**WHAT ARE THE SPECIFIC DIFFERENCES BETWEEN VERSION 5.5 AND VERSION 5.6 OF THE RESEARCH ETHICS COMMITTEE STANDARD APPLICATION FORM?**

<table>
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<tr>
<th>Application Form Cover Sheet</th>
<th>Application Form Table of Contents</th>
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<tr>
<td>- Addition of Application Version No. in Version 5.6</td>
<td>- Section G title changed from ‘Radioactive Material / Diagnostic of Therapeutic Radiation’ to ‘Radiation’ only in Version 5.6. (deletion)</td>
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<tr>
<td>- Addition of Application Date in Version 5.6</td>
<td>- Section J title changed from ‘Indemnity’ to ‘Indemnity and Insurance’ in Version 5.6.</td>
</tr>
<tr>
<td>- Remove ‘Principal Investigator’ (deletion)</td>
<td>- Section K title changed from ‘Cost and Resource Implications and Funding’ to ‘Cost and Resource Implications, Funding and Payments’ in Version 5.6.</td>
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<tr>
<td>- Remove ‘Applicant’s Signature’ (deletion)</td>
<td>- Section L title changed from ‘Ethical Issues’ to ‘Additional Ethical Issues’ in Version 5.6.</td>
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**Application Form – All Sections**

The following instruction which appears in the Table of Contents is no longer repeated at intervals throughout the application form in Version 5.6: ‘IMPORTANT NOTE: This application form permits the applicant to delete…..’ (deletion)

**Application Form – Section A**

- Questions A3 (a) in Version 5.5 “Is this a multi-site study?” has moved to become Question A2 (a) in Version 5.6.
- **An important distinction is introduced between multi-site and single-site studies in Version 5.6, and the response to this question affects the questions which follow.**
- For multi-site studies, applicants are asked to provide the details of the principal investigator, to list all sites, to provide details of all lead co-investigators at these sites, and of the outcome of relevant research ethics committee reviews (A2 (b)(c)(d))
- ‘Lead co-investigator’ is a new term in Version 5.6, replacing the term used in Version 5.5 which was ‘lead investigator’
- For single-site studies, applicants are asked to provide details of the principal investigator only and to name the site. (A2 (e) and (f))
- Question A4 in Version 5.5 ‘Details of Co-investigators’ has moved to become Question A3 in Version 5.6.
- A telephone number, and email is now requested for co-investigators in Version 5.6 (A3)
- The role in the research must be specified in Version 5.6 e.g. statistical / data / laboratory analysis
- Question A5 in Version 5.5 ‘Lead contact person’ has moved to become Question A4 in Version 5.6
- An address for correspondence is requested for the lead contact person in Version 5.6.
- Question A6 (lay description) in Version 5.5 has moved from Section A to Section B in Version 5.6 (B3)
- Question A7 (a) in Version 5.5 ‘Is this study being undertaken as part of an academic qualification?’ has moved to become Question A5 (a) in Version 5.6.
- **A new question appears in Version 5.6 (A5 (c)) requesting academic supervisor details**
- Question B6 in Version 5.5 ‘start date’ has **moved** to become Question B1 in Version 5.6
- Question B7 in Version 5.5 ‘study duration’ has **moved** to become Question B2 in Version 5.6
- Question A6 (lay description) has **moved** to become Question B3 in Version 5.6.
- The new Question B3 in Version 5.6 is **extended**: Please provide a brief plain English lay description of the study. Please ensure the language used in your answer is at a level suitable for use in a research participant information leaflet.
- Question B1 in Version 5.5 ‘study background’ has **moved** to become Question B4 in Version 5.6.
- Question B2 in Version 5.5 ‘aims and objectives’ has **moved** to become Question B5 in Version 5.6.
- Question B3 in Version 5.5 ‘endpoints’ has **moved** to become Question B6 in Version 5.6.
- The new Question B6 in Version 5.6 is **extended** to explain endpoints as measurable outcomes.
- Question B4 ‘design’ in Version 5.5 has **moved** to become Question B7 in Version 5.6.
- Question B5 ‘methodology’ in Version 5.5 has **moved** to become Question B8 in Version 5.6.
- Question B8 (b) ‘statistical approach’ in Version 5.5 has **moved** to become Question B9 in Version 5.6.
- Question B8 (c) ‘sample size’ in Version 5.5 has **moved** to become Question B10 (a) in Version 5.6.
- Question B8 (d) ‘sample size continued’ in Version 5.5 has **moved** to become Question B10 (b) in Version 5.6.
- Question B8 (a) ‘how many research participants’ in Version 5.5 has **moved** to become B11 in Version 5.6.
- Part of Question C1.1 (numbers in each group) in Version 5.5 has **moved** to become Question B12 (a) in Version 5.6.
- Question B12 (a) **appears** as a table.
- A new question appears in Version 5.6: **B12 (b)** Please provide details of randomisation (where applicable)
- Part of Question C1.1 (numbers at each site) in Version 5.5 has **moved** to become Question B13 in Version 5.6.
- Question B13 **appears** as a table.

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**Application Form – Sub-sections C1, and C2**

- Question C1.1 ‘numbers’ in Version 5.5 has **moved** to become two questions in Section B in Version 5.6.
- Question C1.2 ‘selection’ in Version 5.5. has **moved** to become question C1.1 in Version 5.6
- Question C1.3 ‘recruitment’ in Version 5.5. has **moved** to become question C1.2 in Version 5.6
- Question C1.4 ‘inclusion criteria’ in Version 5.5. has **moved** to become question C1.3 in Version 5.6
- The Question C1.3 no longer refers to the main inclusion criteria, **(deletion)** and now refers to justifying inclusion criteria only where necessary.
- Question C1.5 ‘exclusion criteria’ in Version 5.5. has **moved** to become question C1.4 in Version 5.6
- The Question C1.4 no longer refers to the main exclusion criteria, **(deletion)** and now to justifying exclusion criteria only where necessary.
- Question C1.6 ‘participation in other research’ in Version 5.5. has **moved** to become question C1.5 in Version 5.6
- Question C2.1 (b) in Version 5.6 is now **extended**: You must provide a full and detailed explanation as to why informed consent will not be obtained.
- Question C2.1 (c) in Version 5.6 is now **extended**: If yes, please outline the consent process in full. (How will consent be obtained, when, by whom and from whom?)
- Question C2.3 (c) in Version 5.6 is **extended**: If no, please justify and explain why an instantaneous decision is reasonable having regard to the rights of prospective research participants and the risks of the study.
Application Form – Subsection C3
- The heading of sub-section C3 has been **expanded** to read: C3 Adult Participants (18 and over) - Capacity
- C3.1 (a) in Version 5.5 ‘capacity’ is a ‘Yes/No’ question in Version 5.6. The option ‘non-applicable’ has been removed. (Deletion)
- C3.1 (c) in Version 5.5 has **moved** to become Question C3.2 in Version 5.6.
- C3.2 in Version 5.6 is now **extended** by the phrase ‘Please elaborate’. This question now requires more than a ‘yes/no’ response.
- A new question appears in Version 5.6: C3.3 ‘Is the research expected to provide direct benefit to the research participants (who lack capacity), or if there is no prospect of direct benefit, are the risks no more than minimal? Please elaborate.’
- A new question appears in Version 5.6: C3.4 ‘What arrangements are in place to ascertain the wishes of research participants, who although they lack decision-making capacity, have some ability to understand the significance of the research?’
- Question C3.1 (d) in Version 5.5 has **moved** to become Question C3.5 in Version 5.6.

Application Form – Subsection C4
- A new question appears in Version 5.6: C4.1 (c) if yes to persons <16, please specify:
  - Pre-term neonates
  - Full-term neonates
  - Infants and toddlers 0-3
  - Children 5-8
  - Children 9-12
  - Adolescents 13-15
- Question C4.2 has been **extended** in Version 5.6 by the phrase ‘Please elaborate.’ This question now requires more than a ‘yes/no’ answer.
- A new question appears in Version 5.6: C4.3 Is the purpose of the research to generate knowledge about the health and social care needs of children?
- A new question appears in Version 5.6: C4.4 Is the research expected to provide direct benefit to child participants, or if there is no prospect of direct benefit, are the risks no more than minimal? Please elaborate.
- C4.4 ‘information for children’ in Version 5.5 has **moved** to become C4.5 in Version 5.6, and the question has been **reworded** slightly: Will each child receive information about the risks and benefits of the study according to his/her capacity to understand? Please elaborate and provide copies.
- C4.5 ‘children’s wishes’ in Version 5.5 has **moved** to become C4.6 in Version 5.6.
- The new Question C4.6 in Version 5.6 has been **adjusted** to refer to ‘investigators’ as opposed to ‘the lead investigators, co-investigators and principal investigator’
- The new Question C4.6 in Version 5.6 has been **expanded** as follows: Please outline the assent process in full (How will assent be obtained, when and by whom etc.)
- C4.6 ‘involvement of parents’ in Version 5.5 has **moved** to become C4.7 in Version 5.6. The phrase ‘if any’ has also been **deleted** from within the question. (-deletion)
- C4.7 ‘when the child reaches 18’ in Version 5.5 has **moved** to become C4.8 in Version 5.6.
- C4.3 ‘children at risk’ in Version 5.5 has **moved** to become C4.9 in Version 5.6.
Application Form – Subsection C5

- The lead text for this section has been revised and extended: “Please confirm if persons from any of the following groups will participate in this study. This is a quick checklist to assist research ethics committee members and to identify whether study participants include persons from vulnerable groups and to establish what special arrangements, if any, have been made to deal with issues of consent. It is recognised that not all groups in this listing will automatically be vulnerable or lacking in capacity. Please refer to the HSE’s National Consent Policy, particularly Part 3, Section 5. Committees are particularly interested to know if persons in any of these groups are being targeted for inclusion, as per the inclusion criteria.”

- The numbering in this section has changed with one overall question number in Version 5.6 (C5.1)

- The formatting and use of bullets in this section has changed.

- A new category has been introduced in Version 5.6 of ‘persons in dependent or unequal relationships’ – see C5.1 (d) in RECSAF 5.6

- A new category has been introduced in Version 5.6 of ‘persons with a life limiting condition’ – see C5.1 (f) in RECSAF 5.6

- Question 5.9 ‘prisoners’ in Version 5.5 no longer appears in Version 5.6. (deletion)

- Question 5.10 ‘residents of nursing homes’ in Version 5.5 has been deleted in Version 5.6 (deletion)

- Residents of Nursing Homes are now covered in a new category: ‘Persons in residential care’

- Question 5.16 ‘persons aged >65 years’ no longer appears in Version 5.6 (deletion)

- Question C5.17 in Version 5.5 now appears as Question C5.2 in Version 5.6 and has been reworded: If yes to any of the above, please comment on the vulnerability of the research participants, and outline the special arrangements in recognition of this vulnerability (if any)

- Questions C5.11 ‘pregnant women’, 12 ‘women of child-bearing potential’ and 13 ‘breastfeeding mothers’ in Version 5.5 have been merged in Version 5.6 to create a new question: C5.3: Please comment on whether women of child-bearing potential, breastfeeding mothers, or pregnant women will be included or excluded in this research study.

Application Form – Sections D and E

- Question D1 has been reworded in Version 5.6 and now appears as two Questions D1 (a) and (b) D1 (a) What activities, procedures or interventions (if any) are research participants asked to undergo or engage in for the purposes of this research study? D1 (b) What other activities (if any) are taking place for the purposes of this research study e.g. chart review, sample analysis etc?

- Question D2 has been extended in Version 5.6 as follows: Please provide details below of any potential harm that may result from any of the activities, procedures, interventions or other activities listed above.

- Question D4 (a) has been extended to allow for a ‘non-applicable response’

- Question D5 has been split into two Questions D5 (a) and D5 (b) in Version 5.6. Question D5 (a) refers to monitoring during the study, and question D5 (b) refers to monitoring after the study.

- Question D6 (a) has been extended to allow for a ‘non-applicable response’

- Question D9 has been amended to include the word ‘that’: Will the research participant’s general practitioner be informed that the research participant is taking part in the study (if appropriate).

- Question D10 has been amended to include the word ‘that’: Will the research participant’s hospital consultant be informed that the research participant is taking part in the study (if appropriate).

Application Form – Section E

- Question E2.6 has been changed to refer to site(s) (plural) in Version 5.6
Application Form – Section 5 Subsections F3, F4 & F5
- Question F3.6 (b) has been reworded to read: If no, please justify why existing consent is considered sufficient, or why a waiver of consent from the research ethics committee is warranted.
- Questions F4.1 (a), (d) and (f) have been changed to refer to institution(s) (plural) in Version 5.6.
- Question F5.1 (b) is expanded in Version 5.6 to read ‘If yes, please specify the nature and purpose of the genetic testing.’
- 5 new questions appear in Version 5.6: F5.2 (a) Will consent be obtained? F5.2 (b) if yes, please set out the steps that will be taken and the information that will be provided to study participants prior to genetic testing and processing of genetic data in relation to any potential implications for the health of the study participant which may become known as a result of the genetic testing and the processing of genetic data. F5.3 (a) Please set out the strategy and arrangements that will be in place to address any significant results or information arising from the genetic testing or processing of genetic data with the study participant. F5.3 (b) What strategy / arrangements will be in place regarding third party disclosure, in particular, to family members or others? F5.4 Please set out what arrangements will be in place to ensure the privacy and confidentiality of study participant’s genetic data throughout the life cycle of the study.

Application Form – Section G, subsection G1
- The title of the Section G reads ‘Radiation’ only in Version 5.6. (deletion)
- The first question (G1.1 (a)) refers to ‘radiation’ only in Version 5.6. (deletion)
- Question G1.1 (b) has been extended in Version 5.6 to include the category of ‘other’ and details are requested.
- Question G1.2 (a) in Version 5.6 no longer includes the phrase ‘to radioactive materials or diagnostic or therapeutic ionising radiation’ (deletion)
- Question G1.3 has been reworded in Version 5.6 to refer as follows: Please specify if this study is due to take place at a: - (i) Radiation Oncology Unit; (ii) Diagnostic Imaging Facility; (iii) Clinical Laboratory; (iv) Academic Research Centre; (v) Other....
- A new question appears in Version 5.6: Has each study site/institution in the Republic of Ireland been licensed by the Radiation Protection Society of Ireland?

Application Form – Subsection G2
- Question G2.1 and G2.2 from Version 5.5 have been combined into one question in Version 5.6: G2.1 Does the study / trial involve exposure of patients to radiotherapy?
- Question G2.3 in Version 5.5 has moved to become Question G2.2 (a) in Version 5.6, and the text has been extended: Is the planned radiotherapy part of standard treatment or is it experimental in terms of dose / technique / rationale?
- A new question appears in Version 5.6: G2.2 (b) If experimental, please elaborate.
- Question G2.4 ‘radiotherapy information’ in Version 5.5 has moved to become Question G2.3 in Version 5.6.
- Question G2.4 (b)(i) ‘technique’ in Version 5.5 has moved to become Question G2.3 (a) in Version 5.6 and the question has been expanded: Dose Delivery Technique to be used e.g. 3-DCRT (3-dimensional conformal..
Application Form – Subsection G2 (continued)
..radiation therapy), IMRT (intensity modulated radiation therapy)
- Question G2.4 (b)(ii) ‘technique’ in Version 5.5 has moved to become G2.3 (b) in Version 5.6 and the question has been expanded:
  Imaging / Verification Technique to be used e.g. IGRT (image guided radiation therapy)...Question G2.4 (c) ‘Radiation Treatment Schedule’ in Version 5.5 has moved to become Question G2.3 (c) in Version 5.6
- A new heading appears in Version 5.6: Question 2.4 RADIOTHERAPY PLANNING
- Question G2.4 (a) ‘volumes of interest’ in Version 5.5 has moved to become Question G2.4 (a) in Version 5.6 G2.4 (a) and expanded slightly to read: - Planning Volumes of interest (tumour related volume and organs at risk)
- Question G2.4 (d) ‘dose volume constraints’ in Version 5.5 has moved to become Question G2.4 (b) in Version 5.6 and expanded slightly to read: - Planning Dose volume constraints (DVCs) for organs at risk (OARs)
- Question G2.4 (f) in Version 5.6 ‘patient positioning’ has moved to become Question G2.4 (c) in Version 5.6 and has been expanded as follows: Details of patient positioning/set-up/immobilization, inclusive of pre-treatment preparation e.g. bladder filling protocol, IV contrast etc.
- Question G2.4 (g) ‘evaluation parameters’ in Version 5.5 has moved to become Question 2.4 (d) in Version 5.6.
- Question G2.4 (h) ‘toxicity scoring’ in Version 5.5 has moved to become Question 2.4 (e) in Version 5.6.
- Question 2.5 (a) has been expanded: Standard alternatives. Please ensure to detail and contrast the experimental protocol with ‘standard’ therapy.
- Question 2.5 (b) has been expanded: Potential additional risks/toxicities associated with the experimental protocol.
- Question G2.7 has been expanded in Version 5.6 to read: Clinical Monitoring / Assessment during radiotherapy and supportive care: please provide a detailed summary of the clinical monitoring of patients included in the study / trial.
- A new question appears in Version 5.6: G2.8 – Criteria for Radiotherapy Adverse Event Reporting

Application Form – Section H
- Question H3 ‘clinical investigations’ in Version 5.5 has been split into two questions in Version 5.6.
- The two new questions appear as:
  H3 (a) Is this an application to conduct a clinical investigation of a medical device?
  H3 (b) If yes, will the Medical Devices Section of the Health Products Regulatory Authority (HPRA) be reviewing this study?
- The name change for the Irish Medicines Board is also reflected.
### Application Form – Subsection G3
- Question G3.2 (a) ‘Dose and Risk Assessment’ is **split** into two questions in Version 5.6: G3.2 (a) and G3.2 (b)
- Question G3.2 (b) ‘Declaration’ in Version 5.5 has **moved** to become Question G3.2 (c) in Version 5.6

### Application Form – Section J
- The heading of this section has **changed** from ‘Indemnity’ to ‘Indemnity and Insurance’
- All Questions in this section have been **completely redrafted**.
- All Reference to the Clinical Indemnity Scheme (CIS) has been **removed**.
- Question J1 in Version 5.6 requests confirmation that insurance/indemnity is in place for each site: J1. Please confirm and provide evidence that appropriate insurance / indemnity is in place for this research study at each site.
- Question J2 in Version 5.6 requests confirmation that insurance/indemnity is in place for each investigator: J2. Please confirm and provide evidence that appropriate insurance / indemnity is in place for this research study at each site.
- All reference to sponsor has been removed, and question J3.1 now states ‘Please give the name and address of the organisation / or individual legally responsible for this research study? ’
- Following on from this, applicants who list an organisation as legally responsible are asked to specify in J3.2 what type of organisation this is e.g. a pharmaceutical company, medical device company etc.
- Question J3.3 in Version 5.6 requests details of any specific additional insurance / indemnity arrangements which have been put in place by the organisation / individual.

### Application Form – Section K
- The title of this section has been **changed** to include the additional word ‘payments’ at the end.
- The questions in this section have been **divided into four sub-sections**. Sub-section headings are included, and the numbering of questions reflects four sub-sections.
- Questions K1 (a) and (b) ‘cost and resources’ in Version 5.5 have been **merged** in Version 5.6 to form one single question: K1.1 The merged question has been **extended** and now reads 'Please provide details of all cost / resource implications related to this study (e.g. staff time, office use, telephone, printing costs etc.) The merged question now requires an answer, and is no longer a ‘yes/no’ question.
- K2 (a) ‘is funding in place’ in Version 5.5 has been **renumbered** as K2.1 (a) in Version 5.6, and the formatting has been changed to ‘centre’
- K2 (b) ‘if no, has funding been sought’ in Version 5.5 has been **renumbered** as K2.1 (b) in Version 5.6, and the formatting has been changed to ‘right’
- K2 (c) ‘source of funding’ in Version 5.5 has been **renumbered** as K2.1 (c) in Version 5.6.
- The new question K2.1 (c) has been **expanded**: If yes, please state the source of funding (industry, grant or other), the name of the funder, the amount of funding and duration of funding.
- The new question K2.1 (c) has been re-formatted to appear as a table.
- K2 (g) ‘management of funds’ in Version 5.5 has been moved to become Question K2.1 (d) in Version 5.6.
- K2 (d) ‘external agency’ in Version 5.5 has been deleted from Version 5.6 and no longer appears: Is this study funded by an external agency? (deletion)
- K2 (e) ‘for profit’ in Version 5.5 has been renumbered in Version 5.6 as K2.1 (e). The new wording is ‘Is the study funded by a for-profit organisation?’
- K2 (f) ‘conflicts of interest’ in Version 5.5 has been **split** to become two questions in Version 5.6: K2.2 (a) Do any conflicts of interest exist in relation to funding or potential funding? K2.2 (b) If yes, please elaborate.
- K3 ‘payments to investigators’ in Version 5.5 has been **split** into two questions in Version 5.6: K3.1 (a) and (b). The first question is now a ‘Yes/No’ question. K3.1 (a) reads ‘Will any payments (monetary or otherwise) be made to investigators? K3.1 (b) reads ‘If yes, please provide details of payments, including amount.
- K4 ‘payments to participants’ in Version 5.5 has been **split** into two questions in Version 5.6: K4.1 (a) and (b). The first expanded question is now a ‘Yes/No’ question. K4.1 (a) reads ‘Will any payments / reimbursements (monetary or otherwise) be made to participants? K3.1 (b) reads ‘If yes, please provide details of payments / reimbursements, including amount.'
<table>
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<tr>
<th>Application Form – Section L</th>
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<tbody>
<tr>
<td>- The heading of this section has <strong>changed</strong> from ‘Ethical Issues’ to ‘Additional Ethical Issues’</td>
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<tr>
<td>- This section is now <strong>no longer</strong> a mandatory section.</td>
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<tr>
<td>- The first question has been <strong>changed</strong> to ‘yes/no’ question to reflect the fact that this section is now optional: <strong>L1 (a)</strong> Does this study raise any additional ethical issues? <strong>Yes/No</strong></td>
</tr>
<tr>
<td>- Question L1 ‘ethical issues’ in Version 5.5 has <strong>moved</strong> to become Question L1 (b) and starts with ‘If yes.....’</td>
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**WHAT ARE THE BROAD DIFFERENCES BETWEEN VERSION 5.5 AND VERSION 5.6 OF THE RESEARCH ETHICS COMMITTEE STANDARD APPLICATION FORM GUIDANCE MANUAL?**

In broad terms, the Guidance Manual which accompanies Version 5.6 of the Standard Application Form has been updated in line with the Questions in application form 5.6. In addition:

- All quotes from the Declaration of Helsinki (2008) have been replaced with equivalent quotes from 2013 document. (The 2013 Declaration as compared to the 2008 Version also appears as Appendix 2)

- Most references to Irish Medicines Board (IMB) have been replaced with the Health Products and Regulatory Authority (HPRA).

- Most references to the Department of Health and Children (DoHC) have been replaced with the Department of Health (DoH)

- There are extensive quotes and references to the HSE National Consent Policy (2013) throughout.

**However, key changes which should be noted are:**

- The provision of an explicit definition for the ‘Principal Investigator’ as follows: ‘The Principal Investigator is the Principal Researcher on the research team who is responsible for the conduct, and in many instances also the design, of this research study.’ (-Guidance Notes: A2 (b) and (e))

- The introduction of the concept of lead co-investigator in multi-site studies, and the definition of the lead co-investigator as follows: ‘The lead co-investigator takes responsibility for the study at a site. S/he should be an employee of the site in question who is appropriately qualified to oversee the conduct of the study at the site.’ (-Guidance Note: A2 (c))

- The provision of Guidance Note B7, which is an excerpt from this publication: C. Collins (2008) *Irish College of General Practitioners Guide to Conducting Research.*

- All guidance Notes in Section C have been updated in line with legal advice, and policy.

- All guidance Notes in Section F3 have been updated in line with the HSE National Consent Policy (2013), and quotes from the Irish Council Bioethics Recommendations for Collection, Use and Storage in Research (2005) have been replaced with quotes from the HSE National Consent Policy (2013)

- Guidance Notes in Section F5 have been updated in line with legal advice, and policy.

- New guidance notes have provided for Section J, which reflect the fact that all questions in this section have been redrafted.

Endnotes have been updated in line with legal advice.