facilitate efficient ethical review and should improve the calibre of application completed by researchers and submitted to RECs. It will also be key in facilitating communication and interaction between researchers and ethics committees, allowing both to work together as partners in the process of ethical review.

Dr. Siobhan O'Sullivan
Scientific Director
Irish Council for Bioethics
July 2010

INTRODUCTION

This Guidance Manual accompanies the Standard Application Form developed for health-related research studies not covered by SI 190. Its purpose is to guide applicants when completing the form. It is a reference document that provides detailed context for the questions asked and directs applicants to other related sources of information. The Guidance Manual will be reviewed and updated on a regular basis. The need for a Guidance Manual was identified during the development of the Standard Application Form.

This edition of the Guidance Manual reflects

(i) the release by the Health Services Executive of a National Consent Policy in May 2013;

(ii) the publication by the World Medical Association of an amended version of the Declaration of Helsinki in October 2013;

(iii) feedback received from research ethics committees and applicants to research ethics committees on the previous version of the Standard Application Form, and Guidance Manual;

(iv) the re-naming and re-branding of the Irish Medicines Board in July 2014.

Applicants are requested to read this Guidance Manual in conjunction with Part Three of the Health Service Executive National Consent Policy (May 2013) or any subsequent editions of this policy.

Guidance Note E3.2 (b) – Access to Healthcare Records without Consent

Applicants are advised that, although the Office of the Data Protection Commissioner has expressed reservations about the wording of the Guidance Note E3.2 (b), the decision of research ethics committees using the form is to retain this wording at the present time.

Applicants framing a response to Question E3.2 (b) may wish to avail of the advice of the Office of the Data Protection Commissioner on a case by case basis.

Although *The Data Protection Guidelines on Research in the Health Sector 2007* are referenced in this Guidance Manual, it is acknowledged that these guidelines are out of date. An updated version is not available at the time of going to print.

September 2014

KEY DEFINITIONS

STANDARD APPLICATION FORM: Application Form for the Ethical Review of Health-Related Research Studies which are not clinical trials of medicinal products for human use as defined in Statutory Instrument 190/2004. Standard Application Form is available on the Molecular Medicine Ireland website and from research ethics committees.

DEPARTMENT OF HEALTH FORM: Application Form for ethical review of clinical trials of medicinal products for human use as defined in S.I. 190/2004. This application form is available on the Department of Health website and from research ethics committees.

Clinical trial of a Medicinal Product:
Any investigation in human subjects, other than a non-interventional trial, intended to:

(a) discover or verify the clinical, pharmacological or other pharmacodynamic effects of one or more investigational medicinal products, or
(b) identify any adverse reactions to one or more such investigational medicinal products, or
(c) study absorption, distribution, metabolism and excretion of one or more such investigational medicinal products, or
(d) discover, verify, identify or study any combination of the matters referred to at subparagraphs (a), (b), and (c),

with the object of ascertaining the safety or efficacy of such products, or both.

(European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations, 2004 (S.I. No. 190 of 2004)

Local Committee Checklist/ Local Committee Declaration and Signatory Page: Research ethics committees using the Standard Application Form may wish to draft a 'Local Committee Checklist' outlining local documentation requirements, and a 'Local Committee Declaration and Signatory Page' outlining local signatory requirements. (See Appendices Three and Four for templates)

Principal Investigator: The Principal Investigator is the Principal Researcher on the research team who is responsible for the conduct, and in many instances also the design, of the research study

IN DEPTH INSTRUCTIONS ON HOW TO COMPLETE EACH QUESTION IN THE STANDARD APPLICATION FORM

SECTION A GENERAL INFORMATION

A1 Title of the Research Study:
[TYPE ANSWER]

A2 (a) Is this a multi-site study? (Please answer 'yes' if this study is taking place at more than one site) Yes / No

Action: If you chose 'yes' please delete A2 (e) and (f)

Action: If you chose 'no' please delete A2 (b)(c) and (d)

A2 (b) If yes, **please name the principal investigator with overall responsibility for the conduct of this multi-site study.** (The Principal Investigator is the Principal Researcher on the research team who is responsible for the conduct, and in many instances also the design, of this research study. Please note the strong links between this question and Questions J3.1 and J3.2 in Section J. Please pause at this point to refer to and respond to Questions J3.1 and J3.2. Please provide a 2 page curriculum vitae of the Principal Investigator for review.

Research Ethics Committees which have decided formally to adopt this application form (see Appendix Five) may wish to review their local requirements in light of this definition, for example, an institutionally-based research ethics committee may require principal investigators who are not employees (e.g. academic staff and students) to be mentored, supported, sponsored, supervised etc. by an employee. In addition, an institutionally-based committee may require such a principal investigator where s/he seeks to conduct research on patients to provide evidence that those with clinical responsibility for patients are fully aware / supportive of this study taking place.

Applicants are requested to liaise with the institutional ethics committee – local requirements of this nature are typically outlined in the local committee checklist (see Appendix Three) or local committee declaration and signatory page (see Appendix Four))

Title: Dr. / Ms. / Mr. / Prof.
Name: [TYPE ANSWER]
Qualifications: [TYPE ANSWER]
Position: [TYPE ANSWER]
Dept: [TYPE ANSWER]
Organisation: [TYPE ANSWER]
Address: [TYPE ANSWER]
Tel: [TYPE ANSWER]
E-mail: [TYPE ANSWER]

A2 (c) For multi-site studies, **please name each site where this study is proposed to take place, state the lead co-investigator for each of these sites and state if you have got an outcome from the relevant research ethics committee(s).** (The Lead Co-Investigator takes responsibility for the study at a site. S/he should be an employee of the site in question who is appropriately qualified to oversee the conduct of the study at the site. Please ensure that you have provided copies of any approvals which you have referred to in your response.)

Site:	Lead Co-Investigator for each site:	Research Ethics Committee Outcome
[TYPE ANSWER]	[TYPE ANSWER]	[TYPE ANSWER]
[TYPE ANSWER]	[TYPE ANSWER]	[TYPE ANSWER]

Action: Please add rows to the above table should you wish to add a site.

A2 (d) For multi-site studies, **please provide details of the Lead Co-Investigators at each site.**

Title: Dr. / Ms. / Mr. / Prof. **Name:** [TYPE ANSWER]
Qualifications: [TYPE ANSWER]
Position: [TYPE ANSWER]
Dept: [TYPE ANSWER]
Organisation: [TYPE ANSWER]
Address: [TYPE ANSWER]
Tel: [TYPE ANSWER] **E-mail:** [TYPE ANSWER]

Action: Please copy and paste the headings in Question A2 (d) should you wish to add a Lead Co-Investigator.

A2 (e) If no, **please name the principal investigator with overall responsibility for the conduct of this single-site study.** (The Principal Investigator is the Principal Researcher on the research team who is responsible for the conduct, and in many instances also the design, of this research study. Please note the strong links between this question and Questions J3.1 and J3.2 in Section J. Please pause at this point to refer to and respond to Questions J3.1 and J3.2. Please provide a 2 page curriculum vitae of the Principal Investigator for review.

Research Ethics Committees which have decided formally to adopt this application form (see Appendix Five) may wish to review their local requirements in light of this definition, for example, an institutionally-based research ethics committee may require principal investigators who are not employees (e.g. academic staff and students) to be mentored, supported, sponsored, supervised etc. by an employee. In addition, an institutionally-based committee may require such a principal investigator where s/he seeks to conduct research on patients to provide evidence that those with clinical responsibility for patients are fully aware / supportive of this study taking place.

Applicants are requested to liaise with the institutional ethics committee – local requirements of this nature are typically outlined in the local committee checklist (see Appendix Three) or local committee declaration and signatory page (see Appendix Four))

Title: Dr. / Ms. / Mr. / Prof. **Name:** [TYPE ANSWER]
Qualifications: [TYPE ANSWER]
Position: [TYPE ANSWER]
Dept: [TYPE ANSWER]
Organisation: [TYPE ANSWER]
Address: [TYPE ANSWER]
Tel: [TYPE ANSWER] **E-mail:** [TYPE ANSWER]

A2 (f) For single site studies, **please name the only site where this study will take place.**
[TYPE ANSWER]

A3. Details of Co-investigators: (Please provide the details of the Main 'Co-Investigators' i.e. those investigators who play key roles in relation to the conduct of this study e.g. statistical analysis (Section B), selection, recruitment and consent (Section C), data collection and analysis (Section E) and laboratory analysis (Section F) etc.)

Name of site (if applicable): [TYPE ANSWER]
Title: Dr. / Ms. / Mr. / Prof. **Name:** [TYPE ANSWER]
Qualifications: [TYPE ANSWER]
Position: [TYPE ANSWER]
Dept: [TYPE ANSWER]
Organisation: [TYPE ANSWER]

Address: [TYPE ANSWER]
Tel: [TYPE ANSWER] **E-mail:** [TYPE ANSWER]
Role in Research e.g. statistical / data / laboratory analysis: Answer

Action: Please copy and paste the headings in Question A3 should you wish to add a Co-Investigator

A4. Lead contact person who is to receive correspondence in relation to this application or be contacted with queries about this application.
(For administrative and correspondence purposes, committees require a person who is familiar with this study to be available to address queries as they arise. This person can be the Principal Investigator, or any person who has been delegated this task by the Principal Investigator.)
Name: [TYPE ANSWER]
Position: [TYPE ANSWER]
Organisation: [TYPE ANSWER]
Address for Correspondence: Answer
Tel (work): [TYPE ANSWER] **Tel (mob.):** [TYPE ANSWER]
E-mail: [TYPE ANSWER]

A5 (a) Is this study being undertaken as part of an academic qualification? (Students are encouraged not to complete this application form without the assistance of an academic supervisor) Yes / No

Action: If you chose 'no' please delete A5 (b) and (c)

A5 (b) If yes, **please complete the following:**
Student Name(s): [TYPE ANSWER]
Academic Course: [TYPE ANSWER]
Academic Institution: [TYPE ANSWER]

A5 (c) Academic Supervisor(s):

Title: Dr. / Ms. / Mr. / Prof. **Name:** [TYPE ANSWER]
Qualifications: [TYPE ANSWER]
Position: [TYPE ANSWER]
Dept: [TYPE ANSWER]
Organisation: [TYPE ANSWER]
Address: [TYPE ANSWER]
Tel: [TYPE ANSWER] **E-mail:** [TYPE ANSWER]

SECTION B STUDY DESCRIPTORS

APPLICANTS MAY COPY AND PASTE FROM STUDY PROTOCOLS AS A STARTING POINT WHEN RESPONDING TO THE QUESTIONS IN SECTION B. PLEASE HOWEVER AVOID STATEMENTS SUCH AS 'SEE ATTACHED PROTOCOL FOR DETAILS'

B1. What is the anticipated start date of this study?
[TYPE ANSWER]

B2. What is the anticipated duration of this study?
(Please state the anticipated duration of this research study in months or years.)
[TYPE ANSWER]

B3. Please provide a brief lay (plain English) description of the study. Please ensure the language used in your answer is at a level suitable for use in a research participant information leaflet.

(The lay summary should be in simple language between 100 and 500 words in length only. There is a word limit in place.)

[TYPE ANSWER]

B4. Provide brief information on the study background

(Committees are interested in knowing where the idea for this study came from, if a literature review has been carried out and what the rationale for the study is. Your answer should be between 100 – 500 words in length to include a maximum of five references. There is a word limit in place. If a study protocol is available, please ensure that the study protocol has been provided for the review of the committee. Please note that study protocols are not distributed to all committee members. However, all committee members will receive a copy of this application form.)

[TYPE ANSWER]

B5. List the study aims and objectives.

(Any study proposed which cannot answer the research question posed is unethical)

[TYPE ANSWER]

B6. List the study endpoints / measurable outcomes (if applicable).

(For quantitative research, a study 'endpoint' is a measurable outcome designed to answer the research question.)

[TYPE ANSWER]

B7. Provide information on the study design.

(The study design chosen should be appropriate to achieving the aims and objectives stated in response to B5.)

"The different types/patterns and designs of research can sometimes be confusing. The purpose here is to provide definitions and explanations of the main terms.

Types/Patterns of Research

The terms used to describe the different types of social research are:

- Basic – to understand and describe social phenomena;
- Applied (policy/action research) – to provide useful knowledge to apply to a problem or inform change;
- Evaluative (assessment/appraisal) – to establish the efficiency, effectiveness and/or success of a program/intervention.

The terms used to describe the different types of medical research are:

- Basic – investigation of human or animal samples (e.g. biochemical, genetic) carried out in a laboratory;
- Epidemiological – the study of disease occurrence (distribution and determinants);
- Clinical – the study of patients who have a particular condition.

Other terms you may encounter are:

- Exploratory – referring to the fact that the subject area is being explored and little is currently understood about it;
- Causal – referring to the fact that you are looking for 'cause and effect' in the subject area.

Research Design – the broad decisions

➢ Observational or Experimental

Observational research collects information on subjects with no intervention. It comprises descriptive studies (description only) and analytical studies (analyzing relationships between variables; cross-sectional, case-control, cohort and ecological studies).

Experimental research is where the researcher affects what happens to the subjects by varying some factor which the researcher can control and then investigates the effects of the intervention. It comprises clinical trials and field trials (individual level and aggregated - community trials) and is also known as intervention research/studies.

- Prospective or Retrospective

Prospective means that the events to be measured have not occurred when the study commences; hence data is collected about future events.

Retrospective means that the events to be measured have already occurred when the study commences; hence data is collected about past events (and may come from existing sources).

Experimental research is prospective, whereas observational research may be either prospective or retrospective.

- Cross-sectional or Longitudinal

Cross-sectional study is where data is collected at one point in time.

Longitudinal study is where data is collected at more than one point in time – usually to investigate changes over time.

Research Design – study types

- Descriptive study

A simple description, based on routinely available data or on data from a dedicated survey. This is often the first step in an epidemiological study. May examine patterns but does not analyze the relationship between exposure and outcome. Includes case-study/report and case-series where the characteristics of one or more patients, respectively, are described.

- Cross-sectional study

Also known as a prevalence study. Individuals are the unit of observation. Data on both exposure(s) and outcome(s) is collected at the same single point in time. Relatively easy and economical to conduct with a short timeframe as no subject follow-up involved. May be based on a random sample from a defined population or a presenting sample of patients with a particular condition. Suitable for studying prevalence, behaviour and attitudes and estimating health needs. It is not easy to assess the reasons for the associations observed or to ascertain whether the outcome or exposure occurred first - not an issue for exposures that do not change over time; questions about past and current exposures could be asked.

- Case-control study

May (less often) be called a case-reference study. Individuals are the unit of observation. It involves comparing people with a specific outcome of interest (e.g. a particular disease) with a group of people who do not have this outcome; hence subjects are recruited based on the presence of absence of this outcome. Exposure among cases is compared to exposure among non-cases. Suited to rare/long induction diseases. Not suitable to measure incidence or the effectiveness of an intervention. Used to identify causes of disease or rare effects of treatment. Relatively easy and economical to conduct (usually smaller sample size compared to a cohort study). Retrospective in the sense that data is collected on past exposure. Prone to selection bias (must ensure that the controls are from the same study population as the cases) and information/recall bias (due to cases recalling exposures more accurately than controls or more detailed interviewing of cases). Most efficient design is an equal number of cases and controls although two or more controls (no more than four) can be taken if the number of cases is limited. Matching ensures an equal distribution of confounders among cases and controls. You can match for variables known to be associated with the exposure and the outcome, or to the outcome only but not variables associated with the exposure only or factors intermediate in the casual pathway between exposure and outcome. Matching can be paired (individual) or frequency (distribution). Over-matching can cause difficulties and can not be adjusted at the analysis stage.

- Cohort study

Also known as a follow-up or incidence study. Individuals are the unit of observation. People (free of the outcome variable) are classified according to their exposure (either exposed/not exposed or various degrees of exposure) and followed over a period of time to determine outcome. Usually classification is done at the start of the study and is not an explicit part of the design although occasionally exposure status is identified in advance and a sample taken from each group separately. It is possible to examine multiple outcomes. It is the observational study that most closely resembles experimental studies, except that allocation of exposure is not controlled by the researcher. Expensive and time-consuming and may require long periods of follow-up (a historical cohort may be available to reduce both). Useful to investigate late or chronic effects. Can also be used to investigate different approaches to service delivery and management. Not suited to rare diseases (due to sample size problems) or to measure the effectiveness of an intervention. Follow-up time may be fixed (all subjects followed for the same, defined period) or variable (analyzed using person years of follow-up or clinical life tables).

- Ecological study

Also known as a correlational study. A population or a group of people is the unit of observation. Compares different countries at the same time or the same country at different times. Usually relies on data collected for other purposes therefore full exposure data may not be available. The individual link between exposure and outcome is not possible. An association observed at the group level does not necessarily represent that which exists at the individual level. Used for estimating the frequency of disease. May lead to more detailed epidemiological work.

- Clinical Trial

More often referred to as a randomised controlled trial (RCT). Also known as a therapeutic trial or a secondary prevention trial. It is an experiment to evaluate the effectiveness of an intervention or therapy; hence individual patients are usually the unit of observation. The researcher has direct control over many aspects of the investigation, and in particular over the allocation of individuals to different treatment groups. Subjects on a treatment/therapy (called the treatment or intervention group) are followed up and their outcome compared with subjects who have the same condition who are not so treated (the control group). The control group either receives no treatment or an established treatment. The outcome may be the recovery from existing disease or the development of new disease. Defined selection criteria are required for patient enrolment into the trial. Patients are randomly allocated to the groups. Confounding and bias can be eliminated through the design of the trial and the implementation of that design using randomisation, single-blinding and double-blinding. Single-blinding refers to the patient not knowing which group s/he is allocated to and is often achieved through the use of a 'placebo'. Double-blinding is where neither the patient nor the doctor/researcher who is managing the patient or evaluating response knows which group the patient is allocated to. All patients in the trial must be managed similarly in terms of the number of check-ups etc. A full list of criteria for withdrawing the patient from the trial (regardless of group) should be compiled before commencement. Some measure of patient compliance should be included. Should only be conducted if there is a doubt as to which treatment is better. Analysis ideally conducted on the basis of intention to treat. Many trials undertaken are too small to detect treatment effects and result in non-significant differences. The smaller the effect, the larger the trial required; the larger the trial, the greater the power to detect differences. Even if non-significant, the effect may be of clinical/medical importance.

- Field Trial

Also known as a primary prevention trial. It involves people who are disease-free but presumed to be at risk. It evaluates if the intervention reduces the risk of developing an outcome/disease among those free from it. Usually huge logistic and financial considerations. Can be used to evaluate interventions aimed at reducing exposure without measuring the occurrence of an outcome – and therefore carried out on a small scale at lower cost. In community trials (also known as community intervention studies), the treatment groups are communities rather than individuals. Particularly appropriate for outcomes that have their origins in social conditions that can be influenced by intervention directed at group behaviour as well as at individuals. Random allocation of communities is not possible and usually only a small number of communities can be included. It is also difficult to avoid contamination, that is, to isolate the intervention communities from general social changes.

The ethical issues associated with all research should be considered. However, they are paramount in the design of experimental research and will be dealt with in a future article."

- C. Collins (2008) Irish College of General Practitioners 'Guide to Conducting Research'

[TYPE ANSWER]

B8 Provide information on the study methodology.

(Please provide a comprehensive answer to this question. Please ensure that you provide copies of any instruments / questionnaires etc. referred to in your response.)

[TYPE ANSWER]

B9 Provide information on the statistical approach to be used in the analysis of your results (if appropriate) / source of any statistical advice.
(It is important to get the advice of a statistician in relation to all research studies. The statistician will advise if a statistical approach is relevant to this particular research study.)

[TYPE ANSWER]

B10 (a) Please justify the proposed sample size and provide details of its calculation (including minimum clinically important difference).
(It is important to obtain the advice of a statistician in relation to all research studies. Specific advice on determination of sample size is also available on page 23 of ICGP Guide to Conducting Research (2008) available from www.icgp.ie)

[TYPE ANSWER]

B10 (b) Where sample size calculation is impossible (e.g. it is a pilot study and previous studies cannot be used to provide the required estimates) then please explain why the sample size to be used has been chosen. (It is important to obtain the advice of a statistician in relation to all research studies.)

[TYPE ANSWER]

B11 How many research participants are to be recruited in total?
(State total number of participants.)

[TYPE ANSWER]

B12 (a) How many research participants are to be recruited in each study group (where applicable)? Please complete the following table (where applicable).

Name of Study Group:	**Name of Study Group:**	**Name of Study Group:**	**Name of Study Group:**	**Name of Study Group:**
[Type Answer=TA]	[TA]	[TA]	[TA]	[TA]
Number of Participants in this Study Group:	**Number of Participants in this Study Group:**	**Number of Participants in this Study Group:**	**Number of Participants in this Study Group:**	**Number of Participants in this Study Group:**
[TA]	[TA]	[TA]	[TA]	[TA]

Action: Please add rows to the above table should you wish to add a study group.

B12 (b) Please provide details on the method of randomisation (where applicable)

[TYPE ANSWER]

B13 How many research participants are to be recruited at each study site (where applicable)? Please complete the following table.
(You have already provided the overall totals in your response to Question B11, and B12 (a). The overall totals are relevant in respect of research design and statistical analysis.
The focus of this question (B13) is different and is on the totals at each site. Committees will have a particular interest in knowing the numbers of participants at the site or sites for which they provide an ethical review. This question is particularly relevant for as long as the conduct of multi-site research requires review and approval of studies by multiple ethics committees.

Site:	**Number of Research Participants at this site**

[TYPE ANSWER]	[TYPE ANSWER]
[TYPE ANSWER]	[TYPE ANSWER]

Action: Please add rows to the above table should you wish to add a site.

SECTION C STUDY PARTICIPANTS

C1 PARTICIPANTS – SELECTION AND RECRUITMENT

C1.1 How will the participants in the study be selected?

(Please outline how you will identify the participants for the study e.g. referral list to hospital clinic, random selection of patients from GP Register etc.)

[TYPE ANSWER]

C1.2 How will the participants in the study be recruited?

(Please indicate how and who will identify the participants for the study e.g. letter of invitation, verbal approach when attending the clinic, poster advertisement, web advertisement etc. Please ensure that you provide copies of all letters and advertisements referred to in your response for review)

[TYPE ANSWER]

C1.3 What are the inclusion criteria for research participants? (Please justify, where necessary)

(Please be careful when responding to this question especially if there is more than one grouping of research participants. Please state the inclusion criteria for each group of research participants.)

[TYPE ANSWER]

C1.4 What are the exclusion criteria for research participants? (Please justify, where necessary)

(Please be careful when responding to this question especially if there is more than one grouping of research participants. Please state the exclusion criteria for each group of research participants.)

[TYPE ANSWER]

C1.5 Will any participants recruited to this research study be simultaneously involved in any other research project?

(Researchers should consider the effect of over-burdening participants in terms of the number of research projects they are invited to participate in.) Yes / No / Not to my knowledge

C2 PARTICIPANTS – INFORMED CONSENT

"For the consent to be valid, the service user must:

- have received sufficient information in a comprehensible manner about the nature, purpose, benefits and risks of an intervention/service or research project;
- not be acting under duress; and
- have the capacity to make the particular decision."

HSE National Consent Policy May 2013[1]

"26. In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits

[1] Page 23

and potential risks of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study…………Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information. After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed."

World Medical Association Declaration of Helsinki, 2013

"25. Participation by individuals capable of giving informed consent as subjects in medical research must be voluntary. Although it may be appropriate to consult family members or community leaders, no individual capable of giving informed consent may be enrolled in a research study unless he or she freely agrees."

World Medical Association Declaration of Helsinki, 2013

C2.1 (a) Will informed consent be obtained? Yes / No

Action: If you chose 'no' please delete C2.1 (c), C2.2 (a)(b) and C2.3 (a)(b) and (c)

Action: If you chose 'yes' please delete C2.1 (b)

C2.1 (b) If no, **please justify. You must provide a full and detailed explanation as to why informed consent will not be obtained.**
(Your response to this question may in some cases have considerable links to further sections of this Guidance Manual e.g. page 24-research in emergency settings; page 29-data protection; page 38-research using archival material and page 40-genetic research. Where this occurs, please revisit your response to this question to ensure the consistency of your responses)

[TYPE ANSWER]

C2.1 (c) If yes, **please outline the consent process in full. (How will consent be obtained, when, by whom and from whom etc)**
(Only appropriately qualified and competent persons should take informed consent. Please ensure you provide copies of any Information Leaflets, Consent Forms and Assent Forms referred to in response to this question. Please refer to the HSE National Consent Policy for guidance in relation to sample information to be provided, as appropriate, when preparing information leaflets and consent documentation.[2])

[TYPE ANSWER]

C2.2 (a) Will participants be informed of their right to refuse to participate and their right to withdraw from this research study?
("A patient's refusal to participate in research must not influence your care of that patient in any way."

Guide to Professional Conduct and Ethics for Registered Medical Practitioners 2009

"26. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal."

World Medical Association Declaration of Helsinki 2013

"Prospective research participants must be informed from the outset that they can withdraw from a study at any time that they need not offer any explanation for wishing to withdraw and their decision will not impact on the services being provided to them.

Where an individual wishes to have his/her biological material or data withdrawn from the study, every effort should be made to respect his/her wishes. However, it is recognised that this might not always be feasible e.g. once the research results have been published or disseminated in other way, such as by being deposited in a publicly accessible database.

[2] Pages 65-67 and Figure 1, Part 1 Section 3.

Therefore consent documentation should clearly indicate what circumstances would prohibit the withdrawal of biological material or personal data.

In the case of anonymous biological material/data, prospective research participants should be informed during the consent process that it will not be possible to withdraw their material and/or data"[3]

"Prospective participants… should be assured that they can withdraw from the research study at any time and that their decision will not have any negative repercussions….The contact details of researchers should be provided to research participants should s/he require clarification on any issue relating to the research."[4])

Yes / No

C2.2 (b) If no, **please justify.**

[TYPE ANSWER]

C2.3 (a) Will there be a time interval between giving information and seeking consent? (Research participants should be given a reasonable period of time and support in order to make a decision about whether or not they wish to participate in a research study. Ideally, there should be adequate time for the participant to consult with family, friends and general practitioners before making a decision.

"It is particularly important to ensure this is the case for those with limited literacy skills and those who may have difficulty making decisions including those with communication difficulties, intellectual disability or cognitive impairment."[5]

It is recognised however that some studies are low-risk and participants may be asked to make a decision with regard to participation there and then. In other cases, it may be impossible due to the nature of the study for participants to be given an extended period of time to make a decision.

It should be noted that the HSE National Consent Policy states that "prospective research participants should be given enough time to fully consider their participation and to ask questions" [6] which suggests that best practice is to allow a reasonable time interval between the giving of information and seeking of consent. Therefore, if a study is low-risk you will need to consider whether it is reasonable for participants to be asked to make a decision there and then or whether a longer time-period should be provided.) Yes / No

Action: If you chose 'no' please delete C2.3 (b)

Action: If you chose 'yes' please delete C2.3 (c)

C2.3 (b) If yes, **please elaborate.**

(Please comment on how much time participants will be given to make a decision and explain how you will consider an individual's particular requirements e.g. limited literacy skills etc., in this regard.)

[TYPE ANSWER]

C2.3 (c) If no, **please justify and explain why an instantaneous decision is reasonable having regard to the rights of the prospective research participants and the risks of the study.**

[TYPE ANSWER]

3 HSE National Consent Policy (May 2013), page 88
4 HSE National Consent Policy (May 2013), Page 66
5 HSE National Consent Policy (May 2013), Page 27
6 Page 65

C3 ADULT PARTICIPANTS (AGED 18 OR OVER) - CAPACITY

C3.1 (a) Will all adult research participants have the capacity to give informed consent?

An adult is defined as a person aged 18 years or over. [I]

Capacity is defined as the ability to understand the nature and consequences of a decision in the context of available choices at the time the decision is to be made. [II]

A person lacks the capacity to make a decision if he or she is unable -
(a) to understand the information relevant to the decision,
OR
(b) to believe the information,
OR
(c) to retain that information long enough to make the decision,
OR
(d) to use or weigh that information as part of the process of making the decision,
OR
(e) to communicate his or her decision (whether by talking, using sign language or any other means [III]

In addition, the HSE's National Consent Policy provides that if there is "sufficient reason to question the presumption of capacity," the following should be assessed:

- The service user understands in broad terms and believes the reasons for and nature of the decision to be made.
- The service user has sufficient understanding of the principal benefits and risks of an intervention and relevant alternative options after these have been explained to them in a manner and in a language appropriate to their individual level of cognitive functioning.
- The service user understands the relevance of the decision, appreciates the advantages and disadvantages in relation to the choices open to them and is able to retain this knowledge long enough to make a voluntary choice.[7]

Yes / No

Action: If you chose 'yes' please delete C3.1 (b), C3.2 – 5.

C3.1 (b) If no, **please elaborate.** (Please state clearly how capacity to participate in this research study will be determined. Please also state clearly how the issue of consent and assent will be managed for those research participants who lack capacity.

"In accordance with the functional approach to capacity there may be instances where a person might have limited capacity and may require assistance in deciding whether or not to participate in research. In such cases, researchers must ensure efforts are made to assist people in reaching their decision and that they are provided with the appropriate tools to maximise their decisions-making ability.

The objectives, risks and benefits should be explained fully to prospective participants given their level of understanding. The information should be provided using easily comprehensible language and the prospective participant should be informed of their right to withdraw from the study at any time without there being any repercussions."[8]

Where capacity to consent is lacking, best practice suggests that the following principles should be adhered to:

- The research should only be undertaken if the required knowledge cannot be obtained by conducting research involving adults with decision making capacity.

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[7] Part 1, Section 5.5 (page 31)
[8] HSE National Consent Policy (May 2013), page 74

- The research is expected to provide a direct benefit to the participants or to provide knowledge about the cause or treatment of the impairing or similar condition. Where there is no prospect of direct benefit for participants, the risks involved should be no more than minimal.
- Consent for participation must be sought from the person's legal representative.
- A REC must approve the participation of adults lacking decision making capacity in research taking all of the above factors into consideration.
- The explicit wish of the participant to refuse participation in or to be withdrawn from the study should be respected.
- Where a prospective research participant lacks decision-making capacity but has some ability to understand the significance of the research, the researcher should ascertain the wishes of that individual with respect to his/her participation.
- Under the EC (Clinical Trials of Medicinal Products for Human Use) Regulations 2004, consent for research participation on behalf of an adult lacking decision-making capacity must be obtained from the person's legal representative. A legal representative has been defined as a person not connected with the conduct of the trial who by virtue of his/her family relationship with that adult is suitable to act as the legal representative and is willing and able to do so. If there is no such person, a person who is not connected with the trial, who is a solicitor nominated by the relevant healthcare provider. However, outside of clinical trials there is currently no legal framework for a person who lacks decision-making capacity to participate in research. The HSE National Consent Policy recommends that, in the absence of legislation, as a matter of best practice the same principles as those which apply to clinical trials should be applied. This means that consent for participation in any form of research on behalf of an adult lacking decision-making capacity must be obtained from the person's legal representative. However, this approach does not have a legislative/legal basis.
- Refusal to participate should be respected.[9])

[TYPE ANSWER]

C3.2 Is the research of such a nature that it can only be carried out on adults without capacity? (If this research study can validly take place using adult participants with capacity, adult participants without capacity should not be included.
"The research should only be undertaken if the required knowledge cannot be obtained by conducting research in adults with decision making capacity"[10])

Yes / No

C3.3 Is the research expected to provide direct benefit to the research participants (who lack capacity), or if there is no prospect of direct benefit, are the risks no more than minimal? Please elaborate. ("The research is expected to provide a direct benefit to the participants or to provide knowledge about the cause or treatment of the impairing or similar condition. Where there is no prospect of direct benefit to participants, the risks involved should be no more than minimal"[11])

[TYPE ANSWER]

C3.4 What arrangements are in place to ascertain the wishes of research participants, who although they lack decision-making capacity, have some ability to understand the significance of the research? ("Refusal to participate in research by an individual lacking decision making capacity should be respected"[12])

[TYPE ANSWER]

C3.5 What arrangements are in place for research participants who regain their capacity during the study? (A strategy for re-consenting participants

[9] Pages 74 - 75
[10] HSE National Consent Policy (May 2013), page 74
[11] HSE National Consent Policy (May 2013), page 74
[12] HSE National Consent Policy (May 20130, page 75

should be set out here. If capacity has been regained, the adult should be advised that he/she was a participant and the full consent process should be gone through which is applicable to adults who have capacity.[13])

[TYPE ANSWER]

C4 PARTICIPANTS UNDER THE AGE OF 18

C4.1 (a) Will any research participants be under the age of 18 i.e. children?

(A "child" is a person under the age of 18 years as per Section 2 of the Child Care Act 1991)

Yes / No

Action: If you chose 'no' please delete all remaining questions in C4.

C4. 1 (b) If yes, please specify:

"The following principles should be adhered to when conducting research involving children:

- The research should only include children where the relevant knowledge cannot be obtained by conducting research involving adults
- The purpose of the research is to generate knowledge about the health or social care needs of children
- The research does not pose more than minimal risk unless there is a prospect of direct benefit for the participants
- The research has been designed to minimise pain, discomfort, fear and any other foreseeable risk to the child or his/her stage of development
- Consent to the child's participation must be obtained from a parent/legal guardian
- Whenever s/he has sufficient competence to provide it, the child's assent must be sought in a child-appropriate manner;
- A child's refusal to participate or continue in research should be respected."[14]

- Consent from one parent/legal guardian for a child's participation in research unless the REC has found that the risks involved in participation in research require the consent of both.[15]

Neonates: Research involving full term or pre-term neonates is in principle similar to research involving children as decision making power rests with their parents/legal guardians. Additional issues relating to consent may arise, e.g. if there was a difficult/distressing/ premature birth.[16]

Persons < 16 (Persons under the age of 16[IV] cannot give consent to take part in most research studies, and (if consent is being sought) it should be sought from one parent or one legal guardian. It is recommended however that persons under the age of 16 be assented to participate in a manner appropriate to their age and level of understanding. It is strongly recommended that expert advice be sought where the research study involves persons under 16.)

Yes / No

Persons aged 16 – 18 (Persons between the ages of 16 and 18 form a special category of persons under the age of 18 who can legally give consent for medical, surgical and dental treatment.[V] It can be argued that this entitlement does not extend to participation in medical research.[VI] This has not been tested in the Irish courts. However the HSE National Consent Policy takes the following approach: - "For the purposes of participation in clinical trials, anyone over the age of 16 years can consent on his/her

[13] HSE National Consent Policy (May 2013), Page 89

[14] HSE National Consent Policy (May 2013), Page 70

[15] HSE National Consent Policy (May 2013), Part 3 Section 3, page 71 - See important Endnote IV

[16] HSE National Consent Policy (May 2013), Page 73

own behalf. For all other research, the person must be over the age of 18 years in order to provide consent."[17]

Hence the best practice approach would be (if consent is being sought) to approach one parent or one legal guardian to give consent on their behalf and for the persons between 16-18 to read an Information Leaflet appropriate for young persons and to sign an Assent Form. This matter however will need to be dealt with on a case by case basis, as some research studies involve the collection of data only.[VII VIII] It is strongly recommended that expert advice be sought where the research study involves persons between 16 – 18)

Yes / No

Children in Care (The recruitment of children who are in care (as participants in research) is legally complex and problematic. It involves establishing the precise care arrangement that is in place (voluntary care, emergency care order, interim care order or full care order) and who has the legal authority to make decisions in relation to participation in research and to undergo study interventions. The legislation and regulations governing children in care and foster arrangements do not address consent to participation in research.[IX] HIQA National Standards for Foster Care set out standards for health and development and provides a very useful guidance note on medical consent in the context of medical treatment of children in foster care or placement with relatives[X]. However, neither the Standards nor the Guidance Note addresses the issue of consent to participation in research.)

The HSE National Policy on Consent states that:

"Research involving children in care is permitted once the criteria listed above..[please refer back to page 20 of this Guidance Manual for criteria]....are adhered to. In order to conduct research involving a child in care researchers should first get consent from the responsible legal guardians, e.g. a parent and/or the child's health/social care providers or someone with a duty of care to the child. This consent must be supplemented with the child's assent.

Given the vulnerability of children in care, researchers should consider appointing an advocate, agreed by the child. The task of the advocate would be to ensure that the child is not exploited, coerced or subjected to undue influence or harm during the course of the research and that the child has freely given his or her assent to participation."[18]

Notwithstanding this statement, having regard to the complexity outlined above, it is strongly recommended that expert advice be sought where the research study involves children in care. [XI]

Yes / No

C4.1 (c) If yes to persons <16, **please specify:**
Pre-term neonates Yes / No
Full-term neonates Yes / No
Infants and Toddlers 0 - 4 Yes / No
Children 5 - 8 Yes / No
Children 9 – 12 Yes / No
Adolescents 13 -15 Yes / No

C4.2 Is this research of such a nature that it can only be carried out on children? Please elaborate. (Research carried out on children should only be undertaken if the required knowledge cannot be obtained by conducting research involving adults with decision-making capacity.[19])

[TYPE ANSWER]

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[17] Page 70

[18] Page 73

[19] HSE National Consent Policy (May 2013), Page 74

C4.3 Is the purpose of the research to generate knowledge about the health or social care needs of children? (Please refer back to page 20 of this Guidance Manual)

[TYPE ANSWER]

C4.4 Is the research expected to provide direct benefit to child participants, or if there is no prospect of direct benefit, are the risks no more than minimal? Please elaborate. (Please refer back to page 20 of this Guidance Manual)

[TYPE ANSWER]

Action: The following questions apply only if consent is being sought as per your response to Question 2.1 (a).
If you responded 'no' to Question C2.1 (a), please delete C4.4 - 9.

C4.5 Will each child receive information about the risks and benefits of the study according to his/her capacity to understand? Please elaborate and provide copies. (Age appropriate information leaflets and assent forms are important in this respect e.g. an information leaflet should be designed for 12-16 year olds, for 8 to 12 year olds and for children under 8. While children over 8 may read the information leaflet themselves, children under 8 should have the information leaflet read to them.

Applicants should consider, based on the age of the child and the nature of the study, whether it might be appropriate, or helpful for the information to be provided to the child while a family member (e.g. parent/guardian) is present.

"Older children, who are more capable of giving assent (i.e. children over the age of 7 years) should be selected before younger children, unless there are valid, scientific, age-related reasons for involving younger children first. Children should be as fully informed as possible given their age and competence, about the nature of the study and methods to be employed from the outset. Information for children aged 5 and under should be predominately pictorial. For older children, information sheets should be provided that explain briefly and in simple terms the background and aim of the study, so they can consider assent. It should also explain that their parents/legal guardians will be asked for consent. It should be explained to children that they may choose to withdraw from the study if they are uncomfortable with continuing. The objection of a child to participate should be adhered to unless the intervention being tested were to offer an important, direct benefit to the child."[20])

[TYPE ANSWER]

C4.6 Will the explicit wish of the child who is capable of forming an opinion and assessing information to refuse to participate or to be withdrawn from the study be considered by the investigators? Please elaborate, outlining the assent process in full. (How will assent be obtained, when and by whom etc.) (Where the child refuses to participate or wishes to be withdrawn from a study, the wishes of the child should be considered and adhered to unless the interventions being tested were to offer an important direct benefit to the child.[21])

[TYPE ANSWER]

C4.7 Please comment on the involvement of Parents / Legal Guardians of the child in the consent process. (HSE National Consent Policy states that it is sufficient for one parent or one legal guardian to sign a Consent Form in order for the child to participate in a research study, unless there is a significant risk to the child and therefore consent from both

[20] HSE National Consent Policy (May 2013), Pages 71 - 72
[21] HSE National Consent Policy (May 2013), Page 72

parents/legal guardians should be obtained.[22] Please also refer to the Endnotes at the rear of the Guidance Manual.

"A parent or legal guardian who provides consent on a child's behalf should be given the opportunity, to a reasonable extent, to observe the research as it proceeds."[23]

Researchers must be aware of the possibility of parental therapeutic misconceptions when determining how to explain the potential benefits and risks of research participation during the consent process.[24])

[TYPE ANSWER]

C4.8 Please explain your approach to reviewing assent where research subjects reach the age of 18 during the course of the study.
(Researchers must respect the developing capacity of children and upon turning 18, the consent of the adult should be obtained and consented in the way you would all other adult participants.[25])

[TYPE ANSWER]

C4.9 Please comment on what will occur if the researcher discovers that a child is <u>at risk</u> during the course of this study? (It is recommended that all researchers familiarise themselves with the Children's First National Guidelines for the Protection and Welfare of Children[XII]. In addition, if a child reveals to the researcher observes/receives evidence that they are at significant risk of harm, the researcher must divulge this information to the appropriate authorities. This should only occur following discussion with the child. The child and legal guardian(s)/parent(s) should be informed of this obligation during the consent/assent process and it should be highlighted in participant information leaflets. A strategy for information disclosure should be submitted to the REC for approval.[26]

[TYPE ANSWER]

C5 PARTICIPANTS - CHECKLIST

"19. Some groups and individuals are particularly vulnerable and may have an increased likelihood of being wronged or of incurring additional harm. All vulnerable groups and individuals should receive specifically considered protection.
20. <u>Medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research</u>.'

World Medical Association Declaration of Helsinki, 2013

C5.1 Please confirm if persons from any of the following groups will participate in this study. This is a quick checklist to assist research ethics committee members and to identify whether study participants include persons from vulnerable groups and to establish what special arrangements, if any, have been made to deal with issues of consent. <u>It is recognised that not all groups in this listing will automatically be vulnerable or lacking in capacity. Please refer to the HSE's National Consent Policy, particularly Part 3, Section 5.</u>[27]

[22] Page 72
[23] Page 71
[24] Page 72
[25] HSE National Consent Policy (May 2013), Page 89
[26] HSE National Consent Policy (May 2013), Page 72
[27] Pages 76 - 78

Committees are particularly interested to know if persons in any of these groups are being targeted for inclusion, as per the inclusion criteria.

(a) Healthy Volunteers (It is not uncommon for researchers to seek healthy volunteers in particular as act as 'controls' in respect of a given research study.) Yes / No

(b) Patients (Patients should be made aware that should they decide not to participate in a research study that this will have not have any impact on their care. Patients may be vulnerable and may find it difficult to say 'no' especially in cases where the researchers are also involved in their care. This difficulty may increase in cases where patients are chronically ill, severely ill or terminally ill and are in a dependent relationship with the investigators) Yes / No

- **Unconscious patients** (Unconscious patients cannot give consent. Where possible however, to use the terminology in the HSE Consent Policy, *'consent'* should be obtained from the *'legal representative.'* This *'consent'* where it applies to research interventions / procedures, and not to the 'processing of personal data,' has no legal value but performs the function of informing the next of kin that the patient is participating in a research study. In relation to the 'processing of personal data' only, valid consent can be given by the certain named classes of next of kin.[XIII] – Please refer to Section E also on this point. Patients should be informed of their involvement in a research study upon regaining capacity and consent should be obtained from patients themselves at this time.[XIV]) Yes / No
- **Current psychiatric in-patients** (A number of committees provide an ethical review for research studies taking place in psychiatric in-patient facilities. It is strongly recommended that expert advice be sought where the research study involves current psychiatric in-patients.) Yes / No
- **Patients in an emergency medical setting** (Patients should be made aware that should they decide not to participate in any research study that this will not have any impact on their care. Patients in an emergency setting may be vulnerable and may find it difficult to say 'no' especially in cases where the researchers will also be involved in their care. Secondly, trauma, shock or injury may also affect capacity on a case by case basis. Thirdly, many patients in an emergency setting may be unconscious, intubated etc. Research in emergency situations involves individuals who have a life-threatening medical condition that necessitates urgent intervention and who because of that condition cannot give consent. When not possible to obtain consent from the prospective participant, *consent* of the participant's *legal representative*[XV] should be sought. If there is no *legal representative*, the individual can only be enrolled in research if the following criteria are met:

- The research addresses the emergency needs of the individual involved;
- The experimental interventions have a realistic probability of benefit equal to or greater than standard interventions; and
- The risks associated with the research are reasonable in view of the critical nature of the condition and the risks associated with standard interventions.)

Participants who regain capacity (or their legal representatives once located) should be given all the relevant information and new consent to continue participation should be obtained as soon as is reasonably possible. The option to withdraw and seek destruction of any biological material/data collected as part of the study should also be given.[28]) Yes / No

(c) Relatives / Carers of patients (Relatives or Carers of Patients recruited due to their relationship with the patient must be consented separately for their own involvement in any research study.) Yes / No

(d) Persons in dependent or unequal relationships (Dependent or unequal relationships might include those between: health and social care professionals and residents in care, teachers and students, penal institutions and prisoners, employers and employees, or governments and refugees. Being in a dependent or unequal relationship may influence a person's decision to participate in research. Researchers should consult Section 5.3 Part 3 of the HSE National Consent Policy in this regard.[29]) Yes / No

- **Students** (A number of committees provide an ethical review for studies taking place in schools and educational facilities. In these cases, students can be primary, post-primary or third level students. A number of further committees provide an ethical review for studies in healthcare settings. Students in this context can therefore include undergraduate medical and nursing students etc. Students in training towards a professional qualification may be vulnerable and unable to say 'no' in terms of participation in a research study by virtue of their position in the organisation or their relationship with the investigators.) Yes / No
- **Employees / staff members** (Employees and staff members may be vulnerable and unable to say 'no' in terms of participation in a research study by virtue of their position in the organisation or their relationship with the investigators. This is particularly the case where employees or staff members are in a dependent relationship with the investigators. You must consult the Health Service Executive's National Consent Policy in this regard.[30]) Yes / No
- **Persons in residential care** (A number of committees provide an ethical review for research studies taking place in community settings including private and public nursing homes, other residential care homes and community sheltered housing schemes etc.) Yes / No
- **Persons highly dependent on medical care** (The reliance on medical treatment of people who are highly dependent on medical care (e.g. people in intensive care or the terminally ill) may impact on their willingness to consent to research participation and this raises significant ethical issues. Such research should only be undertaken when:
  It is likely that the research will led to an increased understanding of, or an improvement in, the care of that population; and any risk or burden of the proposed research to a particular participant is justified by the potential benefits that might accrue to him/her. Researchers should consult Section 5.2 of Part 3 of the HSE National Consent Policy in this regard.) Yes / No

[28] HSE National Consent Policy (May 2013), Page 76

[29] HSE National Consent Policy (May 2013), Page 78

[30] Page 78

(e) Intellectually impaired persons (Some research participants may lack capacity by virtue of an intellectual disability. However, capacity should be assessed on a case by case basis. There is no available definition for 'intellectual impairment' and hence this term should be taken to refer to both learning disability and intellectual disability. A number of committees provide an ethical review for research occurring in the community, including specifically the 'intellectual disability' services.) Yes / No

(f) Persons with a life-limiting condition
("A life limiting condition is defined as any condition…….where there is no reasonable hope of cure and from which the……[person]…. will die…….Conditions may include those for which the curative treatment has failed e.g. cancer, irreversible organ failure; conditions which require long periods of intensive treatment, but which are often associated with premature death e.g. cystic fibrosis, muscular dystrophy; progressive conditions without curative option e.g……. mucopolysaccharoidosis; conditions with severe neurological disability that may deteriorate unpredictably e.g. severe brain or spinal injury, severe cerebral palsy.

– A Palliative Care Needs Assessment for Children (2005))

Yes / No

(g) Persons with an acquired brain injury (Some research participants may lack capacity by virtue of an acquired brain injury. However, capacity should be assessed on a case by case basis.) Yes / No

C5.2 If yes to any of the above, **please comment on the vulnerability of the potential participants, and outline the special arrangements which have been made in recognition of this vulnerability)?** (Special arrangements, for example, may relate to consent / assent / recruitment / approach etc. It is recognised that not ALL groups in the above listing will automatically require special arrangements in relation to consent and assent. Secondly, you may have already provided the necessary information in your response to Question C3.1 (b). There can be a crossover between groups which may be vulnerable, groups which may require special arrangements in relation to consent and assent and persons who lack capacity. Researchers are advised to consult the HSE's National Consent Policy in this regard.)

[TYPE ANSWER]

C5.3 Please comment on whether women of child-bearing potential, breastfeeding mothers, or pregnant women will be included or excluded in this research study.
(Committees are interested to know if these groups are being recruited to a study. This applies to studies involving exposure to radiation in particular. Secondly, a number of research ethics committees provide an ethical review specifically on behalf of maternity hospitals.)

[TYPE ANSWER]

SECTION D RESEARCH PROCEDURES

D1 (a) What activities, procedures or interventions (if any) are research participants asked to undergo or engage in for the purposes of this research study?
(This means research procedures or interventions which the participants are undergoing or engaging in as part of the research study, and not those procedures and interventions which participants are undergoing or engaging in as part of routine care (or equivalent) i.e. which would occur irrespective of involvement in this research study.

'Research Procedures' is a very broad term which encompasses medical examinations, laboratory tests, x-rays, other imaging, phlebotomy, physiotherapy sessions, counselling sessions, psychological assessments, questionnaires, interviews and focus groups i.e. any type of intervention or measure which research participants may undergo or engage in.

It is further noted that not all research participants will be patients. For a healthy volunteer or staff member taking part in a research study, no procedures or interventions will be 'clinically indicated' or 'part of routine care.' Nevertheless, please also list interventions or procedures which healthy volunteers or staff members will undergo due to their involvement in this research study only.)

[TYPE ANSWER]

D1 (b) What other activities (if any) are taking place <u>for the purposes of this research study</u> e.g. chart review, sample analysis etc?
(For example, committees are also interested in knowing if there are any extra tests or analyses being done on samples taken which are over and above those tests done as part of routine clinical care. Please also refer to tests / analyses in response to this question where this applies.)

[TYPE ANSWER]

D2. Please provide details below of any potential harm that may result from any of the activities, procedures, interventions or other activities listed above.
(All research on human beings carries the possibility of harm. Whether the risk of harm is acceptable or not depends on the importance of the question being addressed and the likelihood of a meaningful result from the study.
Harms can be physical, psychological, psychosocial, financial or other and can include pain, discomfort, inconvenience or change to lifestyle. Even seemingly innocuous questionnaires can upset patients and / or change the way they view or manage their illness.
It is also wise to classify the harms listed. Harms can be classified as serious, non-serious, transient etc.
It is also useful to committees if you state the risk (probability) of the harms occurring, where this is possible: the risk of harms occurring can in some studies be stated with accuracy. It is recognised however that for many studies the risk (probability) of harm occurring will not be quantifiable.
Where relevant, please also state in your answer what measures will be put in place, if any, to ensure that risk of these harms occurring is minimised.
<u>Important Note:</u> Please ensure any relevant harms listed in response to this questions are clearly outlined in any Information Leaflets related to this study.
Important Note: All serious adverse events occurring during the course of this research study must be reported as per each committee's local guidelines in this matter.
Note: The term 'serious adverse event' is more typically associated with clinical trials of medicinal products. A generic definition for a 'serious adverse event' outside of S.I. 190/2004 is not available. Hence, please report all Serious Adverse Events in line with each committee's local definitions and guidelines in this matter.)

[TYPE ANSWER]

D3. What is the potential benefit that may occur as a result of this study? (There may be a direct benefit for research participants. There may be a benefit for the researcher in terms of academic qualification or career advancement. There may be a benefit for the healthcare system in general or for an organisation / site or service. There may be a benefit to a pharmaceutical company, device manufacturer, charity etc.)

[TYPE ANSWER]

D4 (a) Will the study involve the withholding of treatment? ('Treatment' may include prescribed drugs, surgery, radiotherapy, physiotherapy, occupational therapy etc.)

Yes / No / Non-applicable

Action: If you chose 'no' or 'non-applicable' please delete D4 (b) and (c)

D4 (b) Will there be any harms that could result from withholding treatment? Yes / No

Action: If you chose 'no' please delete D4 (c)

D4 (c) If yes, **please elaborate.**

[TYPE ANSWER]

D5 (a) How will the health of participants be monitored <u>during</u> the study, and who will be responsible for this?

(Some research studies may involve special arrangements in this regard. However, it is recognised that in many research studies, especially those involving staff members, monitoring of the health of participants is neither appropriate nor necessary.

Please provide details however if the health of participants is being monitored. Participants should also be informed of this monitoring in all relevant Information Leaflets.

Committees will also have a particular interest in knowing if the study/trial itself is being monitored / overseen by an Independent Data Safety Monitoring Board. Again, a DSMB is neither appropriate nor necessary for many research studies)

[TYPE ANSWER]

D5 (b) How will the health of participants be monitored <u>after</u> the study, and who will be responsible for this?

[TYPE ANSWER]

D6 (a) Will the interventions provided during the study be available if needed after the termination of the study? Yes / No / Non-applicable

Action: If you chose 'no' please delete D6 (b)

D6 (b) If yes, **please state the intervention you are referring to and state who will bear the cost of provision of this intervention?** (This question should be interpreted in a broad sense e.g. in a study which provides a broadband connection free of charge to research participants, 'free broadband' is the intervention and the question relates to whether this will continue to be provided after the study has finished.)

"34. In advance of a clinical trial, sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial. This information must also be disclosed to participants during the informed consent process."

World Medical Association Declaration of Helsinki, 2013

[TYPE ANSWER]

D7. Please comment on how individual results will be managed.

(It is extremely important for researchers to decide in advance if research participants will receive individual results in relation to this study, or alternatively, if study results will be sent to the research participant's general practitioner or consultant (subject to consent).

Secondly, a definite plan needs to be decided in terms of what referral or care pathways will be in place in case of a negative finding / result / outcome for any individual research participant.

Finally, a definite plan needs to be decided in terms of 'incidental findings.' 'Incidental findings' are findings which are discovered during the course of a research study which are 'incidental' i.e. a researcher may not be conducting research into cholesterol, but during the course of his / her research study may 'incidentally' discover that a participant has high cholesterol.

It should be decided in advance whether 'incidental findings' will be relayed to the research participant, noting that the HSE Consent Policy recommends that "prospective research participants should be provided with the option of whether or not they wish to have medically relevant incidental findings disclosed to them.[31]

It is recognised however that not all research studies generate results which have individual meaning and not all research studies include the possibility of either 'negative findings' or 'incidental findings.'

[31] Page 86

Please read Part 3, Section 8 of the HSE National Consent Policy[32].)

[TYPE ANSWER]

D8. Please comment on how aggregated study results will be made available.

Researchers should decide in advance in so far as possible what their intention is in terms of release of overall study results. This may include publication in peer-reviewed journals, poster and verbal presentations, or submission of a final thesis to a university.

"35. Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject."

World Medical Association Declaration of Helsinki, 2013

Researchers may also wish to consider if it will be appropriate or meaningful to inform individual participants or collectives of research participants (e.g. Patient Organisations) of the overall outcome of the research study. The guidance in the Declaration of Helsinki is as follows:

"26. All medical research subjects should be given the option of being informed about the general outcome and results of the study."

World Medical Association Declaration of Helsinki, 2013

[TYPE ANSWER]

D9. Will the research participant's general practitioner be informed that the research participant is taking part in the study (if appropriate)?

(If yes, please ensure permission is sought from the research participant for the researcher to make contact with the research participant's general practitioner. If the general practitioner is being informed, please provide a copy of the letter to the GP for review by the committee. Patient Safety should the key factor in deciding whether it will be necessary to inform the participant's General Practitioner.) Yes / No / Non-applicable

D10. Will the research participant's hospital consultant be informed that the research participant is taking part in the study (if appropriate)?

(If yes, please ensure permission is sought from the research participant for the researcher to make contact with the research participant's consultant. If the hospital consultant is being informed, please provide a copy of the letter to the hospital consultant for review by the committee. Patient Safety should the key factor in deciding whether it will be necessary to inform the participant's hospital consultant.)

Yes / No / Non-applicable

SECTION E DATA PROTECTION

E1 DATA PROCESSING - CONSENT

RESEARCHERS ARE REMINDED THAT THE DATA PROTECTION LEGISLATION APPLIES IN RESPECT OF THE PROCESSING OF 'PERSONAL DATA' OF LIVING PERSONS.

DURING STUDY DESIGN STAGE RESEARCHERS ARE ADVISED TO ASK THEMSELVES THESE QUESTIONS:

1. Does this study involve the processing[33] of personal data of living persons?

[32] Pages 86 - 87

[33] Processing is defined as 'performing an operation or set of operations on the information or data, whether or not by automatic means including:

2. Is it possible for this study to be undertaken using irrevocably anonymised data?
3. Is it possible for this study to be undertaken using pseudonymised data?

"Irrevocable anonymisation of personal data puts it outside data protection requirements as the data can no longer be linked to an individual and therefore cannot be considered to be personal data."

"Equally, it is recognised that the need to link episodes of care and prevent duplication of data in research, in some instances, requires that information may need to be capable of being matched or linked. This can be achieved through appropriate pseudonymisation (e.g., use of initials, coding) methods without the need to retain all identifying characteristics with the data."

"Similar to the advice above in relation to anonymisation, where pseudonymisation methods are used, it is recommended that extra efforts, beyond use of initials etc, be incorporated where a condition is particularly rare. Where sufficient measures are put in place to ensure that personal data is not accessible or likely to be identifiable by parties external to the data controller, the requirement to capture consent to use the data for research purposes, in such circumstances, will no longer apply"

Data Protection Guidelines on Research in the Health Sector, 2007

STUDIES WHERE <u>WRITTEN</u> CONSENT OF RESEARCH PARTICIPANTS IS OBTAINED FOR THE PROCESSING OF <u>PERSONAL</u> DATA ARE THE GOLD STANDARD.
THE DATA PROTECTION LEGISLATION HOWEVER ALSO PERMITS CONSENT TO BE GIVEN BY PERSONS OTHER THAN THE DATA SUBJECT WHERE HE/SHE LACKS CAPACITY TO GIVE CONSENT FOR PROCESSING OF PERSONAL DATA.

Section 2A(1) of the Acts provides that, where a person by reason of his or her physical or mental incapacity or age, is or is likely to be unable to appreciate the nature and effect of giving consent, such consent may be given by a parent or guardian or a grandparent, uncle, aunt, brother or sister of the person provided that the giving of such consent is not prohibited by law.[XVI]

"Research participants who have given appropriate consent have a right to expect that identifiable data about themselves, either provided or discovered in the course of research, will not be shared with others without their consent. Anonymous data is beyond the scope of the Data Protection Act, therefore consent is not required to conduct research using this form of data. However, the use of anonymous data is not always possible or indeed desirable in a research context.

De-identifying data (i.e. where identifiable is substituted for a code to which only the data controller would have the key) is another way of protecting confidentiality. In order to safeguard a research participant's rights to privacy, data should be de-identified by the <u>data controller</u> as early as possible. <u>In the case of HSE-run facilities, the HSE is the data controller</u>.

<u>In cases where research is to be undertaken by external third parties (e.g. researchers who are not directly involved in the care of the prospective research participants), where identifiable information will be used then the explicit consent of the prospective research participants must be obtained.</u>

In cases where research is to undertaken by external third parties and the data has been de-identified, prior to being transferred, the consent of the research participant for such a transfer is not required."[34]

HSE National Consent Policy (May 2013)

(a) Obtaining, recording or keeping the information or data;
(b) Collecting, organising, sharing, altering or adapting the information or data;
(c) Disclosing the information or data by transmitting, disseminating or otherwise making it available or;
(d) Aligning, combining, blocking, erasing or destroying the information or data

[34] Pages 87 and 88

Please refer to your response to Question C2.1 (a) before responding to Question E1.1 (a)

E1.1(a) Will consent be sought for the processing of data? (Consent is an absolute requirement for the processing of 'personal data' only. 'Personal data' is defined in the Data Protection Acts as follows: "data relating to a living individual who is or can be identified either from the data or from the data in conjunction with other information that is in, or is likely to come into, the possession of the data controller." It covers any information that relates to an identifiable, living individual. However, it needs to be borne in mind that data may become personal from information that could likely come into the possession of a data controller. Often a case by case assessment must be made taking account of some of the above considerations as to whether data could be deemed to be personal.)

Yes / No

Action: If you chose 'yes' please delete E1.1 (b)

E1.1(b) If no, **please elaborate.** (If consent is not being sought irrevocably anonymised data and/or appropriately pseudonymised data may be processed ONLY. The 'appropriateness' of the pseudonymisation proposed should be assessed on a case by case basis.

"Consent is an absolute requirement for the processing of sensitive data. *Sensitive personal data* means personal data as to:

(a) The racial or ethnic origin, political opinions or religious or philosophical beliefs of the data subject.
(b) Whether the data subject is a member of a trade union;
(c) The physical or mental health or condition or sexual life of the data subject;
(d) The commission or alleged commission of an offence;
(e) Any proceedings for an offence committed or alleged to have been committee by the data subject."[35]

HSE National Consent Policy (May 2013)

[TYPE ANSWER]

E2 DATA PROCESSING - GENERAL

E2.1 Who will have access to the data which is collected? (Please ensure to inform research participants about who will have access to the collected data in all relevant Information Leaflets.)

[TYPE ANSWER]

E2.2 What media of data will be collected? (Data can be hard copy or electronic; data can be visual e.g. video recordings, clinical photographs, images; data can be audio data e.g. tape recordings.)

[TYPE ANSWER]

E2.3 (a) Would you class the data collected in this study as anonymous, irrevocably anonymised, pseudonymised, coded or identifiable data? (Please note that different media may be classed differently. Questionnaires for example may be completely anonymous rendering it impossible to ascertain which research participant completed an individual questionnaire. In a research study involving an anonymous questionnaire it would be impossible for a research participant to withdraw from the study once data collection has occurred. Images may be identifiable in particular where images are clearly marked with a patient's name or medical record number. Photographs of the face and video-recordings, for example, are identifiable. The term 'irrevocably anonymised' applies when the data which was originally identifiable has been rendered 'anonymous' e.g. to delete the patient name, medical record number from an 'x-ray' would irrevocably anonymise the X-Ray. It should be noted that it can be more difficult to successfully de-identify

[35] Pages 84 - 86

photographs of the face and video-recordings. The term 'pseudonymised' is a form of anonymisation wherein duplication is avoided by the use of 'initials / year of birth' for example. Finally, data is often coded i.e. it is possible to identify the participant from the data via a code which is retained by the researcher.)

[TYPE ANSWER]

E2.3 (b) If 'coded', **please confirm who will retain the 'key' to re-identify the data?** (It is recommended that the key to re-identify 'coded' data remain at the site of origin of the data. It is further recommended that the person who holds the 'key' to re-identify be the lead investigator at the site.)

[TYPE ANSWER]

E2.4 Where will data which is collected be stored? (Please note that different media may be stored in different fashions.)

[TYPE ANSWER]

E2.5 Please comment on security measures which have been put in place to ensure the security of collected data. (These measures would include locked filing cabinets, password protected computers, encryption of desktop computers and portable devices and encryption of individual files. It is strongly advised that 'personal' data is not stored on portable devices or home-based desktops. However, where this is absolutely necessary, encryption software should be installed. Researchers should be aware of their responsibilities under the data protection legislation to keep electronic and hard copy 'personal data' safe and secure.)

[TYPE ANSWER]

E2.6 (a) Will data collected be at any stage leaving the site(s) of origin?

Yes / No

Action: If you chose 'no' please delete E2.6 (b)

E2.6 (b) If yes, **please elaborate.** (Please state what data, what medium of data, what class of data etc. will be sent and state where and to whom this data will be sent? Please ensure to inform research participants in all relevant Information Leaflets of the details which you supply in response to this question. It is particularly important to inform research participants if data is leaving the country, and especially if the data is leaving the European Economic Area. EEA Transfers of personal data to non-EEA countries must take place in compliance with the Data Protection Acts, e.g. where the individual has consented to that transfer. It is recommended that only non-identifiable data leave the EEA where at all possible.)

[TYPE ANSWER]

E2.7 Where will data analysis take place and who will perform data analysis (if known)? (While is advisable to obtain the advice of a statistician while designing any research study, it may not be known at the point of submitting an ethics application where the data analysis will take place at the end of the study or throughout the study and/or it may not be known who will be performing the data analysis. However, if there is a possibility that data will be leaving the site of origin for the purposes of data analysis, it is important to inform the research participant.)

[TYPE ANSWER]

E2.8 (a) After data analysis has taken place, will data be destroyed or retained?

[TYPE ANSWER]

E2.8 (b) Please elaborate. (Different media of data may be treated differently in respect of retention / destruction. Similarly, different classes of data may be retained e.g. identifiable data may be destroyed, while irrevocably anonymised data may be retained for the purposes of future publication.)

[TYPE ANSWER]

E2.8 (c) If destroyed, how, when and by whom will it be destroyed? (Please note different media may be destroyed in different fashions)

[TYPE ANSWER]

E2.8 (d) If retained, for how long, for what purpose, and where will it be retained? (Please inform research participants in all relevant Information Leaflets of the details which you supply in response to this question. Researchers should be aware of their responsibilities under the data protection legislation not to retain 'personal data' for longer than is necessary to fulfil the purpose for which the data was originally collected. There are no such time restrictions in place with regard to the retention of anonymous or irrevocably anonymised data. Please note that although a number of committees may specify timelines that research data must be retained for e.g. 5 years / 7 years, the only legal requirement is that data should not be held for longer than necessary to fulfil the purpose for which it was originally collected. Where the data forms part of the patient's healthcare record however, the timelines listed in the NHO Code of Practice on Records Management apply.)

[TYPE ANSWER]

E2.9 Please comment on the confidentiality of collected data. (Identifiable data should only be disclosed to third parties if consent is in place for this disclosure to take place. If there is a possibility of a situation arising where it may become necessary to breach confidentiality, research participants should be informed of this in all relevant Information Leaflets.)

[TYPE ANSWER]

E2.10 (a) Will any of the data collected consist of audio recordings / video recordings?

Yes / No

Action: If you chose 'no' please delete E2.10 (b)

E2.10 (b) If yes, **will participants be given the opportunity to review and amend transcripts of the tapes?**

[TYPE ANSWER]

E2.11 (a) Will any of the data collected consist of photographs / video recordings?

Yes / No

Action: If you chose 'no' please delete E2.11 (b)

E2.11 (b) If yes, **please elaborate.** (Please focus on consent in your response, in particular, if it is proposed to publish or present photographs / video recordings.)

[TYPE ANSWER]

E3 ACCESS TO HEALTH CARE RECORDS

E3.1 (a) Does the study involve access to healthcare records (hard copy / electronic)?

Yes / No

Action: If you chose 'no' please delete all the remaining questions in Section E3

E3.1 (b) If yes, **please elaborate.** (Please state what healthcare records will be accessed (e.g. hard copy charts, computer systems etc.), for what purpose healthcare records will be accessed and what data it is proposed to collect from these records.)

[TYPE ANSWER]

E3.1 (c) Who will access these healthcare records? (Research participants should be informed in any information leaflets or consent forms who will have access to their healthcare records.)

[TYPE ANSWER]

Studies in which written consent is in place to access healthcare records are the gold standard.
The ideal situation is one where written consent is sought to access healthcare records.

E3.1 (d) Will consent be sought from patients for research team members to access their healthcare records? (Research participants should be informed in any Information leaflets or consent forms that it will be necessary to access their healthcare records as part of their participation in this study.)

Yes / No

Action: If you chose 'yes' please delete Questions E3.2 (a) and E3.2 (b)

In cases where consent is not being sought to access healthcare records, the following issues should be considered by the researcher. It is common, for example, for healthcare records to be accessed without consent at an early stage in any research study for the purposes of identifying patients who fulfil the inclusion / exclusion criteria prior to recruitment.

E3.2 (a) Who or what legal entity is the DATA CONTROLLER in respect of the healthcare records?

(Data Controllers are those who, either alone or with others, control the contents and use of personal data.
Examples of Data Controllers:

- Data Controllers can be either legal entities such as companies, government departments or voluntary organisations, or they can be individuals such as GPs, pharmacists or sole traders.
- The data controller can be an individual hospital consultant in the case of private patients.
- The data controller is however the hospital board in respect of independent teaching hospitals.
- The data controller is the HSE in respect of HSE hospitals.
- The data controller can be the individual GP in respect of patients attending a General Practice but can in certain cases be the practice itself.

The Data Subject is an individual who is the subject of personal data.)

[TYPE ANSWER]

E3.2 (b) What measures have been put in place by the data controller which may make access to healthcare records permissible without consent?

(Will the data controller nominate the researcher as an agent? Will the researcher enter into a confidentiality agreement with the data controller? Does a memorandum of understanding or other agreement exist between the legal entity which is the data controller and the legal entity to which the researcher is affiliated? Is the researcher involved in the direct care of the patient(s) whose healthcare records he / she proposes to access? Is the researcher bound by confidentiality via the terms of his / her contract of employment or his / her code of professional conduct? Is it possible for the data controller to access the healthcare records on the researcher's behalf and to issue irrevocably anonymised or pseudonymised data only to the researcher? Is it possible for the data controller to act as 'gatekeeper' and select / recruit patients on behalf of the researcher?
IMPORTANT NOTE: Access to Healthcare Records should occur in line with local institutional / organisational policies in this area.
IMPORTANT NOTE: A list of patients should not be provided to a third party or health professional not involved in the care of these patients for the purposes of making contact unless patients have specifically consented to this.)

[TYPE ANSWER]

SECTION F HUMAN BIOLOGICAL MATERIAL

It is recommended that all researchers familiarise themselves with the Irish Council for Bioethics Guidelines:
Human Biological Material: Recommendations for Collection, Use and Storage in Research 2005

F1 BODILY TISSUE / BODILY FLUID SAMPLES - GENERAL

"A human biological specimen is any material derived from a human subject-such as blood, urine, tissues, organs, hair, nail clippings, or any other cells or fluids-whether collected for research purposes or as residual specimens from diagnostic, therapeutic, or surgical procedures."
United States Department of Veteran Affairs VA Tissue Banking Program

F1.1 (a) Does this study involve human biological material? Yes / No

Action: If you chose 'no' please delete all remaining questions in Section F and all sub-sections of Section F

F2 BODILY TISSUE / BODILY FLUID SAMPLES PROSPECTIVELY COLLECTED

F2.1 Does this study involve the prospective collection of human biological material? Yes / No

If you chose 'no' please delete the remaining questions in Section F2

F2.2 Please state the type of human biological material which is being prospectively collected.
[TYPE ANSWER]

F2.3 Who or what institution will be the custodian of the prospectively collected human biological material?
(Please note that for applications to set up a biobank, the custodian should be an institution as opposed to an individual e.g. a hospital / a university etc.
For all other research applications, "the investigator responsible for collecting and maintaining the material (the custodian) should control access to this material for the duration of his/her studies."
Human Biological Material: Recommendations for Collection, Use and Storage in Research 2005)
[TYPE ANSWER]

F2.4 (a) Will the human biological material be collected as part of routine clinical care? (The participant may be undergoing surgery requiring the taking of a biopsy, or may be giving blood samples as part of routine clinical care.)
Yes / No

F2.4 (b) Will the human biological material be collected specifically for the purposes of this research study? (The participant may for example be undergoing a procedure which does not normally involve taking of a tissue sample and therefore a sample is being taken for the purposes of this study.)
Yes / No

F2.4 (c) With reference to your responses to Question F2.4 (a), F2.4 (b), please provide more detail, in particular, in relation to whether participants will be consented to the taking of a sample or to the use of a sample (or part of a sample) which will be taken anyway for clinical

reasons. (Please ensure that the consent for either the taking of a sample for research or for the use of a sample which it is planned to take for clinical reasons 'is clearly separated from' CONSENT FOR SURGERY / CONSENT FOR TREATMENT. A Study Information Leaflet and Consent Form specific to this research study is required. The consent form used for surgery or treatment is insufficient in this regard.)

[TYPE ANSWER]

F2.5 (a) With respect of human biological material which it is proposed to prospectively collect for the purposes of this research study, after the laboratory analysis which this research study involves, will any human biological material remain?

Yes / No

Action: If you chose 'no' please delete F2.5 (b) (c) (d) (e) (f) and (g)

F2.5 (b) If yes, **will this remaining biological material be retained?** (This question refers to the human biological material which is taken for the purposes of this research study. It is understood that if material has been collected as part of routine clinical care, hospital laboratory practices and procedures will apply in relation to retention)

Yes / No

Action: If you chose 'no' please delete F2.5 (c) (d) (e) (f) and (g)

F2.5 (c) If yes, **for how long and where will samples be retained?**

[TYPE ANSWER]

F2.5 (d) If yes, **for what purpose will samples be retained?**

[TYPE ANSWER]

F2.5 (e) If yes, **please comment on consent for retention of biological material.**

[TYPE ANSWER]

F2.5 (f) If yes, **will this human biological material and/or any data derived from it be used for any other purpose (including future research projects)?**

Yes / No

Action: If you chose 'no' please delete F2.5 (g)

F2.5 (g) If yes, **please comment on consent for future use of human biological material.** (RESEARCHERS ARE ADVISED TO CONSULT THE HSE NATIONAL CONSENT POLICY IN THIS REGARD AND SPECIFICALLY PART 3, SECTION 7[36])

[TYPE ANSWER]

F2.6 (a) Will the human biological material be collected specifically for the purposes of depositing this human biological material in a biobank? (A 'biobank' is a collection or repository of human biological material. "While any biological sample archive can be termed a 'biobank' the term is normally applied to a centralised archive of material from which materials are made available for approved research."

Human Biological Material: Recommendations for Collection, Use and Storage in Research 2005)

[36] Pages 84 - 86

Yes / No

Action: If you chose 'no' please delete F2.6 (b) and (c)

F2.6 (b) If yes, **please provide specific information in relation to this proposed biobank.** (Researchers should consider setting up a steering committee for the biobank. There should be procedures and guidelines in place as to when exactly permission will be granted for access to the biobank for future research studies to occur.)

[TYPE ANSWER]

F2.6 (c) If yes, **will research participants be informed in all Information Leaflets and Consent Forms that this is a biobank?** (Researchers should emphasise the permanency of a biobank and indefinite nature of retention of human biological material (if this is the case). They should further emphasise that the material may be used in future research projects as yet undevised. Participants need to be clearly informed if this is a commercial biobank, or if there is any possibly of profit being made. Participants should be informed if research ethics committee approval will be required in order to use biobank material in the future. Finally, the extent to which the participants are giving permission for their material to be used in the future must be clearly stated. RESEARCHERS ARE ADVISED TO REFER TO PART 3, SECTION 7 OF THE HSE NATIONAL CONSENT POLICY'[37]

[TYPE ANSWER]

F3 BODILY TISSUE / BODILY FLUID SAMPLES RETROSPECTIVELY COLLECTED

F3.1 Does this study involve accessing retrospectively collected human biological material? Yes / No

Action: If you chose 'no' please delete the remaining questions in Section F3

F3.2 Please state the type of human biological material which is being accessed.

[TYPE ANSWER]

F3.3 Who will access the material?

[TYPE ANSWER]

F3.4. Who (or which institution) is the current custodian of the material?

[TYPE ANSWER]

F3.5 Please state for what purpose the human biological material was originally collected and please comment on the nature of consent for the collection of this material.

[TYPE ANSWER]

F3.6 (a) Do you intend to contact patients to seek their consent to use stored human biological material?

Yes / No

Action: If you chose 'yes' please delete Question F3.6 (b)

Before responding the next question, please refer to Part 3, Section 6.6 and 9 of the HSE National Consent Policy (May 2013), as follows: -

[37] Pages 85 - 86

"Section 6.6 – Research involving archival material[38]
Researchers may want to use biological material of data that was previously accumulated for clinical purposes or that was collected by other researchers. This raises privacy issues, such as whether the archival material or data contains personal identifiers, or whether it can be linked to such identifiers and, if so, by whom. If consent was required for the original collection or use of the archival material or data, then secondary uses may be constrained by the conditions specified in the initial consent. Consequently, it is essential that the consent process anticipate, where feasible, any foreseeable plans for future research using the material or data.

There are, however, certain circumstances under which archival biological material or data may be used for research purposes where consent is not required. For instance, where archival biological material or data was obtained from persons for research or clinical purposes, where the material or data is not individually identifiable (i.e. anonymous), and where there are no potential harms to the person from whom the material or data was obtained, consent requirements may be waived.

Where existing material or data is individually identifiable, researchers should make every effort to obtain consent from individuals for the use of their archival biological material or data. A REC may waive the consent requirement subject to conditions outlined below.

Researchers who have not obtained consent from participants for secondary use of their archival biological material or data should only use such material or data if they can satisfy a REC that:

- The use of the material/data without the participant's consent is unlikely to adversely affect the welfare of individuals involved;
- The researchers will take appropriate measures to protect the privacy of individuals, and to safeguard the material/data;
- The researchers will comply with any known preferences previously expressed by individuals about any use of their material/data;
- It is impossible or impracticable to seek consent from individuals to whom the material/data relates; and

It is important to note that the word 'impracticable' refers to excessive difficulty or onerousness that jeopardises the conduct of the research as opposed to inconvenience.

As a condition of access, archival biological material or data should be de-identified by the data controller (for more information, see Section 9 Consent and Controlling access to data)"[39]

"Section 9 – Consent and controlling access to data
Research participants who have given appropriate consent have a right to expect that identifiable data about themselves, either provided or discovered in the course of research, will not be shared with others without their consent.
Anonymous data is beyond the scope of the Data Protection Acts, therefore, consent is not required in order to conduct research using this form of data. However, use of anonymous data is not always possible, or indeed desirable, in a research context.

De-identifying data (i.e. where identifiable information is substituted with a code to which only the data controller would have the key) is another way of protecting confidentiality. In order to safeguard a research participant's privacy, data should be de-identified by the data controllers as early as possible. In the case of HSE-run facilities, the HSE is the data controller.

In cases where research is to be undertaken by external third parties (e.g. researchers who are not directly involved in the care of the prospective research participants), where identifiable information will be used then the explicit consent of the prospective research participants must be obtained.

In cases where research is to be undertaken by external third parties and the data has been de-identified, prior to being transferred, the consent of the research participant for such transfer is not required."

[38] Pages 83 - 84
[39] Pages 87 - 88

"Section 12– Research where consent may not be required
Waiver of consent is to be regarded as an exception to the rule and studies seeking waiver of consent must receive REC approval. Before a waiver of consent may be granted the researcher must satisfy the REC that:

- the overall benefit of the research is real and substantial
- the benefits from the research justify any risks of harm associated with not seeking consent;
- it is impracticable to obtain consent (for example, due to the quantity, age of accessibility of records);
- there is no known or likely reason for thinking that participants would not have consented if they had been asked;
- there is sufficient protection of their privacy; and
- there is an adequate plan to protect the confidentiality of data"

F3.6 (b) If no, **please justify why existing consent is considered sufficient, or why a waiver of consent from the research ethics committee is warranted.**

[TYPE ANSWER]

F4 BODILY TISSUE / BODILY FLUID SAMPLES – SAMPLE MOVEMENT

F4.1 (a) Will human biological material at any stage leave the institution(s) of origin?

Yes / No

Action: If you chose 'no' please delete all the remaining sections in Section F4

F4.1 (b) If yes, **for what purpose?**

[TYPE ANSWER]

F4.1 (c) If yes, **please state where samples will be sent?**

[TYPE ANSWER]

F4.1 (d) If yes, **please state if the samples leaving the institution(s) of origin will be anonymous, irreversibly anonymised, coded, identifiable etc?**

[TYPE ANSWER]

F4.1 (e) If 'coded', **please confirm who will retain the 'key' to re-identify the samples?** (It is recommended that the key to re-identify 'coded' samples remain at the site of origin of the samples. It is further recommended that the person who holds the 'key' to re-identify be the principal / lead investigator at the site or the custodian of the samples.)

[TYPE ANSWER]

F4.1 (f) Does a Memorandum of Understanding (or agreement / contract) exist between the institution(s) of origin and the institution(s) to which the samples will be sent? Please elaborate. (Researchers should note the value of putting such agreements in place in order to avoid misunderstandings as to how samples can be used in the future. There may however be no intention to put an agreement between institutions in place, or an agreement between institutions may not be in place at the time of submission of the ethics application for review.)

[TYPE ANSWER]

F5 GENETIC TESTING

The Disability Act, 2005 Part 4 sets out certain legal requirements for genetic testing to be lawful. In particular, Section 42 of the Disability Act, 2005 prohibits genetic testing unless the requirements of that section are met and makes it an offence to contravene the requirements of that section.

Section 42 provides as follows:-

"1) Genetic testing shall not be carried out on a person unless:-

(a) the testing is not prohibited by law; and

(b) the consent of the person to the processing of any genetic data to be derived from the testing has been obtained in accordance with the Acts.

2) A person shall not engage in the processing of genetic data in relation to—

(*a*) the employment of a person save in accordance with the provisions of section 12A of the Data Protection Act 1988 (as inserted by the Data Protection (Amendment) Act 2003),
(*b*) a policy of insurance or life assurance,
(*c*) a policy of health insurance or health-related insurance,
(*d*) an occupational pension, a retirement annuity contract or any other pension arrangement,
(*e*) the mortgaging of property.

(3) A person shall not process genetic data unless all reasonable steps have been taken to provide the data subject with all appropriate information concerning—

(*a*) the purpose and possible outcomes of the proposed processing, and
(*b*) any potential implications for the health of the data subject which may become known as a result of the processing.

(4) A person who contravenes *subsection (2)* or *(3)* shall be guilty of an offence; an offence under this subsection shall be deemed to be an offence to which section 31 of the Data Protection Act 1988 applies."

Section 42 of the Disability Act 2005

F5.1 (a) Does this research study involve 'genetic testing'? ("genetic testing" means the examination of samples taken from a living person for the purpose of analyzing the person's deoxyribonucleic or ribonucleic acid by means of chromosomal analysis or by any other means for the purpose of (*a*) confirming the identity or nature of an existing symptomatic disease; (*b*) ascertaining whether the person has a genetic predisposition or susceptibility to a disease, or (*c*) identifying the carrier of a disease. "Genetic Data" means data relating to a living person derived from genetic testing of the person. These definitions are taken from Section 4 of the Disability Act 2005)

Yes / No

Action: If you chose 'no' please delete F5.1 (b), F5.2 (a)(b), F5.3 (a)(b), and F5.4 (a).

F5.1 (b) If yes, **please specify the nature and purpose of the genetic testing** (It is important that this information should be prominently placed in any Information Leaflets or Consent Forms. It is extremely important that research participants be told whether they have a particular disease or that they are a 'control' in this research study. Participants may not understand the term 'control' and may need this to be explained to them. It is very important that the implications of any testing be stated clearly in any Information Leaflets, in particular, if there are implications for next of kin, offspring or future offspring)

[TYPE ANSWER]

F5.2 (a) Will consent be obtained?
(The Disability Act 2005 Part 4 states that consent for the processing of any genetic data to be derived from testing must be obtained and prohibits genetic testing in the absence of such consent. The Act also stipulates that

a person shall not process genetic data unless all reasonable steps have been taken to provide the data subject with all of the appropriate information concerning:

- The purpose and possible outcomes of the proposed processing; and
- Any potential implications for the health of the data subject which may become known as a result of the processing.

Processing has the meaning assigned to it by the Data Protection Acts, 1998 and 2003. Therefore, the definition of processing is extensive. Processing is defined as:-

"Performing an operation or set of operations on the information or data, whether or not by automatic means including:

(a) obtaining, recording or keeping the information or data;
(b) collecting, organising, sharing, altering or adapting the information or data;
(c) retrieving, consulting or using the information or data;
(d) disclosing the information or data by transmitting, disseminating or otherwise making it available or;
(e) aligning, combining, blocking, erasing or destroying the information or data."

Therefore, researchers have a legal obligation to inform each study participant of the nature and purpose of the genetic testing; any potential implications for the health of the individual which may become known as a result of the testing and processing of genetic data and the purpose and possible outcomes of the proposed processing of genetic data.

The HSE National Consent Policy addresses genetic testing in Section 6. It recommends that researchers must formulate a strategy regarding third party disclosure in particular to family members. Results of genetic research might create a need for alternative life decisions, e.g. production, dietary modification and career choices.

When participants or their relatives are to be informed about genetic data the disclosure strategy should provide access to genetic and clinical advice/counseling or clearly recommend to participants that they may seek these services. Advice of the results needs to include a clear explanation of the difference between research and clinical testing and clarify the need for the clinical confirmation of research results by an accredited laboratory.

When people are asked to consent to collection of genetic material or data for research they should be advised:

- that by its nature, genetic material is in principle identifiable, even if personal identifiers are not collected or are removed
- That they are free to decline participation without giving reasons
- About arrangements to ensure the privacy and confidentiality of their genetic data with regard to both family members and others
- Whether the research may reveal information of potential importance to their future health, or the future health of their blood relatives
- That a genetic test may reveal unexpected relationships, such as non-paternity (i.e. a different biological father); and
- That, if it is proposed to approach blood relatives, consent to do so will first be sought from the participant.

Identifiers of genetic material or related data:

- Should not be removed without the consent of participants, if removal would make it difficult to communicate personal results; and
- Should be removed if participants request it, provided they have been informed that the material or data would remain potentially identifiable
- Researchers should not transfer genetic material or related data to any researcher not engaged in the research project unless:
    - Where the material of data is identifiable, participants have been informed about the transfer and have explicitly consented to it; or
    - A REC has judged that the conditions for transfer have been met"[40])

[40] HSE National Consent Policy (May 2013), Pages 79-80

Yes / No

Action: If you chose 'no' please delete F5.2 (b).

F5.2 (b) If yes, **please set out the steps that will be taken and the information that will be provided to study participants prior to genetic testing and processing of genetic data in relation to any potential implications for the health of the study participant which may become known as a result of the genetic testing and the processing of genetic data.**

[TYPE ANSWER]

F5.3 (a) Please set out the strategy and arrangements that will be in place to address any significant results or information arising from the genetic testing or processing of genetic data with the study participant.

[TYPE ANSWER]

F5.3 (b) What strategy / arrangements will be in place regarding third party disclosure, in particular, to family members or others?

[TYPE ANSWER]

F5.4 Please set out what arrangements will be in place to ensure the privacy and confidentiality of study participants' genetic data throughout the life cycle of the research.

[TYPE ANSWER]

F6 COMMERCIAL VALUE

F6.1 (a) Will the human biological material in this research study or the data derived from the analysis of the human biological material be commercially valuable or is there the possibility that it will become commercially valuable? ("Researchers should discuss with research participants the potential commercial uses of their biological material, and also make clear that they will not be entitled to share in any profits that might ensue from their biological material. Donors must be allowed to withhold their consent for commercial use of products developed from their biological material, as an exercise of control over the terms and conditions of their participation in the research. Disclosure of potential commercial applications is further indicated because of the practical consequences for research if people come to distrust doctors and researchers because they feel they were deceived or treated unjustly."

Human Biological Material: Recommendations for Collection, Use and Storage in Research 2005)

Yes / No

Action: If you chose 'no' please delete F6.1 (b)

F6.1 (b) If yes, **please elaborate.** (It is important that this information should be prominently placed in any Information Leaflets or Consent Forms)

[TYPE ANSWER]

SECTION G RADIATION

G1 RADIATION – GENERAL

"10.1. Medical exposure for biomedical and medical research shall not be permitted save in accordance with such criteria as may be directed by the Medical or Dental Councils and approved by the local medical ethics committee.

10.2. Without prejudice to the generality of paragraph 10.1, the practitioner shall ensure that for each biomedical and medical research project each participating individual shall participate voluntarily, the practitioner shall seek where practicable to obtain previous diagnostic information or medical records relevant to the individual, that the individual is informed about the risks of this exposure and that he or she gives his or her informed consent in writing and that a dose constraint is established for that individual.

10.3. In the case of patients who voluntarily accept to undergo an experimental diagnostic or therapeutic practice and who are expected to receive a diagnostic or therapeutical benefit from this practice, the target levels of doses shall be planned on an individual basis by the practitioner"

Communities (Medical Ionising Radiation Protection) Regulations, 2002 (S.I. No. 478 of 2002)

G1.1 (a) Does this study / trial involve exposure to radiation? Yes / No

Action: If you chose 'no' to Question G1.1. (a) please delete all remaining questions in section G and all sub-sections of section G

G1.1 (b) If yes, **please specify:**

i) Exposure to radioactive materials

(Radioactive materials can be administered, either by injection, inhalation or oral administration. One diagnostic example of the use of radioactive materials would be the use of radioactive iodine in the imaging of the thyroid gland.

A therapeutic example would be the use of radioactive materials to kill cancerous tissue, reduce the size of a tumour, or reduce pain e.g. teletherapy (an intense beam of radiation), brachytherapy (surgical implant or injection of radioactive materials), and therapeutic nuclear medicine (high doses of radioactive material ingested or injected). An example of therapeutic nuclear medicine would be the use of radioactive iodine to destroy or shrink a diseased thyroid.)

Yes / No

ii) Therapeutic ionising radiation

(An example of therapeutic ionising radiation is radiotherapy or radiation treatment)

Yes / No

iii) Diagnostic ionising radiation

(Examples of diagnostic ionising radiation are x-rays and CT scans, but not MRI scans or ultrasounds)

Yes / No

iv) Other

(Other forms of radiation, for example, environmental or incidental)

Yes / No

Details: [TYPE ANSWER]

G1.2 (a) Does this study / trial involve ADDITIONAL radiation exposure other than normally received as part of standard care? Yes / No

Action: If you chose 'no' please delete Question G1.2 (b)

G1.2 (b) If yes, **please elaborate.**

(Please elaborate in simple terms e.g. research participants will undergo one additional x-ray / CT scan. Please state a reasonable estimate of the total research protocol dose from the exposure and what component of this is the additional dose over and above standard practice, and state the risks associated with this dose. It is advisable to cross-check your response to Question D1 to ensure consistency.
NOTE: For radiotherapy/radionuclide studies the applicant may refer to details as outlined in the dose/risk assessments in sub-section G2 and sub-section G3 respectively.)

[TYPE ANSWER]

G1.3 Please specify if this study is due to take place at a: -

- **i) Radiation Oncology Unit** Yes / No
- **ii) Diagnostic Imaging Facility** Yes / No
- **iii) Clinical Laboratory** Yes / No
- **iv) Academic Research Centre** Yes / No
- **v) Other** Yes / No **Details:** [TYPE ANSWER]

G1.4 Has each study site/institution in the Republic of Ireland been licensed by the Radiation Protection Society of Ireland?

"The RPII is the competent authority in relation to the protection of workers and members of the public from the harmful effects of exposure to ionising radiation. By law, all practices which use radioactive sources and/or irradiating apparatus (such as an X-ray unit) must hold a valid licence from the RPII, unless they have been exempted" -The Radiation Protection Institute of Ireland

Yes / No

IMPORTANT NOTE PRIOR TO COMPLETING SECTIONS G2, G3 & G4:

IT IS ADVISABLE TO DISCUSS THE PROPOSED RESEARCH STUDY AT AN EARLY STAGE WITH A MEDICAL PHYSICIST AND A RADIATION ONCOLOGIST WHO SHOULD CARRY OUT THE ASSESSMENTS REQUIRED AS PART OF SECTIONS G3 & G4.

G2 RADIOTHERAPY TRIALS

(THE PRINCIPAL INVESTIGATOR FOR EXPERIMENTAL RADIOTHERAPY TRIALS INVOLVING PATIENTS MUST be A RADIATION ONCOLOGIST. Please revisit responses in Section A if applicable.)

(It is recognised however that rare exceptions will occur to the above rule, for example in a dermatology trial where radiotherapy is administered by a radiation therapist and overseen by a dermatologist, it may be inappropriate to name a radiation oncologist as the principal investigator. Nevertheless, as both a medical physicist and a radiation oncologist are required to carry out the assessments required as part of Sections G2 and G4, at the very least, a radiation oncologist should be listed as a co-investigator in such a trial.)

G2.1 Does the study/trial involve exposure of patients to radiotherapy? Yes / No

Action: If you chose 'no' please delete all remaining questions in Section G2

G2.2 (a) Is the planned radiotherapy part of standard treatment or is it experimental in terms of dose / technique / rationale?

Standard Treatment / Experimental

Action: If you chose 'Standard' please delete Section G2.5

G2.2 (b) If experimental, **please elaborate.**

(Itemise what components of radiotherapy treatment/technique/technology is non-standard: i.e. localisation, verification, imaging, planning, dose, delivery and/or immobilisation)

[TYPE ANSWER]

G2.3 <u>IN RELATION TO THE RADIOTHERAPY PLEASE PROVIDE DETAILS OF THE FOLLOWING:</u>

G2.3 (a) Dose Delivery Technique to be used, e.g. 3-DCRT (3-dimensional conformal radiation therapy), IMRT (intensity modulated radiation therapy).
(Be as specific as possible e.g. fixed gantry IMRT -vs- VMAT. If different techniques are to be used then all must be listed.)

[TYPE ANSWER]

G2.3 (b) Imaging/Verification Technique to be used, e.g. IGRT (image guided radiation therapy), etc.
(Pease include your IGRT protocol for this trial i.e. number of scans, tolerance, correction strategy etc.)

[TYPE ANSWER]

G2.3 (c) <u>Radiation treatment schedule:</u>

(i) Total dose:

[TYPE ANSWER]

(ii) Dose per fraction

[TYPE ANSWER]

(iii) Number of fractions per day

[TYPE ANSWER]

G2.3 (d) Expected spectrum of acute and long-term radiation-induced side effects
(Please crosscheck this with information provided in the patient information leaflet for completeness.)

[TYPE ANSWER]

G2.4 RADIOTHERAPY PLANNING

G2.4 (a) Planning Volumes of interest (tumour related volume and organs at risk)

[TYPE ANSWER]

G2.4 (b) Planning Dose Volume Constraints (DVCs) for organs at risk (OARs). (Please ensure all OARs have a DVC.)

[TYPE ANSWER]

G2.4 (c) Details of patient positioning / set-up / immobilisation, inclusive of pre-treatment preparation e.g. bladder filling protocol, IV contrast etc.

[TYPE ANSWER]

G2.4 (d) Details of radiotherapy plan evaluation parameters (i.e. planning target volume [PTV] coverage)

[TYPE ANSWER]

G2.4 (e) What toxicity scoring criteria are to be used?

[TYPE ANSWER]

G2.5 <u>For experimental radiotherapy</u>, please provide the following information:

(a) Standard alternatives. Please ensure to detail and contrast the experimental protocol with 'standard' therapy.

[TYPE ANSWER]

(b) Potential additional risks/toxicities associated with the <u>experimental</u> protocol.

(This should include a discussion of degree of increased risk of secondary cancer.)

[TYPE ANSWER]

G2.6 (a) Radiotherapy quality assurance at delivery:
Please describe the quality assurance programme i.e. PHYSICS quality assurance (beam and dose).

(Please indicate what dosimetry protocols are followed. Also describe the machine QA recommendations followed, indicating the level of compliance i.e. partially or completely. Please give details of participation in external dose audits, either in a formal or informal basis.)

[TYPE ANSWER]

G2.6 (b) Radiotherapy quality assurance at delivery:
Please describe the quality assurance programme i.e. CLINICAL quality assurance.

(Outline patient setup tolerances and correction strategies, the type and frequency of the set-up verification methods used, and details of in-vivo dose measurements taken.)

[TYPE ANSWER]

G2.7 Clinical Monitoring/Assessment during radiotherapy and supportive care: please provide a detailed summary of the clinical monitoring of patients included in the study / trial.

(Indicate how often patients are reviewed on-treat and by whom. Is a questionnaire used? What tests are monitored (e.g. full blood count) during RT? What treatment may be recommended for anticipated side-effects?)

[TYPE ANSWER]

G2.8 Criteria for Radiotherapy Adverse Event Reporting

(To include the definition of a serious adverse event (SAE) and any protocol specific reporting exceptions)

[TYPE ANSWER]

G3 RADIONUCLIDES

"A Radionuclide is an isotope of artificial or natural origin that exhibits radioactivity. Radionuclides serve as agents in nuclear medicine and genetic engineering, play a role in computer imaging for diagnosis and experiment, and account for a percentage of background radiation to which humans are exposed. In cancer therapy, radionuclides that localise to certain organs (e.g. radioactive iodine or gallium) deliver cytotoxic radiation doses to tumours. Similarly, radionuclides can be yoked to monoclonal antibodies engineered to attach specific populations of cancerous cells. In positron emission tomography, glucose molecules tagged with radionuclides are injected into the bloodstream. The gamma radiation emitted by the decay of radionuclides reveals areas of active glucose uptake and thus offers a guage of cell metabolism and function."

Biology Online Dictionary

Please complete the tables below for __each radionuclide__ to be administered

G3.1 (a) Will any of the study/trial participants be patients? Yes / No

Please ensure to choose 'no' if you chose 'no' to the relevant Question in Subsection C5 (Patients)

Action: If you chose 'no' please delete the table which follows:

Details of patients to be studied				
Number (whole study)	**Age range**	**Sex**	**Clinical condition**	**Total effective or target tissue dose per individual**
[TA]	[TA]	[TA]	[TYPE ANSWER=TA]	[TA]

Action: Please add rows to the table above to add a radionuclide.

G3.1 (b) Will any of the study/trial participants be healthy volunteers? Yes / No

Please ensure to choose 'no' if you chose 'no' to the relevant question in Subsection C5 (Healthy Volunteers)

Action: If you chose 'no' please delete the table which follows:

Details of healthy volunteers to be studied			
Number (whole study)	**Age range**	**Sex**	**Total effective dose per individual**
[TA]	[TA]	[TA]	[TYPE ANSWER=TA]

Action: Please add rows to the table above to add a radionuclide.

__G3.2 Dose and Risk Assessment__

Please note, special attention must be paid to pregnant/potentially pregnant women or those who are breast feeding or other potentially vulnerable groups.

G3.2 (a) What is the total research protocol dose from the exposure (if any)?

[TYPE ANSWER]

G3.2 (b) What component of this is the additional dose over and above standard practice? What are the risks associated with this dose?

[TYPE ANSWER]

__G3.2 (c) DECLARATION BY MEDICAL PHYSICIST (for Section G3 Radionuclides)__

I am satisfied that the information in sub-section G3.1 and the assessment in sub-section G3.2 provide a reasonable estimate of the ionising radiation exposure planned in this research and the associated risks.

Signature: ______________________ **Date:** ______________________

Please Print Name: ______________________

G4 CLINICAL ASSESSMENT

Please note, special attention must be paid to pregnant/potentially pregnant women or those who are breast feeding or other potentially vulnerable groups.

G4.1 Will the exposure exceed the exposure that might be received as part of normal care? Yes / No

G4.2 Assessment of additional exposure

G4.2 (a) Please explain how the planned exposure compares with normal practice and assess whether it is appropriate, using language comprehensible to a lay person. Consideration should be given to the specific objectives of the exposure, the characteristics of participants, the potential diagnostic or therapeutic benefits to the participant, the potential benefits to society, the risk to the participant and the availability of alternative techniques involving less, or no, ionising radiation.

[TYPE ANSWER]

Please refer to your answer to Question C5.3 before answering the next question.

G4.2 (b) If pregnant or breastfeeding mothers are to be studied **give reasons and details of special radiation protection measures to be taken.**

[TYPE ANSWER]

G4. 3 DECLARATION BY RADIATION ONCOLOGIST

I am satisfied that the exposure to ionising radiation planned in this research study (as defined in sub-section G2 and/or G3) is reasonable and that the risks are adequately described in the participant information sheet for the study.

Signature: ______________________ **Date:** ______________________

Please Print Name: ______________________

SECTION H MEDICAL DEVICES

H1 (a) Is the focus of this study/trial to investigate/evaluate a medical device? (The term 'medical device' covers all products, except medicines, used in healthcare for the diagnosis, prevention, monitoring or treatment of illness or disability. It includes contact lenses and condoms; heart valves and hospital beds; resuscitators and radiotherapy machines; surgical instruments and syringes; wheelchairs and walking frames or other assistive technology products; pregnancy tests, blood glucose monitors and pacemakers - many thousands of items used each and every day by healthcare providers and patients. Medical devices do not include ambulance vehicles, general workshop equipment such as power or machine tools, or general purpose laboratory equipment. Pre-filled devices, for example, drug inhalers, syringes and certain other drug / device combinations are classed as medicines, not medical devices. Health Products Regulatory Authority) Yes / No

If you are uncertain as to the definition of a medical device, please contact the Health Products Regulatory Authority

Action: If you chose 'No' please delete all remaining questions in Section H.

H1 (b) If yes, **what is the name of the medical device or device nomenclature (system of naming the medical device)?**

[TYPE ANSWER]

H1 (c) If yes, **please provide a general description of the medical device.**

[TYPE ANSWER]

H2 (a) Does the device have a CE mark? (CE stands for 'Conformité Européene' and is mandatory conformity mark on many products placed on the single market in the European Economic Area. If the device has a CE Mark, please ensure to enclose the relevant certificate for review.) Yes / No

Action: If you chose 'no' please delete question H2 (b) (c) (d);
Action: If you chose 'yes' please delete question H2 (e)

H2 (b) If the device has a CE Mark, is it proposed to use the device within the terms of its CE mark or outside the terms of its CE mark? Within / Outside

Action: If you chose 'within' please delete question H2 (c);

H2 (c) If outside, **please elaborate:**

[TYPE ANSWER]

H2 (d) CE MARK NUMBER: (This is a unique 4 digit code which refers to the 'Notifying Body' which awarded the CE Mark and can be found in the bottom right hand corner of the CE Mark)

[TYPE NUMBER]

H2 (e) If the device does not have a CE Mark, is this study being undertaken for the purposes of obtaining a CE mark? Yes / No

H3 (a) Is this an application to conduct a 'clinical investigation of a medical device'?

("The term clinical investigation is defined in ISO Standard 14155, 'Clinical Investigations of Medical Devices for Human Subjects as any designed and planned systematic study in human subjects undertaken to verify the safety and/or performance of a specific device. The term 'clinical investigation' rather than clinical trial is generally used when referring to device-related research."

- HPRA Guide to Ethics Committees on Clinical Investigation of Medical Devices (2010))

Yes / No

H3 (b) If yes, **will the Medical Devices section of the Health Products Regulatory Authority (HPRA) be reviewing this study?** (Please note that review by the HPRA will generally be required if you completed H2 (c) or stated 'yes' in response to H2 (e) above. For other instances when HPRA review applies, please refer to the Medical Devices Section of the Health Products Regulatory Authority website.) Yes / No

SECTION I MEDICINAL PRODUCTS / COSMETICS / FOOD AND FOODSTUFFS

I.1 NON-INTERVENTIONAL TRIALS OF MEDICINAL PRODUCTS

Clinical trials of medicinal products that require authorisation in accordance with SI 190 of 2004 will not be accepted on this application form. You are referred to the Department of Health Application Form should you wish to make an application for the ethical review of a clinical trial of a medicinal product.

I 1.1 (a) Does this study involve a medicinal product? (Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis. Further information on the definition of a medicinal product is provided in the Irish Medicines Board Guide to the Definition of a Human Medicine.) Yes / No

Action: If you chose 'No' please delete Questions I 1.1 (b), I 1.2 (a) and I 1.2 (b)

IMPORTANT NOTE: If you chose 'No' to Question I 1.1. (a) this study is not a 'clinical trial of a medicinal product' and you are completing the correct application form.

I 1.1 (b) If yes, **please state:**

I. the trade name of the medicinal product:
[TYPE ANSWER]

II. the name of the active substance: (To source the active substance: see the Human Medicines Product List located in the Health Products Regulatory Authority (HPRA) website.)
[TA]

III. the formulation: (To source the formulation, see the Human Medicines Product List.)
[TA]

IV. the authorisation / product number: (To source the authorisation / product number, see the Human Medicines Product List. Please note if there is no product authorisation number, then the study is an interventional trial)
[TA]

Action: Please copy and paste the headings above to add a medicinal product.

Before responding the next question, please log on to the European Commission Website scroll to Chapter V: Additional Information 'Questions and Answers Document' and refer to the algorithm appended to this document.

If you have difficulty in locating this algorithm, a copy is also placed at the rear of this Guidance Manual for ease of reference (See Appendix One)

If after referring to this algorithm, you remain unsure if this study is a clinical trial of a medicinal product or a non-interventional trial of a medicinal product, please send a brief summary of the study to the Health Products Regulatory Authority requesting their advice (clinicaltrials@hpra.ie). If the definition of non-interventional is not met, the study should be considered interventional and requires authorisation in accordance with SI No 190 of 2004.

I 1.2 (a) Is this an application to conduct a non-interventional trial of a medicinal product?

(“non-interventional trial’: a study where the medicinal product(s) is (are) prescribed in the usual manner in accordance with the terms of the marketing authorisation, where the assignment of the patient to a particular therapeutic strategy is not decided in advance by a trial protocol but falls within current practice, where the prescription of the medicine is clearly separated from the decision to include the patient in the study and where no additional diagnostic or monitoring procedures shall be applied to the patients and epidemiological methods shall be used for the analysis of collected data.)

Yes / No

I 1.2 (b) Is this trial a <u>post-authorisation safety study</u>?

(A pharmacoepidemiological study or a clinical trial carried out in accordance with the terms of the marketing authorisation, conducted with the aim of identifying or quantifying a safety hazard relating to an authorised medicinal product. Post authorisation safety studies fall under the definition of non-interventional trials and should be conducted in accordance with the requirements outlined in Volume 9A of the Rules Governing Medicinal Products in the European Union, Guidelines on Pharmacovigilance for Medicinal Products for Human Use available from the European Commission Website. Scroll to Volume 9A)

Should you answer ‘yes’ to question I 1.2 (b), the trial can be notified to the Irish Medicines Board.

Yes / No

<u>IMPORTANT NOTE:</u> If you responded ‘No’ to Question 1.2 (a) and ‘No’ to Question 1.2 (b) there is a strong possibility that this study is a clinical trial of a medicinal product. Please liaise with the Health Products Regulatory Authority if you are unsure. You are referred to the Department of Health Application Form should you wish to make an application for the ethical review of a clinical trial of a medicinal product.

I.2 COSMETICS

I 2.1 (a) Does this study involve a <u>cosmetic</u>? (“any substance or preparation intended to be placed in contact with the various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance and/or correcting body odours and/or protecting them or keeping them in good condition”

Council Directive 76/768/EEC and amendments.)[XVII]

Yes / No

Action: If you chose ‘no’ please delete Question I 2.1 (b)

I 2.1 (b) If yes, **please state:**

I. the trade name of the cosmetic:

[TYPE ANSWER]

II. **the ingredients/composition:** (the Cosmetics Directive sets out a list of substances which cannot be included in the composition of cosmetic products (Annex II) and a list of substances which cosmetic products may contain only under the restrictions and conditions laid down (Annex III), and lists of colourings (Annex IV), preservatives (Annex VI) and UV filters (Annex VII) permitted in cosmetic products. The Directive also outlines the requirements for labelling)

[TA]

Action: Please copy and paste the headings above to add a cosmetic.

I.3 FOOD AND FOOD SUPPLEMENTS

I 3.1 (a) Does this study involve <u>food or food supplements</u>? "food supplements" means foodstuffs the purpose of which is to supplement the normal diet and which are concentrated sources of nutrients or other substances with a nutritional or physiological effect, alone or in combination, marketed in dose form, namely forms such as capsules, pastilles, tablets, pills and other similar forms, sachets of powder, ampoules of liquids, drop dispensing bottles, and other similar forms of liquids and powders designed to be taken in measured small unit quantities;
(b) "nutrients" means the following substances:
(i) vitamins,
(ii) minerals.

Yes / No

Action: If you chose 'no' please delete Question I 3.2 (b)

I 3.2 (b) If yes, **please elaborate:**

[TYPE ANSWER]

IMPORTANT NOTE: a food supplement that is used in a trial to treat or prevent disease in human beings may be considered a medicinal product and as such may require authorisation in accordance with SI 190 of 2004. Further information on the definition of a medicinal product is provided in the Health Products Regulatory Authority Guide to the Definition of a Human Medicine.

SECTION J INDEMNITY AND INSURANCE

J1 Please confirm and provide evidence that appropriate insurance/indemnity is in place for this research study <u>at each site.</u>
(You have listed the sites where this study will take place in Section A. It is important that the research work at each of these sites has appropriate insurance/indemnity provisions in place. Please liaise with the sites to assess what insurance they have in place and what insurance the research study is required to supply, and provide copies of any relevant Certificates of Insurance/Indemnity, where applicable.

- At a minimum work at every site must be covered by some form of a Public Liability insurance policy.
- Where there are clinical risks associated with the study then the work at each site must be covered by some form of a medical / clinical malpractice insurance policy.
- Public health facilities will be covered for clinical risks by the state sponsored Clinical Indemnity Scheme (CIS).
- Pay particular attention to any sites which are PRIVATE healthcare facilities e.g. private hospitals and general practice. These facilities are outside of the cover provided by the CIS and they must have their own privately held medical / clinical malpractice insurance policy.

If you are uncertain whether the healthcare facility is PRIVATE or PUBLIC, contact the site for clarification.

Please also take note of any expiry dates on any Certificates provided, and ensure that insurance/indemnity will last for the duration of this study / be renewed when necessary)

[TYPE ANSWER]

J2 Please confirm and provide evidence that appropriate insurance/indemnity is in place for this research study <u>for each investigator.</u>
(You have listed the investigators who will be involved in this study in response to Section A. It is important that each of these investigators has appropriate insurance / indemnity in place either individually or as provided by their hosting/employing institution. Please liaise with the investigators to assess what insurance they have in place, and provide copies of any relevant Certificates of Insurance/Indemnity.

- At a minimum all persons must be covered by some form of a Public Liability insurance policy.
- Where there are clinical risks associated with the study then each person engaging in clinical activities must be covered by some form of a medical / clinical malpractice insurance policy.

- Persons employed via the public health system and operating within same will be covered for clinical risks by the state sponsored Clinical Indemnity Scheme (CIS).
- Pay particular attention to any investigators who work in PRIVATE capacity e.g. general practitioners, allied healthcare professionals with PRIVATE PRACTICES. These persons will need to carry their own private clinical / medical malpractice cover.
- Investigators who are in doubt should seek advice from their employer or insurer.

Please also take note of any expiry dates on any Certificates provided, and ensure that insurance/indemnity will last for the duration of this study / be renewed when necessary)

[TYPE ANSWER]

Note: there may be significant crossover between Answers to J1 and J2.

J3.1 Please give the name and address of the organisation / or individual legally responsible for this research study?

(Please give some thought before answering this question, as the answer will vary considerably from study to study.

Responsibility in the context of this question means responsibility for 'the initiation and management of this research study.'

The person responsible may be Principal Investigator himself / herself.

The organisation responsible may be a pharmaceutical company, a medical device company, a university, a charity, or the organisation in which the Principal Investigator works, for example.

If the Certificate of Insurance for this person / organisation has not already been provided in response to previous answers in this section, this should be provided now.)

[TYPE ANSWER]

Action: If the answer to Question J3.1 was an individual, please delete question J3.2

J3.2 Where an organisation if legally responsible, **please specify if this organisation is:**

A pharmaceutical company Yes / No
A medical device company Yes / No
A university Yes / No
A registered charity Yes / No
Other Yes / No **If yes, please specify:** Answer

J3.3 Please confirm and provide evidence of any specific additional insurance / indemnity arrangements which have been put in place, if any, by this organisation / or individual for this research study?

(Additional indemnity arrangements would include entering into a contract of indemnity with the site, or ensuring that product liability is in place where required, or the taking out of additional insurance.
Please ensure that you have provided a copy of any certificates or contracts referred to in your response to this question)

[TYPE ANSWER]

SECTION K COST AND RESOURCE IMPLICATIONS, FUNDING AND PAYMENTS

K1 COST AND RESOURCE IMPLICATIONS

K1.1 Please provide details of all cost / resource implications related to this study (e.g. staff time, office use, telephone / printing costs etc.) (This refers to all cost and resource implications both for the researcher and for the institution(s) at which the research study is proposed to take place.)

[TYPE ANSWER]

K2 FUNDING

K2.1 (a) Is funding in place to conduct this study?
(Non-disclosure of funding will result in revocation of ethical approval) Yes / No

Action: If you chose 'yes' please delete question K2. 1 (b); If you chose 'no', please delete question K2.1 (c).

K2.1 (b) If no, **has funding been sought to conduct this study? From where? Please elaborate.** (An important part of any research study is ensuring that funding is in place to conduct it)

[TYPE ANSWER]

K2.1 (c) If yes, **please state the source of funding (industry, grant or other), the name of the funder, the amount of funding and duration of funding.**

Source of funding (industry, grant or other):
[TYPE ANSWER]
Name of Funder:
[TYPE ANSWER]
Amount of Funding:
[TYPE ANSWER]
Duration of Funding
[TYPE ANSWER]

K2.1(d) Please provide additional details in relation to management of funds. (Schedule of Payments, how payments will be made, how payments will be phased, name of bank account into which funds will be lodged)

[TYPE ANSWER]

K2.1(e) Is the study funded by a 'for profit' organisation? Yes / No

K2.2 (a) Do any conflicts of interest exist in relation to funding or potential funding? ("53.6 If you are paid, directly or indirectly, by pharmaceutical, medical device or other commercial companies or organisations to conduct medical research, you must make sure that such payment does not influence your study design or interpretation of research data."
"53.7 If you receive payment, directly or indirectly, from pharmaceutical, medical device or other commercial companies or organisations in connection with medical research, you must address any potential conflict of interest arising from such payment and make an appropriate disclosure in any publication of research results."
Guide to Professional Conduct and Ethics for Registered Medical Practitioners 2009.)

See also the International Committee of Medical Journal Editors for more information on conflicts of interest. Researchers will be required to disclose all conflicts of interest prior to publication.) Yes / No

Action: If you chose ‘no’, please delete question K2.2 (b)

K2.2 (b) If yes, **please elaborate.**
[TYPE ANSWER]

K3 PAYMENTS TO INVESTIGATORS

K3.1 (a) Will any payments (monetary or otherwise) be made to investigators? Yes / No

Action: If you chose ‘no’, please delete question K3.1 (b)

K3.1 (b) If yes, **please provide details of payments (including amount).**
[TYPE ANSWER]

K4 PAYMENTS TO PARTICIPANTS

K4.1 (a) Will any payments / reimbursements (monetary or otherwise) be made to participants? (There may be instances where research participants will be paid for any inconvenience and time given to the study. Payments may be financial or non-financial, e.g. entry into prize draws, gifts vouchers, book tokens. Payment that is disproportionate to the time involved or is likely to encourage participants to take risks, is ethically unacceptable. The timing of payments must be such that they do not constitute under inducement.

Where researchers wish to offer payment to prospective research participants, they must justify to a REC their reasons as well as the amount/reward being offered. Payments or rewards that undermine reward being offered. Payments or rewards that undermine a person's ability to exercise free choice would be deemed to invalidate his/her consent. - HSE National Consent Policy Page 79 – 80

Research participants may be reimbursed for lost earnings, travel costs and other expenses incurred. Another acceptable form of reimbursement might be the provision of free medicines services. Compensation for the time and inconvenience involved in research participation (e.g. payment at minimum wage level) might also be permissible as research participants should not be expected to bear the costs that relate to taking part in a study. However, it is important to note that compensation is understood to mean a recompense for losses sustained e.g. time away from work.

Any reimbursements or compensation that might be offered to prospective participants should first be approved by a REC in order to ensure that they are measurable and do not reflect any undue inducement by encouraging people to act against their better judgment or take unnecessary risks.)
Yes / No

Action: If you chose ‘no’, please delete question K4.1 (b)

K4.1 (b) If yes, **please provide details of payments / reimbursements (including amount).**
[TYPE ANSWER]

SECTION L ADDITIONAL ETHICAL ISSUES

L1 (a) Does this project raise any additional ethical issues?
(It may be prudent to think carefully before automatically replying 'no' in response to this question.) Yes / No

If you chose 'no' please delete Question L1 (b)

L1 (b) If yes, please identify any particular additional ethical issues that this project raises and discuss how you have addressed them.

[TYPE ANSWER]

Please ensure this application form is fully completed as incomplete submissions will not be reviewed

APPENDIX ONE: EUROPEAN COMMISSION ALGORITHM REQUIRED TO ANSWER QUESTION I 1.2 (a)

Q I 1.2 (a) IS IT A CLINICAL TRIAL OF A MEDICINAL PRODUCT?

This algorithm and its endnotes will help you answer that question. Please start in column A and follow the instructions. Additional information is provided in the notes at the end of the table. If you have doubts about the answer to any of the questions contact the clinical trials unit of your competent authority.

A	B	C	D	E
A CLINICAL TRIAL OF A MEDICINAL PRODUCT?				**A NON-INTERVENTIONAL CLINICAL TRIAL?**
Is it a medicinal product (MP)?[i]	**Is it not a medicinal product?**	**What effects of the medicine are you looking for?**	**Why are you looking for those effects?**	**How are you looking for those effects?**
If you answer no to <u>all</u> the questions in column A, the activity is not a clinical trial on a MP. If you answer yes to <u>any</u> of the questions below go to column B.	If you answer yes to the question below in column B the activity is not a clinical trial on a MP. If you answer no to this question below go to column C.	If you answer no to <u>all</u> the questions in column C the activity is not a clinical trial under the scope of Directive 2001/20/EC. If you answer yes to <u>any</u> of the questions below go to column D.	If you answer no to <u>all</u> the questions in column D the activity is not a clinical trial under the scope of Directive 2001/20/EC. If you answer yes to <u>any</u> of the questions below go to column E.	If you answer yes to <u>all</u> these questions the activity is a non-interventional trial which is outside the scope of Directive 2001/20/EC. If your answers in columns A,B,C & D brought you to column E and you answer no to <u>any</u> of these questions the activity is a clinical trial within the scope of the Directive.
A.1 Is it a substance[ii] or combination of substances presented as having properties for treating or preventing disease in human beings ? A.2 Does the substance function as a medicine? i.e. can it be administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action or to making a medical diagnosis or is otherwise administered for a medicinal purpose? A.3 Is it an active substance in a pharmaceutical form?	B.1 Are you <u>only</u> administering any of the following substances? • Human whole blood[iii]; • Human blood cells; • Human plasma; • Tissues except a somatic cell therapy medicinal product[iv]; • A food product[v] (including dietary supplements) not presented as a medicine; • A cosmetic product[vi] • A medical device	C.1 To discover or verify/compare its clinical effects? C.2 To discover or verify/compare its pharmacological effects, e.g. pharmacodynamics? C.3 To identify or verify/compare its adverse reactions? C.4 To study or verify/compare its absorption, distribution, metabolism or excretion?	D.1 To ascertain or verify/compare the efficacy[vii] of the medicine? D.2 To ascertain or verify/compare the safety of the medicine?	E.1 Is this a study of one or more medicinal products, which have a marketing authorisation in the Member State concerned? E.2 Are the products prescribed in the usual manner in accordance with the terms of that authorisation? E.3 Does the assignment of any patient involved in the study to a particular therapeutic strategy fall within current practice and is not decided in advance by a clinical trial protocol[viii]? E.4 Is the decision to prescribe a particular medicinal product clearly separated from the decision to include the patient in the study? E.5 Will no diagnostic or monitoring procedures be applied to the patients included in the study, other than those which are applied in the course of current practice? E.6 Will epidemiological methods be used for the analysis of the data arising from the study?

[i] Article 1.2 of Directive 2001/83/EC is replaced by Article 1.1 of Directive 2004/27/EC which provides the definition of "medicinal product" which applies for the purposes of Directive 2001/20/EC.

[ii] Substance is any matter irrespective of origin e.g. human, animal, vegetable or chemical that is being administered to a human being.

[iii] This does not include derivatives of human whole blood, human blood cells and human plasma that involve a manufacturing process.

[iv] Somatic cell therapy medicinal products use somatic living cells of human (or animal) origin, the biological characteristics of which have been substantially altered as a result of their manipulation to obtain a therapeutic, diagnostic or preventative effect (in humans) through metabolic, pharmacological and immunological means.

[v] Any ingested product which is not a medicine is regarded as a food. A food is unlikely to be classified as a medicine unless it contains one or more ingredients generally regarded as medicinal and indicative of a medicinal purpose.

[vi] The Cosmetic Directive 76/768/EC, as amended harmonises the requirements for cosmetics in the European Community. A "cosmetic product "means any substance or preparation intended for placing in contact with the various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and mucous membranes of the oral cavity with the view exclusively or principally to cleaning them, perfuming them or protecting them in order to keep them in good condition, change their appearance or correct body odours.

[vii] Efficacy is the concept of demonstrating scientifically whether and to what extent a medicine is capable of diagnosing, preventing or treating a disease and derives from EU pharmaceutical legislation.

[viii] Assignment of patients to a treatment group by randomisation planned by a clinical trial protocol cannot be considered as current practice.

APPENDIX TWO:

WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI 2013, AS COMPARED TO 2008

(Modifications and insertions highlighted; and compared to previous 2008 wording.
Changes in focus commented on where they appear)

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964
and amended by the:
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
52nd WMA General Assembly, Edinburgh, Scotland, October 2000
53rd WMA General Assembly, Washington DC, USA, October 2002 (Note of Clarification added)
55th WMA General Assembly, Tokyo, Japan, October 2004 (Note of Clarification added)
59th WMA General Assembly, Seoul, Republic of Korea, October 2008
64th WMA General Assembly, Fortaleza, Brazil, October 2013

Preamble

1. The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data.

The Declaration is intended to be read as a whole and each of its constituent paragraphs should be applied with consideration of all other relevant paragraphs.

2. Consistent with the mandate of the WMA, the Declaration is addressed primarily to physicians. The WMA encourages others who are involved in medical research involving human subjects to adopt these principles.

General Principles

3. The Declaration of Geneva of the WMA binds the physician with the words, “The health of my patient will be my first consideration,” and the International Code of Medical Ethics declares that, “A physician shall act in the patient's best interest when providing medical care.”

4. It is the duty of the physician to promote and safeguard the health, well-being and rights of patients, including those who are involved in medical research. The physician's knowledge and conscience are dedicated to the fulfilment of this duty.

5. Medical progress is based on research that ultimately must include studies involving human subjects.

6. The primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments). Even the best proven interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality.

7. Medical research is subject to ethical standards that promote and ensure respect for all human subjects and protect their health and rights.

8. While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects.

[Old wording: In medical research involving human subjects, the well-being of the individual research subject must take precedence over all other interests]

New Focus: rights and interest of the individual research subjects.

9. It is the duty of physicians who are involved in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects. The responsibility for the protection of research subjects must always rest with the physician or other health care professionals and never with the research subjects, even though they have given consent.

10. Physicians must consider the ethical, legal and regulatory norms and standards for research involving human subjects in their own countries as well as applicable international norms and standards. No national or international ethical, legal or regulatory requirement should reduce or eliminate any of the protections for research subjects set forth in this Declaration.

11. Medical research should be conducted in a manner that minimises possible harm to the environment.

[Old wording: Appropriate caution must be exercised in the conduct of medical research that may harm the environment]

12. Medical research involving human subjects must be conducted only by individuals with the appropriate ethics and scientific education, training and qualifications. Research on patients or healthy volunteers requires the supervision of a competent and appropriately qualified physician or other health care professional.

[Old wording: Medial research involving human subjects must be conducted only by individuals with the appropriate scientific training and qualifications…..]

New Focus: training in ethics

13. Groups that are underrepresented in medical research should be provided appropriate access to participation in research.

[Old wording: Populations….]

14. Physicians who combine medical research with medical care should involve their patients in research only to the extent that this is justified by its potential preventive, diagnostic or therapeutic value and if the physician has good reason to believe that participation in the research study will not adversely affect the health of the patients who serve as research subjects.

15. Appropriate compensation and treatment for subjects who are harmed as a result of participating in research must be ensured. [NEW]

New Focus: compensation and treatment of subjects in case of harm.

Risks, Burdens and Benefits

16. In medical practice and in medical research, most interventions involve risks and burdens.

Medical research involving human subjects may only be conducted if the importance of the objective outweighs the risks and burdens to the research subjects.

17. All medical research involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and groups involved in the research in comparison with foreseeable benefits to them and to other individuals or groups affected by the condition under investigation.

[Old wording: communities]

Measures to minimise the risks must be implemented. The risks must be continuously monitored, assessed and documented by the researcher. [NEW]

New Focus: continuous monitoring of risks by the researcher

18. Physicians may not be involved in a research study involving human subjects unless they are confident that the risks have been adequately assessed and can be satisfactorily managed.

When the risks are found to outweigh the potential benefits or when there is conclusive proof of definitive outcomes, physicians must assess whether to continue, modify or immediately stop the study.

[Old wording: Physicians must immediately stop a study when the risks are found to outweigh the potential benefits or when there is conclusive proof of positive and beneficial results]

New Focus: on assessing whether to continue or modify or stop as opposed to stop.

Vulnerable Groups and Individuals

19. Some groups and individuals are particularly vulnerable and may have an increased likelihood of being wronged or of incurring additional harm.

All vulnerable groups and individuals should receive specifically considered protection.

[Old wording: Some research populations are particularly vulnerable and need special protection.]

20. Medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research.

[Old wording: Medical research involving a disadvantaged or vulnerable population or community is only justified if the research is responsive to the health needs and priorities of this population or community and if there is a reasonable likelihood that this population or community stands to benefit from the results of the research.]

New Focus: criteria for inclusion of vulnerable groups.

Scientific Requirements and Research Protocols

21. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and, as appropriate, animal experimentation. The welfare of animals used for research must be respected.

22. The design and performance of each research study involving human subjects must be clearly described and justified in a research protocol.

The protocol should contain a statement of the ethical considerations involved and should indicate how the principles in this Declaration have been addressed. The protocol should include information regarding funding, sponsors, institutional affiliations, potential conflicts of interest, incentives for subjects and information regarding provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study.

In clinical trials, the protocol must also describe appropriate arrangements for post-trial provisions.

[Old wording: The protocol should describe arrangements for post-study access by study subjects to interventions identified as beneficial in the study or access to other appropriate care or benefits.]

Research Ethics Committees

23. The research protocol must be submitted for consideration, comment, guidance and approval to the concerned research ethics committee before the study begins. This committee must be transparent in its functioning, must be independent of the researcher, the sponsor and any other undue influence and must be duly qualified. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards but these must not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration.

[Old wording: The research protocol must be submitted for consideration, comment, guidance and approval to a research ethics committee before the study begins. This committee must be independent of the researcher, the sponsor and any other undue influence. It must take into consideration the laws and regulations of the country or countries.........]

New Focus: transparency, and training

The committee must have the right to monitor ongoing studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse events. No amendment to the protocol may be made without consideration and approval by the committee.

[Old wording: No change to the protocol may be made without consideration and approval by the committee.]

After the end of the study, the researchers must submit a final report to the committee containing a summary of the study's findings and conclusions. [NEW]

New Focus: final report to ethics committee

Privacy and Confidentiality

24. Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information.

Informed Consent

25. Participation by individuals capable of giving informed consent as subjects in medical research must be voluntary. Although it may be appropriate to consult family members or community leaders, no individual capable of giving informed consent may be enrolled in a research study unless he or she freely agrees.

[Old wording: Participation by competent individuals…..]

26. In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post-study provisions [NEW] and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information.

New Focus: post-study provisions

After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed.

All medical research subjects should be given the option of being informed about the general outcome and results of the study.

[Old wording: At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study…..]

New Focus: option to receive results

27. When seeking informed consent for participation in a research study the physician must be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress. In such situations the informed consent must be sought by an appropriately qualified individual who is completely independent of this relationship.

28. For a potential research subject who is incapable of giving informed consent, the physician must seek informed consent from the legally authorised representative. These individuals must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the group represented by the potential subject, the research cannot instead be

performed with persons capable of providing informed consent, and the research entails only minimal risk and minimal burden.

[Old wording: - population]

29. When a potential research subject who is deemed incapable of giving informed consent is able to give assent to decisions about participation in research, the physician must seek that assent in addition to the consent of the legally authorised representative. The potential subject's dissent should be respected.

30. Research involving subjects who are physically or mentally incapable of giving consent, for example, unconscious patients, may be done only if the physical or mental condition that prevents giving informed consent is a necessary characteristic of the research group. In such circumstances the physician must seek informed consent from the legally authorised representative. If no such representative is available and if the research cannot be delayed, the study may proceed without informed consent provided that the specific reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee. Consent to remain in the research must be obtained as soon as possible from the subject or a legally authorised representative.

31. The physician must fully inform the patient which aspects of their care are related to the research. The refusal of a patient to participate in a study or the patient's decision to withdraw from the study must never adversely affect the patient-physician relationship.

32. For medical research using identifiable human material or data, such as research on material or data contained in biobanks or similar repositories, physicians must seek informed consent for its collection, storage and/or reuse. There may be exceptional situations where consent would be impossible or impracticable to obtain for such research. In such situations the research may be done only after consideration and approval of a research ethics committee.

[Old wording: For medical research using identifiable human material or data, physicians must normally seek consent for the collection, analysis, storage and/or re-use. There may be situations where consent would be impossible or impracticable to obtain for such research or would pose a threat to the validity of the research. In such situations the research may be done only after consideration and approval by a research ethics committee.]

New Emphasis: exceptional situations

Use of Placebo

33. The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best proven intervention(s), except in the following circumstances:

Where no proven intervention exists, the use of placebo, or no intervention, is acceptable; or

[Old wording: The use of placebo, or no treatment, is acceptable in studies where no current proven intervention exists; or]

Where for compelling and scientifically sound methodological reasons the use of any intervention less effective than the best proven one, the use of placebo, or no intervention is necessary to determine the efficacy or safety of an intervention

[Old wording: Where for compelling and scientifically sound methodological reasons the use of placebo is necessary to determine the efficacy or safety of an intervention.]

and the patients who receive any intervention less effective than the best proven one, placebo, or no intervention will not be subject to additional risks of serious or irreversible harm as a result of not receiving the best proven intervention.

[Old wording: and the patients who received placebo or no treatment will not be subject to any risk of serious or irreversible harm.]

New Focus: any risks moves to additional risks

Extreme care must be taken to avoid abuse of this option.

Post-Trial Provisions

34. In advance of a clinical trial, sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial. This information must also be disclosed to participants during the informed consent process.

[Old wording: At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study and to share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits.]

New Focus: have a plan from the outset for post-trial access.

Research Registration and Publication and Dissemination of Results

35. Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject.

[Old wording: Every clinical trial must be registered in a publically accessible database before recruitment of the first subject.]

New Focus: all research studies required to register

36. Researchers, authors, sponsors, editors and publishers all have ethical obligations with regard to the publication and dissemination of the results of research. Researchers have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. All parties should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results must be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest must be declared in the publication. Reports of research not in accordance with the principles of this Declaration should not be accepted for publication.

[Old wording: Authors, editors and publishers all have ethical obligations with regard to the publication of the results of research. Authors have a duty…….]

New Focus: broadening of scope to include sponsors etc.

Unproven Interventions in Clinical Practice

37. In the treatment of an individual patient, where proven interventions do not exist or other known interventions have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorised representative, may use an unproven intervention if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. This intervention should subsequently be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information must be recorded and, where appropriate, made publicly

Declaration of Helsinki 2013 downloaded from WMA Website, 27/11/13

APPENDIX THREE TEMPLATE LOCAL CHECKLIST

LOCAL COMMITTEE CHECKLIST:

COMMITTEE CONTACT DETAILS:

Name of Committee:

Contact Person:

Position:

Address:

Tel:

E-Mail:

Website (if any):

COMMITTEE REMIT:

Reviews applications to conduct research in:

SECTIONS OF STANDARD APPLICATION FORM TO BE COMPLETED:

Complete all Sections with the Exception of Sections:

LOCAL REQUIREMENTS (IF ANY):

LOCAL RESTRICTIONS (IF ANY):

FEES:

DOCUMENTS REQUIRED (IF APPLICABLE):

Documents Required:	Number of Copies Required:	Yes / No / N/A	Document Version / Date
Local Checklist			
Standard Application Form			
Local Declaration and Signatory Page			

APPENDIX FOUR TEMPLATE LOCAL DECLARATION AND SIGNATORY PAGE

LOCAL COMMITTEE DECLARATION AND SIGNATORY PAGE:

Name of Committee:

Title of Study:

DECLARATION OF PRINCIPAL INVESTIGATOR:

- The information on this form is accurate to the best of my knowledge and I take full responsibility for it.
-
-
-
-
-
-
-
-
-
-

Name of Principal Investigator: ______________________________________

Signature of Principal Investigator: ____________________________________

Date Proposal Form Submitted: ________/_______/_______

APPENDIX FIVE

LIST OF COMMITTEES USING THE 'STANDARD APPLICATION FORM'

The following Research Ethics Committee (RECs) have independently decided to adopt the Standard Application Form and Guidance Manual:

1. Adelaide and Meath Hospital incorporating the National Children's Hospital / St. James's Hospital
2. Beacon Hospital
3. Beaumont Hospital
4. Bons Secours Health System
5. Children's University Hospital (Temple Street)
6. Connolly Hospital
7. Coombe Women's and Infant's University Hospital
8. Cork Teaching Hospitals
9. Daughters of Charity Services for Intellectual Disability
10. Galway University Hospitals
11. HSE Midland Area
12. HSE North East
13. HSE South Eastern Area
14. Irish College of General Practitioners
15. Laura Lynn Children's Hospice
16. Letterkenny General Hospital
17. Mater Misericordiae University Hospital / Mater Private Hospital
18. Naas General Hospital
19. National Maternity Hospital (Holles Street)
20. National Rehabilitation Hospital (Dun Laoghaire)
21. Our Lady's Children's Hospital, Crumlin, Dublin 12
22. Rotunda Hospital (Parnell Square, Dublin 1)
23. Royal College of Physicians in Ireland
24. Royal Victoria Eye and Ear Hospital
25. Sligo General Hospital
26. Sisters of Charity of Jesus and Mary Services
27. Sports Surgery Clinic (Santry)
28. St. Francis Hospice (Raheny)
29. Saint John of God Hospitaller Ministries
30. St. Luke's Radiation Oncology Network
31. St. Patrick's University Hospital
32. St. Vincent's Healthcare Group
33. St. Vincent's Hospital (Fairview)
34. University of Limerick Hospitals

List Valid, September 2014

WORKING GROUP MEMBERS

CONSULTATION GROUP 2009–14 In alphabetical order:

Bradley, Colin	Irish College of General Practitioners
Byrne, Damien	Sports Surgery Clinic (Santry)
Byrne, Ned	St. Vincent's Hospital (Fairview)
Callinan, Sinead	Beacon Hospital
Collins, Claire	Irish College of General Practitioners
Connaire, Kevin	St. Francis Hospice (Raheny)
Fitzgerald, Barbara	Naas General Hospital
Gargan, Angela	National Maternity Hospital
Hillis, Rowan	Laura Lynn Ireland Children's Hospice
Jensen Kavanagh, Mette	Sligo General Hospital
Kelly, Aine	Saint John of God Hospitaller Ministries
Kennedy, Jan	St. Vincent's Hospital (Fairview)
Kirkham, Colin	Rotunda Hospital
Lamb, Caroline	HSE South East
Lee, Bernie	National Rehabilitation Hospital (Dun Laoghaire)
Leonard, Marie	Our Lady's Children's Hospital
Lynch, Dan	AMNCH / St. James's Hospital
Marsden, Paul	HSE Midland Area
Mayne, Philip	Children's University Hospital
McCourt, John	Dublin Centre for Clinical Research
McDonnell, Joan	St. Vincent's Healthcare Group
McLoughlin, Declan	St. Patrick's University Hospital
O'Neill, Sarah	Mater Misericordiae University Hospital
Nolan, Maeve	National Rehabilitation Hospital (Dun Laoghaire)
Nolan, Treasa	Beacon Hospital
McQuillan, Regina	St. Francis Hospice (Raheny)
Owens, Valerie	St. Luke's Hospital (Rathgar)
Quinn, Claire	Laura Lynn Ireland Children's Hospice
Quinn, Rosie	HSE North East
Rice, Claire	Our Lady's Children's Hospital
Ryan, Ursula	AMNCH / St. James's Hospital
Saunders, Jean	Mid Western Regional Hospital Complex
Stanton, Alice	Beaumont Hospital
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The Consultation Group's mandate comes from its members who voluntarily agreed to collaborate on the development and revision of a Standard Application Form, and accompanying Guidance Manual.

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ACKNOWLEDGEMENTS

For the generous provision of pro-bono legal review, without which, publication of this Guidance Manual would not have been possible, particular thanks to:

Christle, Cliona	A&L Goodbody Solicitors
Herron, Michaela	A&L Goodbody Solicitors

For provision of expert advice and text in relation to Section J (Insurance/Indemnity):

Coulahan, Peter	Corporate and Legal Office, University College Dublin
Shipsey, Ruth	Medisec Ireland Ltd

For independently collaborating on the amendments to Section G (Radiation):

Callinan, Sinead	Beacon Hospital
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For nominating a representative to the Consultation Working Group to speak on their behalf between 2009 and 2014, thank you to the chairpersons and members of the following committees:

- Adelaide & Meath Hospital, Dublin, incorporating National Children's Hospital / St. James's Hospital
- Beaumont Hospital
- Beacon Hospital
- Children's University Hospital
- HSE Midland Area
- HSE North East
- HSE South East
- Irish College of General Practitioners
- Laura Lynn Ireland Children's Hospice
- Our Lady's Children's Hospital
- Mater Misericordiae University Hospital and Mater Private Hospital
- Mid Western Regional Hospital Complex / University of Limerick Hospitals
- Naas General Hospital
- National Maternity Hospital
- National Rehabilitation Hospital (Dun Laoghaire)
- Rotunda Hospital
- Saint John of God Hospitaller Ministries
- Sligo General Hospital
- Sports Surgery Clinic (Santry)
- St. Francis Hospice (Raheny)
- St. Luke's Hospital (Rathgar)
- St. Patrick's University Hospital
- St. Vincent's Healthcare Group
- St. Vincent's Hospital (Fairview)

For formally evaluating the Draft Standard Application Form during the Pilot Phase of this Project in 2010, thank you to the chairpersons, committee members and administration teams of the following committees: -

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- Adelaide & Meath Hospital, Dublin, incorporating National Children's Hospital / St. James's Hospital (Chair: Dr. Ray McDermott; Administrator: Ms. Ursula Ryan)
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- Mater Misericordiae University Hospital and Mater Private Hospital (Chair: Dr. Malcolm Kell; Administrator: Ms. Sarah O'Neill)

For generous assistance and support of this project between 2009 and 2012:

Dr. Ruth Barrington	Molecular Medicine Ireland (MMI)

For graciously agreeing to act as facilitator and chairperson at all Working Group Meetings between 2009 and 2012:

Towns, Jeremy	Dublin Centre for Clinical Research

For the patient provision of IT expertise and support at all Working Group Meetings between 2009 and 2012:

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For generous assistance and invaluable expert advice between 2009 and 2012, in alphabetical order: -

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O'Sullivan, Ciara M.	Office of Data Protection Commissioner
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Ryan, Kieran	Irish College of General Practitioners (previously Royal College of Surgeons in Ireland)

For support of this project at the pre-consultation stage, to include presenting or facilitating at seminars held in May and June 2009. In alphabetical order:

Barrington, Ruth	Molecular Medicine Ireland
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BIBLIOGRAPHY

Age of Majority Act 1985
A Palliative Care Needs Assessment for Children 2005
Child Care Act 1991
Children First Bill 2014
Children in Foster Care Regulations 1995
Council Directive 76/768/EEC and amendments
Criminal Law (Sexual Offences) Act 2006
Department of Children and Youth Affairs, Children First National Guidelines for the Protection and Welfare of Children 2011
Data Protection Act 1988
Data Protection (Amendment) Act 2003
Data Protection Guidelines on Research in the Health Sector 2007
Disability Act 2005
European Commission Volume 9A of the Rules governing Medicinal Products in the European Union – Guidelines on Pharmacovigilance of Medicinal Products for Human Use 2008
Guide to Ethics Committees on Clinical Investigation of Medical Devices, HPRA, 2010
European Communities (Medical Ionising Radiation Protection) Regulations, 2002 (S.I. No. 478 of 2002)
European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations, 2004 (S.I. No. 190 of 2004)
Fitzpatrick v K (2008) IEHC 104
ICH GCP Guidelines 1996
Intoxicating Liquor Act 1988
Irish College of General Practitioners Guide to Conducting Research 2008
Irish Council for Bioethics Human Biological Material: Recommendations for Collection, Use and Storage in Research 2005
Irish Medical Council Guide of Professional Conduct for Registered Medical Practitioners 2009
Irish Medicines Board Guide to the Definition of a Human Medicine 2013
National Consent Policy, HSE, May 2013
National Hospital's Office Code of Practice on Records Management 2007
National Standards in Foster Care, HIQA, April 2003
Non-Fatal Offences Against the State Act 1997
Public Health (Tobacco) Act 2002
World Medical Association Declaration of Helsinki 2013

WEBSITES

Biology Online Dictionary
Data Protection Commissioner
Department of Health
European Commission
Health Products Regulatory Authority
International Committee of Medical Journal Editors
Irish Medical Council
Irish Statute Book
Radiation Protection Institute of Ireland
State Claims Agency
United States Department of Veteran Affairs
World Medical Association
World Health Organisation

LEGAL REVIEW AND INTRODUCTION TO ENDNOTES

We have amended the guidance to align its content with the [HSE National Consent] policy. As the policy may be subject to alteration, it would be wise to advise researchers and REC members of this and to suggest that they would consult the [policy] document as the guidance manual and end notes reflects the position as of September 2013. A link to the [policy] document on the HSE website would facilitate future reference.

Adult Participants Capacity: We have retained endnotes I and III, and have amended endnote II. The Assisted Decision Making Capacity Bill is referred to, but endnote II reflects that it is not law and until there is a change in law, the safest course of action is to apply the test for capacity in Fitzpatrick v K which is set out in endnote III.

C3.1 (b) - reference to legal representative: The National Consent Policy recommends the use of a legal representative in research outside clinical trials as this is the statutory requirement provided for in relation to clinical trials. It is important to note that this recommendation is not supported by any legislative basis. Therefore following this best practice recommendation does not equate to having a legally effective proxy consent. In the context of the Assisted Decision Making Bill 2013, there is an opportunity to lobby the relevant Minister to remedy the gap in the law and make provision for consent by a legal representative for an adult lacking decision making capacity in the case of research which is not a clinical trial. It is important for legislatures to support the research community and enable them to practice within a clear legal framework which respects the rights of the incapacitated adult.

Children: We have reflected the HSE National Consent Policy which recommends that it is sufficient to obtain consent from one parent / legal guardian unless the REC has found that the risks involved require the consent of both. This is a pragmatic approach but it is one which will require the exercise of judgment on a case by case basis by researchers and RECs. We have noted in our endnote how the courts have interpreted the role of joint legal guardians of a child. Clearly the courts become involved where there is dispute between legal guardians. Having said that, it is none the less clear from the approach which the courts have adopted that in matters of importance concerning the welfare of a child each guardian is entitled to be consulted and that the guardians should reach joint decisions. The cases reflect that the obligation is on the guardians to consult with eachother. However the court's interpretation of the role of joint guardians has implications for those designing systems of healthcare or delivering healthcare to children (including the opportunity to participate in research) as they clearly need to have regard to the rights of joint legal guardians. Therefore, in each case the researchers and the REC will need to consider whether, in the context of the individual research proposal, the decision to participate is a decision of importance to the welfare of the child. Endnote IV sets out the legal position regarding guardianship and footnote 15 directs readers to the relevant endnote.

Children who are 16 but not yet 18: S23 of the Non Fatal Offences Against the Person Act 1997 has not to our knowledge been interpreted by the Irish courts and is capable of a narrow construction which would exclude consent for research. Given this, we continue to recommend obtaining the consent of parent or guardian accompanied by the assent of the child. Again there is a policy issue here that the legislature ought to address namely are 16 year olds to be conferred with decision making authority in relation to all health decisions including research…..[The HSE Consent Policy states that for research other than clinical trials, the person must be over the age of 18 years to provide consent]…..

Children in Care: Children in care as participants in research is presented in the National Consent Policy as being straightforward and …[we]…don't believe that is it the case in practice. The text in the guidance manual reflects the complexity of the issues which arise in identifying who has legal authority to consent as well as reflecting the guidance provided by the National Consent Policy.

Data Protection: [We] have made some amendments to this section and have included various definitions which are relevant including the definition of processing and sensitive personal data. [We] note you will be consulting with the Data Protection Commissioner (DPC). There are a number of issues you might wish to consider:

1. More and more research is conducted on a multi-site collaborative basis, involving research consortia which include healthcare and academic institutions. There may or may not be formal agreements in place between the members of the research

consortia. It is not always clear who is the data controller for an individual project where it involves the collection and processing of personal data / sensitive personal data. Therefore it would be appropriate to ask the question 'Who or what legal entity if the data controllers for personal data / sensitive personal data collected and / or processed in research?' In addition, it would be important for research participants to know to whom they should address any complaint or data access request.

2. In keeping with the increased multinational dimension to research the issue of transfer of data outside the EEA arises from time to time. The obligations rest with the data controller to ensure compliance with data protection law. However the DPC may have a view as to whether, in addition to the consent of the study participant to the transfer of data, additional steps such as the use of Model Form contracts ought to be required by the data controllers and the non EEA based recipient of data or samples / materials for analysis.

Genetic Testing: [We] have strengthened this section to reflect the legal requirements of the Disability Act 2005 and the recommendations of the National Consent Policy and have broadened the questions to reflect the issues which need to be addressed. If you agree with the proposed questions, they should be reflected in the application form. Other than amending F5.1 (b), [we] have not amended this section of the application form.

Section J Insurance: RECs need access to expert insurance advice and this can be facilitated by their institution with input from the institution's brokers.

I note the feedback that you are engaging with the Clinical Indemnity Scheme (CIS). I think it would be useful for CIS to prepare a more detailed statement of the scope of cover provided to research and to identify exclusions and when an indemnity agreement is required. It would be also be helpful to confirm the process which ought to be followed to obtain clarification in individual cases. The State Claims Agency (SCA) have engaged AON to advise them in relation to the adequacy of insurance cover and indemnity in drug trials and drug trials are referred to AON for confirmation of cover under CIS.

It is easy to identity enterprises covered by CIS and generally the individuals within the enterprise are covered. As a general statement, CIS provides cover for personal injury claims, including death, where the claim is by or on behalf of a patient of the enterprise where they allege that they were injured as a result of a negligent act or omission in the provision of a professional medical service. A professional medical service is defined as treatment of any illness, disease injury or medical condition. The cover extends to doctors, nurses and allied health professionals.

Even where the enterprise and the individual are covered by CIS the nature of the research and the risks involved may fall outside the scope of cover. Examples of this might include where the research is not on patients; where the researcher is not an employee on the institution; where the risk which arises is not personal injury e.g. breach of data protection or confidentiality or failure to obtain informed consent to participation in the research or where the research does not involve the treatment of patients for any illness or disease or injury or medical condition. It would be useful to tease through these issues with CIS to achieve greater clarity on what is outside scope.

Each institution (with input from their insurance brokers) should provide guidance to their REC in relation to the scope of the insurances / indemnity that are in place for research undertaken by the institution and clarify in what circumstances researchers / their institutions of origin / external research organisations must provide evidence of adequate insurance cover, the scope and level of cover that is required for individual projects and when an indemnity agreement should be put in place.

[We] hope that these comments are helpful.

Ms. Cliona Christle and Ms. Michaela Herron
A&L Goodbody Solicitors
September 2013

ENDNOTES

[I] "Adult" does not have a legislative definition in Ireland, however, pursuant to the Age of Majority Act, a person who has not attained full age (i.e. 18 years of age) and who is not or has never been married prior to attaining full age, is a minor. By way of implication an adult is a person who has attained 18 or a person who has married prior to that age

[II] The HSE National Consent Policy, May 2013. This however is not a legislative definition.

Interestingly, the recently published *Assisted Decision Making Capacity Bill includes the following definition*

" A person shall lack the capacity to make a decision if he or she is unable,

(a)to understand the information relevant to the decision
(b)to retain that information
(c)to use or weigh that information as part of the process of making the decision (whether by talking, using sign language, assisted technology or any other means) or, if the decision requires the act of a third party to be implemented to communicate by any means with that third party".
This should also not be relied upon unless and until the Bill becomes Law.

[III] For present purposes the interpretation of capacity should be that as held by Laffoy J in *Fitzpatrick v K* which is that in determining whether a patient does not have capacity (cognitive ability) the test is *"whether the patient's cognitive ability has been impaired to the extent that he or she does not sufficiently understand that nature, purpose and effect of the proffered treatment and the consequences of accepting or rejecting it in the context of the choices available at the time the decision is made".*

The following is helpful in applying the test, also from *Fitzpatrick v K,* "The patient's cognitive ability will have been impaired to the extent that he or she is incapable of making the decision to refuse the proffered treatment if the patient: -

A. has not comprehended and retained the treatment information and, in particular, has not assimilated the information as to the consequences likely to ensue from not accepting the treatment,
B. has not believed the treatment information and, in particular, if it is the case that not accepting the treatment is likely to result in the patient's death, has not believed that outcome is likely and;
C. has not weighed the treatment information, in particular the alternative choices and the likely outcomes, in the balance in arriving at the decision."

[IV] The preponderance of legal opinion is that under sixteen's in Ireland have no personal power to consent to medical treatment. The seed of this reasoning is the special position of the family based on marriage, recognised in Article 41 of the Irish Constitution, which vests authority for decisions in relation to the family within the family and therefore in effect vests decision making authority with the parents. A constitutional referendum concerning children's rights was held on 10 November 2012. While the proposal was approved at referendum, the signing of theconstitutional amendment into law has been delayed by a legal challenge brought in the HighCourt. The outcome of that legal challenge is awaited.In the case of a child whose parents are married to each other both parents are legal guardians of the child. In the non-marital family, the natural mother is legal guardian and a natural father may be appointed guardian by agreement or by order of the District Court. The Irish High Court has considered what acting jointly entails in guardianship matters and has held that it requires guardians to consult with each other and reach joint decisions on matters of importance pertaining to the welfare of a child. It should also be noted that where sole custody has been awarded to one legal guardian, that such an order does not negate the rights of the non-custodial parent as guardian of the child and he/she has a right to be consulted on all matters of importance affecting the welfare of the child as distinct from day-to-day matters which will be the responsibility of the custodial parent. Therefore, in each case the researchers and the REC members will need to consider whether, in the context of the individual research proposal, the decision to participate is a decision of importance to the welfare of a child in which event consent of both legal guardians should be obtained.

[V] Section 23 of the Non Fatal Offenses against the Person Act 1997 states that a minor who has attained the age of 16 can consent to any “surgical, medical or dental treatment” and such consent shall be as effective as if it were given by a person of 18 years of age or over. In this section “surgical, medical or dental treatment” includes any procedure undertaken for the purposes of diagnosis, and this section applies to any procedure which is ancillary to any treatment as it applies to that treatment. Sixteen and Seventeen year olds have the power to consent to medical treatment in relation to “surgical, medical or dental treatment” only. So, for the purposes of psychiatric treatment a person is only considered an adult from the age of 18

[VI] Section 43.2 Guide to Professional Conduct and Ethics for Registered Medical Practitioners 2009, page 41

[VII] The minimum age at which a person can give consent to having their personal data processed is not specified in the Data Protection Acts.

[VIII] The legal age to consent to sexual intercourse is 17 under the Criminal Law (Sexual Offences) Act 2006. The legal age to buy alcohol is 18 under Section 31 Intoxicating Liquor Act 1988. The legal age to buy cigarettes is 18 under the Section 45 Public Health (Tobacco) Act 2002.

[IX] Childcare Act 1991 as amended Children in Foster Care Regulations 1995

[X] National Standards in Foster Care HIQA April 2003

[XI] Participation in research is unlikely to constitute “necessary treatment or assessment” and therefore these children ought to be excluded from participation in clinical trials and research as the HSE (or Foster Parents or Relatives acting under a Court Order), do not have the authority to grant consent to their participation in such research. Where it is felt that participation in a clinical trial or other research is in the best interests of an individual child or children, then an application can be made to the District Court under Section 47 of the Child Care Act 1991.

[XII] Children First: National Guidance for the Protection and Welfare of Children 2011 (Part II).

[XIII] Legally valid consent can be given on behalf of an adult without capacity whether due to physical or mental incapacity or age, by a parent, guardian, grandparent, uncle, aunt, brother or sister of the data subject. There is a noted omission in the data protection legislation of consent from a spouse or a son or daughter. Such persons would normally be the subject’s next of kin and should be consulted. Even though they are not authorised under the data protection legislation to consent, their views should be considered.

[XIV] Persons who regain capacity should be given a full explanation and they have the right to revoke permission and withdraw from the trial or research. The effect of this is that information/data gathered about them or samples obtained from them, cannot be used in the research and must be deleted or destroyed.

[XV] See C3.1(b) for explanation of legal representative and lack of legal basis in research outside clinical trials.

[XVI] See ‘XIII’

[XVII] Council Directive 76/768/EEC as amended was transposed into Irish Law by the European Communities (Cosmetic Product) Regulations 2004 81870/2004 (as amended) collectively The European Communities (Cosmetic Products) Regulations 2004-2013