Guidance on interpretation of IR(ME)R 2017 and IR(ME)R (Northern Ireland) 2018 in NHS research involving ionising radiation in England, Northern Ireland or Wales

Executive Summary

"One of the key priorities for the UK Clinical Research Delivery (UKCRD) programme is to streamline and reform the set-up and delivery of clinical trials through digitalisation and reduction of unnecessary bureaucracy freeing up workforce capacity to deliver clinical trials." (UKCRD Study Set-up Project)

One area identified by the UKCRD study set-up project, as a barrier to further streamlining, is inconsistent interpretation of the research specific requirements of IR(ME)R by NHS organisations. These inconsistencies result in unnecessary steps in the set-up of research studies involving ionising radiation exposures, adding to delay.

This guidance provides the following clarifications on national research review processes and IR(ME)R legislation, to help make study set-up and the delivery of research easier:

- The Total Research Protocol Dose (TRPD) is a concept developed to support the UK Research Ethics Committees (RECs) in giving an ethical opinion on the risk-benefit ratio of a research study and the way in which this is communicated to potential participants. It is an indicative value only. It is not a strict cap upon local exposure.

- In some cases, the TRPD is exceeded due to equipment or standard practice at site. In these instances, following the research protocol and exceeding the TRPD does not invalidate the REC approval, as long as the site adheres to clinical protocols and has justified and optimised the exposures. During research the professional community should not delay study set-up by routinely re-calculating the TRPD.

- There are requirements in IR(ME)R to calculate individual target levels of dose for experimental radiological practice (IR(ME)R (12)(4)(d)), or dose constraints for exposures that are of no medical benefit to the participant (IR(ME)R (12)(4)(c)). Most exposures in health research will not fall into these categories.

- Where exposures are experimental, or they do not provide medical benefit to the research participant, the REC approved TRPD can be helpful to the local site as a guide on dose constraint or target levels of dose.

- Where research exposures do not require a dose constraint or dose target TRPD is not intended to act as a strict cap.

- The purpose of each exposure will be clearly identified and described in the UK Radiation Assurance provided to site/employer, where this has been undertaken, and sites should use the information provided therein to inform the appropriate IR(ME)R requirements locally. For research that has not been through Radiation Assurance, sites/employers should take account of the stated purpose of each exposure in the protocol and Lead CRE review and apply the requirements of IR(ME)R, as set out here, accordingly

- Standardised statements relating to risk arising from research exposure to ionising radiation are available for inclusion in participant facing information. Risk statements are scrutinised by REC, and ARSAC for studies involving radioactive substances. It is not generally expected that approved risk statements in the participant information would require amendment where local optimisation or local standard practice mean the TPRD is exceeded, because of the tolerances inherent and assumed in the Lead MPE calculations and Lead CRE review. This is as long as the number of exposures has been provided to the participant.

For the avoidance of doubt, nothing in this guidance should be interpreted as removing or alleviating any duty or responsibility held by any party under IR(ME)R. Nor does this guidance remove any right for sites to notify the REC of exposures that were not disclosed to the REC for its review, or to raise concerns that local exposures significantly exceed those calculated for central review and communicated to potential research participants (which is to say, when it is the opinion of the site that the variation is of significant orders of magnitude to justify reconsideration by the REC of its opinion).

To allow for variation at individual sites, there are inherent significant tolerances built into Radiation Assurance and central REC review processes, however the usual REC complaints (or third party breach) policies are available where exposures have been missed or in instances of significant local variation.

This guidance should prompt a review of NHS site governance processes, SOPs for research study set-up and employer's procedures. This review should ensure that these local processes are aligned with this guidance and in all cases involve local R&D offices working in conjunction with those departments involved in delivering ionising radiation to patients/participants.

Introduction

This guidance is for all those involved in the set-up and delivery of research studies involving ionising radiation as part of medical (diagnostic or therapeutic) exposures delivered in the NHS in England, Northern Ireland or Wales. This includes R&D personnel and individuals in clinical services concerned with the optimisation, justification, planning and delivery of medical exposures

This guidance is provided by the Health Research Authority (HRA) and is written to apply in the NHS in England, Northern Ireland and Wales. It follows consultation with Care Quality Commission (CQC), UK Health Security Agency (UKHSA) and Medical Physics Experts (MPE), Clinical Radiation Experts (CRE) and other expert parties. In England, this is formal HRA regulatory guidance on the principles of good practice in the management and conduct of health and social care research, to which NHS Trusts and Foundation Trusts must have regard, in accordance with the Care Act 2014 (111(7)).

In this document we use NHS to refer to the NHS in England and Wales and the HSC in Northern Ireland. Questions relating to this document should be directed to the HRA at queries@hra.nhs.uk. It is intended that this guidance is kept under ongoing review, with a formal 6-month review date from publication.

Purpose

The main purpose of the guidance is to provide a common understanding (as a basis for further streamlining of study set-up) amongst the radiation and research communities of the research specific requirements of the **Ionising Radiation (Medical Exposures) Regulations 2017** (IR(ME)R17), as applied in England and Wales, and the **Ionising Radiation (Medical Exposures) Regulations (Northern Ireland) 2018** (IR(ME)R18) applicable to Northern Ireland, and subsequent amendments. These regulations are referred to collectively here as IR(ME)R.

IR(ME)R

IR(ME)R place obligations on specific duty holders and provide a framework intended to protect individuals from the hazards associated with medical exposures involving ionising radiation.

Guidance on IR(ME)R is available:

1. DHSC Guidance to the Ionising Radiation (Medical Exposure) Regulations 2017
2. IR(ME)R: Implications for clinical practice in diagnostic imaging, interventional radiology and diagnostic nuclear medicine (currently under review and due to be re-published shortly)
3. IR(ME)R: Implications for clinical practice in radiotherapy (currently under review and due to be re-published shortly)
4. Medical & Dental Guidance Notes

5. ARSAC Notes for Guidance

The responsibility for compliance with IR(ME)R lies with the employer and each of the entitled duty holders. IR(ME)R applies to all exposures to ionising radiation; however, it makes additional provisions for exposures undertaken as part of research studies. The specific research provisions are outlined in **Appendix 1**, alongside guidance for how NHS organisations can ensure that they are meeting these requirements.

ARSAC

For research involving the administration of radioactive substances, ARSAC Research Approval is required. This is in addition to HRA and HCRW Approval, equivalent review processes in Northern Ireland, and Research Ethics Committee (REC) processes. Employers and practitioners wishing to take part in any ARSAC approved research study must ensure the specified procedure codes are included on their existing employer/practitioner licences (ARSAC Notes for Guidance).

Research Exposures

During research, exposures to ionising radiation may be required by the research study protocol.

Exposures given during and as part of research that are integral to and required by the research study protocol, are defined as **research exposures**. Research exposures are described in detail with examples in IRAS help guidance.

Research exposures may be the same in type or number as those usually given to patients on a clinical pathway in any given organisation, or they may be different. IR(ME)R set out additional specific requirements for research exposures that are

1. experimental diagnostic or therapeutic practice, or;
2. not expected to result in medical benefit for that participant.

Some research exposures will be solely for answering the research question (“no direct medical benefit for the individual is expected from the exposure”) and hence subject under IR(ME)R to research-specific dose constraint.

Some research exposures will be experimental in nature but for the purpose of care (“experimental diagnostic or therapeutic practice from which the patients are expected to receive a diagnostic or therapeutic benefit”) and hence subject under IR(ME)R to research-specific individual target level doses.

Most research exposures, as set out in the research study protocol, will be neither solely for the purpose of answering the research question, nor experimental in

nature, but will be for the purpose of the care of that individual patient. Their purpose will be to monitor patient safety or treat the condition.

Any research exposures required by a research study protocol, that are above or different to a usual care pathway, are not necessarily experimental and may be intended to provide medical benefit.

Research exposures that are not experimental but are intended to provide medical benefit will not require local individual target levels of dose (IR(ME)R (12)(4)(d)), or dose constraints (IR(ME)R (12)(4)(c)). This is separate from the requirement for all therapeutic exposures of target volumes to be individually planned.

Where research exposures do not require local individual target levels of dose or dose constraints, and even where research exposure is the same as for usual care purposes, each exposure must still be justified prior to the exposure being made ((IR(ME)R) (11)) and optimised (IR(ME)R (12).

Research ethics approval, radiation technical assurance and local set-up

The UK Radiation Assurance process, where it is undertaken, helps study set-up by ensuring that all exposures associated with a research study are identified and consistent across the documentation, and that the purpose of each is determined.

The Total Research Protocol Dose (TRPD) is an indicative value calculated by a Lead Medical Physics Expert (MPE) to allow the Lead Clinical Radiation Expert (CRE) and REC to make a judgement on the risk/benefit of a notionally average exposure given by a notionally average local process and equipment to a notionally average sized research participant. As with all healthcare radiation exposures, locally optimised doses required by the protocol will vary dependent upon patient size and other local factors.

The TRPD is not intended to represent a limit, nor impose any restriction on locally optimised and justified practice. TRPD may support the calculation of local individual target levels of dose (where exposures are experimental), and dose constraints (where exposures are not intended to benefit the patient or participant). In instances where sites identify that TRPD has omitted exposures, or where local doses would be significantly in excess of the TPRD such that reconsideration of REC opinion is justified, sites should escalate to the REC as a formal complaint.

The Lead MPE makes their assessment of imaging doses based on National Diagnostic Reference Levels (NDRLs) or National Dose Reference levels (NDoRLs), where they exist. If a NDRL doesn't exist, the Lead MPE will use a published

reference level as outlined in the guidelines for Lead MPE review. This is more likely where the exposures are not standard radiological practice or where the detailed nature of the exposure is specified in a study imaging manual.

The REC favourable opinion applies even when local equipment used for the study means that the total dose given to a participant may exceed the calculated Total Research Protocol Dose (TRPD) provided to the REC, as long as the number of exposures is in accordance with the REC (and ARSAC approval, for studies using radioactive substances). If a site becomes aware that exposures were omitted from the information reviewed by the REC, this should be addressed via the usual REC complaints process. If the local DRL exceeds the national DRL, all research exposures that are not experimental can be undertaken locally for research if they are optimised and undertaken locally for routine clinical care. Equipment and imaging protocols that are optimised for justified exposures outside of research should be regarded as equally suitable for research exposures.

The radiation risk statement in the REC approved participant information is produced based on the Lead MPE and CRE dose assessment and represents a broadly drawn description of risk, considered by the central assessment to be appropriate to the study population. Local variation within a reasonable margin from the TRPD does not affect the validity of the risk statement and, whilst concerns may be escalated to the REC via the usual complaints procedure, it is expected that this would occur only exceptionally. Standardised statements relating to risk arising from research exposure to ionising radiation are provided by this central technical review and scrutinised by REC (and ARSAC, for studies involving radioactive substances). It is not generally expected that the approved risk statement would require amendment where local optimisation exceeds TPRD, because of the tolerances inherent and assumed in the MPE calculations and CRE review.

Risk statements usually reflect research exposure that is additional to standard care (though overall risk is likely to also be addressed). Approved risk statements should not usually need amending because of local standard care at site differing from that used to create the risk statement. The Lead CRE and REC are content with the overall risk and the risk statement takes account of tolerances inherent and assumed in the Lead MPE calculations, Lead CRE and REC reviews.

For research that has not been through Radiation Assurance, sites/employers should take account of the stated purpose of each exposure in the protocol and Lead CRE review and apply the requirements of IR(ME)R, as set out here, accordingly.

If a site becomes aware that a research study protocol requires research exposures not identified to the REC, this should be escalated immediately to the REC via the usual complaints procedure.

Reviews undertaken by Lead MPEs and Lead CREs are indemnified through their normal professional and employment arrangements. As per the UK Policy Framework for Health and Social Care, “the HRA indemnifies NHS research sites that accept assurances from the HRA against any claim covered by the NHS Litigation Authority arising as a result of incorrect assurances” (9.15)

With thanks to all partners in developing this guidance. Particular thanks to expert advisors:

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Appendix

IRMER requirements specific to research exposures

The table below shows the IR(ME)R requirements that are specifically for research exposures. It also details how NHS organisations taking part in research can meet the research requirements of IR(ME)R, including where they may use national research review processes to inform local research set-up and delivery.

IR(ME)R Requirement	What employers need to ensure when taking part in research	Source of evidence for the employer	How national research review processes can support site set up
11(1)(d) In the case of an exposure taking place in the course of a research programme under **[regulation 3(1)(c)],** that programme has been approved by an ethics committee and, in the case of the administration of radioactive substances, approved by an expert committee who can advise on the administration of radioactive substances to humans;	Favourable opinion from a properly constituted REC has been given for the study and there is also ARSAC approval where needed	Favourable opinion from a properly constituted REC is evidenced through receipt of the REC Favourable Opinion letter (as part of HRA and HCRW Approval processes, or equivalent processes in Northern Ireland) ARSAC will undertake an assessment of the research study and provide approval. The ARSAC approval must be provided to site, by or on behalf of the sponsor.	In some cases, the TRPD is exceeded due to equipment or standard practice at site. In these instances, following the research protocol and exceeding the TRPD does not invalidate the REC approval, as long as the site adheres to clinical protocols and has justified the exposures. During research the professional community should not delay study set-up by routinely re-calculating the TRPD.

IR(ME)R Requirement	What employers need to ensure when taking part in research	Source of evidence for the employer	How national research review processes can support site set up
11.(1) A person must not carry out an exposure unless— **(a)** in the case of the administration of radioactive substances, the practitioner and employer are licensed to undertake the intended exposure;	Employers and practitioners wishing to take part in any ARSAC approved research study, must ensure the specified procedure codes are included on their existing employer/practitioner licences (ARSAC Notes for Guidance).	Employers and practitioners wishing to take part in any ARSAC approved research trial, must ensure the specified procedure codes are included on their licences for the purpose of research	
12 (4) (a) consent to take part in the research programme is given by or, where appropriate, on behalf of, the individuals concerned; **(b)** the individuals concerned **[**or their representative (if there is one) where appropriate,**]** are informed in advance about the risks of the exposure;	The participant consents freely and understands the risks and benefits involved in taking part in the research	The site's SOPs and employer's procedures should ensure that they are in receipt of and use the currently REC approved participant information. The procedures should require that local staff follow the REC approved processes and documentation to support participant consent, including documenting consent in medical notes.	The radiation risk statement in the REC approved participant information is produced based on the Lead MPE and CRE dose assessment and represents a broa dly drawn description of risk, considered by the central assessment to be appropriate to the study population. Standardised statements relating to risk arising from research exposure to ionising radiation are provided by this central technical review and scrutinised by REC (and ARSAC, for studies involving radioactive substances). It is not generally expected that

IR(ME)R Requirement	What employers need to ensure when taking part in research	Source of evidence for the employer	How national research review processes can support site set up
			the approved risk statement would require amendment where local optimisation exceeds TPRD, because of the tolerances inherent and assumed in the MPE calculations and CRE review.
6(5)(d) establish dose constraint for individual effective or equivalent doses over a defined appropriate time period (i)for biomedical and medical research programmes **[**falling within regulation 3(1)(c)**]** where no direct medical benefit for the individual is expected from the exposure. **12(4)(c)** the dose constraint set down in the employer's procedures for individuals for whom no direct medical benefit is expected from the exposure is adhered to;	Exposures that are not for medical (therapeutic or diagnostic) benefit to the participant, have dose constraints applied	Applies only to research exposures of no medical diagnostic or therapeutic benefit. Sites should follow their employer's procedure under IR(ME)R to establish a dose constraint.	The purpose of each exposure will be clearly identified and described in the Radiation Assurance provided to site/employer, where this has been undertaken. For research that has not been through Radiation Assurance, sites/employers should take account of the stated purpose of each exposure in the protocol and Lead CRE review and apply the requirements of IR(ME)R, as set out here, accordingly.
Reg 12(4)(d): individual target levels of doses are planned by the practitioner, either alone or with	Exposures that are of an experimental practice and are for medical (therapeutic or diagnostic)	Applies only to research exposures that are of an	The purpose of each exposure will be clearly identified and described in the Radiation Assurance

IR(ME)R Requirement	What employers need to ensure when taking part in research	Source of evidence for the employer	How national research review processes can support site set up
the input of the referrer, for patients who voluntarily undergo an experimental diagnostic or therapeutic practice from which the patients are expected to receive a diagnostic or therapeutic benefit.	benefit have individual target level doses applied (Employers should determine individual target dose levels for each participant when they present for the exposure).	experimental diagnostic or therapeutic practice Sites should follow their employer's procedure under IR(ME)R to establish a target dose.	provided to site/employer, where this has been undertaken. Where Radiation Assurance has not been undertaken, sites/employers should take account of the stated purpose of each exposure in the protocol and Lead CRE review and apply the requirements of IR(ME)R, as set out here, accordingly.
IR(ME)R Schedule 2 Employer Procedure **1(g):** to determine whether the practitioner or operator is required to effect one or more of the matters set out in regulation **12(4)** including criteria on how to effect these matters, in particular procedures for the use of dose constraints established by the employer for biomedical and medical research programmes falling within **Reg 3(c)**	Employers' Procedures are in place	This procedure should be reviewed to ensure that matters described above are addressed.	

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The research exposure(s) must also be justified for the individual participant by the IR(ME)R practitioner (entitled by the employer) before the exposure is given. Research sites carrying out research that involves exposures to ionising radiation should be aware that a referral must be made by an entitled referrer, who must be a registered health care professional. Each exposure will require a referral to be made and the research study the individual is participating in should be clearly identifiable within the referral. For the avoidance of doubt, Employers retain responsibility for ensuring that research exposures are delivered safely; that entitled duty holders are appropriately supported; and that any concerns relating to radiation risk, exposure purpose or protocol implementation are identified and addressed promptly through local governance arrangements to minimise impact on trial delivery and to ensure patient safety at all times.			