IRISH RESEARCH NURSES NETWORK

CLINICAL RESEARCH NURSE ORIENTATION PACK

June 2015

An introduction to the role of the research nurse and to the regulations and guidelines governing clinical research in Ireland
Irish Research Nurses National Orientation Program

Foreword

On behalf of the Irish Research Nurses Network (IRNN) I am delighted to present this orientation program to facilitate you, the research nurse, as you start working in the area of clinical research. I hope it will help guide you through some of the complex processes involved in this multifaceted role and help steer you in the direction of further information.

This program was compiled by members of the IRNN as part of its commitment to support the educational and professional needs of clinical research nurses, working in a variety of settings in Ireland. The IRNN recognised the need to develop an orientation program to help standardise the training of all clinical research nurses. It is hoped that this document will also prove a useful tool for mentors in orientating staff into their new role. Aspects of this document are equally applicable to other members of the clinical research team and may be used for their orientation also.

I hope you find this document beneficial and on behalf of the IRNN team I wish you well in your career in clinical research.

Mary Clarke Moloney, Chairperson, Irish Research Nurses Network.

For more information about the Irish Research Nurses Network see: http://irnn.ie

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Acknowledgements

We would like to acknowledge the Dublin Centre for Clinical Research (DCCR) and the UK Clinical Research Facility (UKCRF) Network who kindly allowed us to adapt sections from their orientation, competency and induction framework documents for inclusion in this folder. Version 1 of this resource was based on the DCCR Research Nurse Orientation Pack originally developed for use in DCCR affiliated clinical research centres. The IRNN Clinical Research Nurse Orientation Pack, Version 2, June 2015, is a revision of Version 1, published in September 2013. The resource was revised in response to our survey of the use of the pack, and to reflect changing legislation and guidelines. Further revisions and addendums will be provided as necessary to reflect changing policies and practices in the clinical research setting.
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USING THIS ORIENTATION PACK

This pack has been designed for use during a period of orientation to a new workplace setting. Ideally it should be utilised as part of an orientation process supported by a mentor or line manager.

Section 1.3 provides recommended timelines for completion of various elements of an orientation process. This can be adapted according to local circumstances, and according to the inductee’s prior experience. It is recommended that a signed and dated checklist be used to record achievement and completion of these processes. This can be a locally developed tool, or you can use the sample checklist/signature sheets provided (Appendix i).

**New staff member/Inductee**

- Discuss orientation/induction needs with mentor/line manager, taking into considerations prior experiences and responsibilities associated with new role
- In conjunction with mentor/line manager identify objectives to be achieved and timelines for completion
- Identify and avail of opportunities and resources available to achieve agreed objectives
- Sign and date completed objectives in a timely manner
- Identify barriers to completion of objectives or areas of non-completion of expected targets
- Should issues of concern arise about failure to meet objectives identify these in a timely manner and address them in line with local management and Human Resources policies

**Mentors/Line Managers**

- Access orientation and induction needs of new staff member
- In conjunction with inductee identify objectives to be achieved and timelines for completion
- Provide opportunities and resources for inductee to achieve agreed objectives
- Sign and date completed objectives in a timely manner
- Identify barriers to completion of objectives or areas of non-completion of expected targets
- Should issues of concern arise about failure to meet objectives identify these in a timely manner and address them in line with local management and Human Resources policies
SECTION 1

Orientation Process
1.1. INTRODUCTION

Congratulations on your new position in Clinical Research. The training and educational needs of research nurses and study coordinators are complex due to the level of specialist knowledge necessary to fulfil the role at a professional level. Responsibilities include the care of patients and their families as well as the planning, coordination and administration of the clinical research itself. This necessitates the development of a wide range of skills, knowledge, training, education and experience.

1.2. OBJECTIVES OF THE ORIENTATION PROGRAMME

The aim of this programme is to standardise the orientation and of clinical research nurses and midwives in Ireland. It will orientate you to the clinical research environment and the role and responsibilities of the clinical research nurse. Learning about clinical research, the people involved, systems and procedures is likely to be an incremental process during the coming months and much learning will occur informally in the workplace. This pack will provide a structure for self-directed and/or supported orientation, and an introduction to clinical research processes and governance. It will provide you with information about the relevant legislation and regulations underpinning clinical research and the role and responsibilities of a clinical research nurse.

Protected time should be allocated as part of an induction and training process to allow you to work through this folder. Ideally, your manager or mentor should agree objectives with you and agree on a timeframe to achieve your targets. It is recommended that, as outlined on page 3, you complete a structured orientation process to ensure you have received an introduction to all aspects of clinical research applicable to your role (see Sample Checklist, Appendix i).

The opportunities available to you will depend on your workplace. Training methods for orientation and continuing professional development may include:

- In-service induction & training programmes
- Shadowing experienced staff members to observe practice
- Introduction to appropriate departments/personnel etc.
- Reviewing relevant literature and web resources
- Attendance at relevant local and national research meetings and seminars
### 1.3. ORIENTATION PROCESS

This section contains suggested induction processes and timelines that can be adapted to individual needs.

<table>
<thead>
<tr>
<th>Areas Of Induction</th>
<th>Target Timelines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Local Orientation</strong></td>
<td>First day on premises</td>
</tr>
<tr>
<td>• Tour of facility and familiarisation with layout including building opening times, authorised access and emergency exits, toilets and hand-washing facilities, tea/coffee facilities</td>
<td></td>
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<tr>
<td>• Shared resources (e.g. fax, photocopier)</td>
<td></td>
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<tr>
<td>• Allocation of workspace, computer, access to phone etc.</td>
<td></td>
</tr>
<tr>
<td>• Hours/time of working day</td>
<td></td>
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<tr>
<td>• Fire, emergency &amp; cardiac arrest information</td>
<td></td>
</tr>
<tr>
<td><strong>Introductions</strong></td>
<td>At first opportunity after commencement</td>
</tr>
<tr>
<td>• Introduction to core staff and associate staff within the facility</td>
<td></td>
</tr>
<tr>
<td>• Introduction to porters and building administration staff</td>
<td></td>
</tr>
<tr>
<td>• Introduction to affiliated hospital personnel as required</td>
<td></td>
</tr>
<tr>
<td><strong>Institutional Orientation</strong></td>
<td>Prior to or as soon as possible after commencement</td>
</tr>
<tr>
<td>• Tour of institution and explanation of history, ethos and mission of the institution</td>
<td></td>
</tr>
<tr>
<td>• Introduction to institutional resources – Library, website etc.</td>
<td></td>
</tr>
<tr>
<td>• Familiarisation with institutional HR policies – annual leave, sick leave, etc.</td>
<td></td>
</tr>
<tr>
<td><strong>Organisation of identity badge/swipe card, computer and e-mail access</strong></td>
<td>1st week in post</td>
</tr>
<tr>
<td>• Passwords</td>
<td></td>
</tr>
<tr>
<td>• Remote access to server</td>
<td></td>
</tr>
<tr>
<td><strong>Training in and access to electronic systems for</strong></td>
<td>First Month</td>
</tr>
<tr>
<td>• Scheduling and reporting time allocated to specific activities</td>
<td></td>
</tr>
<tr>
<td>Task</td>
<td>Duration</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>• Managing patient bookings</td>
<td></td>
</tr>
<tr>
<td>• Using study specific databases</td>
<td></td>
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<tr>
<td>• Using hospital/HSE reporting systems e.g. for lab results</td>
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<tr>
<td><strong>Meeting with the nurse manager, department manager and/or your designated mentor to:</strong></td>
<td></td>
</tr>
<tr>
<td>• Identify specific learning needs, and book attendance at training days: for example, ICH GCP, lab safety, venepuncture &amp; cannulation, CPR, First Aid, and other mandatory or optional training sessions</td>
<td>First 2 weeks</td>
</tr>
<tr>
<td>• Organise shadowing with other research nurses, specialist nurses, etc. as indicated</td>
<td></td>
</tr>
<tr>
<td>• Provide information about education and training resources, Research Nurse Network mailing list &amp; other resources as applicable</td>
<td></td>
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<tr>
<td>• Set objectives and targets for current role</td>
<td></td>
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<tr>
<td>• Arrange schedule for future PPD meetings as per local policy</td>
<td></td>
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<tr>
<td><strong>Training in Standard Operating Procedures, policies and guidelines.</strong></td>
<td></td>
</tr>
<tr>
<td>• Seek guidance from your mentor/manager regarding which are specific to your trials or activities.</td>
<td>From day 1 to 6 weeks</td>
</tr>
<tr>
<td>• Sign and date to indicate that each SOP has been read and understood.</td>
<td></td>
</tr>
<tr>
<td>• Complete associated training as necessary, for example, use of specific equipment</td>
<td></td>
</tr>
<tr>
<td><strong>Introduction to Principal Investigator/Research Team</strong></td>
<td></td>
</tr>
<tr>
<td>• Introduction to the research team and the research specialty multidisciplinary team for allocated studies</td>
<td>First 2 weeks</td>
</tr>
<tr>
<td>• Read protocols and specific trial information including Patient information Sheets and Consent forms</td>
<td></td>
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<tr>
<td>• Meet study monitor and complete study specific training (provided by Monitor or study team) before starting any study activity</td>
<td></td>
</tr>
<tr>
<td>• Orientation to wards, outpatient departments etc. associated with allocated studies</td>
<td></td>
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<tr>
<td><strong>Understanding of importance of delegation logs</strong></td>
<td></td>
</tr>
<tr>
<td>• You must have received training in ICH GCP, the study protocol training and trial specific activities before performing any delegated duties for a clinical trial</td>
<td>First month</td>
</tr>
</tbody>
</table>
1.4. INTRODUCTION TO THE RESEARCH NURSE ROLE

‘Clinical research nursing is nursing practice with a specialty focus on the care of research participants. In addition to providing and coordinating clinical care, clinical research nurses have a central role in assuring participant safety, ongoing maintenance of informed consent, integrity of protocol implementation, accuracy of data collection, data recording and follow up’  http://clinicalcenter.nih.gov/nursing/crn/crn_2010.html

1.4.1. AREAS OF RESPONSIBILITY

The Irish Research Nurses Network identifies three key areas of responsibility associated with the CRN role: clinical, managerial and educational. (http://irnn.ie)

Clinical

The research nurse acts as the primary advocate for the patient, both prior to and throughout their participation in a research study. They also educate the patient and family about their disease process, study related procedures and alternative choices. The research nurse is also involved in the informed consent process. The research nurse schedules procedures and performs initial patient interviews, nursing assessments and clinical duties such as venipuncture, drug administration and adverse event management.

Managerial

The most significant and extensive aspect of the role of the research nurse is the management and co-ordination of individual research studies. Whilst always working within his/her scope of practice and delegated responsibilities, the research nurse may be responsible for:

- preparation of study protocols
- the preparation, submission and maintenance of ethics and regulatory documents
- developing study related documents
- screening and recruitment of patients
- data collection, data entry, adverse event reporting
• preparation of biological samples for shipment to reference laboratories
• financial account management
• establishment of Standard Operating Procedures

**Educational**

Education is a vital role of the research nurse. Patients are educated about studies and procedures and on occasion the research nurse educates the clinical team about the studies. There is also a responsibility for research nurses to continue their own education through literature review, meeting and workshop attendance relevant to their clinical area or research specialty.

**1.4.2. THE RESEARCH NURSE ROLE WITHIN THE CLINICAL RESEARCH TEAM**

Numerous reports on the status of clinical research in the Irish setting allude to the role of the clinical research nurse, and its value in forwarding the research agenda, but there is still little formal recognition or definition of the role. A report compiled by Dr Sarah Condell for the Health Research Board and National Council for the Professional Development of Nursing and Midwifery was published in 2008. It identified a number of challenges associated with the role:

• Variety of titles, with different grades and pay scales and large variance in contracts, conditions and entry criteria

• Lack of visibility – role of CRN largely unknown

• Wide range of roles and responsibilities; Role is diverse depending on setting, type & stage of study, composition of research team

• No standardisation of professional development and lack of opportunity for role progression

However, the report also identified that nurses enjoy the role:

• Tasks within the role cluster around the centre of the research continuum

• Role utilises nurse/midwife clinical practice skills

• Role itself is good source of job satisfaction
• Potential to build nursing & midwifery research in parallel with medical-led research

*Ref: NCNM (2008) Report on the Role of the Nurse or Midwife in Medical-led Clinical Research HRB/NCNM Dublin*

The research nurse is responsible for the day to day running of research studies including identification and recruitment patients into studies according to agreed protocols, assisting in the informed consent process and management of study related procedures and data. The research nurse must have the ability to work independently, to prioritise his/her own workload, to communicate effectively with all members of the research team, and be able to meet tight deadlines. All clinical research activity must be compliant with the ethically approved study protocol and conducted in line with current legislation and guidelines.

<table>
<thead>
<tr>
<th>Key CRN Responsibilities</th>
<th>Key CRN Attributes</th>
</tr>
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<tbody>
<tr>
<td>• Patient identification and recruitment</td>
<td>• Clinical experience</td>
</tr>
<tr>
<td>• Patient consent – varies depending on study type</td>
<td>• Knowledge of research theory and the research process</td>
</tr>
<tr>
<td>• Organisation and completion of study visits</td>
<td>• Professional approach to care</td>
</tr>
<tr>
<td>• Completion and maintenance of study documents</td>
<td>• Attention to detail - organisation / managerial</td>
</tr>
<tr>
<td>• Maintenance of Investigator Site Files</td>
<td>• Time management!</td>
</tr>
<tr>
<td>• Liaison with PI/research team/clinical staff</td>
<td>• Ability to work autonomously</td>
</tr>
<tr>
<td>• Liaison with CRA/Sponsor/Institutions</td>
<td>• Good communication skills and interpersonal relationships</td>
</tr>
</tbody>
</table>

**Associated skills**

• Patient assessment
• Venepuncture and cannulation
• Ability to learn new skills or techniques as needed
• Safe Laboratory practice
• Data entry
• Teaching skills
• Organisation and time management
• Effective communication

Advanced areas of responsibility associated with the CRN role may include:

• Protocol development
• Preparing and submitting Ethics and/or Regulatory submissions
• Budget assessment and negotiation
• Feasibility assessment
• Grant applications and management of funds
• Reporting studies and dissemination of results
• Nurse-led research

1.5. THE CLINICAL RESEARCH SITE

Clinical research studies should be conducted in an environment that is suitable for its purpose and ensures a positive experience for research participants. The area for clinical research activity / review will be designated by your institution. Increasingly, clinical research is located in dedicated clinical research facilities or units, usually under the auspices of an academic institution, but physically located on a hospital campus. Research for specific disease areas (e.g. Oncology) may be located within the specialist department. CRNs not located in such a unit may face challenges securing dedicated space for clinical trial activity, and this should be factored into the planning stage of proposed trials.

Clinical Research Team Members

Depending on the location and the resources available, members of a Clinical Research team may include:

- Director/Head of Department
- Nurse manager
- Administrator
- Research nurses
- Research assistants
- Investigators
- Data managers
- Laboratory technicians
- Clinical informatics manager
- Statistician

Some of these roles are discussed further in Section 3.2 of this document.
**Training Records**

All Clinical Research Nurses/Midwives should develop and maintain their own Training Record which can be used to show evidence of experience and training during an audit or inspection. Typically this would include an up-to-date Curriculum Vitae, training certificates, with hand-outs from training if applicable, agendas from meetings or conferences attended, certification of professional registration or qualification, publications, and any other evidence of experience, qualification and continuing professional development. Local SOPs may be available to outline this process further.

**Training in Good Clinical Practice (GCP) and Research Governance**

It is mandatory that all Research Staff have training in good clinical practice, including ICHGCP, EU Directives and Regulations and Irish legislation. Training opportunities should be identified during the orientation process. All clinical research staff should complete GCP training, regardless of whether their research involves a medicinal product.

**Skills and competencies**

As with all areas of nursing practice, Research Nurses must work within their scope of practice. This requires that you do not accept delegation for tasks which fall outside your present skills and competence. The orientation period, and ongoing personal development processes in your organisation, should be used to identify areas of practice to be developed and opportunities to develop skills and competencies.

**Research Support/Training**

Relevant training opportunities are generally advertised on institutional websites and sent via email to the staff mailing list. Research nurses may need to liaise with hospital nurse educators to avail of additional training from the nursing perspective.

**1.6. POST-GRADUATE TRAINING OPPORTUNITIES**

The following are examples of specific clinical research postgraduate education programmes which may be of interest to nurses working in the clinical research area in Ireland:

**Postgraduate Certificate in Nursing (Clinical Research):**

Offered by the School of Nursing and Midwifery, RCSI, this Level 9 programme is delivered
part-time over 6 months and includes 3 modules: Clinical Research Design & Methodology, Ethics & Regulatory Affairs and Clinical Research Practice and Management. Each module is awarded 10 credits, and, under the European Credit Transfer and Accumulation System (ECTS), progression to MSc can be facilitated either in RCSI or in other academic institutions. Modules can be taken on a stand-alone basis by nurses and other members of the healthcare research team for academic credit. For more details contact the programme coordinator: Deirdre Hyland (dhyland@rcsi.ie), or visit http://www.rcsi.ie/nursing

**MSc in Clinical Research:**
Offered by NUI Galway, this is a two-year part-time programme of academic study in Clinical Research Methodology. Year 1 will be spent at NUIG and Year 2 is completed by a combination of distance learning through modules delivered by McMaster University and NUI Galway, and on-site modules delivered by NUI Galway. A full-time one-year option is available to students who wish to complete the MSc in a full-time capacity. For more details see: http://www.nuigalway.ie/courses/taught-postgraduate-courses/clinical-research.html

**Graduate Certificate Clinical and Translational Research:**
Offered by the School of Medicine and Medical Science in UCD is a one-year part time course. Credits from this course may be applied towards requirements for a Graduate Diploma in Clinical & Translational Research, and/or an MSc. in Clinical & Translational Research. For more details see:
http://www.ucd.ie/medicine/studywithus/graduatestudies/clinicalresearch/mscclinicaltranslationalresearch/

**MSc Clinical & Translational Research:** offered by the School of Medicine and Medical Science in UCD is a two year part time course. Learning is through a combination of formal teaching on campus for 6-8 hours on three sequential days during six blocks, directed home studies with review of selected educational material, and completion of projects for continuous assessments.
http://www.ucd.ie/medicine/studywithus/graduatestudies/clinicalresearch/mscclinicaltranslationalresearch/
SECTION 2:

Regulations & Legislation Governing

Clinical Research
2.1. BACKGROUND TO CLINICAL RESEARCH PRACTICE GUIDELINES AND LEGISLATION

Research involving human participants is necessary in order to advance knowledge in the field of biomedical science. However, there are many examples throughout history of human research subjects being treated unethically, and of atrocities in relation to human research having occurred throughout the world. Therefore, regulations, guidelines and ethical codes of conduct are required to ensure that the rights and welfare of research participants are protected and to ensure that similar events are not repeated. The following sections provide an overview of the important guidelines and legislation with regard to clinical trials, from an Irish and European perspective in particular.

2.2. THE NUREMBERG CODE

The Nuremberg Code, formulated in August 1947, is a set of research ethics principles for human experimentation drawn up as a result of the Nuremberg Trials held at the end of the Second World War. It is a seminal document in the history of the ethics of medical research and the first of its kind to ensure the rights of subjects. Specifically, the principals were set in response to the inhumane human experimentation, carried out in concentration camps during WW2, by Nazi doctors such as Dr Josef Mengele. The Nuremberg code includes such principles as informed consent and absence of coercion; properly formulated scientific experimentation; and beneficence towards experiment participants.

The ten points of the Nuremberg Code

1. The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understood and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonable to be expected; and the effects upon his health or person which may possibly come from his participation in the
experiment. The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study and not random and unnecessary in nature.

3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.

4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.

5. No experiment should be conducted where there is a prior reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.

6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.

7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.

8. Only scientifically qualified persons should conduct the experiment. The highest degree of skill and care should be required through all stages of the experiment of those that conduct or engage in the experiment.

9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.

10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgement required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.
2.3. DECLARATION OF HELSINKI

The Declaration of Helsinki is the World Medical Association's best-known policy statement. The first version was adopted in 1964 and the document has been amended many times since, most recently at the WMA General Assembly in October 2013 (See full document in Appendix ii). The current (2013) version is the only official one; all previous versions have been replaced and should not be used or cited except for historical purposes. The declaration is not legally binding but its power lies in the extent to which its underlying principals have been incorporated into guidelines and law internationally. It is a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects.

The key principles of the Declaration of Helsinki are:

- In medical research involving human subjects, the well-being of the individual research subject must take precedence over all other interests.
- It is the duty of the physician to protect the life, health, privacy and dignity of the human subject.
- Medical research involving human subjects must conform to generally accepted scientific principles.
- Effects on the environment and welfare of animals used for research must be considered.
- Each experimental procedure should be fully described in a protocol and be considered by an ethical review committee.
- The research protocol should contain a statement of the ethical aspects of the research study.
- Medical research must be conducted by scientifically qualified personnel supervised by a clinically competent medical person.
- Predictable risks and burdens should be assessed in comparison with foreseeable benefits for the subject and others.
- Physicians should cease any investigations if the risks outweigh the potential benefits.
- The importance of the objective should outweigh the risks and burden to the research subject.
- The subjects must be volunteers and informed participants.
The right of research subjects to safeguard their physical and mental integrity and privacy must be respected.

Each potential subject must be adequately informed of every aspect of the research study and their freely given consent sought in writing.

For subjects in a dependent relationship with the researcher, informed consent should be sought by an independent physician.

For legally incompetent subjects the investigator must seek consent from a legally authorised representative.

Where the legally incompetent subject is able to give assent to decisions about participation in research that assent should be sought in addition to consent of the legally authorised representative.

If research is intended on subjects who cannot consent, it must be justified to, and be approved by the ethics committee.

Results of all trials conducted according to these principals should be accurately published and be made available.

2.4. INTERNATIONAL CONFERENCE OF HARMONISATION, GOOD CLINICAL PRACTICE

ICH GCP is a phrase that you will hear frequently during your work in research and is the code of good practice that must be adhered to.

“Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with Good Clinical Practice and the applicable regulatory requirements”

Until 1996 there were several documents in existence relating to good clinical practice (GCP). An international committee for the harmonisation of good clinical practice (ICH GCP) was formed to produce a mutually accepted standard, which was agreed by the European Union, Japan and the United States of America. These guidelines were implemented in the participating countries and had the advantage of facilitating mutual acceptance of data by the regulatory authorities of these countries, thus avoiding replication of studies.

The ICH GCP guidelines (1996) are very comprehensive and list responsibilities for all involved in research activity. It includes specific sections listing responsibilities of ethics
committees, investigators and sponsors. There are also sections detailing the format of trial protocols, investigator brochures and essential documents required for clinical trials. The guidelines were an attempt to unify GCP standards but they, of themselves, lacked the legal status needed to enforce their use. Although most sponsor companies adopted the guidelines from the outset there were some that did not. In particular academic research units found the cost implications were too great to implement the guidelines, and some ethics committees were reluctant to adhere to the extra requirements that ICH GCP guidelines made of them, since they were not legally obliged to do so. However in 2001 the European Union (EU) issued a clinical trial directive (2001/20/EC) which required the ICH GCP guidelines to be adopted into national legislation in member states, ensuring that all parties practising research now have to adhere to the guidelines.

The Main Principles of ICH GCP

- Before a trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefits for the individual trial subjects and society. A trial should be initiated and continued only if the anticipated benefits justify the risks.
- The rights, safety and well-being of the trial subjects are the most important consideration and should prevail over interests of science and society.
- The available non-clinical and clinical information on an investigational product should be adequate to support the proposed clinical trial.
- Clinical trials should be scientifically sound and be described in a clear detailed protocol.
- A trial should be conducted in compliance with the protocol that has received prior institutional review board (IRB)/research ethics committee (REC) approval/favourable opinion.
- 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.
- Each individual involved in conducting a trial should be qualified by education, training and experience to perform his or her respective task(s).
- Freely given informed consent should be obtained from every subject prior to clinical trial participation.
- All clinical trial information should be recorded, handled and stored in a way that allows its accurate reporting, interpretation and verification.

- 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).

- 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.

- Systems with procedures that assure the quality of every aspect of the trial should be implemented.

**Clinical investigation of medical devices for human subjects -- Good Clinical Practice**

ICH GCP does not apply to device trials – this area of research is guided by ISO 14.155. ISO 14155:2011 addresses good clinical practice for the design, conduct, recording and reporting of clinical investigations carried out in human subjects to assess the safety or performance of medical devices for regulatory purposes. It specifies general requirements intended to protect the rights, safety and well-being of human subjects, ensure the scientific conduct of the clinical investigation and the credibility of the results, define the responsibilities of the sponsor and principal investigator, and assist sponsors, investigators, ethics committees, regulatory authorities and other bodies involved in the conformity assessment of medical devices.

**2.5. EUROPEAN DIRECTIVE ON GOOD CLINICAL PRACTICE IN CLINICAL TRIALS**

The EU Clinical Trials Directive of 2001 (2001/20/EC), and subsequent amendments, aimed to harmonise and streamline clinical trial conduct and IMP manufacture throughout the member states. It relates to all trials involving medicinal products for human use, and encompasses all personnel involved with clinical trial activities. Member states were required to implement the directive by May 2004. In Ireland the EU directive was transposed into law under Statutory Instrument 190 (S.I 190 of 2004) European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations, 2004. S.I. 190 of 2004 has been amended to include S.I. 878 of 2004 and S.I. 374 of 2006, reflecting
amendments to the EU directive. These regulations replaced the Control of Clinical Trials Acts, 1987.

**Guidance provided by the EU Directive includes:**

- Properly obtained and documented informed consent must be obtained.
- Adherence to Data Protection directive 95/46/EEC is required.
- Indemnity and insurance to cover liability of investigator and sponsor is required.
- Subjects must be given a contact point from where further information can be obtained.
- Extensive details relating to the conduct of clinical trials using those unable to give consent.
- A single ethics committee opinion is required for national multi-centre studies.
- 60 days maximum is allowed for an ethics committee to provide an opinion (35 days for an amendment).
- Extension to these approval times apply when studies involve gene/cell therapies.
- A database with details of European trials and adverse health events will be set up.
- Adverse event reporting to be standardised.
- GCP inspections to become mandatory.
- Controls to be placed on the manufacture and labelling of investigational products.
- Studies can be stopped in the event of sponsor and/or investigator non-compliance.

SI 190 also provided for the establishment of recognised ethics committees for provision of a single ethics opinion for trials that fall under the legislation and for regulatory inspection of clinical trials by the Irish Medicines Board (now renamed as the Health Products Regulatory Authority (HPRA)).

**New EU Regulations**

On 16 April 2014 the EU adopted a new Regulation on clinical trials on medicinal products for human use; EU No 536/2014 (the "Clinical Trials Regulation"), thereby repealing Directive 2001/20/EC. The Regulation entered into force on 16 June 2014 but will apply no earlier than 28 May 2016. The Clinical Trials Regulation aims to create an environment that is favourable for conducting clinical trials, with the highest standards of patient safety, for all EU Member States. Intrinsic to this is the simplification of current rules, for example:
• A streamlined application procedure via a single entry point - an EU portal and database, for all clinical trials conducted in Europe. Registration via the portal will be a prerequisite for the assessment of any application;

• A single authorisation procedure for all clinical trials, allowing a faster and thorough assessment of an application by all Member States concerned, and ensuring one single assessment outcome and authorisation per Member State;

• The extension of the tacit agreement principle to the whole authorisation process which will give sponsors and researchers, in particular SMEs and academics, more legal certainty;

• Strengthened transparency for clinical trials data.

2.6. MEDICAL RESEARCH ETHICS COMMITTEES

A Medical Research Ethics Committee (REC) reviews applications to undertake medical research. Its remit is to protect the safety and welfare of research participants, and primarily to weigh the risks and benefits for research participants, of individual research projects. A REC must at all times be ICH/GCP compliant.

Clinical Trials of Investigational Medicinal Products (IMPs)

At present a clinical drug trial, and some device trials, cannot take place in any EU member state without obtaining a favourable approval from a recognised Research Ethics Committee (REC), and from the Health Products Regulatory Authority. There are currently 12 RECs in Ireland that have been recognised by the Department of Health and Children to review applications for clinical trials of medicinal products for the whole of Ireland. In addition, the drug trial must have a European Clinical Trial (EudraCT) number https://eudract.ema.europa.eu/

Legislation for the formulation of a recognised ethics committee is very specific and sets out how many members the committee should have, and what proportion of these must be lay members. S.I 190 sets out how many members must be at a meeting in order to have a quorum. It also sets out specific timelines within which a REC must make a decision in relation to a clinical trial and in relation to amendments to a clinical trial.

Clinical trials of IMPs, which are primarily funded by pharmaceutical companies, require an
indemnity agreement, and a clinical trial agreement, which are both legal contracts, drawn up between the sponsor and the hospital/principal investigator. Adequate insurance must be in place in case of an injury occurring to a trial participant.

**Approval of ‘Other Research’**

A REC reviews many other types of research other than IMP trials. For example, it reviews clinical investigations of medical devices, e.g. stents and pacemakers. There are statutory instruments in place also in relation to medical devices, which the committee must comply with. Unlike drug trials however the device legislation does not allow a REC to give a central favourable opinion for Ireland. Some medicine device trials also require HPRA approval.

Academic or non-interventional research taking place in a hospital must also be reviewed by the local REC. A large percentage of research taking place in a teaching hospital would fall into the category of research other than clinical trials, and there is no specific legislation governing the REC’s role in this area. However more general pieces of legislation which the committee must comply with include Data Protection Legislation, Freedom of Information Legislation, HSE National Consent Policy (2014), Human Tissue Legislation (at consultation stage only) and common law on consent for medical treatment and research. In addition, there are relevant publications from the Irish Council for Bioethics to consider and many professional organisations have guidelines in place e.g. the Nursing & Midwifery Board of Ireland (NMBI) and The Irish Medical Council.

**Documents required for REC Approval of a Clinical Trial**

1. Cover Letter
2. REC Application Form
3. Application Fee
4. Protocol with all current amendments
5. Narrative Summary
6. Irish Medicines Board approval letter
7. Consent Form (on headed notepaper)
8. Patient Information Leaflet (on headed notepaper)
9. Indemnity Form between the hospital and the sponsor (if applicable)
10. Insurance Certificate
11. Copy of letter of notification to patient’s GP (on headed notepaper)
12. Principal Investigator’s up-to-date Curriculum Vitae
13. Any questionnaire which participant may be asked to complete
14. Any advertisement or circular used in recruitment

Additional application documents required under European Communities (Clinical Trials on Medicinal Products for Human Use Regulations 2004) Statutory Instruments S. I. No. 190 of 2004:
1. Request for authorisation of a clinical trial on a medicinal product for human use to the Competent Authority and for opinion of the Ethics Committee in the Community
2. Agreement between the Principal Investigator and the sponsor
3. List of Competent Authorities to which the application has been submitted and details of decisions, if available
4. Summary of the protocol in the national language
5. Peer review of the scientific value of the trial, when available, not compulsory
6. Investigators brochure
7. Summary of Product Characteristics (SmPC) (for products with marketing authorisation in the Community
8. Outline of all active trials with the same Investigational Medicinal Product (IMP)
9. Facilities for the trial
10. Site specific assessment form
11. CV of the co-ordinating investigator responsible for the conduct of the trial in a site in the Member State concerned (principal investigator)
12. Provision for indemnity or compensation in the event of injury or death attributable to the clinical trial.
13. Any insurance or indemnity to cover the liability of the investigator and sponsor. This should include the insurance policy associated with the Certificate of Liability Insurance (confirm that the interest of any institution in this jurisdiction in which it is proposed this trial will be conducted and the interest of any clinician conducting the trial will be noted on the policy. It will be necessary to examine whether the aggregate limit is adequate in the
context of the number of participants in the trial world-wide and the levels of awards, which might be anticipated, in different jurisdictions)

14. Compensation to subjects
15. Compensation to investigators
16. Agreement between the sponsor and the trial site
17. Agreement between the investigators and the trial sites
18. Certificate of agreement between sponsor and investigator when not in the protocol

**Documents required for REC Approval of an Academic/Non-interventional Study**

1. Cover Letter
2. REC Application Form
3. Protocol with all current amendments
4. Narrative Summary
5. Consent Form (on headed notepaper)
6. Patient Information Leaflet (on headed notepaper)
7. Copy of letter of notification to patients GP (on headed notepaper)
8. Principal Investigators up-to-date Curriculum Vitae
9. Any questionnaire which participant may be asked to complete
10. Any advertisement or circular used in recruitment

**2.7. HEALTH PRODUCTS REGULATORY AUTHORITY (PREVIOUSLY IRISH MEDICINES BOARD)**

The HPRA is the regulatory or competent authority in Ireland. It was established in 1995 (as the Irish Medicines Board (IMB)) and replaced the National Drugs Advisory Board which was established in 1966. The fundamental role of the HPRA is to protect and enhance public and animal health through the regulation of medicines, medical devices and healthcare products. Among its many activities, the HPRA regulates clinical trials / the use of medicines for clinical research purposes. Written regulatory approval must be obtained from the HPRA prior to any clinical trial procedures being carried out. The HPRA reviews the scientific aspects of the application and reaches a conclusion on the likely balance of any benefits versus risk of the product before arriving at a decision. The HPRA has the authority to audit sponsors, investigators and sites involved with clinical trials to assess patient protection and protocol compliance.
Other HPRA Responsibilities:

- Following clinical trials on a medicinal product and before a medicinal product can be authorised for use (product authorisation), an application must be made to the HPRA and this must contain all of the necessary data supporting its quality, safety and efficacy.
- Monitoring and inspecting of products on the market to ensure their quality, safety and efficacy consistent with current medical and scientific knowledge.
- Monitoring the quality of medicines by conducting inspections at sites of manufacture and distribution of medicines and by random sampling of products both pre and post authorisation.
- Competent Authority for the implementation of EU and national legislation relating to Blood and Blood Components and also for Tissues & Cells.
- In addition to its regulatory activities the HPRA also carries out enforcement of many of the regulations for which it has responsibility. Enforcement activities include investigation of potential breaches of regulations and a range of measures, including prosecution, may be applied.

2.8. MEDICAL DEVICE TRIALS

The term 'medical device' covers all products, except medicines, used in healthcare for the diagnosis, prevention, monitoring or treatment of illness or disability. The HPRA is responsible for the regulation of medical devices on the Irish market. The range of products classified as medical devices is diverse. It includes: contact lenses and condoms; heart valves and hospital beds; resuscitators and radiotherapy machines; surgical instruments and syringes; wheelchairs and walking frames or other assistive technology products; pregnancy tests, blood glucose monitors and pacemakers - many thousands of items used each and every day by healthcare providers and patients. Medical devices do not include ambulance vehicles, general workshop equipment such as power or machine tools, or general purpose laboratory equipment. Pre-filled devices, for example, drug inhalers, syringes and certain other drug / device combinations are classed as medicines, not medical devices. There are three types of medical devices outlined in the legislation. These are:

- General medical devices
- Active implantable medical devices
• *In-vitro* diagnostic medical device

Medical devices are divided into classes dependent on risk, which can be low, medium and high risk. The principle legislation covering medical devices are:

- Directive 90/385/EEC concerning Active Implantable Medical Devices (AIMDD)
- Directive 93/42/EEC concerning General Medical Devices (MDD)
- Directive 98/79/EC concerning *In-vitro* Diagnostic Medical Devices (IVDs)

The above Directives have been transposed into national law, as follows:


Clinical investigations are usually required to gather clinical data that is sufficient to demonstrate conformity of a non-CE marked medical device to the requirements of the Medical Devices Regulations.

**When does the HPRA get involved in Device Trials?**

When clinical investigations of non-CE marked devices are to be carried out in Ireland, an application is required to be sent to HPRA. Typically applications are submitted by medical device manufacturers. Clinical investigation applications will receive a unique identification number, CIV ID, (if not previously assigned) for the purposes of notification to the EUDAMED database. The HPRA reviews the regulatory, technical and clinical aspects of the application. If the review has a satisfactory outcome, the sponsor will be issued with a “Letter of no objection”. In order for any clinical investigation to commence in Ireland, both the HPRA and the Ethics Committee must have issued a final positive opinion. The final opinion of the Ethics Committee must be submitted to the HPRA prior to commencement of the investigation. Some clinical investigations, such as those using CE marked devices within their intended purpose, may not require review.
2.9. DATA PROTECTION

Data protection pertains to the individual’s fundamental right to privacy. The Irish Data Protection Office (DPO) states that “anonymisation of patient records and/or freely given and informed patient consent to access records for the purposes of research are the foundation stones of how the DPO wishes to see medical research undertaken from a privacy perspective”.

Data Protection Acts

The main Irish law dealing with data protection is the Data Protection Act 1988. The 1988 Act was amended by the Data Protection (Amendment) Act 2003. An informal consolidated version of the two Acts is available. The 2003 Amendment Act brought our law into line with the EU Data Protection Directive 95/46/EC. All Sections of the Acts are in force, except Section 4 (13) (enforced subject access). Anyone processing personal data must comply with the 8 data protection principles of good practice:

1. Data must be fairly and lawfully processed
2. Data must be obtained for specified explicit and legitimate purposes
3. Data must be processed in ways compatible with the purpose for which it was first given to you
4. Data must be held securely
5. Data must be accurate and up-to-date
6. Data must be accurate, relevant and not excessive
7. Data must not be kept for longer than necessary for the specified purpose
8. Data must be provided to the subject upon request

In situations where data is being transferred to countries outside the EU, the researcher must ensure that the country in question provides an adequate level of data protection. The nature of research implies that there is a large amount of paper and electronic data held about the research subject. Research staff, have a responsibility to their research subjects and their employer regarding data protection.

- Data should be stored in a secure room
- Data must be locked away if unattended
- No one should access subject data unless authorised to do so by research personnel
and/or data protection officer.

- Research subject confidentiality should be maintained by the use of initials and/or research numbers as unique identifiers on research material.
- Electronic data must be password protected.
- Personal data that could potentially identify research subjects should be kept in a secure place, separate from research files.

For more information visit [https://www.dataprotection.ie](https://www.dataprotection.ie)

2.10. UPCOMING CHANGES IN RESEARCH GOVERNANCE IN IRELAND

Long awaited changes in the governance of ‘all other research’ will be implemented in the coming years. The Health Information Bill is expected to be finalised by the end of 2015 but it may be some time after that before the new structures it will recommend are in place. Researchers can anticipate changes in terms of re-structuring of ethics committees in Ireland in the next few years, with the Health Information Quality Authority (HIQA) assuming responsibility for oversight of ethics committees.

The cumulative effect of these changes is it will soon be possible for researchers to apply to one ethics committee only, when conducting any research study at any state-funded site in the Republic of Ireland. There is as yet no indication of a system for inspection of research that does not come under the remit of the HPRA. There is no date yet for the publication of the Human Tissue Act, which is intended to provide clearer guidance on the use of biological tissue for research.
SECTION 3:

Clinical Research
3.1 OVERVIEW OF TRIAL PROCESS

There are many definitions as to what constitutes a clinical research trial. The most commonly performed clinical trials evaluate new drugs, medical devices, biologics, new approaches to surgery or other interventions on patients. Clinical trials are usually designed to assess the safety and efficacy of an experimental therapy, or to assess whether the new intervention is better than standard therapy, or to compare the efficacy of two standard or marketed interventions. Post marketing surveillance / observational studies are another aspect of clinical research.

Pharmaceutical companies, academic institutions or individual investigators may sponsor clinical trials. Funding for clinical trials by academic institutions or investigators may be via grants or partial funding from pharmaceutical companies.

Most research trials follow a similar pathway from beginning to end.

- Protocol development: a protocol is developed by a sponsor, usually in collaboration with an investigator.
- Ethics approval: Ethics committees usually meet monthly and are composed of people from varying backgrounds. All research protocols and associated paperwork have to be submitted to and approved by the ethics committee. They may refuse approval, grant conditional approval subject to changes, or grant full approval. All projects require full approval before subject recruitment can begin. The EU Directive stipulates time deadlines for EC decisions. Ethics committees should be notified in writing when a study ends and of any serious adverse events that happen over the course of the study.
- Regulatory approval: The HPRA must approve all clinical trials before subject recruitment can begin.
- Indemnity: is required only for trials involving drugs supplied by pharmaceutical companies. The standard HSE Form of Indemnity should be used.
- Recruitment: once all of the above have been completed, patient recruitment may start. All research protocols stipulate strict inclusion and exclusion criteria, which all research personnel should be familiar with prior to approaching patients. Informed
consent is the most important aspect of any research trial. Written consent needs to be obtained for everything, including potential storage of and access to data/material. A subject should not undergo any research related procedure until written informed consent has been obtained.

- Visits as per protocol: the type of study will dictate the visits. Every procedure that a patient receives as part of a research trial must be documented accurately and clearly. Any reasons for non-compliance with the protocol must be documented. It is important that the research subjects have a name and number for the study team to contact between visits should they have any concerns.

- Study Close-out: All documentation is complete and data queries are resolved. Patients revert back to standard care in OPD or to their GP. Data are analysed and reported. The Investigator or sponsor will decide when the trial documents can be archived. For trials that are subject to inspection by the HPRA files must be readily accessible if needed for regulatory inspection.

3.2 ROLES AND RESPONSIBILITIES

Please note: Some of the main responsibilities of research team members are outlined below however this is by no means an exhaustive list. Not every research trial will have a data manager and/or a research pharmacist available and in this instance the research nurse may fulfil these roles.

**Study Sponsor**

A Sponsor is ‘An individual, company, institution, or organization which takes responsibility for the initiation, management and/or financing of a clinical trial’ (ICH GCP 1.53)

The study sponsor is responsible for:

- Providing the investigational products, as well as appropriate information to support the safe use of these products.

- Ensuring that the trial is conducted in accordance with sound scientific principles and good clinical practice.

- Selection of investigators.
• Provision of clinical trial protocol and ensuring protocol compliance.

• Establishing the distribution of trial related responsibilities.

• Providing procedures and staff management of the clinical trial, record keeping, monitoring and quality assurance.

• Ensuring compliance with applicable legal, ethical and regulatory requirements.

• Provision of compensation and indemnity for trial related injury according to local laws and regulations.

**Principal Investigator (PI)**

An investigator is ‘A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.’ (ICH GCP 1.34)

It is the responsibility of the PI to conduct the study according to the protocol and to ensure that he/she has the patient availability to conduct the study within the period defined in the study protocol. The PI also holds additional responsibilities:

• To ensure that the study is conducted in full conformance with the principles of the Declaration of Helsinki

• To ensure that the study is performed in accordance with the international Good Clinical Practice standards and according to all local laws and regulations concerning clinical studies.

• Submission of the protocol, patient information sheets and consent forms to local ethics committee for approval.

• To ensure that all staff involved in the study have a full understanding of the protocol and its requirements.

• Obtaining and recording patient consent.

• To withdraw a patient from the clinical trial for any reason that is in the best
interests of the subject.

- To ensure subjects anonymity is maintained.

- To ensure the completeness and accuracy of case report forms.

- To agree to allow the monitor/auditor/inspector to have access to any or all of the study materials needed for source data verification and proper review of the study progress.

- To report all adverse events in the case report form.

- To publish the clinical study results as soon as possible following study completion. In a multi-centre study, the principle investigator must ensure that the data from one centre is not published before the publication of the whole study without his/her consent.

- To retain all essential documents until after 2 years after the approval of the marketing application or longer if required by the regulatory requirements.

- To comply with the study sponsor and regulatory authority requirements regarding the auditing of the study.

**Co-Investigator/ Sub Investigators**

The co-investigator/Sub-Investigator is responsible for medical care of patients participating in research studies, working under the supervision of the principle investigator.

- The co-investigator holds additional responsibilities:

  - To ensure that the study is performed in accordance with the international; Good Clinical Practice standards and according to all local laws and regulations concerning clinical studies.

  - Obtaining and recording patient and/or parental consent.

  - To withdraw a patient from the clinical trial for any reason that is in the best interest
of the subject.

- To ensure subjects anonymity is maintained.

- To perform protocol directed medical care including assessment, examination, and prescription of study and support medication.

- To ensure the completeness and accuracy of case report forms. To agree to allow a monitor/auditor/inspector to have access to any or all of the study materials needed for source data verification and proper review of the study progress.

- To retain all essential documents until after two years after the approval of the marketing application or longer if required by the regulatory authority requirements regarding the auditing of the study.

**Clinical Research Manager**

The responsibilities of the clinical research manager are:

- Management of the research network team.

- To ensure that there are sufficient resources in terms of time, staff and facilities to conduct the trial.

- To ensure that all protocols are reviewed, by all relevant departments in order to facilitate the conduct of the study.

- To ensure that ethical approval has been granted prior to any patient entering the trial.

- To monitor workload levels and delegate duties and responsibilities accordingly.

- To ensure that appropriate training and education has been provided in order to conduct the clinical trials.

- To act as liaison between study sponsors, investigator, the clinical trials research team and any other departments involved in the conduct of the trial.
• Where necessary, to maintain the flow of information regarding the progress of clinical trial activity within the research team and relevant groups

• Education of all staff of all grades in relation to clinical trials.

• Production of annual reports and monthly reports for trial meetings.

Clinical Research Nurse (CRN)

Taking account of the previous discussion about the complexity and variation of the CRN role, within the research team research nurses are typically responsible for:

• Co-ordinating the clinical trial in terms of patient recruitment, organising screening procedures, randomisation and management of procedures necessary during subsequent patient visits.

• Confirmation of patient eligibility according to the inclusion/exclusion criteria stated in the protocol in collaboration with the clinicians.

• Collaboration with clinicians in assessing patients and making treatment decisions according to the protocol.

• To submit local ethics approval/research and development applications.

• To ensure they have attended the initiation meeting and received any appropriate training prior to the trial commencement.

• Accountability of investigation agents/treatments.

• Handling, processing, labelling, storage and shipping of biological samples.

• Ensuring that source documentation is a true reflection of decisions and actions taken for each individual patient.

• Completion of case report forms and ensuring quality of life data is collected from patient.

• Timely reporting of serious adverse events.
• Liaison with study sponsor regarding the conduct of the trial.

• Patient education and dissemination of trial related information to relevant staff and departments

• Staff education and training.

**Data Managers**

Data managers work closely with investigators, research nurses and study coordinators to ensure accurate and appropriate data collection. They can be responsible for:

• Designing, developing, and modifying databases to meet study requirements
• Assisting with development of paper and electronic case record forms
• Writing data management guidelines, policies and SOPs and monitoring their implementation and adherence
• Providing support in identifying and defining site data requirements
• Training and supporting other members of the research team in any aspect of data management, when required.
• Ensure all data protection legislation is adhered to within all study activities
• Ensure IT systems and electronic databases in use comply with GCP guidelines and applicable legislation
• Carry out or supervise data entry and validation
• Prepare data for analysis and reporting

**Research Assistant**

A research assistant may be employed for study specific or task specific duties at a research site. Duties may include:

• Providing an efficient secretarial/administrative support service to the research project(s) and Principal Investigator or his/her nominee.
• Supporting the research activities of the Principal Investigator or his/her nominee.
• Liaising with related departments and project leaders within the research area to help co-ordinate their research activities.
• Liaising with the Principal Investigator and colleagues on matters relating to the research project.
• Data entry or validation (paper or electronic)
• Sample processing, shipping etc.
• Carrying out laboratory procedures
• Laboratory and equipment care and maintenance

**Research Pharmacist**

As the number and variety of trials continues to increase it is vital that there is good communication between the sponsor company, the research team and the trials pharmacist. This will ensure that issues are raised and resolved at an early stage, allowing the trial to run smoothly and effectively. Early input from pharmacy in the planning of a clinical trial enables early recognition of potential pharmaceutical issues; pharmacy should be given a copy of the protocol at the earliest opportunity.

• The design of prescription so the correct trial supplies are ensured.
• How blinding of trial medication is to be achieved and maintained.
• The requirements for documentation and record keeping.
• Labelling requirements.
• Drug receipt, delivery, re-ordering and stock checks.
• The mechanism for continuation of supplies, if appropriate, once the trial period has finished.
• Storage conditions of the trial medication.
• Size of packaging, which has implications for storage space.
• For parenteral administration of medicinal products there may be a requirement for aseptic preparation.
3.3. STANDARD OPERATING PROCEDURES (SOP’S)

Standard operating procedures are defined in the ICH GCP guidelines as ‘detailed written instructions to achieve uniformity of the performance of a specific function’

The aims of SOPs are to ensure that any procedure performed as part of a research trial/study is done to a consistently high standard, thus enhancing the quality of the data produced. SOPs are of particular importance when a trial is being run over several sites, and involves a number of research personnel. SOPs are relevant to all aspects of a research study. That is general study organisation, pre-study procedures, actual study procedures and end of study procedures. Before commencing a trial specific procedure the appropriate SOP should be read and understood. If applicable, training in the procedure outlined should be completed before performing the procedure.

The format of SOPs will normally include:

- Title and Number of SOP
- Purpose
- Other related procedures
- Personnel involved with procedure
- When and how the procedure should be performed
- Date of approval and/or implementation of version in use
- Name of author and approval signature(s)

3.4. CASE REPORT FORMS

A Case Report Form (CRF) is a record of all the data and other information on each subject, required by the research protocol. ICH GCP guidelines include strict guidance relating to CRF completion as they are the official documentation of the trial. CRF’s, along with the source documentation, will be closely examined during the monitoring visits and in the event of a regulatory audit therefore accurate and thorough completion is essential. Data contained within the CRF should match exactly that data, which has been recorded in the subject’s source notes.

The CRF should collect necessary information about:
The subject
Administration of the study drug
Study specific procedure
Outcome of any assessments
Details of any adverse/serious adverse events

Following the study initiation visit only those personnel authorised on the delegation log by the principal investigator should complete CRF’s. These may include co-investigators, research nurses, radiographers and data managers. CRF’s should be completed during, or as soon as possible after the associated study visit/patient assessment, to ensure the information is up-to-date and accurate.

The following guidelines should be taken into account when completing paper CRF’s:

- Black ball point pen must always be used to complete the CRF.
- If the CRF is on carbon duplication paper, ensure that an appropriate separator is inserted.
- Never leave blank spaces. If a section cannot be completed write: as appropriate, not known, not done etc.
- Never enter a research subject’s full name on a CRF.
- CRF’s must be signed off by the principal investigator at the end of the trial or as appropriate throughout the trial, to indicate that they believe the information to be complete and correct.
- All entries must be legible.
- Corrections must be made as follows:
  - Cross out incorrect entry with a single line, so that the original entry is still legible.
  - Enter the correct data
  - Initial and date correction.

Increasingly, electronic CRF’s (eCRF’s) are being utilised in clinical trials. Electronic systems must meet the same essential elements of data quality that are expected of paper records.
3.5. ADVERSE EVENTS

An adverse event (AE) is defined as any unfavourable and unintended sign including any abnormal laboratory finding, symptom or disease associated with the use of an investigational medicinal product (IMP), regardless of whether or not it is considered to be caused by the IMP.

Expected Adverse Event:
Those adverse events that have been identified in nature, severity, or frequency in the current investigator brochure, investigational protocol and current patient information leaflet/informed consent form (PIL/ICF).

Unexpected Adverse Event:
Any adverse event whose nature, severity or frequency of which is not consistent with the current investigator brochure; or with the risk information described in the PIL/ICF. Unexpected refers to an experience that has not been previously observed. This includes events that are more serious than expected or occur more frequently than expected.

Grading of Adverse Events:
All adverse events should be categorised according to severity. Each protocol may have a unique approach to grading AEs and the Principal Investigator/site staff should consult the protocol for specific grading scales. Multi-centre studies generally include such a table, sometimes called a toxicity table within the protocol.

Medical Events of Special Interest
On occasion a protocol will require reporting of an event – such as an altered laboratory value – that would not normally be considered an adverse event but is of particular interest in the context of the study. This may be due to the results of preclinical studies.

Nurses working on a trial must be fully knowledgeable of trial specific adverse events, their grading and necessary actions and reporting specifics as detailed in each trial protocol.
3.6. INFORMED CONSENT

Freely given informed consent is the cornerstone of ethical research. Each prospective participant and/or the legal representative must:

- Understand the nature of research
- Be informed of purpose, risks, and benefits and alternative therapies
- Make a **voluntary decision** about study participation

Informed consent must be obtained prior to any protocol specific testing being conducted. If protocol specific testing is done the same day as informed consent is obtained, there must be clear documentation of the chronological order in the patients’ medical record.

Details of how informed consent is to be obtained, by whom and details of the research project the participant must be provided with to adequately provide an “informed” decision to participate is clearly detailed in the ICH GCP booklet. The person obtaining consent should have sufficient knowledge about the research and be capable of answering questions from prospective participants (HSE 2014).

The Health service executive (HSE) National Consent Policy (2014) states that a person over 16 can consent for clinical trials on his/her own behalf, and that, for all other research, the person must be 18 years or over. The policy advocates that, while children should never be exploited, or inappropriately enrolled in research, they should be allowed to participate in research that might benefit them. In this case parents or guardians provide legal consent, but children should be provided with age appropriate information, and given the choice of providing assent to participate should they wish to do so.

**All research personnel must be familiar with ICH GCP guidelines and legislation for obtaining valid informed consent.**

HSE (2014) National Consent Policy available at:  

Accessed on line 18/05/2015
SECTION 4:

General Information
4.1. INFORMATION TECHNOLOGY

- All research personnel must ensure that only authorised persons enter the workplace, to prevent unauthorised access to confidential patient information.
- All computer equipment must be located away from public access. If this is not possible then equipment must always be supervised, or locked when unattended.
- Printed materials must be retrieved from printers or fax machines as quickly as possible in order to prevent unauthorised observation.
- Desks must be cleared of information sources (patient data, contact information etc.) when the office is unattended.
- All computers/laptops must be switched off at the end of the day before leaving the office.
- Computers must not be left logged in when staff are away from their desk or out of the office.
- All old information must be disposed of securely. Paper based items must be shredded.

Personal Computer/Laptop Security

- All accounts & database systems must have secure password access only.
- Passwords must be kept secret at all times; use of a co-worker’s password is forbidden, and passwords should never be recorded where they may be visible to a casual observer.
- Up to-date anti-virus software must be installed on an ongoing basis.
- Personal fire-walling must be installed if the internet is to be accessed from outside the hospital network or from home. The firewall will protect the computer/laptop by preventing unauthorised access.
- Free software programs must not be downloaded from the internet as they may contain viruses etc. which could cause damage to the computer and/or the data on it.
- Laptops must be kept in a secure location when not in use.
- All laptops must be encrypted in order to prevent unauthorised access to data should the equipment be lost or stolen.

You are expected to be aware of, and adhere to, your organisations IT policies and procedures
4.2. GLOSSARY OF COMMON TERMS (As per HPRA)

“adult” means a person who has attained the age of 16 years;

“adverse event” means any untoward medical occurrence in a subject to whom a medicinal product has been administered, including occurrences that do not necessarily have a causal relationship with this treatment;

“adverse reaction” means any untoward and unintended response in a subject to an investigational medicinal product which is related to any dose administered to that subject;

“Advisory Committee for Human Medicines” means the Committee established under section 9(1)(a) of the Irish Medicines Board Act 1995 (No. 29 of 1995);

“appointing authority” means the institution on whose behalf application for recognition of an ethics committee in accordance with Regulation 7(1) is made and for the purposes of this definition “institution” means a health board, a hospital, a University or other similar body involved in higher education or in the award of post-graduate specialist medical or dental qualifications or in the provision of continuing medical or dental education;

“authorised health care professional” means a registered medical practitioner or registered dentist;

“Board” means the Irish Medicines Board established by section 3 of the Irish Medicines Board Act 1995 (No. 29 of 1995);

“chief investigator” means -

(a) in the case of a clinical trial conducted at a single trial site, the investigator for that site, or

(b) in the case of a clinical trial conducted at more than one trial site, the authorised health care professional, whether or not he or she is an investigator at any particular site, who takes primary responsibility for the conduct of the trial;

“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;

“clinical trial protocol” means a document that describes the objectives, design, methodology, statistical considerations and organisation of a clinical trial and includes any successive versions of the protocol and protocol amendments;


“conditions and principles of good clinical practice” means -

(a) The principles of and guidelines for good clinical practice set out in a measure adopted pursuant to Article 1(3) of the Directive, and

(b) The conditions and principles for the protection of clinical trial subjects specified in Schedule 1;

“conducting a clinical trial” includes -

(a) Administering, or giving directions for the administration of, an investigational medicinal product to a subject for the purposes of that trial,

(b) Giving a prescription for an investigational medicinal product for the purposes of that trial,

(c) Carrying out any other medical or nursing procedure in relation to that trial, and

(d) Carrying out any test or analysis -

(i) To discover or verify the clinical, pharmacological or other pharmacodynamic effects of the investigational medicinal products administered in the course of the trial,

(ii) To identify any adverse reactions to those products, or

(iii) To study absorption, distribution, metabolism and excretion of those products,

but does not include any activity undertaken prior to the commencement of the trial which consists of making such preparations for the trial as are necessary or expedient;


“EMEA” means the European Agency for the Evaluation of Medicinal Products established by Council Regulation (EEC) No. 2309/93;

“ethics committee” means a committee established or recognised in accordance with Part 2 of these Regulations;

“European Economic Area” means the European Economic Area created by the EEA Agreement;

“health care professional” means -

(a) a registered medical practitioner,

(b) a registered dentist,

(c) a registered nurse,

(d) a registered pharmacist,

(e) a person registered in the Register of Optometrists established under the Opticians Acts 1956 and 2003, or

(f) any other person holding another such professional qualification that would entitle him or her to provide health care;

“insurance or indemnity” includes a contract of insurance, a contract of indemnity, a guarantee, a surety, a warrant and a bond and which in any case shall be available to cover the liability of the sponsor and the investigator to provide for compensation in the event of any injury, loss or damage to, or the death, of any subject arising out of the arrangement for, or conduct of, the clinical trial and which the sponsor, or investigator, shall become liable to pay to such subject, or in respect of such subject, by way of damages or costs;

“investigational medicinal product” means a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including a medicinal product that is already the subject of a marketing authorisation, but—

(a) is used, formulated or packaged in a way different from the form that is the subject of the authorisation,

(b) is used for an indication that is not included in the summary of product characteristics under the authorisation for the product, or

(c) is used to gain further information about the form of the product that is the subject of the authorisation;
“investigator’s brochure” means a document containing a summary of the clinical and non-clinical data on the investigational medicinal product which are relevant to the study of the product in human subjects;

“investigator-sponsor” means, in relation to a clinical trial, a chief investigator who is also acting as the sponsor for that clinical trial;

“medicinal product” has the meaning assigned to it by Directive 2001/83/EC;

“multi-centre clinical trial” means a clinical trial conducted according to a single protocol but at more than one site, and therefore by more than one investigator, in which the trial sites may be located in a single Member State, in a number of Member States or in a Member State or Member States and a third country or third countries;

“non-interventional trial” means a study of one or more medicinal products which have 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;


“qualified person” means -

(a) a person who as respects qualifications and experience satisfies the requirements set out in Part 1 of Schedule 6, or
(b) a person who, without satisfying the requirements referred to in paragraph (a) has been engaged in activities equivalent to those to be performed in accordance with Regulation 40(2) in respect of investigational medicinal products for a period of at least one year prior to 1 May 2004;

“serious adverse event or serious adverse reaction” means any adverse event or adverse reaction that at any dose -
(a) results in death,
(b) is life-threatening,
(c) requires hospitalisation or prolongation of existing hospitalisation,
(d) results in persistent or significant disability or incapacity, or
(e) consists of a congenital anomaly or birth defect;

“sponsor” means, in relation to a clinical trial, the person who takes on responsibility for the initiation and management (or for arranging the initiation and management) of, and the financing (or arranging the financing) for that clinical trial;

“subject” means, in relation to a clinical trial, an individual, whether a patient or not, who participates in a clinical trial—

(a) as a recipient of an investigational medicinal product or of some other treatment or product, or

(b) without receiving any treatment or product, as a control;

“trial site” means a hospital, nursing home, health centre, surgery or other establishment or facility at or from which a clinical trial, or any part of such a trial, is conducted;

“unexpected adverse reaction” means, in respect of an investigational medicinal product, an adverse reaction, the nature or severity of which is not consistent with the information about that medicinal product as set out -

(a) in the case of a product which is the subject of a marketing authorisation, in the summary of product characteristics for that product,

(b) in the case of any other investigational medicinal product, in the investigator's brochure relating to the particular clinical trial.

4.2.1 Other Definitions:

Confidentiality Agreement
A legal agreement to protect confidential information being revealed during discussions or negotiations with another party; applicable where either or both parties are individuals or an organisation. The agreement also contains the following clauses;
- Protection against the copying or retention of confidential information.
- Protection against disclosure to third parties of information not already in the public domain.
- Remedy for any breach of the agreement.

Department of Health and Children (DOHC)
The aim of the DOHC is to improve the health and wellbeing of people in Ireland. Their
website contains information, publications and links to other health related information sources. See: www.dohc.ie

**EUDRACT: (The European Clinical Trials Database)**
EUDRACT is designed to be a register of all clinical trials in the Community, information on the content, commencement and termination of the clinical trials and on inspections. See: http://eudract.emea.europa.eu

**EudraVigilance**
EudraVigilance is the European data-processing network and database management system for the exchange, processing and evaluation of Individual Case Safety Reports (ICSRs) related to medicinal products authorised in the European Economic Area (EEA). See: http://www.eudravigilance.org/

**FDA (Food and Drug Administration USA)**
The FDA is the federal agency within the USA responsible for ensuring that foods are safe, wholesome and sanitary; human and veterinary drugs, biological products, and medical devices are safe and effective; cosmetics are safe; and electronic products that emit radiation are safe. FDA also ensures that these products are honestly, accurately and informatively represented to the public. See: http://www.fda.gov/

**GMP (Good Manufacturing Practice)**
GMP refers to principles and specifications for good manufacturing of medicinal products that are set by the Federal Therapeutic Goods Administration (FTGA), in accordance with international standards (known as Codes of GMP). These are the standards manufacturers must comply with to provide safe and reliable products for consumers.

**Insurance Indemnity**
Indemnity provides protection against any action by an individual, a group or an organisation that believe they received bad or negligent services, and incurred a loss as a result. Most professional bodies have professional indemnity cover; in some cases it is compulsory. The limit of an indemnity policy relates to the maximum amount of money that an individual or organisation will pay out in the event of a claim being made.

**Investigational Medicinal Product (IMP)**
An investigational medicinal product is an active substance or placebo being tested or used as a reference in a clinical trial. It includes licensed medicinal products that are being used either off licence, within the licence but where the study involves assessing the efficacy and/or safety of the product, or assembled (formulated or packaged) in a way different from the form of the product authorised under the authorisation.

**Pharmacovigilance**
Pharmacovigilance is defined as watchfulness in guarding against danger from drugs or providing for safety of drugs. It may also be a dedicated department whose role is to monitor toxicity and safety of drugs both in the development phase and post marketing.
### 4.3. GLOSSARY OF ABBREVIATIONS USED IN CLINICAL RESEARCH

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>ABPI</td>
<td>Association of the British Pharmaceutical Industry</td>
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<tr>
<td>ADR</td>
<td>Adverse Drug Reaction</td>
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<tr>
<td>AE</td>
<td>Adverse Event</td>
</tr>
<tr>
<td>AR</td>
<td>Adverse Reaction</td>
</tr>
<tr>
<td>CA</td>
<td>Competent Authority(s)</td>
</tr>
<tr>
<td>CIP</td>
<td>Clinical Investigation Plan (Protocol)</td>
</tr>
<tr>
<td>CIOMS</td>
<td>Council for International Organizations of Medical Sciences</td>
</tr>
<tr>
<td>CIS</td>
<td>Clinical Indemnity Scheme</td>
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<tr>
<td>CONSORT</td>
<td>Consolidated Standards of Reporting Trials</td>
</tr>
<tr>
<td>CRA</td>
<td>Clinical Research Associate</td>
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<td>CRC</td>
<td>Clinical Research Centre</td>
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<tr>
<td>CRF</td>
<td>1. Clinical Research Facility  2. Case Report Form</td>
</tr>
<tr>
<td>CRN</td>
<td>Clinical Research Nurse</td>
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<tr>
<td>CRO</td>
<td>Contract Research Organization</td>
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<tr>
<td>CSET</td>
<td>Centres for Science, Engineering &amp; Technology</td>
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<tr>
<td>CSFP</td>
<td>Clinician Scientist Fellowship Programme</td>
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<tr>
<td>CSTAR</td>
<td>Centre for Support and Training Analysis Research</td>
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<tr>
<td>CT</td>
<td>Clinical Trial</td>
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<tr>
<td>CTA</td>
<td>Clinical Trial Agreement</td>
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<tr>
<td>CTCAE</td>
<td>Common Terminology Criteria for Adverse Events</td>
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<tr>
<td>CTIF</td>
<td>Clinical Trial Indemnity Form</td>
</tr>
<tr>
<td>CTIMP</td>
<td>Clinical Trial for Investigational Medicinal Product</td>
</tr>
<tr>
<td>CV</td>
<td>Curriculum Vitae</td>
</tr>
<tr>
<td>DAMC</td>
<td>Dublin Academic Medical Centre</td>
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<tr>
<td>DCCR</td>
<td>Dublin Centre for Clinical Research</td>
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<tr>
<td>DM</td>
<td>Data Management</td>
</tr>
<tr>
<td>DSMB</td>
<td>Date safety Monitoring Board</td>
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<tr>
<td>DSMC</td>
<td>Data and Safety Monitoring Committee</td>
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<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<tr>
<td>DOHC</td>
<td>Department of Health and Children</td>
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<tr>
<td>EC</td>
<td>Ethics Committee</td>
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<tr>
<td>eCRF</td>
<td>electronic Case Report Form</td>
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<tr>
<td>EI</td>
<td>Enterprise Ireland</td>
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<tr>
<td>EMEA</td>
<td>European Agency for the Evaluation of Medicinal Products</td>
</tr>
<tr>
<td>EPA</td>
<td>Environmental Protection Agency</td>
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<tr>
<td>ERI</td>
<td>European Research Infrastructure Consortium</td>
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<tr>
<td>EU</td>
<td>European Union</td>
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<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
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<tr>
<td>FSAI</td>
<td>Food Safety Authority of Ireland</td>
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<tr>
<td>GCP</td>
<td>Good Clinical Practice</td>
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<tr>
<td>GLP</td>
<td>Good Laboratory Practice</td>
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<tr>
<td>GMO</td>
<td>Genetically Modified Organism</td>
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<tr>
<td>GMP</td>
<td>Good Manufacturing Practice</td>
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<tr>
<td>GMS</td>
<td>General Medical Services</td>
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<tr>
<td>HEA</td>
<td>Higher Education Authority</td>
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<tr>
<td>HETAC</td>
<td>Higher Education and Training Awards Council</td>
</tr>
<tr>
<td>HIQA</td>
<td>Health Information and Quality Authority</td>
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<tr>
<td>HPRA</td>
<td>Health Products Regulatory Authority</td>
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<tr>
<td>HRB</td>
<td>Health Research Board</td>
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<td>HRG</td>
<td>Health Research Group</td>
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<tr>
<td>HSE</td>
<td>Health Service Executive</td>
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<tr>
<td>IB</td>
<td>Investigator’s Brochure</td>
</tr>
<tr>
<td>IC</td>
<td>Informed Consent</td>
</tr>
<tr>
<td>ICORG</td>
<td>All-Irish Cooperative Oncology Research Group</td>
</tr>
<tr>
<td>ICH</td>
<td>International Conference on Harmonisation</td>
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<tr>
<td>ICMJE</td>
<td>International Committee of Medical Journal Editors</td>
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<tr>
<td>ICRIN</td>
<td>Irish Clinical Research Infrastructure Network</td>
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<tr>
<td>IDA</td>
<td>Industrial Development Authority</td>
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<tr>
<td>IMDA</td>
<td>Irish Medical Devices Association</td>
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<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<tr>
<td>IMI</td>
<td>Innovative Medicines Initiative</td>
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<tr>
<td>IMP</td>
<td>Investigational Medicinal Product</td>
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<tr>
<td>IP</td>
<td>Intellectual Property</td>
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<tr>
<td>IPHA</td>
<td>Irish Pharmaceutical Healthcare Association</td>
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<tr>
<td>IPPOSI</td>
<td>Irish Platform for Patient Organisations, Science and Industry</td>
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<tr>
<td>IRB</td>
<td>Institutional Review Board</td>
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<tr>
<td>ISBER</td>
<td>International Society for Biological and Environmental Repositories</td>
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<tr>
<td>IT</td>
<td>Information Technology</td>
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<tr>
<td>ITT</td>
<td>Intention to Treat</td>
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<tr>
<td>IVRS</td>
<td>Interactive Voice Response System</td>
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<tr>
<td>IWRS</td>
<td>Interactive Web Response System</td>
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<tr>
<td>MedDRA</td>
<td>Medical Dictionary for Regulatory Activities</td>
</tr>
<tr>
<td>MED</td>
<td>Minimal Effective Dose</td>
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<tr>
<td>MMI</td>
<td>Molecular Medicine Ireland</td>
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<tr>
<td>MRCG</td>
<td>Medical Research Charities Group</td>
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<tr>
<td>MTD</td>
<td>Maximum Tolerated Dose</td>
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<tr>
<td>NSAI</td>
<td>National Standards Authority of Ireland</td>
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<tr>
<td>NSAFP</td>
<td>National SpR/SR Academic Fellowship Programme</td>
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<tr>
<td>NUIG</td>
<td>National University of Ireland, Galway</td>
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<tr>
<td>OECD</td>
<td>Organisation for Economic Cooperation and Development</td>
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<tr>
<td>OREC</td>
<td>Office for Research Ethics Committees</td>
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<tr>
<td>PD</td>
<td>Pharmacodynamic</td>
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<tr>
<td>PI</td>
<td>Principal Investigator</td>
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<tr>
<td>PIL</td>
<td>Patient/participant Information Leaflet</td>
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<tr>
<td>PIAG</td>
<td>Patient Information Advisory Group</td>
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<tr>
<td>PK</td>
<td>Pharmacokinetic</td>
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<tr>
<td>PMS</td>
<td>Post Marketing Surveillance</td>
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<tr>
<td>PRTLI</td>
<td>Programme for Research in Third Level Institutions</td>
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<tr>
<td>QA</td>
<td>Quality Assurance</td>
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<tr>
<td>QC</td>
<td>Quality Control</td>
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<tr>
<td>Acronym</td>
<td>Description</td>
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<tr>
<td>QM</td>
<td>Quality Management</td>
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<tr>
<td>QMS</td>
<td>Quality Management System</td>
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<tr>
<td>RCSI</td>
<td>Royal College of Surgeons in Ireland</td>
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<tr>
<td>RCT</td>
<td>Randomised Controlled Trial</td>
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<tr>
<td>REC</td>
<td>Recognised Ethics Committee</td>
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<tr>
<td>SAE</td>
<td>Serious Adverse Event</td>
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<td>SAR</td>
<td>Serious Adverse Reaction</td>
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<td>SCA</td>
<td>State Claims Agency</td>
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<td>SDV</td>
<td>Source Data Verification</td>
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<td>SFI</td>
<td>Science Foundation Ireland</td>
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<td>SI</td>
<td>Statutory Instrument</td>
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<tr>
<td>SIV</td>
<td>Site Initiation Visit</td>
</tr>
<tr>
<td>SMEs</td>
<td>Small to Medium Enterprises</td>
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<tr>
<td>SMF</td>
<td>Study Master File</td>
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<tr>
<td>SOP</td>
<td>Standard Operating Procedure</td>
</tr>
<tr>
<td>SpR/SR</td>
<td>Specialist Registrar/ Senior Registrar</td>
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<tr>
<td>SSA</td>
<td>Site Specific Assessment (form)</td>
</tr>
<tr>
<td>SUSAR</td>
<td>Suspected Unexpected Serious Adverse Reaction</td>
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<tr>
<td>TCD</td>
<td>Trinity College Dublin</td>
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<td>UCC</td>
<td>University College Cork</td>
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<tr>
<td>UCD</td>
<td>University College Dublin</td>
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<tr>
<td>UKCRF</td>
<td>United Kingdom Clinical Research Facilities (Network)</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organisation</td>
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<tr>
<td>WMA</td>
<td>World Medical Association</td>
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**APPENDIX I. SAMPLE ORIENTATION CHECKLIST**

Name: ______________________     Commencement Date: ________________________

Preceptor/Mentor: ______________________

<table>
<thead>
<tr>
<th>SECTION 1 - INTRODUCTION TO SITE PERSONNEL</th>
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<tr>
<td><strong>Area of Induction</strong></td>
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<tr>
<td>1. Outline of role</td>
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<tr>
<td>2. Introduction to core research staff</td>
</tr>
<tr>
<td>3. Introduction to Medical Research Ethics Committee Administrator</td>
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<tr>
<td>4. Introduction to core support staff</td>
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<table>
<thead>
<tr>
<th>SECTION 2 - CONDITIONS OF EMPLOYMENT</th>
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</thead>
<tbody>
<tr>
<td><strong>Area of Induction</strong></td>
</tr>
<tr>
<td>1. Contract of employment, working hours, &amp; breaks and period of notice</td>
</tr>
<tr>
<td>2. Electronic &amp; paper timesheet (as applicable)</td>
</tr>
<tr>
<td>3. Holidays &amp; local arrangements for leave</td>
</tr>
<tr>
<td>4. Sickness Policy &amp; how to report sickness</td>
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<thead>
<tr>
<th>SECTION 3 - CRC STANDARD OPERATING PROCEDURES</th>
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<tr>
<td><strong>Area of Induction</strong></td>
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<tr>
<td>1. Location of SOP’s</td>
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<tr>
<td>2. Policy for reviewing and signing SOPs</td>
</tr>
<tr>
<td>3. Process for updating and distributing amended SOPs</td>
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</table>
## SECTION 4 – INTRODUCTION TO FACILITIES

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<thead>
<tr>
<th>Area of Induction</th>
<th>Date</th>
<th>Signature of Preceptor</th>
<th>Signature of New Employee</th>
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<tbody>
<tr>
<td>1. Tour of research facilities</td>
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<tr>
<td>2. Access &amp; security procedure</td>
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<tr>
<td>3. Changing room/lockers and toilet facilities</td>
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<tr>
<td>4. Fire exits &amp; System for raising alarms</td>
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<tr>
<td>5. Awareness of drug key storage</td>
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<td>6. Telephone operation</td>
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<td>7. Notice boards</td>
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<tr>
<td>8. Identity badge / Swipe card</td>
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<tr>
<td>9. IT set up and passwords (Email, Hospital Information System)</td>
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<tr>
<td>10. Attend Occupational Health for introduction (if applicable)</td>
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<tr>
<td>11. Tour of the hospital if appropriate (Introduction to key outpatient, pharmacy and radiology staff)</td>
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<td>12. Staff restaurants</td>
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<td>13. Parking arrangements - check permit issued (if appropriate)</td>
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## SECTION 5 - ADMINISTRATIVE PROCESSES

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<tr>
<th>Area of Induction</th>
<th>Date</th>
<th>Signature of Preceptor</th>
<th>Signature of New Employee</th>
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<tbody>
<tr>
<td>1. Data protection / Patient confidentiality</td>
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<tr>
<td>2. Hospital admissions procedures</td>
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<tr>
<td>3. Making Hospital outpatients appointments</td>
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</tbody>
</table>
4. Process of organising screening investigations & retrieving results

5. Process for obtaining and tracking medical records

6. Training in hospital information system

7. Training in study manager system

### SECTION 6 - HEALTH & SAFETY

<table>
<thead>
<tr>
<th>Area of Induction</th>
<th>Date</th>
<th>Signature of Preceptor</th>
<th>Signature of New Employee</th>
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<tbody>
<tr>
<td>1. Attendance at fire training</td>
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<tr>
<td>2. Attendance at infection control training (Hand Hygiene)</td>
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<td>3. Attendance at manual handling training</td>
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<td>4. Personal security</td>
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<tr>
<td>5. Awareness of overnight study guidelines (if applicable)</td>
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<td>6. Awareness of lone worker policy (if applicable)</td>
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<td>7. Awareness of risk assessments</td>
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<td>8. Safe handling of biological samples</td>
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<td>9. Safe handling of dry ice</td>
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<tr>
<td>10. Sharps policy</td>
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<tr>
<td>11. Spills policy</td>
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<tr>
<td>12. Vaccination screening</td>
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### SECTION 7 – CLINICAL SKILLS

Some of the clinical procedures that you may be involved in are listed in the table below; Your mentor will help to identify the skills associated with your role, and other skills should be added as appropriate

<table>
<thead>
<tr>
<th>Area of Induction</th>
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<th>Signature of New Employee</th>
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<tr>
<td>1. ICH Good Clinical Practice Training and certification</td>
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<tr>
<td>2. Phases of Clinical trials</td>
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<tr>
<td>3. Study protocols</td>
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<tr>
<td>4. Investigator's Brochure</td>
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<tr>
<td>5. Role and composition of research ethics Committees</td>
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<tr>
<td>6. REC application and approval process including protocol amendments</td>
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<tr>
<td>7. Case report form completion (Source documents, data verification)</td>
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<td>8. Legal issues i.e. indemnity</td>
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<tr>
<td>9. Declaration of Helsinki</td>
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<tr>
<td>10. Good Laboratory Practice</td>
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<tr>
<td>11. Introduction to Site Files &amp; Filing</td>
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</tbody>
</table>
12. Introduction to Informed Consent Process (Examples of PIL/ICF’s)

13. Study Co-Ordination Training (Initiation visit, pt visit, monitoring visit)

14. Study archiving

15. Safety Reporting
   (Adverse events/Serious adverse events)

### SECTION 9 - EMPLOYEE INVOLVEMENT AND COMMUNICATION

<table>
<thead>
<tr>
<th>Area of Induction</th>
<th>Date</th>
<th>Signature of Preceptor</th>
<th>Signature of New Employee</th>
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<tbody>
<tr>
<td>1. Staff meetings</td>
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<tr>
<td>2. Journal club meeting / research meetings</td>
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<td>3. Social and sports club</td>
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<tr>
<td>4. Irish Research Nurses Network</td>
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### SECTION 10 – Miscellaneous

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*It is the responsibility of each nurse to ensure that they seek further training if they feel they need it;*

*Acknowledged by ______________________ on date ______________________*
APPENDIX ii: WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI

ETHICAL PRINCIPLES FOR MEDICAL RESEARCH INVOLVING HUMAN SUBJECTS


Preamble

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

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

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

General Principles

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

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

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

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

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

8. While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects.
9. It is the duty of physicians who are involved in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects. The responsibility for the protection of research subjects must always rest with the physician or other health care professionals and never with the research subjects, even though they have given consent.

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

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

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

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

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

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

Risks, Burdens and Benefits

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

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

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

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

18. Physicians may not be involved in a research study involving human subjects unless they are confident that the risks have been adequately assessed and can be satisfactorily managed. When the risks are found to outweigh the potential benefits or when there is conclusive proof of definitive outcomes, physicians must assess whether to continue, modify or immediately stop the study.
Vulnerable Groups and Individuals

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

All vulnerable groups and individuals should receive specifically considered protection.

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

Scientific Requirements and Research Protocols

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

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

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

Research Ethics Committees

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

The committee must have the right to monitor ongoing studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse events. No amendment to the protocol may be made without consideration and approval by the committee. After the end of the study, the researchers must submit a final report to the committee containing a summary of the study’s findings and conclusions.

Privacy and Confidentiality

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

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

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

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

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

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

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

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

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

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

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

Use of Placebo

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

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

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

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

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

Post-Trial Provisions

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

Research Registration and Publication and Dissemination of Results

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

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

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