

# IRISH RESEARCH NURSES NETWORK



## **CLINICAL RESEARCH NURSE ORIENTATION PACK**

*September 2013*

*An introduction to the role of the research nurse  
and the regulations and guidelines governing  
clinical research in Ireland*



## ***Irish Research Nurses National Orientation Program***

### ***Foreword***

This orientation program was compiled by members of the Irish Research Nurses Network (IRNN) as part of its commitment to support the educational and professional needs of clinical research nurses working in Ireland. Mindful that research nurses in Ireland work in a variety of settings, from established clinical research facilities, to independently working within hospital departments, we recognised the need to develop this orientation program to help standardise the training and educational needs of all clinical research nurses.

We wish you well as you embark in what will hopefully be a rewarding career choice and we hope you find this program a useful training tool.

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, for this we are most grateful.

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

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**SECTION 1:**

***Orientation Process***



### **1.1. Introduction**

Congratulations on your new position in Clinical Research. Learning about clinical research, the people involved, systems and procedures is likely to be an incremental process across the coming months and most learning will occur informally on the job.

The training and educational needs of research staff are complex due to the depth of specialist knowledge necessary to master components of the job at a professional level. These components include both care of the patient and their families along with the planning, coordination and administration of the clinical research itself. This will require a wide range of skill, knowledge, training, education and experience.

### **1.2. Objectives of this Orientation program**

The aim of this program is to standardise the training and education of clinical research nurses in Ireland. It will provide you with information on 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 the induction and training process to allow you to work through this folder. Your manager will agree a learning contract with you and a timeframe will be agreed upon to complete a series of competency assessment questionnaires. Also in conjunction with your manager you will complete an orientation checklist to ensure you have received direction in all aspects of clinical research (sample checklist, Appendix 1).

Training methods may include:

- Ongoing development through reading, internet searches etc
- In-service training & induction programmes
- Shadowing experienced staff members to observe practice
- Introduction to appropriate departments / personnel etc
- Attendance at relevant national research meetings and seminars

### 1.3. Induction process and checklist

The following pages contain suggested induction processes and timelines, and an orientation checklist to be adapted to individual needs.

Areas Of Induction	Target Timelines
<p>Local Induction</p> <ul style="list-style-type: none"> <li>• Tour of facility and familiarisation with layout including opening times, authorised access and emergency exits,</li> <li>• Fire, emergency &amp; cardiac arrest information &amp; telephone numbers</li> <li>• Toilets and hand-washing facilities</li> <li>• Office equipment (e.g. fax, photocopier)</li> <li>• Tea/coffee facilities</li> <li>• Hours/time of working day</li> </ul>	<p>First day on premises</p>
<p>Introductions</p> <ul style="list-style-type: none"> <li>• Introduction to core staff and associate staff within the facility</li> <li>• Introduction to porters and building administration staff</li> <li>• Introduction to affiliated hospital personnel as required</li> </ul>	<p>At first opportunity after commencement</p>
<p>Institutional Induction</p> <ul style="list-style-type: none"> <li>• Tour of institution and explanation of history, ethos and mission of the institution</li> <li>•</li> </ul>	<p>Prior to or as soon as possible after commencement</p>
<p>Issue of forms to arrange identity badge/swipe card, computer and e-mail access (Administrator)</p>	<p>1<sup>st</sup> week in post</p>
<p>Training in and access to systems for:</p> <ul style="list-style-type: none"> <li>• Scheduling and reporting time allocated to specific activities</li> <li>• Managing patient bookings</li> </ul>	<p>First Month</p>
<p>One-to-one meeting with the nurse manager and/or your designated mentor to:</p> <ul style="list-style-type: none"> <li>• Identify specific learning needs, and book attendance at study days, for example, ICH GCP, lab safety, venepuncture &amp; cannulation, CPR, First Aid, other mandatory or optional training</li> <li>• Organise shadowing with other research nurses, specialist nurses, etc as indicated</li> <li>• Secure access to education and training resources, Research Nurse Network mailing list &amp; meetings</li> <li>• Set objectives and targets</li> <li>• Arrange schedule for future PPD meetings as per local policy</li> </ul>	<p>First 2 weeks</p>
<p>Read Standard Operating Procedures, policies and guidelines. Seek guidance from your mentor/manager regarding which are specific to your trials or activities. Sign and date to indicate that each SOP has been read and understood. Complete associated training as necessary, for example, use of specific equipment</p>	<p>From day 1 to 6 weeks</p>

Principal Investigator/Research Team <ul style="list-style-type: none"> <li>• Introduction to the research team and the research specialty multidisciplinary team for allocated studies</li> <li>• Read protocols &amp; specific trial information, screening, recruitment, Investigators Brochure, Adverse Event Reporting, informed consent including Patient information Sheets &amp; Consent forms</li> <li>• Meet study monitor and complete study specific training (by Monitor or study team) before starting any study activity)</li> </ul>	First 2 weeks
PI to delegate tasks on the delegation log once attended ICH/GCP training, had protocol training and had trial specific training	First month
The Orientation Pack will be provided by your manager or mentor. Use to learn or revise your knowledge of the clinical research process, regulations and guidelines, and your role and responsibilities. Once complete and signed off, scan and email to your line manager, and retain original in your training folder	First month in post, with timelines for additional training agreed

#### **1.4. Introduction to the Research Nurse Role**

The research nurse is responsible for the day to day running of research studies including screening of potential patients, recruiting patients into studies according to agreed protocols, assisting in the informed consent process and management of all the study related data.

The research nurse must have the ability to work independently, to prioritise their own workload and to communicate effectively with all members of the research team with the ability to meet tight deadlines.

All clinical research activity must be compliant and conducted in accordance with European Union (EU) Directive, SI 190 (2004), ICH/GCP International Conference on Harmonisation and Good Clinical Practice (GCP).

There are many different abbreviations within Research, a glossary can be found in section C.

#### **The Clinical Research Environment.**

Research participants should be seen in comfortable surroundings ultimately improving their experience in clinical research studies. The area for clinical research activity / review will be designated by your institution.

#### **Clinical Research Staff**

Members of a Clinical Research team generally include:

- Director:
- Nurse manager
- Administrator
- Research Nurses
- Data entry officers
- Lab technicians
- Clinical Informatics manager
- IT Manager



## **Training for Research Nurses**

All Research Nurses must have and maintain their own Training File which can be inspected/audited on request. Please refer to the relative local SOP

### **ICH/GCP/EU Directive Training**

It is a legal requirement that all Research Staff have training in ICH/GCP, the EU Directives and Irish Regulations. Training opportunities are to be identified during the orientation process. Staff members must attend ICH GCP training

### **Skills and competencies**

Details of skills and competencies required for clinical research nursing is provided in the competencies assessment booklet available locally.

### **Research Support/Training**

Relevant training opportunities are usually advertised on each institutions website and sent via email to the staff mailing list.

### **Further post-graduate training opportunities**

Please discuss all opportunities for study and support with your line manager. The following are examples of clinical research specific postgraduate courses which may be of interest to nurses working in the clinical research area in Ireland.

**Postgraduate Certificate in Nursing (Clinical Research):** offered by the Faculty of Nursing and Midwifery, RCSI, is a Minor Award, Level 9, course delivered part-time over 6 months and includes 3 modules of education and practical seminars. Progression to MSc can be facilitated either in RCSI or in local institution. For more details see;  
[http://www.rcsi.ie/cat\\_course\\_detail.jsp?n=769&itemID=60](http://www.rcsi.ie/cat_course_detail.jsp?n=769&itemID=60)

**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/>

### **1.5. Site specific operational details**

#### **Annual leave**

Each research nurse must request Annual Leave from their manager. Nurses employed by an investigator must liaise with PI and other members of their research team prior to taking leave.

#### **Sickness**

Sickness & absence must be reported to your line manager **and** to your research team. Please adhere to the Sickness/Absence policy, along with other Human Resources policies, available from your organisation.

#### **Hours of Operation**

Hours of operation are:

Mon-Fri: \_\_\_\_\_

Weekend: \_\_\_\_\_

#### **Useful contact numbers:**

Name	Number	E-mail address
_____	_____	_____
_____	_____	_____
_____	_____	_____

**SECTION 2:**

***Regulations & Legislation Governing***

***Clinical Research***



## ***Back ground 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.

### ***2.1. 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 very important 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 the war, 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

Process Of Induction: All staff to attend ICH GCP training and certification
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## **2.2. 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 has been amended six times since, most recently at the General Assembly in October 2008. The current (2008) 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 the underlying principals have been incorporated into law in some countries. It is a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects.

The key points of the declaration 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 principals.
- 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.

Process Of Induction: All staff to attend ICH GCP training and certification
Recommended Reading: <a href="http://www.wma.net">www.wma.net</a>
Useful Contacts: The local Ethics committee

### ***2.3. International Conference of Harmonisation, Good Clinical Practice (ICH GCP)***

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.

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 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.

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“

The ICH GCP guidelines 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 ICH GCP guidelines were an attempt to unify GCP standards but they were only ever guidelines and lacked the legal status needed in order that everyone adopted them. Although most sponsor companies adopted the guidelines from the outset there were some that did not. In particular academic research units found the cost load implications were too great to implement the guidelines. Also 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 in local law 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 weighted 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.

Process Of Induction: All staff to attend ICH GCP training and certification
Recommended Reading: <a href="http://www.emea.europa.eu">www.emea.europa.eu</a>
Useful Contacts: Local research ethics committee

## 2.4 European Directive on Good Clinical Practice in Clinical Trials

The EU Clinical Trials Directive of 2001 (2001/20/EC) aimed to harmonise and streamline clinical trial procedures throughout the member states, and relates to all trials involving medicinal products for human use, and encompasses all personnel involved with the clinical trial procedure.

The regulations came into force on 1st May 2004 when a statutory instrument (S.I. 190 of 2004) passed the parent EU Regulation into Irish law. These regulations replace those controls that previously applied to such trials under the Control of Clinical Trials Acts, 1987 and 1990. S.I. 190 now governs clinical drug trials in Ireland. (S.I. 190 of 2004 has been amended by S.I. 878 of 2004 and S.I. 374 of 2006.)

Guidance provide by the EU Directive:

- 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.



## **2.5. 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 time be ICH/GCP compliant.

### ***Clinical Drug Trials***

A clinical drug trial can not take place in any of the EU countries without central favourable approval from its national REC. There are currently 13 REC's in Ireland which have been recognised by the Department of Health and Children, to review applications for clinical trials of medicinal products for the whole of Ireland. One of these REC's and the Irish Medicines Board (regulatory) must approve a clinical drug trial for it to proceed in Ireland. In addition, the drug trial must have a European Clinical Trial number, called a EudraCT number.

Legislation on clinical drug trials is very specific and sets out how many members the committee is allowed to have, and what proportion of these must be lay members. The maximum number of members is 21, one third of which 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 drug trial, and in relation to amendments to a clinical drug trial.

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

### ***Other Research***

A REC reviews many other types of research other than clinical drug 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. Not all clinical investigations of medical devices require Irish Medicines Board approval either.

Academic research, which takes place in a hospital must also be reviewed by its 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, 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 e.g. An Bord Altranais 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
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 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 Clinical Trial 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

Process Of Induction: Informal presentation and discussion.
Useful Contacts: Local medical research ethics committee

## **2.6. Regulatory Authority (Irish Medicines Board)**

The Irish Medicines Board (IMB) is the regulatory or competent authority in Ireland. It was established in 1995 and replaced the National Drugs Advisory Board which was established in 1966. The fundamental role of the IMB is to protect and enhance public and animal health through the regulation of medicines, medical devices and healthcare products.

Among its many activities, the IMB regulates clinical trials / the use of medicines for clinical research purposes. Written regulatory approval must be obtained from the IMB prior to any clinical trial procedures being carried out. The IMB 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 IMB has the authority to audit sponsors, investigators and sites involved with clinical trials to assess patient protection and protocol compliance.

### ***Other IMB roles:***

- 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 IMB and this must contain all of the necessary data supporting its quality, safety and efficacy.
- The IMB is also responsible for the monitoring and inspecting of products on the market to ensure their quality, safety and efficacy consistent with current medical and scientific knowledge.
- The IMB also monitors 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.
- The IMB is also the 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 IMB 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.

Process Of Induction: Informal presentation and discussion.
Recommended Reading: <a href="http://www.imb.ie">www.imb.ie</a>
Useful Contacts: Irish Medicines Board, Earlsfort Terrace, Dublin 2. Tel (01) 6764971

## 2.7. 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 IMB is responsible for the regulation of medical devices on the Irish market. The range of products is very wide. 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. They are as follows:

- 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:

- S.I. No. 253 of 1994, European Communities (Active Implantable Medical Devices) Regulations, 1994 that became mandatory on 1st January 1995.
- S.I. No. 252 of 1994, European Communities (Medical Devices) Regulations, 1994 that became mandatory on 14th June 1998.
- S.I. No. 304 of 2001, European Communities (*In-vitro* Diagnostic Medical Devices) Regulations, 2001 that became mandatory on the 7th December 2003.

A number of key guidance notes have been prepared to assist the medical device sector on the use of the Directives and related Regulations. In addition a number of application forms have been prepared to ensure that all data required by the IMB is included with correspondence. These documents can be found on the publications section of the website. These forms can also be obtained in the European Commission Guideline on a Medical Device Vigilance System Meddev 2.12-1, rev 5. Within the Medical Devices Department there are three sections, details of which can be found on the website:

- Pre-Market Evaluation Section
- Post-Market Evaluation Section
- Auditing & Surveillance Section

**The IMB provide advice on conducting clinical investigations involving medical devices.**

The IMB is happy to talk to clinicians or manufacturers about conducting clinical research/investigations involving medical devices in Ireland. The IMB encourage sponsors of clinical investigations requiring IMB review to meet with them prior to submission of the application. This allows for opportunity to discuss the investigation, the device and the process/review of the IMB. The contact details are: [www.medicaldevices@imb.ie](mailto:www.medicaldevices@imb.ie)

**Ethics Committee Opinion is required prior to applying to the Irish Medicines Board to conduct a clinical investigation of a non-CE marked device.**

Currently a favourable Ethics Committee opinion is required from each site at which a clinical investigation involving a non-CE marked medical device is conducted in Ireland. Certain Ethics Committees can provide opinion, which are applicable to several hospitals/investigational centres. A clinical investigation involving a non-CE marked medical device, which requires notification to the IMB cannot proceed unless both the relevant Ethics Committee provides a favourable opinion and the IMB has no objection following its review.

Process Of Induction: Informal presentation and discussion
Recommended Reading: <a href="mailto:www.medicaldevices@imb.ie">www.medicaldevices@imb.ie</a>
Useful Contacts: Irish Medicines Board, Earlsfort Terrace, Dublin 2. Tel (01) 6764971

## 2.8. 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 the case 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.

Process of Induction: Informal presentation and discussion.
Recommended Reading: <a href="http://www.dataprotection.ie">www.dataprotection.ie</a>
Useful Contacts: Data Protection Commissioner, Canal House, Station Road, Portarlinton, Co. Laois Telephone: 1890 252 231 or 057 8684800

**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 Irish Medicines Board 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.



### **3.2 Roles and Responsibilities**

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

#### **Study Sponsor**

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)**

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 (revised version 2008)
- 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, which 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 (SubI)**

The co-investigator/Sub I 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 which 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.

### **Research Nurse**

Within every clinical trial named research nurses are 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, spinning labelling, storage and shipping of blood and urine pharmacokinetic 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 Entry Staff**

The data managers will work closely with the research nurses to ensure accurate and appropriate data collection.

- To ensure that they have attended the initiation meeting and received any appropriate training necessary in order to conduct the trial safely and efficiently.
- Entry of patients into clinical trials, utilising appropriate randomisation procedures when necessary.
- Completion of case report forms.
- Ensuring that all data is available for monitoring visits.
- Assist research nurses in submission to ethics/research and development.
- (In some centres) archiving of all clinical trial related documents according to regulatory requirements.

- Shipping of blood and urine pharmacokinetic samples.
- Entering and updating databases.

### **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 parenterally administered 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.

SOPs will normally include:

- Number and title of procedure
- Purpose
- Other related procedures
- Personnel involved with procedure
- When and how the procedure should be performed
- Date 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 signed into the signature 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 now 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 in the protocol.

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

### **3.6. Informed Consent**

Informed consent registering the research participants voluntary agreement to be part of a research trial is of paramount importance. Details of how it is to be obtained, by whom and what details the research participant must be provided with, to adequately provide an “informed” decision to participate is clearly detailed in the ICH GCP booklet.

**All research staff must be familiar with ICH GCP regulations and the legislation surrounding informed consent.**



## **SECTION 4:**

### ***General Information***



#### ***4.1. Information Technology***

1. All staff must ensure that only authorised personnel enter the workplace, to prevent computer hackers or criminals gaining access to patient information.
2. All computer equipment must be located away from public access. If this is not possible then equipment must always be supervised.
3. Computer printouts must be retrieved from printers as quickly as possible in order to prevent unauthorised observation.
4. Desks must be cleared of information sources (Data, contact information etc.) when the office is unattended.
5. All computers/laptops must be switched off at the end of the day before leaving the office.
6. Computers must not be left logged in when staff are away from their desk or out of the office.
7. All old information must be disposed of securely. Paper based items must be shredded.

#### ***Personal Computer/Laptop Security***

1. All accounts & database systems must have secure passwords. Blank passwords will allow unauthorised individuals to gain access to the computer and it's data.
2. Passwords must be kept secret at all times; use of a co- worker's password is forbidden, and passwords should never be stored anywhere near the computer.
3. Up to-date anti-virus software must be installed on an ongoing basis.
4. 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 shutting out any unauthorised access.
5. 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.
6. Laptops must be kept close to hand, never assuming it will be safe lying around.
7. All laptops must be encrypted in order to prevent data access should the equipment be stolen.

#### **4.2. Glossary of Common Terms (IMB Definitions)**

**“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;

**“Commission Directive 2003/94/EC”** means Commission Directive 2003/94/EC<sup>2</sup> of 8 October 2003 laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and for investigational medicinal products for human use, but only insofar as that Directive applies to investigational medicinal products;

**“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;

**“Directive”** means Directive 2001/20/EC<sup>1</sup> of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use;

**“Directive 2001/83/EC”** means Directive 2001/83/EC<sup>3</sup> of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use;

**“EMA”** means the European Agency for the Evaluation of Medicinal Products established by Council Regulation (EEC) No. 2309/93<sup>5</sup>;

**“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”** means the authorised health care professional responsible for the conduct of a clinical trial at a trial site and if a trial is conducted by a team of authorised health care professionals at a trial site, the investigator is the leader responsible for that team;

**“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;

***“principles and guidelines of good manufacturing practice”*** means the principles and guidelines set out in Commission Directive 2003/94/EC;

***“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.

### **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](http://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)**

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.

### **Sponsor**

The concept of a „sponsor“ for a clinical trial was introduced by the EU Clinical Trials Directive (2001/20/EC). The definition of sponsor for trials of investigational medicinal products is the individual, organisation or group of organisations/individuals that take responsibility for the initiation, management and financing (or arranging financing) for the study.



**Appendix 1. Sample Orientation checklist**

<b>RESEARCH NURSE ORIENTATION CHECKLIST</b>			
Name: _____		Commencement Date: _____	
Preceptor/Mentor: _____			
SECTION 1 - INTRODUCTION TO SITE PERSONNEL			
Area of Induction	Date	Signature of Preceptor	Signature of New Employee
1. Outline of role			
2. Introduction to core research staff			
3. Introduction to Medical Research Ethics Committee Administrator			
4. Introduction to core support staff			
SECTION 2 - CONDITIONS OF EMPLOYMENT			
Area of Induction	Date	Signature of Preceptor	Signature of New Employee
1. Contract of employment, working hours, & breaks and period of notice			
2. Electronic & paper timesheet (as applicable)			
3. Holidays & local arrangements for leave			
4. Sickness Policy & how to report sickness			
SECTION 3 - CRC STANDARD OPERATING PROCEDURES			
Area of Induction	Date	Signature of Preceptor	Signature of New Employee
1. Location of SOP's			
2. Policy for reviewing and signing SOPs			
3. Process for updating and distributing amended SOPs			

SECTION 4 – INTRODUCTION TO FACILITIES			
Area of Induction	Date	Signature of Preceptor	Signature of New Employee
1. Tour of research facilities			
2. Access & security procedure			
3. Changing room/lockers and toilet facilities			
4. Fire exits & System for raising alarms			
5. Awareness of drug key storage			
6. Telephone operation			
7. Notice boards			
8. Identity badge / Swipe card			
9. IT set up and passwords (Email, Hospital Information System)			
10. Attend Occupational Health for introduction (if applicable)			
11. Tour of the hospital if appropriate (Introduction to key outpatient, pharmacy and radiology staff)			
12. Staff restaurants			
13. Parking arrangements - check permit issued ( if appropriate)			
SECTION 5 - ADMINISTRATIVE PROCESSES			
Area of Induction	Date	Signature of Preceptor	Signature of New Employee
1. Data protection / Patient confidentiality			
2. Hospital admissions procedures			
3. Making Hospital outpatients appointments			
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			
<b>SECTION 6 - HEALTH &amp; SAFETY</b>			
Area of Induction	Date	Signature of Preceptor	Signature of New Employee
1. Attendance at fire training			
2. Attendance at infection control training (Hand Hygiene)			
3. Attendance at manual handling training			
4. Personal security			
5. Awareness of overnight study guidelines (if applicable)			
6. Awareness of lone worker policy (if applicable)			
7. Awareness of risk assessments			
8. Safe handling of biological samples			
9. Safe handling of dry ice			
10. Sharps policy			
11. Spills policy			
12. Vaccination screening			
<b>SECTION 7 – CLINICAL SKILLS</b>			
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			
Area of Induction	Date	Signature of Preceptor	Signature of New Employee
1. CPR training			
2. CRC Medical Emergency policy			
4. Laboratory techniques			
5. Dry ice training			
6. Anthropometry			

7. Phlebotomy			
8. ECG recording			
9. Central Laboratory (Lab kits, processing, packaging & shipping)			
<b>SECTION 8 - RESEARCH GOVERNANCE</b>			
Area of Induction	Date	Signature of Preceptor	Signature of New Employee
1. ICH Good Clinical Practice Training and certification			
2. Phases of Clinical trials			
3. Study protocols			
4. Investigator's Brochure			
5. Role and composition of research ethics Committees			
6. REC application and approval process including protocol amendments			
7. Case report form completion (Source documents, data verification)			
8. Legal issues i.e. indemnity			
9. Declaration of Helsinki			
10. Good Laboratory Practice			
11. Introduction to Site Files & Filing			
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**

Area of Induction	Date	Signature of Preceptor	Signature of New Employee
1. Staff meetings			
2. Journal club meeting / research meetings			
3. Social and sports club			
4. Irish Research Nurses Network			

**SECTION 10 – Miscellaneous**

Area of Induction	Date	Signature of Preceptor	Signature of New Employee

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

**Acknowledged by \_\_\_\_\_ on date \_\_\_\_\_**





**CLINICAL RESEARCH NURSE ORIENTATION PACK**  
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