

CONSULTATION RESPONSE

Human Tissue Authority Consultation on the Codes of Practice

Response by the Medical Research Council and the Wellcome Trust

November 2008

Introduction

1. The Wellcome Trust is the largest charity in the UK. It funds innovative biomedical research, in the UK and internationally, spending around £600 million each year to support the brightest scientists with the best ideas. The Wellcome Trust supports public debate about biomedical research and its impact on health and wellbeing.
2. The Medical Research Council (MRC) is dedicated to improving human health through the best scientific research. Its work, on behalf of the UK taxpayer, ranges from molecular level science to public health medicine, including patient and volunteer based research involving human tissue samples.
3. Both the MRC and the Wellcome Trust fund substantial amounts of research involving human tissue. The MRC also has five of its own units that hold Human Tissue Authority (HTA) licences, two of which have had phase 2 inspections. Both organisations welcome the recognition by the HTA of the need for a Code of Practice dealing specifically with research and overall we find this to be a useful document.
4. In this response we have made general comments on the Research Code, followed by comments relating to specific paragraphs. We have then made some further specific points relating to Code 1 (Consent) and 5 (Disposal of Human Tissue) which are also relevant to research involving human tissue. The Wellcome Trust has also responded separately to Code 7 (Public Display).
5. We also commend the HTA on the process of drafting these Codes - including the extensive consultation, through different mechanisms, with research funders and the wider research community. We look forward to continued dialogue on these Codes.

General Comments

6. We would reiterate the point made in our previous responses to Code of Practice consultations that it needs to be made absolutely clear as to which statements reflect legal requirements and which are statements of good practice. We would refer the HTA to the approach of the Charity Commission, which does this by using "must" to denote a legal requirement and "should" to denote good practices. They also use a symbol throughout their guidance to indicate what are legal requirements and this would be most helpful. Their guidance states¹:

¹ <http://www.charity-commission.gov.uk/publications/cc3.asp#c2>

'C2. 'Must' and 'should': what we mean

In this guidance, where we use **'must'**, we mean it is a specific legal or regulatory requirement affecting trustees or a charity. Trustees must comply with these requirements. To help you easily identify those sections which contain a legal or regulatory requirement we have used the **L** symbol next to the short answer in that section.

We use **'should'** for items we regard as minimum good practice, but for which there is no specific legal requirement. Trustees should follow the good practice guidance unless there's a good reason not to'.

Code 9: Research

7. This Code addresses a need of the research community to be clear as to the specific requirements the HTA places on them. It is a great improvement to have these set out in a single Code rather than in parts of other Codes. The MRC has developed a Toolkit on Data and Tissue use² in research to which the HTA has contributed and the Authority may find it useful to refer researchers to this resource, in particular the research summaries.
8. The Code is clearly written but is too long in its current form. We consider that much of the opening section (paragraphs 1 to 31) is not necessary in the context of this Code. For example detailed reference to linked legislation and also reference to other sectors, such as transplantation in paragraphs 13 and 14 is not often likely to be relevant for medical researchers. The references embedded in the text could be moved to an appendix as it would be an infrequent occurrence for researchers to wish to access primary and secondary legislation. In some places the Code is repetitive.
9. The exemplars are particularly helpful and we would support inclusion of more. If the HTA would like further examples they could be provided from the MRC and/or the Wellcome Trust. A further section of 'Q and As' could be added to provide another means of dealing with specific examples.
10. The flow chart provided is well set out. It is our view that more such diagrams would provide further assistance. It is our experience that researchers find these a useful way to receive information. However, we appreciate that it may be difficult to ensure complex information is appropriately conveyed through summary diagrams. It may be preferable to include references to parts of the Code in the diagrams.
11. The Code has a particular strength in clarifying the difference between the legislative requirements for consent and the requirements for licensing under the HT Act. The regulatory framework could be further clarified by being more explicit about which areas are the responsibilities of Research Ethics Committees (RECs). It is wise of the HTA not to overlap this Code with areas RECs will deal with but it may be helpful to researchers to make quite clear where requirements and expectations of the HTA are distinct from those of RECs.
12. Where appropriate, there could be more linking to the relevant sections of other Codes, especially with reference to the Consent and Import and Export Codes.

Specific Comments on draft Code 9

13. Paragraph 3 – Should make it clear that it is the storage activity that is licensed, as in Paragraph 35.

² <http://www.dt-toolkit.ac.uk/home.cfm>

14. Paragraph 7-9 – This section should include the part of the Act that is applicable to Scotland. DNA/genetic analysis should be specifically mentioned. As it stands it reads that the Human Tissue Act 2004 (HT Act) is not applicable to Scotland. Similarly in paragraph 26.
15. Paragraph 29 – The MRC Data and Tissues Tool Kit (www.dt.toolkit.ac.uk) should be mentioned here.
16. Paragraph 31 - Add the word 'are' between 'purposes' and 'defines research' in the sentence 'This code begins by explaining what scheduled purposes are and defines research'.
17. Paragraph 34 – This is a good and workable definition of research. We acknowledge the difficulties in reaching this definition and that the HTA has been responsive to previously expressed views on this definition. We would hope that this definition has been developed in consultation with other relevant organisations, e.g. National Research Ethics Service (NRES), for consistency across the research sector.
18. Paragraph 35 – Case examples of the scheduled purpose and the activity might assist in understanding this important difference.
19. Paragraph 38 – Reference could be made (in a footnote) to guidance on capacity and on research involving children, such as that of the MRC. Reference should be made to the situation in Scotland as regards children as this differs from the rest of the UK.
20. Paragraph 39 – It would be helpful to expand upon what 'necessary assurance' means and how the HTA would wish this to be evidenced.
21. Paragraph 42 – It should be clarified that it is the holding of bodily material with the intent of analysing DNA that is regulated under s45 of the HT Act by the HTA, not the analysis itself. Reference to this being applicable UK-wide should be made.
22. Paragraph 46 - For ease of reference and clarity, paragraph 46 should spell out at the beginning that it applies to tissues from the deceased. The second sentence is not clear – would such a family not wish to reclaim the tissue consent is being sought for? The tissue should be returned as the first priority.
23. Paragraph 47 – It is our understanding that this exemption can only apply to people who have died prior to the implementation of the Act (2006) but as currently worded that is not the case, for example, the 100 years exemption would not apply to material from a person who dies in the year 2107 but as written it is implied that it would.
24. Paragraph 48 – The last sentence of this paragraph provides an example of the general point made above that this level of detail on Directions will not be required by researchers and in fact may be confusing.
25. Paragraph 49 – It would be helpful to include paragraph 52 in this paragraph and a case example would be helpful. The issue of degree of linkage within anonymisation is of key importance to medical researchers.
26. Paragraph 50– In paragraph 64 it is explicitly stated that other RECs eg University RECs are not approved Authorities for the purposes of the Act and the HTA. This would be better placed in this section (or possibly even earlier in the guidance), with the explanation that this pertains throughout the Code.
27. Paragraph 51 – This is specifically relevant to licensing and would be easier to read if it was placed in that section.
28. Paragraph 53 – We strongly support the guidance on broad consent in this paragraph.
29. Paragraph 54 – The guidance from the GMC deals with conduct of research but is not specific to ethical approval. It could be clarified that the HTA supports adherence to this guidance but this seems out of place in this paragraph. Following this paragraph reference

should be made to the Consent code to provide information on who can give consent for it to be appropriate or qualifying.

30. Paragraph 55 (Licensing) - There is a need to state the regulations pertaining to the use of imported tissue on licensed or non-licensed premises here or at the very least link through to the import/export code. The need for UK recognised REC approval for projects being carried out in non-licensed premises using imported tissue needs to be stated.
31. Paragraph 56 – The distinction between HTA licence and REC approval is helpful.
32. Paragraph 60 - 62 - This section is rather confusing. It would be useful (perhaps via examples) to point out what is not covered by the exception here. It would also be of assistance to researchers to clarify that this exemption can also apply to temporary storage of tissue while a single assay is performed if this is indeed the case.
33. Paragraph 61 – We recognize the divergence of views in the research sector on this paragraph. On balance we believe it is helpful to place some timescale around what 'temporary' means. However, we also share concerns that a strict deadline of a week may, in exceptional cases, cause difficulty. This could perhaps be indicated in wording recognising that in very exceptional cases this might occur.
34. Paragraph 62 - The example in paragraph 62 states the "researchers using the serum should have evidence to ensure that the laboratory process rendered the relevant material acellular." Members of the research community have suggested that it would be useful for the HTA to list a set of general methods used to make samples 'acellular'. This would standardise any analysis procedures and make verification by the HTA on inspection an easy process rather than the HTA having to wade through a plethora of different methods and then confirm the validation – which could be complicated and time consuming. The MRC and Wellcome Trust would be happy to work with the HTA and the research community to facilitate any such list.
35. Paragraph 63 – This is a further example of wording that is overly 'legalistic' and unlikely to assist researchers. It could simply be stated that this is a further exception.
36. Paragraph 68 – This should state that the researchers receiving relevant material from the appropriate tissue banks do not require a licence to store the material for the period of the research project.
37. Paragraph 69 – Relates to REC approval and does not seem relevant to this Code of Practice.
38. Paragraphs 74 – 79 – Overall, this section is much less clear than others in the Code and would benefit from being rewritten with an emphasis on the difference between tissue from the living and the deceased. It also needs more clarity that tissue for diagnosis can be used for research, subject to the requirements of these sections. This is an important resource for research that is currently underused and researchers are unclear as to how it may legally be used.
39. Paragraphs 76 and 77 – These could be made clearer as to the difference between requirements for consent for tissue obtained from the living as compared to the deceased.
40. Paragraph 78 – The exemption from consent for anonymised tissue only applies to tissue obtained from the living – again the different requirements for tissue from the living and the deceased need to be made clear. An example of the research use of pathology samples would help add clarity here.
41. Paragraph 77 – This should reference paragraphs 55-71, not 54 - 71.
42. Paragraph 82 - Members of the research community have indicated that they would welcome an example here.
43. Paragraph 83 – We recognise that the HTA has had extensive discussions with both of our organisations, and many others on this issue. In view of the difficulties in ascertaining when original cells are present it does seem reasonable to leave this to the researcher's

judgment. However, examples of how this might be assessed would be helpful; MRC and Wellcome Trust are willing to assist in clarifying this point further if it would assist.

44. Paragraph 84 – Replace ‘tissue’ with ‘bodily material’
45. Paragraph 85 - In the first line, replace the phrase ‘any human material’, with ‘bodily material’. The term Research Ethics authority should be used not REC. There are additional excepted purposes than those that are quoted that may be relevant for the research sector. In the example given, it would be useful to clarify the situation if the researcher was to analyse the DNA rather than simply extracting it.
46. Paragraphs 86 – 90 – These are much less clear than many other aspects of the Code. If it would assist, MRC and Wellcome Trust would be willing to discuss further how they could be redrafted. The use of terms ‘stem cells’ and ‘stem cell lines’ should be carefully reviewed to ensure the correct terms are being used. For example, in the first sentence of paragraph 86 it is adult and fetal stem cells that need to be stored on licensed premises – not embryonic cells or stem cell lines derived from any of the three sources.
47. Paragraph 86 – We remain concerned that use of stem cell therapies must be regulated in a clear and non-duplicative manner. It is difficult to predict which type of stem cell therapies will require licensing by the three authorities potentially involved. We hope that all will remain in discussion with each other and other relevant bodies, including ourselves to ensure there is proportionate regulation in this area.
48. Paragraph 87 – The HFEA does not regulate embryonic stem cell lines but rather the creation of the embryos from which they are derived. The sentence could be amended to clarify that the three authorities regulate steps in production of embryonic stem cell lines.
49. Paragraph 88- -It is unclear to us what ‘relevant material for a clinical trial which will not be used in human application’ means. If this section only relates to clinical trials of stem cells this should be made explicit in the section title. It appears that this section also includes other tissue and cells for human application and if so this should be stated. It is the case that material may be used in therapeutic trials and further clarity is needed that such applications apply to all human material, not just stem cells.
50. Paragraph 97 onwards – The HTA may wish to consider whether all of these standards need or should be listed in the Code of Practice. They are available on the website and also may be subject to amendment as systems and processes for licensing are updated over time.
51. Appendix A – Storage of tissue from the living flowchart:
 - Consent required unless is ‘non-identifiable...,’ this could be interpreted as irrevocably unlinked, which is not what is meant;
 - REC approved project should say RE Authority-approved (or approval is pending), as the exemptions do not apply to university REC approval; and
 - it should be made clear that although a Research Tissue Bank may have REC approval, they require a licence. As the flowcharts stand it could be interpreted that storage under a specific REC-approved project is a valid exemption for Research Tissue Banks.
52. Glossary - Should include definitions of:
 - anonymised (reversible and non-reversible);
 - audit;
 - bodily material;
 - public health monitoring; and
 - relevant material: Cells manufactured outside the body should be specifically excluded from the definition.

Code 1 - Consent

53. Please refer to the general comments on Code 9 above which also apply to Code 1 – in particular the comments on the length of the opening sections before the main body of the Code begins at paragraph 35.

Specific Points

54. Paragraph 28 – The Code is helpful in explaining the different regulatory framework in Scotland. However, the Authority could be more precise as to what standards are expected by the Scottish Executive. Scottish researchers are advised to 'read this code'. It would be of more assistance to indicate that they should treat it as Best Practice, while having an obligation to comply with the HT (Scotland) Act, if that is indeed the expectation.

55. Paragraph 35 – The differentiation of these aspects of consent is helpful and clear.

56. Paragraph 45 – This could be slightly amended to reflect that relatives and friends would only be involved where appropriate and (for a living person) also subject to the agreement of the person in question.

57. Paragraph 48– We strongly support the position in the Codes that it is preferable to obtain generic consent when possible and with appropriate information. This also applies to tissue from the deceased, whereas this paragraph refers only to that from the living, where it may not be appropriate to recontact relatives to obtain further consent for broader purposes than an original specific consent.

58. Paragraph 52 – It is not clear what the reference to rules on duration of consent for adults who lack capacity refers to. We are not aware of specific limitations as regards consent for research in this regard. This paragraph references Code 9, however, code 9 paragraph 42 references this code. It is important that a definitive summary of consent for research relating to adults who lack capacity is provided in one of these two codes and that this is then referenced from the other code. The MRC has produced guidance³ on this topic and MRC and the Wellcome Trust would be willing to discuss further how the HTA Codes could be clarified.

59. As researchers in Scotland are advised to consider these Codes they should also include the fact that there is different legislation in Scotland in this regard.

60. Paragraph 54 – This seems unnecessary.

61. Paragraph 68 – It should be pointed out that there is different legislation in Scotland as regards adults who lack capacity.

62. Paragraph 81 – It is not clear as to why the HTA makes requirements of Designated Individuals in relation to images when these are not subject to the HT Act, nor apparently part of the HTA remit. It would be preferable if this paragraph was removed or amended to be clearer as to the role and expectations of the HTA in this regard.

63. Paragraph 87 –We are concerned about the implications of this paragraph as regards use of tissue for research. This is a very sensitive area and we appreciate that the wishes of relatives must be given serious considerations. However, the concluding sentence implies that the balance between the wishes of the deceased and of relatives would rest with the latter; this does not reflect the HT Act and the need for respect for a person's own wishes and explicit consent before death. We appreciate that in some cases donation should not proceed against the relatives wishes but in some circumstances it may be appropriate, this paragraph strongly suggests that the default position would be for relatives to have a veto,

³ <http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC002409>

despite the acknowledgement in the preceding paragraph that there is no legal basis for this.

64. Paragraph 96 – The last sentence should be amended to clarify that consent from a qualifying relative is not required if there is a personal consent from the deceased or consent from a nominated representative. Read in isolation this paragraph implies consent from a relative is always required.
65. Paragraph 115 – Add the word 'and' between '*examination*' and '*for public display*'.
66. Paragraph 123, Part ii – Add the word 'needed' or 'required' between 'than the time' and 'for the coroner'.
67. Paragraph 123, Part ii – Add the words 'evidence concerning' between the words '*pathologist that it bears on*' and '*the cause of death*'.
68. Paragraph 124 – Remove the word 'following' between '*scheduled purposes where*' and '*the coroner's authority*'.
69. Paragraph 137 – The last sentence should be reworded to 'in cases where researchers do not have consent to use patient data...'
70. Paragraph 140 – This should make it clear that it is a Research Ethics Authority-approved project. Replace '*... or a project for which ethical approval has been sought*' with '*...or a project for which ethical approval is pending*'.
71. Paragraph 146 – The age stated for an adult as defined by the HT Act is incorrectly quoted here as 16 or over. It should read '*18 or over*', as in paragraph 102.
72. Paragraph 163 – The statement '*The guidance in this section also applies to RNA analysis*' should not be included in the Code. Whilst we would advocate that the principles of good practice that govern research using DNA should also apply to RNA, RNA is not included in the HT Act and is therefore outside the remit of the HTA. We would be happy to look into including a section on RNA in current guidance from the MRC and the Wellcome Trust on DNA and genetic analysis.
73. Paragraph 165 – Given that the JCMG report mentioned in paragraph 165 was published before the HTA issued its guidance and Codes of Practice and is an '*interpretation of likely effects on practice*' of the HT Act and its main focus is not research, we would ask that the HTA also add the following guidance: 'Research and the Human Tissue Act - DNA Analysis' (October 2007)⁴ either here or in the relevant section in Code 9 on Research. This guidance is particularly relevant in the context of research; it was compiled after the implementation of the HT Act and in consultation with the HTA.
74. This paragraph needs to explain more clearly that the HT Act deals with being in possession of bodily material with the intent of analysing DNA, as opposed to the analysis itself. It would be helpful to clarify for researchers and others what 'bodily material' means (as compared to 'relevant material').
75. Paragraph 167 – Our understanding is that the hierarchical relationships for consent should be respected for this situation – although this is not stipulated in the HT Act. It would be useful if the HTA could confirm in this paragraph if this is indeed the case.
76. Paragraph 170 – '*As with other tissue from the living, research... must be ethically approved*'. This is an important point that would benefit from being included in Part 3: Tissue from the Living.
77. Appendices – Overall, the tables are a clear explanation of the main points made in this Code of Practice. However, in Appendix B storage and/or use for research, it should be

⁴ http://www.ukcrc-rgadvice.org/Documents/MRC_DNA_Analysis_Summary_Consent.pdf

clarified that ethical approval is from a Research Ethics Authority and the approval can be pending.

78. Glossary - should include the following:

- Existing holdings – should state the date 1 September 2006;
- Bodily material; and
- RNA (if this is to be included in the Code).

Code 5 – Disposal of Tissue

79. Please refer to the general comments on Code 9 above which also apply to Code 5 – in particular the comments on the length of the opening sections before the main body of the Code begins at paragraph 35.

Specific Points

80. Paragraph 41 - Part v. Add the word 'for' to read 'the methods of and reason for disposal'.
81. Paragraph 52 - Change 'of' to 'or' in the last sentence 'They may make their own arrangements for cremation *or* burial'.
82. Before paragraph 67 (Disposal of surplus tissue) - it would be useful to include a section headed 'Disposal of tissue from the living' as disposal of material from the living other than that classified under 'surplus tissue' or as an 'existing holding' is not dealt with directly anywhere else. There is a statement in Section 74 which refers to existing holdings from the living - 'these may be incinerated in the same way as any other tissue taken from a living person'. This new section should cover both identifiable and unidentifiable material, stating that "Identifiable and unidentifiable tissue taken from the living may be incinerated, subject to the considerations outlined in paragraph 47.
83. Paragraph 75 - Remove extra 'of' in the last sentence 'and are therefore covered by of this guidance'.
84. Heading before paragraph 86 - add the words 'from the deceased' to the 'Identifiable tissue' heading to make it clear.
85. Paragraph 92 – This should be amended to be clear as to which circumstances it applies – for example, the identity of the person will need to be disclosed to relatives in many cases
86. The addition of a flow chart is a very good idea, gives an easy-to-understand overview and enables quick referencing without having to read through pages of text.