R&D Operational Framework

2020

R&D Operational Arrangements

University Partnership

As a University Health Board, SWANSEA BAY UHB has signed a Memorandum of Understanding (MOU) with Swansea University which summarises and agrees the Research Partnership between the two Organisations.

Joint Clinical Research Facility (JCRF)

Within the context of the Partnership arrangements, the JCRF operates as a University initiative housed within the Institute of Life Sciences 2, situated on Singleton Hospital campus in collaboration with SWANSEA BAY UHB and encompasses a sister Unit housed within Morriston Hospital.

The JCRF contains clinical facilities to support clinical trials within SWANSEA BAY UHB and the University. The governance approvals and indemnity of JCRF trials is provided by the NHS via SWANSEA BAY UHB R&D Department and through individual study contracts (c.f. MOU clause 1.8) with operational delivery provided by a team of research nurses, data officers and administrative staff employed by the University (whilst maintaining several NHS conditions, such as pension rights) and overseen by the JCRF Operational Board. The JCRF research team all have honorary NHS contracts with Swansea Bay UHB.

Swansea University

The University Partnership extends to include co-sponsorship collaboration with Swansea University. In addition, methodological support is provided by Swansea Trials Unit (STU) the UKCRC registered Trials Unit. STU is the partner trials unit for Swansea Bay UHB, offering expert methodological advice and support to NHS staff engaging in research. The Director of the Trials Unit is a member of the SWANSEA BAY UHB R&D Committee.The Trials Units across Wales are core-funded by Welsh Government, via the Health and Care Research Wales infrastructure, to support research within their regional NHS Partner Organisations.

The Swansea University co-sponsorship arrangement is governed by a Framework Agreement and Joint Working Protocol.

Joint Study Review Committee (JSRC)

The JSRC is a Joint SWANSEA BAY/Hywel Dda UHB and Swansea University Committee which meets monthly. It provides sponsor oversight as well as scientific and peer review for research studies which involve SWANSEA BAY/Hywel Dda UHB and have not undergone robust peer-review elsewhere. This will include SWANSEA BAY UHB sponsored studies, Swansea University Studies (usually from Faculty of Health and Life Sciences) and high risk Swansea University sponsored student studies. Alongside pure scientific review, the JSRC provides wider governance support to the R&D Department, receiving monthly Quality Assurance (QA) reports from the SWANSEA BAY UHB R&D QA Officer, agreeing

the most appropriate course of redress for studies encountering difficulties or challenges. JSRC also agrees classification decisions of Service Evaluation/development; members receive monthly updates of external sponsored studies opened within the Health Board and act as the Sponsor Oversight Committee receiving assurances on the conduct and delivery of co-sponsored studies. Membership of the JSRC is constituted by SWANSEA BAY/Hywel Dda UHB Clinicians, R&D representatives and representatives from Swansea University academic colleges engaged in SWANSEA BAY UHB R&D activity.

Standard Operating Procedures (SOP)

The Health Board utilises the portfolio of research SOPs developed by STU, with some additional SOPs developed for local research management issues.

Human Tissue

Swansea Bay UHB operates satellite sites under the main Swansea University Human Tissue Authority (HTA) licence no. 12651. The HTA Governance Officer acts in a joint SWANSEA BAY UHB and Swansea University role under the direction and oversight of the Designated Individual for HTA licence 12651. A joint HTA quality management system (QMS) forms the basis of the governance around the use of human tissue in research in both organisations. A number of tissue banks and licenced collections are managed under the joint HTA licence. The HTA Governance Officer is a member of the Swansea University HTA Sub-committee, Swansea Bay UHB HTA Assurance Committee and Swansea Bay UHB HTA Operational Group and also reports to the Swansea Bay UHB R&D Committee.

A review of studies is performed alongside Health Board Capacity and Capability (C&C) and amendment checks to ensure compliance with the requirements of the HT Act and a register of REC approved studies that use and store relevant material is maintained to mitigate the risk of breach at study end. Responsibilities for tissue transferred in or out of SWANSEA BAY UHB are defined in an appropriate agreement.

Advice and guidance on compliance with the Human Tissue Act legislation and best practice in the use of human samples in research is available to Health Board researchers.

Research Involving Ionising Radiation

Please refer to procedure attached.

Research Contracts

As a requirement of the UK Policy Framework for Health and Social Care Research, all interventional commercial or non-commercial studies (excluding educational) sponsored or hosted by a Health Board are governed by a research contract. Non-interventional studies will be contracted using a national organisation information document (OID).

UK Clinical Research Collaboration (UKCRC) has developed national model template agreements for use by NHS Organisations and Sponsors of research studies and these model templates are accepted by SWANSEA BAY UHB.

For SWANSEA BAY UHB co/sponsored studies, a Conditions of Sponsorship agreement is signed by the Chief Investigator (CI) to confirm the delegation of study responsibilities from the Health Board to the CI.

Research contract signatories for SWANSEA BAY UHB are the AMD R&D, MD or Chief Executive.

Contract Modifications

The R&D Manager has responsibility for contract review. Non-modified model templates may be reviewed by the Assistant R&D Manager. All modifications to the model templates or non-model templates must be reviewed by the R&D Manager.

Modifications to any of the below listed clauses may be escalated by the R&D Manager for external review to NWSSP Legal and Risk Services:

- Modifications to Liabilities and Indemnity
- Modifications to Insurance*
- Modifications to the ABPI Form of Indemnity
- Modifications to Financial Liabilities*
- Modifications to Clinical Trial Compensation guidelines

*If external Sponsor insurance provision is less than the agreed UK standard of £5 million for clinical drug trials, the R&D Finance Manager will refer to Director of Finance for agreement to accept the modified insurance level. Equally, modifications to the capped financial liability clauses as agreed to apply to the NHS will be escalated for Director of Finance authorisation.

Grant Contracts

Collaborative grant and funding contracts are reviewed by the R&D Manager and R&D Finance Manager.

R&D Financial Control

The R&D Budget is set in accordance with the Health and Care Research Wales Needs Based Funding model...

Commercial Studies

SWANSEA BAY UHB Health Board utilises the NIHR Industry Costing Template and NIHR Tariffs. All commercial studies are costed and verified by the R&D Finance team against the costing template protocol and contract to ensure all costs impacting on SWANSEA BAY UHB are fully reimbursed. It is possible for the R&D Budget to be used to cover costs associated with supporting commercial research however this will be on the basis of full cost recovery from the commercial Sponsor.

The costing template carries a Market Force Factor (MFF) of 1.9 to enable capacity building within the Health Board for future engagement in R&D.

Joint Clinical Research Facility (JCRF)

All studies conducted within the JCRF adhere to the above costing methods and governance review by the R&D Department. The Health Board R&D team will invoice the Sponsor companies for receipt of funds, however Swansea University is recompensed for the services supporting those studies. The R&D Finance team invoice the Sponsor company upon onset of study recruitment. Recruitment to the studies is actively monitored by the R&D team on a monthly basis.

Non-Commercial

Cost attribution

For all non-commercial portfolio studies, the Sponsor apply the ACORD guidance to determine the cost attribution of each intervention required by the study protocol. Each intervention is classified in line with guidance and definitions within ACORD.

All NHS Support Costs are met by the R&D Service Support Budget stream. The classification of costs is determined through agreement with the Research Teams and with verification from the support departments/directorates involved in the study. The needs for delivering a study is monitored monthly and reported monthly to Health and care Research Wales performance monitoring team as part of the needs based funding requirements.

Threshold of accepting Excess Treatment Costs (ETC)

Where an intervention is identified as a NHS Treatment cost but which is excess to current standard treatment, the following principle is used to decide whether subvention funding will be applied for from Health and Care Research Wales Welsh Government.

ETC Principle

Studies with total excess treatment costs of £3000 or more per service department will have an ETC application made to Health and Care Research Wales***. If the total ETC amounts to less than £3000 per service department, SWANSEA BAY UHB may decide to meet costs from central R&D funds***. This will be decided on a case to case basis, as the decision may depend upon available funding from our Needs Based Funding allocation.

SWANSEA BAY UHB sponsored studies

For SWANSEA BAY UHB sponsored studies, the ACORD methodology applies in addition to Research Sponsorship costs being met from the R&D Budget Researcher Support & Portfolio Development (RS&PD) funding stream.

Invoicing & Re-charging

All commercial studies are invoiced via the R&D Finance team. For studies hosted by the JCRF, the invoicing process is also managed by HB R&D finance. For non-commercial studies where NHS support costs have been identified and agreed to be met from the R&D Budget, the R&D Finance team will reimburse the relevant directorates upon receipt of recruitment/activity data. If a study has grant funding with an allocation set aside for participating sites, the research costs will be invoiced to the study sponsor by the R&D Finance team.

Research Codes

All commercial studies will have an identified cost centre. Non-commercial studies do not have individual cost centres but will be coded to the central R&D Cost centres L201/L202. In some instances, there will be a requirement for their own identifiable analysis code to be set up; this must be agreed with the R&D Finance team.

Budget sign off

The R&D Budget is signed off annually by the AMD R&D in agreement with Health and Care Research Wales Welsh Government.

R&D Expenditure sign off

In accordance with the HB Finance Standing Operating Procedures, the R&D management team has financial responsibility for sign off of expenditure against the Budget.

Financial Authorisation Limits

AMD R&D – Limit of £75,000

R&D Manager – Limit of £5,000

Finance Roles & Responsibilities

It is the responsibility of the local Investigator teams to liaise with the R&D Finance team at an early stage of study set up, either to agree commercial costings or to apply the ACORD cost attribution guidance for non-commercial and SWANSEA BAY UHB sponsored studies. Upon approval of a study, the Principal Investigator (PI) must advise the R&D team of activity and recruitment within the study, receipt of study information will be tracked by the central R&D team.

Delegated accountability for the R&D budget is the responsibility of the AM R&D Director, responsibility for managing the R&D Budget correctly in line with Health and Care Research Wales Policy is delegated to the R&D Manager, supported by the R&D Finance team.

Intellectual Property (IP)

Issues relating to Background and Foreground IP are included in research contracts. For instances where SWANSEA BAY UHB owns the IP Right (IPR) associated to the R&D activity, SWANSEA BAY UHB IP Policy is applied. The IP Policy includes a revenue sharing scheme to ensure fair reward and incentivisation for SWANSEA BAY UHB staff.

Decisions to progress the exploitation or protection of R&D associated IPR is decided through the structures outlined within the SWANSEA BAY UHB IP Policy. Such decisions would include agreement to cover costs associated to IPR exploitation through the use of R&D funds or the agreement to proceed with licensing the IPR to a third party.

Clinical Academics have the choice to exploit associated IPR via their university role or clinical role. However, there is a requirement for Clinical Academics to report IP to the R&D department as evidence of innovation, whilst offering fair opportunity for SWANSEA BAY UHB to consider options for collaborative exploitation and commercialisation.

R&D Quality Assurance (QA)

Following SWANSEA BAY UHB R&D approval, SWANSEA BAY UHB sponsored or SU co-sponsored clinical interventional studies (Drug/Surgical/Device) are monitored and audited according to their risk profile, as determined by the Sponsor/CI risk assessment during study development stages. SWANSEA BAY UHB (co-)sponsored clinical trials have highest priority for QA monitoring and audit, due to the legal sponsorship for those studies resting with the Health Board.

For (co-)sponsored studies adopted by STU, monitoring will be delegated to the STU via the contract agreement and in accordance with the overarching MOU and Joint Working document describing the co-sponsorship model in operation with SU. Periodic auditing of site files is undertaken by the SWANSEA BAY UHB/SU QA Officers.

For all other studies sponsored by SWANSEA BAY UHB, periodic auditing by the R&D team will be undertaken in line with the Research Governance Framework (RGF).

Commercial studies have regular on-site monitoring undertaken by the Sponsor companies; therefore, the R&D QA team will receive the external monitoring reports and will audit at the discretion and request of the Sponsor in the event of a local Suspected Unexpected Serious Adverse Reactions (SUSAR) or breach of protocol/Good Clinical Practice (GCP).

For non-SWANSEA BAY UHB sponsored non-commercial studies, including student projects which access SWANSEA BAY UHB patients, staff or resource, the sponsor has responsibility to monitor unless delegated to SWANSEA BAY UHB site via the study contract. Periodic auditing by the SWANSEA BAY UHB QA team will be undertaken in line with the RGF (10% of studies per year).

The R&D QA Officer has responsibility to audit studies to verify compliance with GCP standards. The R&D QA also undertakes regular audits of processes within Pharmacy and Laboratory Medicine. Audit reports are prepared, reviewed and authorised by the QA Officer before being issued to the research team and notified to the JSRC and the HB R&D Committee.. Corrective and preventative actions and timescales are agreed with the research team prior to the next scheduled audit visit, or earlier depending on the level of resulting risk.

Where SWANSEA BAY UHB is an investigator site, the SWANSEA BAY UHB R&D QA team and external Sponsors have a reciprocal responsibility to communicate audit and monitoring findings to allow both to mitigate risks. This responsibility is defined in a contract or agreement.

Conditions of SWANSEA BAY UHB sponsorship agreements are signed by the Chief Investigators in both CTIMP and non-CTIMP studies.

Unless classified as high risk, in accordance with JSRC review, student studies are subject to clinical supervision and are not subject to GCP audit visits.

Internal audits against the published Human Tissue Authority standards for the research sector are conducted as part of the joint quality management system (QMS) for HTA licence. Audit processes including follow up actions are described fully in the QMS Internal Audit SOP.

Department Risk register

The R&D Manager has responsibility for managing the department risk register and escalating high level risks to the R&D Committee for mitigation of the risk concerned.

The R&D QA Officer has responsibility for maintaining the R&D Study QA monitoring and audit trackers.

Managing R&D Risk

The R&D QA Officer reports on a monthly basis to the JSRC on all study audit visits undertaken in the preceding month. The QA report includes reference to any issues of GCP non-compliance, difficulties with study continuity, reportable Serious Adverse Events (SAEs) arising in those of the SWANSEA BAY UHB sponsored studies and/or Suspected Unexpected Serious Adverse Reactions (SUSARS) which have arisen in the externally sponsored studies. SAEs arising in non-HB sponsored studies are reported by the Trials team to the Study sponsor, in line with regulation requirements. Issues are also reported on Datix, the HB incident and risk management platform.

Individual Data Safety and Ethics Committees (DMECs) for SWANSEA BAY UHB co/sponsored clinical interventional studies receive notification of all SAEs relating to the study and are reviewed for trend analysis. The lead nominated statistician for the study undertakes the trend analysis, contributing key advice to Committee members. Following consideration of the clinical events arising in a study and the trend analysis, the members make necessary recommendations to SWANSEA BAY UHB as study (Co-)Sponsor, via the Trial Manager. The R&D Manager will report the recommendations to the JSRC as Sponsor Oversight Committee, to agree appropriate course of actions vis. to continue the study, temporarily halt the study or stop the study. Issues arising in externally sponsored hosted studies will be reported via the external monitoring process and escalated to JSRC, via the QA report, where escalation is deemed necessary.

Student Research

Students requiring access to SWANSEA BAY UHB to undertake research must have their studies assessed for capacity and capability by the R&D department and reviewed through

the permissions process as well as obtain a favourable ethical opinion from a NHS Research Ethics Committee, in line with standard procedural requirements.

It is the expectation of SWANSEA BAY UHB that all student research is sponsored by the host Academic Institution and is clinically supervised.

Permissions

SWANSEA BAY UHB R&D Department complies with the Health and Care Research Wales Permissions process. The role of the R&D department is to confirm the HB has appropriate capacity and capability to undertake any given research programme proposed. Comprehensive governance checks are undertaken on all studies by the central permissions governance team, ensuring appropriate legislative and regulatory compliance is evident prior to issuing the study with HCRW approval.

For studies co/sponsored by SWANSEA BAY UHB, approval by the JSRC is required prior to submission to the Permissions Unit and Ethics Committee unless there is evidence of a satisfactory level of external peer review, such as from a recognised Funder. Study substantial amendments for approved SWANSEA BAY UHB sponsored studies must also be submitted and approved by JSRC prior to regulatory submissions for approval amendment (i.e. R&D/Ethics/Medicine Healthcare Regulatory Authority (MHRA)).

A summary list of all studies approved by the R&D department is reported to the JSRC, for notification purposes, along with those sponsored by SWANSEA BAY UHB but which have received external peer review.

Defining Research

The JSRC has responsibility for reviewing study proposals, in accordance with the National Research Ethics Service ‘Defining Research’ guidance to determine and agree whether a study may proceed on the grounds of its classification as a service evaluation/development or audit, thereby exempting the need for R&D and ethical approval.

Research Passports

In accordance with the UKCRC Research Passport Scheme, launched across the UK in 2007, researchers’ external to SWANSEA BAY UHB are issued with either an Honorary Research Contract (HRC), if their planned research activity has a direct impact on the quality of patient care or a Letter of Access (LOA) if there is no direct impact on patient care.

The R&D team is responsible for processing Research Passport applications. Letters of access may be issued through the R&D department along with template Honorary Research Contracts, as agreed by SWANSEA BAY UHB HR Department.

Confirmation of pre-engagement checks is necessary for either a HRC or LOA to be issued. The Passport scheme algorithm is applied by the R&D team to determine which pre-engagement checks apply, depending on the proposed activity outlined in the research application.

R&D Targets/ Key Indicators (KIs)

SWANSEA BAY UHB is measured on its R&D performance against Key Indicators as set by Welsh Government. Health and Care Research Wales Support Centre is responsible for performance managing all Health Board R&D Departments against WG KIs.

The R&D department utilises the national Local Performance Management System (LPMS) as its main information system, ensuring timely upload of a minimal data set including monthly recruitment activity, excluding those studies which upload directly to the Central Portfolio Management System (CPMS).

Healthcare Standard 21

The R&D Manager is Corporate Lead for Healthcare Standard 21 relating Research and Innovation. Directorate and Locality Healthcare Standard Leads have delegated responsibility for compliance to Standard 21 within their Directorate/Localities, providing evidence of compliance to the Corporate Lead. The Corporate Lead has responsibility to ensure proper advice and guidance is provided to the Directorate and Locality Leads to achieve compliance and is responsible for reviewing and reporting the evidence to the Board, through the annual Healthcare Standard self-assessment return.

Research Misconduct

The HB will follow the process steps/guiding principles outlined in the MRC Policy when it comes to assessing any alleged instances of misconduct and as appropriate follow relevant Health Board policy in line with Counter Fraud/HR advice.

R&D Reporting Structure

Health Board

R&D reports are submitted to the Board of SWANSEA BAY UHB in January and July each year.

Quality & Safety Committee

The Quality & Safety Committee is responsible for monitoring the implementation of Quality and Safety across the organisation including the integration of quality activities. The Terms of Reference of this Committee are set out in the Standing Orders approved by the Health Board and available on the Intranet.

The Quality and Safety Committee will be supported in its role by a number of key specialty Groups/Committees which are overseen by the Quality & Safety Forum which is an Executive Management Group. **Appendix 6 of the Risk Management Strategy & Policy** sets out the main specialty groups/Committees reporting to the Forum. The Standards for Health Services in Wales Scrutiny Panel is a formal sub Committee of the Quality & Safety committee chaired by a Non Officer member.

Research & Development Committee

The Research & Development Committee reports into the Q&S Committee as a specialist quality & safety Committee via the AMD R&D who reports as Chair of the R&D Committee to the Medical Director as Executive Lead for R&D. As a specialist quality & safety Committee, the R&D Committee is overseen by the Quality & Safety Forum.

Joint Scientific Review Committee (JSRC)

The JSRC is a monthly R&D governance operational group which reports into the R&D Committee of SWANSEA BAY UHB.

Directorate/Locality Groups

Each Locality/Clinical Directorate has a Clinical Governance Committee to which R&D related issues within the directorate/locality are reported. Some Directorate/Localities have specialist R&D sub groups to oversee research and development activity. All Directorate/Locality R&D Leads are members of the R&D Committee.

Joint Clinical Research Facility Operational Board

The JCRF Operational Board reports both to Swansea University/SWANSEA BAY UHB Partnership Board and provides update reports to the Health Board R&D Committee.

Swansea Trials Unit Executive Committee and Joint Advisory Group

The STU Executive Committee oversee the management of STU in accordance with appropriate regulatory requirements, especially those of the MHRA, GCP, UKCRC, Health and Care Research Wales, SU and SBM UHB. The STU Executive report to the R&D Committee of SWANSEA BAY UHB and to REIS Department of Research and Innovation at Swansea University.

STU Document Review Group

The Document Review Group is responsible for managing, developing, monitoring, reviewing and refining the STU portfolio of SOPs in accordance with relevant requirements, especially those of the MHRA, GCP, UKCRC, WG, SU and SBU HB.

Procedure for Obtaining Approval of New Research Studies Involving *Ionising Radiation Exposures* and Achieving Regulatory Compliance at Participating Sites

Purpose

To ensure that all medical research studies restrict any dose of ionising radiation to the minimum required to achieve the intended clinical objective and comply with regulatory requirements and guidance.

Only research projects involving medical exposures and therefore needing to comply with the *Ionising Radiation (Medical Exposure) Regulations 2017* (IR(ME)R) are covered by this procedure.

It is assumed that all associated research permissions (e.g. Joint Scientific Review Committee) have been granted.

Procedure

The following procedure describes both the process for obtaining approval for a new research study as a lead site (A) and ensuring compliance with IR(ME)R at all participating research sites (including the lead site) (B).

(A) Obtaining Approval for New Research Studies as a Lead Site

Approval process

1. All proposed research studies must involve the following personnel;

a. *Chief Investigator (CI)* is the investigator with overall responsibility for the conduct of research. The CI is responsible for gaining Radiation Assurance from the HRA and submitting the IRAS application to the main REC together with all supporting documentation (including the protocol and participant information sheet). The CI is responsible for the completeness and accuracy of all submissions.

b. *Principal Investigator (PI)* is the lead investigator responsible for the conduct of the research at each particular site (if multi-site project) and for applying to the local R&D office. The PI will usually be the same person as the CI for the lead site.

c. *Lead Clinical Radiation Expert (CRE)* must be a registered healthcare professional (e.g. with Health and Care Professions Council, HCPC) with clinical expertise in the modality involved in the study and must be registered with the HRA as an expert reviewer. The CRE should understand the characteristics of the research population and the associated detriment that exposure may cause (typically a radiologist, clinical oncologist or nuclear medicine specialist).

d. *Lead Medical Physics Expert (MPE)* must be a registered healthcare professional (e.g. with HCPC) and formally recognised as an MPE in the UK under IR(ME)R 2017. The selected lead MPE must be registered with the HRA as an expert

reviewer with expertise relevant to the modality involved in the study. The MPE should understand the characteristics of the research population in order to provide a suitable dose and risk assessment.

2. All studies involving NHS patients or volunteers that are exposed to ionising radiation must first gain Radiation Assurance from the NHS Health Research Authority (HRA). Depending on the nature of the study (e.g. commercially sponsored, multi-site etc) it will either become an "HRA-managed" or "Self-managed" study. In either case the study will be validated and registered by the HRA.

3. Depending on whether the study is HRA-managed or Self-managed affects how the CRE and lead MPE are selected. In HRA-managed studies the applicant may indicate a preferred CRE and/or lead MPE to conduct the review. The HRA will then approach and endeavour to use these individuals subject to their availability.

In Self-managed studies the applicant chooses the CRE and/or lead MPE reviewers and arranges the reviews themselves. This is often most convenient when applicants wish internal experts to review the study for reasons of speed and familiarity. Applicants should be aware that there is a review fee for all new studies payable to each expert reviewer. This is either paid directly to HRA (HRA-managed studies) or arranged locally with the reviewing health board (Self-managed studies). Further details are available on the HRA website.

4. In order to achieve HRA validation the applicant must complete the relevant sections of the HRA *Research Exposures Form*. Part F1 of the form requires that all radiation exposure details are accurately and consistently documented by the applicant to permit later review by the relevant experts (CRE and lead MPE) and completion of parts F2 and F3.

The quality and adequacy of Information provided by applicants in part F1 and any supporting documentation (including an HRA registration form) is validated by HRA prior to granting approval and issuing to the relevant reviewing experts.

5. Once HRA validation has been granted (usually within 14 calendar days) the applicant is able to send all validated documents to the relevant reviewers to allow them to conduct their expert reviews. Each reviewer completes the relevant section of the Research Exposures Form (parts F2 and F3) and returns the form to the applicant. The applicant then returns the finalised form to HRA and awaits confirmation that they have Radiation Assurance and subsequent registration.

6. Following notification of Radiation Assurance all studies must be approved by a *medical* Research Ethics Committee (REC). All applications to this body are made using the National Research Ethics Service (NRES) Integrated Research Application System (IRAS) – https://www.myresearchproject.org.uk/

7. Applicants completing the IRAS form must follow the NRES guidance, '*Approval for research involving Ionising radiation, v2.0* (2008)'. This document is available via the NRES website at: http://www.hra.nhs.uk/documents/2013/10/approval-of-research-involving-ionising-radiation-2.pdf. Adherence to this guidance will ensure that the research is conducted in accordance with IR(ME)R.

8. The content and structure of parts F1, F2 and F3 of the Research Exposures Form previously approved by HRA and contributed to by the expert reviewers allows the applicant to copy/paste the requested information into the relevant fields of Part B, Section 3 (Exposure to Ionising Radiation) of the IRAS form. Once completed the applicant will then request the formal authorisations from the CRE and lead MPE reviewers who will confirm that their review has been copied to the relevant sections unchanged.

9. Once all other authorisations have been gained e.g. Sponsor, Chief Investigator, the study is then finalised in IRAS and ready for submission to the REC and for any other necessary regulatory approvals (e.g. site/ individual licencing for administration of radioactive materials, if applicable, through a licencing authority such as ARSAC).

10. All applications must also be submitted to each Host NHS Organisation R&D Department for approval in accordance with NHS policies and procedures which are consistent with the Research Governance Framework for Health & Social Care. R&D approval is required for all studies involving recruitment of patients from within the health board or studies using health board facilities or staff. NHS R&D Permission will not be granted without evidence of HRA registration, a favourable ethical opinion & scientific peer review.

TECHNICAL CONSIDERATIONS

11. For each research project involving exposure to individuals for whom no direct medical benefit is expected from the exposure the CRE will approve a dose constraint based on the benefit to society on advice from the lead MPE. This dose constraint must not be exceeded. See Table 1.

Table 1

Benefit to Society	Dose Constraint (mSv)[a]
Minor	< 0.1
Intermediate	0.1 – 1
Moderate	1 – 10
Substantial	> 10

a. These figures can be increased by a factor of 5-10 for those over 50 years. In the event of approval of research on children they should be reduced by a factor of 2 or 3.

12. For research projects involving exposure to individuals for whom a diagnostic or therapeutic benefit is expected the above dose constraints are not appropriate and the CRE will approve a target level of dose on the advice of the lead MPE which will be specified in the submission. This target level of dose should be set at a level which it is anticipated will not be exceeded, but may be exceeded if the clinical benefit of additional exposure outweighs the radiation detriment.

13. The dose assessment by the lead MPE will allow proposal of an approximate total dose for an average patient for the whole study (Total Research Protocol Dose,

(TRPD)). The assessment will be based upon the CRE's statement on normal/additional exposures required for the study.

14. The CI will ensure that submission to the REC and local R&D Department specifies for all exposures required by the research protocol, whether or not they are over and above those required for normal clinical management, the set TRPD and corresponding risks. This will be facilitated by completion of the form F1 described above.

15. The CI will satisfy him/herself that the individuals concerned participate voluntarily in the research programme and ensure that they have been informed in advance about the risks of the exposure. The CI is responsible for preparing and submitting to the REC a Participant Information Sheet (PIS), which should be supplied in advance to all individuals concerned containing the risks of the planned exposures. Advice must be sought from the lead CRE and lead MPE on the content and wording of the information regarding radiation exposures in the PIS.

16. The CRE and lead MPE must make full use where applicable of the Generic Risk Statements provided by the HRA in advising on the wording of the risk communication in the IRAS form and PIS. It is the responsibility of the lead MPE to ensure that the chosen risk statements are accurate and appropriate.

(B) IR(ME)R Compliance at Participating Research Sites

The following applies to both the lead site and participating sites undertaking radiation exposures as part of an approved research study.

1. All participating research sites must involve the following personnel;

- **a.** *Principal Investigator (PI)* – the lead investigator responsible for the conduct of the research at each site (if multi-site project) and for applying to the local R&D office. The PI will usually be the same person as the CI for the lead site.
- **b.** *Local Medical Physics Expert (MPE)* - The Local MPE should be a registered healthcare professional (e.g. with Health and Care Professions Council, HCPC) and formally recognised as an MPE in the UK under IR(ME)R 2017 with expertise relevant to the modality involved in the study. The Local MPE should also understand the characteristics of the research population in order to review and approve the dose and risk assessment completed by the lead MPE. It may be necessary for several modality specific MPEs to be involved in a single study with a nominated "Reviewing MPE" responsible for coordinating a joint review.
- **c.** *IR(ME)R Practitioner* – All exposures must be justified locally by an entitled IR(ME)R Practitioner. For lead site studies this role is expected to be fulfilled by the same individual as undertakes the CRE role. The Practitioner should be a registered healthcare professional (e.g. with HCPC) with clinical expertise in the modality involved in the study (typically a radiologist, clinical oncologist or nuclear medicine specialist).

2. Despite approval of a study by the REC, local IR(ME)R procedures must still be followed at all participating sites. It should be ensured that;

- **a)** Dose constraints are established and adhered to in studies where there is no health benefit to be expected from the exposure.
- **b)** Target dose levels are established where there is some expected health benefit for participants.
- **c)** Exposures are individually justified by an IR(ME)R practitioner.
- **d)** Individuals participate voluntarily.
- **e)** Participants are informed of the risks of the exposure.

3. All studies must be approved by the local R&D Department for approval in accordance with NHS policies and procedures which are consistent with the Research Governance Framework for Health & Social Care. R&D approval is required for all studies involving recruitment of patients from within the health board or studies using health board facilities or staff. NHS R&D Permission will not be granted without HRA registration, a favourable ethical opinion & scientific peer review.

4. The PI at each participating research site (not the lead site), will arrange for completion of a Site-Specific Information Form (SSI Form) in IRAS. The SSI Form and full submission dataset is sent for Health Board R&D Permission.

5. For all research projects involving ionising radiation exposure of individuals the local PI will identify and make contact with a suitable local IR(ME)R practitioner and an appropriate Local Medical Physics Expert (MPE) to review the submission.

6. The local IR(ME)R practitioner is responsible for reviewing the trial protocol and main REC application and confirm in writing to the local PI and R&D Department that the local site can adhere to the protocol, local patients are covered by the main REC (Ethical) submission and any additional exposure is justified having regard to IR(ME)R.

Studies involving several exposure modalities e.g. radiotherapy, nuclear medicine, diagnostic radiology will require involvement of multiple practitioners to cover each discrete modality for which they are entitled to act as practitioner.

Further considerations for prior justification are contained in the NRES guidance referenced above however in most cases it is expected that the practitioner will be able to justify the exposures having regard to the assessment made by the lead CRE for the project as a whole.

7. In accordance with the local IR(ME)R procedure it may be preferable for authorisation of certain research exposures to be carried out by an entitled operator acting in accordance with guidelines issued by the practitioner.

8. The local MPE is responsible for reviewing the trial protocol and main REC application to confirm to the PI that the estimated ranges of doses made by the lead MPE for the research are reasonable and achievable at the participating site.

Studies involving several exposure modalities e.g. radiotherapy, nuclear medicine, diagnostic radiology will require collaborative involvement of multiple MPE's to cover each discrete modality.

A local dose constraint or target dose should be established and this should be in line with the total research protocol dose (TRPD) estimated in the main REC application. Any concerns must be addressed with the lead MPE for the research.

The MPE in Nuclear Medicine (if applicable) will also advise on whether site and/or individual licensing by an approved licensing authority (e.g. ARSAC) is required.

A formal MPE radiation governance report covering the above checks will be submitted to the PI by the Reviewing Local MPE on behalf of all contributing MPEs involved in the study.

9. The local MPE and IR(ME)R practitioner should also check that the approved PIS accurately reflects the additional radiation dose and risk to which local participants will be exposed. Any concern should be referred to the PI for discussion with the CI.

10. In order facilitate the above actions the PI will send a copy of the approved research protocol to the manager of the service carrying out the exposures (e.g. Radiology Services Manager) indicating which exposures are required as part of the study.

11. As with standard medical radiation exposures, a record of the exposure factors should be made, to enable an estimate of the effective dose to individuals and to ensure compliance with the set dose constraint or target dose.

12. All departments responsible for delivering radiation exposures as part of the study will maintain a register of ongoing approved research studies including details of the individual exposures and dose constraints and will ensure that the total dose from all exposures associated with the protocol does not exceed the set dose constraint or target dose.

13. The PI will satisfy him/herself that the individuals concerned participate voluntarily in the research programme and ensure that they have been informed in advance about the risks of the exposure. The latter is facilitated by issue of the PIS approved by the main REC. The generic PIS should normally be used with no changes other than to customise for local use e.g. local contact details, employer headed paper.

14. Pregnant women and children should not normally be accepted as volunteers unless the project concerns their population group specifically. Adults who lack the capacity to consent must be excluded as volunteers.

15. In order to comply with IR(ME)R a registered healthcare professional must be identified as *Referrer* for the study in question. Only approved referrers complying with the selection criteria may refer participants for the study. The *referrer* who signs requests for research exposures will ensure that reference to the named research study is clearly identified on the referral document.

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References

1. NHS Health Research Authority Radiation Assurance, 2018. https://www.hra.nhs.uk/about-us/committees-and-services/technical-assurances/radiation-assurance/applying-radiation-assurance/

2. Approval for research involving Ionising radiation, v2.0 (2008). http://www.hra.nhs.uk/documents/2013/10/approval-of-research-involving-ionising-radiation-2.pdf.

3. Department of Health. The Ionising Radiation (Medical Exposure) Regulations 2017. London: The Stationery Office, 2017.

Appendix 1 Glossary

ARSAC	Administration of Radioactive Substances Advisory Committee. ARSAC certificates are required by clinicians wishing to administer radioactive medicinal products to humans.
CI	Chief Investigator
CRE	Clinical Radiation Expert
HRA	Health Research Authority
HTA	Human Tissue Authority
IRAS	Integrated Research Application System
Modality	Imaging/treatment method
MPE	Medical Physics Expert
NRES	National Research Ethics Service
PI	Principal Investigator
PIS	Participant Information Sheet
R&D	Research & Development

REC	Research Ethics Committee
SSI Form	Site-Specific Information Form (available in IRAS)
TRPD	Total Research Protocol Dose