

Maynooth University Research Ethics Policy

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Revised and Approved by Academic Council 13th December 2019

1. Introduction to the Maynooth University Research Ethics Policy and Committee

1.1 Introduction

Maintenance of high ethical standards in research is a central and critical responsibility of the Maynooth University. This policy should be interpreted in a manner consistent with the University's commitment to the highest standards of professional conduct.

Members of the academic community have a responsibility not only to themselves but also to society, to act in accordance with the highest standards of integrity and to comply with the law and University codes of practice and policies. This policy addresses issues of ethics in the conduct of research. Researchers should also be mindful of the following related policies:

- Maynooth University Research Integrity Policy
- Maynooth University Research and Commercialisation Conflict of Interest Policy
- Maynooth University Policy and Procedure for the Protection of Children
- Maynooth University Health and Safety policy document on research involving blood, tissue and/or other biological samples from human subjects
- Maynooth University Data Protection Policy and Data Privacy Impact Assessment
- Your own department's policy on health and safety

This Policy will be reviewed no later than June 2024.

1.2 Maynooth University Research Ethics Committee

The Maynooth University Research Ethics Committee, on behalf of Governing Authority, will consider and, if appropriate, approve work, which requires the approval of a University Research Ethics Committee before it can receive external authorisation to proceed (and/or draw down funds from a research grant.) The committee will have discretion on behalf of the University and in the light of ethical considerations to disallow the proposed research or to require such modifications as it may think fit. The committee will advise the President on research projects having important ethical implications for the University. The committee has two subcommittees which review protocols specific to different formats of research (See Section 2 on governance).

Any research project carried out under the auspices of Maynooth University must undergo an ethical review when the research involves:

- The participation of humans
- Taking blood or tissue or other biological samples from humans, human remains or cadavers, or the use of physiological measurements or other invasive techniques involving humans
- Data derived from secondary sources, e.g. interviews about an individual(s)
- Identifiable private information about individual(s)
- Non-human vertebrate animals as set out in EU Directive 2010/63/EU and SI. 543 of 2012
- Genetically modified organisms
- Biohazardous agents.

Please see Section 2 for ethical review procedures.

1.3 Maynooth University Ethics Policy document

This policy is subdivided into the following sections:

1. Introduction to Maynooth University Policy and Committee
2. Governance and Procedures for Ethical Review
3. Ethics Policy for social research carried out involving human participants (with the **exception** of research that involves the taking blood or tissue or other biological samples from humans, human remains or cadavers, or the use of physiological measurements or other intrusive techniques involving humans).
4. Ethics Policy for biomedical research involving human participants that involves the taking blood or tissue or other biological samples from humans, human remains or cadavers, or the use of physiological measurements or other intrusive techniques involving humans
5. Ethics Policy for research carried out with non-human vertebrate animals as set out in EU Directive 2010/63/EU and SI. 543 of 2012
6. Ethics Policy for research carried out with biohazardous agents (above level 1)
7. Ethics Policy for Research carried out with Genetically Modified Organisms
8. Ethics Policy for Clinical trials/investigations

2. Governance and Procedures for Ethical Review

2.1 Introduction

The Maynooth University Research Ethics Committee is a standing subcommittee of the Research Committee with devolved responsibility to make decisions on ethical approval of research and to assist Maynooth University academic staff and research students in negotiating ethical issues in research. The committee is further divided into two subcommittees as follows:

2.1.1. The Social Research Ethics Subcommittee

This subcommittee reviews proposals of research with human participants or secondary use of personally identifiable data derived from human participants or human biological material (with the **exception** of research that involves taking blood or tissue or other biological samples from humans, human remains or cadavers, or the use of physiological measurements or other intrusive techniques involving humans).

2.1.2. The Biomedical and Life Sciences Research Ethics Subcommittee

This subcommittee reviews proposals of:

- research with humans that involves taking blood or tissue or other biological samples from humans, human remains or cadavers, or the use of physiological measurements or other intrusive techniques involving humans
- research with non-human vertebrate animals as set out in EU Directive 2010/63/EU and SI. 543 of 2012
- research using genetically modified organisms
- research using biohazardous agents.

2.2 Terms of Reference for Maynooth University Research Ethics Committee and subcommittees

2.2.1. Maynooth University Research Ethics Committee (REC)

The REC:

- is responsible for the development and recommendation of policies and procedures in relation to ethics in research, which may from time to time become necessary.
- shall discuss and make decisions regarding any ethical issues in research arising at Maynooth University.
- shall receive copies of all applications to its subcommittees, and their decisions.
- shall review any applications that the subcommittees feel are contentious.
- may set up further subcommittees if the need arises.

2.2.2. Biomedical and Life Sciences Research Ethics Subcommittee

This subcommittee is responsible for:

- the review of applications regarding ethical issues of:
 - a) conducting research with humans that involves that involves taking blood or tissue or other biological samples from humans, human remains or cadavers, or the use of physiological measurements or other intrusive techniques involving humans
 - b) conducting research with vertebrate animals

- c) conducting research using genetically modified organisms
- d) conducting research using biohazardous agents
- the communication of all approvals/denials to REC
- the proposal of recommendations to the REC on ethical policy in research related to a-d

2.2.3. Social Research Ethics Subcommittee

This subcommittee is responsible for:

- the review of applications regarding ethical issues of conducting research with human participants or secondary use of personally identifiable data derived from human participants or human biological material (with the **exception** of research that involves taking blood or tissue or other biological samples from humans, human remains or cadavers, or the use of physiological measurements or other intrusive techniques involving humans)
- the communication of all approvals/denials to REC
- the proposal of recommendations to the REC on ethical policy in research with human participants.

2.3 Membership of Maynooth University Research Ethics Committee

REC should have at least ten members, and may co-opt experts where required. A vice chair should be elected from the membership. Committee members should sit for a maximum of three years. Committee members should rotate on a staggered basis to ensure continuity for new members.

- Vice President for Research (Chair);
- Non-voting Secretary;
- Members of the Social Research Ethics Subcommittee;
- Members of the Biomedical and Life Sciences Research Ethics Subcommittee;
- An academic staff member with academic qualifications and research experience in law or a barrister or solicitor, not affiliated to Maynooth University (appointed by the Chair);
- A lay person who brings an impartial view to the committee (appointed by the Chair).

The REC also has powers to co-opt additional members who shall provide expert advice on particular questions, as required.

2.4 Membership of Research Ethics Subcommittees

The subcommittees should have at least eight members, and the Chair may co-opt more experts where required. A vice chair should be elected from the membership. Committee members should sit for a maximum of three years. Committee members should rotate on a staggered basis to ensure continuity for new members.

2.4.1. Biomedical and Life Sciences Research Ethics Subcommittee:

- Chair - An academic member of staff with experience in the biomedical and life sciences nominated by the VPRI
- Vice Chair – elected from the members listed below
- A secretary who may be provided from Research Development Office staff
- Three academic staff members with academic qualifications and research experience in

Medical/Biological sciences

- A designated veterinarian or expert who is charged with advisory duties in relation to the well-being and treatment of the animals
- An animal care and welfare officer who is responsible for overseeing the welfare and care of the animals in the user establishment,
- An academic staff member with academic qualifications and research experience in psychology
- A statistician or person with expertise in statistical analysis
- And/or an academic representative from any department that may from time to time require ethical approval from the Biomedical and Life Sciences Research Ethics Subcommittee.
- A lay-person who may or may not be a member of Maynooth University staff provided they outside of the disciplines under review.

2.4.2. Social Research Ethics Subcommittee:

- Chair – An academic member of staff with experience in Social research nominated by the VPRI
- Vice Chair – elected from the members listed below
- A secretary who may be provided from Research Support Office staff
- At least two academic staff members with academic qualifications and research experience in sociological research
- At least one academic staff member with academic qualifications and research experience in anthropological research
- At least one academic staff member with academic qualifications and research experience in psychological research
- At least one academic staff member with academic qualifications and research experience in educational research
- At least one academic staff member with academic qualifications and research experience in a humanities discipline
- A person with knowledge of, and current experience in, the professional care, counselling or treatment of people and/or additional academic representatives from any department in any faculty that may from time to time require ethical approval from the Social Research Ethics Subcommittee.

2.5 Procedures

2.5.1. When is ethical review required and who may/must submit research for ethical review

When a research proposal is required to be critically ethically assessed, either from within Maynooth University or by a funding agency, it is referred to the REC.

Protocols for ethical review of research projects are accepted only from Maynooth University staff or students; Maynooth University staff involved (whether as the researcher or as the supervisor of a student researcher) must be qualified in relevant theory and method. Maynooth University staff who are carrying out research are responsible for determining if their project is required to undergo ethical review; Maynooth University staff who are supervising student research are responsible for determining if a student's research is required to undergo ethical review, and are responsible for advising their students on the process.

Proposals from postgraduate students registered for a level 9 degree (by research) or PhD that meet

the criteria outlined above should be submitted to the Research Ethics Committee for review and approval. Research proposals from students registered for a professional doctorate may be reviewed by a departmental process provided these proposals are subsequently submitted to the Research Ethics Committee Tier 1 evaluation for formal approval. All other student research that requires ethical review (e.g. research projects within undergraduate or taught masters programmes), should undergo review at departmental level. The Research Ethics committee will periodically review departmental policies and processes.

The Research Ethics Committee acknowledges the work that is completed at departmental level in training and supervising a wide variety of undergraduate and taught postgraduate research. Departments are responsible for training students, including training about ethical conduct in research, and for supervising the research projects completed during the course of their studies. Departments should submit to the Research Ethics Committee their policy and processes for ensuring that non-doctoral student research projects comply with the Maynooth University Research Ethics Policy. These may be submitted electronically to the Research Ethics Secretariat.

Non-research students undertaking any research with participants must receive departmental approval. Approval of research that undergoes ethical review at departmental level must be recorded and the record held by the Department.

If departments have specific concerns about particular student research projects, we recommend that these projects are submitted electronically to the Research Ethics Secretariat for review, with a note from the department review committee explaining their concerns.

The Research Ethics Committee may require an understanding of the ethical procedures of each department for undergraduate and taught postgraduate research. The Committee may conduct a sample audit of these research projects on an annual basis. Maynooth University staff should be aware of the risks to themselves and to the institution if they proceed with research without reference to the Research Ethics Committee when this is required. Ethical review of multi-centered research

Research projects which are carried out with other universities, institutes, companies, hospitals, etc., should undergo ethical approval both at Maynooth University and the collaborating organisations. Research projects which are carried out with hospitals using the Research Ethics Committee Standard Application Form (RECSAF) should complete only the sections on the Maynooth University form that are not in the RECSAF. All other sections should reference the appropriate section from the RECSAF. This information along with the hospital form should be submitted for review.

2.5.2. Ethical review of research in other jurisdictions or countries

Maynooth University staff/students requiring ethical review who intend to carry out research in other countries should demonstrate to the REC that they are aware of the permission procedures for that country and that they are taking steps to negotiate those procedures. Researchers should also be aware and address issues related to cultural differences and other sensitivities related to different jurisdictions. For example for research carried out in resource-poor settings please refer to the Global Code of Conduct for Research in Resource Poor Settings.

2.5.3. Submission of research proposals

Submission of the ethical protocol is the responsibility of the Maynooth University staff or student researcher who will carry out the research project. Supervisors of students should be closely involved with their students' submissions. The Principal Investigator submits his/her ethical protocol electronically to the Research Ethics Secretariat. Postgraduate researchers and doctoral level

students should submit their ethical protocols along with a letter of support from their supervisor indicating their suitability and experience to carry out the proposed research project.

The ethical protocol should be submitted prior to any research activity being undertaken. Care should be taken to anticipate the timing of the review process to insure that the process will be completed before the projected start date of the research.

The person submitting the ethical protocol should determine to the best of her/his ability which subcommittee is the appropriate one to carry out the review, and should complete the appropriate form for that subcommittee. Protocols should be filled out completely and should include appropriate participant information sheets/consent forms. The completed protocol should be sent to the Secretariat of the REC where it will be checked for completeness; incomplete protocols will be returned to the sender to be completed before being forwarded on to the appropriate subcommittee.

Each subcommittee has its own procedures posted on the REC website, and it is the responsibility of researchers submitting protocols to be familiar with these.

The committees will review protocols on a regular basis and may release a protocol with or without comments, or may ask for clarification or additional information. Once released from the committee, a formal letter of approval will be issued to the applicant.

3. Ethics policy for social research carried out involving human participants

(with the exception of research that involves taking blood or tissue or other biological samples from humans, human remains or cadavers, or the use of other intrusive techniques involving humans)

3.1 Respect for human dignity: guiding principles

The rights and dignity of human participants in research must at all times be maintained. We acknowledge the diversity between people and the need to act with an ethic of respect and equality throughout our research activities.

Researchers have a primary ethical obligation to the people they study; this obligation can supersede the goal of obtaining new knowledge through research. Where conflicts emerge it might be appropriate not to undertake or to discontinue a research project.

Researchers have a responsibility to individual participants, as well as to the wider communities in which they live. The consequences of research may reverberate at many levels, including the local community of participants, the professional community and the wider society. Researchers should be cognizant of this and sensitive to issues arising from inequalities of power.

Maynooth University's ethical review process encourages researchers to consider and work through the complexities inherent in social research – this ethical policy provides guidance to support ethical decision making. Researchers will also need to refer to codes of ethics of relevant disciplines, but should understand that the policy of Maynooth University is overriding.

Maynooth University requires due consideration to the following concerns whenever research involving human subjects takes place:

3.2 Minimising risk

Researchers have a primary responsibility to protect participants from harm, physical or otherwise, during the investigation. Participants should not be exposed to risks beyond what might reasonably be encountered in daily life.

Researchers should be cognizant of how participants are experiencing the research process, sensitive to the potential impacts of their research and prepared to manage unanticipated outcomes.

Due care must be taken by the researcher to consider the wider context and how any individual's participation in the research may lead to repercussions for that participant or for others beyond the immediate research context. Consideration should be given to appropriate methods of data storage (See Maynooth University Research Integrity Policy regarding Data protection and Maynooth University Data Protection Policy and Procedures). Researchers should consider any potential tensions that may arise from existing relationships between participants, funders or others involved in the research process.

3.3 The right of confidentiality

In many circumstances a commitment to confidentiality for participants is a necessary part of the research process. This right to confidentiality is an important, but not absolute, principle that the University will strive to uphold by lawful means.

Subject to the requirements of legislation, including the Data Protection Act and the Freedom of Information Act, researchers should protect the confidentiality of research participants. Researchers have a responsibility to ensure that participants understand the extent of anonymity and confidentiality offered at all stages of the research from data gathering to dissemination. Participants should be apprised of the limits of confidentiality.

It must be recognized that, in some circumstances, confidentiality of research data and records may be overridden by courts in the event of litigation or in the course of investigation by lawful authority. In such circumstances the University will take all reasonable steps within law to ensure that confidentiality is maintained to the greatest possible extent. In so doing, research data and records may be accessed and held by the University (through the President or Vice President for Research) and its legal advisers, to determine their relevance to any proceedings.

When participants choose to be identified in research outputs, their explicit, unambiguous informed consent must be obtained. While endeavouring to respect participants' wishes, researchers should consider whether this puts participants at unanticipated or unacceptable risk. Researchers should be aware of the potential risks in transferring any confidential material in print or any other technological medium.

As one example of consideration of limits to confidentiality, the Sociological Association of Ireland guidelines state that:

Research participants should be given the opportunity to refuse the use of data-gathering devices such as tape recorders and video cameras. Researchers should be careful, on the one hand, not to give unrealistic guarantees of confidentiality and, on the other, not to permit communication of research films or records to audiences other than those to which the research participants have agreed.

3.3.1 Steps to be taken if an outside agency seeks access to confidential Maynooth University Research Data

The following steps should be taken if any external agency or person seeks access to confidential Maynooth University research data.

1. Any such demand or request should be referred immediately to the VP Research.
2. If necessary, the VP Research, working with the academics involved, will seek legal advice to establish the lawful authority of the request.
3. The VP Research will negotiate with the requesting body to attempt to agree on an acceptable course of action that would protect the confidentiality of the data and the participants. The VP Research will hold securely any data or equipment that is the subject of the request.
4. If it is not possible to protect appropriately the confidentiality of the data or the participants by negotiation and agreement, then the University would consider what other steps to take, including making an application to an appropriate court to protect the confidentiality of the research and the participants.
5. The University will abide by the court's decision, subject to any appeal mechanisms which it may be feasible and reasonable to pursue.
6. Every effort will be made to ensure that, if confidential non-anonymised, data must be released, and in so far as possible, any person to whom a commitment of confidentiality has

been made will be informed prior to the data being released to an outside agency or person.

3.4 Informed consent

The right of the individual to give informed consent is paramount. Informed consent must be recorded but does not necessarily have to be obtained in written form; the quality and the record of the consent is more important than the format. Under no circumstances should participation in research be coerced by any means. The researcher should inform participants about all aspects of the research process that might reasonably be expected to influence willingness to participate, including limits to confidentiality. Consent should be an ongoing, negotiated process, particularly in circumstances where the research is carried out over an extended period of time or through repeated data collection sessions. Researchers should clearly indicate to participants their right to withdraw from the research without negative consequences.

Data collected should be collected and stored in a secure and accessible form; electronic data should be stored in an encrypted format.

Personal Data collected in an identifiable format should be held only for a specific purpose and length of time in accordance with the Maynooth University Data Protection Policy and Procedures, the Maynooth University Research Integrity Policy and General Data Protection Regulations 2018.

Personal Data is defined by the General Data Protection Regulations as:

“ any information relating to an identified or identifiable natural person ('data subject'); an identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person;”

3.4.1 Inducements

Participants should not normally be paid or otherwise compensated to participate in research. However, it is reasonable to note that in some countries, particularly developing countries, some forms of payment may be expected and necessary. It is important therefore to take account of the research environment. If a form of payment is to be given it should not be so attractive as to induce participants to undertake risk against their better judgment. Excessive payments or compensations constitute undue inducement and are considered unethical.

3.5 Working with students as research participants

In some research situations, the recruitment of students in educational institutions, including the University, is integral to the research protocol. This is particularly true of research related to the scholarship of teaching and learning, curriculum development and teaching methods. Researchers should be cognizant of their academic and ethical obligations towards students and should carefully consider the ethical implications of the research in terms of their own dual roles as researcher/educator and the potential vulnerable position of students as research participant/student. Researchers should be particularly diligent in ensuring that participation is not coerced in any way and that the individual's right to discontinue participation without penalty is respected.

3.6 Working with vulnerable groups

Researchers have a special responsibility for safeguarding the interests of vulnerable groups. It is the responsibility of the researcher to consider carefully whether proposed research participants may be considered vulnerable in some way. This may also include research located in contexts or raising issues that create possible vulnerability for participants.

Even though there is a special obligation to highlight the situation of such groups, vulnerable persons may not always be best equipped to protect their interests in relation to research. Suitable procedures to promote understanding of the nature of the research and process of participation should be used so that participants may give consent to the extent that their capabilities allow. Researchers should seek the collaboration of guardians or responsible others involved in their care to assist participation in the research. Researchers need to ensure that they have adequate training to conduct and support such research.

3.7 Research with children

In accordance with the UN Convention on the Rights of the Child and the Maynooth University Policy for Child Welfare, the best interests of the child must be central to any research conducted. Young people should be given the right to informed consent in a manner suited to their age, maturity and competence. Researchers should seek the consent and collaboration of guardians or responsible others involved in their care to support young people's participation in the research. A young person's right to refuse to participate or to discontinue participation should be respected even if parents or responsible others have given consent. Researchers should give due consideration to the limits of confidentiality and to the appropriate communication of such limits both to parents/guardians and to the children themselves.

Researchers must ensure that they, and any other members of their research team, comply with legal requirements and professional standards in relation to working with young people. If research is to be completed with persons under the age of 18 years, researchers are required to obtain Garda clearance before the research commences. For Maynooth University researchers, procedures for obtaining Garda Vetting are outlined in the Child Protection Procedures.

For further information guidelines when carrying out research with children please go to the Maynooth University Child Protection Policy and Procedures.

3.8 Research using observational methods in public spaces

The observation of individuals in what would normally be considered a public space can only be undertaken without explicit consent in situations where those observed would normally expect to be observed by strangers. Investigators should be considerate of the possibility of intrusion upon personal privacy in situations where individuals, while in a public space, feel they are unobserved.

3.9 Ethics in research dissemination

Researchers have responsibility for the way in which their research is disseminated and should be cognizant of where this may present difficulty, especially in situations of competing social interests. They should be aware of the possible consequences of publication of their research for participants and should ensure that published data does not enable the actual or potential identification of

research participants without their explicit consent.

In addition, research which aims to gather information on the behaviour of persons and groups should avoid using designations, which could give rise to unreasonable generalisation, resulting in possible stigmatisation of particular social groups.

4. Ethics policy for biomedical research carried out involving human participants

(involving taking blood or tissue or other biological samples from humans, human remains or cadavers, or the use of physiological measurements or other intrusive techniques involving humans)

4.1 General considerations

There are three basic ethical principles to which all research involving human participants should adhere, viz:

- respect for persons
- beneficence
- justice.

4.1.1. Respect for persons

There are at least two important considerations under this principle and these are:

- Respect for autonomy, which requires that those who are capable of deliberation about their personal choices should be treated with respect for their capacity for self-determination; and
- Protection of persons with impaired or diminished autonomy, which requires that those who are dependent or vulnerable be afforded security against harm or abuse.

4.1.2. Beneficence

This principle enshrines the ethical obligation to maximise benefit and to minimise harm. In practice this principle guides decision and judgment in terms of weighing up the risks of the research against expected benefits (risk/benefit analysis). It also motivates the requirement that the research design is sound, and that the investigators involved are competent both to conduct the research and to safeguard the welfare of the research participants. Beneficence further proscribes the deliberate infliction of harm on persons; this aspect of beneficence is sometimes expressed as a separate principle, nonmaleficence (do no harm).

4.1.3. Justice

For research involving human participants, this principle largely requires the equitable distribution of both the burdens and the benefits of participation in research. Differences in distribution of burdens and benefits are justifiable only if they are based on morally relevant distinctions between persons; one such distinction is vulnerability. "Vulnerability" refers to a substantial incapacity to protect one's own interests owing to such impediments as lack of capability to give informed consent, lack of alternative means of obtaining medical care or other expensive necessities, or being a junior or subordinate member of a hierarchical group. Accordingly, special provision must be made for the protection of the rights and welfare of vulnerable persons. The concept can be generalised beyond the individual to groups, communities and countries. For example, researchers should not take advantage of the relative inability of other countries to protect their own interests and those of their citizens.

Justice requires also that the research be responsive to the health conditions or needs of vulnerable participants. Justice requires that the participants selected should be the least vulnerable necessary to accomplish the purposes of the research. Risk to vulnerable participants is most easily justified when it arises from interventions or procedures that hold out for them the prospect of direct health-related benefit. Risk that does not hold out such prospect must be justified by the anticipated benefit to the population of which the individual research participant is representative. Specific considerations

The above principles are developed further to yield the following set of considerations which are pertinent to research involving human participants. Applications for ethical approval should address these considerations where appropriate.

4.1.4 Necessity

A clear statement of the justification for the study and its scientific significance must be provided. If there have been previous studies on this topic it is important to make a clear statement and justification of why additional or replicated research is required. Unnecessary research is not ethical.

4.1.5 Potential benefits

It is important that the applicant makes a compelling case for the research in terms of the benefits of the research. Ethical research should minimise, pose no more risk than a participant would face in the normal daily lives or if possible, avoid all risk to the participants. More typically a reasonable balance is struck between potential benefits and risks. Much of the research undertaken at Maynooth University requires interventions that do not hold out the prospect of direct diagnostic, therapeutic or preventive benefit for the individual and therefore must be justified in relation to the expected benefits to society as generalisable knowledge. Such risks must be reasonable in relation to the significance of the knowledge to be gained.

4.2 Will the research plan proposed be effective in answering the scientific questions?

While the research may be justified in terms of scientific value the Research Ethics Committee requires evidence that the research plan envisaged will be effective in creating scientific information of sufficient quality to merit the research.

4.2.1. Facilities

Are there appropriate facilities available to allow the research to be executed as successfully as possible? Have the required health and safety aspects been addressed?

4.2.2. Required competencies

The Research Ethics Committee must be satisfied that the team involved has the requisite experience, qualifications and competency to carry out this research in an effective, professional and ethical manner. It is important to highlight who is responsible for the research and that a description of the team involved is provided.

4.2.3. Experimental design

A poorly designed experiment will not be effective in generating good scientific information. Such research therefore is not ethically justified as it holds no scientific value. In order that the Research Ethics Committee can make a judgment on this aspect of the research applicants are requested to provide the following information:

- The objectives of the trial or study, its hypotheses or research questions, its assumptions, and its variables
- The number of research participants needed to achieve the study objective, and how this was statistically determined
- Justification for the choice of participants needed for the study objective especially if the cohort selected would be classed as vulnerable due to the nature of the study objectives.
- Rules and criteria according to which the study may be terminated. For example, an intermediate process might determine that the research study will be ineffective therefore it would be unethical to continue the experiment further.

4.2.4. Clinical Trials/Investigations

The term 'clinical trial/investigation' for the purpose of this policy also includes but is not limited to terms such as 'clinical trials', 'pre-clinical trials/research', 'clinical investigations', 'first in man trials' or 'first in man investigations or research'.

A clinical trial/investigation differs from general patient-oriented or healthy volunteer research in that it usually involves experimental and/or novel biomedical or behavioural products, interventions or therapies for the diagnosis, treatment, prevention or cure of a human disease or condition. This primarily involves testing, evaluating and/or investigating the effects of new products, interventions and/or therapies on human subjects, with a view to assessing the safety, efficacy, benefits, and/or adverse reactions of that product, intervention or therapy. It may also however include testing of existing medicines on human subjects in order to study longer term effects of that medicine.

The clinical trial/investigation may include but is not limited to, investigative medicinal products, drugs, medical devices, instruments, appliances, software, radiopharmaceuticals, cells and other biological products, and/or natural health products. The product may be new or an already approved product and may be used alone or in combination.

All research that involves clinical trial research presently falls outside the normal professional indemnity insurance and a specific insurance policy must be put in place before any such projects commence. Clinical trial research projects are also governed by law and regulated by Irish Medicines Board and it is imperative that both regulatory and ethical approval is given before any subjects are approached regarding the proposed investigation.

Please consult section 8 of this policy 'Ethics Policy for Clinical Trial Research' for more detailed information.

Any potential involvement in a clinical trial/investigation must be brought to the attention of the VP for Research and Innovation, prior to any agreement being put in place regarding Maynooth University's Role in the clinical trial/investigation.

4.3 Distributive justice.

The Research Ethics Committee must determine whether or not the research imposes an equitable distribution of both the burdens and the benefits of participation. If it does not, the committee must determine if the balance given is justifiable in light of other considerations.

4.3.1 Externally sponsored research

All external sponsoring organisations and investigators should submit the research protocol for ethical and scientific review in the country of the sponsoring organisation, and the ethical standards applied should be no less stringent than they would be for research carried out in that country. The health authorities of the host country, as well as a national or local ethical review committee, should ensure that the proposed research is responsive to the health needs and priorities of the host country and meets the requisite ethical standards.

4.3.2 Overuse of groups

In the case of Maynooth University this refers to the student body and researchers junior to the investigator. See dedicated section later.

4.3.3 Informing participants about the results of the study

Participants should be afforded the opportunity to be informed about the results of the study at their discretion and/or when the research is complete.

4.4 Informed consent

This aspect is derived from the principle of respect for persons under general considerations. Informed consent is a decision made by an individual to participate in research. Such decisions can only be taken by sufficiently competent individuals who have received and understood (to an acceptable level) the research procedure. Such individuals must be freely allowed to consider this information and arrive at a participation decision without coercion, undue influence or intimidation.

It is important to protect the individual's autonomy and freedom to choose. Independent review should be provided for those individuals with limited capacity to give adequately informed consent such as children.

4.4.1 Responsibilities of the investigators in obtaining informed consent

Ethical research requires that investigators:

- Refrain from unjustified deception, undue influence, or intimidation. Intimidation and undue influence can manifest itself in subtle ways such as an investigator recruiting their own research students for experimentation – this is discussed in a later section.
- Seek consent only after ascertaining that the prospective participant has adequate understanding of the relevant facts and of the consequences of participation and has had sufficient opportunity to consider whether to participate. In particular the investigators should be completely objective in their account of any pain, discomfort, risks and hazards associated with the experiment, and the limits to confidentiality.
- Should obtain informed consent from each participant
- Informed consent must be recorded either in written form or audio recorded, which may be later transcribed into written format in compliance with the General Data Protection Regulations 2018.
- Renew the informed consent of each participant if there are significant changes in the conditions or procedures of the research or if new information becomes available that could affect the willingness of participants to continue to participate
- Renew the informed consent of each participant in long-term studies at pre-determined intervals, even if there are no changes in the design or objectives of the research.

Investigators should make absolutely clear to participants that understand they may withdraw from the research at any time including retrospectively without any negative consequences.

When a prospective participant is not capable of informed consent, permission will be obtained from a duly authorised person. In the case of a child who is sufficiently mature to understand the implications of informed consent but has not reached the legal age of consent, that knowing agreement, or assent, will be obtained, as well as the permission of a parent, or a legal guardian or other duly authorised representative.

4.4.2 The process of obtaining consent

The process of obtaining consent begins with first contact with the participants. The investigator should therefore describe the means proposed to obtain individual informed consent and the procedure planned to communicate information to prospective participants, including the name and position of the person responsible for obtaining consent. This should include the process of recruitment, e.g., advertisements, and the steps to be taken to protect privacy and confidentiality during recruitment. Template consent forms may be found on the REC website.

4.4.3 Collection, Use and storage of data from medical records and/or biological specimens

Data collected from personal Medical records and/or biological specimens should be collected and stored in a secure and accessible form; electronic data should be stored in an encrypted format.

Personal Data collected in an identifiable format should be held only for a specific purpose and length of time in accordance with the Maynooth University Data Protection Policy and Procedures, the Maynooth University Research Integrity Policy and General Data Protection Regulations 2018.

Personal Data is defined by the General Data Protection Regulations as:

“ any information relating to an identified or identifiable natural person ('data subject'); an identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person;”

Medical records and biological specimens taken in the course of clinical care may be used for research without the consent of the patients/participants only if completely anonymised and if the patient originally gave consent for their material to be further used for research once anonymised. Refusal or reluctance of individuals to agree to participate would not be evidence of impracticability sufficient to warrant waiving informed consent.

4.4.4 Secondary use of research records or biological specimens.

Investigators may want to use records or biological specimens that another investigator has used or collected for use, in another institution in the same or another country. This raises the issue of whether the records or specimens contain personal identifiers, or can be linked to such identifiers, and by whom. If informed consent or permission was required to authorise the original collection or use of such records or specimens for research purposes, secondary uses are generally constrained by the conditions specified in the original consent. Consequently, it is essential that the original consent process anticipate, to the extent that this is feasible, any foreseeable plans for future use of the records or specimens for research. Thus, in the original process of seeking informed consent a member of the research team should discuss with, and, when indicated, request the permission of, prospective participants as to:

- i. whether there will or could be any secondary use and, if so, whether such secondary use will be limited with regard to the type of study that may be performed on such materials
- ii. the conditions under which investigators will be required to contact the research participants for additional authorisation for secondary use
- iii. the investigators' plans, if any, to destroy or to strip of personal identifiers the records or specimens
- iv. the rights of participants to request destruction or anonymisation of biological specimens or of records or parts of records that they might consider particularly sensitive, such as

photographs, videotapes or audiotapes.

4.4.5 Inducements

Participants should not normally be paid or otherwise compensated to participate in research. However, it is reasonable to note that in some countries, particularly developing countries, some forms of payment may be expected and necessary. It is important therefore to take account of the research environment. If a form of payment is to be given it should not be so attractive as to induce participants to undertake risk against their better judgment. Excessive payments or compensations constitute undue inducement and are considered unethical.

4.4.6 Research using observational methods in public spaces

The observation of individuals in what would normally be considered a public space can only be undertaken without explicit consent in situations where those observed would normally expect to be observed by strangers. Investigators should be considerate of the possibility of intrusion upon personal privacy in situations where individuals, while in a public space, feel they are unobserved.

4.4.7 Debriefing

Participants should be debriefed immediately after the experiment if possible and applicable at which stage the investigator may provide the participant with additional information that may help the participant better understand the research. The debriefing session is also an opportunity to check for any unforeseen negative experiences or misunderstandings.

4.5 Research involving vulnerable persons

Vulnerable persons may be considered those relatively incapable of protecting their own interests and ethical justification of their involvement and usually requires that:

- the research could not be carried out equally well with less vulnerable participants
- the research is intended to obtain knowledge that will lead to improved diagnosis, prevention or treatment of diseases or other health problems characteristic of, or unique to, the vulnerable group — either the actual participants or other similarly situated members of the vulnerable group
- the risks attached to interventions or procedures that do not hold out the prospect of direct health-related benefit will not exceed those associated with routine medical or psychological examination of such persons.

4.5.1 Research involving children

The investigator must ensure that:

- the research might not equally well be carried out with adults
- the purpose of the research is to obtain knowledge relevant to the health needs of children
- a parent or legal representative of each child has given permission
- the agreement (assent) of each child has been obtained to the extent of the child's capabilities
- a child's refusal to participate or continue in the research will be respected.

If research is to be completed with persons under the age of 18 years, researchers are required to obtain Garda clearance before the research commences.. Further guidelines when carrying out research with children are available in the Maynooth University Child Welfare Policy

4.6 Confidentiality

The investigator should describe the provisions for protecting the confidentiality of personal data, and respecting the privacy of participants, including the precautions that are in place to prevent disclosure of the results of a participant's genetic and/or other tests to immediate family relatives without the consent of the participant.

They should also provide information about how the code, if any, for the participants' identity is established, where it will be kept and when, how and by whom it can be broken in the event of an emergency. Also any foreseen further uses of personal data or biological materials should be described.

The above provisions should be described to the participant.

Confidentiality of research data and records may, in some circumstances, be overridden by courts in the event of litigation or in the course of investigation by lawful authority. In such circumstances the University will take all reasonable steps within law to ensure that confidentiality is maintained to the greatest possible extent. In so doing, research data and records may be accessed and held by the University (through the President or Vice President for Research) and its legal advisers, to determine their relevance to any proceedings.

4.6.1 Steps to be taken if an outside agency seeks access to confidential Maynooth University Research Data

The following steps should be taken if any external agency or person seeks access to confidential MAYNOOTH UNIVERSITY research data.

1. Any such demand or request should be referred immediately to the VP Research.
2. If necessary, the VP Research, working with the academics involved, will seek legal advice to establish the lawful authority of the request.
3. The VP Research will negotiate with the requesting body to attempt to agree on an acceptable course of action that would protect the confidentiality of the data and the participants. The VP Research will hold securely any data or equipment that is the subject of the request.
4. If it is not possible to protect appropriately the confidentiality of the data or the participants by negotiation and agreement, then the University would consider what other steps to take, including making an application to an appropriate court to protect the confidentiality of the research and the participants.
5. The University will abide by a court's decision, subject to any appeal mechanisms which it may be feasible and reasonable to pursue.
6. Every effort will be made to ensure that, if confidential non-anonymised, data must be released, and in so far as possible, any person to whom a commitment of confidentiality has been made will be informed prior to the data being released to an outside agency or person.

4.7 Self review

It is important that investigators reflect upon all potential ethical issues and considerations that may rise during their study. Investigators should be proactive rather than reactive in describing how these ethical issues will be dealt with.

4.8 Deception

Participants should not be given false information or have information withheld if it is likely that they will feel upset or otherwise uncomfortable when the true information is communicated during the debriefing session. The deliberate deception of participants in all other cases is only tolerated in situations where it is impossible to study the object of investigation through other means. Such cases of deception require strong scientific justification.

4.9 Research with students

Research with students require additional consideration in the research process due to the potential for undue influence, or unintentional pressure to participate where research is being conducted by staff members who have an existing relationship with the student. This includes academics but also post doctorates or post graduate students who are tutors or demonstrators in their departments.

Consideration must be given to ensure that the quality of students' experience is not negatively affected by multiple requests to participate in research. Researchers should also be aware when sourcing student participants, that as a result of their availability they may be more exposed to invitations to take part in research as a result of being a 'captive audience'.

5. Ethics policy for conducting research with vertebrate animals

5.1 Introduction

The development of knowledge necessary for the improvement of health and well-being of humans, as well as other animals, requires in vivo research with a wide variety of animal species. Animal research is an important way of understanding how basic systems of the body work, and what goes wrong with them to cause disease. They are also necessary to prove the efficacy and safety of proposed treatments and indeed may be legally required. However, in accordance with the EU Directive 2010/63/EU and SI. 543 of 2012, scientists must avoid using vertebrate animals whenever possible. Alternatives to animal work such as use of cell cultures, tissue cultures, computers and lower organisms such as bacteria or plants should be considered, particularly in the preliminary stages of research. Researchers must give sound scientific reasons for studies involving vertebrate animals and explain why there are no realistic alternatives (refer to 3Rs section on HPRAs website for sources e.g. NC3Rs, ARRIVE and PREPARE guideline). Research with vertebrate animals is regulated under the EU Directive 2010/63/EU, SI 543 of 2012 and SI. 558 of 2018.

Any establishment in the EU involved in breeding, supply and scientific use of animals is regulated by the Health Products Regulatory Authority (HPRA) under EU Directive 2010/63/EU, to ensure protection and welfare of those animals across all member states. The directive came into effect in 2010 and has since been transposed into Irish law as SI. 543 of 2012, with amendments in SI. 553 of 2018. The Directive achieves its aim in a variety of ways particularly with strong promotion of the 3Rs. Prior to any work being carried out the project must be ethically reviewed and approved by the MU Research Ethics Committee and subsequently authorised (individual and project) by the HPRAs.

5.2 General considerations

5.2.1. The 3Rs

As part of our commitment to animal welfare, Maynooth University requires researchers to adhere to the principles of the 3Rs (refer to 3Rs section on HPRAs website for sources eg NC3Rs, ARRIVE and PREPARE guidelines).

- Replacement of vertebrate animals with humane alternatives wherever possible
- Reduction in the numbers of animals used
- Refinement of husbandry and procedures to minimise any pain and suffering the animals may experience and to improve animal welfare.

Animal research must use the most appropriate species of animal.

Maynooth University expects researchers who use vertebrate animals to consider the ethical issues associated with:

- keeping animals in captivity
- killing animals
- causing animals distress or pain.

Researchers should use the smallest number of animals that can answer the question posed, ensure studies are well-designed to produce scientifically valid data and take every practical step to avoid distress or suffering to the animals involved. All staff involved in vertebrate animal research and in the breeding, housing and care of animals, must be properly trained in accordance with the HPA guidelines.

5.3 Responsibilities of the relevant parties:

5.3.1. Responsibilities of researchers and associated veterinary and animal care staff

Researchers are responsible for the design and conduct of research using vertebrate animals. In addition to fulfilling any legal responsibilities, they are primarily responsible for applying the principles in this guidance, with support from Maynooth University. Animal care and veterinary staff also bear responsibility for the conduct of research involving vertebrate animals and can provide guidance to the researchers. Researchers, associated animal care and veterinary staff should adopt a culture of care with regard to the animals. This includes keeping themselves informed of developments in good practice and advances in the 3Rs.

Researchers are expected to give appropriate consideration to the 3Rs in any research involving vertebrate animals. In addition, researchers must explain in their research proposals (in applications to both funding bodies and ethics committees) how the 3Rs have been taken into account.

5.3.2. Responsibilities of Maynooth University Research Ethics Committee

The Maynooth University Research Ethics Committee considers ethical issues related to the following areas: a) the areas of scientific use for which animals will be used including replacement, reduction and refinement in the respective areas; b) experimental design, including statistics where appropriate; c) veterinary practice in laboratory animal science of wildlife veterinary where appropriate; d) animal husbandry and care, in relation to the species that are intended to be used (article 38 of Directive 2010/63/EU).

5.4 Specific considerations

Maynooth University requires due consideration of the following principles whenever carrying out research or training involving the use of vertebrate animals:

5.4.1. Directive 2010/63/EU and SI 543 of 2012 mandates the principles of replacement, reduction and refinement should be implemented. When no alternative method is available, the numbers of animals should be reduced by experimental design and refine the techniques used. Chosen procedures should in as far as is possible aim to:

- (a) Use the minimum number of animals; whilst using sufficient numbers to provide statistically valid data
- (b) Involve animals with the lowest capacity to experience pain, suffering, distress or lasting harm;
- (c) Cause the least pain, suffering, distress or lasting harm; and are most likely to provide satisfactory results.

5.4.2. Refer to 'Guidelines for the welfare of non-farming ('other') species during commercial transport' when considering the transportation, of vertebrate animals

5.4.3. In accordance with the EU Directive 2010/63/EU & SI. 543, of 2012 (i) all vertebrate animals used in regulated scientific procedures must be bred and obtained from designated and registered breeding establishments, and (ii) all regulated scientific procedures must be performed in designated registered premises. In accordance to 14(b) of SI. 543 of 2012 wild

animals may be captured from the wild with HPRA permission

5.4.4. The general health and welfare of all vertebrate animals must be checked daily to ensure that the health and well-being of animals is maintained. Animals which are undergoing scientific procedures must be inspected as per approved protocols.

5.4.5. Procedures involving vertebrate animals should be designed and performed with due consideration of their relevance to human or animal health, the advancement of knowledge.

5.4.6. Proper use of vertebrate animals, including the avoidance or minimisation of discomfort, distress, and pain when consistent with sound scientific practices, is imperative. Unless the contrary is established, investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals.

5.4.7. Procedures involving vertebrate animals, where possible or deemed necessary, should use appropriate sedation, analgesia and/or anaesthesia.

5.4.8. Humane end-points should be agreed and adhered to so all should be monitored as detailed in the HPRA project approval during the project.

5.4.9. The living conditions of vertebrate animals should be appropriate for their species and contribute to their health and comfort. Animals should be housed and fed appropriately. In any case, veterinary care shall be provided as indicated. The aim is to maintain vertebrate animals in good health and physical condition: behaving in a manner normal for the species and strain and with a reasonably full expression of their behavioural repertoire; amenable to handling; and suitable for the scientific procedures for which they are kept.

5.4.10. Investigators and other personnel shall be appropriately qualified and experienced for conducting procedures on living vertebrate animals. Adequate arrangements shall be made for their in-service training* including proper and humane care and use of laboratory vertebrate animals.

5.4.11. The Animal Welfare Body oversees the care of laboratory vertebrate animals as set out in EU Directive 2010/63/EU and SI. 543 of 2012 which are involved in or held for scientific procedures at Maynooth University. Individual responsibility falls to: (i) the Institution authorised to carry out animal research; (ii) those holding individual and project authorisations who are responsible for all animals submitted to procedures under the terms of his or her authorisation; (iii) the person named as responsible for the day to day care of the animals; (iv) the designated veterinary surgeon (or in, exceptional circumstances, another suitably qualified person) who monitors and advises on the health and welfare of the animals

5.4.12. All personnel performing regulated procedures must be both individually licensed (individual authorization) as well as licensed for specific projects (project authorization) and (i) be competent to take primary responsibility for the animals involved in procedures; (ii) have appropriate education and training; (iii) know the relevant techniques for the species concerned; (iv) know the signs of pain, suffering or distress in the species to be used; (v) understand the needs for any aftercare following the procedure; (vi) know how to care for the animals.

5.4.13. In accordance with the EU Directive 2010/63/EU and SI. 543 of 2012 full and accurate records must be maintained of the source, use and final disposal of all vertebrate animals protected by the legislation in the University. In addition, suitable records must be maintained of the

environmental conditions in the rooms in which animals are held.

5.4.14. Standard Operating Procedures (approved by the Animal Welfare Body) and relevant Health and Safety Risk Assessments should be in place prior to commencement of any procedures.

*All personnel involved with animal research must have successfully completed a HPRA approved training course

6. Ethics policy for conducting research using biohazardous agents

6.1 Introduction

A biohazardous agent can be defined as material of biological origin that constitutes a hazard to humans, animals or to the environment, for example an infectious microorganism or a toxin of biological origin. Research involving biohazardous agents has both safety and environmental implications and must be conducted in accordance with relevant legal requirements for the handling and use of such materials prior to the commencement of any research work involving their use.

6.2 EU and national regulations

All researchers must familiarise themselves with European Union and National regulations for the handling and use of such materials prior to the commencement of any research work involving their use. The University Safety Policy Statement clearly sets out all relevant obligations on staff and students as well as setting out a Risk Assessment Protocol which must be carried out prior to commencing research work.

6.3 University regulations

All researchers should familiarise themselves with the Department and University regulations for handling hazardous materials.

6.4 Biohazardous agents

The regulations governing the use and storage of biohazardous agents are set out in Statutory Instrument No. 146 of 1994 (SI 146 (1994)16 and SI 248 of 1998¹⁷. These Statutory Instruments are entitled 'Safety, Health and Welfare at Work (Biological Agents) Regulations, 1994' and 'Safety, Health and Welfare at Work (Biological Agents) Regulations 1998', respectively.

These documents clearly set out all the regulations and duties pertinent to the use of biohazardous agents. They also classify biohazardous agents into four categories – category 4 being the most hazardous- as well as listing all containment measures required for handling all biohazardous agents.

All relevant researchers must be familiar with the legislation governing the use of biohazardous agents prior to commencing any research involving the use of biohazardous agents. Furthermore, all necessary containment facilities and measures must be in place prior to beginning such work.

Specific authorisation may be required from the Health & Safety Authority for the first time use of a biological agent. Consult the Departmental Safety Advisor or University Safety Office if authorisation is required before storing the biological agent on campus.

7. Ethics policy for conducting research using genetically modified organisms

7.1 Introduction

The terms genetic modification, genetic manipulation, genetic engineering or recombinant DNA technology are interchangeable. These terms are usually defined to mean the propagation of heritable material by the insertion of that material, prepared by whatever means outside a cell or organism, into a cell or organism in which it does not occur naturally, either directly or into a vector system which is then incorporated into the cell or organism.

This type of research can contribute to understanding of normal and abnormal biological processes in all living organisms. Current and future potential applications of the research include prevention and treatment of diseases and feeding the hungry.

7.2 Specific issues

Ethical issues that should be considered when generating or using genetically modified organisms (GMOs) include:

- What is the intention of the research?
- What are the known health/environmental risks associated with transgenic organisms?
- What unintended consequences could result?

All work with GMOs is regulated in the European Union, see below.

All those working with Genetically Modified Organisms/Microorganisms (GMOs/GMMs) must notify the Environmental Protection Agency (EPA) of their work prior to commencement, see Section 7.4 below. In the first instance, all draft notifications should be reviewed by the Departmental Biological Safety Officer and then submitted to University Biological Safety Committee for approval. Notifications are then submitted to the EPA. Updated annual reports must be submitted to the EPA and regular site inspections are carried out by the EPA.

7.3 EU regulations

Genetically modified organisms (Contained Use) Regulations, 2001 (S.I. No. 73 of 2001) gives effect to Directive 98/81/EC of the European Commission on the contained use of GMO's in Ireland.

SI 73 of 2001 introduces a GMO classification system based on a risk assessment which results in the classification of contained use activities into one of four classes:

- Class 1: activities of no or negligible risk
- Class 2: activities of low risk
- Class 3: Activities of moderate risk
- Class 4: Activities of high risk to the environment and human health.

7.4 Risk assessment

All work with GMO/GMMs is regulated by the Environmental Protection Agency (EPA, <http://www.epa.ie/whatwedo/licensing/gmo/>). The EPA is the competent authority for the purpose of implementation of SI No. 73 of 2001 in Ireland. Prior to commencing work with GMO/GMMs, all users must undertake a risk assessment and notify, in writing, the Environmental Protection Agency (EPA) as to the classification of the proposed work.

All necessary information required to make a risk assessment is supplied in SI No. 73 of 2001. Further information can be obtained from the University Safety Officer and the University Biological Safety Committee. All correspondence with the EPA should be copied to the Departmental Biological Safety Officer and all applications to the EPA should be sent firstly to the University Biological Safety Committee for Review.

It should be noted that Class 1 and 2 contained use of GMMs incur a cost of €250 and €1250, respectively, when making an application for use to the EPA. These costs should be borne in mind when making grant applications involving the application and use of GMMs. Currently there are no costs relating to GMO applications.

8. Ethics policy for clinical trial/investigations

This section should be read in conjunction with section 4 of the Ethics policy: 'Ethics policy for biomedical research carried out involving human participants (involving taking blood or tissue or other biological samples from humans, human remains or cadavers, or the use of physiological measurements or other intrusive techniques involving humans)'

8.1 Definition of clinical trial/investigation for the purpose of the Maynooth University Research Ethics Policy

The term 'clinical trial/investigation' for the purpose of this policy also includes but is not limited to terms such as 'clinical trials', 'pre-clinical trials/research', 'clinical investigations', 'first in man trials' or 'first in man investigations or research'.

A clinical trial/investigation differs from general patient-oriented or healthy volunteer research in that it usually involves experimental and/or novel biomedical or behavioural products, interventions or therapies for the diagnosis, treatment, prevention or cure of a human disease or condition. This primarily involves testing, evaluating and/or investigating the effects of new products, interventions and/or therapies on human subjects, with a view to assessing the safety, efficacy, benefits, and/or adverse reactions of that product, intervention or therapy. It may also however include testing of existing medicines on human subjects in order to study longer term effects of that medicine.

The clinical trial/investigation may include but is not limited to, investigative medicinal products, drugs, medical devices, instruments, appliances, software, radiopharmaceuticals, cells and other biological products, and/or natural health products. The product may be new or an already approved product and may be used alone or in combination.

Any potential involvement in a clinical trial/investigation must be brought to the attention of the VP for Research, prior to any agreement being put in place regarding MAYNOOTH UNIVERSITY's Role in the clinical trial/investigation. The VP for Research supported by the Commercialisation Office, advised by a legal representative, will be responsible for the making the final decision regarding MAYNOOTH UNIVERSITY's role in clinical trial/investigation.

8.2 Specific Considerations

8.2.1 Risk versus benefit

The principles of any research project involving human subjects must be based on the obligation to weigh up the balance of benefit *versus* risk. The aim of a clinical trial/investigation is to provide new or improved interventions or therapies that will offer greater understanding and improvement of human health and human disease. It is imperative that the underlying principle of this type of research is the protection of human beings, and not exposing people to undue risk because, without prior evidence, experimental product, interventions and therapies pose a higher risk than that of general human related research with existing validated approaches. The rights, safety, confidentiality and well-being of subjects are paramount.

Clinical trial/investigations should only be carried out where absolutely necessary and only after all *in vitro*, *in vivo* and/or animal models have been completed. A clinical trial/investigation should be

properly designed, be ethically acceptable and with appropriate risk management procedures in place.

Clinical trial/investigations must be carried out in a clinical setting, hospital or Clinical Research Centre (CRC), under the direction of authorised health care professionals. Other specific considerations include the regulatory and legal frameworks as well as insurance.

Ethical approval must be given from one of the nationally approved ethics committees before any clinical trial/investigation subjects are approached.

8.3 Regulatory requirements

8.3.1. Definitions

For the purposes of the regulatory framework, clinical trial/investigations carried out for medicinal products (Section 8.6) and medical devices (Section 8.7) are managed by separate legislation and regulatory processes, with some significant differences including the use of distinctive terminology. However, all clinical trial/investigations require a Sponsor, an Investigator and a Monitor.

8.3.2. The Sponsor

All clinical trial/investigations must have a Sponsor (as defined by both ICH GCP 1.53 and ISO 14155:2011). The Sponsor is the person or organisation who takes responsibility for the design, initiation and management of the clinical trial/investigation and who also takes responsibility for the financing, or arranging of finance for the clinical trial/investigation. The Sponsor submits the required documents for regulatory approval. All communication with the regulatory authority is through the Sponsor. The Sponsor may delegate all the clinical trial/investigation related functions to a hospital or company or CRC but still remains responsible for compliance with all EU legislation and clinical trial regulations.

The Sponsor may be:

- An individual
- A pharmaceutical or medical device or diagnostic company
- A government agency or organisation
- An academic institution
- A private or other organisation

It is only in exceptional circumstances that Maynooth University would agree to act as Sponsor in a clinical trial/investigation. Maynooth University may consider acting as Sponsor for a clinical trial/investigation when data from 'first in man' trials is required in order to spin out or license out a new product, only in situations where there is no industrial interest or involvement.

In cases where a company has a vested interest (i.e. directly funding, either in full or in part, and/or has a license option of IP from Maynooth University) in a new product then Maynooth University expects the company to act as Sponsor, even for collaborative clinical trial/investigations that may be led and/or part funded by Maynooth University.

In cases where a new product or a change of use for a product is based on an existing license from Maynooth University, and the company has a license option for the potential new product, then Maynooth University expects the company to act as Sponsor, even for collaborative clinical

trial/investigations that may be led and/or part funded by Maynooth University.

Any potential involvement in a clinical trial/investigation must be brought to the attention of the VP for Research, prior to any agreement being put in place regarding Maynooth University's Role in the clinical trial/investigation. The VP for Research & Innovation supported by the Commercialisation Office, advised by a legal representative, will be responsible for the making the final decision regarding Maynooth University's role in clinical trial/investigation.

8.3.3. The Investigator

All clinical trial/investigations must have an Investigator. This is the health care professional who is responsible for the conduct of a clinical trial/investigation at the trial site (hospital or CRC). Where a clinical trial/investigation is conducted with a team of health care professionals, the Investigator is the leader responsible for the team. Sponsor and Investigator may be one and the same person in which case they are referred to as 'Investigator-Sponsor'.

The Investigator should be someone with 'suitable qualifications' and should possess knowledge of:

- The product technology and application;
- The research protocol and/or methodology;
- The diagnosis and management of target condition.

8.3.4. Monitor

The role of the Monitor is to ensure the monitoring process is implemented throughout the research clinical trial/investigation. The Monitor, who may be the Sponsor or someone employed by the Sponsor, oversees the progress of a clinical trial/investigation and ensures that it is conducted, recorded and reported in accordance with the agreed clinical investigation plan or protocol, and/or subsequent amendments, standard operating procedures (SOPs), GCP and the applicable regulatory requirements.

ISO 14155 of 2011 (Clinical Investigations of medical devices for human subjects – good clinical practice) describes the Monitor as a person:

- Qualified in the field of the international standards for GCP through training, experience as well as scientific or clinical knowledge;
- Knowledgeable on the use of investigational devices and relevant requirements, clinical investigation plan and informed consent processes;
- Trained on the Sponsor's clinical quality assurance and quality control system as well as any special procedures for monitoring a specific clinical investigation.

8.4 Legal requirements

8.4.1. Legal framework

A highly regulated legal framework covering clinical trial/investigations exists. This ensures both a high standard of research design and quality, and that the same standards apply across the European Community, as many research projects of this nature are multi-centred and multi-national. All clinical trial/investigations carried out with medicinal products in Ireland must have approval from the regulatory authority as well as a nationally approved ethics committee before subjects can be

recruited. It is not sufficient to have institutional ethical approval only.

8.4.2. Clinical Trial Agreement

There will likely be a number of parties involved in a clinical trial/investigation namely; the university; the clinical research organisation or hospital; the Investigator; clinicians or other medical staff; and possibly a company. For this reason a legally binding Clinical Trial Agreement (CTA) should be put in place. The CTA ensures the protection of the university, the Investigator and the subjects of the clinical trial/investigation. The Commercialisation Office should be contacted regarding a CTA.

A CTA is a legal agreement between all parties involved in a clinical research. It sets out all the obligations of each party during and after the clinical trial/investigation. The agreement ensures that all parties are aware of their responsibilities... Typically CTAs should address:

- The protocol, SOPs and Good clinical practice (GCP);
- Regulatory requirements, approvals, inspections and audits;
- Insurance and indemnification;
- Personnel, subcontracting and assignment;
- Confidential information and publication;
- Management of results and IP/execution of documents for IP;
- Record and sample retention, access and utilisation;
- Notifications for fraud, misconduct and amendments.
- Budget

8.4.3. Data Protection

All data collected by Maynooth University researchers is governed by the Maynooth University Data Protection Policy and Procedures and the Maynooth University Research Integrity Policy, and should be in compliance with the General Data Protection Regulations 2018. Individuals have the right to privacy and protection of their health related data; therefore, it is imperative that best practice is followed for obtaining consent, data collection, recording, storage and disposal.

Data collected should be collected and stored in a secure and accessible form; electronic data should be stored in an encrypted format.

Personal Data collected in an identifiable format should be held only for a specific purpose and length of time in accordance with the Maynooth University Data Protection Policy and Procedures, the Maynooth University Research Integrity Policy and General Data Protection Regulations 2018.

Personal Data is defined by the General Data Protection Regulations as:

“ any information relating to an identified or identifiable natural person (‘data subject’); an identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person;”

Data in health research must comply with the Health Research Regulations (S.I. No. 314 of 2018).

A data controller (organisation or individual that holds the data) who is processing or further

processing personal data for the purposes of health research shall ensure that arrangements are in place so that personal data shall be processed in order to achieve the objective of the health research and not in a manner that may be damaging or distressing to participants. The controller will also implement measures to ensure the security of the data and arrangements to anonymise, archive or destroy personal data once the health research has been completed

The data collected from a clinical trial/investigation must be held by the Data Controller (organisation or individual that holds the data) but if anonymised may be given to third parties without further consent as long as the individual initially consented to their data being used for further research purposes.

If the data is not anonymised then the Data Controller must seek further explicit consent from the subjects for use of that data for any other purpose with the exception of Regulation 6(4) (a) of the Data Protection Health Research Regulations where it is determined that:

‘the public interest of the research significantly outweighs the public interest in requiring the explicit consent of the individual whose data is being processed’

In such cases an application for a ‘consent declaration’ may be made to the Health Research Consent Declaration Committee. The Committee shall consider applications under sections 5 and 6 of the Data Protection Health Regulations.

In accordance with S.I. No. 374/2006 all essential documents related to clinical trials of medicinal products should be retained for a least 5 years after the completion of the trial and for a longer period where so required.

8.5. Insurance

All researchers in a university have professional indemnity insurance cover. This cover usually does not extend to clinical trial/investigations. If your research project involves a ‘clinical trial/investigation’ as defined in 8.1, an intervention or proposed therapy you should check with the Research Support and Development Office to ensure that sufficient insurance is in place prior to commencement of the project.

Health care professionals in public hospitals are covered by a national scheme called ‘The Clinical Indemnity Scheme’ (CIS). The CIS was established in 2002 in order to rationalise previous indemnity held by clinicians and other practitioners and is managed by the State Claims Agency. Under the CIS, the state assumes full responsibility for the indemnification and management of certain clinical negligence claims. The CIS will cover claims from patients whose treatment was part of a clinical trial/investigation only under the following criteria:

- The clinical trial/investigation has received ethical approval from a relevant ethics committee;
- The clinical trial/investigation is designed by an entity or employee, covered by the scheme;
- Where a clinical trial/investigation is sponsored by an external organization, the CIS cover extends to treatment only and does not cover claims arising from protocol design or product liability.

The CIS covers health care professionals employed in public hospitals and/or other HSE

organisations. Healthcare professionals in private hospitals are not covered by the CIS but should have their own private policies in place.

In clinical trial/investigations where the protocol is designed by a hospital employee the CIS cover will extend to claims arising from the clinical trial/investigation design or protocol. In clinical trial/investigations where the protocol is designed by an investigator from an outside organisation, such as a university, CIS cover does not extend to claims arising from the clinical trial/investigation design or protocol. Therefore, all organisations involved in the project are required to have their own insurance.

The HSE will seek an indemnification from collaborating partners for clinical trial/investigations not designed by employees of the HSE. If a clinical trial/investigation involves a product manufactured by a private organisation or company, all partners should seek indemnification from that organisation or company prior to commencement of the research clinical trial/investigation. If Maynooth University is not sponsoring a clinical trial/investigation then indemnification must be sought from each of the clinical trial/investigation partners.

The levels of insurance cover for:

- Product liability from a company manufacturing a device;
- Public liability at the clinical trial/investigation site;
- Professional indemnity for all partners;

must be checked by the Research Support and Development Office to ensure that all partners have sufficient insurance cover for a clinical trial/investigation.

8.6. Good Clinical Practice

Good Clinical Practice (GCP) is an international standard of ethical and scientific quality for research and/or clinical trial/investigations that involve the participation of human subjects.

GCP should be implemented when designing, conducting, recording and reporting on human clinical trial/investigations in order to ensure that the rights, safety and wellbeing of subjects are protected and consistent with the principles of the Declaration of Helsinki and also that the data recorded is accurate and credible (EU Directive 2005/28/EC for trials of medicinal products).

In 1996 the International Conference on Harmonisation (ICH) produced a consolidation guidance document for GCP (Notice for guidance on good clinical practice: Consolidation guideline (ICH GCP) CPMP/ICH/135/95) This ICH GCP was developed through consideration of current good clinical practices in the EU, US, Japan, Australia, Canada, The Nordic countries and the World Health Organisation (WHO). The objective of ICH CGP is to provide a unified standard that would be mutually accepted by the regulatory authorities across all these jurisdictions.

GCP should be implemented for all research clinical trial/investigations that involve human subjects, regardless of whether the research is or is not required to be submitted for regulatory review.

The principles of Good Clinical Practice outlined by ICH GCP are as follows:

1. Clinical trials/investigations should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s);

2. Before a clinical trial/investigation is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject and society. A clinical trial/investigation should be initiated and continued only if the anticipated benefits justify the risks;
3. The rights, safety, and well-being of the clinical trial/investigation subjects are the most important considerations and should prevail over interests of science and society;
4. The available nonclinical and clinical information on an investigational product should be adequate to support the proposed clinical trial/investigation;
5. Clinical trials should be scientifically sound, and described in a clear, detailed protocol;
6. A clinical trial/investigation should be conducted in compliance with the protocol that has received prior Institutional Review Board (IRB) or Independent Ethics Committee (IEC) approval/favourable opinion;
7. The medical care given to, and medical decisions made on behalf of, subjects should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist;
8. Each individual involved in conducting a clinical trial/investigation should be qualified by education, training, and experience to perform his or her respective task(s);
9. Freely given informed consent should be obtained from every subject prior to clinical trial/investigation participation;
10. All clinical trial/investigation information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation, and verification;
11. The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s);
12. Investigational products should be manufactured, handled, and stored in accordance with applicable Good Manufacturing Practice (GMP). They should be used in accordance with the approved protocol;
13. Systems with procedures that assure the quality of every aspect of the clinical trial/investigation should be implemented;

8.7 Consent

For Clinical clinical trial/investigations with medicinal products consent should be given in accordance with S.I. No. 190/2004 and for medical devices, the common law on consent is applied. Subjects of a clinical trial/investigation must give informed consent. (See section 4.5 for general information on consent). An interview should be arranged between the Investigator and the subject. The subject should be made aware of and should be given the opportunity to understand the nature, objectives, significance, implications and risks and inconvenience of the clinical trial/investigation and the conditions under which the clinical trial/investigation will be conducted. The subject should be informed of his/her right to withdraw from the clinical trial/investigation at any time. That consent

should be for a specific purpose, written, dated and signed.

Consent for an incapacitated adult, not in the position to give consent, must be given by the subject's legal representative. Consent for minors should be given by every person with parental responsibility. Consent for minors should be given in consultation with the registered medical practitioner who has been treating the minor. The minor should also be given information about the risks and benefits of the clinical trial/investigation, suitable for his/her understanding. This information should be given by a person who has professional experience with minors. The explicit wish of a minor, who is capable of forming an opinion and assessing the information given, to withdraw or be excluded from a clinical trial/investigation must be considered by the Investigator. The clinical trial/investigation must relate directly to a condition from which the minor suffers.

8.8 Clinical Investigations with Medical Devices

8.8.1. Definitions

A clinical trial/investigation carried out with a medical device is, in the regulatory documentation, is termed, 'A Clinical Investigation'. Clinical investigations aim to assess the safety and clinical performance of a medical device to evaluate if the device is suitable for both the purpose and the population for which it is intended.

A clinical investigation is defined as;

*'any systematic **investigation** or study in or on one or more human subjects, undertaken to assess the safety and/or performance of a medical device.'* (SG5/N1:2007)

A medical device is defined by Directive 93/42/EEC as:

*"**device**' means any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application intended by the manufacturer to be used for human beings for the purpose of -*

- i. Diagnosis, prevention, monitoring, treatment or alleviation of disease,*
- ii. Diagnosis, monitoring, treatment, alleviation of or compensation for an injury of handicap,*
- iii. Investigation, replacement or modification of the anatomy of a physiological process, or*
- iv. Control of conception; and*

Does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, even if assisted in its function by such means;'

Medical devices are categorised primarily as general, active implantable or *in vitro* diagnostic devices depending on where they are used on or in the body. They are further classified, based on risk, into four classes, Class I, IIa, IIb and III with risk increasing from class I to III. Classification is decided on the basis of the intended use of the device, how invasive it may be, where it will be located within the body and also any existing evidence from other similar devices.

A series of four directives cover the safety and marketing of medical devices with the EU:

- Active implantable medical devices, S.I. 253 of 1994 and Directive 90/385/EEC;
- General medical devices S.I. 252 of 1994 and Directive 93/42/EEC;
- In vitro diagnostic medical devices S.I. 304 of 2001 and Directive 98/79/EC;
- Medical devices incorporating stable derivatives of human blood or human plasma, Directive 2000/70/EC amending Directive 93/42/EEC.

8.8.2. Requirements for regulatory approval

It will usually be necessary to carry out a clinical investigation for a medical device when a new device is to be tested (non-CE marked) where there is no previous existing documentation or evidence of the features or components of that device in a clinical setting. This also applies to existing devices that are:

- to be modified such that the safety and or clinical performance may be affected;
- have new materials and/or components not previously tested in the human body;
- are to be used for a longer period of time in the body, in a different location of the body or to be used for a new function (change of use).

The Sponsor will be responsible for submitting, to the regulatory authorities, a clinical investigation plan including the device risk analysis, design and materials documentation, cytotoxicity and biocompatibility data, sterilisation, pre-clinical and existing clinical data, patient information and consent forms and the investigator's brochure.

A Data Monitoring Committee (DMC) may be established by the Sponsor to give oversight to the investigation, the safety data or the critical performance end points. The DMC will make recommendations to the Sponsor whether to continue, suspend, modify or stop the clinical investigation.

The Monitor is separate from the DMC and ensures the quality of the study and oversees the progress of an investigation. Serious adverse events, serious adverse device effects and unanticipated serious adverse effects must be reported by the monitor to the Sponsor and to the regulatory authorities.

1. A serious adverse event may be an event that:
 - Led to death;
 - Led to serious deterioration in the health of the subject, that either resulted in
 - A life-threatening illness or injury, or
 - A permanent impairment of a body structure or a body function, or
 - In-patient or prolonged hospitalization, or
 - Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function;
 - Led to foetal distress, death or congenital abnormality or birth defect.
2. A serious adverse device effect (SADE) is an effect that results in any of the consequences characteristic of a serious adverse event.
3. An unanticipated serious adverse effect (UNSADE) is an effect which by its nature, incidence, severity or outcome is an effect which was not originally anticipated when carrying out the risk analysis (ISO 14155:2011(E)).

The Sponsor must prepare a close out report for all close-out activities, including routine close out and a final report of the clinical investigation, even if the investigation was terminated prematurely.

In certain circumstances, regulatory approval may not be required whilst carrying out a clinical investigation of a medical device. These exceptions include studies carried out by academia and clinical researchers where there is no intent to commercialise the results and there is no intent to seek commercial gain based on the data generated. The relevant regulatory body should be consulted for a complete list of regulatory requirements and also to determine definitively whether approval is required or not.

8.8.3. Conducting a clinical investigation

A device must be manufactured in such a way that the risks, to human subjects, of infection, toxicity, physical injury, exposure to radiation, electrical energy sources or magnetic fields is eliminated or reduced as far as is possible.

Where possible, pre-clinical testing of any medical device should be carried out to test biocompatibility and potential cytotoxicity prior to clinical testing. Testing may involve *in vitro* investigations, *ex vivo* tissue tests; appropriate modelling and/or animal models (please see section 4 of this policy for ethical requirements for animal based research). A risk analysis should be performed based on published or unpublished data and any pre-clinical testing that has been carried out.

The design of the investigation should determine whether the device is suitable for the purpose and the population for which it is intended and the design should ensure the results obtained have clinical relevance and scientific validity, addressing the clinical investigation objective.

Clinical Investigations should reflect the latest scientific and technical knowledge; and must include enough subjects and a robust statistical plan to guarantee the validity of the results. The procedures selected must be appropriate for the device and carried out under similar conditions for the normal use of the device. The Investigators must possess knowledge of the device technology, methodology and the diagnosis and management of the subject's condition.

Some of the factors that must be considered for a clinical investigation include:

- Type of device and its classification;
- Previous testing and/or novelty of the technology;
- Types of clinical applications;
- Exposure to the body of the product;
 - Surface
 - Implanted
 - Ingested
- All associated risks;
- Sterilisation of the device and/or components;
- Device labelling including instructions for use;
- Components – materials and/or substances;
- Patient population and disease;
- Cultural, demographic and geographic considerations (e.g. race, gender, age etc.);
- Impact of device failure;
- Period of exposure and lifetime of the device;
- Alternative treatments.

8.9 Clinical trials with Medicinal Products

8.9.1. Definitions

A clinical trial/investigation carried out with medicinal products is termed, by the legislation, 'A Clinical Trial' and/or 'Non interventional Trial'.

The legislation that covers investigative medical products includes:

- The relevant provisions of Regulation (EU) 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and will repeal the previous Directive 2001/20/EC.
- The aim of Regulation (EU) 536/2014 is to simplify and harmonise the authorisation of clinical trials across the European Union. The new Regulation is expected to enter into force six months after the full functionality of a new EU Database and single online EU Portal created under the new Regulation (Currently estimated to be in 2019).
- Clinical Trials on Medicinal Products for Human Use (S.I. 190 of 2004) which implemented the EU directive, Clinical Trial Directive on Good Clinical Practice in Clinical Trials (2001/20/EC)
- These regulations were further amended in 2004 (S.I. 878 of 2004) and in 2006 (S.I. 374 of 2006) which implemented the EU directives 2001/20/EC and 2005/28/EC which detailed guidelines for good clinical practice for medicinal products for human use.
- These regulations establish procedures relating to the conduct and review of clinical trials on medicinal products for human use and therefore replace the Control of Clinical Trial Acts of 1987 and 1990.

A 'Clinical Trial' is defined by S.I. 190/2004:

'clinical trial means any investigation in human subjects, other than a non-interventional trial, intended

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

'Non-Interventional Trial' means a study of one or more medicinal products which a marketing authorisation, where the following conditions are met:-

- (a) the products are prescribed in the usual manner in accordance with the terms of that authorisation,
- (b) the assignment of any patient involved in the study to a particular therapeutic strategy is not decided in advance by a clinical trial protocol but falls within current practice,
- (c) the decision to prescribe a particular medicinal product is clearly separated from the decision

- to include the patient in the study,*
- (d) no diagnostic or monitoring procedures are applied to the patients included in the study, other than those which are ordinarily applied in the course of the particular therapeutic strategy in question, and*
 - (e) epidemiological methods are to be used for the analysis of the data arising from the study.'*

And a medicinal product is defined by directive 2001/83/EC, as:

- (a) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or*
- (b) 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.*

8.9.2. Requirements for regulatory approval

It is necessary to apply for regulatory approval to carry out a clinical trial and also for authorisation for the manufacture and/or marketing of a medicinal product which includes;

- Placebo products;
- Authorised and unauthorised medicines with an active substance;
- Homeopathic and herbal products.

Approval for the use of authorised medicines is required where the medicine is to be used in a manner that is different from that which the authorization was given (e.g. change of dose, application, and indication).

Applications for a clinical trial must be first registered with EU through EudraCT. The EU guidelines should be followed when preparing the protocol. Applications must be submitted to the regulatory authorities by the Sponsor in line with the authority's guidelines. A clinical trial protocol describing the objectives, design, methodology, statistical considerations, and organisation of the clinical trial and successive or amended versions of the protocol must be submitted to the regulatory authorities (S.I. 190/2004).

If the product to be used in the trial contains a genetically modified organism/microorganism a separate license is also required which should be provided with the clinical trial application.

Products must be labelled in accordance with the requirement of Annex 13 to the EU Guide to Good Manufacturing Practices on 'Manufacture of Investigational Medicinal Products' (Eudralex, Vol 10, Chapter 3).

The authorisation will depend on the type of medicinal product used in the study.

There are two categories of products:

- General medicinal products, biological and biotechnological products
- Advanced therapy medicinal products (gene therapy, somatic cell therapy, tissue engineered products or products containing genetically modified organisms).

It is the responsibility of the Monitor to report any suspected serious adverse reactions (SUSARs) that

occur during the clinical trial according with regulatory requirements. Detailed records of all adverse events must be kept, must be available to the regulatory authorities upon request, and should be cognisant of guidelines released such as 'Detailed Guidance on the Collection, Verification and Presentation of Adverse Reaction Reports arising from Clinical Trials on Medicinal Products for Human use, CT-3'(2011/C 172/01).

An end of trial report must be submitted regardless of whether the trial is completed or terminated prematurely. The European Commission's guidelines and the relative regulatory body should be consulted for a complete list of regulatory requirements.

8.9.3. Conducting a clinical trial

Clinical trials are conducted to test an investigative medicinal product against either an existing treatment or product or placebo (control).

All clinical trials should be conducted according to GCP (see section 8.2.3: Good Clinical Practice). In addition other guidelines for the quality, safety and efficacy of investigative medicinal products should be taken into account;

- 'Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95)
- The 'Detailed Guidance on the Collection, Verification and Presentation of Adverse Reaction reports arising from Clinical Trials on Medicinal Products for Human Use, CT-3'. Compliance is necessary to Annex 13 to the 'GMP Guide on Manufacture of Investigational Medicinal Products.

All sites involved in the trial may be subject to GCP inspection and must operate to the GCP standards, for example:

- Investigator site or multiple sites if applicable;
- Manufacturing site of the investigative medicinal product;
- Labs used for trial analyses;
- Sponsor's site;
- Contract organizations performing some of the functions for the Sponsor.

Clinical trials are normally conducted in phases:

- I. Researchers test a new medicinal product with a limited group of subjects for the first time to evaluate its safety, determine a safe dosage range, and identify side effects;
- II. The product is given to a larger set of subjects to test its affect and to further evaluate safety;
- III. The product is given to large cohort of subjects to confirm effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow product to be used safely;
- IV. Studies are carried after the product has been marketed to gather information on its effect in various populations and any side effects associated with long-term use.

8.10 Conflict of Interest

The integrity and the honesty/objectivity of a clinical trial/investigation are paramount in the protection of the welfare of human subjects. Any risk of undue influence due to a conflict of interest could result in subjects being adversely affected and the reputation of the organizations involved being severely damaged.

For definitions of and guidelines and management processes for conflicts of interest, please refer to the Maynooth University, Research and Commercialisation Conflict of Interest: Policy and guidelines.