ESTABLISHING REGULATORY APPROACHES TO ENABLE ALL SURPLUS TISSUE SAMPLES TO BE POTENTIAL RESEARCH SAMPLES

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ABSTRACT

Human tissue is routinely removed from patients in the course of diagnosis and treatment. Surgical procedures such as tumour excision or biopsies often involve removing relatively large amounts of tissue after which only a small amount is required for diagnostic purposes. The remainder is stored in a diagnostic archive in case further testing should be required. However, where all or some stored tissue is no longer required for diagnostic purposes it may have value for health research purposes, for which these diagnostic archives can be a rich source of tissue samples. Health research is generally considered to be something which is a 'good' and in the best interest of society, as the knowledge which is generated from research positively impacts on all members of society, whether directly or indirectly.

Consent is the fundamental principle which underpins the lawful storage and use of tissue for research purposes. However, where tissue is removed during clinically directed procedures and is surplus to diagnostic requirements, the opportunity to request consent is often missed and obtaining consent retrospectively can be problematic. The Human Tissue Act 2004 does provide for the secondary research use of surplus tissue in the absence of consent where certain safeguarding mechanisms are in place. The research must be ethically approved and the research must be carried out in circumstances such that the person carrying it out is not in possession of information which could identify the person from whom it was removed. Whilst the Human Tissue Act 2004 is permissive of the secondary research use of surplus tissue in the absence of consent, there remain barriers to accessing such tissue samples for research purposes. My thesis aims to establish regulatory approaches which if implemented in practice, could be more enabling of the secondary research use of surplus tissue samples, whilst also safeguarding individual patient interests.

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PART 1: THE BACKGROUND

CHAPTER 1

THE PROBLEM

Human tissue is routinely removed from patients in the course of diagnosis and treatment. Surgical procedures such as tumour excision or biopsies[1] often involve removing relatively large amounts of tissue after which only a small amount is required for diagnostic purposes[2]. The remainder is stored in a diagnostic archive in case further testing should be required[3]. However, where all or some stored tissue is no longer required for diagnostic purposes it may have value for health research purposes, for which these diagnostic archives can be a rich source of tissue samples[4]. Health research is generally considered to be something which is a 'good' and in the best interest of society[5], as the knowledge which is generated from research positively impacts on all members of society, whether directly or indirectly[6]. It is fundamental to the prevention, diagnosis and treatment of health-impacting conditions and, in some cases, ensures patients can have access to novel treatments which may have

[1] Dowsett M. New Hurdles for Translational Research. *Breast Cancer Research*. 2000 **2** 241-243
Dowsett T et al. The value of Archival Tissue Blocks in Understanding Breast Cancer biology. *Journal of Clinical Pathology.* 2014 **67** 272-275
[2] van Diest P J. No Consent Should be Needed for using Leftover Body Material for Scientific Purposes. *British Medical Journal*, 2002 **325** 648-649
[3] Nuffield Council on Bioethics (2011) Human Bodies: Donation for Medicine and Research. Available at www.nuffieldbioethics.org/publications/human-bodies-donation-for-medicine-and-research
Nuffield Council on Bioethics (1995) Human Tissue: Ethical and Legal Issues. Available at www.nuffieldbioethics.org/publications/human-tissue
[4] Bathe O F and McGuire A L. The Ethical use of Existing Samples for Genome Research. *Genetics in Medicine* 2009 **11(10)** 712-715
[5] McHale J. Reforming the Regulation of Health Research in England and Wales: New Challenges and Pitfalls. *Journal of Medical Law and Ethics*. 2013 **1(1)** 23-42
[6] Schaefer O, Emanuel E and Wertheimer A. The Obligation to Participate in Biomedical Research. *Journal of the American Medical Association.* 2009 **302(1)** 67-72

positive life-changing, extending or even saving effects[7]. Moreover, it can also have a positive socio-economic impact by improving the efficiency of NHS services[8].

As much health research is publicly funded however, whether this is via the Government or charities, there is also a responsibility to ensure cost efficiency in research[9]. The promotion and facilitation of efficient healthcare research is therefore considered to be something which is in the public interest[10], yet the requirement to protect the rights and interests of research participants must also play a key role and is enshrined into research ethics practice - most notably by virtue of the Declaration of Helsinki, produced by the World Medical Association[11]. Whilst the Declaration of Helsinki is not in itself legally binding, it does provide ethical principles which are considered to have primacy and are intrinsically embedded in ethical, and to some degree legal, standards[12]. It is important to achieve an effective balance between facilitating important health research and safeguarding the interests of those who are the subject of such research. However, in 2011 the Academy of Medical Sciences (AMS) suggested that there was imbalance in health research governance with regards to ensuring safeguarding of patients and the public and facilitating quality health research[13]. In its report 'A new pathway for the regulation and governance of health research', the AMS stated that the balance was tipped too far towards safeguarding which had resulted in unnecessarily complex over-regulation. Whilst safeguarding was considered to be of high importance, it was suggested that a governance

[7] Academy of Medical Sciences (2011) A New Pathway for the Regulation and Governance of Health Research. Available at acmedsci.ac.uk/policy/policy-projects/a-new-pathway-for-the-regulation-and-governance-of-health-research
[8] *Ibid*
[9] *Ibid*
[10] *Ibid*
[11] World Medical Association (2013) WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects. Available at www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/
[12] Rid A, Schmidt H. The 2008 Declaration of Helsinki – First Among Equals in Research Ethics. *Journal of Law, Medicine & Ethics*. 2010 **38(1)** 143-148
[13] Academy of Medical Sciences (2011) A New Pathway for the Regulation and Governance of Health Research. Available at acmedsci.ac.uk/policy/policy-projects/a-new-pathway-for-the-regulation-and-governance-of-health-research

structure which delays or prohibits quality research also risks harming future patients and society more broadly, and therefore this should be avoided[14].

Empirical evidence strongly indicates that when asked, people are generally not only accepting of their surplus tissue being used for secondary research purposes, but in some cases people have expressed a desire for their tissue to be used for such purposes and have questioned why this does not happen more often[15]. However, there are significant barriers to obtaining surplus tissue samples for secondary research purposes, despite patients often expressing a willingness to donate samples for such purposes[16]. Moreover, the governance structures within which such activities sit are often not conducive to the sharing of surplus tissue samples where consent for secondary research purposes has not been requested and recorded in a format which is easily accessible. The Human Tissue Act 2004 (HT Act 2004) regulates the storage and use of tissue for scheduled purposes, activities which are lawful when undertaken with consent[17], and is explicit in its intention to make consent the fundamental principle which underpins the lawful storage and use of human tissue[18]. However, the HT Act 2004 also provides for surplus tissue to be used for research purposes without consent, where the research is ethically approved and the research will be carried out in circumstances such that the person carrying it out will not be in possession of information which could identify the person from whom the tissue was removed[19]. This provision was included as an amendment to the Human Tissue Bill during its passage through Parliament following lobbying from the scientific and research

[14] Academy of Medical Sciences (2011) A New Pathway for the Regulation and Governance of Health Research. Available at acmedsci.ac.uk/policy/policy-projects/a-new-pathway-for-the-regulation-and-governance-of-health-research

[15] Ipsos MORI (2018) Consent to use Human Tissue and Linked Health Data in Health Research. A Public Dialogue for Health Research Authority and Human Tissue Authority. Available here www.hra.nhs.uk/documents/1570/Consent_to_use_human_tissue_and_linked_health_data_in_health_research_FINAL.pdf
Ipsos MORI (2019) *A Public Dialogue on Genomic Medicine: Time for a New Social Contract?* Available at www.ipsos.com/ipsos-mori/en-uk/public-dialogue-genomic-medicine-time-new-social-contract

[16] Nuffield Council on Bioethics (2011) *Human Bodies: Donation for Medicine and Research*. Available at www.nuffieldbioethics.org/publications/human-bodies-donation-for-medicine-and-research

[17] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Schedule 1 Part 1

[18] *Ibid* Explanatory notes paragraph 4

[19] *Ibid* Part 1 s. 1 ss. (7 - 9)

community due to concerns that a blanket requirement for consent to use all tissue samples would stifle important research[20]. However, surplus tissue which is stored within a diagnostic archive is an under-utilised resource and there appears to be hesitancy by regulators such as the Human Tissue Authority (HTA) to accept the 'consent exemption' provision too abundantly.

Whilst consent is the fundamental principle which underpins the lawful storage and use of tissue[21] and has been extolled as the 'golden thread' which runs through the legislation[22], the logistics and scale of tissue removal procedures which are undertaken in the NHS are not always conducive to obtaining consent, and recording it in a way which can easily be accessed by pathologists when asked to provide samples for research purposes[23]. The consequence is that surplus tissue which has potential research value is often stored in diagnostic archives without consent for secondary research use. Moreover, the tissue may be surplus to diagnostic requirements and have potential research value but is not always being made available for secondary research purposes - an issue which my thesis aims to address. My thesis proposes that, due to the significant public benefit in health research and the potential research value of surplus tissue, all tissue which is removed during a clinically directed procedure and is surplus to diagnostic requirements should have the *potential* to be a research tissue sample. In making this assertion, my thesis establishes regulatory approaches which, if implemented in practice, could be more enabling of surplus tissue being used for secondary research purposes compared to the current situation. The regulatory approaches which I propose primarily relate to England. However, they may also be transferrable in whole or in part to all UK nations.

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[20] Liddell K and Hall A. Beyond Bristol and Alder Hey: The Future Regulation of Human Tissue. *Medical Law Review.* 2005 **13(2)** 170-223

[21] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Explanatory notes paragraph 4

[22] Furness P. The Human Tissue Act: Reassurance for Relatives, at a Price. *British Medical Journal*. 2006 **333(512)**

[23] Macklin P et al. Barriers to the Release of Human Tissue for Clinical Trials in the UK: A National Survey of Cellular Pathology Laboratories on Behalf of the National Cancer Research Institute's Molecular Pathology (CM-Path) Initiative. *Journal of Clinical Pathology.* 2019 **72** 52-57

In achieving the aim of enabling all surplus tissue samples to be potential research samples, my thesis focuses on tissue which is stored in diagnostic archives and is surplus to diagnostic requirements but may have secondary research value. My reasons for focusing on tissue samples which are stored in diagnostic archives are twofold. First, this is an area of regulation relating to research involving human tissue which is not as widely discussed or established in practice, a gap which my thesis aims to address. Second, I aim to establish a more *normative* regulatory approach to the secondary research use of surplus tissue, which aims to increase patient awareness of the potential research value of surplus tissue and provides greater choice - but does not require explicit consent where the law provides for this. A regulatory approach which increases patient awareness of the potential research value of surplus tissue arguably also has the potential to provide a more solid regulatory foundation which in turn *supports* more established biobanking practices. In focusing on surplus tissue samples which are stored in diagnostic archives, my thesis does not intend to suggest that these tissue samples should be accessed as an *alternative* to established biobanks where there is explicit consent for the use of tissue samples and data. It does however suggest that tissue samples which are stored in a diagnostic archive should not be prevented from being used for health research purposes *because* consent was not requested or recorded when the tissue was removed - where the law provides for this.

In achieving the aim of enabling all surplus tissue samples to be *potential* research samples, my thesis aims to define and address potential regulatory barriers which limit the availability of surplus tissue for use in health research because patient consent was not requested or recorded. To achieve this, my thesis establishes regulatory approaches which if implemented in practice could better enable the secondary research use of surplus tissue samples in the absence of consent. Moreover, the regulatory approaches established in my thesis aim to maximise the research value of surplus tissue samples by also facilitating the linking of tissue samples with associated patient information. The real value of surplus tissue samples in health research is where samples are linked with associated data about the person from whom the samples were removed - the tissue samples alone have limited research

value[24]. However, provision in the HT Act 2004 which permits the use of tissue samples for research purposes in the absence of consent requires for the research to be undertaken in circumstances such that the person undertaking it is not in possession of information which could identify the person from whom the tissue was removed. Therefore, to gain the optimal research value from surplus tissue samples in the absence of consent, it is important to establish a regulatory approach which enables tissue samples and relevant patient information to be linked for secondary research purposes.

Chapter 10 explores whether a 'safeguarding' approach, as provided for via the General Data Protection Regulation (GDPR) and the Data Protection Act 2018 (DPA 2018) for the use of personal data in health research, could better enable the availability of surplus tissue linked with associated data which is necessary to achieve the research aim. In proposing an approach which better acknowledges the value in sharing surplus tissue linked with associated data which is necessary to meet research aims (which I refer to as a 'share and protect' approach), I suggest this does not necessarily lessen the protection afforded by the 'consent or anonymise' approach under the HT Act 2004. A 'share and protect' approach does however consider the sharing of surplus tissue linked with associated patient information as a valuable activity which should be facilitated, whilst also safeguarding individual patient interests. Moreover, the provision in the data protection legislation with regards to safeguarding of personal data does not negate the common law duty of confidence, i.e. that information held in confidence should not be disclosed in a form which could identify the person without their consent[25]. However, Section 251 of the NHS Act 2006 provides for the duty of confidence to be temporarily set aside by the Health Research Authority (HRA), on the advice of the Confidentiality Advisory Group (CAG)[26], where this is deemed to be justified. This therefore does provide some flexibility to undertake research which is in the public interest where consent has not

[24] Regidor E. The use of Personal Data from Medical Records and Biological Material: Ethical Perspectives and the Basis for Legal Restrictions in Health Research. *Social Science & Medicine*. 2004 **59** 1975-1984
[25] Department of Health (2003) Confidentiality: NHS Code of Practice. Available at www.gov.uk/government/publications/confidentiality-nhs-code-of-practice
[26] In England and Wales. Different arrangements apply in Scotland and Northern Ireland.

been obtained for secondary research use and where obtaining consent retrospectively would not be feasible.

My intention in exploring whether a broader 'safeguarding' approach, rather than a requirement for absolute non-identifiability when linking tissue and patient information, is to establish a regulatory approach which would be more enabling of such materials being used in health research and which also protects patient interests. This is important because there is a public benefit in better facilitating health research which uses surplus tissue, as such research is crucial to improving the diagnosis and treatment of diseases which have significant impacts on individual health as well as society more broadly, such as cancer and heart disease[27]. Moreover, such research requires access to large numbers of tissue samples as well as associated patient information to achieve meaningful and generalisable outcomes.[28] Therefore a more enabling approach which better facilitates the sharing of surplus tissue linked with associated patient information, in a way which also safeguards patient interests, could better balance the public interest with individual patient interests.

To enable all tissue samples which are surplus to diagnostic requirements to be *potential* research samples it is also important that all NHS organisations apply consistent policies, which are conducive to the secondary research use of samples and acknowledge the logistical challenges and limitations of obtaining consent from all patients for all samples which may have research value. Chapter 11 highlights extant inconsistency across different NHS organisations with regards to the sharing of surplus tissue for secondary research purposes and requirements for consent to be obtained prior to sharing for such purposes. In highlighting extant inconsistency, chapter 11 argues that there is an unfair distribution of opportunities for patients associated with the donation of surplus tissue samples for secondary research purposes and furthermore, this inconsistency means that public benefits cannot be fully realised. The public benefits referred to here are the benefit of maximising the

[27] Meslin E and Quaid K. Ethical Issues in the Collection, Storage, and Research of Human Biological Materials. *Journal of Laboratory Clinical Medicine*. 2004 **144(5)** 229-234
[28] *Ibid*

availability of surplus tissue samples and the benefit in trust which comes from governance and regulation, including procedures to request permission for the secondary research use of surplus tissue samples. In suggesting that a more consistent approach would mean fairer distribution of opportunities and better meet public interest claims, chapter 11 suggests that a consistent approach across NHS organisations which permits the use of surplus tissue samples where there is no evidence of objection would be the fairest approach and would have the greatest overall public benefit. Moreover, to ensure fair opportunity for patients to object, mechanisms to record an objection to the secondary research use of surplus tissue should be well-publicised, simple and accessible.

Chapter 12 of my thesis considers requirements for an HTA research licence for diagnostic archives which provide surplus tissue samples for secondary research purposes. The HT Act 2004 includes provision that tissue which is stored for research purposes should be under the authority of a research licence[29]. However, there is a legal grey area where tissue samples are collected during clinical or surgical procedures, stored in a diagnostic archive and surplus to diagnostic requirements - as they are stored for clinical purposes but may subsequently be identified as having secondary research value. Obtaining a research licence requires clear procedures for seeking and obtaining consent[30]. However, where surplus tissue is stored in a diagnostic archive and surplus to diagnostic requirements, it is often the case that consent for secondary research use was not obtained or has not been recorded in a way which can be confirmed. This therefore creates potential issues for diagnostic archives which store tissue samples for clinical purposes without consent for secondary research use but subsequently want to provide surplus tissue samples for such purposes - an issue which my thesis aims to address.

The HTA code of practice on research *implies* that a research licence is required where a diagnostic archive provides tissue samples for research on a *regular* basis, particularly if there are governance

[29] Human Tissue Act 2004. Part 2 s.16 ss. (2) (e)
[30] Human Tissue Authority (2016) *HTA Code E Standards and Guidance*. Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20E%20standards.pdf

procedures in place to manage requests to access tissue samples. Whilst the code of practice is not clear on the matter, the implication is that where a diagnostic archive provides tissue samples on a regular basis and where there are established governance procedures, then the establishment is also functioning as a research tissue bank - an activity which must be under the authority of an HTA research licence to be lawful. Chapter 12 suggests that the wording in the code of practice is not sufficiently clear and risks avoidance of practices relating to the research use of surplus tissue as well as being 'over regulation' within a regulatory framework which sufficiently protects the interests of patients without applying additional licensing requirements. The intention here is to establish a regulatory approach which would be more proportionate to the actual risks associated with the activities being undertaken and more facilitative of the secondary research use of surplus tissue.

In achieving the aim of establishing a regulatory approach which is more facilitative of diagnostic archives providing surplus tissue samples for secondary research purposes, chapter 12 suggests that we should consider diagnostic archives which provide surplus tissue samples to be undergoing a transitionary process. Moreover, by viewing diagnostic archives which transition to also function as research tissue banks as a *process*, rather than a leap from one state to a new state, we can better conceptualise the activities being undertaken and therefore apply a more proportionate and enabling regulatory approach to governance and licensing which is proportionate to the actual activities being undertaken.

My thesis concludes by suggesting that the regulatory approaches which I establish could, if implemented in practice, better enable the secondary research use of surplus tissue samples. Moreover, I suggest that these regulatory approaches should be supported by clear authoritative guidance from regulators and a culture change towards a more normative approach to the secondary research use of surplus tissue which ensures that patients are accepting and supportive of such practices.

CHAPTER 2

THE BACKGROUND TO THE HUMAN TISSUE ACT 2004

MACABRE HOARDING OR VALUABLE RESOURCE?

2.1 Organ and Tissue Retention: Bristol and Alder Hey

The use of surplus tissue in health-related research is currently regulated under the HT Act 2004. This piece of legislation was created in response to findings that human tissue and organs were being retained *post-mortem* for teaching and research purposes without the full awareness of families of the deceased[31]. Whilst it has been suggested that this legislation was 'born under the wrong star'[32], due to its scope reaching beyond that of human tissue and organs removed from the deceased and to include tissue removed from living persons, the history of how the HT Act 2004 came about provides important context to the current regulatory situation with regards to the use of surplus tissue in health-related research. In 1998 Frank Dobson, the (then) Secretary of State for Health, announced an investigation into paediatric cardiac services at the Bristol Royal Infirmary between 1984 – 1995[33]. This investigation, Chaired by Professor Sir Ian Kennedy, was initiated in response to a notably high mortality rate of children undergoing complex heart surgery[34].

[31] McHale J. The Human Tissue Act 2004: Innovative Legislation – Fundamentally Flawed or Missed Opportunity? *Liverpool Law Review* 2005 **26** 169-188
Price D. The Human Tissue Act 2004: *The Modern Law Review*. 2005 **68(5)** 798-821
[32] Mason J K and Laurie G T. (2006) *Mason & McCall Smith's Law and Medical Ethics: Seventh Edition*. Oxford: Oxford University Press
[33] Department of Health (2002) *Learning from Bristol: The Department of Health's Response to the Report of the Public Inquiry into children's heart surgery at the Bristol Royal Infirmary 1984-1995*. Available at www.gov.uk/government/publications/the-department-of-healths-response-to-the-report-of-the-public-inquiry-into-childrens-heart-surgery-at-the-bristol-royal-infirmary
[34] Dyer C. Bristol inquiry condemns hospital "club culture". *BMJ news article*. 2001 **323**

Whilst the scope of this inquiry was primarily focused on clinical care received by the babies prior to their death, it was also noted that hearts were being routinely retained *post-mortem* and used for research purposes - often without the awareness or understanding of the parents[35]. Moreover, when giving evidence at the inquiry, a statement was made by Professor Robert Anderson, Professor of Paediatric Cardiac Morphology at Great Ormond Street Hospital and a member of the inquiry's expert group, which subsequently had a cataclysmic impact on the regulatory landscape in relation to the storage and use of human tissue in the UK. When reflecting on the benefits of retaining hearts *post-mortem* for research and teaching purposes, Professor Anderson informed the inquiry that retention was common practice and commented that the most extensive collection of hearts was housed at The Royal Liverpool Children's Hospital (Alder Hey)[36]. This revelation, whilst intended to provide reassurance about the improvements in clinical care for babies with complex cardiac conditions which can result from research using retained hearts in teaching and research, was picked up by the media and led to the publication of sensationalist headlines[37].

In response to the media surrounding the revelation about heart retention at Alder Hey, parents whose children had died contacted the hospital to request details of whether their child's heart had been retained *post-mortem*[38]. This led to further questioning of whether other organs were also being retained. The government subsequently initiated an inquiry, under the provisions of Section 2 of the National Health Service Act 1977, into the removal, retention and disposal of organs and tissue following post-mortem examinations[39]. During investigations as part of this inquiry, the collection of

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[35] Miola J (2011) Law, Ethics, and Human Tissue Research: Integration or Competition? In Lenk C, Hoppe N, Beier K, Wilderman C. (eds.) *Human Tissue Research: A European Perspective on the Ethical and Legal Challenges* (pp 79 – 86) Oxford: Oxford University Press.

[36] McHale J. The Human Tissue Act 2004: Innovative Legislation – Fundamentally Flawed or Missed Opportunity? *Liverpool Law Review* 2005 **26** 169-188

Hall D. Reflecting on Redfern: What Can We Learn from the Alder Hey Story? *Arch Did Child* 2001 **84** 455-456

The Royal Liverpool Children's Inquiry (2001) *Royal Liverpool Children's Inquiry Report. Chair, Michael Redfern QC*. Available at www.gov.uk/government/publications/the-royal-liverpool-childrens-inquiry-report

[37] Furness P. Research using Human Tissue – a Crisis of Supply? *Journal of Pathology* 2001 **195** 277-284

[38] The Royal Liverpool Children's Inquiry (2001) *Royal Liverpool Children's Inquiry Report. Chair, Michael Redfern QC*. Available at www.gov.uk/government/publications/the-royal-liverpool-childrens-inquiry-report

[39] Brazier M. (2006) The Human Body and its Parts. In Brazier M and Cave E (eds.) *Patients and the Law (sixth edition)* (pp 545 – 564) Manchester: Manchester University Press

retained organs and tissues held by Professor Dick van Velzen at the Myrtle Street building, part of the Royal Liverpool Children's Hospital, was discovered. This collection included organs and tissues from approximately 850 post-mortem examinations undertaken between September 1988 and December 1995 and included over 2,000 containers holding whole organs and tissue fragments[40]. Whist the scale of the collection is notable, the poor conditions in which the collection was stored also raised concerns. Identification of some of the tissues was extremely difficult because the labels on some containers had become dilapidated and the writing faded over the years, which was compounded by a lack of adequate record keeping[41].

In response to these findings, the Government announced that there would be a public inquiry into the activities at Alder Hey, chaired by Michael Redfern QC. This subsequent inquiry had a primary focus to examine the retention of tissues and organs *post-mortem* and the extent to which the Human Tissue Act 1961 had been complied with[42]. This inquiry included evidence from parents whose children had died and who had subsequently found out that organs and tissues had been retained. The primary concern expressed by the parents was that they had not been aware that their child's organs and tissues would be retained - and therefore they had not agreed to the retention[43]. On reading the Royal Liverpool Children's Enquiry Report, the Secretary of State for Health at the time, Alan Milburn, stated that it was the most shocking thing he had ever read[44]. Gillott[45] suggests that this may be due to the emotive tone with which the findings were presented and furthermore, this emotive reaction may also have perpetuated a view amongst the public and politicians that the storage and use of all tissue samples for research and teaching purposes was in itself wrong. In his book 'Bioscience, Governance and Politics', Gillott quotes from an interview which he conducted with Margaret Brazier when

[40] The Royal Liverpool Children's Inquiry (2001) *Royal Liverpool Children's Inquiry Report. Chair, Michael Redfern QC.* Available at www.gov.uk/government/publications/the-royal-liverpool-childrens-inquiry-report
[41] *Ibid*
[42] *Ibid*
[43] Dewar S and Boddington B. Returning to the Alder Hey report and its Reporting: Addressing the Confusions and Improving Enquiries. *Journal of Medical Ethics*. 2004 **30** 463-469
[44] Gillott J. (2014) *Bioscience, Governance and Politics*. Basingstoke: PALGRAVE MACMILLAN
[45] *Ibid*

working towards his PhD thesis[46]. Gillott quotes Brazier reacting to Alan Milburn's comment, saying that to suggest that the findings from the investigation into organ retention at Alder Hey is the most shocking thing he has ever read is hard to believe, when only a few years previous he had also read the Shipman Report; a GP who was responsible for the deaths of almost 300 people[47]. Moreover, Dewar and Boddington suggest that such reactions by the media and leading politicians to the findings at Alder Hey Hospital perpetuated macabre mental images of organs and body parts being hoarded by 'mad and bad scientists' with wicked intent[48]. The reality however was that the retention and use of tissue and organs *post-mortem* for research and teaching purposes was something that happened routinely and was not something doctors considered to be illegal or immoral at the time, let alone scandalous and macabre which was how such practices appeared to be portrayed in the media and by leading politicians[49].

In describing the collections of organs and tissues which had been retained and stored at the Myrtle Street building, the Royal Liverpool Children's Inquiry Report does however acknowledge the role which the collections played in furthering medical knowledge and the benefit which had been attained from this knowledge. The report acknowledges that 'there can be no doubt that the use of the heart collection has been invaluable in terms of research education and training'[50]. Moreover, the report suggests that:

> 'Perhaps the most compelling evidence of the value of the collection was the dramatic reduction in the mortality rate following complex cardiac surgery….. The mortality rate

[46] Gillott's PhD thesis titled the Changing Governance of Science? A Critical Inquiry into the Contemporary Politics and Governance of Natural Scient Research as Explored through the Human Tissue and Embryo Cases in the UK

[47] Gillott J. (2014) *Bioscience, Governance and Politics*. Basingstoke: PALGRAVE MACMILLAN

[48] Dewar S and Boddington B. Returning to the Alder Hey report and its Reporting: Addressing the Confusions and Improving Enquiries. *Journal of Medical Ethics*. 2004 **30** 463-469

[49] Dobson R. Doctors Subjected to 'Harsh Treatment' over organ retention says report. *British Medical Journal*. 2001 **322(1566)**

[50] The Royal Liverpool Children's Inquiry (2001) *Royal Liverpool Children's Inquiry Report. Chair, Michael Redfern QC.* Available at www.gov.uk/government/publications/the-royal-liverpool-childrens-inquiry-report pg. 96

following all such surgery has fallen from 20 per cent in 1970 to 3.6 per cent in 1999. ……. There are now more than 1,600 living children who would have died in infancy or childhood without the improvements in surgical techniques and care which were pioneered in Liverpool'.[51]

Furthermore, the evidence given during the inquiry from some parents indicated not only an acceptance of the role which such organs and tissues play in research and training but also a frustration that their children's retained organs and tissues had been retained without clear purpose - as they had *not* been used for such purposes:

'Their overriding concern is why the organs were retained. If some useful research had been carried out it might have comforted them. They regard storage without research as totally futile'[52]

'The parents fully accept that the medical profession will never discover anything in the future without research'.[53]

'Even after discovering retention of their son's heart and lungs without their knowledge or consent they would have considered leaving the organs with Alder Hey had they been useful for research/training purposes.'[54]

This is important in the overall context of my thesis because empirical work indicates that people are generally supporting of existing surplus tissue being used for secondary research purposes[55]. However,

[51] The Royal Liverpool Children's Inquiry (2001) *Royal Liverpool Children's Inquiry Report. Chair, Michael Redfern QC.* Available at www.gov.uk/government/publications/the-royal-liverpool-childrens-inquiry-report pg. 97
[52] *Ibid* pg. 394
[53] *Ibid* pg. 396
[54] *Ibid* pg. 398
[55] Ipsos MORI (2018) *Consent to use Human Tissue and Linked Health Data in Health Research. A Public Dialogue for Health Research Authority and Human Tissue Authority*. Available at www.hra.nhs.uk/documents/1570/Consent_to_use_human_tissue_and_linked_health_data_in_health_research_FINAL.pdf
Williams A M et al. Consent to Donate Surgical Biospecimens for Research: Perceptions of People with Colorectal Cancer. *Cancer Nursing.* 2016 **39(3)** 221-227

people want to be aware, have the opportunity to object and for any such objection to be respected[56]. Attaining a balance between facilitating the secondary research use of surplus tissue in the broader public interest which comes from increasing medical knowledge through research and respecting individual interests is a key theme throughout my thesis.

The Royal Liverpool Children's Inquiry concluded that the provisions within the Human Tissue Act 1961 had not been sufficient to adequately regulate practices with regards to the retention of organs and tissues *post-mortem*[57]. The Human Tissue Act 1961 provided that in the absence of clear instruction from a person prior to their death:

> '….the person lawfully in possession of the body of a deceased person may authorise the removal of any part from the body for use for the said purposes [medical education or research] if, having made such reasonable enquiry as may be practicable, he has no reason to believe –
>
> (a) that the deceased had expressed an objection to his body being so dealt with after his death, and had not withdrawn it; or
>
> (b) that the surviving spouse or any surviving relative of the deceased objects to the body being so dealt with.[58]

Hamilton S et al. Consent Gained from Patients after Breast Surgery for the use of Surplus Tissue in Research: An Exploration. *Journal of Medical Ethics*. 2007 **33** 229-233
Soto C et al. Consent to Tissue Banking for Research: Qualitative Study and Recommendations. *Archives of Diseases in Childhood*. 2012 **97** 632-636

[56] Ipsos MORI (2018) *Consent to use Human Tissue and Linked Health Data in Health Research. A Public Dialogue for Health Research Authority and Human Tissue Authority*. Available at www.hra.nhs.uk/documents/1570/Consent_to_use_human_tissue_and_linked_health_data_in_health_research_FINAL.pdf

[57] The Royal Liverpool Children's Inquiry (2001) Royal Liverpool Children's Inquiry Report. Chair, Michael Redfern QC. Available at www.gov.uk/government/publications/the-royal-liverpool-childrens-inquiry-report p 367

[58] *Human Tissue Act 1961*. Available at www.legislation.gov.uk/ukpga/Eliz2/9-10/54/2002-12-17 s. 2

This wording subsequently led to a suggestion by Margaret Brazier, the Chair of the Retained Organs Commission, established as a Special Health Authority[59] to oversee the process of returning retained organs to families[60], that the Human Tissue Act 1961 was a 'toothless tiger imposing fuzzy rules with no provision for sanctions or redress.'[61]. The lack of legislative sanctions was reiterated by the fact that Professor van Velzen did not face any criminal charges over his actions. The Crown Prosecution Service considered the case and concluded that there was no realistic prospect of demonstrating that a criminal offence had been committed[62]. Professor van Velzen was however subsequently struck off the medical register by the General Medical Council[63].

The Royal Liverpool Children's Inquiry report[64] concluded with several recommendations. These included that the Human Tissue Act 1961 should be amended to include provision that informed consent should be sought for the retention of parts of the body from deceased persons *post-mortem* and that there should be criminal penalty for breach of compliance with this requirement[65]. A census conducted by the Chief Medical Officer (CMO), Professor Liam Donaldson, which was published in 2001, identified over 54,000 tissues, body parts, foetuses and stillborn babies retained by pathology services in hospitals and medical schools in England[66]. The CMO subsequently went on to publish 'The Removal, Retention and use of Human Organs and Tissue from Post Mortem Examination'[67]. This report acknowledged the findings from the inquiries into the practices with regards to organ retention at the Bristol Royal Infirmary and Alder Hey and concurred that regulatory change was required to

[59] *The Retained Organs Commission (Establishment and Constitution) Order 2001*. Available at www.legislation.gov.uk/uksi/2001/743/enacted
[60] Brazier M. Retained organs: Ethics and Humanity. *Legal Studies*. 2002 **22(4)** 550-569
[61] Brazier M. Organ Retention and Return: Problems of Consent. *Journal of Medical Ethics.* 2004 **29** 30 – 33 p31
[62] Bmj.com news roundup. GMC hearing opens into doctor at centre of organ retention scandal. *British Medical Journal*. 2005 **330**
[63] Dyer, O. Alder Hey Pathologist Is Struck Off Medical Register. *British Medical Journal*. 2005 **330(7506)**
[64] The Royal Liverpool Children's Inquiry (2001) *Royal Liverpool Children's Inquiry Report. Chair, Michael Redfern QC.* Available at www.gov.uk/government/publications/the-royal-liverpool-childrens-inquiry-report
[65] *Ibid* 10 s 11 ss 11.1
[66] Price D. The Human Tissue Act 2004. *The Modern Law Review*. 2005 **68(5)** 798-821
[67] Department of Health, Chief Medical Officer (2001) *The Removal, Retention and use of Human Organs and Tissue from Post Mortem Examination: Advice from the Chief Medical Officer*. Available at webarchive.nationalarchives.gov.uk/ukgwa/20130123204009/http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4064942

ensure that similar practices of organ and tissue retention *post-mortem* did not continue and to restore public confidence[68].

The report concluded with a number of recommendations, broadly covering post-mortem practices and the handling of organs and tissue. Moreover, the CMO report reiterated the recommendations made by Michael Redfern QC in the Royal Liverpool Children's Inquiry report that the Human Tissue Act 1961 should be amended to be explicit that consent is required from those with parental responsibility for organs and tissues to be retained from children following a post-mortem examination (recommendation 1). The report further recommended amendments to the Coroners Rules 1984 to clarify that pathologists have no independent right to retain organs following post-mortem examination, except where this is under the authority of the Coroner (recommendation 2). The report also recommended the establishment of an independent commission to oversee the return of organs and tissues to families; (later to become the *Retained Organs Commission* Chaired by Professor Margaret Brazier) (recommendation 5).

Whilst these recommendations aimed to address some of the issues in the short term, a further recommendation was made which indicated that there would be a fundamental review of the law relating to the removal, storage and use of organs and tissues with a view to introducing a system of regulatory control. Moreover, it was recommended that the scope of this fundamental review of the law should encompass the removal, storage and use of organs and tissues from living persons as well as from those who are deceased (recommendation 6). This last recommendation therefore widened the scope of regulatory reform which subsequently led to the current regulatory framework for research use of human tissue - including tissue which is removed during clinically directed procedures and is surplus to diagnostic requirement.

[68] Department of Health, Chief Medical Officer (2001) *The Removal, Retention and use of Human Organs and Tissue from Post Mortem Examination: Advice from the Chief Medical Officer*. Available at webarchive.nationalarchives.gov.uk/ukgwa/20130123204009/http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4064942

In July 2002 the Department of Health (England) and the NHS Department of the Welsh Assembly Government (Wales) published a consultation report – *Human Bodies, Human Choices: The Law on Human Organs and Tissue in England and Wales*. This consultation report sought views in relation to the future legislative provisions for 'the removal, retention and use of human organs and tissue from the living and those who have died'[69], taking forward the fundamental review of the law which had been recommended by the CMO. Whilst the report does set out some interim arrangements with regards to *post-mortem* practices and communication with families, the intention was to undertake a fundamental and comprehensive review of the law without the additional short-term legislative amendments proposed by the CMO. The reason cited for this was that substantial amendment would have been required to the existing Human Tissue Act 1961 which would have pre-empted the views being sought via the broader consultation process[70].

The subsequent consultation summary report included a number of key messages, including that consent should be the fundamental basis for a future legislation and regulatory framework. Whilst the expectation of consent was evidently front and centre, the report acknowledged that this should not unintentionally restrict or prevent important research from taking place, an appropriate balance needed to be struck[71]. Achieving an appropriate balance between facilitating important health research using surplus tissue stored in diagnostic archives, whilst also protecting patient interests, is a key theme throughout my thesis. Moreover, finding ways to better achieve this balance forms the basis of arguments throughout my thesis when proposing regulatory approaches to enable all surplus tissue samples to be potential research samples.

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[69] Department of Health/Welsh Assembly Government (2002) *Human Bodies, Human Choices: The Law on Human Organs and Tissue in England and Wales: A consultation Report*. Available at webarchive.nationalarchives.gov.uk/ukgwa/20090318211500/http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4109272 s. 1

[70] *Ibid* ss. 4.3

[71] Department of Health (2003) *Human Bodies, Human Choices – Summary of Responses to the Consultation Report*. Available at https://webarchive.nationalarchives.gov.uk/ukgwa/20090430232110/http://www.dh.gov.uk/en/Consultations/Responsestoconsultations/DH_4069366

The requirement for consent to be a key element of future legislation was seemingly based on the assumption that individuals may have interests in their tissues once removed from the body, as the tissue retains some part of their identity or characteristics, and therefore continues to be part of the person[72]. Moreover, for some people, their tissues have religious relevance, even after they have been removed from the body. For example, Orthodox Jews sometimes seek the storage of amputated limbs so that they can be buried with them when they die[73]. This view that tissue remains part of the person even after removal therefore suggests that people have an interest in retaining some degree of *control* over what happens to their tissue - which is seemingly to be achieved by setting a requirement for tissue to only be used with the person's consent. With this in mind, it is important to ensure that there is a regulatory framework for the secondary research use of surplus tissue which recognises such views and therefore protects individual interests in a way which acknowledges and respects that tissue may be considered part of a person even once removed from the body.

For some people however, their tissue becomes waste materials once removed and they no longer retain any personal interest[74]. Where there is value for the greater good, such as health research, then people often accept and even welcome the fact that their waste materials could be used for such purposes[75]. Harris therefore suggests that there should be a cautious approach when developing legislation and guidelines which does not focus too heavily on individual attitudes[76]. Liddell and Hall further suggest that reasonable yet diverging views about human tissue are to be expected in a modern society as people will 'endorse diverse moral beliefs due to conflicting and complex evidence

[72] Liddell K and Hall A. Beyond Bristol and Alder Hey: The Future Regulation of Human Tissue. *Medical Law Review.* 2005 **13(2)** 170-223
[73] McGuinness S and Brazier M. Respecting the Living Means Respecting the Dead Too. *Oxford Journal of Legal Studies*. 2008 **28(2)** 297-316
[74] McHale J. Waste, Ownership and Bodily Products. *Healthcare Analysis*. 2000 **8** 123-135
[75] Hamilton S et al. Consent gained from patients after breast surgery for the use of surplus tissue in research: an exploration. *Journal of Medical Ethics*. 2007 **33** 229-233
Williams A M et al. Consent to Donate Surgical Biospecimens for Research: Perceptions of People with Colorectal Cancer. *Cancer Nursing*. 2016 **39(3)** 221-227
Soto C et al. Consent to Tissue Banking for Research: Qualitative Study and Recommendations. *Archives of Diseases in Childhood.* 2012 **97** 632-636
[76] Harris J. Law and Regulation of Retained Organs: The Ethical Issues. *Legal studies*. 2002 **22(4)** 527-549

that bears on the selection of moral values'[77]. This 'moral pluralism' is an important, but also challenging, issue for policy makers as consequently, laws and guidance are unlikely to please all of the people all of the time. It is therefore necessary to base laws and guidance on principles which can be justified on grounds which most people can agree are reasonable[78]. This is important in the broader context of my thesis, which proposes regulatory approaches which if implemented in practice could better facilitate the availability of surplus tissue for secondary research purposes, because it highlights the importance of also respecting individual and cultural perceptions of tissue once removed from the body.

2.2. The Human Tissue Bill

The Human Tissue Bill (also referred to here as the Bill) was introduced to the House of Commons on 3 December 2003 and subsequently brought up to the House of Lords on 29 June 2004, eventually receiving Royal Assent on 15 November 2004. The introduction of the Human Tissue Bill raised a number of concerns, most notably that it would criminalise research practices which utilised tissue and lead to a culture of over caution where pathologists and clinicians would avoid research using human tissue samples rather than falling foul of legislative sanctions - which in turn risked stymying important research[79]. The Bill was described as using a sledgehammer to crack a nut[80], also mockingly referred to as a sledgehammer which misses the nut[81], as well as a knee-jerk reaction to the public outcry which followed the inquiries at the Royal Bristol Infirmary and Alder hey[82].

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[77] Liddell K and Hall A. Beyond Bristol and Alder Hey: The Future Regulation of Human Tissue. *Medical Law Review.* 2005 **13(2)** 170-223 pg. 9.

[78] Liddell K and Hall A. Beyond Bristol and Alder Hey: The Future Regulation of Human Tissue. *Medical Law Review.* 2005 **13(2)** 170-223

[79] *Ibid*

Furness P and Sullivan R. The Human Tissue Bill: Criminal Sanctions Linked to Opaque Legislation Threaten Research. *British Medical Journal*. 2004 **328** 533-534

[80] Pincock S. Human Tissue Bill Could Jeopardise Research, Scientists Warn. *British Medical Journal* 2004 **328** 1034 quoting Lord May.

[81] Baroness O'Neil (2004) *'Human Tissue Bill'* Hansard: House of Lords Debates 22 July. c. 396

[82] Zimmern J. Consent and Autonomy in the Human Tissue Act 2004. *King's Law Journal* 2007 **18(2)** 313-328

During the passage of the Human Tissue Bill through Parliament, it was questioned whether the Bill placed too much emphasis on individual rights, to the detriment of social benefit achieved through health-related research[83]. The initial draft of the Bill required for there to be valid consent for the research use of *all* tissue samples removed from the living, including tissue samples which are held in diagnostic archives and are surplus to diagnostic requirements. Historically, such tissue samples would have been used for research and teaching purposes without consent from the person from whom they were removed and there was concern that a requirement for consent would have a significant impact on the ability of pathologists and researchers to undertake these important activities[84].

This prompted significant pushback from the research community which resulted in a meeting with organisations with a vested interest in the research use of surplus tissue, such as medical charities, research funders and professional associations[85]. The concern expressed by the research community was that important research could be severely limited if there was a requirement for consent to be in place for all surplus tissue samples which are held within a diagnostic archive[86]. A requirement for consent for the research use of surplus tissue would require an infrastructure which ensured that consent was requested, recorded and stored in a way which meant that pathologists could confirm whether patients had given consent. Without such an infrastructure, important health research would be significantly limited and could in turn impact all society by restricting future development in the medical field[87]. Almost twenty years later, there is still no established infrastructure to request, record and access patient preferences with regards to potential future research use of their surplus tissue, an issue which my thesis aims to address.

[83] Furness P and Sullivan R. The Human Tissue Bill: Criminal Sanctions Linked to Opaque Legislation Threaten Research. *British Medical Journal*. 2004 **328** 533-534
[84] Furness P. Research using Human Tissue - A Crisis of Supply? *Journal of Pathology* 2001 **195** 277-284
[85] Liddell K and Hall A. Beyond Bristol and Alder Hey: The Future Regulation of Human Tissue. *Medical Law Review.* 2005 **13(2)** 170-223
[86] Price D. The Human Tissue Act 2004. *The Modern Law Review*. 2005 **68(5)** 798-821
[87] *Ibid*

Lobbying by the research community resulted in an amendment being made to the Human Tissue Bill which meant that consent would not be required for the use of tissue which was removed during a clinically directed procedure under certain conditions. These conditions were that the research must be approved by an authorised research ethics committee and the research must be carried out in circumstances such that the person conducting the research is not in possession of information which could identify the person from whom the tissue was removed[88]. Lord Warner, when addressing the House of Lords during the second reading of the Bill, stated that the amendment was important because it recognised the research value in surplus tissue, whilst also preserving the integrity of the rights being protected by requirements for consent[89]. This amendment was well received during the second reading of the Bill in the House of Lords. Baroness O'Neill acknowledged the importance of recognising the practical aspects relevant to the use of tissue samples which were removed during clinical directed procedures[90]. Moreover, Lord Clement-Jones stated that the amendment providing for tissue from living persons to be used in research in the absence of consent resulted in the Bill being in 'far better shape'[91]. This approach was also supported by scholars such as Liddell and Hall who suggested that the HT Act 2004 was fairer and more practical with regards to the availability of surplus tissue for research than earlier versions of the Bill[92].

However, is has also been suggested that any use of human tissue without the consent of the person from whom it was removed is unacceptable. Porteri and Borry suggest that consent is a fundamental requirement which should not be a mere formality or legal standard but should truly demonstrate respect for those persons whose tissue is being used for research purposes[93]. Moreover, they suggest that anonymisation of samples should not be an alternative to the respect which is demonstrated

[88] Liddell K and Hall A. Beyond Bristol and Alder Hey: The Future Regulation of Human Tissue. *Medical Law Review.* 2005 **13(2)** 170-223; *Human Tissue Act 2004* Part 1 Section 1 (9)
[89] Lord Warner (2004) *'Human Tissue Bill'* Hansard: House of Lords Debates 22 July. c. 369
[90] *Ibid*. c. 396 Baroness O'Neil
[91] *Ibid.* c. 374 Lord Clement-Jones
[92] Liddell K and Hall A. Beyond Bristol and Alder Hey: The Future Regulation of Human Tissue. *Medical Law Review.* 2005 **13(2)** 170-223
[93] Porteri C and Borry P. A Proposal for a Model of Informed Consent for the Collection, Storage and use of Biological Materials for Research Purposes. *Patient Education and Counselling*. 2008 **71** 136-142

through consent and therefore, identifiable samples should be treated in the same way as non-identifiable samples in this regard[94]. Garwood-Gowers[95] advises caution when it comes to removing requirements for consent for the research use of human tissue, suggesting that such an approach may lead to sacrificing respect for individuals purely to meet the research demand for tissue samples.

However, the suggestion that all uses of human tissue should only be with the consent of the person from whom the tissue was removed appears to assume that consent is always *necessary*. Brownsword suggests that a fixation which over-values consent can in itself be as risky as under-valuation of consent[96]. In following this thinking, Brownsword suggests that a requirement for consent should only be applied where an action would violate a 'right' if undertaken without their consent - where no such rights exist then consent is not *necessary*[97]. In the context of surplus tissue being used for secondary research purposes within a legal framework which permits such activities, the 'rights' which consent aims to protect are intended to be mitigated by safeguards provided via the HT Act 2004. The rights which I refer to here are the right for surplus tissue not to be used for research purposes which patients may find morally reprehensibly, such as research into biological weapons[98], mitigated by the requirement for research to be ethically approved, and the right to privacy, mitigated via the requirement for the person undertaking the research to not be in possession of information which could identify the person from whom the tissue was removed.

Brownsword further suggests that applying consent requirements where it is not necessary, moves from a beneficial *culture* of consent towards a non-beneficial *cult* of consent. He further suggests that the danger arises where consent is applied as a free-standing detached principle, rather than applied in support of other principles[99]. Whilst respect for persons whose tissue has been removed and stored

[94] *Ibid*
[95] Garwood-Gowers A. (2011) Respect as a precondition for use of human tissue for research purposes. In Lenk C, Hoppe N, Beier K and Wiseman C. (eds.) *Human Tissue Research: A European Perspective on the Ethical and Legal Challenges* (pp 25 – 34) Oxford: Oxford University Press
[96] Brownsword R. The Cult of Consent: Fixation and Fallacy. *King's Law Journal*. 2004 **15(2)** 223-251
[97] *Ibid*
[98] Furness P. Research using Human Tissue - A Crisis of Supply? *Journal of Pathology* 2001 **195** 277-284
[99] Brownsword R. The Cult of Consent: Fixation and Fallacy. *King's Law Journal*. 2004 **15(2)** 223-251

in a diagnostic archive is undoubtedly important, this does not in itself mean that using such tissue samples for research purposes without explicit consent is *necessarily* wrongful towards that person. During the second reading in the House of Lords in July 2004, Baroness Hayman expressed concern that the Bill over emphasised issues with regards to consent for the use of surplus tissue in health-related research and suggested that work should be undertaken to build public awareness and confidence in research rather than applying consent requirements which would essentially be a tick-box exercise, in its most literal sense[100].

The amendment to the Human Tissue Bill which permitted the use of stored surplus tissue in health-related research, where the research is ethically approved and the identity of the person from whom the tissue was removed is not known to the researcher, aimed to achieve a balance between protecting the interests of individuals and societal benefit[101]. However, as consent was considered to be the fundamental principle which underpinned the lawful use of human tissue[102], the perception that consent is *necessary* is apparent in practice, even where the law is permissive in this regard. A study undertaken in 2016/7, on behalf of the National Cancer Research Institute's Molecular Pathology (CM-Path) initiative, surveyed the views of people working in pathology departments in the UK[103]. This study found that 42% of institutions had implemented a system of obtaining consent for the future research use of surplus tissue and of these, only 50% stated that the system in place was sufficiently robust to ensure that consent was routinely requested and appropriately recorded.

Whilst the HT Act 2004 does provide for the sharing of surplus tissue in the absence of consent under certain circumstances, obtaining consent is recommended as good practice where practical[104].

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[100] Baroness Hayman (2004) *'Human Tissue Bill'* Hansard: House of Lords Debates 22 July. cc. 408-409
[101] Zimmern J. Consent and Autonomy in the Human Tissue Act 2004. *King's Law Journal* 2007 **18(2)** 313-328
[102] Human Tissue Act 2004. Available at www.legislation.gov.uk/ukpga/2004/30/contents Explanatory notes para 4
[103] Macklin P et al. Barriers to the Release of Human Tissue for Clinical Trials in the UK: A National Survey of Cellular Pathology Laboratories on Behalf of the National Cancer Research Institute's Molecular Pathology (CM-Path) Initiative. *Journal of Clinical Pathology*. 2019 **72** 52-57
[104] Human Tissue Authority (2020) HTA Code A: Guiding Principles and the Fundamental Principle of Consent. Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20A.pdf

However, respondents highlighted issues in relation to consent such as confusion whether consent forms covered tissue release, and inadequate communication, knowledge and awareness of consent generally. Moreover, this survey highlighted that significant underfunding and understaffing in NHS departments, resulting in a lack of time, was an issue[105]. The consequence of a lack of time in clinical situations when completing standard consent forms likely means that insufficient attention will be paid to additional sections regarding secondary research use of surplus tissue[106]. As such, an ineffective consent infrastructure can become a barrier to accessing surplus tissue for use in health-related research rather than an enabler and therefore consent outcomes are often a reflection of factors other than patient choice.

In chapter 6 of my thesis I highlight the inconsistent approaches, with regards to sharing surplus tissue samples for secondary research purposes and requirements for consent, across different NHS organisations. Here I argue that a consistent approach applied across all NHS organisations would be fairer as it would ensure equal opportunities for patients in relation to the donation of surplus tissue for secondary research purposes. The opportunities which I refer to here are the opportunity for patients to donate surplus tissue and therefore to knowingly act on altruistic interests. Chapter 6 concludes that the approach which would best achieve overall benefits for both individual patients and broader public interests in health research, if implemented consistently across NHS organisations, would be for surplus tissue samples to be accessible for secondary research where there is no evidence of objection. Moreover, this approach should be supported by a well-publicised mechanism via which patients can register an objection which is simple and accessible. This proposed approach aims to address the issue of ineffective consent infrastructures becoming a barrier to accessing surplus tissue

[105] Macklin P et al. Barriers to the Release of Human Tissue for Clinical Trials in the UK: A National Survey of Cellular Pathology Laboratories on Behalf of the National Cancer Research Institute's Molecular Pathology (CM-Path) Initiative. *Journal of Clinical Pathology*. 2019 **72** 52-57

[106] Wheeler J et al. Experiences from the Front-Line Routine Consenting of Surplus Surgically Removed Tissue: Without Investment by the National Health Service Fully Informed Consent is Not Available. *Journal of Clinical Pathology.* 2007 **60** 351-354

for secondary research purposes and to better facilitate patient choice and engagement with regards to the potential research value of surplus tissue.

Part of the issue with regards to the secondary research use of surplus tissue is that the legal and governance framework which underpins tissue release from diagnostic archives is complex and unclear[107]. Where tissue samples are collected and stored for research purposes then the need for consent under the HT Act 2004 is clear - appropriate consent is required[108]. However, where tissue is removed as part of a clinically directed procedure, surplus to any further diagnostic requirements and stored in a diagnostic archive then the legal and governance framework is less clear. The requirement for consent to access archived tissue samples is implicitly defined via the licensing requirements under the HT Act 2004. The Act includes provisions which require that the storage of human tissue for research purposes (except for a research project which has ethical approval or where ethical approval is pending[109]) to be under the authority of a research licence. Moreover, the HTA code of practice on research states the following:

> 'Where a diagnostic archive functions as a resource for researchers as it invites applications for the release of samples and/or in any way advertises the archive as a research resource, it is functioning as a research tissue bank. It must therefore be encompassed within the HTA's licensing framework.'[110]

The HTA licensing framework requires compliance with four broad standards, one of which is consent:

> 'Establishments meeting the consent Standards will be able to demonstrate that their processes for seeking and gaining consent comply with the HT Act and the HTA's Codes of

[107] Macklin P et al. Barriers to the Release of Human Tissue for Clinical Trials in the UK: A National Survey of Cellular Pathology Laboratories on Behalf of the National Cancer Research Institute's Molecular Pathology (CM-Path) Initiative. *Journal of Clinical Pathology*. 2019 **72** 52-57
[108] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 1 s 1 ss (1) (d) and Schedule 1 Part 1 6
[109] *Human Tissue Act 2004 (Ethical Approval, Exceptions from Licensing and Supply of Information about Transplants) Regulations 2006*. Available at www.legislation.gov.uk/uksi/2006/1260/note/enacted
[110] Human Tissue Authority (2017) *HTA Code E: Research*. Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20E.pdf paragraph 95

> Practice. The standards also cover the documentation and information used to support the establishment's consent procedures, and ensure that the staff involved in seeking consent are suitably trained and equipped for the task.'[111]

Whilst the HTA codes of practice are not clear on the matter, the implication is that where a diagnostic archive is also functioning as a research tissue bank, and therefore must meet the HTA's licensing standards, there must be valid consent for secondary research use of the samples. However, as previously indicated, the current underfunding and understaffing of NHS departments is not conducive to ensuring an effective consent infrastructure which represents the desires of patients with regards to their surplus tissue[112]. Moreover, the distinction between a diagnostic archive providing samples on request and also functioning as a research tissue bank, and therefore coming under the HTA's licensing framework, is unclear. The HTA code of practice on research states:

> 'The HTA's position is that if a diagnostic archive releases tissue occasionally upon request, its status as a diagnostic archive is clear. However, if there is an expectation that tissue will be released on a regular basis then it may cease to be a purely diagnostic archive, particularly where there are developed governance / decision-making structures and procedures for applying for tissue.'[113]

In not setting clear standards for diagnostic archives in relation to when an HTA research licence is required, and therefore consent must be obtained, the code of practice on research arguably adds to an already complex and confusing situation. There is currently no literature which challenges the ambiguity of the current UK guidance on licensing requirements of diagnostic archives which supply tissue for use in health-related research. Chapter 12 of my thesis discusses this issue in more detail,

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[111] Human Tissue Authority (2016) *HTA Code E: Standards and Guidance*. Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20E%20standards.pdf paragraph 1

[112] Macklin P et al. Barriers to the Release of Human Tissue for Clinical Trials in the UK: A National Survey of Cellular Pathology Laboratories on Behalf of the National Cancer Research Institute's Molecular Pathology (CM-Path) Initiative. *Journal of Clinical Pathology*. 2019 **72** 52-57

[113] Human Tissue Authority (2017) *HTA Code E: Research*. Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20E.pdf paragraph 94

aiming to fill this gap in the literature. Here I argue that viewing diagnostic archives becoming research tissue banks as a transitionary process with an 'in-between' state means that we can apply proportionate regulation which is appropriate for the actual activities being undertaken. Furthermore, in acknowledging the 'in-between' state which exists, when a diagnostic archive transitions to also function as a research tissue bank, there can be greater clarity with regards to regulatory requirements for individuals undertaking research practice involving surplus tissue which is stored in diagnostic archives.

In 2009, onCore UK conducted a survey in response to work undertaken by the National Cancer Institute's Task Force on Pathology and Research[114], to explore the effect of regulation and governance on pathology research in the UK[115]. This was in response to anecdotal evidence that researchers were finding it difficult to access existing tissue samples for research purposes[116]. Over half of the respondents to the survey stated that they found undertaking research difficult due to the lack of clear guidance available and 13% of respondents said that because of this, they do not undertake research at all. For 83% of respondents, they would be more likely to be more research active if there was clear, consistent guidance which was easily accessible and endorsed by regulators.

It was noted that where guidance did exist, it was often in different places and published by different sources which could be confusing. Respondents stated that the most common places to seek advice would be local Research and Development (R&D) offices or trusted colleagues. The report published by onCore UK in July 2009 concluded that the existing regulatory and governance environment was affecting the willingness and ability of those working in pathology to undertake research. My thesis aims to address this issue by proposing regulatory approaches which if implemented across the NHS

[114] A time limited and scope restricted Task Force formed by the National Cancer Research Institute (NCRI) in response to concerns raised that research regulation was limiting pathology research

[115] onCore UK (2009) *The Effect of Regulation and Governance on Research Led by Pathologists or Involving Pathology in the UK*. Available at www.pathsoc.org/news/30/oncore_uk_report_effect_of_regulation_governance_survey

[116] Clotworthy M. Human Tissues for Research Purposes: A Conference in the House of Lords. *Cell Tissue Banking*. 2011 **12** 329-331

could provide a clear and consistent infrastructure to enable all surplus tissue samples to be potential research samples - in a way which safeguards individual patient interests and facilitates health research in the public interest.

CHAPTER 3

BALANCED AND PROPORTIONATE REGULATION

3.1. An Evolving Regulatory Picture

In 2011 the Academy of Medical Sciences (AMS) published a report titled, 'A new pathway for the regulation and governance of health research'[117]. This report highlighted imbalance in health research governance with regards to ensuring safeguarding of patients and the public on the one hand, and facilitating quality health research on the other - suggesting that the balance was tipped too far towards safeguarding which had resulted in unnecessarily complex over-regulation. Whilst safeguarding was considered to be of high importance, it was suggested that a governance structure which delays or prohibits quality research also risks harming future patients and society more broadly, and therefore this should be avoided. Moreover, it was noted that health research governance had become complex and difficult to navigate for those wanting to undertake research.

This complex regulatory picture resulted in a lack of clarity and misinterpretation of legislation[118]. Consequently, some organisations had introduced systems which were over and above what was required, as well as some researchers avoiding undertaking research in this field. This complex regulatory landscape had built up over a number of years, creating a fragmented regulatory system with multiple layers of bureaucracy and overlap of roles and responsibilities[119]. A review of the governance of health-related research, including research involving human tissue, was undertaken, resulting in four key principles and seventeen recommendations. The AMS proposed that research regulation should:

[117] Academy of Medical Sciences (2011) *A New Pathway for the Regulation and Governance of Health Research*. Available at acmedsci.ac.uk/policy/policy-projects/a-new-pathway-for-the-regulation-and-governance-of-health-research
[118] Gillott J. (2014) *Bioscience, Governance and Politics*. Basingstoke: PALGRAVE MACMILLAN
[119] *Ibid*

- Safeguard the well-being of research participants
- Facilitate high-quality health research to the public benefit
- Be proportionate, efficient and co-ordinated
- Maintain and build confidence in the conduct and value of health research through independence, transparency, accountability and consistency

These principles are relevant in the context of my thesis, which aims to develop regulatory approaches which if implemented in practice could better enable the availability of surplus tissue for secondary research purposes. This is because the regulatory approaches which I develop throughout my thesis aim to safeguard individual patient interests whilst also better facilitating access to surplus tissue for secondary research purposes, in ways which are proportionate to the activities being undertaken and also promote patient engagement and awareness.

Chapter 7 of the AMS report covers the regulation of research involving human tissue and embryos in research. Respondents to the calls for evidence, which had been issued as part of the work to develop the report, indicated a view that the regulatory requirements around the use of human tissue in research were disproportionate to the actual views of patients. It was suggested that patients should routinely be offered the opportunity to donate their surplus tissues for use in health-related research. However, it was also noted that the existing regulatory framework was unclear, and the absence of an established risk-based approach had led to inconsistent interpretation of the HT Act 2004 and its regulatory provisions[120], an issue which my thesis aims to address. In chapter 11 I use the policies from 12 different NHS organisations in England as a case study to demonstrate that there is currently inconsistency across the NHS with regards to accessing surplus tissue for secondary research purposes and in particular with regards to requirements for consent. Moreover, I argue that this inconsistency

[120] Academy of Medical Sciences (2011) *A New Pathway for the Regulation and Governance of Health Research*. Available at acmedsci.ac.uk/policy/policy-projects/a-new-pathway-for-the-regulation-and-governance-of-health-research

is unfair because it does not allow equal opportunities for patients to donate surplus tissue for secondary research purposes, nor does it meet broader public interest claims.

The impact of a complex regulatory framework which has developed at different times over a number of years has been the subject of much debate. Laurie and Harmon[121] refer to the 'regulatory thicket' which they describe as the creation of a complex and fragmented accumulation of legal instruments, institutions and mechanisms which require greater knowledge and awareness and become ever increasingly difficult to navigate. Moreover, Laurie[122] suggests that the piecemeal way in which health research regulation has developed over the years, partly as a knee jerk reaction to events such as the findings from Bristol Royal Infirmary and Alder Hey, has created a silo approach to regulation. Consequently, areas such as the use of tissue and patient data in research are regulated under separate legal instruments and regulatory bodies which have at times been uncoordinated. Moreover, it has not always been clear how the different legislative provisions and regulatory bodies should be ranked or prioritised when conflicts or discrepancies arise[123]. This can be difficult for those holding tissue and/or data, as well as researchers wanting to access such valuable research resources, when trying to comply with the law yet also wanting to avoid stymying health research unnecessarily[124].

The report by the AMS recommended that to address this issue, a health research regulatory body should be established[125]. The Government responded by establishing the Health Research Authority (HRA) as a Special Health Authority via Statutory Instrument 2011/2323, The Health Research Authority (Establishment and Constitution) Order 2011, and later as a Non-Departmental Government

[121] Laurie G and Harmon S. (2015) Through the Thicket and Across the Divide: Successfully Navigating the Regulatory Landscape in Life Sciences Research. In Cloatre E and Pickersgill M (eds.) *Knowledge, Technology and Law*. (pp 121 – 136) Oxon: Routledge

[122] Laurie G. Liminality and the Limits of Law in Health Research Regulation: What Are We Missing in the Spaces In-Between? *Medical Law Review*. 2016 **25(1)** 47-72 2016

[123] Gibbons S MC. (2012) Mapping the Regulatory Space. In Kaye J, Gibbons S MC, Heeney C, Parker M, Smart A (eds.) *Governing Biobanks: Understanding the Interplay Between Law and Practice* (pp 51 – 92) Oxford: Hart Publishing ltd.

[124] *Ibid*

[125] Academy of Medical Sciences (2011) *A New Pathway for the Regulation and Governance of Health Research*. Available at acmedsci.ac.uk/policy/policy-projects/a-new-pathway-for-the-regulation-and-governance-of-health-research

body via the Care Act 2014. The formal remit of the HRA extends to England only. The aim of the HRA was to provide co-ordination and standardisation of practices relating to health-related research, as well as taking over some practical functions relating to the appointment and oversight of Research Ethics Committees (RECs) and the Confidentiality Advisory Group (CAG)[126].

Since the HRA was established in 2011, a key function has been to implement a centralised governance assessment and approval process in England, for research being undertaken in the NHS,[127] which assesses against UK wide standards. The UK-wide standards confirm research project compliance with legislation such as the HT Act 2004 and the common law duty of confidentiality, as well as established NHS governance mechanisms such as Material Transfer Agreements (MTA)[128] - which are a legal agreement defining the conditions under which researchers are granted access to tissue and data[129]. In addition to the streamlining of NHS research governance checks, a key benefit of the HRA has been the potential for more consistent advice which has a clear authoritative basis[130]. The role of the HRA and RECs with regards to the regulation of research involving surplus tissue is important in the context of my overall thesis because I aim to establish clear and consistent regulatory approaches which could better and more proportionately facilitate the research use of such tissue within a broader regulatory framework. Therefore, the existence and functions of relevant regulatory bodies provides important structure and synergy within a broader regulatory framework; something which will be discussed in more detail in chapter 12.

The AMS report considered a recommendation from Government, which had been proposed the previous year following a review of Government arm's-length bodies, that the HTA's research

[126] *Care Act 2014*. Available at www.legislation.gov.uk/ukpga/2014/23/contents/enacted s 110 ss (1)
[127] *Health Research Authority. HRA Approval* (2021) Available at www.hra.nhs.uk/approvals-amendments/what-approvals-do-i-need/hra-approval/
[128] Health Research Authority (2016) *HRA Approval: Assessment Criteria and Standards Document*. Available at www.hra.nhs.uk/documents/217/hra-approval-assessment-criteria-standards-document.pdf
[129] National Cancer Research Institute (2009) *Samples and Data for Research: Template for Access Policy Development.* Available at tdcc-blog.azurewebsites.net/wp-content/uploads/2016/06/Initiatives-Biobanking-2-Access-template-1.pdf
[130] McHale J. Reforming the Regulation of Health Research in England and Wales: New Challenges and Pitfalls. *Journal of Medical Law and Ethics*. 2013 **1(1)** 23-42

functions should be transferred to a new research regulator[131] - later to become the HRA. The AMS issued a call for evidence in relation to a single research regulator and responses commonly cited the view that regulation which is complex and multi-layered does not necessarily protect the interests of individuals but can stymie important research[132]. However, there was also concern raised that bringing all research regulators under one organisation could be too research focused and lose sight of broader non-research issues[133]. The AMS report was supportive of the recommendation to transfer the research regulation functions of the HTA to the proposed new research regulator[134]. However, when the HRA was subsequently established, it did not explicitly take on the research regulation functions of the HTA. The Care Act 2014 did however provide a statutory responsibility on the HRA to co-operate with the HTA (amongst other government bodies) in relation to health and social care research functions to ensure standardisation of practice[135].

Whilst the scope of the HTA is broader than research, as it also covers the regulation of activities such as post-mortem examinations, live and deceased organ donation and tissue and cells for human application[136], it does have a statutory responsibility where tissue is being stored for use in research[137]. The HT Act 2004 provides for scheduled purposes, including the storage and use of tissue[138], to be under the authority of a licence granted by the HTA[139]. However, there is an exemption to the licensing requirements for research which has ethical approval, or where ethical approval is pending, from an authorised research ethics committee. This is confirmed via provision in Statutory Instrument

[131] Department of Health (2010) *Liberating the NHS: Report of the Arm's-Length Bodies Review*. Available at assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/216278/dh_118053.pdf
[132] Academy of Medical Sciences (2011) *A New Pathway for the Regulation and Governance of Health Research.* Available at acmedsci.ac.uk/policy/policy-projects/a-new-pathway-for-the-regulation-and-governance-of-health-research s. 9.2.2
[133] *Ibid*
[134] *Ibid*
[135] *Care Act 2014*. Available at www.legislation.gov.uk/ukpga/2014/23/contents/enacted 111 s. 1
[136] www.hta.gov.uk/about-us
[137] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Schedule 1 Part 1
[138] Relevant material
[139] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 2 s. 16 ss. (1)-(2)(e) (ii)

2006/1260, The Human Tissue Act 2004 (Ethical Approval, Exceptions from Licensing and Supply of Information about Transplants) Regulations 2006. The HT Act 2004 and its associated statutory instruments do therefore provide a clear legal separation of the roles and responsibilities of the HTA and research ethics committees, with regards to tissue which is held for research purposes. However, UK policy has also introduced some overlap.

The HTA has a statutory responsibility to licence establishments which store human tissue for the purpose of research and additionally, the UK research ethics service provides a voluntary ethical review scheme for research tissue banks[140]. Whilst HTA licensing requirements and ethical review do have distinct areas of scope, there is some overlap when it comes to consent as this is an area which both the HTA and research ethics committees consider. One key benefit to applying for ethical approval of a research tissue bank is that a generic approval can be obtained which covers all research projects which obtain tissue samples and data from the bank and are within the scope of the generic approval - thereby avoiding the need for each project to be ethically approved and for consent to obtained on a project specific basis[141]. Moreover, consent is a key component of the licensing standards applied by the HTA[142]. Therefore, whilst there are some benefits to applying for ethical approval of research tissue banks, there is also some regulatory duplication when it comes to reviewing consent. The roles of the HTA, the HRA and research ethics committees in relation to the secondary research use of surplus tissue are considered in more detail in chapter 12.

This is important context for my thesis because subsequent chapters (chapters 10, 11 & 12) challenge existing approaches to regulation, establishing regulatory approaches which if implemented, could better facilitate the secondary research use of surplus tissue samples. It is therefore important to establish the roles and responsibilities of key regulatory actors in the field of tissue research to provide

[140] *Health Research Authority. Research Ethics Committee Standard Operating Procedures* (2021) Available at www.hra.nhs.uk/about-us/committees-and-services/res-and-recs/research-ethics-committee-standard-operating-procedures/
[141] Melham K. Enacting Regulation: Tissue in Practice. *Diagnostic Histopathology*. 2013 **19(9)** 343 – 349
[142] Human Tissue Authority (2016) *HTA Code E: Standards and Guidance.* Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20E%20standards.pdf

context for later discussion. The next section sets out the Government's approach to ensuring proportionality in regulation, focusing on a particular approach which was developed by the Council for Healthcare Regulatory Excellence (CHRE), which became the Professional Standards Authority for Health and Social Care (PSAHSC) under the Health and Social Care Act 2012, and is referred to as 'right touch' regulation[143].

3.2. Proportionate Regulation

In 1997 the UK Government established the Better Regulation Task Force (BRTF) which aimed to improve the framework of regulation in the UK. The BRTF produced five principles of good regulation: transparency, consistency, proportionality, targeting and accountability and recommended that regulators should produce Regulatory Impact Assessments (RIA) when proposing new policies and initiatives[144]. In 2005 the BRTF published a report, 'Better Regulation – Less is More' and in the same year, a report was published (The Hampton Report) detailing the outcome of a review led by Philip Hampton, who was a leading businessman, which looked at reducing administrative burdens[145]. These reports indicated a shift of direction towards an even more 'risk-based' approach which meant that there would be no inspection, form filling or providing of information without clear justification[146]. There have been various proportionate regulatory approaches proposed and discussed in the academic literature, such as responsive regulation[147], really responsive regulation[148] and smart regulation[149]. Each of these approaches aims to provide a regulatory framework which targets

[143] Professional Standards Authority for Health and Social Care (2015) *Right-Touch Regulation 2015*. Available at www.professionalstandards.org.uk/publications/detail/right-touch-regulation-2015
[144] *Parliament. Chapter 8: Improving the Framework of Regulation* (2004) Available at publications.parliament.uk/pa/ld200304/ldselect/ldconst/68/6810.htm
[145] *Parliament. The Hampton Report* (2013) Available at publications.parliament.uk/pa/cm201213/cmselect/cmspeak/1069/106911.htm
[146] Baldwin R. Better Regulation in Troubled Times. *Health Economics, Policy and Law.* 2006 ***1*** 203-207
[147] For more information about responsive regulation see Ayres I and Braithwaite J. (1992) *Responsive Regulation: Transcending the Deregulation Debate*. New York: Oxford University Press
[148] For more information about really responsive regulation see Baldwin R and Black J. Really Responsive Regulation. *The Modern Law Review*. 2008 **71(1)** 59-94
[149] For more information about smart regulation see Gunningham N and Sinclair D. (1995) Smart Regulation. In Drahos P (ed*) Regulation Theory: Foundations and Applications*. (pp 133 – 148) Acton: Australian National University Press.

resources based on the assessment of risks associated with activities rather than a blanket approach to regulatory enforcement[150].

One proportionate regulatory approach which has been proposed is known as 'right touch' regulation. This approach to regulation is of particular relevance in the context of my thesis because the HTA strategy 2019-22 states that its strategic approach is based on 'right touch' regulation. Furthermore, chapter 12 of my thesis challenges whether ambiguity in the HTA code of practice on research, with regards to licensing requirements for diagnostic archives which provide surplus tissue samples for secondary research, is truly in keeping with the 'right touch' regulation strategic aim of the HTA. This is therefore an approach to proportionate regulation which has particular prominence in this section to provide context for further discussion later in my thesis.

The principle of 'right touch' regulation was based on previous work undertaken by the Better Regulation Executive in 2000, which resulted in the five key principles referred to earlier in this section (regulation should be proportionate, consistent, targeted, transparent and accountable)[151]. The CHRE added a sixth principle, that regulation should be agile, based on the idea that regulation should be forward facing and should anticipate change, rather than focusing on preventing mistakes which had occurred in the past[152]. Whilst the remit of the PSAHSC is the regulation of registered health professionals, the principles of right touch regulation are transferable to other areas of regulation. Right touch regulation is a risk-based approach to regulation which considers the achievement of a desired outcome as being of equal importance with managing any risks. This requires for risks to not just to be identified, but also quantified via a process of risk assessment, so that the actual problems are being addressed through regulation, rather than perceived problems or risks which are already being managed. Right touch regulation means that regulation should only be applied where it is

[150] Baldwin R and Black J. Really Responsive Regulation. *The Modern Law Review*. 2008 **71(1)** 59-94
[151] Professional Standards Authority for Health and Social Care (2015) *Right-Touch Regulation 2015*. Available at www.professionalstandards.org.uk/publications/detail/right-touch-regulation-2015
[152] Bilton D and Clayton H. Finding the Right Touch: Extending the Right-Touch Regulation Approach to the Accreditation of Voluntary Registers. *British Journal of Guidance and Counselling*. 2013 **41(1)** 14-23

necessary and simple solutions, rather than overly complex regulatory systems, should be applied wherever possible[153]. This approach acknowledges that more regulation does not necessarily lead to better quality or safer practices, and in fact can result in additional and unnecessary cost; to those being regulated and also to society more broadly where over regulation restricts or prevents intended outcomes from being achieved.

In achieving a right touch regulation approach, the HTA aims to assess risks, be proportionate and targeted in its approach to regulation so that it uses the minimum intervention necessary to achieve compliance and to take the role of professional bodies and other regulators into account[154]. Chapter 12 considers the right touch regulation strategic approach of the HTA in the context of requirements for an HTA research licence where diagnostic archives provide surplus tissue samples for use in health-related research. Here I suggest that the HTA code of practice on research implies that an HTA research licence may be required, where diagnostic archives provide surplus tissue samples for secondary research purposes, where this is not *necessarily* required to comply with the HTA Act 2004. In doing so, a regulatory framework exists which is not in keeping with the principle of right touch regulation. This is because it risks unnecessary regulatory duplication, due to the perception that an HTA research licence is required where this is not necessarily required to comply with the HT Act 2004, or it risks stymying important research due to surplus tissue not being provided for secondary research use due to fear of falling foul of legislative sanctions.

In this section I have provided an overview of the regulatory framework which underpins research involving human tissue in England, including the responsibilities of key regulatory actors. I have further provided an overview of approaches which promote proportionality in regulation, focusing on a 'right touch' regulation approach which is the stated strategic approach of the HTA. This is intended to

[153] Cayton H and Webb K. The Benefits of a 'Right-Touch' Approach to Health Care Regulation. *Journal of Health Services Research & Policy*. 2014 **19(4)** 198-199
Bilton D and Clayton H. Finding the Right Touch: Extending the Right-Touch Regulation Approach to the Accreditation of Voluntary Registers. *British Journal of Guidance and Counselling*. 2013 **41(1**) 14-23
[154] *Human Tissue Authority. Our Strategic Approach* (2019) Available at archive.hta.gov.uk/our-strategic-approach-0

provide context for later discussion (chapter 12), which considers the extant regulatory framework in relation to the secondary research use of surplus tissue and argues that a more enabling approach should be applied. A key component of regulatory requirements with regards to the research use of tissue is consent. Whilst my thesis focuses on the secondary research use of surplus tissue in the absence of consent, where the law is permissive of this, consent remains a key issue within this area and therefore something which I consider in detail in the next section.

CHAPTER 4

CONSENT – THE 'GOLDEN THREAD'

4.1 Consent: Legal and Moral Foundations

The HT Act 2004 makes consent the fundamental principle which underpins the lawful storage and use of human tissue[155]. However, often it is the case that any research value of the tissue is not known at the time the tissue is removed and therefore consent is not obtained for future research use[156]. The HT Act 2004 is permissive of the use of such tissue in the absence of consent, where the research is ethically approved and the research will be carried out in circumstances such that the person carrying it out is not in possession of information which could identify the person from whom the tissue was removed[157]. However, whilst the focus of my thesis is to better facilitate the secondary research use of surplus tissue under this 'consent exemption', the significance of consent for the research use of tissue means that it warrants further discussion in the context of my thesis.

Consent as a concept can be complex[158] with roots in both legal and moral contexts[159]. With this in mind, I think it is important that consent is viewed conceptually as consisting of different components which serve different legal and ethical purposes. Consent provides a legal basis under statutory instruments[160] and in common law[161], establishing entitlements, creating obligations and shifting risks and responsibilities from one to another[162]. Moreover, consent reflects the decision to accept a course

[155] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Explanatory notes paragraph 4
[156] Riegman P and van Veen E. Biobanking Residual Tissues. *Human Genetics.* 2011 **130** 357-368
[157] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 1 s 1 ss (9)
[158] Nelson-Marten P and Rich B. A Historical Perspective of Informed Consent in Clinical Practice and Research. *Seminars in Oncology Nursing*. 1999 **5(2)** 81-88
[159] Faden R R and Beauchamp T L. (1986) *A History and Theory of Informed Consent*. New York: Oxford University Press
[160] For example, The Human Tissue Act 2004, The Medicines for Human Use (Clinical Trial) Regulation 2004
[161] For example, in relation to the common law duty of confidence
[162] Johnston D. (2005) A History of Consent in Western Thought. In Miller F and Wertheimer A (eds.) *The Ethics of Consent: Theory and Practice.* Oxford University Press Scholarship Online

of action as well as the authorisation for that course of action to occur[163]. However, consent has a broader function ethically. It is commonly associated with the principle of autonomy, acting as a mechanism by which autonomous individuals can exercise their autonomous rights by choosing whether to give or withhold their consent[164]. Whilst the HT Act 2004 provides a legal framework with regards to consent, including provision for the secondary research use of surplus tissue, consent also provides moral justification and therefore extends beyond a mere legal basis. It is this component of consent which I did not want to lose sight of in my thesis, despite focusing on the secondary research use of surplus tissue samples in a legal framework which is permissive of such activities in the absence of consent.

This section is comprised of two parts. The first part sets out international and national instruments and key guidance relating to consent and choice with regards to the use of human tissue in health-related research. This is intended to provide a basis for later discussion which aims to establish regulatory approaches to better enable to the secondary research use of surplus tissue. The second part discusses approaches to consent and choice for the secondary research use of tissue which are noteworthy in the academic literature. Whilst the primary focus of my thesis is enabling access to surplus tissue samples in the absence of consent where the law provides for this, these approaches are important in providing key principles which ensure respect for patients – a key issue which I did not want to lose sight of when establishing regulatory approaches to better enable access to surplus tissue samples for secondary research purposes.

4.2. Consent: International and National Guidance

Here I set out the key policy and guidance instruments which apply to the secondary research use of surplus tissue and associated patient information, with particular focus on expectations with regards

[163] Beauchamp T. (2005) 'Autonomy and Consent' in Miller F, Wertheimer A (eds.) *The Ethics of Consent: Theory and Practice* Oxford University Press Scholarship Online
[164] Faden R R and Beauchamp T L. (1986) *A History and Theory of Informed Consent*. New York: Oxford University Press

to patient choice and consent. This is relevant in the context of my thesis because I will go on to propose regulatory approaches which, if implemented in practice, could better enable the availability of surplus tissue samples for secondary research purposes. For these regulatory approaches to be accepted in practice, it is important that they comply with, or at least do not significantly deviate from, established principles such as those set out in international and UK guidance relating to choice and consent for the use of tissue and associated patient information for secondary research purposes.

4.2.1. International Instruments and Guidance

The modern day understanding of consent as an ethical principle in medical research stems from the Nuremberg Code[165], containing ten principles which predicated ethical research, produced as part of the response to trials into Nazi war crimes. This led to the Declaration of Helsinki, produced by the World Medical Association[166], initially in 1964 although has been through a number of revisions and iterations during the intervening period[167]. Whilst the Declaration of Helsinki is not in itself legally binding, it does provide ethical principles which are considered to have primacy and are intrinsically embedded in ethical, and to some degree legal, standards[168]. In the current version (October 2013), paragraphs 25-32 relate to informed consent. However, only paragraph 32 relates to the use of human biological material or patient information:

> 'For medical research using identifiable human material or data, physicians must normally seek consent for the collection, analysis, storage and/or reuse. There may be situations where consent would be impossible or impractical to obtain for such research or would pose a threat

[165] Carlson R V, Boyd K M and Webb D J. The Revision of the Declaration of Helsinki: Past, Present and Future. *British Journal of Clinical Pharmacology.* 2004 **57(6)** 695 - 713

[166] World Medical Association (2013) *WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects*. Available at www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/

[167] Mason J K and Laurie G T. (2006) *Mason & McCall Smith's Law and Medical Ethics: Seventh Edition.* Oxford: Oxford University Press

[168] Rid A, Schmidt H. The 2008 Declaration of Helsinki – First Among Equals in Research Ethics. *Journal of Law, Medicine & Ethics*. 2010 **38(1)** 143-148

to the validity of the research. In such situations the research may be done only after consideration and approval of a research ethics committee.'[169]

Notably this paragraph refers to 'identifiable' human material and data, as the scope of the Declaration of Helsinki is limited to medical research which includes research on identifiable human material and data[170]. However, the notion of identifiability is not something that is a clear binary entity, particularly where tissue samples and associated patient information are *pseudonymised,* and therefore a coded link to the identifiable data is retained - the code to which is only accessible to persons with legitimate access to the identifiable information[171]. Identifiability in the context of the secondary research use of surplus tissue samples is an important concept in the broader context of my thesis because the real research value in surplus tissue is where tissue samples are linked with associated patient information[172]. Moreover, linking tissue samples and data necessarily raises issues of identifiability and therefore issues of privacy and confidentiality – this is something which I consider in more detail I chapter 5 of my thesis.

In 1997 the Council of Europe issued the Convention on Human Rights and Biomedicine[173] (Oviedo Convention), which is a legally binding instrument on human rights in relation to biology and medicine for Member States of the Council of Europe, as well non-Member States, which chose to be signatories. The UK was not a signatory of the Oviedo Convention and therefore it does not apply as a legally binding instrument in the UK. However, whilst not legally binding the UK, it is an important international instrument and therefore worthy of inclusion when considering UK regulation with regards to the secondary research use of surplus tissue in the context of international instruments and

[169] World Medical Association (2013) *WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects*. Available at www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/ paragraph 32
[170] *Ibid* paragraph 1
[171] Lowrance W. (2012) *Privacy, Confidentiality and Health Research.* Cambridge: Cambridge University Press
[172] Regidor E. The use of Personal Data from Medical Records and Biological Material: Ethical Perspectives and the Basis for Legal Restrictions in Health Research. *Social Science & Medicine*. 2004 **59** 1975-1984
[173] Council of Europe (1997) *Convention for the Protection of Human Rights and Dignity of the Human Being with regards to the Application of Biology and Medicine (Oviedo Convention).* Available at www.coe.int/en/web/conventions/full-list/-/conventions/treaty/164?module=treaty-detail&treatynum=164

guidelines. The Oviedo Convention does not include explicit reference to research involving human tissue. However, article 22 states that 'when in the course of an intervention any part of the human body is removed, it may be stored and used for a purpose other than that for which it was removed, only if this is done in conformity with appropriate information and consent procedures'[174]. In 2005 the Council of Europe published an 'Additional protocol to the Convention om Human Rights and Biomedicine, concerning Biomedical Research'[175]. This instrument aims to protect the dignity and identity of persons involved in 'interventional research', and therefore does not include the secondary research use of surplus tissue which was removed during clinically directed procedures and is surplus to diagnostic requirements within its scope. However, the Council of Europe has since published Recommendation Rec(2016)6, (which is a revised version of recommendation Rec(2006)4), of the Committee of Ministers to Member States on research in biological materials of human origin, which includes research involving human tissue which was previously collected for another purpose within its scope. Moreover, this document includes clarification regarding when human tissue is considered to be 'identifiable' and when it is considered to be 'non-identifiable'.

> '"identifiable biological materials" are those biological materials which, alone or in combination with data, allow the identification of the persons from whom the materials have been removed, either direct or through the use of code(s).'[176]

> '"non-identifiable biological materials" are those materials which, alone or in combination with data, do not allow, with reasonable efforts, the identification of the persons from whom the materials have been removed.'[177]

[174] Council of Europe (1997) *Convention for the Protection of Human Rights and Dignity of the Human Being with regards to the Application of Biology and Medicine (Oviedo Convention).* Available at www.coe.int/en/web/conventions/full-list/-/conventions/treaty/164?module=treaty-detail&treatynum=164 Article 22
[175] *Ibid*
[176] Council of Europe (2016) *Recommendation CM/Rec(2016)6.* Available at www.coe.int/en/web/bioethics/biobanks Article 3 paragraph 1 (i)
[177] *Ibid* Article 3 paragraph 1 (ii)

This distinction between 'identifiable' and 'non-identifiable' may be seen as a helpful clarification as it moves away from potential misconceptions around 'anonymisation' of data and samples[178], an issue which I consider in more detail in chapter 10. Where tissue samples which have been removed for another purpose and are 'non-identifiable', recommendation Rec(2016)6 permits the use of these samples for future research use as long as this is within the provisions of national legislation[179].

Whilst the HT Act 2004 (covering England, Wales and Northern Ireland[180]) does provide a legal basis for the use of surplus human tissue without consent where the samples will be non-identifiable to the person undertaking the research[181], the interpretation of 'non-identifiability' does differ from that defined in recommendation Rec(2016)6. This differing interpretation of identifiability is not a legal issue as such, as the UK was not a signatory to the Oviedo Convention or its additional protocols and moreover, Recommendation Rec(2016)6 is not legally binding. However, whilst there is no formal regulatory enforcement, these guidance documents do have importance as they provide consistent standards which can be applied internationally[182]. Moreover, differing interpretations of identifiability of human tissue samples risks adding to an already confused area of bioethics and law and to misunderstanding between different parties caused by varied terminology and can also limit international collaboration[183].

In 2016 The Council for International Organisations of Medical Sciences (CIOMS), in collaboration with the World Health Organisation (WHO), published 'International Ethical Guidelines for Health-related

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[178] Beier K and Lenk C (2011) 'A Unified European Approach on Tissue Research and Biobanking? A Comparison'. In Lenk C, Sándor J and Gordijn B (eds.) *Biobanks and Tissue Research: The Public, the Patient and the Regulation* (pp 143 – 164) Dordrecht: Springer

[179] Council of Europe (2016) *Recommendation CM/Rec(2016)6.* Available at www.coe.int/en/web/bioethics/biobanks Article 11 paragraph 3

[180] The Human Tissue Scotland Act 2006 applies in Scotland

[181] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 1 s. 1 ss. (7) – (9)

[182] Gibbons S MC. (2012) Mapping the Regulatory Space. In Kaye J, Gibbons S MC, Heeney C, Parker M, Smart A (eds.) *Governing Biobanks: Understanding the Interplay Between Law and Practice.* Oxford: Hart Publishing ltd.

[183] Elger B and Caplan A. Consent and anonymization in research involving biobanks. *European Molecular Biology Organization*. 2006 **7(7)** 661-666

Gibbons S MC. (2012) Mapping the Regulatory Space. In Kaye J, Gibbons S MC, Heeney C, Parker M, Smart A (eds.) *Governing Biobanks: Understanding the Interplay Between Law and Practice* (pp 51 – 92) Oxford: Hart Publishing ltd.

Research Involving Humans'[184]. These guidelines were the fourth version of the CIOMS guidelines, revising the 'International Ethical Guidelines for Biomedical Research Involving Human Subjects' previously issued in 2002, and merging with the 'International Guidelines for Ethical Review of Epidemiological Research', previously issued in 2009. The scope of the 2016 guidelines was broadened from 'biomedical research' to 'health-related research' to better incorporate research activities such as observational research, biobanking and epidemiological studies[185]. The aim of these guidelines, which are based on established ethical guidance documents such as the Declaration of Helsinki[186] and the Universal Declaration on Bioethics and Human Rights[187], is to provide internationally applicable ethical principles[188]. Guideline 11 of the 'International Ethical Guidelines for Health-related Research Involving Humans' provides guidance with regards to the collection, storage and use of biological materials and related data. Guideline 11 say that surplus tissue may be used for secondary research purposes where there are informed opt-out procedures which meet the following conditions - patients must be aware of the existence of the option to opt-out and the option to withdrawn any data, with a genuine option to opt-out being offered, and research which uses such samples and data should have important social value[189].

The acceptability and standards of an opt-out procedure for the secondary research use of surplus tissue are of particular relevance in the broader context of my thesis. In chapter 11 I identify

[184] Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO) (2016) *International Ethical Guidelines for Health-Related Research Involving Humans.* Available at cioms.ch/publications/product/international-ethical-guidelines-for-health-related-research-involving-humans/

[185] *Ibid* Preface pg ix

[186] World Medical Association (2013) *WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects.* Available at www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/

[187] United Nations Educational, Scientific and Cultural Organisations UNESCO (2005) *Universal Declaration on Bioethics and Human Rights*. Available at unesdoc.unesco.org/ark:/48223/pf0000142825.page=80 pg. 74 - 80

[188] van Delden J J M and van der Graaf R. Revised CIOMS International Ethical Guidelines for Health-Related Research Involving Humans. *Journal of the American Medical Association*. 2016 **317(2)** 135-136

[189] Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO) (2016) *International Ethical Guidelines for Health-Related Research Involving Humans.* Available at cioms.ch/publications/product/international-ethical-guidelines-for-health-related-research-involving-humans/ pg. 41

inconsistency across NHS organisations with regards to consent requirements for the secondary research use of surplus tissue, using 12 NHS organisations in England as a case study. In chapter 11 I conclude that a consistent policy approach across NHS organisations would be fairer, as it would allow equal opportunities for patients with regards to the donation of surplus tissue for secondary research purposes. Moreover, I conclude that the approach which, if applied consistently across all NHS organisations, would best address individual as well as broader societal interests, would be for surplus tissue samples to be available for secondary research purposes where there is no evidence of objection. Furthermore, I suggest that this approach should be supported by a well-publicised mechanism via which patients can record an objection (op-out), which is simple and easily accessible.

The CIOMS guidelines set out further requirements for the secondary research use of surplus tissue samples in the absence of consent, including where researchers propose to access tissue samples where there are no established opt-out procedures are in place[190]. The guidance says that research projects which intend to access surplus tissue samples without consent from the patient for secondary research use should be reviewed by a research ethics committee. Furthermore, the research ethics committee should consider whether the research could be carried out in circumstances such that consent has been given by patients, whether the research project has important social value and whether the research would pose no more than minimal risk to the patient. The CIOMS guidelines further require that research involving tissue samples should be undertaken in circumstances such that the confidentiality of the persons from whom the tissue was removed is respected and protected, whether by anonymisation of samples or by the use of key codes to link samples with data, in ways which mean that those undertaking the research do not have access to identifiable information[191].

[190] Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO) (2016) *International Ethical Guidelines for Health-Related Research Involving Humans.* Available at cioms.ch/publications/product/international-ethical-guidelines-for-health-related-research-involving-humans/ pg. 41

[191] *Ibid*

Safeguarding approaches when linking surplus tissue samples with associated patient information is an issue which I discuss in more detail in chapter 10.

This review of international instruments and guidance indicates that the UK position with regards to the secondary research use of surplus tissue samples in the absence of consent is broadly aligned with international standards. These international instruments and guidance do *prima facie* acknowledge the complexities with regards to obtaining consent for the secondary research use of surplus tissue samples and moreover that research ethics committees may have an important role in determining the acceptability of such practices on a cases by case basis - ensuring that donor interests would not likely be violated and that the research aims to address an important and valid research question. However, this is notwithstanding the question of whether provision in the HT Act 2004, with regards to tissue not being identifiable to the researcher, would meet the 'non-identifiability' standard as defined in recommendation Rec(2016)6. The HT Act 2004 is permissive of the secondary research use of surplus tissue samples in the absence of consent, where the research is ' carried out in circumstances such that the person carrying it out is not in possession, and not likely to come into possession, of information from which the person from whose body the material has come can be identified'[192]. This includes where a coded link is retained between the tissue sample and the person from whose body it originated, the code to which is not known to those undertaking the research and held securely by someone with legitimate authority to know the identity of the person[193].

4.2.2. UK National Instruments and Guidance

In the UK, the Department of Health published guidance regarding obtaining consent, originally in 2001 and re-published in 2009. This document primarily focuses on consent for examination, treatment and care. However, the revised edition also includes a section on the subsequent use of

[192] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 1 s 1 ss (9)(b)
[193] Thomas G (2014) Access to Human Cells and Tissues. In Coleman, R (ed.) *Human-Based Systems for Translational Research*. (pp 1 – 16) Royal Society of Chemistry

removed tissue[194], due to the HT Act 2004 having been enacted in 2006, bringing a change in legal requirements with regards to consent for the use and storage of tissue. This document does not provide explicit guidance, it merely summarises what the HT Act 2004 says with regards to consent requirements and refers the reader to the HTA code of practice on consent. However, this is an important document in the broader context of my thesis. In chapter 6 I use policies for the secondary research use of surplus tissue and requirements for consent from 12 NHS organisations in England as a case study to highlight the variation and inconsistency of approaches across different NHS organisations. In highlighting this, I suggest that this inconsistency of approach results in an unfair distribution of opportunities for patients to choose whether to donate surplus tissue samples for secondary research purposes and therefore to knowingly act on altruistic interests. The policies which I identified as part of this work all relate to obtaining consent for examination or treatment and are policies which include a section on the subsequent use of surplus tissue removed during clinically directed procedures. Therefore, whilst the Department of Health reference guide to consent for examination or treatment has a role in the context of the secondary research use of surplus tissue, it does not appear to be conducive to achieving a fair and consistent approach across NHS organisations in England, as chapter 6 will demonstrate.

Further UK guidance with regards to consent requirements for the research use of tissue is provided in the HTA code of practice on consent[195]. The HTA has a statutory responsibility to publish codes of practice and moreover, the HTA Act 2004 is explicit that such codes should deal with consent[196]. Whilst non-compliance with the codes of practice is not in itself unlawful[197], compliance with the codes does ensure compliance with the legislative provisions set out in the HT Act 2004 and moreover, the HTA has statutory authority to take any observations of non-compliance into consideration when carrying

[194] Department of Health (2009) *Reference Guide to Consent for Examination or Treatment (second edition).* Available at www.gov.uk/government/publications/reference-guide-to-consent-for-examination-or-treatment-second-edition S 1 paragraph 24-28
[195] Human Tissue Authority (2020) *HTA Code A: Guiding Principles and the Fundamental Principle of Consent.* Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20A.pdf
[196] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 2 s 26 ss 3
[197] *Ibid* S 28 ss 1

out its licensing functions and may result in revocation of a research licence[198]. The code of practice on consent sets out the HTA's guiding principles on consent, explains in detail the importance of consent as the fundamental principle in the HT Act 2004 and sets out the statutory requirements for consent provided via the Act[199].

The HTA code of practice on consent sets out the provision in the HT Act 2004, that the storage and use of tissue from living persons, where the research is ethically approved, and the research is to be carried out in circumstances such that the person carrying it out is not in possession of information which could identify the person from whom it was removed[200]. The code of practice indicates that although consent is not legally required, it is considered to be good practice when practical[201], but does not provide any further guidance with regards to the circumstances under which obtaining consent would or would not be considered to be practical.

In November 2014, the Medical Research Council (MRC) [202] published a guidance document entitled 'Human Tissue and Biological Samples for Use in Research: Operational and Ethical Guidance'[203]. This document further reiterates the importance of consent which is based on the principle that individuals should be afforded the choice with regards to their participation in research and that any such choice should be on the basis of appropriate information. However, in recognising that there are circumstances when it would not be practical to obtain consent, such as where surplus tissue is stored in a diagnostic archive, and that the law is permissive under certain circumstances, the MRC guidance puts forward two 'reasonableness tests' to determine if proceeding without consent would be

[198] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents s. 28 ss. 2
[199] Human Tissue Authority (2020) *HTA Code A: Guiding Principles and the Fundamental Principle of Consent.* Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20A.pdf
[200] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 1 s. 1 ss. (9)
[201] Human Tissue Authority (2020) *HTA Code A: Guiding Principles and the Fundamental Principle of Consent.* Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20A.pdf
[202] There is an expectation that this guidance is followed where research is funded wholly or in part by the MRC. However, guidance published by the MRC is generally considered to have authority for health research projects more broadly and therefore I consider this guidance worthy of reference in this context.
[203] Medical Research Council (2014) *Human Tissue and Biological Samples for use in Research: Operational and Ethical Guidelines.* Available at www.ukri.org/publications/human-tissue-and-biological-samples-for-use-in-research/

acceptable[204]. Consideration should be given to whether a reasonable person would likely have refused permission for their surplus tissue samples to be used for health research purposes and whether a reasonable person would likely be distressed if they discovered that their samples had been used for such a purpose[205]. However, as previously suggested (ss. 2.1), reasonable yet diverging views about human tissue are to be expected in a modern society as people will 'endorse diverse moral beliefs due to conflicting and complex evidence that bears on the selection of moral values'[206]. This therefore means that applying objective standards of reasonableness, which comply with individual preferences with regards to the secondary research use of surplus tissue, may be an imperfect approach.

In chapter 11 I argue that a consistent approach, to the availability of surplus tissue for secondary research purposes and requirements for consent, should be applied across NHS organisations as this would allow equality of opportunity for patients to choose whether their surplus tissue samples are used for such purposes. Moreover, I suggest that the approach which would best achieve individual patient and also public interest claims would be for surplus tissue to be available for secondary research use where there is no evidence that the patient has objected. Such an approach could supplement the reasonableness test provided by the MRC, by allowing tissue holders to confirm whether patients have registered an objection, thereby strengthening the reasonableness test with regards to whether individuals would likely refuse their permission for the secondary research use of their surplus tissue samples.

[204] Medical Research Council (2014) Human Tissue and Biological Samples for use in Research: Operational and Ethical Guidelines. Available at www.ukri.org/publications/human-tissue-and-biological-samples-for-use-in-research/

[205] *Ibid*

[206] Liddell K and Hall A. Beyond Bristol and Alder Hey: The Future Regulation of Human Tissue. *Medical Law Review*. 2005 **13(2**) 170-223 pg. 9.

4.3. Consent for the Secondary Research use of Tissue

4.3.1. Broad Consent

During the passage of the Human Tissue Bill through Parliament, questions were raised with regards to whether consent needed to be specific in relation to individual research projects or whether it could be broad, with one consent covering a range of research projects including future as yet undefined research projects[207]. Lord Warner was explicit in confirming that there would be no expectation that consent should be required for each individual research project and that a broad and enduring approach to consent would be permissible[208]. This is confirmed via the HTA code of practice on consent[209] which states that consent may either be specific to a research project or it may be broad consent which includes use of tissue in future, as yet undefined research projects. The HTA code of practice on consent recognises that broad consent offers the widest potential benefit for future research use, as well as the importance of ensuring that broad consent is supported by appropriate safeguards to ensure that any research use is within the terms of the consent given[210].

The acceptability of broad consent for the use of surplus tissue has been the subject of much debate. Petrini suggests that broad consent is often considered to be a favourable approach for the research use of surplus tissue because this type of research is generally considered to be low risk, often the exact detail of the research is unknown at the time of consent and it also avoids the burden associated with ongoing contact for each individual project[211]. Grady et al provide five reasons for obtaining consent for the research use of surplus tissue; respect for the person from whom the tissue was removed, enabling some control over what happens to the samples, an opportunity to accept potential risks or burdens and to decide whether to contribute to research as well as ensuring

[207] Lord Warner (2004) *'Human Tissue Bill'* Hansard: House of Lords Debates 22 July c. 369
[208] *Ibid*
[209] Human Tissue Authority (2020) *HTA Code A: Guiding Principles and the Fundamental Principle of Consent.* Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20A.pdf
[210] *Ibid*
[211] Petrini C. 'Broad' Consent, Exceptions to Consent and the Question of Using Biological Samples for Research Purposes Different from the Initial Collection Purpose. *Social Science and Medicine*. 2010 **70** 217-220.

transparency[212]. They suggest that broad consent does protect these interests whilst also helping to facilitate important research[213]. Moreover, they suggest that whilst people often indicate that they like to be asked whether they agree to their tissue being used for research purposes, their decision to donate tissue samples is often not affected by the detail of the future research[214].

Whilst there is generally support for a broad consent model for the secondary research use of surplus tissue, there is a general opinion that this should come with some limitations and safeguards. A broad consent model is considered to differ from a 'blanket' consent model because it is not open ended and does limit the purposes for which the tissue can be used[215]. A broad consent model is based upon the public interest argument and this therefore means that the tissue can only be used for research which people will generally consider to be acceptable and should not be used for purposes which would be inconsistent with the values of the person from whom the tissue was removed[216]. This may be achieved by ensuring that any research uses of surplus tissue under a broad consent model are ethically approved[217]. Moreover, a broad consent model should require that personal information is safeguarded, to protect confidentiality and privacy rights, and there should be a clear and easy way to withdraw consent at a later point[218].

Arguments against a broad consent model include that it does not provide the same level of respect for tissue donors as specific consent[219]. However, Hansson et al suggest that this argument is only

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[212] Grady C et al. Broad Consent for Research with Biological Samples: Workshop Conclusions. *The American Journal of Bioethics.* 2015 **15(9)** 34-42
[213] *Ibid*
[214] *Ibid*
[215] Nuffield Council on Bioethics (2011) *Human Bodies: Donation for Medicine and Research*. Available at www.nuffieldbioethics.org/publications/human-bodies-donation-for-medicine-and-research
Buden-Løsne I et al. Dynamic Consent: a potential solution to some of the challenges of modern biomedical research. *Journal of Medical Ethics*. 2017 **18(4)**
[216] Wendler D. Consent for Research with Biological Samples: One-Time General Consent Versus a Gift Model. *Annals of Internal Medicine*. 2012 **156(8)** 596-598
[217] Hansson M G et al. Should Donors be Allowed to Give Broad Consent to Future Biobank Research? *Lancet Oncology* 2006 **7** 266-69
[218] *Ibid*
Petrini C. 'Broad' Consent, Exceptions to Consent and the Question of Using Biological Samples for Research Purposes Different from the Initial Collection Purpose. *Social Science and Medicine*. 2010 **70** 217-220.
[219] *Ibid*

reasonable if obtaining specific consent does not limit the amount and/or the quality of the research which is undertaken[220]. Whilst individuals generally express that they would like to retain some control over whether their tissue samples are used for research purposes, they are generally also willing to allow research ethics committees to decide appropriate uses for their tissue samples without a requirement for specific detail about each individual research project[221].

In 2017 Ipsos MORI was commissioned by the Health Research Authority (HRA) and the Human Tissue Authority (HTA) to undertake a public dialogue to explore peoples' views in relation to consent for the use of human tissue and associated patient information in health-related research[222]. Participants were asked about their perception of broad consent and indicated a general acceptance of a broad consent model. While participants expressed that they would want to know what their tissues and data would be used for, there was a general acceptance that this should not prevent or restrict important research from taking place[223]. This view by members of the public reflects similar views expressed during an evaluation of public views about the HTA undertaken by Ipsos MORI[224] in 2007. This work found that there was a high level of confidence in the regulation of human tissue (52% confident, 24% not confident and 24% had no opinion) and as such, participants were supporting of their tissues being used for research purposes. Moreover, it was noted that acceptance of some risk was deemed to be reasonable where there was a regulatory and ethical framework which predefined acceptable and non-acceptable uses of tissue.

Hansson M G et al. Should Donors be Allowed to Give Broad Consent to Future Biobank Research? *Lancet Oncology* 2006 **7** 266-69

[220] Hansson M G et al. Should Donors be Allowed to Give Broad Consent to Future Biobank Research? *Lancet Oncology* 2006 **7** 266-69

[221] Wendler D. Consent for Research with Biological Samples: One-Time General Consent Versus a Gift Model. *Annals of Internal Medicine*. 2012 **156(8)** 596-598

[222] Ipsos MORI (2018) *Consent to use Human Tissue and Linked Health Data in Health Research. A Public Dialogue for Health Research Authority and Human Tissue Authority.* Available at www.hra.nhs.uk/documents/1570/Consent_to_use_human_tissue_and_linked_health_data_in_health_research_FINAL.pdf

[223] *Ibid*

[224] Ipsos MORI (2007) *Human Tissue Authority Stakeholder Evaluation: General Public Qualitative and Quantitative Research*. Available at www.ipsos.com/sites/default/files/migrations/en-uk/files/Assets/Docs/Archive/Polls/hta.pdf

Where research use of human tissue was contained within this framework then concerns about risks associated with the use of tissue was lessened and participants were willing to accept a broad awareness rather than more detailed information about each individual research use[225]. The secondary research use of surplus tissue within a regulatory framework which also applies appropriate regulatory and privacy safeguards is a key focus of my thesis. Furthermore, the importance of patient awareness with regards to the potential research value of surplus tissue, the potential for surplus tissue samples to be used for secondary research purposes to ensure that such activities are what patients expect and accept, and the regulatory and privacy safeguards which are applied, are key issues which are considered throughout my thesis.

4.3.2. Opt-out

Some scholars have argued that an opt out model (also referred to as 'deemed consent') would be preferable as this would increase the amount of research which could be undertaken using surplus tissue samples[226]. An opt-out approach means that a lack of objection is taken to indicate a person's acceptance[227]. However, for a lack of objection to truly represent a person's choice, it is important that an opt-out system is transparent and well organised, so that persons understand what their lack of objection means and any implications of this, and have a fair opportunity to register an objection[228].

Arguably the current legal position under the HT Act 2004 permits an opt-out approach , as there is legal provision for tissue stored in diagnostic archives to be used for research purposes without explicit consent, where the research is ethically approved and the research is carried out in circumstances

[225] Ipsos MORI (2007) *Human Tissue Authority Stakeholder Evaluation: General Public Qualitative and Quantitative Research*. Available at www.ipsos.com/sites/default/files/migrations/en-uk/files/Assets/Docs/Archive/Polls/hta.pdf

[226] Giesbertz N, Bredenoord A and van Delden J. Inclusion of Residual Tissue in Biobanks: Opt-in or Opt-out? *PLOS Biology*. 2012 **10(8)**
Riegman P and van Veen E. Biobanking Residual Tissues. *Human Genetics.* 2011 **130** 357-368
Van Veen E-B. Obstacles to European Research Projects with Data and Tissue: Solutions and further Challenges. *European Journal of Cancer*. 2008 **44** 1438-1450

[227] Giesbertz N, Bredenoord A and van Delden J. Inclusion of Residual Tissue in Biobanks: Opt-in or Opt-out? *PLOS Biology*. 2012 **10(8)**

[228] Riegman P and van Veen E. Biobanking Residual Tissues. *Human Genetics.* 2011 **130** 357-368

such that the person carrying it out is not in possession of information which could identify the person from whom the tissue was removed[229]. Moreover, the CIOMS 'International Guidelines for Health-Related Research Involving Humans'[230] permits reliance on informed opt-out procedures, as an alternative to requirements for consent, for the secondary research use of surplus tissue. However, for an opt-out procedure to be considered sufficient, it must be genuine, and patients must be aware that they can opt-out of their tissue and data being used for secondary research purposes[231]. Evidence suggests that people are often unaware that their surplus tissue samples have a potential research value[232] and therefore in the absence of a well-publicised mechanism to record an objection, lack of objection could not necessarily be taken to indicate a person's choice with regards to the secondary research use of their surplus tissue samples.

Reigman and van Veen favour an opt out approach based on the assumption that when asked, the majority of people are willing to donate their surplus tissue samples because they want to contribute to the public good[233]. Moreover, van Veen suggests that research using surplus tissue should be considered as 'observational' research and therefore should be distinguished from research which is 'interventional', thus an opt out model should be acceptable[234]. This is an important point in the context of my thesis because I focus on research which uses surplus tissue samples which are stored in diagnostic archives and therefore there is a clear separation between the 'intervention' during which the tissue sample was removed and any secondary research use.

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[229] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 1 s1 ss (9)
[230] Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO) (2016) *International Ethical Guidelines for Health-Related Research Involving Humans.* Available at cioms.ch/publications/product/international-ethical-guidelines-for-health-related-research-involving-humans/
[231] *Ibid*
[232] Ipsos MORI (2018) *Consent to use Human Tissue and Linked Health Data in Health Research. A Public Dialogue for Health Research Authority and Human Tissue Authority.* Available at www.hra.nhs.uk/documents/1570/Consent_to_use_human_tissue_and_linked_health_data_in_health_research_FINAL.pdf
[233] Riegman P and van Veen E. Biobanking Residual Tissues. *Human Genetics.* 2011 **130** 357-368
[234] Van Veen E-B. Obstacles to European Research Projects with Data and Tissue: Solutions and further Challenges. *European Journal of Cancer*. 2008 **44** 1438-1450

Giesbertz et al also support an opt-out approach for the use of surplus tissue samples in health-related research[235]. This view is based on research involving surplus tissue being low risk, and also due to the large number of samples which are required to achieve meaningful results. They suggest that acceptability of an op-out approach is supported by the evidence that the majority of people are willing for their samples to be used for research purposes. However, Geisbertz et al also acknowledge the risk that an opt-out approach could lead to negative attitudes where people object to their tissue samples having been used without their explicit consent; potentially resulting in high levels of people opting out[236]. This appears to have been evident with the care.data initiative which provided an opt-out mechanism with regards to the use of primary care data for purposes beyond direct healthcare.

Care.data was implemented in England in 2013 and subsequently paused 6 months later due to overwhelming concern expressed by members of the public as well as professionals, resulting in over a million people opting out of their data being used[237]. One reason posited for this was a failure to instil trust due to inadequate publicity and infrastructure by which to express a choice to op-out[238]. Since the care.data initiative was abandoned, another GP data sharing initiative has been implemented in England. The National Data Opt-Out was introduced in 2018 and means that patients can opt out of their confidential data being used for purposes beyond their direct healthcare, such as for research purposes or for NHS service planning[239]. Whilst the initiative was introduced in 2018, the full roll out has been delayed until 31 March 2022 to ensure that the opt out system which supports this initiative is fit for purpose and to ensure that there has been an effective campaign to raise awareness[240]. In establishing regulatory approaches which are more enabling of surplus tissue being

[235] Giesbertz N, Bredenoord A and van Delden J. Inclusion of Residual Tissue in Biobanks: Opt-in or Opt-out? *PLOS Biology*. 2012 **10(8)**

[236] *Ibid*

[237] Carter P, Laurie G T and Dixon-Woods M. The Social Licence for Research: Why care.data Ran into Trouble. *Journal of Medical Ethics*. 2015 **41** 404-409

[238] *Ibid*

[239] *NHS. Sharing your Health Records* (2018) Available at www.nhs.uk/using-the-nhs/about-the-nhs/sharing-your-health-records/

[240] Lord Bethell (2021) *'NHS Digital: Primary Care Medical Records'* Hansard: House of Lords Debates 8 June c. 1320

available for secondary research purposes, it is therefore important to consider matters beyond what is merely lawful and also consider what would be 'accepted' by patients and the public.

Empirical work has been undertaken to understand peoples' views on the acceptability of an opt out model of consent. Lewis et al[241] undertook a study which involved two approaches, focus groups and the issuing of a questionnaire. This study found that the majority of focus group attendees preferred an opt out approach (57%) compared to an opt in (36%) approach (7% were unsure). The reasons put forward for preferring this approach were that it would ensure that more samples were available for research purposes, it would be less burden administratively as well as less burdensome for patients - while also ensuring that people could retain some control by ensuring that they had the opportunity to refuse if they so wish.

This opinion supports the outcome from work undertaken by Bryant et al[242] and Botkin et al[243] which also found that the majority of people asked preferred an opt out model. However, Lewis et al[244] also found that the majority of questionnaire responders (55%) favoured an opt in approach (28% preferred opt-out, 14% had no preference and 4% did not know). One potential reason posited by Lewis et al as to why the percentage preferring an opt out model was higher in the focus group attendees rather than the questionnaire respondents was that the focus group attendees had been provided with additional information with regards to the value of surplus tissue in research and they were therefore better informed[245]. Giesbertz et al suggest that an opt out model would be justifiable where there is a good level of information available to patients to ensure that they are aware of the potential research use of their surplus tissues and to ensure that they have a clear understanding of

[241] Lewis C, Clotworthy M, Hilton S et al. Consent for the use of Human Biological Samples for Biomedical Research: A Mixed Methods Study Exploring the UK Public's Preferences. *British Medical Journal Open*. 2013 **3**
[242] Bryant et al. Ownership and uses of Human Tissue: What are the Opinions of Surgical In-Patients? *Journal of Clinical Pathology* 2008 **61** 322-326
[243] Botkin J R, Anderson R, Stark L A, Mitchell J. Public Attitudes Regarding the use of Electronic Health Information and Residual Clinical Tissues for Research. *Journal of Community Genetics*. 2014 **5** 205-213
[244] Lewis C, Clotworthy M, Hilton S et al. Consent for the use of Human Biological Samples for Biomedical Research: A Mixed Methods Study Exploring the UK Public's Preferences. *British Medical Journal Open*. 2013 **3**
[245] *Ibid*

the option to opt out which is available to them[246]. Giesbertz et al refer to this as a 'thick' opt out method as it puts significant emphasis on the information which is provided to patients and moreover, it is suggested that this model would not be appropriate where research may have higher risks or burdens, is controversial or research involving sensitive tissue types.

In a study by Williams et al exploring the views of surplus tissue donation for research purposes in patients who had undergone surgical resection of a malignant colorectal tumour, it was noted that in some cases, an opt *in* method of consent was not found to be as empowering for patients as had been anticipated[247]. Patients who participated in this study commonly expressed that donation of any surplus tumour tissue for future research use was 'no big deal', certainly compared to the experience of cancer diagnosis and treatment, and that they were very supportive of samples being used for research purposes[248].

This view of tissue banking for future research being no big deal compared to the experience of diagnosis and treatment was also noted in in studies by Hamilton et al[249] and Soto et al[250], which sought the views from parents and patients with regards to obtaining consent for the future use of tissue samples removed from patients with cancer, including children. Participants in these studies commented that donating tissue for research was a minor issue compared to the illness and the surgical procedure and was accepted as something that was positive and should be encouraged. Moreover, in the study by Soto et al, it was noted that a more general awareness of tissue banking for

[246] Giesbertz N, Bredenoord A and van Delden J. Inclusion of Residual Tissue in Biobanks: Opt-in or Opt-out? *PLOS Biology*. 2012 **10(8)**

[247] Williams A M et al. Consent to Donate Surgical Biospecimens for Research: Perceptions of People with Colorectal Cancer. *Cancer Nursing*. 2016 **39(3)** 221-227

[248] *Ibid*

[249] Hamilton S et al. Consent Gained from Patients after Breast Surgery for the use of Surplus Tissue in Research: An Exploration. *Journal of Medical Ethics*. 2007 **33** 229-233

[250] Soto C et al. Consent to Tissue Banking for Research: Qualitative Study and Recommendations. *Archives of Diseases in Childhood*. 2012 **97** 632-636

future research would have been welcomed as this was an additional decision to make at what was an already extremely stressful time for the parents and children[251].

The importance of patients having some awareness of biobanking practices and the value which surplus tissue can have for research purposes was also identified by Axler et al[252] when undertaking a review of the literature relating to the reasons cited for donation and refusal to donate tissue. They concluded that one possible reason for patients refusing to donate surplus tissue samples for secondary research use is a lack of awareness about biobanking and tissue research which means that patients are required to understand a concept which may be completely new to them, as well as make a decision about whether to donate their surplus tissue samples, at what may be a difficult time for patients[253]. With this in mind, the value of raising general awareness with regards to tissue research practices, particularly in the context of an infrastructure which enables patients to object to their surplus tissue samples being used for secondary research purposes, is a key part of my thesis - something which is discussed in more detail in chapter 11.

4.3.3. Precautionary Consent

During the passage of the Human Tissue Bill through the House of Lords, discussion also took place with regards to consent for future research use of surplus tissue being taken alongside consent for clinical or surgical procedures and recorded in an additional box on standard consent forms[254]. This approach, where consent is routinely taken from patients when undergoing procedures which involve the removal of tissues is sometimes referred to as 'precautionary' consent[255]. This involves routinely asking patients to consent to future research use, even where there is no clear intention for tissue to

[251] Soto C et al. Consent to Tissue Banking for Research: Qualitative Study and Recommendations. *Archives of Diseases in Childhood*. 2012 **97** 632-636
[252] Axler R E, Irvine E, Lipworth W, Morrell B, Kerridge I H. Why Might People Donate Tissue for Cancer Research? Insights from Organ/Tissue/Blood Donation and Clinical Research. *Pathobiology.* 2008 **75** 323-329
[253] *Ibid*
[254] Baroness Finlay (2004) '*Official Report of the Grand Committee on the Human Tissue Bill*' Hansard: House of Lords 15 September c. GC 419
[255] Gefenas E et al. Turning Residual Human Biological Materials into Research Collections: Playing with Consent. *Journal of Medical Ethics* 2012 **38** 351-355.

be used for research purposes, so that there is consent in place should this be required in the future. However, concerns have been raised with regards to the practicalities of implementing this approach within existing infrastructures.

During the second reading of the Human Tissue Bill in the House of Commons, reference was made to the Royal College of Pathologists having raised concern that it would be necessary to implement a system which ensured that the express decisions of all patients could be efficiently retrieved and confirmed prior to any research use of surplus tissue samples[256]. An effective system to achieve this would likely require significant resource to establish and it was not evident that any such resource would be made available[257]. During the second reading of the Human Tissue Bill in the House of Lords, Baroness Cumberlege referred to an audit undertaken at Leeds Teaching Hospital NHS Trust which found that only 48% of tissue samples received in the laboratory had a corresponding consent form and of these forms, 40% did not have the tissue section completed. This was despite the same study finding that less than 5% of patients expressed an objection to their surplus tissue samples being used for research purposes when asked[258].

Moreover, the study at Leeds Teaching Hospital NHS Trust also identified variation between the health professional roles and departments when completing the section on the surgical consent form which related to future research use of surplus tissue. This study, undertaken by Wheeler et al, looked at all surgical consent forms received in the histopathology department at the Trust between October – November 2002 and October – November 2003[259]. This study identified a marked difference in practice between clinical departments, individual persons and groups of consent takers when it came to completion of the section relating to the future research use of surplus tissue samples. For example, it was identified that 89% of consent forms returned by nurses had a fully completed tissue research

[256] Burstow P (2004) *'Human Tissue Bill'* Hansard: House of Commons Debates 15 January c. 1011
[257] *Ibid*
[258] Baroness Cumberlege (2004) *'Human Tissue Bill'* Hansard: House of Lords Debates 22 July c. 402
[259] Wheeler J et al. Experiences from the Front-Line Routine Consenting of Surplus Surgically Removed Tissue: Without Investment by the National Health Service Fully Informed Consent is Not Available. *Journal of Clinical Pathology.* 2007 **60** 351-354

section but this was true for only 41% of consent forms returned by junior doctors. Moreover, of the completed forms received, clinical departments such as anaesthetics and oncology had a consent rate of 100% whereas the urology department had a consent rate of only 69%[260].

Whilst the study does not draw real conclusions on the reasons for this variation, it was evident that the variation was likely to be due to factors other than mere patient choice[261]. Whilst the study by Wheeler et al was undertaken almost 20 years ago, it does indicate that a 'precautionary' approach to consent is unlikely to be successful in practice without appropriate resources and infrastructure. Moreover, a study undertaken in 2016-17 which surveyed the views of individuals who had some involvement with human tissue research indicated that almost 15 years after the study in Leeds, there was still no effective precautionary consent model in place across the NHS[262]. In some cases, there is no tissue research section within surgical consent forms and where the tissue research section has been included, there is often a lack of understanding and awareness in the clinical setting where consent is being obtained[263].

There are significant practical implications with an approach which requires evidence of consent for the secondary research use of surplus tissue, even on a precautionary consent basis. This is particularly the case when obtaining precautionary consent on a whole population level, such as would be required for all surplus tissue samples to be potential research samples. Obtaining consent for the secondary research use of surplus tissue adds time to routine clinical interactions, which may not be significant on an individual patient level but is significant when considered on a whole population level[264]. An estimate quoted in discussions during the passage of the Human Tissue Bill through

[260] Wheeler J et al. Experiences from the Front-Line Routine Consenting of Surplus Surgically Removed Tissue: Without Investment by the National Health Service Fully Informed Consent is Not Available. *Journal of Clinical Pathology.* 2007 **60** 351-354
[261] *Ibid*
[262] Macklin P et al. Barriers to the Release of Human Tissue for Clinical Trials in the UK: A National Survey of Cellular Pathology Laboratories on Behalf of the National Cancer Research Institute's Molecular Pathology (CM-Path) Initiative. *Journal of Clinical Pathology*. 2019 **72** 52-57
[263] *Ibid*
[264] Coleman M P, Evans B G and Barrett G. Confidentiality and the Public Interest in Medical Research – Will We Ever Get it Right? *Journal of Clinical Medicine.* 2003 **3** 219-228

parliament was that 3 million solid tissue samples are removed during clinically directed procedures each year in the UK[265]. This volume of tissue samples would therefore require significant resource infrastructure to request and record consent for secondary research use, even on a precautionary consent basis. Moreover, precautionary consent which is incorporated within clinical or surgical consent procedures and documents means that where consent is not requested, there is limited opportunity to go back[266].

Where the opportunity to obtain precautionary consent has passed, consideration needs to be given to how to proceed with regards to the secondary research use of such samples, as arguably too much focus on continued attempts to confirm consent, where consent it not required for research activities to be lawful, may result in missed research opportunities[267]. Prohibiting the research use of legitimately held tissue samples, where secondary research use would be lawful, does not necessarily protect any patient interests which would otherwise be breached and moreover, there is no clear public benefit[268]. Therefore, where the law provides for the secondary research use of surplus tissue samples, then an approach which requires consent to be obtained, even on a precautionary basis, is not necessarily the best approach. Moreover, without significant resources being made available to develop and maintain the necessary infrastructure to support such a model, it is unlikely to be wholly successful in practice and therefore inconsistently applied within individual NHS organisations as well as across different NHS organisations, something which I discuss in more detail in chapter 11.

4.3.4. Electronic Recording of Consent

An alternative to the paper consent form approach is electronic recording of consent. Advances in the use of technology to obtain and record consent for research practices, including the secondary

[265] Burstow P (2004) *'Human Tissue Bill'* (2004) Hansard: House of Commons Debates 15 January c. 1011
[266] Riegman P and van Veen E. Biobanking Residual Tissues. *Human Genetics.* 2011 **130** 357-368
Manson N C and O'Neill O (2007) *Rethinking Informed Consent in Bioethics*. New York: Cambridge University Press
[267] Brownsword R. The Cult of Consent: Fixation and Fallacy. *King's Law Journal*. 2004 **15(2)** 223-251
[268] Manson N C and O'Neill O (2007) *Rethinking Informed Consent in Bioethics*. New York: Cambridge University Press

research use of tissue[269], has significant potential to streamline and even personalise mechanisms to request and record consent[270]. Electronic consent models have the potential to reach more people, providing information using on-line platforms which can be layered to provide levels of information preferred by individual patients, and therefore has the potential to enhance patient engagement[271].

In this section I start by setting out two electronic consent models which have been proposed in the academic literature in recent years as potential alternatives to paper based consent models for the secondary research use of tissue and data – dynamic consent and meta consent. To not include reference to these models when discussing electronic consent models would be omissive due to their prominence in the academic literature in the field of tissue and data research. However, as I will go on to suggest, I do not propose that such models should be applied for the secondary research use of surplus tissue which is stored in diagnostic archives. My reason for this is that my thesis aims to develop regulatory approaches which enable the secondary research use of surplus tissue samples in the absence of consent, where the law provides for this. Therefore, the implementation of potentially complex consent models is not in keeping with my overall thesis aim. The second part of this section considers more simplified approaches which I argue could be applied in the context of the secondary research use of surplus tissue samples store in diagnostic archives.

4.3.4.1. Dynamic Consent

The concept of electronically recording consent for future, as yet undefined research uses of surplus tissue and also associated health data, has been discussed under the term 'dynamic consent'[272]. The

[269] Boutin N T et al. Implementation of Electronic Consent at a Biobank: An Opportunity for Precision Medicine in Research. *Journal of Precision Medicine.* 2016 **6(17)** 1-11
[270] Shelton R H. Electronic Consent Channels: Preserving Patient Privacy Without Handcuffing Researchers. *Science Translational Medicine.* 2011 **3(69)** 1-3
[271] Boutin N T et al. Implementation of Electronic Consent at a Biobank: An Opportunity for Precision Medicine in Research. *Journal of Precision Medicine.* 2016 **6(17)** 1-11
[272] Kaye J et al. Dynamic Consent: A Patient Interface for Twenty-First Century Research Networks. *European Journal of Human Genetics.* 2015 **23** 141-146
Williams H et al. Dynamic Consent: A Possible Solution to Improve Patient Confidence and Trust in How Electronic Patient Records Are Used in Medical Research. *JMIR Medical Informatics.* 2015 **3(1)**
Prictor M, Teare H and Kaye J. Equitable Participation in Biobanks: The Risks and Benefits of a "Dynamic Consent" Approach. *Frontiers in Public Health*. 2018 **6(253)**

term dynamic consent was established in 2008 as part of the 'Ensuring Consent and Revocation Project', which aimed to establish ways for persons to have greater control over their tissues and samples, particularly in the field of biobanking where many years can pass from the time the initial consent is given. The proposal as part of this project was that consent should be as easy to turn on and off as a tap[273]. Dynamic consent was intended to be a new approach which could be used to engage individuals with regards to the use of their tissue and data and allows the opportunity to alter their consent choices in real time[274]. This approach may be relevant where there are likely to be multiple and varied uses of data which could require different types of consent over a long period of time[275].

A dynamic consent model uses an electronic platform which can attach and send consent preferences with tissue and data when transferred out of the tissue bank so that the tissue and data are only used for purposes for which the individual has given their consent[276]. This therefore allows the option to have different preferences for different types of research. Moreover, this electronic platform can also be used to inform individuals about research projects which they may want to participate in and provide updates with regards to research projects they have already participated in[277]. Proponents of a dynamic consent approach claim that this approach addresses issues around autonomy of choice and respect for persons in ways which are not achieved by a one-time broad consent model[278]. Furthermore, it is suggested that the electronic approach is preferable to the paper-based approach which has historically been used, where individuals sign a form which is then centrally stored. It is suggested that the paper-based approach is not conducive for secondary research use of tissues and

Stein D T and Terry S F. Reforming Biobank Consent Policy: A Necessary Move Away from Broad Consent Towards Dynamic Consent. *Genetic Testing and Molecular Biomarkers*. 2013 **17(2)** 855-856

[273] Teare H, Prictor M and Kaye J. Reflections on Dynamic Consent in Biomedical Research: The Story So Far. *European Journal of Human Genetics*. 2021 **29** 649-656

[274] Kaye J et al. Dynamic Consent: A Patient Interface for Twenty-First Century Research Networks. *European Journal of Human Genetics.* 2015 **23** 141-146

[275] *Ibid*

[276] *Ibid*

[277] *Ibid*

[278] *Ibid*

data, due to the potentially numerous research projects for which they could be used and the lack of ongoing engagement[279].

A dynamic consent approach is based on a moral principle of autonomy of choice and often extends beyond actual legal requirements of consent for secondary use of tissues and data, as the tissues and data are non-identifiable when they are supplied by biobanks to researchers. Where tissues and data are non-identifiable, broad consent for future research use is *legally* sufficient[280]. However, it has been suggested that a *legal* basis may not be enough and therefore a *moral* basis should additionally be sought. An example of where a *legal* basis was not considered to be sufficient when proposing to use non-identifiable patient information for secondary purposes, including research, was the care.data initiative which aimed to extract data from Primary Care NHS records, unless patients had opted out, for secondary purposes including research[281]. Carter et al suggest that even where the secondary use of patient data in an anonymised format may be lawful, there is an additional requirement to ensure that there is not only public awareness, but also public acceptance[282].

This 'social licence' supporting secondary use of anonymised data may therefore be more permissive than a purely regulatory approach[283]. Whilst those involved in the field of health research may be confident that sharing data using safeguards such as safe havens[284] will protect patient confidentiality, the public understanding of such initiatives is limited[285]. Williams et al considered whether a dynamic consent approach to consenting to the secondary use of primary care data would be preferable[286].

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[279] Kaye J et al. Dynamic Consent: A Patient Interface for Twenty-First Century Research Networks. *European Journal of Human Genetics.* 2015 **23** 141-146

[280] See *R v Department of Health ex parte Source Informatics* [2000] 1 All ER 786 regarding the legal status of the use of non-identifiable patient information.

[281] Carter P, Laurie G T and Dixon-Woods M. The Social Licence for Research: Why care.data Ran into Trouble. *Journal of Medical Ethics*. 2015 **41** 404-409

[282] *Ibid*

[283] *Ibid*

[284] 'Safe Havens' are data repositories where data are stored and accessed securely in a way which reliably maintains the fidelity and quality of the data, but also controls access to the data in ways which ensure that relevant legal and ethical expectations with regards to data access are met.

[285] Williams H et al. Dynamic Consent: A Possible Solution to Improve Patient Confidence and Trust in How Electronic Patient Records Are Used in Medical Research. *JMIR Medical Informatics*. 2015 **3(1)**

[286] *Ibid*

This was on the basis that it would be more inclusive than the opt out approach which was initially proposed under the care.data initiative, as it requires patients to confirm their consent. They suggest that the two way communication element of a dynamic consent model may in itself help to raise awareness and understanding and therefore to achieve a 'social licence' due to secondary research use being something that is expected and therefore more likely to be accepted[287].

Whilst the dynamic consent model does appear to address some concerns with regards to the ongoing use of tissue and data in research, there are some notable limitations with such an approach. Some argue that reliance on electronic systems risks creating a 'digital divide' between those who routinely access electronic platforms and those who do not or are unable to - due to not owning appropriate devices or due to living in a remote area with limited or no internet access[288]. Moreover, questions have been raised with regards to whether individuals really want this level of interaction, communication and choice[289]. Public involvement events where the dynamic consent approach has been presented have indicated that whilst increased choice appears *prima facie* to ensure greater autonomy of choice, in reality updating and amending consent choices was not considered to be something that people would do in practice[290]. Moreover, it has been observed that where biobanks are using the dynamic consent approach[291], individuals rarely amend their consent preferences from those set at the time of initial participation[292].

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[287] Williams H et al. Dynamic Consent: A Possible Solution to Improve Patient Confidence and Trust in How Electronic Patient Records Are Used in Medical Research. *JMIR Medical Informatics*. 2015 **3(1)**

[288] Steinsbekk K S, Myskja B K and Solberg B. Broad Consent Versus Dynamic Consent in Biobank Research: Is Passive Participation an Ethical Problem? *European Journal of Human Genetics.* 2013 **21** 897-902

[289] *Ibid*

[290] Teare H, Prictor M and Kaye J. Reflections on Dynamic Consent in Biomedical Research: The Story So Far. *European Journal of Human Genetics*. 2021 **29** 649-656

Ipsos MORI (2018) *Consent to use Human Tissue and Linked Health Data in Health Research. A Public Dialogue for Health Research Authority and Human Tissue Authority.* Available at www.hra.nhs.uk/documents/1570/Consent_to_use_human_tissue_and_linked_health_data_in_health_research_FINAL.pdf

[291] For example, the RUDY (Rare Diseases of Bone, Joints and Blood Vessels) study. Teare H et al. The RUDY Study: Using Digital Technologies to enable a Research Partnership. *European Journal of Human Genetics* 2017 **25** 816 - 822

[292] Teare H, Prictor M and Kaye J. Reflections on Dynamic Consent in Biomedical Research: The Story So Far. *European Journal of Human Genetics*. 2021 **29** 649-656

There were further suggestions that increasing flexibility to amend consent preferences could negatively impact on research quality if datasets were frequently altering over time[293]. Whilst individuals indicated that they would not likely use a dynamic consent platform to amend their consent choices, there does appear to be a strong preference for greater communication with regards to the research projects being undertaken[294]. However, Steinsbekk et al suggest that this is not something that is particular to a dynamic consent model as such, it's just that a dynamic consent platform could provide this service which is otherwise provided in different ways[295]. Later in this section I refer to more simplified electronic models which could provide opportunities to engage with patients and provide opportunities to choose whether their surplus tissue is used for secondary research purposes.

4.3.4.2. Meta consent

Whilst a dynamic consent platform is intended to provide greater flexibility of choice by affording individuals the opportunity to set different consent preferences for different research uses of tissue and data, it has further been suggested that individuals should be able to choose the type of consent which they give more broadly. Meta consent is a proposed approach whereby individuals have greater choice over the type of consent which they give for research[296]. Similar to a dynamic approach, meta consent uses an electronic interface which presents patients with options to give broad consent for research within defined parameters, the opportunity to consent to each and every project or for blanket agreement or refusal[297].

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[293] *Ibid*

[294] Teare H, Prictor M and Kaye J. Reflections on Dynamic Consent in Biomedical Research: The Story So Far. *European Journal of Human Genetics*. 2021 **29** 649-656

[295] Steinsbekk K S, Myskja B K and Solberg B. Broad Consent Versus Dynamic Consent in Biobank Research: Is Passive Participation an Ethical Problem? *European Journal of Human Genetics.* 2013 **21** 897-902

[296] Ploug T and Holm S. Going Beyond the False Dichotomy of Broad or Specific Consent: A Meta-Perspective on Participant Choice in Research Using Human Tissue. *The American Journal of Bioethics*. 2015 **15(9)** 44-46

[297] Ploug T and Holm S. Meta Consent: A Flexible and Autonomous Way of Obtaining Informed Consent for Secondary Research. *British Medical Journal.* 2015 **350**

Proponents of a meta consent model suggest that this approach better meets the autonomy interests of individuals who agree to participate in biobank research because participation is not a one-off donation of tissue and data, it often requires ongoing access to 'health data' and is therefore an ongoing relationship[298]. Moreover, due to the ongoing access to 'health data' over a potentially long period of time, there is a risk that the nature of the research being undertaken and even the understanding of what is meant by 'health data' can change. Therefore, consent models which do not accommodate an option for ongoing interaction have the potential to expire over time - an issue which is seemingly addressed by a meta consent model[299].

However, the moral importance of respecting autonomy via consent must be balanced with ensuring that important research is not delayed or prevented and therefore, the likely significant cost of a complex consent model which relies on an administrative system which track and respond to individual choices has been highlighted as a potential issue which could limit research[300]. Whilst such costs could arguably be met as part of funding arrangements for some biobanks[301], this is not necessarily the case for NHS based biobanks where resources are limited. Taking the potentially significant costs of a meta consent model into consideration, it has been suggested that to *not* offer the level of individual choice provided by a meta consent model would not actually harm participants[302].

Whilst a meta consent model may be a 'nice to have', all things considered it may not add sufficient real-world value to make the costs and potential limitations on research worthwhile. This is particularly the case within a resource limited NHS where the law is permissive of the secondary

[298] Ploug T and Holm S. The Biobank Consent Debate: Why 'Meta-Consent' is Still the Solution! *Journal of Medical Ethics*. 2019 **45** 295-297
[299] Ploug T and Holm S. The 'Expiry Problem' of Broad Consent for Biobank Research – And Why a Meta Consent Model Solves it. *Journal of Medical Ethics.* 2020 **46(9)** 629-631
[300] Manson N C. The Biobank Consent Debate: Why 'Meta Consent' is not the Solution? *Journal of Medical Ethics.* 2019 **45** 291-294.
[301] Ploug T and Holm S. The Biobank Consent Debate: Why 'Meta-Consent' is Still the Solution! *Journal of Medical Ethics*. 2019 **45** 295-297
[302] Manson N C. The Biobank Consent Debate: Why 'Meta Consent' is not the Solution? *Journal of Medical Ethics.* 2019 **45** 291-294.

research use of surplus tissue samples in the absence of consent. A simple binary choice between participating and not participating, on the basis of broad principles which acknowledge that the future may bring changes may therefore be preferable, particularly where there is emphasis on other safeguarding mechanisms, such as ethical review of research projects proposing to access data and tissue[303].

4.3.4.3. Electronic Mechanisms to Register Objection

So far in this section I have set out two electronic consent models which have been discussed in the academic literature as potential models to obtain and manage preferences for the research use of tissue and data, suggesting that such potentially complex models may not be appropriate for the secondary research use of surplus tissue which is stored in NHS diagnostic archives. I will now go on to consider electronic approaches which may be appropriate in this context, as they allow patients to choose whether their surplus tissue samples are used for such purposes without applying complex consent models. A potential benefit of using electronic models to request and record patient preferences with regards to the secondary research use of their tissue samples is that it provides an alternative to a paper consent form model. As suggested in ss. 4.3.3, one of the challenges with a paper consent form model is ensuring that the pathologist within a diagnostic archive is able to confirm the preferences of the patient with regards to the secondary research use of their tissue samples when deciding whether to release tissue samples to researchers. This relies on the paper form being sent to the diagnostic archive with the tissue sample and for there to be an effective mechanism in place to store this information so that it can be confirmed later if required.

The recording of consent to future research use of surplus tissue samples being linked to electronic medical records does appear to have been the intention of the UK Government when introducing the HT Act 2004. In the second reading of the Human Tissue Bill in the House of Lords, Lord Warner stated:

[303] Chen D T, Rosenstein D L, Muthappen P et al. Research with Stored Biological Samples: What Do Research Participants Want? *Journal American Medical Association Archives of Internal Medicine*. 2005 **165** 652-655

> 'We certainly envisage that once electronic patient records are introduced, mechanisms can be used to record each patients' consent on that record so that it will be clear and available to all health professionals with access to it.'[304]

The actual roll out of electronic health records has however been slow and fraught with problems[305]. In 2014 the NHS set out its plan to better incorporate technology, with the aim of improving care as well as patient access[306]. More recently, in the 2019 NHS Long Term Plan, there was significant focus on digitally enabling access to NHS services[307]. A key part of the digital strategy was the roll out of the NHS App, described by some as the 'the digital front door to the NHS'[308]. The NHS App can be used by patients to undertake activities such as viewing their GP records, booking appointments and requesting repeat prescriptions. However, the NHS App also includes functionality to set preferences with regards to organ donation and the sharing of data for purposes other than direct care[309].

There was been a significant increase in the number of people who had downloaded the NHS App in recent months, due to the NHS App also functioning as a 'vaccination passport', providing evidence of vaccination against SARS-CoV-2 (COVID 19). As of 24 August 2021, the NHS App had recorded 14,184,019[310] signed up users, of which 11,522,141 users had fully verified their identity in the system - which means that they are able to access the full range of services provided by the NHS App. This was a significant increase from 131,321 users who had fully verified their identity in the system (there are no figures available for the number of non-verified users at this time) as of 31 January 2020[311].

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[304] Lord Warner (2004) *'Human Tissue Bill'* Hansard: House of Lords Debates 22 July cc. 429 – 430

[305] Robertson A et al. Implementation and Adoption of Nationwide Electronic Health Records in Secondary Care in England: Qualitative Analysis of Interim Results from National Evaluation. *British Medical Journal*. 2010 **341**

[306] Nelson S J and Allkins S. Technology in Healthcare: The NHS App. *British Journal of Cardiac Nursing*. 2020 **15(1)**

[307] Burki T. A Milestone on the Journey to a Digital NHS. *The lancet.com/digital health*. 2019 1

[308] *Ibid*

[309] *NHS. About the NHS App* (2021) Available at www.nhs.uk/nhs-services/online-services/nhs-app/about-the-nhs-app/

[310] This figure does not necessarily represent unique users as it is possible to have more than one NHS log in and register for the NHS App more than once.

[311] Data provided by NHS Digital in response to a Freedom of Information Request

There is currently no option in the NHS App to confirm preferences with regards to the secondary research use of surplus tissue. However, as my thesis will go on to suggest [ss. 13.2.2], the NHS App could provide an opportunity to allow choice for patients with regards to the secondary research use of their surplus tissues, alongside providing choices with regards to organ donation and secondary uses of health data.

4.3.5. Non-Identifiability as an Alternative to Consent

While consent is often considered to be an 'ethical panacea'[312], the HT Act 2004 does provide for the use of surplus tissue in health-related research without consent under certain circumstances - where the research use is ethically approved, and the research is to be carried out in circumstances such that the person undertaking it is not in possession of information which identifies the person from whom the tissue was removed[313]. This therefore provides an either/or approach to protecting patient interests[314]. Either the patient's interests are satisfied by the giving of consent for their surplus tissue and associated data to be used for research purposes or alternatively, their privacy and confidentiality interests are protected by ensuring that they are not identifiable to those undertaking the research. This approach is sometimes referred to as 'consent or anonymise'.

The inclusion of a consent or anonymise approach in the HT Act 2004 reflected the same approach to personal data which was seemingly a key component of the Data Protection Act 1998, which transposed EU Directive 95/46/EC (protection of individuals with regard to the processing of personal data and on the free movement of such data) into UK law[315]. In the UK these regulations have since been repealed and replaced by Regulation (EU) 2016/679 on the protection of natural persons with

[312] Corrigan O. Empty Ethics: The Problem with Informed Consent. *Sociology of Health and Illness*. 2003 **25(3)** 768-792
[313] *Human Tissue Act 2004.* Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 1 s 1 ss (9)
[314] Laurie G. Liminality and the Limits of Law in Health Research Regulation: What Are We Missing in the Spaces In-Between? *Medical Law Review.* 2016 **25(1)** 47-72
[315] Ibid

regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation), and the Data Protection Act 2018.

The intention of a consent or anonymise approach *prima facie* protects individuals, who have not had an opportunity to give their consent, by removing identifiable data[316]; although linking de-identified data with identifiable data is permitted where a coding system is used and the key to the code is held by someone with legitimate authority[317]. However, whilst de-identification of data aims to mitigate risks associated with breaches of privacy and confidentiality, it can also compromise the usefulness of data. This may be due to restrictions with linking data from different sources or may be due to minimally identifiable data, such as when and where a person was born, their occupation or where they currently live, being important to answer certain research questions[318]. Moreover, identifiability runs a spectrum from overtly identifiable through levels of indirectly identifiable and eventually to fully non identifiable and its status can change depending on factors such as other information, including genetic information, which becomes available[319]. Whilst individual data sets which are linked with tissue samples may not be overtly identifiable, the chances of an individual person being identified increases when data are collated together. Moreover, this risk increases further when there is a possibility of linking with other publicly available information such as the electoral register[320]. This therefore makes any absolute guarantees of non-identifiability problematic and results in a regulatory 'grey area' for researchers and data controllers[321].

[316] Laurie G et al. On Moving Targets and Magic Bullets: Can the UK Lead the Way with Responsible Data Linkage for Health Research? *International Journal of Medical Informatics.* 2015 **84** 933-940
[317] Lowrance W. (2012) *Privacy, Confidentiality and Health Research.* Cambridge: Cambridge University Press
[318] Laurie G et al. On Moving Targets and Magic Bullets: Can the UK Lead the Way with Responsible Data Linkage for Health Research? *International Journal of Medical Informatics.* 2015 **84** 933-940
[319] Lowrance W. (2012) *Privacy, Confidentiality and Health Research.* Cambridge: Cambridge University Press
[320] *Ibid*
[321] *Ibid*

The Information Commissioners Office (ICO), which is the UK authority set up to uphold information rights[322], published guidance on anonymisation and managing data protection risks[323]. This document provides some practical advice for data controllers and suggests that, where there is uncertainty with regards to whether data are considered to be sufficiently anonymised so that re-identification is 'greater than remote' and 'reasonably un-likely', then a 'motivated intruder' test can be applied. This involves an evaluation of whether the anonymised data are likely to result in re-identification of a person and whether anyone would likely have the motivation to attempt to re-identify a person[324]. Whilst absolute anonymisation may not be guaranteed, the motivated intruder test provides a pragmatic approach, particularly where the likelihood of re-identification is low[325].

This is of particular importance in the broader context of my thesis because the real value in the secondary research use of surplus tissue is where the tissue is linked with information about the person from whom the tissue was removed, the tissue alone has limited value[326]. Moreover, data are generated from tissue in the course of research and therefore tissue and data about the person from whom the tissue was removed are inextricably linked. With this in mind, whilst the primary focus of my thesis is enabling the secondary research use of surplus tissue samples, it is also important to ensure that I have addressed issues relating to data, confidentiality and privacy more broadly.

[322] Information Commissioner's Office. Home Page (no date) ico.org.uk/
[323] Information Commissioner's Office (2012) Anonymisation: Managing Data Protection Risks Code of Practice. Available at ico.org.uk/media/for-organisations/documents/1061/anonymisation-code.pdf
[324] *Ibid* Pg. 22
[325] Laurie G et al. On Moving Targets and Magic Bullets: Can the UK Lead the Way with Responsible Data Linkage for Health Research? *International Journal of Medical Informatics.* 2015 **84** 933-940
[326] Quinlan P, Groves M, Jordan L, Stobart H, Purdie C, Thompson A. The Informatics Challenges Facing Biobanks: A Perspective from a United Kingdom Biobanking Network. *Biopreservation and Biobanking.* 2005 **13(5)** 363-370

CHAPTER 5

TISSUE IDENTIFIABILITY – ENSURING LEGAL COMPLIANCE

The research use of patient information in the UK falls within a complex legal framework which spans statutory and common law. Moreover, the grey area between identifiable personal data and completely anonymised data means that the legal context is important, even where there is an intention for tissue samples and patient information to only be provided to researchers in a format which means the person from whom the tissue was removed cannot be identified. The next section therefore provides an overview of the legal framework which regulates the secondary research use of identifiable patient information. This provide important context for later discussion with regards to linking surplus tissue samples with associated patient information for secondary research purposes (chapter 10).

5.1. Data Protection

Regulation (EU) 2016/679 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation - GDPR), is an EU Regulation which has been applicable in EU Member States since May 2018. As the UK was an EU Member State on the day the GDPR came into force, this legislation currently applies in the UK despite the UK no longer being an EU Member State. The GDPR repealed EU Directive 95/46/EC and the UK Data Protection Act 1998 and includes provision for national law to determine the application of certain elements of the GDPR - in the UK this is enacted via the Data Protection Act 2018 (DPA 2018). The GDPR is an extensive regulation which regulates the use of 'personal data', spanning numerous sectors[327]. The GDPR defines personal data as:

[327] Chico V. The Impact of the General Data Protection Regulation on Health Research. *British Medical Bulletin*. 2018 **128** 109-118

> ‘any information relating to an identified or identifiable natural person (data subject); an identifiable person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, psychological, genetic, mental, economic, cultural or social identity of that person’[328].

This includes health related data which is generated and collected when accessing health services[329]. The GDPR includes specific provision, as well as derogation both directly in the GDPR and via provision for national derogation (enacted in the UK via the Data Protection Regulation 2018), for the use of personal data for the purpose of scientific research[330].

Lawful processing of personal data in accordance with the GDPR is based on seven principles which aim to create and promote a culture of data protection within organisations; key aspects of which are openness about how data are processed and data minimisation[331]. The principles require that personal data should be processed in a way which is lawful, fair and transparent[332], as well as limited to what is necessary to achieve the purpose for which they are processed[333]. Personal data should be accurate and kept up to date, with the option available for data to be rectified or erased where this would be reasonable[334]. Personal data should not be kept in an identifiable format any longer than necessary to achieve the purpose for which they are processed[335] and should be processed in a way which ensures appropriate protection, including against unauthorised or unlawful access and the potential for data

[328] *General Data Protection Regulation* (2018) Available at eur-lex.europa.eu/eli/reg/2016/679/oj Article 4 paragraph 1
[329] *Ibid* Article 4 paragraph 15
[330] Staunton C, Slokenberga S and Mascalzoni D. The GDPR and the research exemption: considerations on the necessary safeguards for research biobanks. *European Journal of Human Genetics*. 2019 **27** 1159-1167
[331] Chico V. The Impact of the General Data Protection Regulation on Health Research. *British Medical Bulletin*. 2018 **128** 109-118
[332] *General Data Protection Regulation* (2018) Available at eur-lex.europa.eu/eli/reg/2016/679/oj Chapter II Article 5 1 (a)
[333] *Ibid* Chapter II Article 5 1 (c)
[334] *Ibid* Chapter II Article 5 1 (d)
[335] *Ibid* Chapter II Article 5 1 (e)

loss[336]. Moreover, personal data should be collected for specific purposes and should not be further processed in a way which would be considered incompatible with the purpose of initial collection. However, where secondary processing of data is *inter alia* for the purpose of scientific research, and where it is compliant with Article 89(1), which covers safeguards and derogations relating to research processing of data, then this purpose is not considered to be incompatible with the purpose of collection[337].

The GDPR provides six lawful bases under which personal data must be processed, of which only one need apply for processing to be lawful under the GDPR. Processing of personal data with the consent of the data subject[338] is one legal basis, but this does not have a superior status above the other legal bases[339]. In the context of health-related research, the UK position advised by the Health Research Authority[340] is that consent should not be the legal basis which is relied on when processing personal data for this purpose[341] (more detailed discussion regarding this point is provided in ss. 10.6 pg 162). This does not however mean that consent is not required under a different legal framework, such as the common law duty of confidentiality (discussed in more detail ss. 5.2) or the requirement to obtain consent from participants in clinical trials under the Medicines for Human Use (Clinical Trial) Regulation 2005.

The recommendation that consent should not be the legal basis relied upon under the Regulation for the lawful processing of personal data for the purpose of scientific research, is because the requirements in relation to consent under the GDPR are more stringent and give greater control to the data subject than the requirements which are reasonably and normatively applied in a scientific

[336] *Ibid* Chapter II Article 5 1 (f)
[337] *Ibid* Chapter II Article 5 1 (b)
[338] *Ibid* Chapter II Article 6 1 (a)
[339] Chico V. The Impact of the General Data Protection Regulation on Health Research. *British Medical Bulletin*. 2018 **128** 109-118
[340] *Health Research Authority. Consent in Research* (2018) Available at www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/data-protection-and-information-governance/gdpr-guidance/what-law-says/consent-research/
[341] *Ibid*

research context[342]. For consent to be valid under the GDPR, it must be demonstrable, freely given, clear, in an easily accessible format, and it should be as easy to withdraw any consent given as it was to have given the consent[343]. Whilst these standards *may* also apply in a scientific research context, using consent as the legal basis means that these standards *must* apply for the processing to be lawful. Moreover, a broad consent approach, which is often applied for the secondary research use of surplus tissue and patient information, would not meet the standards required for consent under the GDPR[344]. Recital 33 does acknowledge that for scientific research, the full purpose of processing personal data may not be known at the time of collection and therefore data subjects may consent to certain parts of research. However, the Article 29 working party (now the European Data Protection Board) issued official guidance which stated that when relying on consent as the legal basis to process special category data, which includes health related data[345], the need for consent to be specific would still apply[346]. The guidance states that there would be an expectation that consent would continue to be sought as the research advances[347].

The recommendation in the UK is that the legal bases which should be relied upon to process personal data in a health-related research context are as follows. Where research is being undertaken by an NHS organisation or a university, which are public bodies which carry out research under their official authority[348], the legal basis should be 'processing is necessary for the performance of a task carried out in the public interest or in the exercise of official authority vested in the controller'[349]. Where

[342] *Ibid*
[343] *General Data Protection Regulation* (2018) Available at eur-lex.europa.eu/eli/reg/2016/679/oj Article 7 s. 1-4
[344] Chico V. The Impact of the General Data Protection Regulation on Health Research. *British Medical Bulletin*. 2018 **128** 109-118
[345] *General Data Protection Regulatio)* (2018) Available at eur-lex.europa.eu/eli/reg/2016/679/oj Article 9 s. 1
[346] Peloquin D, DiMaio M, Bierer B and Barnes M. Disruptive and Avoidable: GDPR Challenges to Secondary Research uses of Data. *European Journal of Human Genetics.* 2020 **28** 697-705
[347] European Data Protection Board (2020) *Guidelines 05/2020 on consent under Regulation 2016/679.* Available at edpb.europa.eu/our-work-tools/our-documents/guidelines/guidelines-052020-consent-under-regulation-2016679_en
[348] Chico V. The Impact of the General Data Protection Regulation on Health Research. *British Medical Bulletin*. 2018 **128** 109-118
[349] *General Data Protection Regulation* (2018) Available at *eur-lex.europa.eu/eli/reg/2016/679/oj Article 6 s. 1 (e)*

research is being undertaken by commercial organisations, it is recommended that the legal basis relied upon is 'processing is necessary for the purposes of legitimate interests pursued by the controller…'[350].

As personal data which is processed for the purpose of health-related research is considered to be 'special category data', it is also subject to further provisions under the GDPR and also the DPA 2018. Where special category data are being processed for the purpose of scientific research, the GDPR contains what is sometimes referred to as the 'research exemption'[351]:

> 'processing is necessary for archiving purposes in the public interest, scientific or historical research purposes or statistical purposes in accordance with Article 89(1) based on Union or Member State law which shall be proportionate to the aim pursued, respect the essence of the right to data protection and provide for suitable and specific measures to safeguard the fundamental rights and interests of the data subjects'[352].

Article 9 2(j) provides for further provision via national law, which in the UK is enacted via the DPA 2018, which states that for processing of special category data for the purpose of scientific research to be lawful under Article 9 2(j), it must be:

> ' (a) ..necessary for …… scientific … research,
>
> (b) ..carried out in accordance with Article 89(1) of the GDPR.., and
>
> (c) ..in the public interest'[353]

Article 89(1) requires for the processing of data to be subject to appropriate safeguards, which include technical and organisational measures which ensure respect for the principle of data minimisation,

[350] *Ibid* Article 6 s. 1 (f)
[351] Taylor M J and Whitton T. Public Interest, Health Research and Data Protection Law: Establishing a Legitimate Trade-Off Between Individual Control and Research Access to Health Data. *Laws.* 2020 **9(1)** 6
[352] *General Data Protection Regulation* (2018) Available at *eur-lex.europa.eu/eli/reg/2016/679/oj* Article 9 s. 2 (j)
[353] Data Protection Act 2018. Available at www.legislation.gov.uk/ukpga/2018/12/contents/enacted Schedule 1 Part 1 s. 4

including pseudonymisation[354]. However, it has been suggested that the inclusion of pseudonymised data within the scope of the GDPR could have serious implications for health-related research[355] and cause significant confusion, not least because the terminology with regards to pseudonymisation differs from previous interpretations[356]. This is something which is particularly relevant in the field of biobanking where tissue samples and data are provided to researchers in a non-identifiable format but remain linked to identifiable data via a key code which is held by someone with legitimate authority[357]. The GDPR says that personal data which has undergone pseudonymisation, which could be attributed to a person, should be considered to be identifiable. In determining this, consideration should be given to 'the means reasonably likely used' to identify the person[358]. The word 'reasonable' is important here[359] and the UK position is that where the researcher will not have access to the code, then the data are not considered to be personal data[360], although this position does appear to differ from the EU[361].

In addition to appropriate safeguards, the conditions provided for in Schedule 1 Part 1 of the DPA 2018 require that the data processing must be necessary and in the public interest. Taylor and Whitton suggest that a requirement to demonstrate compliance with a public interest standard could be challenging to achieve in a consistent way due to there not being an existing workable concept of public interests to be applied - and therefore propose an approach which they suggest could be

[354] *General Data Protection Regulation* (2018) Available at eur-lex.europa.eu/eli/reg/2016/679/oj Article 89 s. 1

[355] Mourby M et al. Are 'Pseudonymised' Data Always Personal Data? Implications of the GDPR for Administrative Data Research in the UK. *Computer Law and Security Review.* 2018 **34** 222-233

[356] Peloquin D, DiMaio M, Bierer B and Barnes M. Disruptive and Avoidable: GDPR Challenges to Secondary Research uses of Data. *European Journal of Human Genetics.* 2020 **28** 697-705

[357] *Ibid*

[358] *General Data Protection Regulation* (2018) Available at eur-lex.europa.eu/eli/reg/2016/679/oj Recital 26

[359] Chico V. The Impact of the General Data Protection Regulation on Health Research. *British Medical Bulletin*. 2018 **128** 109-118

[360] *Health Research Authority. Controllers and Personal Data in Health and Care Research* (2018) Available at www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/data-protection-and-information-governance/gdpr-guidance/what-law-says/data-controllers-and-personal-data-health-and-care-research-context/

[361] Peloquin D, DiMaio M, Bierer B and Barnes M. Disruptive and Avoidable: GDPR Challenges to Secondary Research uses of Data. *European Journal of Human Genetics.* 2020 **28** 697-705

suitably generalisable[362]. Their proposed approach acknowledges that where materials (this could be surplus tissue or patient data) derived from patients are to be used in health-related research, in circumstances where obtaining consent would not be practical, there is necessarily a trade-off between the common interest in health and the common interest in ensuring privacy[363]. However, there may be social legitimacy to proceed, preferably with opportunity for those whose tissue and data are to be used to object, where the research use is something which can be justified in terms which are both accessible and acceptable to members of society[364]. Establishing a better balance between safeguarding individual patient interests and the broader public interests associated with the secondary research use of surplus tissue and associated patient information is a key part of my thesis and is an issue which I return to throughout.

In the context of the use of surplus tissue and associated patient information in health-related research, the broader legal and governance framework which applies in the UK also provides a mechanism to confirm compliance with the requirement under the DPA 2018, that data are only processed for scientific research purposes where this is in the public interest, via a requirement for ethical review. The Governance Arrangements for Research Ethics Committees (GAfREC) require that all research which includes participants recruited due to their connection with use of NHS services, including where participation is limited to existing tissue and patient data, may only be conducted where the research has received a favourable opinion from a recognised research ethics committee[365]. Moreover, GAfREC requires that when a research ethics committee reviews a research application, it takes into consideration 'the public interest in reliable evidence affecting health and social care and enable ethical and worthwhile research of benefit to participants or to science and society'[366].

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[362] Taylor M J and Whitton T. Public Interest, Health Research and Data Protection Law: Establishing a Legitimate Trade-Off Between Individual Control and Research Access to Health Data. *Laws.* 2020 **9(1)** 6

[363] *Ibid*

[364] *Ibid*

[365] Health Research Authority (2021) Governance Arrangements for Research Ethics Committees. Available at www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/governance-arrangement-research-ethics-committees/ s. 2.3.5 ss. (a) (d) and (e)

[366] *Ibid* s. 3.2.2

Sorbie suggests that this requirement for public interest to be taken into consideration when reviewing and subsequently approving research projects mitigates a need to provide a generalisable definition of a public interest standard[367]. This is because the research ethics committee can determine whether there is a public interest in that research project, weighed up against risks and benefits for that participant group. Therefore, this *processual* approach to determining whether the public interest requirements which are dictated by law, such as the DPA 2018 and the common law duty of confidentiality (discussed in ss. 5.2), can be met via a practical standard of ethical approval may be preferable to applying conceptual notions of public interest.

This is important in the context of my thesis because the secondary research use of surplus tissue in the absence of consent sits within a regulatory framework which provides for each research project to be reviewed by a research ethics committee and for an opinion to be issued based on an assessment of the benefits and risks - including whether there is sufficient public interest to justify the use of tissue samples in the absence of consent. However, Schaefer et al suggest that there is potential inconsistency with regards to how the public interest test is applied when considering whether public interest claims outweigh any potential risks associated with the secondary research use of tissue and data[368]. Schaefer et al suggest that this may, at least in part, be due to an absence of clear and consistent guidance on what is meant by 'public interest' in the context of the secondary research use of tissue and data in the absence of consent. Moreover, there is a lack of clarity with regards to how public interests claims can be determined, particularly when weighing such claims against other competing interests such as autonomy and privacy[369]. Therefore, whilst a procedural approach to determining whether public interest claims justify the secondary research use of surplus tissue in the

[367] Sorbie A. Sharing Confidential Health Data for Research Purposes in the UK: Where are 'Publics' in the Public Interest? *Evidence & Policy*. 2020 **16(2)** 249-265
[368] Schaefer O G et al. Clarifying How to Deploy the Public Interest Criterion in Consent Waivers for Health Data and Tissue Research. *BMC Medical Ethics.* 2020 21(23)
[369] *Ibid*

absence of consent, some challenges remain with regards to establishing a clear definition which can be consistently applied.

5.2. Patient Confidentiality and the Duty of Confidence

Confidentiality is the handling of information which has been disclosed or generated within a relationship of trust where there is a reasonable expectation that the information will not be shared beyond that relationship[370]. *Coco v A N Clark (Engineers) Ltd [1969]* established three elements which must all be breached to demonstrate a breach of confidence - the information must be of a confidential nature, it must be communicated in circumstances importing an obligation of confidence and there must be an unauthorised use of the information[371]. Patient information[372] is considered to meet elements one and two, as it is disclosed or generated within a relationship of trust with healthcare providers with an expectation that it will not be disclosed, other than for healthcare purposes[373]. However, the case of *R v Department of Health ex parte Source Informatics Ltd* [374] created a legal precedent with regards to whether patient information which has been anonymised would continue to be considered confidential.

R v Department of Health ex parte Source Informatics Ltd [375] concerned the use of anonymised information obtained from prescription forms which had commercial value for pharmaceutical companies with regards to the marketing of their products[376]. A Department of Health circular published in 1997 had taken the view that the use of this data did constitute a breach of

[370] Lowrance W. (2012) *Privacy, Confidentiality and Health Research*. Cambridge: Cambridge University Press
[371] *Coco v A N Clark (Engineers) Ltd* [1969] RPC 41
[372] 'Patient information', is described in the NHS Act 2006 as:
'(a) information (however recorded) which relates to the physical or mental health or condition of an individual, to the diagnosis of his condition or to his care and treatment, and
(b) information (however recorded) which is to an extent derived, directly or indirectly, from such information
[373] Healthcare purposes is described as '..all activities that directly contribute to the diagnosis, care and treatment of an individual and the audit/assurance of the quality of the healthcare provided. They do not include research, teaching, financial audit and other management activities.' Department of Health (2003) Confidentiality: NHS Code of Practice. Available at www.gov.uk/government/publications/confidentiality-nhs-code-of-practice pg. 6
[374] *R v Department of Health ex parte Source Informatics* [2000] 1 All ER 786
[375] *R v Department of Health ex parte Source Informatics* [2000] 1 All ER 786
[376]Grubb A. Breach of Confidence: Anonymised Information. *Medical Law Review.* 2000 **8(1)** 115 - 120

confidentiality, even though it was anonymised. Source Informatics Ltd. challenged this in the High Court, on the basis that the pharmacists who had provided the data had not breached patient confidentiality in doing so. Initially the court ruled that anonymisation did not in itself mean that there had been no breach of confidence and that disclosure of the information in the absence of consent meant that the pharmacists had breached their duty of confidence by disclosing the information. However, this decision was subsequently overturned by the Court of Appeal which concluded that there could be no breach of confidence if the information was anonymised[377]. This case therefore set an important legal precedent that the common law duty of confidence can only be applied where the information is identifiable, and therefore subsequent uses of anonymised data would not breach this common law duty.

A further significant case in relation to breach of confidence under common law came before the High Court in 2004 and was also ultimately unsuccessful in demonstrating a breach of confidentiality, but for different reasons. *Campbell v MGN Ltd*[378] involved the photographing of the celebrity Naomi Campbell outside a Narcotics Anonymous meeting, and subsequent publication of a photo along with details of her attendance at such meetings. The claimant's common law claim had been that there had been a breach of confidentiality due to the sensitive nature of the disclosure which was made by publishing the story – a claim which the courts initially upheld. However, this was later overturned in the Court of Appeal which concluded that the fact she was attending Narcotics Anonymous meetings was not considered to be information of a confidential nature and therefore the publication of this information could not be a breach of confidence. This ruling was subsequently upheld in the House of Lords[379].

[377] *R v Department of Health ex parte Source Informatics* [2000] 1 All ER 786
[378] *Campbell v MGN Ltd.* [2004] UKHL 22, [2004] 2 A.C. 457 HL
[379] *Campbell v MGN Ltd.* [2004] UKHL 22, [2004] 2 A.C. 457 HL

The consent of the person to whom the confidential information relates is the main legal basis under which information may be shared without breaching a duty of confidence[380]. However, confidential information may also be shared where there is an alternative legal basis or where there is a robust public interest claim. The public interest defence was used in the case of *X v Y*[381], which concerned the disclosure of information by a Health Authority employee to a reporter that two General Practitioners had been diagnosed with AIDS. An article was published with an intention for further publications to follow. The Health Authority sought an injunction to prevent any further publication which could identity the doctors, but this was challenged by the claimant who claimed that publication of this information was in the public interest because the public had a right to know that doctors diagnosed with AIDS were continuing to treat patients. The court ruled that the claimant was entitled to a permanent injunction which prevented any further publication of confidential information because the public interest claim was not justified[382].

Two other cases also raised the issue of whether confidential information can be disclosed in the public interest. In the cases of *W v Egdell*[383] and *R v Crozier*[384], two psychiatrists had disclosed information relating to assessments they had made of individuals who were the subject of criminal cases. In both cases, information about the assessment which had been undertaken was disclosed to the courts without following due procedure. In *W v Egdell*[385], the Court of Appeal stated that that doctors do owe a duty to the public as well as a duty to their patients, a ruling which was subsequently relied upon in the case of *R v Crozier*[386]. In both of these cases, the actions of the psychiatrists were found to be justified and the public interest argument upheld.

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[380] Department of Health (2003) *Confidentiality: NHS Code of Practice.* Available at www.gov.uk/government/publications/confidentiality-nhs-code-of-practice
[381] X v Y [1988] 2 All ER 648
[382] Laurie G. (2002) *Genetic Privacy: A Challenge to Medico-Legal Norms.* Cambridge: Cambridge University Press
[383] *W v Egdell* [1990] 1 All E.R 835
[384] *R v Crozier* (1990) 8 BMLR 128
[385] W v Egdell [1990] 1 All E.R 835
[386] *R v Crozier* (1990) 8 BMLR 128

Whilst the public interest defence against a breach of confidence is established in common law, it is unlikely that this defence would in itself be successful in a health research context. However, a public interest claim in health research can influence an alternative legal basis for disclosing confidential patient information under section 251 of the NHS Act 2006 via the Health Service (Control of Patient Information) Regulation 2002. These regulations provide for the lawful processing of confidential patient information, including in the public interest where the Secretary of State considers this necessary[387]. This regulation was invoked in recent years, when responding to the global SARS-CoV-2 (COVID-19) pandemic, via a notification served under Regulation 3(4) of the Health Service (Control of Patient Information) Regulation 2002. This notice not only permitted but *required* organisations to process confidential information - where necessary and solely for COVID-19 purposes, including for purposes of surveillance, monitoring and research[388].

This notice applies for specified and exceptional circumstances for a limited period of time (currently until March 2022). However, section 251 of the NHS Act 2006 and the Health Service (Control of Patient Information) 2002 Regulation also provide a further legal basis for the processing of confidential information for the purpose of health research. This may be appropriate in a research context where obtaining consent is not feasible, such as large-scale cohort studies which access historic datasets. In England and Wales[389] the law provides for the duty of confidentiality to be temporarily set aside so that processing of confidential information can be lawfully undertaken. These legislative provisions permit the Secretary of State to regulate for the processing of patient information where this is for medical purposes and is in the interest of patient care or in the public

[387] *The Health Service (Control of Patient Information) Regulation 2002*. Available at www.legislation.gov.uk/ukdsi/2002/0110398904/data.htm s. 3 ss.(4)
[388] *Department of Health and Social Care. Coronavirus (COVID-19): Notice Under Regulation 3(4) of the Health Service (Control of Patient Information) Regulations 2002 – General.* (2021) Available at www.gov.uk/government/publications/coronavirus-covid-19-notification-of-data-controllers-to-share-information/coronavirus-covid-19-notice-under-regulation-34-of-the-health-service-control-of-patient-information-regulations-2002-general--2
[389] Scotland has the Public Benefit and Privacy Panel for Health and Social Care

interest[390]. In the context of health-related research, the Confidentiality Advisory Group (CAG) has been appointed to advise the Health Research Authority (HRA), which is the organisation appointed by the Secretary of State to authorise access to confidential patient information where consent cannot reasonably be obtained.

Whilst the guidance which is issued by the HRA in relation to the scope, authority and functions of the CAG are not clear with regards to whether section 251 may apply to patient information which is linked to tissue samples, a review of the CAG register of approved research indicates that some research projects which have been approved by the HRA on the advice of the CAG also involve the use of surplus tissue samples without consent[391]. However, the scope of the approval under section 251 of the NHS Act 2006 extends to the use of the patient information only. The legitimacy for the use of the tissue samples comes from the favourable ethical opinion issued by the research ethics committee, which is a condition of the section 251 approval required under the Health Service (Control of Patient Information) Regulation 2002[392]. Confidentiality is associated with information about a person, including where information has been generated through the analysis of tissue samples. However, arguably there are broader *privacy* issues relating to the use of surplus tissue samples in health-related research which extend beyond the scope of confidentiality, something which I discuss in the next section.

5.3. Privacy

Privacy as a concept is complex and its place in UK law is unclear, as there is no overarching cause of action for invasion of privacy[393]. This was evident in the case of *Campbell v MGN Ltd* which relied on a claim of breach of confidentiality due to there being no applicable legal right to privacy, despite

[390] *National Health Service Act 2006*. Available at www.legislation.gov.uk/ukpga/2006/41/contents/enacted s 251
[391] For example, 21/CAG/0010 Peritoneal Mesothelioma Retrospective Sample Collection
[392] *The Health Service (Control of Patient Information) Regulation 2002.* Available at www.legislation.gov.uk/ukdsi/2002/0110398904/data.htm s 2 ss (1) (d)
[393] Laurie G. (2002) *Genetic Privacy: A Challenge to Medico-Legal Norms.* Cambridge: Cambridge University Press

information about a person's private life not in itself being considered to be 'confidential'[394]. Whilst confidentiality and privacy do have a significant overlap in terms of their scope, they are distinct concepts which should not be conflated[395]. Privacy is conceptually broad and as such can be difficult to define[396]. Privacy encompasses areas such as a person's thoughts and actions, their body, the physical space that surrounds them, their home and personal life and information about them[397]. These different areas of privacy may be considered to fall within two broader spheres of privacy, 'informational privacy 'and 'spacial privacy'. However, privacy issues relating to healthcare could be considered to fall within both the information and spacial privacy spheres[398].

Solove suggests that any consideration of privacy, particularly where there is a question of balancing any rights to privacy with other competing interests, such as a potential public interest in health-related research, must be in the context of individual situations[399]. Privacy is conceptually broad, and its relative value is not uniform across all contexts[400]. In the context of sharing surplus tissue samples for use in health-related research there is no clear legal privacy right. The only clear *legal* basis for a right to privacy in the UK is provided for via the European Convention on Human Rights (ECHR), which includes a 'right to respect for private and family life' (ECHR Article 8). In Article 8, the ECHR is explicit that this extends to a person's home and correspondence and states that there should not be interference by a public authority, except where this is provided for via national law, including for the protection of health[401]. The ECHR is enacted into UK law via the Human Rights Act 1998 – with Article 8 providing a right to respect for private and family life, and for there not to be interference by a public

[394] *Campbell v MGN Ltd*. [2004] UKHL 22, [2004] 2 A.C. 457 HL
[395] Laurie G. (2002) *Genetic Privacy: A Challenge to Medico-Legal Norms.* Cambridge: Cambridge University Press
[396] Solove D. (2008) *Understanding Privacy.* Cambridge Massachusetts: Harvard University Press
[397] *Ibid*
[398] Laurie G. (2002) *Genetic Privacy: A Challenge to Medico-Legal Norms.* Cambridge: Cambridge University Press
[399] Solove D. (2008) *Understanding Privacy.* Cambridge Massachusetts: Harvard University Press
[400] *Ibid*
[401] Council of Europe (2021) *European Convention on Human Rights (as amended by Protocol No. 15).* Available at www.echr.coe.int/Pages/home.aspx?p=basictexts&c Article 8 2

authority in the exercising of this right, except in accordance with law[402]. However, there has never been a legal claim brought in the UK relating to accessing surplus tissue samples or personal data breaching a privacy right. A legal claim relating to a breach of 'informational privacy' in the context of identifiable patient information will likely be brought under the common law duty of confidentiality rather than a breach of privacy claim as the duty of confidence is established in common law[403].

Whilst a breach of confidentiality was the approach taken in cases such as *Campbell v MGN Ltd*[404] and *Douglas v Hello! Ltd*[405] (the latter case involved the surreptitious taking and publication of wedding photos), it has since been suggested that the legal basis for such cases should be breach of the tort of misuse of private information. In *Vidal-Hall v Google* [2015], the Court of Appeal considered the potential for a tort of misuse of private information in a case involving the use of information obtained from the claimants' Apple Safari browser, which had been used by advertisers to tailor adverts to individual interests. This case was heard in the Court of Appeal and in giving their judgement, Lord Justice McFarlane and Lady Justice Sharp reflected on previous cases, such as *Campbell v MGN Ltd* and *Douglas v Hello!*, where it was suggested that the misuse of private information had been 'shoe-horned' into a breach of confidentiality. It was suggested that the law of confidentiality had been used to bridge gaps which could more effectively have been addressed by recognising the misuse of private information as a standalone tort – not least because confidentiality and privacy are different concepts which protect different interests[406]. This ruling concluded that actions for breach of confidence and actions for misuse of private information rest on different legal foundations[407] and therefore the misuse of private information should now be recognised as a tort. In reaching this conclusion, it is however suggested that this does not create a new action but rather applies the correct label to an

[402] *Human Rights Act 1998*. Available at www.legislation.gov.uk/ukpga/1998/42/contents Article 8
[403] Loughrey J. The Confidentiality of Medical Records: Informational Autonomy, Patients Privacy and the Law. *Northern Ireland Legal Quarterly*. 2005 **56(3)** 293 - 319
[404] Campbell v MGN Ltd. [2004] UKHL 22, [2004] 2 A.C. 457 HL
[405] Douglas and Others v Hello! Ltd. [2005] EWCA Civ 595
[406] Vidal-Hall v Google Inc. [2015] EWCA Civ 311 para 21
[407] *Ibid* para 25

action which already exists[408]. This ruling has since been supported in subsequent decisions such as *Gulati v MGN Ltd*[409], *Reid v Price*[410], *ZXC v Bloomberg LP*[411], *Sicri v Associate Newspapers Ltd*[412] and *HRH the Duchess of Sussex v Associated Newspapers Ltd*[413].

In addition to a potential legal claim for the misuse of private information, there may be a *moral* claim that a privacy right has been breached, such as where new information is generated from surplus tissue about which the person from whom the tissue was removed is unaware. This is particularly the case where the information could impact on the person's health or influence decisions which they may make regarding their life, such as in the field of genetics where relatives share genetic heritage[414]. Laurie suggests that being made aware of information about ourselves which we did not want to know could be considered to be a breach of a person's spacial privacy and, as our genes are shared by family members, genetic information relating to one person also has the potential to invade the private space of others[415]. For example, if one person is found to be carrying the gene found on the tip of chromosome 4 which predisposes them to Huntington's disease, a degenerative condition affecting the nervous system which does not have symptoms until later in life and ultimately results in death, there is a one in four chance that their siblings will also carry the gene[416]. Awareness of a genetic predisposition to this horrendous disease, and ultimate fate as there is no known cure, can have a significant impact on a person's life well before the onset of any symptoms. This genetic predisposition may impact on insurance options as well as decisions about whether to have children[417]. Therefore, informing a person about any such findings without their agreement is a complex ethical minefield.

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[408] *Ibid* para 51
[409] Gulati v MGN Ltd [2015] EWHC 1482 (Ch)
[410] Reid v Price [2020] EWHC 594 (QB)
[411] ZXC v. Bloomberg LP [2020] EWCA Civ 611
[412] Sicri v. Associated Newspapers Ltd [2020] EWHC 3541 (QB)
[413] HRH the Duchess of Sussex v Associated Newspapers Ltd [2021] EWCA Civ 1810
[414] Laurie G. (2002) *Genetic Privacy: A Challenge to Medico-Legal Norms.* Cambridge: Cambridge University Press
[415] *Ibid*
[416] Jones S. (2000) *The Language of Genes: Revised Edition*. Hammersmith: Flamingo
[417] *Ibid*

Issues relating to the sharing of genetic information with family members have also been raised in the courts. Whilst a right to *not* receive information about a genetic condition was not the cause of action in *ABC v St George's Healthcare NHS Trust*[418], it was suggested by Yip J when ruling on this case that an argument for individuals not wanting to receive such information could represent a hypothetical argument against imposing a broader duty on doctors to locate relatives of patients diagnosed with a genetic condition. The case of *ABC v St George's Healthcare NHS Trust*[419] was brought by the daughter of a patient who was diagnosed with Huntington's Disease when the claimant was pregnant. At the request of the patient, this information was not disclosed by the doctors to the claimant. The claimant stated that had she known this information, she would have undergone testing and if found to have the condition, she would have terminated the pregnancy. She was subsequently tested and was indeed found to have the condition[420].

The initial ruling of the court was that no duty on the doctor to disclose their patient's Huntington's Disease diagnosis to his daughter existed. However, this was subsequently overturned by the Court of Appeal, which held that in principle, doctors did owe a duty of care to their patient's relatives, at least in the field of genetics[421]. This case came before the courts again in 2020, during which the *Caparo* test was invoked, requiring the court to consider whether three criteria were met in this case – that there was foreseeability of harm, there was proximity of relationship and whether it would be fair, just and reasonable to impose a duty of care[422]. The foreseeability of harm was not disputed, and proximity of relationship was found to apply to one of the three defendants. With regards to the third *Caparo* criterion, Yip J ruled that it was fair, just and reasonable to impose a legal duty to balance the

[418] *ABC v St George's Healthcare NHS Trust* [2020] EWHC 455 (QB)
[419] *ABC v St George's Healthcare NHS Trust* [2015] EWHC 1394 (QB)
ABC v St George's Healthcare NHS Trust [2017] EWCA Civ 336
ABC v St George's Healthcare NHS Trust [2020] EWHC 455 (QB)
[420] Gilbar R and Foster C. It's Arrived! Relational Autonomy Comes to the Court: ABC v St George's Healthcare NHS Trust [2017] EWCA 336. *Medical Law Review.* 2017 **26(1)** 125-133
[421] Foster C and Gilbar R. Is There a New Duty to Warn Family Members in English Medical Law? ABC v St George's Healthcare NHS Trust and others [2020] EWHC 455. *Medical Law Review.* 2021 **29(2)** 359-372
[422] *Ibid*

claimant's interests in being informed about the genetic risk against the father's interest in maintaining confidentiality about his condition.

In a research context, there is no requirement to feedback findings which are generated about a person, whether genetic or otherwise. This is particularly the case where it was explicit from the outset that findings would not be fed back, or where tissue samples are anonymous to the person undertaking the research[423]. However, this raises a potential issue with regards to *possession* of information, as generating new information about a person has the potential for a claim that the person has a right to possess information which relates to them. Whilst there is no personal property in information (compared to intellectual property which is not the subject of this discussion)[424], there may be a claim that withholding information is a breach of privacy rights by others knowing information about a person which *that* person does not know about themselves. Where the information is demonstrated to impact on a person's right to respect for private and family life then a claim under the ECHR and Human Rights Act 1998 could be possible, but this is of course purely conjecture. The claimant in *ABC v St George's NHS Trust*[425] argued that withholding information about her father's diagnosis of Huntington's Disease had infringed her rights under Article 8 of the Human Rights Act 1998. However, Irwin LJ suggested that he was unconvinced that reliance on a claim under Article 8 would add to the basis for action provided by common law[426].

In this section I have set out the legal framework in the UK in relation to data protection, confidentiality and privacy - in particular as it relates to the secondary research use of surplus tissue and patient information. This provides important context for discussion later in my thesis (chapter 5) where I aim to establish a regulatory approach to better facilitate the linking of surplus tissue and

[423] Mayor S. Studies Must Have Policies on Feeding Back Health Related Findings to Participants, Says New Guidance. *British Medical Journal*. 2014 **348**

[424] Laurie G. (2002) *Genetic Privacy: A Challenge to Medico-Legal Norms.* Cambridge: Cambridge University Press

[425] *ABC v St George's Healthcare NHS Trust* [2017] EWCA Civ 336

[426] Gilbar R and Foster C. It's Arrived! Relational Autonomy Comes to the Court: ABC v St George's Healthcare NHS Trust [2017] EWCA 336. *Medical Law Review.* 2017 **26(1)** 125-133

associated patient information in the absence of consent. Another area of law which has relevance with regards to human tissue relates to property and ownership of tissue. In particular, whether patients or those who are in possession of tissue after it has been removed from the body, such as pathologists holding tissue in diagnostic archives, hold any proprietary rights over the tissue – this is the subject of the next section.

CHAPTER 6

PROPERTY, OWERSHIP AND ABANDONMENT OF TISSUE

The next section sets out the common law status in relation to ownership and control of tissue once removed from the body. This is important in the context of my thesis because I aim to establish regulatory approaches which better enable the secondary research use of surplus tissue and therefore it is important to define the legislative boundaries with regards to tissue more broadly than the statutory provisions in the HT Act 2004. My intention here is to describe the legal boundaries which exist with regards to common law approaches to ownership and control of surplus tissue and to define where the secondary research use of surplus tissue sits within this framework. To achieving this, I provide a brief overview of the legal history with regards to control and ownership of human bodies, body parts and tissue after which I will go on to discuss the common law position in the specific context of the secondary research use of surplus tissue samples and its relationship with the HT Act 2004.

6.1. A Brief History of Tissue as Property in Common Law

The legal position with regards to the body as property has a history in common law reaching back to the seventeenth century. In 1614 William Haynes was found to have dug up the graves of four people and taken the winding sheets within which the corpses had been buried. The courts considered whether this action constituted theft, as to be guilty of such a crime would necessitate demonstrable ownership of the winding sheets. The courts concluded that the corpse was not capable of ownership and therefore no claim of ownership could be breached by property being removed from the corpse[427]. It is however suggested that the ruling of the courts in this case may have later been misreported to, 'there can be no property in a corpse', and subsequently taken to indicate that the ruling of property related to the corpse and its bodily parts, rather than the question of whether the

[427] Goold I and Quigley M. (2014) Human Biomaterials: The Case for a Property Approach. In Goold I, Greasley K, Herring J, Skene L (eds.) *Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century?* (pp 231 – 262) Oxford: Hart Publishing ltd.

corpse may be considered to hold any rights of ownership[428]. The principle that the corpse and its bodily parts could not be considered as property was reiterated during subsequent cases throughout the eighteenth and nineteenth centuries, not least due to a rise in the exhumation of corpses for use as anatomical specimens for dissection purposes[429].

The question of whether bodies and body parts could be considered property arose again in 1908, coming before the Australian courts in the case of *Doodeward vs Spence*[430]. Here Doodeward had obtained the mummified corpse of conjoined twins and intended to exhibit the body on public display. The corpse was subsequently removed by the authorities due to claims that such an activity would be abhorrent. Doodeward went to the courts to claim that the body should be returned to him and was successfully found to have rights of possession because the body had been subject to 'the lawful exercise of work of skill so…. that it has acquired some attributes differentiating it from a mere corpse awaiting burial.'[431] More recently, the issue of ownership in the context of tissue removed from a living person has been considered in the US courts in the case of *Moore v Regents of the University of California*[432]. This case involved the creation of lucrative cell lines from the excised spleen of a patient, which had been removed as part of medical treatment for hairy cell leukaemia. The patient had consented to the removal of the spleen and had attended numerous follow up appointments during which he underwent further blood sampling on the understanding that this was for the purposes of ongoing clinical care. The doctor treating the patient subsequently filed for a patent for the cell lines which he sold to a drug company for 15 million dollars[433]. The initial ruling of the court was that human tissue was the property of the person from whom it was removed, but this ruling was later reversed

[428] Campbell-Tiech A. A Corpse in Law – Annotation. *British Journal of Haematology* 2002 **117(4)** 809-811
[429] Goold I and Quigley M. (2014) Human Biomaterials: The Case for a Property Approach. In Goold I, Greasley K, Herring J, Skene L (eds.) *Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century?* (pp 231 – 262) Oxford: Hart Publishing ltd.
[430] *Doodeward v Spence* [1908] HCA 45; (1908) 6 CLR 406
[431] Campbell-Tiech A. A Corpse in Law – Annotation. *British Journal of Haematology* 2002 **117(4)** 809-811
[432] *Moore v Regents of University of California* (1990) 51 CAL 3d 120 (Sup Ct Cal); 793 P 2d 479
[433] Mason J K and Laurie G T. (2006) *Mason & McCall Smith's Law and Medical Ethics: Seventh Edition.* Oxford: Oxford University Press

in the Court of Appeal due to concerns that upholding the claim would reflect commodification of the human body[434].

Issues around legal ownership of human tissue have further been considered in the English courts in more recent years. The departure from the body not being considered as property where the body or its parts have been subject to work or skill, which had been applied in the *Doodeward* case, went on to be applied in two English cases. In *R v Kelly and Lindsay*[435], a successful charge of theft was brought against two people who had removed body parts from the Royal College of Surgeons, to be used as casts to create pieces of art for an exhibition. The defence claimed that there could not be a conviction for theft on the basis that the body parts could not be considered as 'property', and therefore could not be the subject of theft. The conviction was however successful on the basis that the body parts had acquired different attributes, due to the application of skill, including dissection or preservation techniques, and therefore were the property of the Royal College.

Later in *AB and others v Leeds Teaching Hospital NHS Trust*[436], the parents of three deceased children brought a multiple representative claim of wrongful interference with their children's bodies following post-mortem examination. The parents of the three deceased children brought a claim that their children's organs had been retained following post-mortem examination without their prior awareness and consent. The court ruled that there could be no claim of wrongful interference because the parents did not have any legal right of possession over the organs and furthermore, as the parents had consented to the post-mortem examinations being carried out, the pathologists carrying out the examination were in lawful possession of the bodies[437]. In delivering this conclusion, Mr Justice Gage

[434] Greasley K. (2014) Property Rights in the Human Body: Commodification and Objectification. In Goold I, Greasley K, Herring J, Skene L (eds.) *Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century?* (pp 67 – 88) Oxford: Hart Publishing ltd.
Lavoie J. Ownership of Human Tissue: Life after Moore v. Regents of the University of California. *Virginia Law Review.* 1989 **75** 1363-1396
[435] *R v Kelly and Lindsay* [1998] 3 All ER 742: (1999) QB 621 (CA)
[436] *AB and others v Leeds Teaching Hospital NHS Trust [2004] EWHC 644 (QB)*
[437] The Human Tissue Act 1961 which was in force at the time provided for the person in lawful possession of the body of a deceased person to authorise removal of part of the body for medical purposes

referred to the ruling in *R v Kelly* having established the principle of body parts being property and subject to property rights due to the application of skill and preservation techniques[438]. Goold and Quigley[439] suggest that the rulings in these cases reflect pragmatism on the part of the courts to reflect actual practice whilst still maintaining the principle that the body, in itself, is not property and cannot be owned.

This common law approach of pragmatically deviating from the principle of the body not being property was further demonstrated in 2009 in *Yearworth v North Bristol NHS Trust*[440]. Here the issue of possession was considered in the context of sperm samples from six men, stored prior to commencing chemotherapy which risked compromising their fertility. The sperm samples were stored in a fertility unit and became irreversibly damaged when the unit failed, and the sperm samples thawed. Claims were brought by the men that they had suffered psychological distress, which required proof of personal injury or loss of their property as a result of negligence. The courts ruled that there could be no claim of personal injury where human tissue has been removed from the body and this claim was therefore rejected. However, in further considering whether there could be a claim of loss of property, it was first necessary to prove that the men held proprietary rights or possessory interests over the sperm samples.

The Court of Appeal ruled that the men did indeed have ownership of the sperm samples because they had created the sperm from their bodies and the purpose of storage was for their sole benefit. Whilst the hospital was responsible for storage of the samples, the hospital had no control over their use beyond the intended use for the men who had created the samples. In finding that the sperm samples could, under these circumstances, be considered to be property, the courts held that the

[438] Petrini C. Ethical and Legal Considerations Regarding the Ownership and Commercial use of Human Biological Materials and their derivatives. *Journal of Blood Medicine*. 2012 **3** 87-96
[439] Goold I and Quigley M. (2014) Human Biomaterials: The Case for a Property Approach. In Goold I, Greasley K, Herring J, Skene L (eds.) *Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century?* (pp 231 – 262) Oxford: Hart Publishing ltd.
[440] *Yearworth and others v North Bristol NHS Trust* [2009] EWCA Civ 37; [2010] QB 1

samples could be considered to be held under bailment and therefore a duty did exist on behalf of the hospital and this duty had been breached[441].

Herring[442] suggests that cases such as *Kelly and Lindsay[443], AB and others[444]* and *Yearworth[445],* indicate that there cannot be a generalisable property claim on the body as some parts have instrumental value while others do not and some circumstances favour a property approach when others do not. As such, it is not the nature of the tissue itself but the circumstances around its removal and retention which lead to a successful claim of 'ownership'. With this in mind, Wall has argued that there is also an important distinction to be drawn between tissue as a *thing* and the *activity* for which the tissue is intended to be used[446]. Wall suggests that applying property law in the context of excised tissue does not sufficiently acknowledge the complexities associated with the uses of excised tissue. This is because a property law approach focuses on exclusionary rights over tissue as a *thing* and provides insufficient flexibility with regards to possible *activities* for which the tissue may be used[447]. Devaney makes a similar point in setting out the distinction between tissue as the *object* and the *relationship* between the object and one or more individuals[448].

The distinction between *thing* and *activity* is helpful when further considering the boundaries of common law and statutory law with regards to body parts and tissue. My rationale for this is that the HT Act 2004 has arguably introduced a shift towards *activity* focused legislation which was not

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[441] Hawes C. Property Interests in Body Parts: Yearworth v North Bristol NHS Trust. *The Modern Law Review*. 2010 **73(1)** 119-140
Skene L. Raising Issues with a Property Law Approach. In Goold I, Greasley K, Herring J, Skene L (eds.) *Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century?* (pp 263 – 280) Oxford: Hart Publishing ltd.

[442] Herring J. Why We Need a Statute Regime to Regulate Bodily Material. In Goold I, Greasley K, Herring J, Skene L (eds.) *Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century?* (pp – 215 – 230) Oxford: Hart Publishing ltd.

[443] R v Kelly [1998] 3 All ER 742: (1999) QB 621 (CA)

[444] AB and others v Leeds Teaching Hospital NHS Trust [2004] EWHC 644 (QB)

[445] Yearworth and others v North Bristol NHS Trust [2009] EWCA Civ 37; [2010] QB 1

[446] Wall J. (2014) The Boundaries of Property Law. In Goold I, Greasley K, Herring J, Skene L (eds.) *Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century?* (pp 109 – 124) Oxford: Hart Publishing Ltd

[447] *Ibid*

[448] Devaney S. Tissue Providers for Stem Cell Research: The Dispossessed. *Law, Innovation and Technology* 2010 **2(2)** 165-191

available when *R v Kelly* and *AB and others v Leeds Teaching Hospital NHS Trust* went before the courts. These cases relied on considering body parts and tissue as *things* which can be the subject of possessory rights, in these cases either due to or with reference to the skill and preservation techniques which had been applied. However, the HT Act 2004 has since provided a more *activity* focused approach via provisions relating to 'scheduled purposes' - activities which require appropriate consent to be lawful and are to be carried out under the authority of a licence.

This is particularly relevant within the broader context of my thesis because the distinction between *thing* and *activity* in the context of the HT Act 2004 helps to define the legislative scope which is relevant in the specific context of the secondary research use of surplus tissue. With this in mind, I suggest that in the context of the secondary research use of surplus tissue, the question of possessory rights established via case law has now to some degree been superseded by statutory duties imposed on holders of tissue via the HT Act 2004. In particular, with regards to consent being obtained for body parts and tissue to be stored and used for scheduled purposes. To further support this assertion, the next section will consider the specific context of the secondary research use of surplus tissue with regards to ownership and abandonment.

6.2. Ownership and Abandonment of Tissue

In 1995 the Nuffield Council in Bioethics published a report entitled 'Human Tissue: Legal and Ethical Issues'[449] which stated the following:

> 'It will be entailed in any consent to **treatment** that tissue removed **in the course of treatment** will be regarded in law as having been abandoned by the person from whom it was removed'[450].

[449] Nuffield Council on Bioethics (1995) *Human Tissue: Ethical and Legal Issues.* Available at www.nuffieldbioethics.org/publications/human-tissue
[450] *Ibid* s. 9.14 ss. 1

Use of the word 'abandonment' in this context has come under some criticism due the legal connotation of abandonment in English property law – 'abandonment' is to give up ownership or possession of something entirely and irrevocably[451]. In applying this specific meaning, distinction must be drawn between abandonment and merely discarding an 'item', as well as transferring possession of an item from one possessor to another. Abandonment requires an item to be discarded in a way which means there are no residual rights or interests and the item is, either temporarily or permanently, in a 'un-possessed' state of *res nullius*; and therefore any future possession of the item could be taken on by anyone for any purpose[452]. Matthews asserts that in English law, the principle of *res nullius*, usually considered to apply to wild animals or plants and in a legal context relating to issues such as whether taking items from a wreck is theft, is not generalisable and would therefore not likely apply in the context of human tissue removed during a surgical procedure[453]. Matthews goes on to suggest that if the principle of abandonment is truly to be applied then full ownership rights could be taken by the first person to claim possession of the tissue and there can be no ongoing interest claimed by the person from whom the tissue was removed[454].

Dworkin and Kennedy suggest that a claim of possession by the person from whom the tissue is removed may exist briefly when the tissue is removed but, where any such claim is not asserted, then possession passes to the hospital[455]. Moreover, Mason and Laurie suggest that possession is transferred from one to another at several stages throughout the process of legitimate handling of tissue[456]. Each person may be said to be in possession of the tissue at different stages, but non may claim ownership. This is more akin to proprietary rights where persons be in possession of the tissue,

[451] Goold I. (2014) Abandonment and Human Tissue. In Goold I, Greasley K, Herring J, Skene L (eds.) *Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century?* (pp 125 – 156) Oxford: Hart Publishing ltd.
[452] *Ibid*
[453] Matthews P. The Man of Property. *Medical Law Review.* 1995 **3** 251-274
[454] *Ibid*
[455] Dworkin G and Kennedy I. Human Tissue: Rights in The Body and Its Parts. *Medical Law Review*. 1993 **1** 291-319
[456] Mason J K and Laurie G T. Consent or Property? Dealing with the Body and its Parts in the Shadow of Bristol and Alder Hey. *The Modern Law Review*. 2001 **64(5**) 710-729

but they may not use it for any purposes of their choosing and therefore cannot claim to have ownership of the tissue[457].

Goold suggests that in English law, the bar to demonstrate abandonment has generally been quite high and requires that there is clear and demonstrable evidence that the person in possession of the item in question has relinquished possession with no residual rights or interests over who may later take possession of the item, and any purposes for which it may be used[458]. Goold further suggests that historically there has been reluctance in English courts to find an item to have been abandoned as in doing so, there are potential consequences - for example a lack of responsibility and therefore accountability such as where an item had been dumped in a public place[459]. Goold asserts that for an abandonment claim to be successful, there must be a divesting ownership which therefore must require for there to be recognition of ownership to be divested[460]. However, ownership in the context of property law cannot exist for human tissue because the law does not recognise human tissue as property[461], except where it has acquired different attributes due to the application of skill, including dissection or preservation techniques[462].

Skene suggests that any ownership rights which may exist in human tissue which is removed during a clinically directed procedure would fall short of ownership in the property sense, suggesting that any such rights are proprietary but not full ownership[463]. This suggestion of proprietary rights rather than full ownership is based on any claims of ownership not being an absolute right but rather a greater right than anyone else. For example, the pathologist who is in possession of tissue removed during a

[457] Mason J K and Laurie G T. Consent or Property? Dealing with the Body and its Parts in the Shadow of Bristol and Alder Hey. *The Modern Law Review*. 2001 **64(5**) 710-729
[458] Goold I. (2014) Abandonment and Human Tissue. In Goold I, Greasley K, Herring J, Skene L (eds.) *Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century?* (pp 125 – 156) Oxford: Hart Publishing ltd.
[459] *Ibid*
[460] *Ibid*
[461] *Ibid*
[462] Goold I and Quigley M. (2014) Human Biomaterials: The Case for a Property Approach. In Goold I, Greasley K, Herring J, Skene L (eds.) *Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century?* (pp 231 – 262) Oxford: Hart Publishing ltd.
[463] Skene L. Legal Rights in Human Bodies, Body Parts and Tissue. *Bioethical Inquiry*. 2007 **4** 129-133

surgical procedure may claim to have proprietary rights over the tissue but they are not permitted to do whatever they choose with the tissue and therefore this falls short of full ownership. Moreover, abandonment in property law must be absolute and therefore cannot be on terms - there cannot be any limitations on what happens to the 'item' after it has been abandoned[464].

Where tissue is removed during clinical or surgical procedures however, it is likely that patients do retain *some* interests in what happens based on what they reasonably expect, and that any future use would be limited to certain activities; such as diagnostic analysis or disposal[465]. There would not likely be a blanket acceptance that *any* activity may be undertaken with the samples. Therefore, in suggesting that consent to undergo treatment could also be taken to mean that any tissue removed in the course of the treatment has been abandoned, the 1995 report by the Nuffield Council on Bioethics is therefore not consistent with abandonment in property law where there cannot be any limitations on future use. Mason and Laurie suggest that in referring to consent being the basis of any claim of abandonment, the Nuffield Council report creates a 'hybrid' by retaining language, such as abandonment and gift, which have recognised connotations within property law, whilst also stating that property is not the basis of any claim of abandonment[466]. Matthews appears to agree in describing the report as an eclectic ad hoc path which takes ideas from different parts of the law[467].

The Nuffield report was notably published prior to the introduction of the HT Act 2004 and the subsequent introduction of this statutory legislation has in some ways clarified the legal position with regards to tissue which has been removed during clinically directed procedures[468]. As previously suggested (ss. 6.1), issues relating to ownership and possessory rights have now to some degree been

[464] Goold I. (2014) Abandonment and Human Tissue. In Goold I, Greasley K, Herring J, Skene L (eds.) *Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century?* (pp 125 – 156) Oxford: Hart Publishing ltd.
[465] Maddox N. 'Abandonment' and the acquisition of property rights in separated human biomaterial. *Medical Law International* 2016 **16(3-4)** 229-251
[466] Mason J K and Laurie G T. Consent or Property? Dealing with the Body and its Parts in the Shadow of Bristol and Alder Hey. *The Modern Law Review*. 2001 **64(5**) 710-729
[467] Matthews P. The Man of Property. *Medical Law Review.* 1995 **3** 251-274
[468] Lucassen A and Wheeler R. Legal Implications of Tissue. *Annals of The Royal College of Surgeons of England.* 2010 **92** 189-192

superseded by statutory duties imposed on holders of tissue via the HT Act 2004 and therefore issues relating to abandonment in a legal sense may no longer be of direct relevance. Moreover, in the context of surplus tissue which has potential secondary research value, reference to abandonment and divested interest in what happens to tissue once removed from the body does not take into account patient interests in the potential benefit to others which the tissue may provide. In the next section I will consider the individual patient and broader societal interests in surplus tissue being 'gifted' for research purposes.

6.3. Gifting Tissue Samples for Research

The donation of tissue samples for use in research is sometimes referred to as 'gifting'[469] the samples, or samples being donated within a 'gift relationship'[470]. Titmuss' seminal work 'The Gift Relationship: From Human Blood to Social Policy'[471] considers the concept of gifting in relation to blood donation, comparing the US commercial system with the UK donation system. His work suggests that the UK 'altruistic' approach is preferred on a social level because a society in which people give with no direct expectation of receiving a gift in return leads to a social structure which is expected to support its citizens, thereby creating an indirect and non-relational giving and receiving model[472]. Titmuss further suggests that whilst traditionally the giving of gifts in society is between associates and based around established occasions, such as Christmas and birthdays, and is often based on reciprocal arrangements of giving and also receiving, there may also be expectations of reciprocity in the donation of tissue to 'strangers'. Reciprocity and altruism are discussed in more detail in ss. 7.3 & 7.4.

In the context of donating tissue samples for research purposes, the terminology 'gifting' is sometimes used to describe the action of giving tissue to avoid expectations of direct reward or payment for the

[469] Nuffield Council on Bioethics (2011) *Human Bodies: Donation for Medicine and Research*. Available at www.nuffieldbioethics.org/publications/human-bodies-donation-for-medicine-and-research
[470] See *Medical Research Council (2014) Human Tissue and Biological Samples for use in Research: Operational and Ethical Guidelines.* Available at www.ukri.org/publications/human-tissue-and-biological-samples-for-use-in-research/
[471] Titmuss R M. (2018) *The Gift Relationship: From Human Blood to Social Policy*. Bristol: Policy Press.
[472] *Ibid*

giving of tissue[473]. A gift requires the voluntary transfer of something to another person without any expectation of receiving anything of value in return[474]. However, this terminology has also been criticised in this context due to connotations of property and ownership which come with a gift model[475]. The transfer of an item from one person to another implies that the tissue is property with rights of ownership being divested along with the giving of the gift. However, as previously indicated (ss. 6.1 & 6.2), the commonly held position is that there can be no property in human tissue, except for where there has been application of skill or preservation techniques. With this in mind, it has been suggested that it may be more appropriate to consider gifting as the voluntary transfer of proprietary rights rather than a transfer of ownership, as this approach addresses issues with connotations of tissue as property[476]. Moreover, a voluntary transfer of proprietary rights approach enables *conditional* gifting which is important in the context of tissue being used for research purposes due to the limitations which some individuals may want to invoke on ethical or religious ground, such as their tissue not being use in animal research[477].

Empirical evidence has also indicated that 'gift' terminology is not how patients being asked to provide tissue for research purposes would perceive the situation. A study by Dixon-Woods et al aimed to establish the views of children with cancer, as well as their parents', with regards to the donation of tissue samples for use in health-related research being considered a 'gift'[478]. In this study, twenty-six families said that they were happy with the gift terminology as it suggested that donation of tissue samples was a positive act and made them feel good about donating. However, twenty-six families

[473] Price D. (2010) *Human Tissue in Transplantation and Research: A Modern Legal and Ethical Donation Framework.* Cambridge: Cambridge University Press
[474] Stewart C, Lipworth W, Aparicio L, Fleming J, Kerridge I. (2014) The Problems of Biobanking and the Law of Gifts. In Goold I, Greasley K, Herring J, Skene L (eds.) *Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century?* (pp 25 – 38) Oxford: Hart Publishing Ltd.
[475] Dixon-Woods M, Cavers D, Jackson C J et al. Tissue Samples As 'Gifts' for Research: A Qualitative Study of Families and Professionals. *Medical Law International*. 2008 **9** 131-150
[476] Stewart C, Lipworth W, Aparicio L, Fleming J, Kerridge I. (2014) The Problems of Biobanking and the Law of Gifts. In Goold I, Greasley K, Herring J, Skene L (eds.) *Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century?* (pp 25 – 38) Oxford: Hart Publishing Ltd
[477] *Ibid*
[478] Dixon-Woods M, Cavers D, Jackson C J et al. Tissue Samples As 'Gifts' for Research: A Qualitative Study of Families and Professionals. *Medical Law International*. 2008 **9** 131-150

expressed a negative view towards the terminology, suggesting that it implied a commercial transaction and the potential for commercial value in the tissue sample (four families were neutral about the terminology)[479]. There was also a perception that the terminology 'gift' was inappropriate due to the term being associated with happy occasions when a gift was given in a positive way. The tumour was perceived to be something very negative, which they just wanted removed, and patients did not associate the tumour as something they would 'gift' to others[480].

Shaw further considers the terminology of 'gift' in the context of donating tissue for use in research, suggesting that terminology which the donors of tissue would use to describe what they are doing should be used[481]. Shaw suggests that the terminology gift is often something devised by ethics committees and research institutes to foster the donation of tissue as a one-way transaction, yet the language isn't what people would generally associate with giving a gift. The terminology of gift in a tissue donation context is usually considered as a gift-*relationship*, rather than focus on the nature of the gift itself[482]. In shifting the focus to the more conceptual 'gift-relationship', this may effectively address issues concerned with ownership and gift giving occasions and better highlight more socially beneficial notions of altruism, solidarity and reciprocity.

In this section I have set out the key issues with regards to the gifting of human tissue, particularly focusing on the gifting relationship between the tissue donor and those undertaking research involving tissue. However, in the broader context of my thesis, which focuses on the secondary research use of surplus tissue which is stored in diagnostic archives, it is also important to acknowledge that patients may not always be aware of such activities. The opportunity to donate tissue for secondary research purposes is associated with the requesting and giving of consent. However, where tissue is surplus to diagnostic requirements and stored in a diagnostic archive, the

[479] Dixon-Woods M, Cavers D, Jackson C J et al. Tissue Samples As 'Gifts' for Research: A Qualitative Study of Families and Professionals. *Medical Law International*. 2008 **9** 131-150
[480] *Ibid*
[481] Shaw R. The Notion of the Gift in the Donation of Body Tissues. *Sociological Research Online.* 2008 **13(6)4**
[482] *Ibid*

research value of the tissue is only realised after consent for the removal of the tissue is given and obtaining consent retrospectively is often not feasible or practical[483]. In this scenario, a broader approach to a *gifting relationship* which gives patients the opportunity to act on their altruistic interests may be required. This is something that is considered in more detail in chapter 11.

[483] Gefanas G, Dranseika V, Cekanauskaite A, Serepkaite J (2011) Research on Human Biological Materials: What Consent is Needed, and When. In Lenk C, Sándor J, Bert Gordijn (eds.) *Biobanks and Tissue Research: The Public, the Patient and the Regulation.* (pp 95 - 110) Dordrecht: Springer

CHAPTER 7

SOCIETY AND CITIZENSHIP IN TISSUE RESEARCH

7.1 The Societal Perspective of Tissue Research

Health research has an important role in society as it provides knowledge and understanding of medical conditions and ways of treating disease[484]. This is important on a societal level as people are relational which means that the health and well-being of us as individuals impacts on those around us, and the health and wellbeing of those around us impacts on us as individuals. This is the case for social and family networks as well as on a broader public health level[485]. The need to balance the interests of individuals against the interests of society is well established in health research legislation, policy and guidance. Discussion about public interests generally involves a balance of interests, and potentially some concession on the part of persons to further a public interest cause[486].

In acknowledging the need to balance the individual interests of the person from whom the tissue was removed with broader societal interests, Forsberg et al suggest that individual persons should also be viewed in their capacity as patient and citizen rather than just the originator of the tissue[487]. Moreover, they suggest that rather than weighing individual interests with public benefit, the interests of the individual as a research subject should be weighed against the interests of the same individual as a

[484] Academy of Medical Sciences (2011) *A New Pathway for the Regulation and Governance of Health Research.* Available at acmedsci.ac.uk/policy/policy-projects/a-new-pathway-for-the-regulation-and-governance-of-health-research

[485] Herring J. Why We Need a Statute Regime to Regulate Bodily Material. In Goold I, Greasley K, Herring J, Skene L (eds.) *Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century?* (pp 215 – 230) Oxford: Hart Publishing ltd.

[486] Meyers EM (2018) Ethics and the Public Interest. In Farazmand A (ed.) *Global Encyclopaedia of Public Administration, Public Policy, and Governance.* Springer International Publishing.

[487] Forsberg JS, Hansson MG and Eriksson E. Biobank Research: Who Benefits from Individual Consent? *British Medical Journal.* 2011 **343**

patient and recipient of healthcare[488]. With that in mind, the line between individual patient interests and broader societal interests may not be clearly defined in this context.

This section considers the key arguments regarding the balance between individual and societal rights when using surplus tissue for health-related research purposes. This is important in the broader context of my thesis because a key justification for my claim that all surplus tissue samples should have the potential to be research samples is that this would better balance individual interests with broader societal interests. Despite evidence that patients are generally supporting of surplus tissue being used for research purposes and a plentiful supply of surplus tissue in diagnostic archives, accessing existing tissue samples has its difficulties[489]. My thesis proposes regulatory approaches which aim to address this problem if implemented in practice. This is because these regulatory approaches come from a more enabling perspective than extant approaches – considering how surplus tissue can be made available for secondary research purposes, in the interest of furthering medical knowledge for broader societal interests, whilst also safeguarding individual patient interests. This enabling approach therefore places greater weight on the societal interests associated with the secondary research use of surplus tissue whilst also ensuring that individual interests are also respected.

7.2. Social Contract and Social Licence

The term 'social contract' is often used in the context of the UK National Health Service (NHS) and is based on principles which bind the community together and ensures all citizens a right to healthcare which is based on a persons need rather than any financial basis[490]. The principle of a 'social contract' lies at the heart of the NHS[491] and is delivered (in England) via the NHS constitution for England (most

[488] Forsberg JS, Hansson MG and Eriksson E. Biobank Research: Who Benefits from Individual Consent? *British Medical Journal.* 2011 **343**

[489] Womack C and Gray N M. Banking Human Tissue for Research: Vision to Reality. *Cell Tissue Banking*. 2009 **10** 267-270

[490] Neuberger J. The NHS as a Theological Institution: The Ideal Remains Strong, but the Practice has to Measure up too. *British Medical Journal*. 1999 **319** 1588-1589

[491] Lord Bishop of St Albans (2016) 'National Health Service' Hansard: House of Lords Debates 14 January c. 412

recent version issued 1 January 2021)[492]. The NHS constitution sets out the common principles on which the NHS was founded and establishes the rights and responsibilities of patients, the public and NHS staff to ensure that the way the NHS operates is fair and effective. The manifestation of a social contract via the NHS constitution is important to ensure that patients have confidence in the NHS.

Trust in public institutions such as the NHS is based on there being a reasonable expectation that such institutions will act in the best interest of the community which they serve, thereby ensuring a collective commonality which is supported by institutional structures and policies[493]. A social contract recognises that the public institution has certain responsibilities and where there is confidence that these responsibilities are being met, those in receipt of services being provided may accept and agree certain concessions. For example, the NHS has a duty to ensure that all information which is disclosed or generated within the fiduciary healthcare professional and patient relationship is kept confidential and is therefore not disclosed to unauthorised persons[494]. Where patients have confidence that their information will be managed in confidence then they may be more willing to concede some degree of an absolute right to confidentiality by permitting their data to be used for broader purposes, including health related research.

However, where confidence that information will be kept confidential is marred, then this can impact on a persons' willingness to accept certain concessions and lead to high levels of objection. This was evident in the response to the care.data initiative, which had a lawful basis for the use of patient data, due to the Health and Social Care Act 2012 having established the Health and Social Care Information Centre (HSCIC) as an Executive Non-Departmental Public Body which was empowered to obtain identifiable patient information from General Practices[495]. However, the initiative did not also have a

[492] Department of Health and Social Care (2021) *NHS Constitution for England*. Available at www.gov.uk/government/publications/the-nhs-constitution-for-england
[493] Horn R and Kerasidou A. Sharing Whilst Caring: Solidarity and Public Trust in a Data-Driven Healthcare System. *BMC Medical Ethics*. 2020 **21** 110
[494] Lowrance W. (2012) *Privacy, Confidentiality and Health Research*. Cambridge: Cambridge University Press
[495] Carter P, Laurie G T and Dixon-Woods M. The Social Licence for Research: Why care.data Ran into Trouble. *Journal of Medical Ethics*. 2015 **41** 404-409

'societal seal of approval'[496] or 'social licence'[497] - and consequently over a million patients opted out of the system[498]. Carter at al suggest that the care.data initiative failed because there was insufficient recognition by public authorities that patients needed to accept the purposes for which their data would be used and consequently, the responsibility to ensure awareness and therefore acceptance was not suitably discharged; resulting in a lack of trust and objection to further data use[499]. A regulation and governance system which is effective and trustworthy is key to ensuring that public institutions maintain public trust[500].

More recently, the National Data Opt-Out initiative has been introduced in England. This initiative allows patients to opt out of their confidential data being used for purposes beyond their direct healthcare, such as for research purposes or for NHS service planning[501]. A more cautious approach appears to be being taken with the National Data Opt-out, compared to the care.data initiative, as the full roll out has been delayed until 31 March 2022 to ensure that the opt out system which supports this initiative is fit for purpose and to ensure that there has been an effective campaign to raise awareness[502]. Empirical work has indicated that whilst patients generally accept their data being used for research and planning purposes within the NHS, there remains concern about sharing data with commercial companies and moreover, awareness of such practices and the National Data Opt-Out

[496] Horn R and Kerasidou A. Sharing Whilst Caring: Solidarity and Public Trust in a Data-Driven Healthcare System. *BMC Medical Ethics*. 2020 **21** 110
[497] Carter P, Laurie G T and Dixon-Woods M. The Social Licence for Research: Why care.data Ran into Trouble. *Journal of Medical Ethics*. 2015 **41** 404-409
[498] Horn R and Kerasidou A. Sharing Whilst Caring: Solidarity and Public Trust in a Data-Driven Healthcare System. *BMC Medical Ethics*. 2020 **21** 110
[499] Carter P, Laurie G T and Dixon-Woods M. The Social Licence for Research: Why care.data Ran into Trouble. *Journal of Medical Ethics*. 2015 **41** 404-409
[500] Academy of Medical Sciences (2011) *A New Pathway for the Regulation and Governance of Health Research*. Available at acmedsci.ac.uk/policy/policy-projects/a-new-pathway-for-the-regulation-and-governance-of-health-research
[501] *NHS. Sharing your Health Records* (2018) Available at www.nhs.uk/using-the-nhs/about-the-nhs/sharing-your-health-records/
[502] Lord Bethell (2021) *'NHS Digital: Primary Care Medical Records'* Hansard: House of Lords Debates 8 June c. 1320

scheme more broadly remains low[503]. The need to establish a basis for a 'social contract' therefore remains and appears to be the basis of the decision to delay full implementation.

Whilst the focus of my thesis is the secondary research use of surplus tissue, it is important to reflect on previous initiatives which raise similar issues to ensure that mistakes of the past are not repeated. My thesis proposes regulatory approaches which aim to better enable the sharing of surplus tissue for secondary research purposes and therefore acceptance of secondary research as part of a social contract is important to ensure a successful outcome. Public dialogue work undertaken by Ipsos MORI[504] in relation to a social contract for genomic medicine indicated that the public consider a social contract within the NHS to be based on three key principles; reciprocity, altruism and solidarity. I will consider each of these principles in more detail below.

7.3. Reciprocity

Reciprocity is a relationship which involves giving and receiving. In his book '*Reciprocity',* Lawrence Becker[505] suggests that as moral agents within a society, we should be more disposed to reciprocity as a matter of moral character; in that where good is received, whether directly or indirectly, we should reciprocate with a good that is commensurate to the good received[506]. Reciprocity as an expected moral standard would ensure consistency and predictability which is not always achieved with individual autonomy, which could be seen as a selective reciprocity, and would increase the overall 'good' and trust in a social group[507]. A culture of 'social reciprocity' was suggested by Titmuss when researching the 'gift' approach to blood donation, who suggested that giving is not always on the understanding of personal and direct reciprocation[508]. Titmuss suggests that the UK blood donation model (compared to the US commercial model) is more effective because it promotes a

[503] Atkin C, Crosby B, Dunn K et al et al. Perceptions of Anonymised Data Use and Awareness of the NHS Data Op Amongst Patients, Carers and Healthcare Staff. Research Involvement and Engagement 2021 **7(40)**
[504] Ipsos Mori (2019) *A Public dialogue on genomic medicine: time for a new social contract?* Available at www.ipsos.com/ipsos-mori/en-uk/public-dialogue-genomic-medicine-time-new-social-contract
[505] Becker L C. (2014) *Reciprocity.* Oxon: Routledge.
[506] *Ibid*
[507] *Ibid*
[508] Titmuss R M. (2018) *The Gift Relationship: From Human Blood to Social Policy.* Bristol: Policy Press.

social structure where citizens give with no direct expectation of receiving, which in turn ensures a society where willingness to give creates a social structure which gives back[509]. Moreover, empirical studies have suggested that some tissue donors consider the opportunity to donate their surplus tissue for use in health-related research as a way to reciprocate for the care and treatment which they have received and to show gratitude to the healthcare institution[510]. In the context of health-related research which uses surplus tissue, reciprocity would suggest that there is mutual return of services and resources between patients whose tissue may be used for research purposes and the researchers and healthcare professionals who seek to improve and to deliver healthcare services[511].

The principle of reciprocity plays an important role in my overall thesis aim, of all surplus tissue samples being potential research samples, because reciprocity may to some degree be *passive*, particularly when compared to the gifting model which was discussed in ss. 6.3. What I mean by this is that where surplus tissue samples which are stored in a diagnostic archive are used for secondary research purposes, the patient becomes a 'passive donor'[512]. However, the gifting of tissue samples for research purposes implies a more active and decisive approach by the patient to give or donate their tissue. Moreover, approaches rooted in reciprocity may be conceptualised as accepting concessions, such as surplus tissue being used for secondary research purposes, based on benefits received in the form of healthcare provided by the NHS. This therefore shifts the focus from individual decisions of control over what happens to surplus tissue and more towards a broader societal acceptance of a social licence - which is more accepting of the need for surplus tissue for research

[509] In the context of health-related research which uses surplus tissue, reciprocity would suggest that there is mutual return of services and resources between patients whose tissues may be used for research purposes and the researchers and healthcare professionals who seek to improve and to deliver healthcare services .
[510] Lewis C, Clotworthy M, Hilton S et al. Consent for the use of Human Biological Samples for Biomedical Research: A Mixed Methods Study Exploring the UK Public's Preferences. *British Medical Journal Open*. 2013 **3** Morrell B. Cancer as Rubbish: Donation of Tumour Tissue for Research. *Qualitative Health Research*. 2011 **21(1)** 75-84
[511] Kanellopoulou N K. (2011) Reciprocity, Trust, and Public Interest in Research Biobanking: In search of a balance. In Lenk C, Hoppe N, Beier K, Wilderman C. (eds.) *Human Tissue Research: A European Perspective on the Ethical and Legal Challenges.* (pp 45 – 54) Oxford: Oxford University Press.
[512] Lensink M A et al. Responsible Research with Human Tissues: The Need for Reciprocity Towards Both Collectives and Individuals. *The American Journal of Bioethics.* 2021 **21(4)** 75-78

purposes and the broader benefits which this brings. However, there are risks with an approach which is based on *passive* reciprocity. First, this assumes that all patients would accept the concessions - something which the failure of the care.data initiative suggests is not necessarily a reasonable assumption. Second, there is a risk that moving away from the *active* decision making in a 'gifting' model towards a *passive* approach could erode not only trust, but also feelings of altruism - due to opportunities to express altruistic interests being lessened. Therefore, when establishing regulatory approaches to better enable the availability of surplus tissue for secondary research purposes, these are important considerations.

7.4. Altruism

The donation of tissue samples for health-related purposes is generally considered to be an act of altruism because this type of research does not have any potential to directly benefit the donor - the benefits are understood to be future patients and society more broadly[513]. This is reflected in common terminology such as 'donation' or 'gifting', terms which are associated with the giving of tissue in a way which is unselfish and altruistic[514]. Altruism relates to the voluntary and intentional desire to help others, whether on an individual person or broader community level, and a belief that doing so is the 'right thing to do' rather than with any expectation of reward[515]. Whilst there may be some reciprocity following an altruistic act, this cannot be a prerequisite. When patients, or parents of children who are patients, are asked about their views in relation to donating surplus tissue for use in health-related research, they commonly express an altruistic preference for the tissues to be used for such purposes because they recognise that their donated tissues can benefit others[516].

[513] Nuffield Council on Bioethics (2011) *Human Bodies: Donation for Medicine and Research*. Available at www.nuffieldbioethics.org/publications/human-bodies-donation-for-medicine-and-research

[514] Lenk C. (2011) Taking Solidarity Seriously: Do Biobank Institutions Have a Moral Obligation to Inform Their Patients About Incidental Findings? In Lenk C, Hoppe N, Beier K, Wilderman C. (eds.) *Human Tissue Research: A European Perspective on the Ethical and Legal Challenges* (pp 55 – 64) Oxford: Oxford University Press.

[515] Morrell B. Cancer as Rubbish: Donation of Tumour Tissue for Research. *Qualitative Health Research*. 2011 **21(1)** 75-84

[516] Lewis C, Clotworthy M, Hilton S et al. Consent for the use of Human Biological Samples for Biomedical Research: A Mixed Methods Study Exploring the UK Public's Preferences. *British Medical Journal Open*. 2013 **3**

Altruism does however usually involve awareness and decision making on some level and altruistic actions with regards to the donation of surplus tissue for secondary research use is usually discharged via the giving of consent. In the context of my thesis, which focuses on tissue which is stored in diagnostic archives in circumstances where consent for secondary research use has not been requested, it is therefore important to establish the relevance and the role of altruism in such scenarios. Earlier in ss. 7.3 I suggested that a passive approach which relies on principles of reciprocity, and therefore accepts the secondary research use of surplus tissue based on the societal benefits which can be gained, risks eroding feelings of altruism. This is an important balance to achieve, not least because of the importance of altruism in health research more broadly. In the context of my thesis I think it is important not to lose sight of the value which altruism and opportunities to act on altruistic interests bring. With this in mind, chapter 11 proposes a regulatory approach which, if consistently applied across the NHS, could better enable the availability of surplus tissue for secondary research purposes as well as ensuring opportunities for patients to act on altruistic interests. I suggest that the opportunity for patients to act on their altruistic interests could be achieved by patients having the opportunity to choose to allow their surplus tissue samples to be used for secondary research purposes, by choosing not to object.

Whilst altruism may be seen to have an important societal role in bringing about good, opportunities for patients to act on altruistic interests may also have benefit on an individual patient level. Empirical evidence indicates that patients recognise the importance of research and perceive the donation of tissue samples to be helping others. However, such altruistic behaviours have also been associated with experiences of surviving or regaining control after a life limiting experience such as cancer and

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Vermeulen E et al. A Trial of Consent Procedures for Future Research with Clinically Derived Biological Samples. *British Journal of Cancer.* 2009 **101** 1505-1512

Hamilton S et al. Consent Gained from Patients After Breast Surgery for the use of Surplus Tissue in Research: An Exploration. *Journal of Medical Ethics.* 2007 **33** 229-233

Williams A M et al. Consent to Donate Surgical Biospecimens for Research: Perceptions of People with Colorectal Cancer. *Cancer Nursing.* 2016 **39(3)** 221-227

Soto C et al. Consent to Tissue Banking for Research: Qualitative Study and Recommendations. *Archives of Diseases in Childhood.* 2012 **97** 632-636

being given an opportunity to donate surplus tissue for use in health-related research may therefore increase a person's sense of control over their illness[517]. Moreover, evidence suggests that patients often express a desire to help other patients who are going through similar experiences and altruism can be a key element of coming to terms with an illness[518].

7.5. Solidarity

The concept of solidarity has largely been brought into the realms of bioethics by Barbara Prainsack and Alena Buyx in recent years. In a report commissioned by the Nuffield Council on Bioethics[519], Prainsack and Buyx present solidarity as shared practices which reflect a collective commitment to carry some degree of cost, whether financial, social, emotional or otherwise, to assist others. This collective commitment originates from a recognition of similarity with others, such as having the same or a similar medical condition or having a loved one with a particular medical condition. Moreover, it is something that occurs on a practical level rather than a purely inner sentiment. It is therefore the willingness to carry actual costs which sets solidarity apart from just having feelings of empathy or sympathy with others[520].

Prainsack and Buyx present a framework of three tiers of solidarity. Tier one is where solidarity occurs on an interpersonal level with individual people recognising some commonality with others and being willing to forego some degree of cost in the interest of others. Tier two is where solidarity occurs on a group level, such as self-help groups where there is an established group within which solidarity amongst its members is manifested due to some common cause. Tier three is where solidarity is

[517] Williams A M et al. Consent to Donate Surgical Biospecimens for Research: Perceptions of People with Colorectal Cancer. *Cancer Nursing.* 2016 **39(3)** 221-227

[518] Bulsara C, Ward A and Joske D. Haematological Cancer Patients: Achieving a Sense of Empowerment by use of Strategies to Control Illness. *Journal of Clinical Nursing*. 2004 **13** 251-258

[519] Prainsack B and Buyx A. (2011) *Solidarity: Reflections on an Emerging Concept in Bioethics_Report Commissioned by the Nuffield Council on Bioethics.* Available at www.nuffieldbioethics.org/publications/solidarity
See allso Prainsack B and Buyx A (2017) *Solidarity in Biomedicine and Beyond.* Cambridge: Cambridge University Press

[520] *Ibid*

manifested via legal or contractual means, such as Government welfare programmes[521]. Dawson and Verweij however, propose two types of solidarity, which they refer to as *rational* and *constitutive*[522]. A *rational* solidarity occurs where there is a collective threat which a group, or even society more broadly, stands against together. A *constitutive* solidarity however is a normative social concept which reflects shared values and norms which do not act to oppose a common threat, but rather act to bring members of a society together based on a common humanity and aims of social betterment[523].

The concept of solidarity has been applied in various field of bioethics, such as big data[524] and biobanking[525]. In the field of biobanking, Prainsack and Buyx[526] propose a solidarity-based approach which moves away from an autonomy dominated focus and towards greater emphasis being given to people's willingness to donate data and tissue samples for health research purposes. This is based on the principle that important moral reasoning for undertaking health-related research should not be overshadowed and risk becoming drowned out by the *equally* powerful moral reasoning for protecting individuals[527]. Empirical evidence repeatedly indicates that people are supporting of health-related research and are willing to donate their data and tissue samples to be used for such purposes[528]. Moreover, Prainsack and Buyx refer to emerging evidence that people are actually more willing to let go of their data and tissues than an autonomy-based model will allow, suggesting that this balance

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[521] *Ibid*

[522] Dawson A and Verweij M. Solidarity: A Moral Concept in Need of Clarification. *Public Health Ethics*. 2012 **5(1)** 1-5

[523] Dawson A and Verweij M. Solidarity: A Moral Concept in Need of Clarification. *Public Health Ethics*. 2012 **5(1)** 1-5

[524] Woods S. (2016) Big Data Governance: Solidarity and the Patient Voice. In Mittelstadt B D and Floridi L (eds.) *The Ethics of Biomedical Big Data* (pp 221 – 238) Cham: Springer

[525] Prainsack B and Buyx A. A Solidarity-Based Approach to the Governance of Research Biobanks. *Medical Law Review*. 2013 **21** 17-91

[526] *Ibid*

[527] Harris J. Scientific Research is a Moral Duty. *Journal of Medical Ethics.* 2005 **31(4)** 242-248

[528] Ipsos MORI (2018) *Consent to use Human Tissue and Linked Health Data in Health Research. A Public Dialogue for Health Research Authority and Human Tissue Authority*. Available at www.hra.nhs.uk/documents/1570/Consent_to_use_human_tissue_and_linked_health_data_in_health_research_FINAL.pdf

Williams A M et al. Consent to Donate Surgical Biospecimens for Research: Perceptions of People with Colorectal Cancer. *Cancer Nursing*. 2016 **39(3)** 221-227

Hamilton S et al. Consent Gained from Patients after Breast Surgery for the use of Surplus Tissue in Research: An Exploration. *Journal of Medical Ethics*. 2007 **33** 229-233

may therefore be tipped too far in favour of individual autonomy at the expense of health research[529]. A solidarity-based approach therefore aims to re-balance individual autonomy with progressing health related research, by accepting that participants are often willing to concede some benefits which may be associated with an exclusively autonomous approach, such as control over data and samples and direct feedback of findings and research outcomes[530].

A solidarity-based approach to biobanking, as proposed by Prainsack and Buyx, would involve participants agreeing to providing data and tissue samples on a 'mission statement' basis, indicating acceptance of broad goals and intentions to support health-related research for the good of society, rather than on the basis of a detailed consent process covering the types of research and research bodies which may use the tissue and data[531]. According to Prainsack and Buyx, a solidarity-based approach is justified, at least in part, on the basis that human beings are relational and as such, we are highly dependent on the wellbeing of others for our own wellbeing[532]. Therefore, policy and practice which aims to promote the health of individuals, including by facilitating and progressing health-related research, is also in the interest of society on a macro level[533]. Consequently, viewing individuals as bounded, self-interested beings and adhering to a deep-rooted fixation on individual autonomy is not only flawed, but actually risks slowing down the progression of medicine within a society to the detriment of its citizens[534]. An approach which is grounded in the principle of solidarity recognises this interconnectedness between individuals within a society, affording equal emphasis to the collective rather than over emphasising the individual[535].

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[529] Prainsack B and Buyx A. A Solidarity-Based Approach to the Governance of Research Biobanks. *Medical Law Review*. 2013 **21** 17-91
[530] *Ibid*
[531] Prainsack B and Buyx A. A Solidarity-Based Approach to the Governance of Research Biobanks. *Medical Law Review*. 2013 **21** 17-91
[532] *Ibid*
[533] *Ibid*
[534] Prainsack B. The "We" in the "Me": Solidarity in Health Care in the Era of Personalized Medicine. *Science, Technology and Human Values*. 2017 **43(1)** 21-44
[535] *Ibid*

There is empirical evidence to suggest that that there is a solidarity basis to donating surplus tissue and associated data to research tissue banks. In a study undertaken by Dixon-Woods et al to explore the views of children with cancer, and their parents, with regards to gifting surplus tissue samples, a strong feeling of solidarity was expressed by those interviewed[536]. Donating surplus tissue samples was seen as something that was very positive and donors felt united with other people, as part of a 'community' in a similar position in pursuit of a common goal[537].

The question of how individual rights can be recognised yet balanced with community interests has previously been explored by Newdick[538] in the context of a solidarity approach within the NHS. Whilst Newdick considers this question in the context of resource allocation within a finite NHS budget, his conclusion that solidarity is about morality within the NHS institution to promote social cohesion rather than individualistic rights claims[539] may be extrapolated into the field of research using surplus tissue. Newdick suggests that emphasising autonomy without also considering reciprocity and solidarity misses an important element within a broader social welfare society, because social citizenship *creates* a sense of solidarity[540]. This is important within the context of my thesis because I aim to establish regulatory approaches which better facilitate the sharing of surplus tissue for secondary research purposes in a way which better balances individual patient interests with broader societal interests by viewing the issue from a more enabling perspective - how can surplus tissue be made available for secondary research purposes in a way which also respects and protects individual interests. These regulatory approaches are therefore rooted in citizenship and solidarity by providing a better balance between individual patient interests and broader societal interests - in the interests of all citizens within society.

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[536] Dixon-Woods M, Cavers D, Jackson C J et al. Tissue Samples As 'Gifts' for Research: A Qualitative Study of Families and Professionals. *Medical Law International*. 2008 **9** 131-150

[537] Dixon-Woods M, Cavers D, Jackson C J et al. Tissue Samples As 'Gifts' for Research: A Qualitative Study of Families and Professionals. *Medical Law International*. 2008 **9** 131-150

[538] Newdick C. Solidarity, Rights and Social Welfare in the HND – Resisting the Tide of Bioethics? *Medicine and Law.* 2008 **27** 547-562

[539] *Ibid*

[540] *Ibid*

7.6. Is There a Duty to Support Health Research?

In recognising the relational nature of human beings within a society, and that there is both an individual and a public interest in the well-being of society, it has been suggested that there may be a duty or obligation to support research practices which maintain and improve health[541]. This suggestion is based on the fact that any benefit which *current* recipients and benefactors of healthcare receive, is on the basis of *previous* persons having participated in health-related research - and therefore previous persons also having accepted any risks or burdens associated with such research[542]. Where persons choose to accept the benefits of previous research by accessing healthcare then there may be a corresponding obligation on current patients to support health-related research which will in turn benefit other or future persons[543]. Harris suggests that whilst any such obligation to support health-related research should not be enforceable, and people should be free to discharge any such duty in ways and at a time which suits them, a duty does indeed exist[544]. Moreover, not only is there a duty to benefit future persons, as those in the past have benefited the current generation, there is also an argument of fairness. The fairness argument suggests that those who accept the benefits of health-related research by accessing healthcare services and do not also concede some cost to support health-related research for the benefit of others, are 'free-riders'[545]. Proponents of the 'free rider'

[541] Caplan A L. Is There a Duty to Serve as a Subject in Biomedical Research? *IRB: Ethics and Human Research*. 1984 **6(5)** 1-5
Harris J. Scientific Research is a Moral Duty. *Journal of Medical Ethics*. 2005 **31(4)** 242-248
Chan S and Harris J. Free Riders and Pious Sons – Why Science Research Remains Obligatory. *Bioethics.* 2009 **23(3)** 161-171.
[542] Caplan A L. Is There a Duty to Serve as a Subject in Biomedical Research? *IRB: Ethics and Human Research*. 1984 **6(5)** 1-5
Harris J. Scientific Research is a Moral Duty. *Journal of Medical Ethics*. 2005 **31(4)** 242-248
Chan S and Harris J. Free Riders and Pious Sons – Why Science Research Remains Obligatory. *Bioethics.* 2009 **23(3)** 161-171.
[543] Caplan A L. Is There a Duty to Serve as a Subject in Biomedical Research? *IRB: Ethics and Human Research*. 1984 **6(5)** 1-5
[544] Harris J. Scientific Research is a Moral Duty. *Journal of Medical Ethics*. 2005 **31(4)** 242-248
[545] Caplan A L. Is There a Duty to Serve as a Subject in Biomedical Research? *IRB: Ethics and Human Research*. 1984 **6(5)** 1-5
Harris J. Scientific Research is a Moral Duty. *Journal of Medical Ethics*. 2005 **31(4)** 242-248

argument suggest that this would be unfair because 'free-riders' knowingly accept the benefits but do not give back.

Whether the arguments put forward to support a moral duty to support and participate in health-related research do indeed demonstrate that any such duty exists has however been questioned[546]. Shapsay and Pimple suggest that participating in health-related research is a moral good, but this does not extend to a demonstrable *duty* to participate as there are many moral goods within society and we cannot reasonably be expected to reciprocate for each and every one[547]. However, Chan and Harris suggest that where there is an opportunity to help others then as moral members of society, we should wherever this would be reasonable[548]. Health-related research is therefore one way to support and promote the welfare of others but is not in itself an activity which should be obliged by all recipients and benefactors of healthcare[549].

Whilst there may be no individual duty to support health-related research, even by those who do reap the benefits of previous research, there may however be a social imperative to ensure that healthcare structures are conducive to supporting and progressing health-related research for the broader benefit of society. This is particularly relevant within the context of the UK NHS as the benefits delivered by the health service and gained by patients are bounded within a single institution[550]. Empirical evidence suggests that people are willing for their surplus tissue and associated data to be used for health-related purposes because they recognise the benefit that such research can bring and

[546] Brassington I. John Harris' Argument for a Duty to Research. *Bioethics*. 2007 **21(3)** 160-168
Shapsay S and Pimple K D. Participation in Biomedical Research is an Imperfect Moral Duty: A Response to John Harris. *Journal of Medical Ethics.* 2007 **33** 414-417
[547] Shapsay S and Pimple K D. Participation in Biomedical Research is an Imperfect Moral Duty: A Response to John Harris. *Journal of Medical Ethics.* 2007 **33** 414-417
[548] Chan S and Harris J. Free Riders and Pious Sons – Why Science Research Remains Obligatory. *Bioethics*. 2009 **23(3)** 161-171.
[549] Shapsay S and Pimple K D. Participation in Biomedical Research is an Imperfect Moral Duty: A Response to John Harris. *Journal of Medical Ethics.* 2007 **33** 414-417
[550] Johns S. (2009) Is There an Obligation to Participate in Medical Research? In Corrigan O, McMillan, Liddel K, Richards M, Weijer C (eds.) *The Limits of Consent: A Socio-Ethical Approach to Human Subject Research in Medicine* (pp 115 – 132) Oxford: Oxford University Press.

because surplus tissue is something which would otherwise go to waste[551]. Arguably therefore, there is an imperative for society to implement effective mechanisms to ensure that tissue and associated data *can* be accessed for use in health-related research, in ways which safeguard the interests of those individuals from whom the tissue and data originated – something which my thesis aims to address.

[551] Williams A M et al. Consent to Donate Surgical Biospecimens for Research: Perceptions of People with Colorectal Cancer. *Cancer Nursing.* 2016 **39(3)** 221-227
Soto C et al. Consent to Tissue Banking for Research: Qualitative Study and Recommendations. *Archives of Diseases in Childhood.* 2012 **97** 632-636

CHAPTER 8

NARROWING THE FOCUS

The aim of my thesis is to highlight and address issues which limit or stymie the availability and value of surplus tissue for secondary research purposes and to establish regulatory approaches which, if implemented in practice, could mean that all tissue samples have the *potential* to be research samples. Moreover, my thesis aims to achieve a better balance between the public interest in facilitating important research which utilises surplus tissue and safeguarding individual patient interests. To achieve this aim effectively, it is necessary to challenge the existing *status quo* in terms of legal and ethical ideals so that a more equal balance can be realised. This section sets out the key legal and philosophical issues which my thesis challenges, with a view to proposing regulatory approaches which, if implemented in practice, could better enable all surplus tissue samples to be potential research samples.

8.1. Legal Approach

The legal and regulatory framework within which the use of surplus tissue and associated patient information for secondary research purposes sits is complex. This is partially due to the piecemeal way in which this area of regulation has built up over a number of years[552]. With this in mind, my thesis challenges two key legal areas, within the broader context of the existing legal and regulatory framework, with the aim of establishing regulatory approaches which if implemented in practice, could better enable the availability of surplus tissue for secondary research purposes.

The first legal issues which I address is in relation to the linking of surplus tissue with associated patient information for secondary research purposes in the absence of consent. The real value in surplus

[552] Laurie G and Harmon S. (2015) Through the Thicket and Across the Divide: Successfully Navigating the Regulatory Landscape in Life Sciences Research. In Cloatre E and Pickersgill M (eds.) *Knowledge, Technology and Law* (pp 121 – 136) Oxon: Routledge

tissue in research can only be realised when the tissue and associated data are linked. This is because linking tissue with information about the person from whom the tissue was removed allows insight into complex interfaces between health, lifestyle, environment and genes which would not be feasible from the tissue alone[553]. Linking tissue and data therefore strengthens the validity and utility of research using surplus tissue[554]. However, linking tissue and data creates further issues relating to data protection and confidentiality because the possibility of identifying the person from whom the tissue was removed increases, particularly where multiple items of data are linked together[555]. Addressing the issue of identifiability in the context of surplus tissue being used for secondary research purposes in the absence of consent is important. This is because the HT Act 2004 provides for tissue to only be used for research purposes without consent where the research is to be 'carried out in circumstances such that the person carrying it out is not in possession, and not likely to come into possession, of information from which the person from whose body the material has come can be identified'[556]. Therefore, to ensure that surplus tissue can be used for secondary research purposes and to obtain the maximum value by linking the tissue with relevant information about the person from whom it was removed, it is important to have an enabling regulatory approach which facilitates such activities in a way which also protects individual patient interests.

Chapter 10 takes a comparative approach between the HT Act 2004 and the Data Protection Act (DPA) 1998 which was in force when the HT Act 2004 was enacted, as well as the General Data Protection Regulation (GDPR) and the Data Protection act 2018, which are currently in force in the UK. The rationale for this is that provision in the HT Act 2004 with regards to tissue not being identifiable to the person carrying out the research appears to reflect wording in the DPA 1998. The DPA 1998 described personal data as data relating to a living person who can be identified 'from those data and

[553] Dörr B, (2014). Collection of Human Tissue Samples in Biobanks: Challenges to Human Rights and Nature. In Albers A, Hoffman T, Reinhardt J (ed) *Human Rights and Nature* (pp 185-196) Dordrecht: Springer
[554] Knoppers B, Isasi R. Stem Cell Banking: Between Traceability and Identifiability. *Genome Medicine*. 2010 **2(73)** 1-7
[555] National Data Guardian (2013) *Information: To Share or Nor to Share? The Information Governance Review.* Available at www.gov.uk/government/publications/the-information-governance-review
[556] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 1 s 1 ss 9 (b)

other information which is in the possession or is likely to come into possession of the data controller'[557]. Moreover, during the passage of the Human Tissue Bill through Parliament, reference was made to the sharing of information which identifies a person breaching the DPA 1998[558], which appears to be a misinterpretation of the DPA – a misinterpretation which was arguably therefore also reflected in the HT Act 2004.

The provision in the HT Act 2004, that tissue can only be used for research purposes in the absence of consent where the researcher is not in possession of information which could identify the person from whom the tissue was removed, appears to apply a 'consent or anonymise' approach. However, a requirement to either have consent or to anonymise data prior to sharing was a common misinterpretation of the DPA 1998[559]. The HT Act 2004 therefore applied a requirement for 'consent or anonymise' without also reflecting broader safeguarding provisions in the DPA 1998. My thesis challenges the provision in the HT Act 2004, which requires that researchers are not be in possession of information which could identify the person from whom the tissue was removed in the absence of consent, exploring whether a broader 'safeguarding' approach could be more effective in facilitating the secondary research use of surplus tissue linked with associated patient information. In practical terms a safeguarding approach would likely apply the same strategies to protect individual patient interests as are currently applied, such as pseudonymisation, and therefore would not lessen the protection which is provided. However, my argument is that approaching the issue from a safeguarding perspective has the potential to shift the focus from a blanket requirement for 'non-identifiability' to a broader 'safeguarding' approach - which considers how surplus tissue and relevant data can be linked effectively to facilitate research whilst also protecting individual patient interests.

The second legal issue which I address is in relation to HTA licensing where diagnostic archives provide surplus tissue samples for health research purposes. The HT Act 2004 provides for licensing of

[557] *Data protection Act 1998*. Available at www.legislation.gov.uk/ukpga/1998/29/contents Part 1 s 1
[558] Baroness Cumberlege (2004) *'Human Tissue Bill'* Hansard: House of Lords Debates 22 July c. 401
[559] Clark S and Weale A (2011) *Information Governance in Health. Research Report. University College London*

specified activities, including the storage and use of tissue for research purposes[560]. The Human Tissue Authority (HTA) code of practice on research[561] provides further detail with regards to when an HTA research licence would be required for a diagnostic archive which supplies surplus tissue for use in health research on request. Chapter 12 challenges the requirements set out by the HTA code of practice on research, suggesting that the code of practice is too ambiguous and implies that a research licence may be required when this is not *necessarily* a requirement under the HT Act 2004. The rationale for this is that over-applying researching licensing requirements has the potential to stymie important research because diagnostic archives may be reluctant to share tissue samples for fear of falling foul of legislative sanctions, leading to a culture of avoidance. Moreover, the implication that an HTA research licence is required where this is not a requirement to comply with the HT Act 2004 is arguably over-regulation which is not proportionate to the actual activities being undertaken.

In challenging the implication that a HTA research licence is required where this is not *necessarily* a requirement under the HT Act 2004, I aim to establish a clearer and more proportionate approach which could better enable the availability of surplus tissue which is held within diagnostic archives. This is within a governance framework which sufficiently protects the interests of patients, whilst also maximising the public interest in health research. This is important in the broader context of my thesis, that all surplus tissue samples should have the potential to be research tissue samples, because a clearer and more proportionate approach to research licensing could help to support diagnostic archives to provide surplus tissue samples for secondary research purposes. Moreover, in establishing a regulatory approach which supports diagnostic archives to provide surplus tissue for secondary research purposes, within a governance framework which safeguards individual patient interests, the intention is to support transitions from diagnostic archive to become establishments which also function as a research tissue bank more broadly.

[560] *Human Tissue Act 2004.* Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 2 s 16
[561] Human Tissue Authority (2017) *HTA Code E: Research.* Available at https://content.hta.gov.uk/sites/default/files/2020-11/Code%20E.pdf

8.2 Philosophical Approach

A key theme throughout my thesis is achieving a balance between protecting individual patient interests and enabling surplus tissue to be used for secondary research in the broader public interest. In 2011 the Academy of Medical Sciences published a report which suggested that the balance in health research regulation was tipped too far towards individual patients, resulting in unnecessarily complex over-regulation[562]. It was suggested that this imbalance risked harming future patients and society more broadly by having the potential to stymie important research[563]. Whilst protecting individual patient interests is of course important, this should not be to the detriment of social benefit achieved through health-related research[564]. Moreover, there is evidence to suggest that people are actually more willing to let go of their data and tissues than an autonomy-based model will allow, suggesting that this balance may therefore be tipped too far in favour of individual autonomy at the expense of health research[565]. With this in mind, my thesis aims to establish regulatory approaches which intend to facilitate the secondary research use of surplus tissue in ways which consider the protection of individual patient and public interests to be more balanced in importance. This is based on the principle that important moral reasoning for undertaking health-related research should not be overshadowed and risk becoming drowned out by the *equally* powerful moral reasoning for protecting individuals[566].

The regulatory approaches which I establish through my thesis are grounded in the principle of solidarity and recognise this interconnectedness between individuals within a society, affording equal emphasis to the collective rather than over emphasising the individual[567]. This solidarity approach

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[562] Academy of Medical Sciences (2011) *A New Pathway for the Regulation and Governance of Health Research.* Available at acmedsci.ac.uk/policy/policy-projects/a-new-pathway-for-the-regulation-and-governance-of-health-research

[563] *Ibid*

[564] Furness P and Sullivan R. The Human Tissue Bill: Criminal Sanctions Linked to Opaque Legislation Threaten Research. *British Medical Journal.* 2004 **328** 533-534

[565] Prainsack B and Buyx A. A Solidarity-Based Approach to the Governance of Research Biobanks. *Medical Law Review.* 2013 **21** 17-91

[566] Harris J. Scientific Research is a Moral Duty. *Journal of Medical Ethics*. 2005 **31(4**) 242-248

[567] Prainsack B. The "We" in the "Me": Solidarity in Health Care in the Era of Personalized Medicine. *Science, Technology and Human Values*. 2017 **43(1)** 21-44

builds on the 'social contract' which lies at the heart of the NHS[568] and ensure that patients can have confidence that their interests will be protected, including with regards to the secondary research uses of tissue and data[569]. Moreover, this approach may be perceived to provide opportunity for patients to reciprocate for the care and treatment which they have received from the NHS and to act on their altruistic interests by permitting the secondary research use of their surplus tissue. Empirical evidence suggests that some patients welcome these opportunities and actually gain some personal benefit from being able to permit their surplus tissue samples being used for such purposes[570]. With this in mind, the secondary research use of surplus tissue may be viewed as an *opportunity* for patients to reciprocate, show solidarity with other patients within a 'health community' and act on altruistic interests - rather than as a concession which patients make as part of a social contract. Chapter 11 argues that there should be a consistent approach applied across all NHS organisations which affords patients the opportunity to choose to donate their surplus tissue, and therefore to act on their altruistic interests, suggesting that this would be fairer for patients than the current varied approach.

8.3. Research questions

8.3.1. *Research question 1.*

Could a 'safeguarding' approach be more effective than a requirement for absolute non-identifiability to facilitate the linking of surplus tissue stored in a diagnostic archive with relevant patient information for secondary research purposes in the absence of consent? (Chapter 10)

A key aim of my thesis has always been to identify ways to better enable the availability of surplus tissue for research purposes, in a way which means that the optimal value could be obtained by allowing linkage with relevant information about the person from whom the tissue was removed. My

[568] Lord Bishop of St Albans (2016) *'National Health Service'* Hansard: House of Lords Debates 14 January
[569] Lucassen A, Montgomery J and Parker M. Ethics and the Social Contract for Genomics in the NHS. In *Annual Report of the Chief Medical Officer 2016: Generation Genome.* Department of Health.
[570] Lewis C, Clotworthy M, Hilton S et al. Consent for the use of Human Biological Samples for Biomedical Research: A Mixed Methods Study Exploring the UK Public's Preferences. *British Medical Journal Open*. 2013 **3** Morrell B. Cancer as Rubbish: Donation of Tumour Tissue for Research. *Qualitative Health Research.* 2011 **21(1)** 75-84

rationale for this is that consent for secondary research use of surplus tissue and associated patient information is often not requested when tissue is removed for clinically directed procedures and obtaining retrospective consent is not always feasible or desirable. Where consent has not been requested from the patient, the linking of associated patient information with surplus tissue samples for secondary research purposes poses a number of legal and ethical challenges, making this a complex area of UK law (see chapter 5). In chapter 10 I consider whether a 'safeguarding' approach when linking surplus tissue and associated patient information could better enable the secondary research use of surplus tissue in a way which maximises the research value in the public interest - whilst also sufficiently respecting and protecting individual patient interests. This is an area which has not previously been addressed in existing literature and is therefore an important question to address in the broader context of my thesis.

8.3.2. Research Question 2.

Would applying a more consistent approach to the secondary research use of surplus tissue samples across NHS organisations be fairer for patients and better address public interest claims compared to the extant inconsistent approach? (Chapter 11)

A dichotomy appears to exist between what patients and the public express when asked about their views with regards to the secondary research use of their surplus tissue, and the approaches taken by organisations to implement the legal provisions set out in the HT Act 2004. Previously undertaken empirical studies and public engagement events have indicated that the majority of people asked express a preference for their surplus tissue samples to be used for research purposes and in some cases, they question why this does not happen more often. Moreover, empirical work had indicated that patients can benefit from being the subject of non-therapeutic research, such as research involving the use of surplus tissue, because they feel solidarity with others and part of a health community (see ss. 7.2 & 7.5). Patients have also expressed that they welcome the opportunity to 'give back' for the care and treatment which they have received (see ss. 7.3 & 7.4).

With this in mind, it appeared to me that an overly risk averse approach to the regulation of surplus tissue was being applied in a way which tipped the balance too far towards regulation and governance, and therefore too far away from research which has a public interest claim, without clear justification. Moreover, inconsistency across NHS organisations which have applied varied policies with regards to the secondary research use of surplus tissue in itself risks further eroding the public interest claim of such research.

Chapter 11 highlights the extant inconsistency across NHS organisations with regards to the secondary research use of surplus tissue samples and discusses the impact which this inconsistency may have on individual patient interests and broader public interest claims. In arguing that a consistent approach should be applied, I suggest that the approach which would have the greatest overall individual patient and also public benefit would be for surplus tissue samples to be available for secondary research purposes where there is no evidence of objection. Furthermore, I suggest that this approach should be supported by well-publicised mechanisms via which patients can record their objection to their surplus tissue samples being used for secondary research purposes would best address both individual and public interests. This conclusion is drawn in the context of the HT Act 2004 providing for the use of surplus tissue samples for secondary research purposes in the absence of consent under certain conditions.

I have not identified any previous work in the academic literature which highlights and challenges the extant inconsistency across NHS organisations with regards to the secondary research use of surplus tissue which is held in diagnostic archives. Moreover, this was an important issues to address in the broader context of my thesis because achieving the overall aim of enabling all surplus tissue samples to be potential research samples requires a more uniform regulatory approach to maximise the sharing of tissue samples for secondary research purposes.

8.3.3. Research Question 3.

Should diagnostic archives which provide surplus tissue samples on request for secondary research purposes require an HTA research licence or would other existing regulatory and governance mechanisms be sufficient to ensure regulatory compliance and safeguarding of patients whose surplus tissue may have research value? (Chapter 12)

The overall aim which this thesis aims to achieve is to better facilitate the availability of surplus tissue for secondary research purposes. I limited the direct focus of this work to tissue samples which are stored in diagnostic archives where consent for secondary research use was not requested. The reason for this was that this area is legally and ethically most contentious and there is currently no clear or consistent infrastructure in the NHS to maximise the availability of this valuable resource. Moreover, it became clear to me that to better enable the potential availability of *all* surplus tissue samples, and therefore to ensure that all surplus tissue samples have the potential to be research samples, this was an important issue to address. There are existing infrastructures which enable surplus tissue samples to be transferred to established research tissue banks with defined consent procedures but there is currently no clear and consistently applied infrastructure to facilitate the secondary use of surplus tissue samples which are surplus to diagnostic requirements where consent was not obtained.

An issue which was important to address in this regard was in relation to requirements for an HTA research licence where surplus tissue is being provided by diagnostic archives for secondary research purposes. Chapter 12 suggests that wording in the HTA code of practice on research implies that a licence is required where this is not necessarily required to comply with the HT Act 2004. Furthermore, this implication risks stymying important research. This is because diagnostic archives sometimes avoid providing tissue samples for secondary research purposes due to concerns that they are undertaking a licensable activity and may fall foul of legislative sanctions. Moreover, an implication that an HTA research licence may be required where this is not *necessarily* required to comply with the HT Act 2004 is arguably over-regulation and therefore is not proportionate to the actual activities

being undertaken. With this in mind, chapter 12 argues that viewing diagnostic archives which provide surplus tissue samples for research purposes, as undergoing a transitionary *process* from a diagnostic archive to also functioning as a research tissue bank, with an in-between state where the establishment is neither a purely diagnostic archive nor yet also functioning as a research tissue bank, could be conducive to a more proportionate regulatory approach.

CHAPTER 9

SUMMARY OF THE ARTICLES

9.1. Article 1: From 'consent or anonymise' to 'share and protect': Facilitating access to surplus tissue for research whilst safeguarding donor interests.

9.1.1. Abstract

There is significant research value in the secondary use of surplus human tissue which has been removed during clinical care and is stored in diagnostic archives. However, this value is limited without access to information about the person from whom the tissue was removed. As the research value of surplus tissue is often not realised until after the patient's episode of care, it is often the case that no consent has been given for any surplus tissue to be used for research purposes. The Human Tissue Act 2004 does permit research use of surplus tissue without consent, but the researcher must not be in possession of information which could identify the person from whom the tissue was removed. Due to the commonly applied 'consent or anonymise' approach, linking tissue and data is challenging and full anonymisation would likely render much research on surplus tissue ineffectual. This article suggests that in recognising the value in surplus tissue linked with information about the person, a 'share and protect' approach which considers safeguards other than anonymisation, where obtaining consent for research use would not be feasible, would better balance the public benefit of health research with the protection of individual rights and interests than a requirement for either consent or anonymisation.

9.1.2. Detailed Summary

This article aims to address the question of whether a 'safeguarding' approach could be more effective than a requirement for absolute non-identifiability to facilitate the linking of surplus tissue stored in a diagnostic archive with relevant patient information for secondary research purpose in the absence of consent. The basis for addressing this issue is that the real research value in surplus tissue is only

realised when tissue is linked with information about the person from whom the tissue was removed - the tissue itself has limited value. Therefore, to achieve the maximum benefit from my overall thesis aim, to enable all surplus tissue samples to be potential research samples, it was important to address this question.

Linking surplus tissue with associated patient information creates complexities with regards to identifiability, not least because data are not necessarily either fully identifiable or fully anonymous, there is a spectrum of varying levels of identifiability in-between and the identifiability of data can change where additional information becomes available. It seemed to me that a regulatory impasse existed whereby important research involving surplus tissue and associated patient information is potentially stymied because consent for secondary research use had not been obtained when the tissue samples were removed and there was a risk that data which is required to achieve a research aim could identify the person from whom the tissue was removed. Therefore, to achieve my overall thesis aim of enabling all research tissue samples to be potential research samples, I wanted to explore a more facilitative approach to the use of surplus tissue linked with associated data which safeguards individual privacy interests, but in a way which is more balanced with the public benefits which come from health research.

To achieve this, I propose a 'share and protect' approach which views the secondary research use of surplus tissue linked with associated patient information from the perspective of, how can these valuable research materials be used for secondary research purposes in a way which also protects individual privacy interests. This approach differs from the current 'consent or anonymise' approach which is commonly applied under the HT Act 2004. In proposing a 'share and protect' approach, this article does not suggest that this approach should be implemented as an *alternative* to consent. This article does however suggest that where consent for the secondary research use of surplus tissue was not obtained, that the research use of such tissue linked with associated patient information should not be prevented *because* consent was not obtained.

This article further argues that provision in the data protection regulations which require 'appropriate safeguards' to protect the rights and freedoms of data subjects, as well as for technical and organisational measures to be in place to comply with the principle of data minimisation, should sufficiently protect individual interests without a need for absolute non-identifiability. With this in mind, applying a safeguarding approach has the potential to be more enabling of the sharing of surplus tissue samples linked with associated data compared to a blanket 'consent or anonymise' approach. This is because applying appropriate safeguards and technical and organisational measures provides a broader scope of mechanisms to protect individual interests and enables consideration of the data necessary to achieve the research aim.

9.2. Article 2: Fair Distribution of Opportunities to Donate Surplus Tissue for Secondary Research? A Case Study.

9.2.1. Abstract

Tissue which is removed during clinically directed procedures and is surplus to diagnostic requirements can be a valuable resource of tissue samples for health-related research. However, there is currently some variation across NHS organisations with regards to whether surplus tissue can be accessed for use in health-related research and whether there is a requirement to evidence that the patient from whom the tissue was removed had agreed to its secondary research use. Using 12 NHS organisations in England as a case study, this article suggests that this inconsistency means that there is an unfair distribution of opportunities for patients in relation to the donation of surplus tissue for use in health-related research. These are opportunities to choose whether tissue is used in research and the opportunity to knowingly act on altruistic interests by choosing to permit its use for this purpose. Moreover, this inconsistency means that the public interest claims associated with maximising the availability of surplus tissue for use in health-related research and maintaining trust cannot be fully met. This article concludes that a uniform and unified approach of ensuring awareness,

which permits the use of surplus tissue samples held in diagnostic archives in the absence of objection from the tissue donor, would be the fairest approach and would maximise public benefit.

9.2.2. Detailed Summary

This article highlights the variation of approach with regards to the sharing of surplus tissue for secondary research purposes and requirements for consent across different NHS organisations, using policies from 12 NHS organisations across England as a case study to demonstrate this point. This article suggests that a varied and inconsistent approach to the sharing of surplus tissue samples for secondary research and requirements for consent across different NHS organisations means that there is an unfair distribution of opportunities for individual patients associated with the donation of tissue samples for health research. The opportunities which I refer to here are the opportunity for patients to choose whether to donate their tissue samples for secondary research purposes and the opportunity to knowingly act on their altruistic interests. Moreover, this article suggests that this variation and inconsistency across different NHS organisations means that public interest claims associated with the secondary research use of surplus tissue cannot be fully realised. The public interest claims which I refer to here are the societal benefit which comes from increased medical knowledge gained from health research and the public interest in trust which comes from regulatory safeguards.

This article identifies four distinct approaches taken by the 12 NHS organisations in the case study with regards to the availability of surplus tissue for secondary research purposes and requirements for consent. I consider each of these approaches from two perspective. First, the perspective of providing opportunities for patients to choose whether their surplus tissue samples are used for secondary research purposes, and therefore to act on their altruistic interests. Second, the perspective of achieving public interest claims associated with increasing medical knowledge and improved healthcare through health research and securing and maintaining trust in healthcare providers. In identifying these four distinct approaches across different NHS organisations, this article suggests that

this variation and inconsistency is unfair because it is not based on any reasoned decision-making process or valid principle of justice.

The inconsistent approaches taken by different NHS organisations denies some patients the opportunity to choose whether to donate their surplus tissue for secondary research purposes, whilst providing this opportunity to others. Allowing autonomy of choice demonstrates respect and therefore, to allow some patients the opportunity to choose whilst denying others the same opportunity arguably treats people different morally. This article therefore suggests that a varied and inconsistent approach across different NHS organisations with regards to the availability of surplus tissue for secondary research purposes and requirements for consent is unfair. Moreover, this article further suggests that this varied and inconsistent approach also means that the public interest claims in health research involving surplus tissue and in establishing and maintaining trust in healthcare providers cannot be met.

This article concludes that the approach which, if applied across all NHS organisations, would best achieve this balance would be for all surplus tissue samples to be available for secondary research purposes where there is no objection recorded. Moreover, this approach should be supported by patient engagement to raise awareness regarding the research value of surplus tissue and mechanisms via which patients can record an objection which are well-publicised, simple and accessible.

9.3 Article 3: Bridging the Gap: Proportionate Regulation for Tissue Sharing by Diagnostic Archives for Research in the UK.

9.3.1. Abstract

Surplus tissue stored in a diagnostic archive can be a valuable resource for health research. The Human Tissue Authority provides guidance on when a diagnostic archive would be considered to also be functioning as a research tissue bank and therefore would require a research licence. This article suggests that the wording is too ambiguous and implies that a research licence *may* be required where

this is not *necessarily* the case; potentially causing unintended consequences of either unnecessarily avoiding sharing samples from diagnostic archives or over regulation by applying licensing standards when not necessarily required. Using the anthropological principle of liminality, diagnostic archives sharing tissue samples for research are viewed as undertaking a transitionary process which has an 'in-between' state. In considering this as a transitionary process, regulation can be applied which is proportionate to the actual activities being undertaken, taking into consideration the different regulatory bodies holding regulatory stewardship roles.

9.3.2. Detailed Summary

This article aims to answer the question, should diagnostic archives which provide surplus tissue samples on request for secondary research purposes require an HTA research licence or could other existing regulatory and governance mechanisms be sufficient to ensure regulatory compliance and safeguarding of patients whose tissue may have research value. This was an important issue to address within my thesis because I considered licensing requirements for diagnostic archives to be a regulatory grey area. This was due to ambiguous wording in the HTA code of practice on research which is not sufficiently clear on whether a diagnostic archive which provides surplus tissue samples on request would be considered to be functioning as a research tissue bank, and therefore should be under the authority of an HTA research licence to comply with the HT Act 2004. Therefore, establishing a clear regulatory approach to requirements for an HTA research licence which is proportionate to the actual activities being undertaken, was crucial to achieve my overall thesis aim of enabling all surplus tissue samples to be potential research samples.

The HTA code of practice on research includes two paragraphs which set out requirements for an HTA research licence where a diagnostic archive provides surplus tissue samples for secondary research purposes:

> 'The HTA's position is that if a diagnostic archive releases tissue for research occasionally upon request, its status as a diagnostic archive is clear. However, if there is an expectation that

tissue will be released on a regular basis, then it may cease to be a purely diagnostic archive, particularly where there are developed governance / decision making structures and procedures for applying for tissue.'[571]

'Where a diagnostic archive functions as a resource for researchers as it invites applications for the release of samples, and/or in any way advertises the archive as a research resource, it is functioning as a research tissue bank.'[572]

Whilst the second paragraph provides a clear definition for when a diagnostic archive is considered to also be functioning as a research tissue bank, as it invites applications to access tissue samples or it advertises itself as a research resource, the first paragraph is not sufficiently clear and implies that an HTA research licence may be required, where this is not *necessarily* required to comply with the HT Act 2004.

This article uses the anthropological principle of liminality to view diagnostic archives which provide surplus tissue samples for secondary research purposes as going through a transitionary *process* which is comprised of three stages. The initial state of a purely diagnostic archive, the 'in-between' state where the establishment is not a purely diagnostic archive but nor is it yet also functioning as a research tissue bank and then the final stage where the establishment invites applications and/or advertises itself as a research resource, and is therefore functioning as a research tissue bank. The rationale for viewing this as a transitional *process* with an in-between state is to establish and apply regulatory approaches which are more proportionate to the actual activities being undertaken. Moreover, this article considers the transitionary process of a diagnostic archive transitioning to become a research tissue bank in the context of a broader regulatory framework which highlights the roles which different regulatory bodies hold at different points through the transitionary process.

[571] Human Tissue Authority (2017) *HTA Code E: Research.* Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20E.pdf paragraph 94
[572] *Ibid* paragraph 95

In considering the transitionary process from purely diagnostic archive to also functioning as a research tissue bank within a broader regulatory framework, this article focuses on three regulatory bodies which hold an authoritative role in the context of tissue samples which are held in a diagnostic archive being available for use in health research. The regulatory bodies which I focus on are the HTA, the HRA and research ethics committees as they also hold a 'regulatory gatekeeper' role - due to having formal responsibility via policy or regulation to undertake a decision-making function which determines whether a research related event proceeds. Moreover, this article further considers these regulatory bodies as regulatory 'stewards', which guide and support through the transitionary process from purely diagnostic archive through to the final state of also functioning as a research tissue bank. In doing so, this article further highlights how these regulatory bodies hold different responsibilities at different points within the transitionary process and how they can work in collaboration to pass the 'regulatory mantle', ensuring that there are no regulatory gaps but also ensuring that there is no unnecessary overlap with regulation which has the potential to stymie important research from proceeding.

I consider this in the context of 'right touch' regulation, which the HTA cites in its 2019-22 strategy as its strategic approach - arguing that the ambiguous wording in the HTA code of practice on research, which implies that an HTA research licence may be required where this is not necessarily required to comply with the HT Act 2004, is not in keeping with the principle of 'right touch' regulation. My rationale for this is that an implication that an HTA research licence may be required where this is not necessarily required to comply with the HT Act 2004 risks avoidance of undertaking research activities and it risks over regulation, neither of which are in keeping with a 'right touch' regulation approach.

PART 2: THE ARTICLES

CHAPTER 10

FROM 'CONSENT OR ANONYMISE' TO 'SHARE AND PROTECT': FACILITATING ACCESS TO SURPLUS TISSUE SAMPLES WHILST SAFEGUARDING DONOR INTERESTS[573].

10.1 Introduction

Health research is generally considered to be something which is a 'good' and in the best interest of society[574], as the knowledge which is generated from research positively impacts on all members of society, whether directly or indirectly[575]. It is fundamental to the prevention, diagnosis and treatment of health-impacting conditions and, in some cases, ensures patients can have access to novel treatments which may have positive life-changing, extending or even saving effects[576]. Moreover, it can also have a positive socio-economic impact by improving the efficiency of NHS services[577]. As much health research is publicly funded however, whether this is via the Government or charities, there is also a responsibility to ensure cost efficiency in research[578]. The promotion and facilitation of efficient

[573] Article published in Health Care Analysis link.springer.com/article/10.1007/s10728-021-00435-z
[574] McHale J. Reforming the Regulation of Health Research in England and Wales: New Challenges and Pitfalls. *Journal of Medical Law and Ethics.* 2013 **1(1)** 23-42
[575] Schaefer O, Emanuel E and Wertheimer A. The Obligation to Participate in Biomedical Research. *Journal of the American Medical Association*. 2009 **302(1)** 67-72
[576] Academy of Medical Sciences (2011) *A New Pathway for the Regulation and Governance of Health Research*. Available at acmedsci.ac.uk/policy/policy-projects/a-new-pathway-for-the-regulation-and-governance-of-health-research
[577] *Ibid*
[578] *Ibid*

healthcare research is therefore considered to be something which is in the public interest[579], yet the requirement to protect the rights and interests of research participants must also play a key role and is enshrined into research ethics practice, most notably by virtue of the Declaration of Helsinki[580]. Whilst the Declaration of Helsinki is not in itself legally binding, it does provide ethical principles which are considered to have primacy and are intrinsically embedded in ethical, and to some degree legal, standards[581].

Human tissue is routinely removed from patients in the course of diagnosis and treatment. Surgical procedures such as tumour excision or biopsies[582] often involve removing relatively large amounts of tissue after which only a small amount is required for diagnostic purposes[583]. The remainder is stored in a diagnostic archive in case further testing should be required[584]. Such 'surplus tissue' may have value for research purposes and these diagnostic archives can be a rich source of tissue samples for such purposes[585]. Accessing existing surplus tissue samples also means that new tissue samples may not always need to be obtained. This reduces the resource required and is therefore more cost effective for the NHS[586]. However, the real value in human tissue for health research purposes comes when the tissue is linked with information about the person from whom the tissue came; the tissue

[579] Academy of Medical Sciences (2011) *A New Pathway for the Regulation and Governance of Health Research*. Available at acmedsci.ac.uk/policy/policy-projects/a-new-pathway-for-the-regulation-and-governance-of-health-research

[580] World Medical Association (2013) *WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects*. Available at www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/

[581] Rid A, Schmidt H. The 2008 Declaration of Helsinki – First Among Equals in Research Ethics. *Journal of Law, Medicine & Ethics.* 2010 **38(1)** 143-148

[582] Dowsett M. New Hurdles for Translational Research. *Breast Cancer Research*. 2000 **2** 241-243

[583] van Diest P J. No consent Should be Needed for using Leftover Body Material for Scientific Purposes. *British Medical Journal* 2002 **325** 648-649

[584] Nuffield Council on Bioethics (1995) *Human Tissue: Ethical and Legal Issues.* Available at www.nuffieldbioethics.org/publications/human-tissue

[585] Bathe O F and McGuire A L. The Ethical use of Existing Samples for Genome Research. *Genetics in Medicine* 2009 11**(10)** 712-715

[586] Academy of Medical Sciences (2011) *A New Pathway for the Regulation and Governance of Health Research.* Available at acmedsci.ac.uk/policy/policy-projects/a-new-pathway-for-the-regulation-and-governance-of-health-research

alone has limited value[587]. Linking tissue with information about the person allows insight into complex interfaces between health, lifestyle, environment and genes which would be impossible from tissue alone[588], thereby strengthening the validity and utility of research involving tissue[589]. This does in turn however create further issues relating to data protection and confidentiality as linkage with information about the person can increase the possibility that the tissue may be considered 'identifiable'[590]. This may be due to the identifiability of the information itself, such as demographic information, or could be the linkage of information which is considered non-identifiable, but when multiple items of such information are linked together, could mean it is it possible for the person to be identified[591], such as can occur when linking multiple datasets of information[592].

The Human Tissue Act 2004 (HT Act 2004) includes research as a 'scheduled purpose' which means that research involving human tissue is something that can be undertaken lawfully with the consent of the person from whom the tissue was removed. However, consent for research use of tissue is often not obtained at the time of removal and it is often not feasible to obtain the person's consent at a later point in time once the research value of surplus tissue in diagnostic archives is identified[593]. Where consent has not been provided for tissue to be used for research purposes, the HT Act 2004, permits use only where the tissue has been removed from a living person, the research has been approved by an authorised Research Ethics Committee and the researcher is not in possession, and will not likely come into possession, of information which could identify the individual from whom the

[587] Quinlan P, Groves M, Jordan L, Stobart H, Purdie C, Thompson A. The Informatics Challenges Facing Biobanks: A Perspective from a United Kingdom Biobanking Network. *Biopreservation and Biobanking.* 2005 **13(5)** 363-370

[588] Dörr B S. (2014) Collection of Human Tissue Samples in Biobanks: Challenges to Human Rights and Human Nature. In Albers M, Hoffmann T and Reinhardt J (eds.) *Human Rights and Human Nature.* (pp 185-196) Dordrecht: Springer

[589] Knoppers B, Isasi R. Stem Cell Banking: Between Traceability and Identifiability. *Genome Medicine.* 2010 **2(73)** 1-7

[590] Identifiability in this context is considered to be information that may reasonably be expected to identify an individual, alone or in combination with other available information

[591] National Data Guardian (2013) *Information: To Share or Nor to Share? The Information Governance Review.* Available at www.gov.uk/government/publications/the-information-governance-review

[592] Lowrance W. (2012) *Privacy, Confidentiality and Health Research.* Cambridge: Cambridge University Press

[593] Regidor E. The use of Personal Data from Medical Records and Biological Material: Ethical Perspectives and the Basis for Legal Restrictions in Health Research. *Social Science & Medicine.* 2004 **59** 1975-1984

tissue was removed. However, this absolute requirement for the researcher to not be in possession of information which could identify the individual does not accommodate the possibility that information which may be considered 'identifiable' may be crucial to be able to achieve a research aim. For example, information such as whether the tissue provider is male or female, when and where they were born, or where they currently live may all be important information to consider alongside analysis of the tissue and other clinical information in answering a research question[594]. The current application of the HT Act 2004 with regards to the researcher not being in possession of information which *could* identify the person makes availability of such data a grey area for researchers and data controllers[595]. This is because this type of information, whilst not overtly in itself identifiable, may mean that an individual could be identified when it is collated together, particularly when you consider the possibility of linking this information with other, publicly available, information such as the electoral register[596].

Whilst identifying the person may take the efforts of a 'motivated intruder'[597], such a grey area in the law often leads to over caution. Even the mere possibility that re-identification could be successful may be cause for data controllers not providing information for research purposes, even when the overall research purpose could not be achieved without the information[598]. Moreover, due to the nature of research which involves surplus tissue and patient information, it may be necessary to source tissue and data from different locations as the patient may have undergone different parts of their care pathway at different NHS hospital trusts. This requires information which is unique to the individual, such as an NHS number, and often a second identifier such as date of birth to verify that

[594] Lowrance W. (2012) *Privacy, Confidentiality and Health Research.* Cambridge: Cambridge University Press
[595] *Ibid*
[596] *Ibid*
[597] The Information Commissioners Office recommend undertaking a 'motivated intruder' test to assess whether information which is considered to be non-identifiable could be used to identify the person to whom the information relates. The 'motivated intruder' is taken to be a person who starts without any prior knowledge but who wishes to identify the individual from whose personal data the anonymised data has been derived.
[598] Academy of Medical Sciences (2011) *A New Pathway for the Regulation and Governance of Health Research*. Available at acmedsci.ac.uk/policy/policy-projects/a-new-pathway-for-the-regulation-and-governance-of-health-research

the tissue and data relate to the correct individual[599]. Therefore, where consent cannot reasonably be obtained retrospectively and where certain information is necessary to achieve the research aim, the value and utility of surplus tissue is limited due to the possibility of identifiability.

This article considers an approach which aims to enable the sharing of surplus tissue where consent was not obtained at the time the tissue was removed and it would not be feasible to obtain consent retrospectively. However, it should be noted that this article does not suggest that this approach should be an *alternative* to obtaining consent where it is reasonable and feasible to do so. Consent, including for the future research use of tissue samples, is important because it demonstrates respect for persons[600] and it allows some degree of choice[601] and control over what happens to those samples. In recent years there has been significant development in approaches to consent for the use of tissue and data in research which is laudable. For example, dynamic consent approaches using electronic platforms which can attach and send consent preferences with tissue and data when transferred from biobanks, thereby allowing greater choice with regards to the types of research which an individual permits their samples to be used for[602]. Moreover, even greater choice is afforded via a meta consent approach which also uses an electronic platform but allows individuals to choose the type of consent which they prefer; whether this is broad consent for research within defined parameters, the opportunity to consent to each individual project or blanket consent which permits any research use[603]. This article does not question the value of consent or the value of engaging with individuals about the potential research value of their surplus tissue samples and data. This article does however suggest that where tissue is removed as part of a clinically directed procedure and is surplus to diagnostic requirements, the tissue linked with associated patient data may have a future research

[599] Lowrance W. (2012) *Privacy, Confidentiality and Health Research.* Cambridge: Cambridge University Press
[600] Dworkin G (1988) *The Theory and Practice of Autonomy*. Cambridge: Cambridge University Press
[601] Faden R R and Beauchamp T L. (1986) *A History and Theory of Informed Consent.* New York: Oxford University Press
[602] Kaye J et al. Dynamic Consent: A Patient Interface for Twenty-First Century Research Networks. European *Journal of Human Genetics.* 2015 **23** 141-146
[603] Ploug T and Holm S. Going Beyond the False Dichotomy of Broad or Specific Consent: A Meta-Perspective on Participant Choice in Research Using Human Tissue. *The American Journal of Bioethics.* 2015 **15(9)** 44-46

value and such secondary uses should not be prevented *because* consent was not requested and would no longer be feasible to obtain. Moreover, this article suggests that in such situations, an approach which safeguards privacy interests by applying data protection mechanisms other than a requirement for anonymisation could be more enabling of health research which is in the public interest.

Empirical evidence suggests that generally people are supporting of their surplus tissue samples[604] and associated data being used for research purposes[605] and furthermore, they welcome the opportunity for their tissue samples to have the potential to help others[606]. In some cases, patients have questioned why this doesn't happen more, due to the minimal impact on the tissue donor compared to the potential benefit which can be gained[607]. However, such altruistic expressions are couched within an expectation that privacy interests will be protected[608]. Moreover, the requirement for the interests of science and society to never outweigh the interests of individuals is the bedrock of research ethics and firmly rooted within the principles of the Declaration of Helsinki[609]. Whilst research involving surplus tissue linked with associated patient data is generally considered to involve minimal risk, it is not entirely risk free[610]. For example, where tissue samples are stored in a diagnostic archive, it is important that sufficient tissue remains for any further analysis required as part of the patients

[604] Ipsos MORI (2018) *Consent to use Human Tissue and Linked Health Data in Health Research. A Public Dialogue for Health Research Authority and Human Tissue Authority*. Available at www.hra.nhs.uk/documents/1570/Consent_to_use_human_tissue_and_linked_health_data_in_health_research_FINAL.pdf

[605] Academy of Medical Sciences (2011) *A New Pathway for the Regulation and Governance of Health Research*. Available at acmedsci.ac.uk/policy/policy-projects/a-new-pathway-for-the-regulation-and-governance-of-health-research

[606] Lewis C, Clotworthy M, Hilton S et al. Consent for the use of Human Biological Samples for Biomedical Research: A Mixed Methods Study Exploring the UK Public's Preferences. *British Medical Journal Open.* 2013 **3**

[607] Hamilton S et al. Consent Gained from Patients after Breast Surgery for the use of Surplus Tissue in Research: An Exploration. *Journal of Medical Ethics.* 2007 **33** 229-233

[608] Kaye J. The Tension Between Data Sharing and the Protection of Privacy in Genomic Research. *Annual Review of Genomics and Human Genetics.* 2012 **13** 415-431

[609] World Medical Association (2013) *WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects*. Available at www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/ principle 8

[610] Thomas G (2014) Access to Human Cells and Tissues. In Coleman, R (ed.) *Human-Based Systems for Translational Research* (pp 1 – 16) Royal Society of Chemistry

clinical care[611], as well as a risk that tissue samples may be used in research which the individual would find morally reprehensible[612]. These risks can be mitigated via governance mechanisms such as access procedures and committees which consider requests to access tissue samples, as well as research ethics committees which ensure that research projects are using tissue samples for ethical purposes. These risks, in the context of any mitigating governance mechanisms, need to be balanced against the potential benefit for society by undertaking health research. This article focuses on risks which are associated with data privacy, which may occur when tissue samples are linked with associated patient data, and considers how an approach which focuses on safeguarding the patient's identity using risk mitigating mechanisms other than complete anonymisation, could better facilitate the use of tissue samples linked with patient data in health research.

10.2. Share and protect

In this article I put forward an argument that, rather than apply a blanket requirement for non-identifiability where obtaining consent is not feasible, the use of surplus tissue in research should follow a more pragmatic approach which allows consideration of the data necessary to achieve a research aim and also respects the rights and interests of individuals by applying 'appropriate safeguards' to protect personal data. I refer to this approach as 'share and protect' because in recognising the potential benefit of combining surplus tissue and data about the person for research purposes, it considers how these resources could be shared with researchers in the public interest, whilst also requiring that there are appropriate data security measures in place which protect personal data, thereby respecting individual rights and interests.

I suggest that the origin of the requirement for non-identifiability in the absence of consent in the HT Act 2004 was based on a misperception that data protection legislation *required* that personal data should not be processed without consent and therefore the only alternative was to anonymise data

[611] Riegman P and van Veen E. Biobanking Residual Tissues. *Human Genetics.* 2011 **130** 357-368
[612] Price D. (2010) *Human Tissue in Transplantation and Research*. Cambridge: Cambridge University Press.

where there was no consent for research use[613]. This 'consent-or-anonymise' approach was included in the HT Act 2004 but was not a requirement under the Data Protection Act 1998, which was in force when the HT Act 2004 was implemented. Furthermore, it is not required by the General Data Protection Regulation 2018 (GDPR 2018) or the Data Protection Act 2018 (DPA 2018) which are currently in force in the UK[614]. Whilst 'consent or anonymise' may have been one way to interpret what was required under the DP Act 1998, this was not the only legitimate, or even the most appropriate interpretation[615]. The DPA 1998, and the subsequent GDPR 2018 and DPA 2018, permit data to be processed under a legal basis other than consent[616]; something which is discussed in more detail later in this article. Moreover, these legislative provisions do not require anonymisation as an alternative but rather set a requirement for 'appropriate safeguards' to be in place to respect the principle of data minimisation; that data should be 'adequate, relevant and limited to what is necessary in relation to the purposes for which they are processed'.

I therefore argue that this interpretation of data protection legislation which facilitates sharing of the minimum data necessary to achieve a research aim, without a *requirement* for consent from the person about whom the data relates or anonymisation of the data where this would render the research ineffectual, should also be applied when sharing surplus tissue linked with data about the person for health research purposes. This is because research involving surplus tissue linked with data about the person has the potential for significant public benefit but, due to the nature of surplus tissue and previously collected data, the opportunity to obtain consent for research use has often passed. Furthermore, anonymisation of the data can reduce its value and even render it ineffectual to achieve

[613] Laurie G et al. On Moving Targets and Magic Bullets: Can the UK Lead the Way with Responsible Data Linkage for Health Research? *International Journal of Medical Informatics.* 2015 **84** 933-940

[614] The General Data Protection Regulation 2018 repealed the Data Protection Directive 95/46/ec which was enacted into statute in the UK via the Data Protection Act 1998. The GDPR 2018 therefore also repealed the DPA 1998 in the UK which was superseded by the Data Protection Act 2018 to enact national provisions provided for in the GDPR 2018.

[615] *Information Commissioner's Office. Accountability and Governance* (no date) Available at ico.org.uk/for-organisations/guide-to-data-protection/guide-to-the-general-data-protection-regulation-gdpr/accountability-and-governance/

[616] National Data Guardian (2013) *Information: To Share or Nor to Share? The Information Governance Review.* Available at www.gov.uk/government/publications/the-information-governance-review

the research aim[617] and therefore a more pragmatic 'share and protect' approach may better achieve the balance between facilitating health research in the public interest and respecting individual rights and interests.

10.3. Background to Research Under the Human Tissue Act 2004

To determine whether a 'share and protect' approach could be applied for the use of surplus tissue and data about the person from whom the tissue was removed, in the absence of consent for research use, it is important to understand how the requirement for non-identifiability to the researcher came about in the HT Act 2004. The HT Act 2004, which was a direct response to events which had been highlighted via the Kennedy and Redfern reports into practices of post mortem organ and tissue retention at Bristol Royal Infirmary and Alder Hey Hospital, aimed to balance the expectations and rights of individuals and families with broader societal interests, including health research[618]. When the Human Tissue Bill was passing through Parliament there was significant discussion about the need to balance the importance of human tissue being available for research and, also to respect and protect the rights and interests of individuals[619]. This balance was seemingly achieved by ensuring that the golden thread which was to run throughout the Act was consent[620]. However, a clause was introduced to the HT Act 2004 via an amendment[621] which allows the use of surplus tissue in research without consent under certain circumstances. This amendment was in response to lobbying from the scientific research community over concern that the Act would stifle or criminalise important research[622]. This approach acknowledged that the opportunity to obtain consent for the use of surplus tissue obtained during routine clinical procedures has often passed, particularly where the research

[617] Academy of Medical Sciences (2006) *Personal Data for Public Good: Using Health Information in Medical Research*. Available at acmedsci.ac.uk/policy/policy-projects/personal-data
[618] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents explanatory notes, summary and background, paragraph 1
[619] For examples of these discussions, see *'Human Tissue Bill'* (2004) Hansard: House of Commons Debate 15 January 2004 cc. 986 & 993 and '*Human Tissue Bill*' (2004) Hansard: House of Lords Debate 22 July 2004 cc. 377, 378 & 380.
[620] Price D. (2010) *Human Tissue in Transplantation and Research.* Cambridge: Cambridge University Press.
[621] Amendment 108
[622] Lansley A (2004) *'Human Tissue Bill'* Hansard: House of Commons Debates 15 January c. 998

value of the tissue is not known at the time of removal, and that obtaining retrospective consent for individual research projects is often impractical and may even be considered unethical; for example the tissue provider may have moved away, or re-contacting a person under such circumstances could bring back difficult memories of a time when they were unwell[623]. The final wording of the Act did therefore recognise that where tissue has previously been collected during the course of routine clinical care and where consent was not obtained for the tissue to be used for research purposes, it may still be used under certain conditions. The conditions are that the tissue must have been removed from a living person, the research is approved by an authorised Research Ethics Committee and the person undertaking the research must not be in possession and will not likely come into possession of information which could identify the person from whom the tissue came. However, as previously indicated, the tissue alone has limited value in a research context and will often need to be linked with information about the tissue donor. Moreover, data about the person will often be generated from tissue in the course of research and therefore tissue and data become inextricably linked.

Human tissue and data are however regulated under different statutory legislation; tissue under the HT Act 2004 and data under the GDPR 2018 and DPA 2018. The GDPR 2018 explicitly references data which is derived from the testing of body parts or bodily substances as personal data concerning health, thereby recognising the relationship between human tissue and personal data about the person from whom the tissue was removed. However, this relationship between tissue and data is not as clearly defined from the perspective of the HT Act 2004 which does not appear to accommodate the complexities of data and more importantly, the complexities of identifiability of data. Identifiability is not something that is static but rather is something that can change as more information becomes available and is a spectrum which runs from fully anonymised to fully identifiable with many levels in-between[624]. In referring only to 'the researcher not being in possession of information which could identify the person', the HT Act 2004 sets a rather absolute standard of non-identifiability which does

[623] Price D. (2010) *Human Tissue in Transplantation and Research*. Cambridge: Cambridge University Press.
[624] Lowrance W. (2012) *Privacy, Confidentiality and Health Research*. Cambridge: Cambridge University Press.

not necessarily allow the flexibility necessary to deal with the complexities of data and identifiability in a research context. Not only can this approach be unduly limiting in terms of accessing surplus tissue and the information necessary to achieve a research aim, its introduction into the Act appears to have been based on a misperception that either consent from the data subject or anonymisation of data was a requirement under data protection legislation. This, as I will go on to demonstrate below, was not in fact the case.

10.4. 'Consent or anonymise' - A misinterpretation of Data Protection Law?

As I have previously suggested, the HT Act 2004 applies an absolute rule of non-identifiability to the researcher for surplus tissue where there is no consent for research use. This does not acknowledge the complexity of identifiability in that identifiability can change when new information becomes available and runs a spectrum from fully anonymous to fully identifiable. I suggest that this approach was implemented due to a misperception that anonymisation was a *requirement* under data protection legislation where there is no consent for research use. In this section I will justify this claim and set out how this misperception resulted in the 'consent or anonymise' approach being included in the HTA Act 2004.

At the time the Human Tissue Bill (HT Bill) was drafted and discussed in Parliament, the EU Directive 95/46/EC and the Data Protection Act 1998 (DPA 1998) (which was the statute enacting the Directive into UK law) were in force. Parliamentary discussions and the final text of the HT Act 2004 do reflect a relationship between these different legislative provisions. For example, the terminology used in the HT Act, 'not in possession, and not likely to come into possession, of information from which the person from whose body the material has come can be identified' is derived from terminology used in the DPA 1998 which defines personal data as data from which a person can be identified……. 'from those data and other information which is in the possession of, or is likely to come into the possession of, the data controller'[625]. Moreover, reference was explicitly made during the HT Bill

[625] *Data protection Act 1998*. Available at www.legislation.gov.uk/ukpga/1998/29/contents Part 1 s. 1 ss. (1)

debates in Parliament to anonymization being necessary to meet the requirements of the DPA 1998[626]. However, such reference to anonymization in this context appears to assume the 'consent or anonymise' rhetoric, which was commonly interpreted as a requirement under the DPA 1998[627]. This led to an apparent perception amongst those debating the HT Bill that the only legal basis under which personal data could be processed for research purposes was where the data subject had given consent for their data to be processed for this purpose and where no consent had been given, the only alternative was to fully anonymise the data.

In referring to a requirement for 'anonymisation', there were numerous calls in Parliament to better define what this meant and, in particular, whether this would mean that tissue and data would be permanently unlinked. Whilst clarification was provided by Lord Warner, Parliamentary Under Secretary in the Department of Health, that a pseudoanonymised link could be maintained, a clear description of what was meant by 'not identifiable to the researcher', remained elusive. Lord Warner simply said that "there is no reason that the researcher should also know the name of the person that the tissue has come from"[628] . This does not address the issue of partially identifiable information which may be required to achieve a defined research aim or the potential need for a unique identifier, such as an NHS number, to link data and tissue from multiple sources. Therefore, on the understanding of the requirement for 'consent or anonymise' and in the absence of acknowledgement that partially identifiable information may need to be linked with surplus tissue to achieve a stated research aim, the principle of consent or anonymise was, to all intents and purposes, reflected in the HT Act 2004[629]. However, according to the Information Commissioner's Office, the interpretation of consent or anonymise being a requirement under the DPA 1998 was not correct and was often applied due to

[626] For examples of these discussions see 'Human Tissue Bill' (2004) Hansard: House of Commons Debates 15 January cc. 997, 1003, 1004 & *'Human Tissue Bill'* (2004) Hansard: House of Lords Debates 22 July c. 375
[627] Clark S and Weale A (2011) *Information Governance in Health. Research Report. University College London*

Laurie G et al. On Moving Targets and Magic Bullets: Can the UK Lead the Way with Responsible Data Linkage for Health Research? *International Journal of Medical Informatics*. 2015 **84** 933-940
[628] *'Human Tissue Bill'* (2004) Hansard: House of Lords Debates 22 July c 427
[629] Laurie G. Liminality and the Limits of Law in Health Research Regulation: What Are We Missing in the Spaces In-Between? *Medical Law Review.* 2016 **25(1)** 47-72

over caution and a desire to prevent any risk of litigation[630]. Whilst a requirement to either obtain the consent of the person or ensure that data are only processed in an anonymised format was one interpretation of the legislation, it was not the only legitimate interpretation[631] and personal data could be processed for research purposes under legal bases other than consent without a requirement for the data to be anonymised. This was permissible under the DPA 1998 due to what is often referred to as the 'research exemption', which permitted the use of personal data for research purposes where the data were fairly obtained, the data were not used to make decisions about the individuals, use of the data would not cause significant damage or distress and no identifiable data are published[632].

So far in this section I have suggested that the wording in the HT Act 2004 requiring for tissue to be non-identifiable to the researcher where there is no consent for research use was based on a misperception that this was required under the DPA 1998. However, as the applicable data protection legislation has changed since the HT Act 2004 was enacted, I will now also consider the position under current legislation, the GDPR 2018 and DPA 2018. The GDPR 2018 requires that for processing of personal data, including health data, a basis under both Articles 6 and 9 of its provisions must apply. Moreover, the GDPR 2018 also states that where personal data have been collected for other purposes, such as when accessing NHS services, any secondary processing of this data would be compatible with the original purpose, then the legal basis may remain the same. The GDPR 2018 is explicit that research should be considered a purpose which is compatible with the purpose for which data were collected, therefore the legal basis under which the personal data were collected may remain the same legal basis under which the data can also be processed for secondary research purposes. As confirmed by the NHS England privacy notice[633], the legal basis under the Article 6, for data being collected as part of interactions with the NHS, is not consent but is 'processing is necessary

[630] Clark S and Weale A (2011) *Information Governance in Health*. Research Report. University College London

[631] *Ibid*

[632] Coleman M P, Evans B G and Barrett G. Confidentiality and the Public Interest in Medical Research – Will We Ever Get it Right? *Journal of Clinical Medicine.* 2003 **3** 219-228

[633] NHS England (2018) *NHS England's Privacy Notice*. Available at www.england.nhs.uk/publication/nhs-englands-privacy-notice/

to perform a task in the public interest' [634]. Moreover, the legal basis under Article 9, as health data is special category data, is 'processing is necessary for the purposes of …… the provision of health or social care or treatment or the management of health and social care systems and services….'[635]. Therefore, consent is not *required* as a legal basis for secondary processing of such data for research purposes. This presumption of compatibility for secondary processing of data for scientific research is however a relaxation from the DPA 1998, which required compatibility to be demonstrated[636]. Furthermore, the UK policy position, confirmed by guidance published by the Health Research Authority[637] and the Information Commissioners Officer[638] is that where personal data are processed for health research purposes, consent should in fact *not* be the legal basis used[639]. The reason for this is that the requirements in relation to consent under the GDPR 2018 are more stringent and give greater control to the data subject than the requirements which are reasonably and normatively applied in a scientific research context[640]. For consent to be valid under the GDPR 2018, it must be demonstrable, freely given, clear, in an easily accessible format, and it should be as easy to withdraw any consent given as it was to have given the consent[641]. Whilst these standards *may* also apply in a research context, using consent as the legal basis means that these standards *must* apply for the processing to be lawful. Moreover, a broad consent approach, which is often applied for the research

[634] GDPR Article 6 1 (e) "processing is necessary for the performance of a task carried out in the public interest or in the exercise of official authority vested in the controller".
[635] GDPR Article 9 2 (h) "processing is necessary for the purposes of preventative or occupational medicine, for the assessment of the working capacity of the employee, medical diagnosis, the provision of health or social care or treatment or the management of health or social care systems and services on the basis of Union or Member State law or pursuant to contract with health professionals and subject to the condition and safeguards referred to in paragraph 3".
[636] Chico V. The Impact of the General Data Protection Regulation on Health Research. *British Medical Bulletin.* 2018 **128** 109-118
[637] *Health Research Authority. Consent in Research* (2018) Available at www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/data-protection-and-information-governance/gdpr-guidance/what-law-says/consent-research/
[638] *Information Commissioners Office. Consent* (no date) Available at ico.org.uk/for-organisations/guide-to-data-protection/guide-to-the-general-data-protection-regulation-gdpr/accountability-and-governance/
[639] Chico V. The Impact of the General Data Protection Regulation on Health Research. *British Medical Bulletin.* 2018 **128** 109-118
[640] *Ibid*
[641] General Data Protection Regulation 2018 Available at eur-lex.europa.eu/eli/reg/2016/679/oj Article 7 ss. 1-4

use of existing collections of tissue and data, would not meet the standards required for consent under the GDPR 2018[642]. Recital 33 does acknowledge that for scientific research, the full purpose of processing personal data may not be known at the time of collection and therefore data subjects may consent to certain parts of research. However, the Article 29 working party (now the European Data Protection Board) issued official guidance which states that when relying on consent as the legal basis to process special category data, which includes health related data[643], the need for consent to be specific would still apply[644] and there would be an expectation that consent would continue to be sought as the research advances[645].

Whilst consent may not be required as a legal basis for the secondary processing of personal health data for research purposes under the GDPR 2018, there remains a question regarding whether anonymisation of the data would therefore be required as an alternative under this statutory provision. The GDPR 2018 refers to requirements to ensure that there are 'appropriate safeguards' in place to protect the rights and freedoms of the data subject. These appropriate safeguards are expected to ensure that there are technical and organisational measures in place, such as contractual arrangements to minimise who can access data and suitable security measures to prevent unauthorised access[646]. Furthermore, these safeguards should ensure that the principle of data minimisation is respected; therefore, data should be 'adequate, relevant and limited to what is necessary in relation to the purposes for which they are processed'. The requirement for appropriate safeguards under the GDPR 2018 therefore applies a broader approach than the blanket requirement

[642] Chico V. The Impact of the General Data Protection Regulation on Health Research. *British Medical Bulletin.* 2018 **128** 109-118

[643] General Data Protection Regulation 2018 Available at eur-lex.europa.eu/eli/reg/2016/679/oj Article 9 ss. 1

[644] Peloquin D, DiMaio M, Bierer B and Barnes M. Disruptive and Avoidable: GDPR Challenges to Secondary Research uses of Data. *European Journal of Human Genetics.* 2020 **28** 697-705

[645] European Data Protection Board (2020) *Guidelines 05/2020 on consent under Regulation 2016/679.* Available at edpb.europa.eu/our-work-tools/our-documents/guidelines/guidelines-052020-consent-under-regulation-2016679_en

[646] *Information Commissioner's Office. Accountability and Governance* (no date) Available at ico.org.uk/for-organisations/guide-to-data-protection/guide-to-the-general-data-protection-regulation-gdpr/accountability-and-governance/

for non-identifiability under the HT Act 2004. In requiring appropriate safeguards to be in place which respect the principle of data minimisation, consideration can be given to the data *necessary* to achieve the research aim and can take a more pragmatic approach in relation to data security which may permit some identifiable data to be retained for a minimum period necessary in relation to the purpose for which it is being processed. Therefore, unlike the HT Act 2004 which is explicit that tissue which is identifiable to the researcher may only be used with appropriate consent, previously the DPA 1998 and currently the GDPR 2018 permit a lawful basis other than consent and give a broader consideration of how individual rights and interests can be protected via safeguards, other than a blanket requirement for anonymization. This therefore allows a more considered approach which takes necessity and purpose into account.

10.5. Balancing public benefit with individual interests

So far in this article I have suggested that research involving human tissue linked with information about the person from whom the tissue was removed is in the public interest as it is cost efficient and can generate valuable data. Empirical studies have indicated that patients are not only supporting of their surplus tissue and data being used for health research purposes[647], this is often their preference and they are surprised to discover that this doesn't happen more often[648]. Moreover, patients who have the opportunity to donate surplus tissue samples for health research purposes have reported that their decision to donate was often based on a feeling of solidarity and desire to help others who may be going through a similar experience[649]. Patients have also reported that feeling solidarity with others by donating their surplus tissue for use in health research had a positive impact on their

[647] Lewis C, Clotworthy M, Hilton S et al. Consent for the use of Human Biological Samples for Biomedical Research: A Mixed Methods Study Exploring the UK Public's Preferences. *British Medical Journal Open*. 2013 **3** Williams A M et al. Consent to Donate Surgical Biospecimens for Research: Perceptions of People with Colorectal Cancer. *Cancer Nursing.* 2016 **39(3)** 221-227

[648] Ipsos MORI (2018) *Consent to use Human Tissue and Linked Health Data in Health Research. A Public Dialogue for Health Research Authority and Human Tissue Authority.* Available at www.hra.nhs.uk/documents/1570/Consent_to_use_human_tissue_and_linked_health_data_in_health_research_FINAL.pdf

[649] Dixon-Woods M, Cavers D, Jackson C J et al. Tissue Samples As 'Gifts' for Research: A Qualitative Study of Families and Professionals. *Medical Law International*. 2008 **9** 131-150

recovery[650]. Whilst patients may not necessarily be aware of individual research uses of previously removed tissue samples which were stored in a diagnostic archive, a general awareness of the potential for research to be undertaken which could benefit other patients may in itself provide some benefit for patients when undergoing investigation or treatment which involves the removal of tissue. However, the public benefit and potential for any individual benefit based on a principle of solidarity, do not negate the need for individual privacy interests to be respected.

In this article I have noted that data protection legislation does permit the processing of personal data, including health data, under legal bases other than consent and applies safeguards which are broader than just anonymisation. In this section I will set out why a similar 'share and protect' approach for surplus tissue and associated information would better achieve a balance between facilitating research which has public benefit and protecting the rights and interests of individuals than the current 'consent or anonymise' approach. The HT Act 2004, the GDPR 2018 and DPA 2018 all aim to balance the interests of individuals with public interests, such as the public benefit which can come from research. Health research generates generalisable knowledge which can have a positive impact on an individual and also societal level[651] and therefore there is a broad interest in achieving an effective balance between respecting the integrity of the individual and improving public health and minimising risks to peoples' health[652]. The requirement for tissue to be non-identifiable to the researcher in the absence of the provider's consent, whilst still permitting use of surplus tissue for research purposes, was intended to be a way of achieving such a balance. However, I suggest that the current application of the requirement for the person undertaking the research to not be in possession of information which *could* identify the person from whom the tissue was removed is too restrictive and therefore does not achieve this balance effectively. This is because in applying the 'consent or

[650] Williams A M et al. Consent to Donate Surgical Biospecimens for Research: Perceptions of People with Colorectal Cancer. *Cancer Nursing.* 2016 **39(3)** 221-227
[651] Academy of Medical Sciences (2011) *A New Pathway for the Regulation and Governance of Health Research*. Available at acmedsci.ac.uk/policy/policy-projects/a-new-pathway-for-the-regulation-and-governance-of-health-research
[652] Hansson O M. Balancing the Quality of Consent. *Journal of Medical Ethics*. 1998 **24** 182-187

anonymise' approach it only considers two key questions: first, is there consent for research use? and second, will the researcher be in possession of information which *could* identify the person? If the answer to the first question is 'no', there is no consent in place, then any answer other than 'no' to the second question would mean that the research cannot proceed. There is no consideration of the potential for public benefit, what the research involves and what data would be required to achieve the intended aim or what other appropriate safeguards could be in place to protect the interests of the individuals.

If we apply the alternative 'share and protect' interpretation, which does consider the data required to achieve the research aim, then this may increase the scope within which surplus tissue and information about the person from whom the tissue was removed can be used for research purposes. This could therefore increase the research being undertaken and thereby also increase the net utility generated from such research. This is because the 'share and protect' approach considers the same scenario from a different perspective. Instead of an assumption that surplus tissue and data cannot be shared because there is no consent in place, the 'share and protect' approach accepts that there is benefit in sharing tissue and data for research purposes but considers what safeguards could be applied to protect the interests of the individual when sharing tissue and data for research purposes. What this therefore means is that there is a more considered approach in terms of what is necessary to achieve the research aim and what data protection measures could be put in place, rather than a blanket requirement for either consent or anonymisation of data.

The use of safeguards other than anonymisation to ensure data security was referenced in a report published by the Academy of Medical Sciences in 2006[653]. The report acknowledged that health research will often require access to identifiable information at some stage and moreover, that anonymisation is often not an 'absolute process'; as there are degrees of anonymisation which depend

[653] Academy of Medical Sciences (2006) *Personal Data for Public Good: Using Health Information in Medical Research*. Available at acmedsci.ac.uk/policy/policy-projects/personal-data

on the context of any particular situation. This may involve retaining a link to a person's identity via a unique code (pseudononymisation) which means that the data are identifiable to those with legitimate access but 'anonymised' to those undertaking research using the data[654]. However, the report published by the Academy of Medical Sciences suggests that a requirement for pseudononymisation with a requirement for the researcher to not have access to the key offers minimal security advantage over coded identifiable data sets which are maintained under strict data security policies. This report also reiterates the responsibilities of organisations undertaking research to ensure that they have appropriate data security arrangements in place, something which is now a statutory requirement under the GDPR 2018 requirement for 'data protection by design and by default'. The GDPR 2018 sets data protection principles which aim to reduce the risk of identifiability, by requiring that secondary processing is not incompatible with the purpose for which it was initially collected, data is limited to what is necessary to achieve the intended purpose, for the minimal time necessary and is processed in a way which ensures appropriate security[655]. This article suggests that where obtaining consent is not feasible, these safeguards should be considered sufficient to permit the linking of surplus tissue and associated patient data, despite the blanket requirement under the HT Act 2004 that the researcher should not be in possession of information which could identify the person from whom the tissue was removed. This is because the data protection principles sufficiently protect the privacy interests of individuals and furthermore, there is a public interest in enabling research which utilises surplus tissue samples and associated patient data.

To demonstrate this point further, consider a hypothetical research project. A researcher wants to undertake a descriptive study which aims to confirm a histopathological variance in anaplastic thyroid cancer in patients diagnosed with the condition over a 15 year period. Anaplastic thyroid cancer is a rare form of cancer which is fast growing and has often metastasised to other parts of the body before

[654] Lowrance W. (2012) Privacy, Confidentiality and Health Research. Cambridge: Cambridge University Press
[655] General Data Protection Regulation 2018 Available at eur-lex.europa.eu/eli/reg/2016/679/oj Article 5 s. 1 ss. (b), (c) (e) and (f)

it is diagnosed and therefore survival rates are low[656]. The hypothesis is that the histopathological variance will be identified in patients who had high levels of iron in their blood and lived within a 10 mile radius of a landfill site in the 3 years prior to diagnosis. The researcher has identified 300 thyroid tissue samples which were obtained via routine clinical care with a confirmed diagnosis of anaplastic cancer. The patients were not asked to give their consent for the tissue to be used for research purposes at the time of removal and consent would not now be feasible as many would have died and re-contacting any survivors may not be reasonable due to the time which has passed and the risk of causing distress to any survivors. The researcher aims to obtain and analyse the tissue samples for evidence of histopathological variance and additionally will require information about the person from whom the tissue was removed to confirm blood iron levels and partial postcode to confirm primary residence for the 3 years prior to diagnosis. Furthermore, additional information will also be required to control for confounding factors; the researcher proposes to collect sex, year of birth, smoking status and occupation. These samples and the information would need to be obtained from a number of different NHS hospital trusts and therefore some identifiers would be required to obtain the clinical information and to validate the accuracy of the data; the researchers propose to use the patient's NHS number and date of birth. Under the 'consent or anonymise' interpretation which is currently applied under the HT Act 2004, the researcher would not be able to have access to this information and therefore the research may not be able to proceed because identifiable information is required to locate and link the relevant tissue and clinical data and also certain information which *could* identify the individual is required to answer the research question. This would be regardless of any potential benefit which the research could achieve and therefore the 'consent or anonymise' approach acts as a limiter to research which may have public benefit.

If we consider the research project from the perspective of a 'share and protect' approach however, then there may be a different outcome. Under this approach, consideration would be given to what

[656] *Healthline. Anaplastic Thyroid Cancer: What You Need to Know* (2019) Available at www.healthline.com/health/anaplastic-thyroid-cancer

data are *necessary* to achieve the research aim and what safeguards would be *appropriate* to protect the interests of the individual. The demographic information, partial postcode, sex, year of birth, smoking status and occupation is required to rule out confounding factors which may otherwise bias the research findings and so is necessary to achieve the research aim. In considering what safeguards could be put in place to protect personal data, a data security policy could be established which imposes limitations in terms of who has access to the data and requires that personal data is kept securely. The NHS number is required to locate tissue and data and the date of birth is required to verify that it relates to the correct person so this data is required for a limited period of time only to achieve a specific function; this data could therefore be replaced with a code once this function has been completed, the key to which is kept securely in a state of limited access. By applying appropriate safeguards which take into consideration the data necessary to achieve the research aim, the potential outcome is that research can be undertaken on surplus tissue with information about the person from whom the tissue came, where obtaining consent for research use would not be feasible, whilst still protecting the interests of those individuals.

10.6. Common Law Duty of Confidentiality

In this article I have considered the relationship between the HT Act 2004 and the GDPR 2018 in relation to whether, in the absence of consent, surplus tissue and data about the person from whom the tissue was removed could be available for research where personal data are necessary to achieve the research aim and applying appropriate safeguards which are broader then just anonymisation. However, the GDPR 2018 also requires that processing of data is lawful, a requirement which is broader than compliance with GDPR 2018 alone, and therefore requires processing to be lawful under other related legislation, as well as the common law duty of confidentiality[657]. Confidentiality is concerned with the control of information which is disclosed within a relationship of trust where there is a reasonable expectation, whether implicit or explicit, that the information will be kept in a state of

[657] Chico V. The Impact of the General Data Protection Regulation on Health Research. *British Medical Bulletin.* 2018 **128** 109-118

limited access[658]. Under common law, it is generally considered that where information is given or generated in circumstances where there is a reasonable expectation that a duty of confidence will apply, such information cannot normally be disclosed without the information provider's consent[659]. Therefore, it is important that the 'share and protect' approach would not breach this common law duty of confidentiality. There is no doubt that the information would be considered to be confidential as the information is about a person who could be identified and was disclosed with an expectation that it would be kept confidential. The question therefore remains whether the disclosure itself would be unlawful and in particular, whether safeguards other than anonymisation would be considered sufficient to avoid a breach of the common law. This is a difficult question to answer definitively, primarily due to the fact that the legal basis for a duty of confidentiality and all circumstances under which it is breached remain unclear[660], particularly in a research context as there is no clear legal precedent. However, in the absence of a test case which confirms whether sharing patient information for health research purposes without consent but with safeguards other than anonymisation would be lawful, a clear legal basis could be provided by the Health Research Authority on the advice of the Confidentiality Advisory Group (CAG)[661] under section 251 of the NHS Act (In England and Wales). The CAG is an independent body established to provide advice in relation to the use of confidential patient information[662]. On the advice of the CAG, the Health Research Authority may permit the common law duty of confidentiality to be temporarily set aside so that personal data can be processed for a defined purpose[663]. This would therefore ensure that processing of confidential information for research purposes remains lawful.

[658] Laurie G. (2002) *Genetic Privacy: A Challenge to Medico-Legal Norms*. Cambridge: Cambridge University Press
[659] Department of Health (2003) *Confidentiality: NHS Code of Practice*. Available at www.gov.uk/government/publications/confidentiality-nhs-code-of-practice
[660] Jackson E (2019) *Medical Law. Text, Cases and Materials. Fifth Edition*. Oxford: Oxford University Press
[661] England and Wales only
[662] *Health Research Authority. Confidentiality Advisory Group* (no date) Available at www.hra.nhs.uk/about-us/committees-and-services/confidentiality-advisory-group/
[663] *Ibid*

This article has primarily focused on establishing a legal basis for the sharing of surplus tissue samples linked with associated patient data, where obtaining consent would not be feasible. However, there are potentially broader implications of sharing such materials for research purposes within a context of confidentiality and trust which extends beyond ensuring such practices are lawful. Carter et al[664] reflect on the failure of the care.data initiative, which aimed to extract Primary Care NHS records for purposes beyond direct patient care with an option for patients to opt out, and suggest that whilst there was a legal basis, the initiative failed due to a lack of social acceptance. This resulted in patients losing confidence and trust in what was happening with their data and consequently, significant numbers of people opted out and the initiative was later abandoned[665]. Moreover, whilst 20 years have passed since the publication of the Redfern report detailing the outcome of the inquiry into organ and tissue retention at Alder Hey, the impact which the findings of the inquiry had on trust and confidence[666] will be remembered by many. Therefore, when considering the acceptability of tissue and data sharing for secondary purposes such as health research, acceptability and reasonable expectation are important factors to consider alongside a potential legal basis.

10.7. Conclusion

The legislation regulating human tissue and data in research have developed at different times and have been driven by different motives which has resulted in areas of non-alignment and contradiction, leading to a lack of clarity and the inevitable over caution which often comes with such legal grey areas. Whilst consent undoubtedly plays an important role when undertaking research on tissue and data, it is also important to recognise that due to the processing being secondary, where tissue was removed as part of clinical care and data generated for purposes other than research, consent is not always feasible when the research value is identified at a later point in time. In such circumstances,

[664] Carter P, Laurie G T and Dixon-Woods M. The Social Licence for Research: Why care.data Ran into Trouble. *Journal of Medical Ethics*. 2015 **41** 404-409
[665] *Ibid*
[666] Dewar S and Boddington. Returning to the Alder Hey Report and its Reporting: Addressing Confusions and Improving Inquiries. *Journal of Medical Ethics.* 2004 **30** 463-469

alternatives to consent which act to safeguard data and respect individual interests should be considered. Furthermore, consistency across different legislation in terms of the acceptability of such safeguards is important to ensure that an effective balance between facilitating research which is in the public interest and respecting and protecting individual rights and interests. Applying the 'share and protect' approach which I have set out in this article may help to align the personal data elements of the HT Act 2004 with the data protection requirements of the GDPR 2018. This may better facilitate access to surplus tissue and information which is necessary to achieve the research aim and, by applying appropriate safeguards which involve strict data protection requirements, may help to lessen the requirement for anonymisation to be the only legitimate alternative to consent. However, this is not without its challenges and, due to the wording of the HTA Act 2004 which is clear that in the absence of consent the researcher must not be in possession of information from which the person from whom the tissue came can be identified, a review of the tissue legislation may be required. Whilst the Codes of Practice, published by the Human Tissue Authority as a statutory requirement of the HT Act 2004, are intended to provide practical guidance, set standards and reflect current interpretation of law and regulatory practice, it is unclear whether appropriate safeguards broader then anonymisation would be acceptable under the current wording of the HT Act 2004. Questions also remain with regards to whether applying safeguards, other than anonymisation in the absence of consent where confidential information is shared for research purposes, would leave researchers liable for a claim of breach of confidentiality without Section 251 support from the Health Research Authority. Moreover establishing a legal basis for the use of surplus tissue and associated patient information which permits privacy safeguards other than just anonymisation would need to be within the parameters of what patients would reasonably accept and expect to ensure that there is broader social acceptance beyond a legal basis.

CHAPTER 11

ACHIEVING FAIR OPPORTUNITY TO DONATE SURPLUS TISSUE FOR SECONDARY RESEARCH PURPOSES IN THE PUBLIC INTEREST

11.1. Introduction

In the UK there is a lack of clear legal and regulatory direction with regards to the requirements and expectations for consent to access tissue for use in health research, where the tissue was removed during clinically directed procedures and subsequently stored in diagnostic archives. Throughout this article, such tissue is referred to as 'surplus tissue'. This has led to a confused and inconsistently applied approach across different NHS organisations, as this article will go on to demonstrate. The legal position, set out in the Human Tissue Act 2004 (herein referred to as the HT Act 2004), is that consent is not required where a research project is ethically approved and the person undertaking the research is not in possession of information which identifies the person from whom the tissue was removed. Recommendation is made by the Human Tissue Authority (HTA)[667] and the Medical Research Council (MRC)[668] that it is 'good practice' to obtain consent where it is practical to do so. However, the code of practice on consent issued by the HTA and the guidance issued by the MRC do not provide any clarification with regards to when it would be appropriate and practical to obtain consent for the secondary research use of surplus tissue. In the absence of clarity on the matter, different NHS organisations have taken different approaches.

[667] Human Tissue Authority (2020) *HTA Code A: Guiding Principles and the Fundamental Principle of Consent*. Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20A.pdf

[668] Medical Research Council (2014) *Human Tissue and Biological Samples for use in Research: Operational and Ethical Guidelines*. Available at www.ukri.org/publications/human-tissue-and-biological-samples-for-use-in-research/

This article highlights the variation and inconsistency between policies covering the use of surplus tissue for secondary research purposes by using 12 NHS organisations across England as a case study. In demonstrating this inconsistency, I argue that this varied approach impacts on both individual patient interests as well as broader public interests associated with the secondary use of surplus tissue in health-related research. On the individual patient level, a consequence is unfair distribution of *opportunities* for individual patients which are associated with the donation and use of surplus tissue for research purposes. In referring to opportunities in this context, I mean the opportunity for persons to choose whether their surplus tissue is available for use in health research, and the opportunity to *knowingly* be a tissue donor for health research and therefore for persons to realise their altruistic interests[669]. This is because the opportunity to choose whether surplus tissue samples are used for secondary research purposes demonstrates respect for persons, and therefore that they matter morally[670], by ensuring self-determination[671]. Additionally, an opportunity for persons to knowingly act on altruistic interests is generally considered to be something which is good, because evidence suggests that altruistic acts can have a positive impact for patients, particularly when they are coming to terms with a serious illness[672]. Opportunities to support research practices which have the potential to improve the diagnosis and treatment of other patients with similar health problems can also invoke feelings of solidarity. Patients are therefore not alone in experiencing difficulties but feel part of a health community, which in itself has been shown to improve how patients deal with their illness[673].

On a societal level, such inconsistent consent requirements across healthcare organisations also means that broader public interest claims cannot be fully realised. The public interest claims I refer to here, are twofold. First, the societal benefit which arguably comes from increased medical knowledge

[669] Ploug T and Holm S. Going Beyond the False Dichotomy of Broad or Specific Consent: A Meta-Perspective on Participant Choice in Research Using Human Tissue. *The American Journal of Bioethics*. 2015 **15(9)** 44-46
[670] Harris J. Law and Regulation of Retained Organs: The Ethical Issues. *Legal Studies.* 2002 **22(4)** 527-549
[671] Beauchamp T. (2010) 'Autonomy and Consent' in Miller F, Wertheimer A (eds.) *The Ethics of Consent: Theory and Practice* Oxford University Press Scholarship Online
[672] Bulsara C, Ward A and Joske D. Haematological cancer patients: achieving a sense of empowerment by use of strategies to control illness. *Journal of Clinical Nursing.* 2004 **13** 251-258
[673] Dixon-Woods M, Cavers D, Jackson C J et al. Tissue Samples As 'Gifts' for Research: A Qualitative Study of Families and Professionals. *Medical Law International.* 2008 **9** 131-150

and improved healthcare by maximising the availability of surplus tissue for use in health-related research. Second, the public benefit in trust which comes from governance and regulatory safeguards, including procedures to request permission, which is an important factor in the fiduciary relationship between healthcare providers and patients[674]. This is in the public interest because maintaining trust is important to ensure that patients access medical care when they are unwell and ensures that new knowledge is generated through participation in research[675].

This article concludes that a consistently applied approach with regards to the secondary research use of surplus tissue would be fairest for patients, as it provides equal opportunity to choose whether surplus tissues samples are used for secondary research purposes and in doing so affords equal moral standing to patients. This argument is justified by respect and self-determination being foundations of social equality and therefore something which all persons should be afforded equally. In suggesting that a consistent approach would be fairest, this article proposes that the approach which should be consistently applied across NHS organisations is that surplus tissue samples are made available for secondary research purposes where there is no recorded objection; via a well-publicised system which is simple and accessible. The rationale for this conclusion is that this approach would have the greatest overall individual and public benefit. As a point of clarification, in referring to secondary research use of surplus tissue this article is referring to research which obtains tissue from diagnostic archives, is ethically approved and where the researcher would not be in possession of information which could identify the person from whom the tissue was removed. In such circumstances there is no legal requirement for consent under the HT Act 2004. Moreover, this article does not suggest that where surplus tissue is being collected for specific research projects, different consent arrangements to those currently in place should apply. This article therefore discusses the various approaches to consent

[674] O'Neil O. (2002) *Autonomy and Trust in Bioethics*. Cambridge: Cambridge University Press.
[675] Vermeulen E et al. A Trial of Consent Procedures for Future Research with Clinically Derived Biological Samples. *British Journal of Cancer*. 2009 **101** 1505-1512

requirements for the use of surplus tissue for secondary research purposes within a regulatory framework which does not *require* consent for such activities to be lawful.

11.2. Background

Health research is generally considered to be something which is positive and in the public interest[676], as it aims to generate generalisable knowledge about the functioning of the human body for the prevention and treatment of ill health[677]. Throughout our lives we all experience a myriad of health issues for which we require some medical intervention and furthermore, preventive medicine means that we can remain well[678], thereby avoiding the need for more intensive and expensive medical treatments. It is therefore in the broad interest of society that health-related research is undertaken and continues to progress medical science. Moreover, health research in the UK is often publicly funded, either by the NHS directly or by universities or charities and therefore there is also a public interest responsibility to ensure that health research is cost effective[679]. One area of health research which has potential for greater cost efficiency is research which involves 'surplus' human tissue. The use of human tissue in health research has helped to increase understanding about a vast range of diseases and treatments[680]. Tissue samples such as blood, urine or biopsy samples, as well as whole organs and diseased tissue, are regularly removed during clinically directed procedures for diagnostic testing and any surplus tissue may be stored in a diagnostic archive and can have significant research value[681]. Access to surplus tissue samples for research purposes could facilitate cost efficiency as it could reduce the requirement to remove additional samples specifically for research purposes.

[676] McHale J. Reforming the Regulation of Health Research in England and Wales: New Challenges and Pitfalls. *Journal of Medical Law and Ethics.* 2013 **1(1)** 23-42
[677] Academy of Medical Sciences (2011) *A New Pathway for the Regulation and Governance of Health Research*. Available at acmedsci.ac.uk/policy/policy-projects/a-new-pathway-for-the-regulation-and-governance-of-health-research
[678] Lowrance W, (2013) *Privacy, Confidentiality and Health Research*. Cambridge: Cambridge University Press
[679] Academy of Medical Sciences (2011) *A New Pathway for the Regulation and Governance of Health Research*. Available at acmedsci.ac.uk/policy/policy-projects/a-new-pathway-for-the-regulation-and-governance-of-health-research
[680] Meslin E and Quaid K. Ethical Issues in the Collection, Storage, and Research of Human Biological Materials. *Journal of Laboratory Clinical Medicine*. 2004 **144(5)** 229-234
[681] Gefenas E et al. Turning Residual Human Biological Materials into Research Collections: Playing with Consent. *Journal of Medical Ethics* 2012 **38** 351-355.

Furthermore, the use of surplus tissue in research, rather than obtaining new samples, could reduce bodily intrusion and therefore also the risks associated with tissue removal.

Public engagement work[682] aiming to understand public opinion with regards to the use of surplus tissue for health research purposes indicates that in general, the public is supporting of surplus tissue being used for research purposes[683]. However, this work has also identified that often patients and the public have little awareness of the potential research value of surplus tissue; the more informed the public are, the more accepting they appear to be of surplus tissue being used for research purposes[684]. Furthermore, public involvement work has indicated that some people consider it wasteful to *not* use surplus tissue for health research purposes and think more should be done to maximise its research use[685]. Studies exploring the views of patients, who have undergone surgical resection for the treatment of cancer, with regards to the secondary research use of their surplus tissue found that patients considered this to be 'no big deal', certainly compared to the experience of cancer diagnosis and treatment, and a view that secondary research use was a 'no brainer'[686].

682

Ipsos Mori (2007) *Human Tissue Authority Stakeholder Evaluation: General Public Qualitative and Quantitative Research.* Available here www.ipsos.com/sites/default/files/migrations/en-uk/files/Assets/Docs/Archive/Polls/hta.pdf

Ipsos MORI (2018) *Consent to use Human Tissue and Linked Health Data in Health Research. A Public Dialogue for Health Research Authority and Human Tissue Authority.* Available at www.hra.nhs.uk/documents/1570/Consent_to_use_human_tissue_and_linked_health_data_in_health_research_FINAL.pdf

683 Liddell K. (2009) Beyond a Rebarbative Commitment to Consent. In Corrigan O, McMillan J, Liddell K, Richards M and Weijer C (eds.) *The Limits of Consent: A Socio-Ethical Approach to Human Subject Research in Medicine* (pp 79 -97) Oxford: Oxford University Press

684 Ipsos MORI (2018) *Consent to use Human Tissue and Linked Health Data in Health Research. A Public Dialogue for Health Research Authority and Human Tissue Authority.* Available at www.hra.nhs.uk/documents/1570/Consent_to_use_human_tissue_and_linked_health_data_in_health_research_FINAL.pdf

685 *Ibid*

Womack C and Gray N M. Banking Human Tissue for Research: Vision to Reality. *Cell Tissue Banking.* 2009 **10** 267-270

686 Williams A M et al. Consent to Donate Surgical Biospecimens for Research: Perceptions of People with Colorectal Cancer. *Cancer Nursing.* 2016 **39(3)** 221-227

Soto C et al. Consent to Tissue Banking for Research: Qualitative Study and Recommendations. *Archives of Diseases in Childhood*. 2012 **97** 632-636

The storage and use of human tissue are regulated under the HT Act 2004 in England, Wales and Northern Ireland and the Human Tissue (Scotland) Act 2006 in Scotland. The Human Tissue (Scotland) Act 2006 only covers tissue which has been removed from the deceased and therefore does not apply to tissue which is removed as part of a clinically directed procedure and surplus to diagnostic requirements. Under the HT Act 2004, research in connection with disorders, or the functioning, of the human body is listed as a scheduled purpose and therefore is an activity which is lawful with 'appropriate' consent (in the context of the HT Act 2004 this refers to consent being given by an appropriate person). Consent is the fundamental principle underpinning the lawful storage and use of human tissue[687] and when the Act came into force was extolled as the 'golden thread' which ran through the legislation[688]. However, the HT Act 2004 provides an exception to the requirement for consent where tissue has been removed from a living person, the research has been ethically approved and the identity of the person from whom the tissue was removed will not be known to the person undertaking the research[689]. This provision was introduced via an amendment to the Human Tissue Bill during its passage through Parliament in response to concerns raised by representatives of the research community, such as medical charities, research funders and professional associations[690]. The concern raised was that important research could be severely limited if there was a requirement for consent to be in place for all surplus tissue samples which are held within a diagnostic archive.

It was suggested that there would be logistical and also ethical issues which would arise if there was a requirement for consent to be in place for the use of surplus tissue samples in health-related research[691]. Moreover, a requirement for consent for the research use of surplus tissue would require an infrastructure which ensures that consent is requested, recorded and stored in a way which means

[687] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents explanatory notes paragraph 4
[688] Furness P. The Human Tissue Act: Reassurance for Relatives, at a Price. *British Medical Journal.* 2006 **333(512)**
[689] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 1 s 1 ss (7) – (9)
[690] Liddell K and Hall A. Beyond Bristol and Alder Hey: The Future Regulation of Human Tissue. *Medical Law Review.* 2005 **13(2)** 170-223
[691] Price D. The Human Tissue Act 2004. *The Modern Law Review.* 2005 **68(5)** 798-821

that pathologists can confirm whether the patient had given consent. Without such an infrastructure, important health research would be significantly limited and could in turn impact all society by restricting future development in the medical field[692]. Almost twenty years later, there is still no established infrastructure in the UK to request, record and access patient preferences with regards to potential future research use of their surplus tissue. Moreover, currently there are inconsistent approaches with regards to the secondary research use of surplus tissue and requirements for consent being applied within NHS organisations, which this article will go on to demonstrate.

The HT Act 2004 also establishes the Human Tissue Authority (HTA) to provide statutory oversight of activities relating to the storage and use of relevant material (human biological material, other than gametes, which consists of or includes human cells). Moreover, the HT Act 2004 gives a statutory responsibility to the HTA to prepare and issue codes of practice for the purpose of giving practical guidance and laying down standards which are expected with regards to activities which are within the remit of the Authority[693]. The HTA code of practice on consent[694], confirms that consent is not legally required where the research is ethically approved, and the researcher is not able to identify the person from whom the tissue was removed. However, the code further indicates that consent is 'recommended as good practice'.

The legal position as well as the good practice standard is also reflected in guidance issued by the Medical Research Council (MRC)[695] which says that 'It is good practice to consider obtaining separate consent for the storage and use of such surplus material for research purposes wherever possible; where this is not reasonably possible appropriate information should be provided so that patients are aware of the potential use of such samples'[696]. However, both the HTA code of practice on consent

[692] Price D. The Human Tissue Act 2004. *The Modern Law Review.* 2005 **68(5)** 798-821
[693] *Human Tissue Act 2004.* Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 2 s 26 ss 1
[694] Human Tissue Authority (2020) *HTA Code A: Guiding Principles and the Fundamental Principle of Consent.* Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20E.pdf
[695] Medical Research Council (2014) *Human Tissue and Biological Samples for use in Research: Operational and Ethical Guidelines.* Available at www.ukri.org/publications/human-tissue-and-biological-samples-for-use-in-research/
[696] *Ibid*

and the MRC guidance on consent fail to provide any further detail in relation to when accessing existing tissue samples from a diagnostic archive would be acceptable without consent. Furthermore, there is no clear guidance in relation to the circumstances under which obtaining consent would be considered 'practical'. In the absence of clearly defined requirements or expectations, or an established infrastructure for obtaining and recording consent, different NHS organisations have implemented different internal policies with regards to the research use of surplus tissue and requirements for consent.

11.3. Inconsistency Across NHS Organisations

To demonstrate the claim that approaches to the research use of surplus tissue are inconsistently applied across NHS organisations, this article refers to policies from 12 different NHS organisations in England. These are all policies for obtaining consent for examination and treatment which make some reference to the availability of surplus tissue for research purposes. These policies were located on the relevant NHS organisation website, were identified via a google search (NHS + "consent to examination and treatment" + tissue + research) and include all secondary and tertiary care organisations in England which were identified via this search method. The intention here is not to demonstrate the full scale of inconsistency across the NHS, but to highlight that there is evidence of *some* inconsistency.

Table 1

NHS Organisation	Use of surplus tissue accepted	Consent required	Evidence of no objection required	Links to policies (All accessed 19 October 2021)
Barnsley District General Hospital	Yes	No	Yes	Available here

Heart of England NHS Foundation Trust	Unclear	Unclear	Unclear	Available here
Royal United Hospitals Bath	Unclear	Unclear	Unclear	Available here
Bolton NHS Foundation Trust	No	N/A	N/A	Available here
County Durham and Darlington NHS Foundation Trust	Unclear	Unclear	Unclear	Available here
Barts Health NHS Trust	Yes	Yes	No	Available here
Gateshead Health NHS Trust	Yes	No	Yes	Available here
Cumbria, Northumberland, Tyne and Wear NHS Foundation Trust	Unclear	Unclear	Unclear	Available here
West Hertfordshire Hospitals NHS Trust	Yes	Yes	No	Available here
Royal Liverpool and Broadgreen University Hospitals NHS Trust	Yes	No	No	Available here
North Cumbria University Hospitals NHS Trust	Yes	No	No	Available here
Surrey and Sussex Healthcare NHS Trust	Yes	No	No	Available here

Table 1 sets out the organisational policies which were identified via the search and detail of the approaches to the availability of surplus issue for secondary research purposes which each organisational policy permitted within that organisation. What this demonstrates is that whether a patient's surplus tissue is accessible for secondary research use and whether that patient will be asked

whether they consent or object, depends on the NHS organisation at which they underwent the tissue-removing procedure. If patient A attended one hospital for a procedure, surplus tissue may be used for research purposes without their consent, patient B may have attended a different hospital and was asked whether they give consent to any surplus tissue being used for secondary research purposes, whereas patient C may have attended a different hospital which had a notice on the wall advising them to inform the clinician if they do not want their surplus tissue to be used for secondary research purposes.

My claim that this is *unfair*, is based on there being an inconsistent distribution of opportunities for patients in relation to the availability and use of surplus tissue for research purposes. Here I mean the opportunity for persons to choose whether their surplus tissue is available for use in health research, and the opportunity to *knowingly* be a tissue donor for health research and therefore for persons to realise their altruistic interests. This is because the opportunity is dependent on the NHS organisation at which the patient underwent a tissue removing procedure and is not based on any reasoned decision-making process or a valid ethical or legal principle of distribution[697]. The following four general approaches have been identified via the 12 NHS policies in this case study:

1. Surplus tissue always available for research use without any requirement for consent[698]
2. Surplus tissue only available for research use with explicit consent[699]
3. Surplus tissue available for research use where there is no objection recorded[700]
4. Surplus tissue never available for research use[701]

In setting out these approaches, I am not suggesting that any one approach is *unacceptable*; each approach can be justified on some level both legally and ethically. What I am suggesting is that this

[697] Beauchamp TL and Childress JF (2013) *Principles of Biomedical Ethics: Seventh Edition*. New York: Oxford University Press
[698] Royal Liverpool and Broadgreen University Hospitals NHS Trust, North Cumbria University Hospitals Trust & Surrey and Sussex Healthcare NHS Trust
[699] Barts Health NHS Trust & West Hertfordshire Hospitals NHS Trust
[700] Barnsley District General Hospital & Gateshead Health NHS Trust
[701] Bolton NHS Foundation Trust

disparate and inconsistent approach is unfair because it does not provide an equal distribution of opportunities. This is because the different approaches are not based on a reasoned decision-making process or a valid principle of distribution[702]. There is no morally justifiable reason why some patients are given opportunities over other patients. The decision with regards to whether a patient is given the opportunity to choose and therefore to knowingly act on their altruistic interests is down to which NHS organisation they attend for their tissue removing procedure.

11.4. Inequality of Opportunity?

To demonstrate the inconsistency, and therefore unfair distribution of opportunities, I refer to the differing approaches identified via the 12 NHS organisation policies in this case study. In approach 1, where all surplus tissue is available for use in health-related research without a requirement for consent, these patients are *de facto* denied the opportunity to choose whether their tissue is used for research purposes. Moreover, in being denied the opportunity to choose to allow surplus tissue to be used for research purposes, patients are denied the awareness that their tissue could be used for this purpose and therefore to knowingly act on their altruistic interests by choosing to allow secondary research use of their surplus tissue. Compare this to approach 2, where surplus tissue is only available for use in health-related research with the consent of the person from whom the tissue was removed. In this scenario, patients do have the opportunity to choose whether their surplus tissue is used for research purposes and therefore also to act on their altruistic interests by knowingly donating their surplus tissue by giving explicit consent. However, for this to truly be the case, an effective infrastructure is necessary to ensure that all patients who undergo a tissue removing procedure are afforded the opportunity to consent or refuse to the secondary research use of their surplus tissue samples. In the absence of an effective infrastructure, there is not only inconsistency with regards to

[702] Beauchamp TL and Childress JF (2013) *Principles of Biomedical Ethics: Seventh Edition*. New York: Oxford University Press

opportunities to choose whether to allow the secondary research use of surplus tissue and to knowingly act on altruistic interests across NHS organisations but also *within* NHS organisations.

In approach 3, where surplus tissue is available for use in health-related research in the absence of objection by the person from whom the tissue was removed, patients also have the opportunity to choose whether their surplus tissue is used for research purposes. However, for this scenario to be truly effective in offering fair distribution of opportunities, there must be an infrastructure in place which means that *all* patients undergoing a tissue removing procedure have awareness, and therefore the opportunity to object to their surplus tissue being available for use in heath research. As with approach 2, absence of such an infrastructure would mean that there is not only inconsistency and therefore inequality across NHS organisations but also within NHS organisations. In ensuring awareness, patients will have the opportunity to choose *not* to object, and therefore to knowingly act on their altruistic interests by allowing their surplus tissue to be available for use in health research. In approach 4 however, where surplus tissue is never available for secondary research use, patients are never given the opportunity to choose to donate their surplus tissue for use in health research and are therefore also always denied the opportunity to act on altruistic interests in being a tissue donor. Whilst this approach removes the risk of surplus tissue from a person who would have strongly objected being used for research purposes, arguably it also prevents the possibility that surplus tissue from those who would strongly agree is made available for this purpose by denying the opportunity to choose.

To be able to truly demonstrate that this inconsistency is *unfair* however, it must be the case that some patients are disadvantaged by the inconsistency of approach across different organisations; something that I will now go on to discuss further. Autonomy, self-determination, and choice are closely linked, with choice often being considered to be predicated on the right of individual persons

to make autonomous decisions about themselves[703] based on their own moral values[704]. Equality between individuals is the basis of much moral theory and generally the view is that equality of opportunity should not be denied persons unless there is some reasoned decision-making process on which inequality can be justified[705]. If it could be demonstrated that some patients are more deserving or worthy of opportunities than other patients, based on reasoning with which most 'rational' persons can agree, then inconsistency of opportunities may be justified. For example, it is generally accepted that the NHS provides greater healthcare resource to those who are in the most need; there is no expectation that every person receives the same amount of healthcare resource. We generally don't resent those with chronic debilitating medical conditions who get to spend more time in hospital than those of us who are generally well and attend a hospital only on rare occasions, because we think this *unfair*.

Powers and Faden[706] suggest that respect and self-determination are critical requirements for achieving social equality and as such, government institutions should aim to ensure *sufficient* levels to maximise opportunities for social equality for members of society. However, where there is no reasoned justification for unequal opportunities then arguably people are being treated *unfairly*. In denying some patients the opportunity to choose whether their surplus tissue is made available for health-related research purposes and to therefore knowingly act on their altruistic interests, where other patients do have this opportunity, these persons are being unfairly denied a right to self-determination. Arguably therefore, in denying some patients a right to self-determination *unfairly*, they are also being treated differently *morally,* as a right to self-determination is closely associated with respect for persons as moral beings. Respect for persons is intrinsic to the morality of human nature[707]. Therefore, *unfair* distribution of the opportunity of self-determination, to choose whether

[703] Maclean A (2009) *Autonomy, Informed Consent and Medical Law.* Cambridge: Cambridge University Press.
[704] O'Neil O. (2002) *Autonomy and Trust in Bioethics*. Cambridge: Cambridge University Press.
[705] Dworkin G (1988) *The Theory and Practice of Autonomy*. Cambridge: Cambridge University Press
[706] Powers M and Faden R. (2006) *Social Justice: The Moral Foundations of Public Health and Health Policy.* Oxford: Oxford University Press.
[707] Harris J. Law and Regulation of Retained Organs: The Ethical Issues. *Legal Studies.* 2002 **22(4)** 527-549

surplus tissue is available for use in health-related research and to knowingly act on altruistic interests, implies that different persons are on a different moral footing and worthy of different levels of respect. According to Powers and Faden[708], the potential consequence of denying respect and self-determination in a broader social context is social inequality, as respect and self-determination are critical foundations for social equality. Therefore, if respect and self-determination hold such a significant moral position within society, to deny some patients opportunities to choose whether to allow their surplus tissue to be used for secondary research purposes and to knowingly act on altruistic interests must be unfair. In making this point I am demonstrating that the unfair distribution of opportunities does have the potential to cause some patients to be disadvantaged by not being afforded opportunities which other patients will receive, and therefore the current disparate approach is unfair.

In this section I have demonstrated that the inconsistent approach to the availability of surplus tissue for use in health-related research means that there is an unfair distribution of opportunities for patients. However, there is arguably a further disadvantage on a broader, societal level, which also results from the inconsistent approach across different NHS organisations, meaning that *public interest* claims cannot be fully realised. This is something which I will go on to discuss in more detail in the next section.

11.5. Public Interest

Whilst a definitive definition of what is meant when we talk about public interest may be illusive[709], I think it important to provide some description of what is meant in referring to public interest in the context of this article. In referring to public interest I am suggesting that as individual members of

[708] Powers M and Faden R. (2006) *Social Justice: The Moral Foundations of Public Health and Health Policy.* Oxford: Oxford University Press.

[709] Taylor M. Health Research, Data Protection and the Public Interest in Notification. *Medical Law Review.* 2011 **19** 267-303

Meyers EM (2018) Ethics and the Public Interest. In Farazmand A (ed.) *Global Encyclopaedia of Public Administration, Public Policy, and Governance.* Springer International Publishing.

society who access healthcare services from the NHS, there is both an individual and a collective interest in health and wellbeing[710]. The approach in the HT Act 2004 of allowing research use of surplus tissue without the need for consent, and the good practice standard of requesting consent which is set out in the HTA code of practice on consent, arguably both have a public interest claim. However, I argue that the inconsistency in how they are applied across different NHS organisations, resulting in unfair distribution of opportunity for patients, means that the public interest claims cannot be fully realised.

The provision in the HT Act 2004, which permits the use of surplus tissue for research purposes without consent under certain specified circumstances was introduced as an amendment to the Human Tissue Bill in response to lobbying from the scientific research community over concern that the legislation would stifle or criminalise important research[711]. This approach is seemingly justified by a claim of public interest, as this provision was intended to maximise the value which could be attained from the tissue, whilst also safeguarding tissue donor rights[712]. The right to confidentiality by requiring that the person undertaking the research is not in possession of information which could identity the person from whom the tissue was removed, and a right for tissue not be used in research projects which a research ethics committee would not consider ethically acceptable. Moreover, the good practice standard of obtaining consent for research use of surplus tissue set out in the HTA Code of Practice on consent may also be considered to have a public interest claim. This is because consent, including consent for the research use of human tissue, amongst other things aims to secure and maintain trust[713]. This is in the public interest because maintaining trust is important to ensure that patients access medical care when they are unwell and ensures that new knowledge is generated through participation in research[714]. However, I suggest that in reality, rather than these *individual*

[710] Lowrance W. (2012) *Privacy, Confidentiality and Health Research.* Cambridge: Cambridge University Press
[711] See Lansley A (2004) *'Human Tissue Bill'* Hansard: House of Commons Debates 15 January c. 998
[712] See Baroness Hayman (2004) '*Human Tissue Bill'* Hansard: House of Lords Debates 22 July c. 409
[713] O'Neil O. (2002) *Autonomy and Trust in Bioethics.* Cambridge: Cambridge University Press.
Eyal N. Using Informed Consent to Save Trust. *Journal or Medical Ethics*. 2014 **40** 437-444
[714] Vermeulen E et al. A Trial of Consent Procedures for Future Research with Clinically Derived Biological Samples. *British Journal of Cancer*. 2009 **101** 1505-1512

approaches promoting public interest, by facilitating research use of surplus tissue (by not requiring consent) or by securing and maintaining trust (by requiring consent), this confused and disparate position fails the public interest claim on both counts because it is inconsistently applied across NHS organisations.

To demonstrate the claim that the public interest claims cannot be fully realised, I refer again to the four approaches identified via the NHS organisation policies set out earlier in this article. In approach 1, surplus tissue is always available for research use without any requirement for consent, this approach has the potential to fulfil both of the previously described public interest claims to some degree. This is because it aims to maximise the availability of surplus tissue and arguably, it also instils trust by the regulatory and governance framework, provided by the HT Act 2004, within which this approach sits. For this approach to be lawful the research must be ethically approved, and the identity of the tissue donor must be safeguarded. The existence of these requirements in statutory law means that there is accountability and possible sanctions for non-compliance; all of which help to secure trust in patients that organisations and individuals will act appropriately. This governance framework therefore helps to build and maintain confidence in the system which in turn has a public benefit[715]. An Ipsos Mori report in 2018, *Consent to use human tissue and linked health data in health research: A public dialogue for Health Research Authority and Human Tissue Authority*[716]*,* identified that those who participated in the public dialogue work had *assumed* that a trusted process is happening. This trust was stated to be based on an existing duty of care within NHS organisations and an understanding that accountability and safeguards are in place. When applied as a general rule across the NHS, this seems plausible. However, I suggest that when this approach is taken by some but not

[715] O'Neil O. (2002) *Autonomy and Trust in Bioethics.* Cambridge: Cambridge University Press.
[716] Ipsos MORI (2018) *Consent to use Human Tissue and Linked Health Data in Health Research. A Public Dialogue for Health Research Authority and Human Tissue Authority*. Available at www.hra.nhs.uk/documents/1570/Consent_to_use_human_tissue_and_linked_health_data_in_health_research_FINAL.pdf

all NHS organisations, there is a risk that the inconsistency could raise doubt about the *sufficiency* of the governance structure which supposedly protects the interests of tissue donors.

Consider approach 1, where surplus tissue is made available for secondary research purposes without a requirement for evidence of consent. Patients may question why other organisations only allow surplus tissue to be accessed for secondary research purposes with the consent of the donor or even refuse to allow access at all. They may question what interests these other approaches, of requiring consent or evidence of no objection before sharing surplus tissue for research purposes or in refusing to share surplus tissue at all, aim to protect which they are being denied. Therefore, whilst the approach in itself may aim to meet the public interests claims, of maximising the availability of surplus tissue for use in health-related research and by building and maintaining trust in patients, the public interest claim of building and maintaining trust arguably fails when this is one approach out of many across NHS organisations.

In approach 2, surplus tissue can only be available for use in health-related research where there is explicit consent. This approach, in complying with the good practice standard set out by the HTA and the MRC, aims to recognise the autonomous interests of patients to choose what happens to their surplus tissue and to act in accordance with their moral agency to support or not support activities with which they agree or object[717]. This in turn aims to build and maintain trust by involving patients in decisions about what happens to their surplus tissue [718]. However, whilst this approach may help to secure the trust of patients within *that* NHS organisation, it risks eroding trust in others attending a different hospital where there is no choice. For example, the policy of Barts Health NHS Trust is that consent is required whereas the policy of the Surrey and Sussex Healthcare NHS Trust, which is approximately 20 miles away, is that surplus tissue can be used without consent from the patient. As

[717] Dworkin G (1988) *The Theory and Practice of Autonomy*. Cambridge: Cambridge University Press
[718] O'Neil O. (2002) *Autonomy and Trust in Bioethics.* Cambridge: Cambridge University Press

a result of this, the broader public interest claim, of building and maintaining trust, arguably fails due to the disparate approach with regards to requirements for consent.

In approach 3, surplus tissue can only be accessed for use in health-related research where there is no evidence that the patient has expressed any objection. This approach aims to meet the public interest claim of building and maintaining trust by allowing patients the opportunity to choose whether their surplus tissue is available for use in health-related research by choosing to object or choosing not to object to secondary research use. Whilst this scenario does not require explicit consent to be given by the patient, a well-publicised system which presumes agreement in the absence of objection would help to ensure that a lack of objection reflects actual choice rather than a mere lack of awareness. This scenario also aims to meet the public interest claim of maximising the availability of surplus tissue by making all such tissue available for use in health-related research unless there is evidence of objection. However, whilst this scenario *prima facie* meets both public interest claims, this may not be the case where this is the approach of some but not all NHS organisations. This is because patients may question either the *sufficiency* or the *necessity* of this approach where other NHS organisations have a more or less robust system which either requires evidence of explicit consent or does not require a record of preferences at all. Moreover, the availability of surplus tissue may be maximised in NHS organisations which make tissue available unless there is evidence of objection, but this is not achieved as a broad public interest claim where other NHS organisation do not allow the same scale of access.

In approach 4, surplus tissue is never available for use in health-related research and therefore does not meet the public interest claim of maximising the availability of surplus tissue on any level. However, this scenario may arguably meet the public interest claim of securing and maintaining trust, by completely removing *any* risk for the persons from whom the tissue was removed. For example, it completely removes the risk of surplus tissue being used in health-related research where the person would have objected to that particular research project and it completely removes any risk of a person

whose tissue is used in health-related research being identified by the person undertaking the research. However, when this scenario is one of several different approaches across the NHS, it arguably also has the potential to diminish trust more broadly. This is because it suggests that the risk to be avoided is sufficient to warrant the public benefit of maximising the availability of surplus tissue for health-related research being overridden; thereby also calling into question whether it is something to be avoided as the potential risks may outweigh any potential benefit.

In setting out these scenarios in the public interest context, my intention is to demonstrate that whilst each individual scenario may be justifiable, the fact that they are inconsistently applied across NHS organisations means that the broader public interest claims cannot be fully realised. In demonstrating that the inconsistent, and therefore unfair, distribution of opportunities limits the public interest claims, I further claim that one scenario which is consistently applied would best maximise the public benefit. In the next section I will consider which approach, if consistently applies across the NHS, would best achieve this aim.

11.6. Which Approach to Take?

So far, this article has argued that inconsistent policy approaches to the use of surplus tissue for health-related research across different healthcare organisations means that there is an unfair distribution of opportunities associated with the donation of surplus tissue for this purpose. Moreover, this unfair distribution of opportunities means that the public interest claims of maximising the availability of surplus tissue for use in health-related research and building and maintaining trust cannot be fully realised. However, a consistently applied policy approach across NHS healthcare organisations may better achieve these public interest claims and furthermore I suggest that this approach should be the scenario which is likely to provide the greatest overall individual and public benefit.

In considering the four approaches set out earlier in this article, I suggest that approach 3 (surplus tissue is available where there is no objection recorded) would best achieve the greatest net benefit.

This is because *on balance*, it is best placed to ensure fair opportunities with regards to the donation of surplus tissue samples and achieve public interests aims. Whilst other scenarios may arguably better achieve *individual* aims, I suggest that scenario 3 best achieves the greatest *overall* benefit. For example, Approach 1 (all surplus tissue is available without a requirement for consent) would *prima facie* best maximise the availability of surplus tissue for use in health-related research, but this scenario fails to allow any choice for patients with regards to the secondary research use of their surplus tissue. Moreover, approach 2 (surplus tissue is only available where the patient has given consent) may arguably be perceived to allow more definitive choice and control over what happens to surplus tissue, but this approach does not meet the public interest aim of maximising the availability of surplus tissue for secondary research purposes. Finally, approach 4 (tissue is never available for secondary research use) does not maximise the availability of tissue, nor does it provide the opportunity to choose whether surplus tissue samples are made available for secondary research purposes.

With approach 3 (surplus tissue samples are available where patients have not objected) however, the availability of surplus tissue will likely be maximised, even taking into account the fact that *some* people will object to their samples being available for use in health-related research. I make this assertion because empirical evidence from public engagement work indicates that a very high percentage of people state that they would agree to the use of their surplus tissue in health-related research if given the opportunity[719] and that not making surplus tissue available would waste a valuable research resource[720]. Furthermore, approach 3 offers choice to patients as it provides an

[719] Furness P N and Nicholson M L. Obtaining Explicit Consent for the use of Archival Tissue Samples: Practical Issues. *Journal of Medical Ethics*. 2004 **30** 561-564
Vermeulen E et al. A Trial of Consent Procedures for Future Research with Clinically Derived Biological Samples. *British Journal of Cancer*. 2009 **101** 1505-1512
Wheeler J et al. Experiences from the Front-Line Routine Consenting of Surplus Surgically Removed Tissue: Without Investment by the National Health Service Fully Informed Consent is Not Available. *Journal of Clinical Pathology.* 2007 **60** 351-354
[720] Ipsos MORI (2018) *Consent to use Human Tissue and Linked Health Data in Health Research. A Public Dialogue for Health Research Authority and Human Tissue Authority*. Available at www.hra.nhs.uk/documents/1570/Consent_to_use_human_tissue_and_linked_health_data_in_health_research_FINAL.pdf

opportunity to choose whether to object, and therefore to act on altruistic interests in donating surplus tissue, or the opportunity to choose not to make surplus tissue available by recording an objection. Previously in this article I have suggested that self-determination to make autonomous choices based on moral values is important because it shows respect for persons as moral beings. If this is indeed the case, then an approach which allows self-determination and autonomous choice must also be important. Whilst the respect and self-determination and autonomous choice afforded by approach 3 may be perceived to be *weaker* than a requirement for explicit consent, the choice to object does still allow patients some control over whether their surplus tissue samples are available for use in health-related research[721]. Previous work has indicated that people express a desire to have awareness of what happens to their surplus tissue samples but generally they do not seek active consent procedures[722].

It is also important to bear in mind that consent may not always be something that is necessary, in which case an approach which enables the secondary research use of surplus tissue samples where there is no evidence of objection may be sufficient. Brownsword refers to the fallacy of necessity with regards to consent, suggesting that a fixation which over-values consent can in itself be as risky as under-valuation of consent[723]. In following this thinking, a requirement for consent should only be applied where an action would violate a right if undertaken without their consent; where no such rights exist then consent is not necessary[724]. Brownsword suggests that applying consent requirements where it is not necessary, moves from a beneficial *culture* of consent towards a non-beneficial *cult* of consent. He further suggests that the danger arises where consent is applied as a free standing, detached principle, rather than applied in support of other principles[725]. Whilst respect

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Womack C and Gray N M. Banking Human Tissue for Research: Vision to Reality. *Cell Tissue Banking.* 2009 **10** 267-270

[721] Giesbertz N, Bredenoord A and van Delden J. Inclusion of Residual Tissue in Biobanks: Opt-in or Opt-out? *PLOS Biology*. 2012 **10(8)**

[722] Bathe O F and McGuire A L. The Ethical use of Existing Samples for Genome Research. *Genetics in Medicine* 2009 **11(10)** 712-715

[723] Brownsword R. The Cult of Consent: Fixation and Fallacy. *King's Law Journal*. 2004 15(2) 223-251

[724] *Ibid*

[725] *Ibid*

for persons whose tissue have been removed and are stored in a diagnostic archive is undoubtedly important, this does not in itself mean that using such tissue samples for research purposes without explicit consent is *necessarily* wrongful towards that person. This is particularly relevant in the context of surplus tissue which is stored in a diagnostic archive being accessed for secondary research purposes because the HT Act 2004 provides a legal framework which protects patient interests, by ensuring that research projects must be ethically approved and that researchers are not in possession of information which could identify the person from whom tissue was removed. Where a legal framework provides protection for individual interests then arguably additional requirements for explicit consent are not *necessary*.

It is also important to acknowledge that equality for the sake of equality is not necessarily always the fairest approach, particularly where this would significantly disadvantage those who would otherwise be better off and only minimally improve the position of the worst off[726]. Applying approach 3 consistently across NHS organisations could achieve equality without levelling down to such a degree that those who would otherwise have had opportunities to choose to donate their surplus tissue for secondary research use and to act on their altruistic interests are denied these opportunities - as would be the case with approach 1 (all tissue is available without a requirement to confirm consent). However, to be confident that patients have truly been given a choice, with an approach which relies on objection rather than explicit consent, there is an imperative to raise awareness to ensure that a lack of objection doesn't reflect a lack of awareness rather than a lack of agreement[727] and patients have a fair opportunity to register an objection[728]. Therefore, a nationally applied approach of surplus tissue being available for secondary research use would ideally be supported by an infrastructure which ensures awareness and means that patients can easily object, and that any objection expressed

[726] Powers M and Faden R. (2006) *Social Justice: The Moral Foundations of Public Health and Health Policy.* Oxford: Oxford University Press.
[727] Giesbertz N, Bredenoord A and van Delden J. Inclusion of Residual Tissue in Biobanks: Opt-in or Opt-out? *PLOS Biology*. 2012 **10(8)**
Riegman P and van Veen E. Biobanking Residual Tissues. *Human Genetics*. 2011 **130** 357-368
[728] *Ibid*

is recorded in a way which can easily be confirmed prior to tissue samples being provided for research purposes.

11.7. Conclusion

This article has highlighted that there is some degree of inconsistency across NHS organisations, using the variation in policies across NHS organisations in England as a case study to demonstrate this point. Furthermore, the inconsistency of approach means that there is an unequal, and therefore unfair, distribution of opportunities for patients, whose tissues have been removed during clinically directed procedure. These are opportunities to *choose* to allow their tissues to be used in health-related research and also therefore to choose to act on their altruistic interests. This is unfair because the variation of approach across different NHS organisations is not based on any reasoned decision-making process and therefore treats equal moral agents unequally without any justified moral reasoning. Moreover, this article has demonstrated that this inconsistent approach means that the public interest claims associated with maximising the availability of surplus tissue for use in health-related research and building trust by allowing self-determination and choice, cannot be fully realised. A consistently applied approach which permits the use of surplus tissue for secondary research purposes in the absence of objection, via mechanisms which are well-publicised, accessible and simple to use would on balance best achieve both individual and public benefit.

CHAPTER 12

BRIDGING THE GAP: PROPORTIONATE REGULATION FOR TISSUE SHARING BY DIAGNOSTIC ARCHIVES FOR RESEARCH IN THE UK

12.1. Introduction

The Human Tissue Act 2004 (HT Act) requires that human tissue[729] which is stored for research purposes must be stored under an HTA research licence[730], except where it is being stored for use in an ethically approved research project or where ethical approval is pending[731]. Where tissue is taken and/or stored for primary research purposes then this is clear, storage should be under the authority of a research licence. However, there is a regulatory grey area where tissue was removed as part of a clinically directed procedure, is stored in a diagnostic archive and has potential secondary research value. It is usual for tissue which has been removed during a clinically directed procedure to be held in a diagnostic archive and this tissue then forms part of the patients' medical record[732]. However, not all of the tissue which is held in a diagnostic archive may be required for this purpose and there is often some 'surplus' tissue which can have value for use in health research[733]. Tissue which is surplus to diagnostic requirements can be a valuable resource for researchers, providing important information about the human body as well as disease processes[734] and biomarkers in drug

[729] Defined in the Human Tissue Act 2004 as 'relevant material' – material, other than gametes, which consist of human cells

[730] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 2 s 16 ss (1) – (2)(e) (ii)

[731] Human Tissue Act 2004 (Ethical Approval, Exceptions from Licensing and Supply of Information about Transplants) Regulations 2006. Available at www.legislation.gov.uk/uksi/2006/1260/note/enacted s (5) ss (b)-(c)

[732] Thomas G (2014) Access to Human Cells and Tissues. In Coleman, R (ed.) *Human-Based Systems for Translational Research*. (pp 1 – 16) Royal Society of Chemistry

[733] Womack C and Gray N M. Banking Human Tissue for Research: Vision to Reality. *Cell Tissue Banking*. 2009 **10** 267-270

[734] Thomas G (2014) Access to Human Cells and Tissues. In Coleman, R (ed.) *Human-Based Systems for Translational Research*. (pp 1 – 16) Royal Society of Chemistry

development[735]. Moreover, health research is generally considered to be in the 'public interest' as it has the potential to improve health at an individual as well as a public health level[736]. The value and importance of health research has been particularly evident in recent times as the world has responded to the threat of the SARS-CoV-2 virus which has resulted in a global pandemic of COVID-19. During this pandemic the number of research projects across the world increased significantly in an attempt to understand the virus and how it interacts with the human body as well as how the resulting disease can be treated and prevented[737]. This has included research using tissue samples taken from individuals who have tested positive for the virus, as well as previously stored samples, to better understand the physiological impact on the human body and, how the virus might be detected and treated[738].

The Human Tissue Authority (HTA), a regulatory body established via provisions in the HT Act 2004, has responsibility for licensing activities which fall under its remit[739]. Moreover, the HTA has a statutory responsibility to publish codes of practice which provide 'practical guidance to persons carrying on activities within its remit'[740] and 'laying down the standards expected in relation to carrying on of such activities'[741]. The code of practice on research aims to define the line between non licensable activities and licensable activities with regards to tissue which is stored in a diagnostic archive and may have secondary research value. The HTA code of practice on research says the following:

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[735] Macklin P et al. Barriers to the Release of Human Tissue for Clinical Trials in the UK: A National Survey of Cellular Pathology Laboratories on Behalf of the National Cancer Research Institute's Molecular Pathology (CM-Path) Initiative. *Journal of Clinical Pathology.* 2019 **72** 52-57

[736] Lowrance W. (2012) *Privacy, Confidentiality and Health Research.* Cambridge: Cambridge University Press

[737] Hofman P. Challenges and issues surrounding the use for translational research of human samples obtained during the COVID-19 pandemic from lung cancer patients. *Translational Lung Cancer Research*. 2020 **9(4)** 1543 - 1553

[738] Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in Different Types of Clinical Specimens. *JAMA*. 2020 **323(18)** 1843-1844

[739] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 2 s 14 ss (1)

[740] *Ibid* Part 2 s 26 ss (1) (a)

[741] *Ibid*

> 'The HTA's position is that if a diagnostic archive releases tissue for research occasionally upon request, its status as a diagnostic archive is clear. However, if there is an expectation that tissue will be released on a regular basis, then it may cease to be a purely diagnostic archive, particularly where there are developed governance / decision-making structures and procedures for applying for tissue.'[742]

This article suggests that the wording of this paragraph in the code of practice on research is too ambiguous and implies that a research licence *may* be required where this is not *necessarily* the case. This ambiguity creates a grey area with regards to accessing tissue samples from diagnostic archives which, as this article will go on to demonstrate, risks two potential adverse outcomes. First, it risks the unnecessary avoidance of accessing existing tissue samples held in a diagnostic archive, and second, it risks unnecessary over-regulation. This article suggests that the ambiguity in the code of practice on research which implies that a research licence *may* be required where this is not *necessarily* the case is not in keeping with the HTA's strategic approach. The HTA's strategic approach is based on 'right-touch regulation' principles; that regulation should be risk proportionate, targeted, taking account of other professional bodies and regulators and using the minimum direct intervention necessary to ensure compliance and improvement[743]. Furthermore, the implication that a research licence is required when this is not *necessarily* the case, risks preventing access to surplus tissue samples which have a potential research value and could be used lawfully for research purposes.

This is a problem in the context of a diagnostic archive because the licensing standards require an establishment to demonstrate that they have suitable arrangements in place to obtain consent from tissue donors for the secondary research use of tissue samples. However, as diagnostic archives are collecting and storing tissue samples for diagnostic rather than research purposes, consent is often

[742] Human Tissue Authority (2017) *HTA Code E: Research.* Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20E.pdf paragraph 94
[743] *Human Tissue Authority. Our Strategic Approach (2019)* Available at archive.hta.gov.uk/our-strategic-approach-0

not obtained for secondary research use[744]. Moreover, the HT Act 2004 permits the use of tissue which is surplus to diagnostic requirements without a requirement for consent where certain conditions are met. These conditions are that the research must be ethically approved by an authorised research ethics committee and the researcher must not be in possession of information from which the person from whom the tissue was removed could be identified[745]. This legislative provision was included in the HT Act 2004 via an amendment to the Human Tissue Bill (The Bill), following lobbying from the scientific and research community due to concerns that a blanket requirement for consent to use all tissue samples would stifle important research[746]. The amendment was well received during the second reading of The Bill and recognised as an important development for health research which meant that The Bill was 'in far better shape'[747]. The amendment to The Bill was also described as being *fairer* as it better balanced individual interests with societal interests[748].

The safeguarding provisions which were put in place were intended to enable the use of surplus tissue which has research value, whilst also recognising that the research value is often not known at the time the tissue is removed and therefore consent may not have been obtained for secondary research use of any tissue which is surplus to diagnostic requirements[749]. Whilst falling short of ensuring autonomous choice for patients with regards to whether their tissue samples are used for research purposes, the safeguarding provisions aimed to protect the privacy interests of the person from whom the tissue was removed and to protect moral interests by ensuring that any secondary research use is approved by an authorised research ethics committee. This was considered, on balance, a fair

[744] Furness P and Sullivan R. The Human Tissue Bill: Criminal Sanctions Linked to Opaque Legislation Threaten Research. *British Medical Journal*. 2004 **328** 533-534
[745] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 1 s 1 ss (7) – (9)
[746] Liddell K and Hall A. Beyond Bristol and Alder Hey: The Future Regulation of Human Tissue. *Medical Law Review.* 2005 **13(2)** 170-223
[747] *'Human Tissue Bill'* (2004) Hansard: House of Lords Debates 22 July c 374
[748] Liddell K and Hall A. Beyond Bristol and Alder Hey: The Future Regulation of Human Tissue. *Medical Law Review.* 2005 **13(2)** 170-223
[749] Lord Warner (2004) *'Human Tissue Bill'* Hansard: House of Lords Debates 22 July c. 369

compromise due to the low risk nature of the activity, the potential research value of stored tissue which is surplus to diagnostic requirements and the public interest in facilitating health research.

Whilst it may be lawful to provide tissue for research purposes without the consent of the person from whom the tissue was removed under certain circumstance, a key standard to be granted a research licence is a requirement to demonstrate clear procedures to obtain consent[750]. Therefore, the implication that a research licence is required where a diagnostic archive provides tissue samples for research purpose on a regular basis, or where there are governance arrangements in place to deal with requests to access samples, creates a potential barrier to research. Consent may not have been taken at the time the tissue was removed and it may not now be feasible to obtain consent for secondary research use of the tissue samples retrospectively, due to the time which has passed since the samples were removed[751]. However, obtaining an HTA research licence would require clear procedures to obtain consent. What this therefore means is that the transition from diagnostic archive to research tissue bank likely requires the implementation of procedures to obtain and record consent at an organisational rather than merely at a pathology department level; due to patient interactions where consent would be taken being distinct from pathology laboratories where samples are subsequently stored.

A well-established precautionary consent model, where patients are routinely asked whether they consent to their surplus tissue samples being used for secondary research purposes[752], may address this issue. However, this is often not the case in practice and where precautionary consent models are in place, they are often limited in how effective they are in confirming and recording patient

[750] Human Tissue Authority (2016) *HTA Code E: Standards and Guidance.* Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20E%20standards.pdf

[751] Gefanas G, Dranseika V, Cekanauskaite A, Serepkaite J (2011) Research on Human Biological Materials: What Consent is Needed, and When. In Lenk C, Sándor J, Bert Gordijn (eds.) *Biobanks and Tissue research: The Public, the Patient and the Regulation* (pp 95 – 110) Dordrecht: Springer

[752] Gefenas E et al. Turning Residual Human Biological Materials into Research Collections: Playing with Consent. *Journal of Medical Ethics* 2012 **38** 351-355.

preferences[753]; something which I will discuss in more detail later in this article. This therefore creates a potential scenario where robust consent arrangements are not in place, the HT Act 2004 permits the use of samples in research which are surplus to diagnostic requirements, but diagnostic archives are potentially discouraged from providing tissue samples or introducing governance arrangements to deal with requests for samples because the HTA code of practice on research implies that a research licence would be required.

This article is comprised of four parts. The first part sets out the legal and regulatory background to the licensing requirements in relation to human tissue, to provide context to later discussions. The second part discusses the impact of unclear or ambiguous regulatory guidance, suggesting that this can result in unintended and adverse consequences. The third part draws on previous work by Graeme Laurie et al applying the anthropological principle of liminality in a health research regulation context. Applying the concept of liminality in this context invites a re-think of how we approach tissue regulation by acknowledging the 'in-between' state which exists within a transitionary process and highlights the potential regulatory gaps and duplication which can occur when different regulatory bodies have different roles and responsibilities within a regulatory space[754]. Here I suggest that a diagnostic archive which provides tissue samples for use in research but does not fully function as a research tissue bank, should be viewed as an 'in-between' state and a proportionate regulatory approach should be applied which takes this into consideration. This section also considers the role of 'regulatory stewards' who guide those involved in providing and accessing surplus tissue for research purposes through the 'in-between' state, when a diagnostic archive transitions from being a purely diagnostic archive to also functioning as a research tissue bank. Furthermore, this section sets out a

[753] Macklin P et al. Barriers to the Release of Human Tissue for Clinical Trials in the UK: A National Survey of Cellular Pathology Laboratories on Behalf of the National Cancer Research Institute's Molecular Pathology (CM-Path) Initiative. *Journal of Clinical Pathology*. 2019 **72** 52-57
Wheeler J et al. Experiences from the Front-Line Routine Consenting of Surplus Surgically Removed Tissue: Without Investment by the National Health Service Fully Informed Consent is Not Available. *Journal of Clinical Pathology.* 2007 **60** 351-354

[754] Laurie G. Liminality and the Limits of Law in Health Research Regulation: What Are We Missing in the Spaces In-Between? *Medical Law Review*. 2016 **25(1)** 47-72

regulatory approach which transitions from a 'research project' regulation model to an 'establishment' regulation model, ensuring a more proportionate regulatory approach for the activities being undertaken. In recognising this as a transitionary process with an in-between state, the fourth part then suggests that the current expectations implied by the HTA code of practice on research with regards to diagnostic archives is not in keeping with the HTAs strategic objective of 'right-touch regulation'.

12.2. Research Licensing

The HT Act 2004 was introduced in response to findings from inquiries into the retention of organs and tissues removed from deceased children *post-mortem* at Bristol Royal Infirmary and Alder Hey Hospital[755]. The investigations which preceded the publication of these reports found that retaining tissues and organs post-mortem was common practice and often without the awareness, let alone agreement, of the deceased child's parents[756]. The Human Tissue Act 1961 which was in force at the time was found wanting, described as a 'toothless tiger'; due to the ambiguity of the legislation which meant that these practices often complied with the letter of the law, but not necessarily the spirit, with no provision for legislative sanctions[757]. The Government committed to reform the law governing human tissue and after a period of consultation, the Human Tissue Bill was published in 2003; with the HT Act 2004 subsequently being enacted in England Wales and Northern Ireland[758] in September 2006[759]. In aiming to put right the wrongs of the past, the HT Act 2004 placed significant emphasis on consent and established the HTA, which would act as a regulatory body with responsibility for the

[755] Price D. The Human Tissue Act 2004. *The Modern Law Review*. 2005 **68(5)** 798-821
[756] Department of Health (2002) *Learning from Bristol: The Department of Health's Response to the Report of the Public Inquiry into children's heart surgery at the Bristol Royal Infirmary 1984-1995*. Available at www.gov.uk/government/publications/the-department-of-healths-response-to-the-report-of-the-public-inquiry-into-childrens-heart-surgery-at-the-bristol-royal-infirmary
The Royal Liverpool Children's Inquiry (2001) *Royal Liverpool Children's Inquiry Report. Chair, Michael Redfern QC*. Available at www.gov.uk/government/publications/the-royal-liverpool-childrens-inquiry-report
[757] Brazier M. Human Tissue Retention – Speech to the Medico-Legal Society. *Medico-Legal Journal* 2004 **72(2)** 39-52
[758] Scotland has the Human Tissue (Scotland) Act 2006
[759] McHale J. The Human Tissue Act 2004: Innovative Legislation – Fundamentally Flawed or Missed Opportunity? *Liverpool Law Review* 2005 **26** 169-188

oversight of practices covered by the HT Act 2004. One such responsibility of the HTA is licensing of activities which the HT Act 2004 refers to as 'scheduled purposes'; activities which can only be lawfully undertaken with 'appropriate' consent. One such scheduled purpose is the storage and use of tissue for the purpose of research in connection with disorders, or the functioning, of the human body.

Where tissue is either removed specifically for the purpose of research, or where tissue which is removed as part of a clinically directed procedure and some surplus tissue is requested for a specific research project or specific research tissue bank, then the research 'purpose' of the sample is clear. Moreover, under these circumstances, the clear research status of the tissue sample means that the legislative provisions with regards to licensing requirements are also clear. However, there is a third scenario in which human tissue samples may be used for research purposes which is not so clearly defined. Where tissue is removed during a clinically directed procedure and is surplus to immediate diagnostic requirements, it is often stored for a period of time after removal, sometimes indefinitely[760], forming part of the patient's medical record in case further analysis is required[761]. The primary purpose of storage is not for use in research and therefore a licence is not required, however the tissue may later be identified as having research value[762], even though it is not necessarily being stored for the *purpose* of research.

Licensing of human tissue was implemented via the HT Act 2004 to 'help restore public confidence in the proper use of human organs and tissue by ensuring compliance with the consent provisions of the Act, so that tissue donation is encouraged for the public good'[763]. The HT Act 2004 says that the storage

[760] National Cancer Research Institute (2009) *Samples and Data for Research: Template for Access Policy Development.* Available at tdcc-blog.azurewebsites.net/wp-content/uploads/2016/06/Initiatives-Biobanking-2-Access-template-1.pdf

[761] Melham K. Enacting Regulation: Tissue in Practice. *Diagnostic Histopathology.* 2013 **19(9)** 343 – 349

[762] Gefenas E et al. Turning Residual Human Biological Materials into Research Collections: Playing with Consent. *Journal of Medical Ethics* 2012 **38** 351-355.

[763] *Human Tissue Act 2004 (Ethical Approval, Exceptions from Licensing and Supply of Information about Transplants) Regulations 2006.* Available at www.legislation.gov.uk/uksi/2006/1260/note/enacted Explanatory Memorandum paragraph 7.3

of 'relevant material which has come from a human body, for use for a scheduled purpose'[764] is required to be undertaken under a licence. Therefore, if tissue is being stored for use in research (a scheduled purpose), the storage should be under a licence. However, if tissue is being stored in a diagnostic archive as part of the patient's medical record (not a scheduled purpose), then storage does not need to be under a licence.

The licensing standards published by the HTA cover four areas which must be complied with for a licence to be obtained; consent, governance and quality systems, traceability and premises, including facilities and equipment[765]. The standards place significant emphasis on consent, stating that the standards aim to reinforce the key principle in the HT Act 2004 that 'consent is paramount in relation to activities involving the removal, storage and use of human tissue'[766] Where tissue is being removed specifically for storage in a research tissue bank, or where there is a clear intention to store tissue removed during a clinically directed procedure in a tissue bank, then a requirement to demonstrate processes to obtain and record consent for the research use of tissue samples is reasonable. However, where a tissue sample is removed during a clinically directed procedure and stored in a diagnostic archive in case further analysis of the tissue is required, and is *later* identified as having research value, then it is often the case that consent for secondary research was not obtained; here compliance with the licensing standards for consent will likely not be met.

One option would be to routinely request consent on a *precautionary* basis, so all patients are asked to consent to the secondary research use of their surplus samples[767]. During the passage of the Human Tissue Bill through Parliament, discussion took place in the House of Lords with regards to the potential for surgical consent forms to include a section to consent for secondary research use of any

[764] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 2 s 16 ss (2) (e) (ii)
[765] Human Tissue Authority (2016) *HTA Code E: Standards and Guidance*. Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20E%20standards.pdf
[766] *Ibid* para 6 (a)).
[767] Gefenas E et al. Turning Residual Human Biological Materials into Research Collections: Playing with Consent. *Journal of Medical Ethics* 2012 **38** 351-355.

surplus tissue[768]. However, concern was raised that this would unlikely be practical within existing infrastructures. Moreover, reference was made to the Royal College of Pathologists having raised concern that it would be necessary to implement a system which ensured that the express decisions of all patients could be efficiently retrieved and confirmed prior to any research use of surplus tissue samples. An effective system to achieve this would likely require significant resource to establish and it was not evident that any such resource would be made available. Moreover, during the second reading of the Bill in the House of Lords, Baroness Cumberlege referred to an audit undertaken at Leeds Teaching Hospital NHS Trust which found that only 48% of tissue samples received in the laboratory had a corresponding consent form and of these forms, 40% did not have the tissue section completed. This was despite the same study finding that less than 5% of patients expressed an objection to their surplus tissue samples being used for research purposes when asked[769].

Moreover, the study at Leeds Teaching Hospital NHS Trust also identified variation between the health professional roles and departments when completing the section on the surgical consent form which related to secondary research use of surplus tissue. This study looked at all surgical consent forms received in the histopathology department at the Trust between October – November 2002 and October – November 2003[770]. The study identified a marked difference in practice between clinical departments, individuals and groups of consent takers when it came to completion of the section relating to the future research use of surplus tissue samples. For example, it was identified that 89% of consent forms returned by nurses had a fully completed tissue research section but this was true for only 41% of consent forms returned by junior doctors. Moreover, of the completed forms received, clinical departments such as anaesthetics and oncology had a consent rate of 100% whereas the urology department had a consent rate of only 69%. Whilst the study does not draw real conclusions

[768] Baroness Finlay (2004) '*Official Report of the Grand Committee on the Human Tissue Bill'* Hansard: House of Lords 15 September c. GC 419
[769] Baroness Cumberlege (2004) *'Human Tissue Bill'* Hansard: House of Lords Debates 22 July c. 402
[770] Wheeler J et al. Experiences from the Front-Line Routine Consenting of Surplus Surgically Removed Tissue: Without Investment by the National Health Service Fully Informed Consent is Not Available. *Journal of Clinical Pathology*. 2007 **60** 351-354

on the reasons for this variation, it was evident that the variation was likely to be due to factors other than mere patient choice[771]. This therefore suggests that a 'precautionary' approach to consent within existing resources and infrastructure may not necessarily be successful in practice. Moreover, a more recent study undertaken in 2016-17 which surveyed the views of individuals who had some involvement with human tissue research indicated that almost 15 years after the study in Leeds, there was still no effective precautionary consent model in place across the NHS. In some cases, there is no tissue research section within surgical consent forms and where the tissue research section has been included, there is often a lack of understanding and awareness in the clinical setting where consent is being obtained[772].

This therefore creates a situation whereby the infrastructure is not in place to ensure that consent can be requested from all patients and recorded in a way which means it can be confirmed within the pathology department, should a potential research use of surplus tissue later be identified. However, the HTA code of practice on research implies that a research licence would be required for the research use of surplus tissue samples if they are being provided on a 'regular' basis or where there are governance arrangements in place to deal with requests to access samples. Furthermore, a key standard which must be complied with to obtain a research licence is to be able to evidence a clear process to request and record consent. This article suggests that the implication that a HTA research licence is required, where a diagnostic archive provides tissue samples on a regular basis or where there are governance procedures in place, is not proportionate to the activity being undertaken and does not take the complexities of obtaining precautionary consent for potential secondary research use into consideration. Consequently, there is a risk that diagnostic archives may not provide some tissue samples for research use unnecessarily or may avoid implementing governance procedures,

[771] Wheeler J et al. Experiences from the Front-Line Routine Consenting of Surplus Surgically Removed Tissue: Without Investment by the National Health Service Fully Informed Consent is Not Available. *Journal of Clinical Pathology*. 2007 **60** 351-354

[772] Macklin P et al. Barriers to the Release of Human Tissue for Clinical Trials in the UK: A National Survey of Cellular Pathology Laboratories on Behalf of the National Cancer Research Institute's Molecular Pathology (CM-Path) Initiative. *Journal of Clinical Pathology*. 2019 **72** 52-57

because it is being inferred that a licence would be required but there is no infrastructure in place to meet the consent requirements to obtain a research licence.

This section has set out the background to the HTA research licensing requirements and highlighted the challenges which occur when applying a consent focused licensing model within a diagnostic archive context. This section is intended to provide the basis for later discussion with regards to the transitional process which occurs when a diagnostic archive is also functioning as a research tissue bank. In the next section, this article will consider the potential for adverse consequences due to ambiguous guidance, in particular the ambiguity which may be caused due to the HTA code of practice on research implying that a research tissue licence is required where this is not *necessarily* the case.

12.3. Ambiguous Guidance Does Not Guide

Ambiguous guidance which aims to support regulatory compliance can result in different organisations taking different approaches[773], which then creates further confusion as different NHS organisation have different requirements and expectations. Human tissue research regulation is often considered to be an area which is confusing and overwhelming and therefore ambiguous guidance within the HTA codes of practice may exacerbate an already unclear situation. In 2009, onCore UK conducted a survey, in response to work undertaken by the National Cancer Institute's Task Force on Pathology and Research[774], to explore the effect of regulation and governance on pathology research in the UK[775]. This was in response to anecdotal evidence that researchers were finding it difficult to access existing tissue samples for research purposes[776]. Over half of the respondents to the survey stated that they found undertaking research difficult due to the lack of clear guidance available and

[773] Academy of Medical Sciences (2011) *A New Pathway for the Regulation and Governance of Health Research*. Available at acmedsci.ac.uk/policy/policy-projects/a-new-pathway-for-the-regulation-and-governance-of-health-research

[774] A time limited and scope restricted Task Force formed by the National Cancer Research Institute (NCRI) in response to concerns raised that research regulation was limiting pathology research

[775] onCore UK (2009) *The Effect of Regulation and Governance on Research Led by Pathologists or Involving Pathology in the UK.* Available at www.pathsoc.org/news/30/oncore_uk_report_effect_of_regulation_governance_survey

[776] Clotworthy M. Human Tissues for Research Purposes: A Conference in the House of Lords. *Cell Tissue Banking.* 2011 **12** 329-331

13% of respondents said that they do not undertake research at all because of this. For 83% of respondents, they would be more likely to be more research active if there was clear, consistent guidance which was easily accessible and endorsed by regulators. It was noted that where guidance did exist, it was often in different places and published by different sources which could be confusing. Respondents stated that the most common places to seek advice would be local Research and Development (R&D) offices or trusted colleagues. The report published by onCore UK in July 2009 concluded that the existing regulatory and governance environment was affecting the willingness ability of those working in pathology to undertake research.

The code of practice on research includes two relevant paragraphs with regards to whether a diagnostic archive may be considered to be functioning as a research tissue bank.

> *'*The HTA's position is that if a diagnostic archive releases tissue occasionally on request, its status as a diagnostic archive is clear. However, if there is an expectation that tissue will be released on a regular basis, then it may cease to be a purely diagnostic archive, particularly where there are developed governance / decision making structures and procedures for applying for tissue.*'*[777]

> *'*Where a diagnostic archive functions as a resource for researchers as it invites application for the release of samples, and/or in any way advertises the archive as a research resource, it is functioning as a research tissue bank. It must therefore be encompassed within the HTA's licensing framework.*'*[778]

Notably, the second statement sets a clear standard by which the status of research tissue bank can be measured, *'*the advertising or inviting of applications for the release of samples for research'. This appears to be a reasonable standard to determine whether a diagnostic archive is also functioning as

[777] Human Tissue Authority (2017) *HTA Code E: Research.* Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20E.pdf paragraph 94
[778] *Ibid* Paragraph 95

a research tissue bank, as advertising samples as a research resource is an unequivocal confirmation of an *intention* to provide tissue samples for use in health research. However, the first statement says that *'*developed governance / decision making structures and procedures for applying for tissue' *may* indicate that the establishment is no longer functioning purely as a diagnostic archive; *implying* that it is therefore functioning as a research tissue bank, an activity which should only be undertaken under the authority of a licence.

This article suggests that such ambiguity has two potential adverse outcomes. It may lead to the over-application of legislative requirements, creating a potential regulatory leap which is disproportionate to the actual activities being undertaken, or it risks creating a culture of avoidance. There is evidence to suggest that the implied need for a research licence, purely on the basis of samples being released from a diagnostic archive on a regular basis, is being inferred as a legal requirement and therefore an over application of regulatory requirements does happen in practice. In relation to barriers to the release of tissue samples for research purposes, Macklin et al make the following assertion, *'*If tissue is released from a diagnostic archive on a regular basis, it is considered a Research Tissue Bank and requires a licence'[779]*.* Whilst in some cases this may indeed be the case, it is not *necessarily* the case and therefore in some cases would be an over application of legislative requirements. Moreover, Furness suggests that there has been evidence of an 'if in doubt, don't do it' attitude, particularly when there is a risk of falling foul of legislative sanctions[780], and Lawrence et al suggest evidence of researchers obtaining new tissue samples rather than using existing samples, because the regulatory hurdles are perceived to be easier to navigate[781]. This therefore suggests that where there is ambiguity

[779] Macklin P et al. Barriers to the Release of Human Tissue for Clinical Trials in the UK: A National Survey of Cellular Pathology Laboratories on Behalf of the National Cancer Research Institute's Molecular Pathology (CM-Path) Initiative. *Journal of Clinical Pathology.* 2019 **72** 52-57

[780] Furness P. The Human Tissue Act: Reassurance for Relatives, at a Price. *British Medical Journal*. 2006 **333(512)**

[781] Lawrence E et al. The Barriers and Motivators to Using Human Tissue for Research: The Views of UK-Based Biomedical Researchers. *Biopreservation and Biobanking*. 2020 **18(4)** 266-273

regarding how regulatory requirements are to be complied with, there is some evidence of a culture of avoidance.

This section has highlighted ambiguity within the HTA code of practice on research in relation to diagnostic archives providing tissue samples for use in health-related research, and the potential consequences of either over-applying the legislative requirements or avoiding related activities for fear of falling foul of legislative sanctions. This article suggests that the potential for unnecessary over regulation or untended consequences of avoidance are not in keeping with the principles of right touch regulation, a regulatory approach which was set out as an aim in the HTA strategy 2019-22; this is something that will be discussed in more detail later in this article. First, in the next section this article uses the anthropological principle of 'liminality' as a conceptual framework by which to view diagnostic archives providing tissue for use in health research as a transitionary *process*.

12.4. Liminality – Recognising the 'In-Between'

This section will start by setting out an overview of the concept of liminality and how it can be applied in a health research regulation setting. The purpose of this is to provide context for later discussion and is not intended to be an in-depth description or analysis[782]. This article uses liminality as a conceptual framework to explore the transitionary processes which occur when a diagnostic archive provides tissue samples for use in health research, thereby transitioning from an establishment which functions purely as a diagnostic archive into an establishment which also functions as a research tissue bank. Moreover, in considering this as a transitionary *process*, rather than a mere change from one state to a new state, this article focuses on the 'in-between' state, where an establishment is neither purely a diagnostic archive, nor is it yet functioning as a research tissue bank. In exploring the transitionary process through the 'lens of liminality', which is a largely theoretical conceptual framework, the intention is to aid later discussion when considering how a more proportionate

[782] For a more detailed description and understanding of this concept, reference should be made to the work of Graeme Laurie et al on 'Confronting the Liminal Spaces of Health Research Regulation'

governance framework could be applied to diagnostic archives which also provide tissue for research purposes.

The concept of liminality originated in an anthropological context in the early 1900s from the work of Arnold van Gennep, when researching rites of passage in tribal communities. Van Gennep's work was later revisited by British Anthropologist Victor Turner after van Gennep's book, *Les Rites de Passage,* was translated from French into English in the 1960s[783]. It was observed that as a generalisable rule, when people transition from one status to a different status, for example when a child transitions into adulthood, they experience three distinct stages. First, they separate from their existing state. Second, they experience a liminal state, a period of 'in-between', where they are neither in their original state, nor have they yet arrived in their new state, and therefore neither *only* the rules of the before nor *only* the rules of the after apply during this period of in-between. Thirdly they transition into their final state[784]. The entire transitionary process may last for a mere nano second or it may endure for a much longer period of time. Furthermore, this transition from one state, through the liminal state in-between and into the final state is facilitated by various *actors* whose role it is to guide safely through the transition to the final state. The role of the guide is of particular importance, because the liminal in-between state is fraught with uncertainty and potential dangers. For example, others may take advantage of the disordered nature of the liminal state and *mis*lead down the wrong path for their own nefarious purposes[785]. 'Actors' therefore take the role of guide to lead through the disordered state in-between, and safely into the final state.

Laurie et al have applied the anthropological concept of liminality to the health research regulatory sphere as part of a programme of work entitled 'Confronting the Liminal Spaces of Health Research'[786]. This work invites consideration of the human element of research and the transitions which occur, for

[783] Bjørn T. (2018) *Liminality and the Modern: Living Through the In-Between*. London: Routledge
[784] *Ibid*
[785] *Ibid*
[786] Laurie G. Liminality and the Limits of Law in Health Research Regulation: What Are We Missing in the Spaces In-Between? *Medical Law Review*. 2016 **25(1)** 47-72

example when a patient becomes a research participant. Moreover, transitionary processes which result in liminal states can be seen to not only occur for persons but also 'objects', such as tissue or data collected as part of routine care being used for research purposes[787]. When such objects are separated from the person from whom they originated then this broadens what must be taken into consideration and therefore necessarily broadens the scope of regulation. The person no longer has full control over their tissue and data once they are separated from the self and therefore regulation acts to protect a person's interests by also protecting these objects in a way which recognises the inextricable link between the person and their tissue and data[788]. This is particularly relevant when there is a transition from a clinical state to a research state as this also results in a shift of expected benefit from benefit to the individual patient to the benefit of science and society more broadly; as well as the corresponding shift in expectations with regards to levels of protection which this brings. Moreover, due consideration should also be given to the transitions which occur in the regulatory sphere, as changes from a clinical and diagnostic state to a research state have implications in relation to the remit of relevant regulatory bodies. For example, the storage of tissue samples in a diagnostic archive as part of the patient's medical record is not a scheduled purpose and therefore is not within the remit of the HTA's licensing responsibilities. However, if the same samples were transferred to a research tissue bank then storage of such samples would be for the purpose of research and would become a licensable activity.

The next section aims to consider some of the individual transitions which occur when surplus tissue which is stored in a diagnostic archive is used for research purposes. In viewing these individual transitions through the lens of liminality, the intention is to demonstrate the in-between state which occurs, and also to highlight the different regulatory bodies which are involved in the broader

[787] Laurie G. Liminality and the Limits of Law in Health Research Regulation: What Are We Missing in the Spaces In-Between? *Medical Law Review*. 2016 **25(1)** 47-72
[788] *Ibid*
Liddell K and Hall A. Beyond Bristol and Alder Hey: The Future Regulation of Human Tissue. *Medical Law Review.* 2005 **13(2)** 170-223

transitionary process; regulatory bodies which each have distinct areas of focus but are required to work collaboratively to facilitate the broader 'tissue research' agenda. Consideration of these regulatory bodies aims to support later discussion in relation to applying a regulatory approach to diagnostic archives which provide tissue samples for use in health research, which is appropriate and proportionate for the actual activities being undertaken.

This section sets out two key transitions which occur when a diagnostic archive provides tissue samples for use in health-related research; each of which are explored in more detail below.

1. The tissue sample transitions from a diagnostic sample to a research sample.
2. The establishment transitions from a diagnostic archive to a research tissue bank.

<u>The tissue sample transitions from a diagnostic sample to a research sample.</u>

Where a tissue sample is removed during a clinically directed procedure and stored in a diagnostic archive in case further analysis of the tissue is required, the sample is a diagnostic sample and the diagnostic purpose of storage is clear. Moreover, if that sample is subsequently used for research purposes then it has transitioned to become a research sample and storage is then clearly for the purpose of research. Here we consider the transitionary process which occurs when a purely diagnostic sample later becomes a research sample and importantly, the liminal state which lies between the purely diagnostic and purely research states.

In considering this transitionary process, it is important to identify the point at which the tissue sample ceases to be a purely diagnostic sample. This is because when the sample ceases to be a purely diagnostic sample then this is the point at which the sample leaves the initial diagnostic state and transitions into the next state, where the sample is neither purely a diagnostic nor purely a research sample. Arguably, the trigger for the tissue sample to transition from being a purely diagnostic sample would be an event which means that there is the *potential* for the sample to be used for research purposes; the liminal state therefore also being a 'state of potentiality' in this context. The tissue

sample has been removed during a clinically directed procedure, it has been stored in a diagnostic archive in case further diagnostic tests are required however, there is a point at which there is *potential* for that tissue sample to be used for research purposes.

The exact scope and nature of that trigger event may vary. For example, a request from a researcher for samples of a specific tumour type may trigger tissue samples of that tumour type to enter the liminal state of potentiality but no other samples which are stored within the diagnostic archive. Alternatively, the triggering event may be the implementation of governance arrangements to manage potential future requests for tissue samples within the archive. In this scenario, notwithstanding any pre-defined exceptions, *all* samples may be considered to transition into the liminal state of potentiality. Moreover, the duration of this liminal state of potentiality, from ceasing to be a purely diagnostic sample to becoming a research sample, may vary. The duration may be relatively short, such as the time from the initial request to the time the sample is provided to the researcher, or it may be indefinite, such as from the time the governance arrangements are implemented to the time a future request for samples to be used for research purposes is made. However, regardless of the scope or the time which elapses, the process of transition remains the same. The tissue sample ceases to be a purely diagnostic sample when an event occurs which means that there is *potential* for the sample to be used for research purposes and the sample further transitions to become a purely research sample when there is *intention* for it to be used for research purposes.

<u>The establishment transitions from a purely diagnostic archive to also functioning as a research tissue bank.</u>

Where tissue samples are being stored for purely diagnostic purposes then the status as diagnostic archive is clear. Moreover, where an establishment is storing tissue samples purely for the purpose of research then its status as a research tissue bank is clear. However, when a diagnostic archive actually, or even potentially, provides tissue samples for use in research then a transition has been triggered

because it ceases to be a *purely* diagnostic archive. The establishment has arguably transitioned out of the diagnostic archive state and into the in-between state of potentiality where it ceases to be a purely diagnostic archive, but it is not *necessarily* functioning as a research tissue bank. The nature of the transitionary trigger event may vary, for example it may be providing the first sample for research use in response to a request from a researcher or may be a pre-emptive action to implement governance procedures in preparation for the eventuality of a researcher making a request for tissue samples stored within the archive.

Furthermore, we must consider how it will be known when the establishment has transitioned out of the in-between state and into the final state of research tissue bank. In a regulatory context, understanding the point at which the transition into the final research tissue bank state occurs is important, as this is also the point at which the establishment must be operating under the authority of a licence to ensure compliance with the HT Act 2004. The HTA code of practice on research is clear that the establishment is functioning as a research tissue bank when it 'invites applications for the release of samples, and/or in any way advertises the archive as a research resource'. However, prior to the point at which the archive invites applications or advertises as a research resource, there is uncertainty with regards to its status. This is particularly the case where there is a question about regularity of providing samples for research and whether there are governance procedures in place. The HTA code of practice on research states that 'if there is an expectation that tissue will be released on a regular basis, then it may cease to be a purely diagnostic archive, particularly where there are developed governance / decision making structures and procedures for applying for tissue'[789]. The transitionary process of the diagnostic archive into an establishment which also functions as a research tissue bank therefore transitions through three distinct states. First, it is functioning purely

[789] Human Tissue Authority (2017) *HTA Code E: Research.* Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20E.pdf paragraph 94

as a diagnostic archive, second it is neither purely a diagnostic archive nor is it yet also functioning as a research tissue bank and finally it is considered to be also functioning as a research tissue bank.

A constant which can be seen throughout each of the transitions described above is the three stages of the purely diagnostic state, the liminal state of being *neither* purely clinical or diagnostic *nor* yet also being a research sample or functioning as a research tissue bank, and then eventually into the research state. In acknowledging these three distinct stages, we can better visualise the transition from a purely diagnostic archive to also functioning as a research tissue bank as a transitional *process* rather than a transitional *leap* from an original to a final state. The overall transition may be completed quickly, maybe in a matter of mere hours or days, or it may take months or years to complete. However, what is important here is that the transition process *can* proceed, or at the very least is it not unnecessarily blocked from proceeding. Previously this article suggested that ambiguity and lack of awareness and understanding of legislative requirements has the potential to either cause over application of legislative requirements or to create a culture of avoidance for fear of falling foul of legislative sanctions. However, in both of these scenarios the transitionary *process* from diagnostic archive to also functioning as a research tissue bank may be viewed as having been unsuccessful; because the in-between state is either being by-passed or it is being avoided altogether.

This section has aimed to demonstrate the individual transitionary processes which occur within the broader transitionary process of a diagnostic archive providing tissue samples for use in health research. This article will now discuss some key regulatory bodies which have guiding roles to support these individual transitions, and discuss how they could interface within the broader transitionary process, to create a proportionate regulatory framework for the secondary research use of surplus tissue which is stored in a diagnostic archive.

12.5. Regulatory Stewardship – Guiding Through In-Between

In the context of liminality, transitionary processes are facilitated by *actors,* whose role is to guide through the uncertain liminal state and safely through to the new state[790]. The role of guide is important to ensure that the transitionary process can be completed successfully and to avoid the potential dangers which lurk within the uncertain and unordered liminal state[791]. This section will consider the relevant 'actors' who take the role of guide where tissue samples which are stored in a diagnostic archive are used for secondary research purposes. In applying the anthropological concept of liminality in a health research regulation sphere, Laurie et al[792] apply the term 'regulatory stewardship', which this article takes to be synonymous with the role of *guide* in the research regulation context. The definition of regulatory stewardship posited by Laurie et al[793] and Dove[794] is, 'the prudent guidance of one or more actors across regulatory thresholds – without which there is a risk of failure, impairment, or harm – with a view to fulfilment of regulatory objectives and collective betterment.'[795] Moreover, Laurie et al suggest that where actors hold a position of authority, this may strengthen their role as regulatory stewards[796]. For example, a regulatory body whose formal role is to advise researchers on how to ensure that they have fully addressed all regulatory requirements to undertake health research may be a stronger regulatory steward than a colleague who shares their experience of having previously submitted one research application.

The concept of regulatory stewardship in a health research regulation context recognises that different regulatory bodies have different roles to deliver research regulation within a broader regulatory framework. Regulatory stewardship extends beyond gatekeeper or oversight functions to

[790] Laurie G et al. Charting Regulatory Stewardship in Health Research: Making the Invisible Visible. *Cambridge Quarterly of Healthcare Ethics* 2018 **27(2)** 333-347
[791] Laurie G. Liminality and the Limits of Law in Health Research Regulation: What Are We Missing in the Spaces In-Between? *Medical Law Review*. 2016 **25(1)** 47-72
[792] Laurie G et al. Charting Regulatory Stewardship in Health Research: Making the Invisible Visible. *Cambridge Quarterly of Healthcare Ethics* 2018 **27(2)** 333-347
[793] *Ibid*
[794] Dove E. (2020) *Regulatory Stewardship in Health Research*. Cheltenham: Edward Elgar Publishing Limited
[795] *Ibid*
[796] Laurie G et al. Charting Regulatory Stewardship in Health Research: Making the Invisible Visible. *Cambridge Quarterly of Healthcare Ethics* 2018 **27(2)** 333-347

also encompass a facilitative role to enable health research which meets ethical and legal standards[797]. The next section considers the regulatory stewardship role of three bodies which hold an authoritative role in the context of tissue samples which are held in a diagnostic archive being available for use in health research: The Human Tissue Authority (HTA), Health Research Authority (HRA)[798] and Research Ethics Committees (RECs). It should be noted that this is not to suggest that these are the *only* bodies which hold such a role. There are different actors within the sphere of human tissue research regulation which may have a regulatory stewardship role occupying different spaces within the sphere. However, this article focuses on those actors which hold a 'regulatory gatekeeper' role within the sphere of health research which uses surplus tissue.

In this context I define 'regulatory gatekeeper' as an actor which has formal responsibility, due to a statutory or policy requirement, to undertake a decision-making process which determines whether a research related event proceeds. This is because regulatory gatekeepers hold a mandatory, and therefore consistent role, and consequently have the potential to be strong regulatory stewards. The next section will provide a brief overview of the individual regulatory stewardship roles for each of the three regulatory bodies, in the context of diagnostic archives providing tissue sample for use in health research. This will be followed by discussion about how the three regulatory bodies may fit together to create a proportionate regulatory framework to facilitate the broader transitionary process of purely diagnostic archive to also functioning as a research tissue bank.

Human Tissue Authority (HTA)

The HTA has a statutory role as a regulator. Its primary functions are ensuring compliance with the HT Act 2004, issuing and monitoring compliance against codes of practice and providing advice and guidance with regards to activities legislated for under the Act[799]. The HTA carries out these functions

[797] *Ibid*
[798] The remit of the HRA applies to England only
[799] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 2 s 15

in part by publishing a wealth of information and codes of practice on its website[800] to support people and organisations to ensure that they are complying with legislative requirements under the HT Act 2004. The HTA refers to itself as a 'compliance-based' regulator, which means that it puts significant emphasis on supporting compliance with the HT Act 2004 through providing support and guidance to ensure that licensing standards can be met[801]. This therefore suggests that the HTA does have a clear regulatory stewardship role as it guides actors across the regulatory threshold when undertaking activities which are within the remit of the HT Act 2004.

In terms of the transitionary process from tissue samples in a diagnostic archive being made available for use in health-related research, the direct responsibility of the HTA is in relation to the licensing of a diagnostic archive which is also functioning as a research tissue bank. This is because the HTA's role is in relation to transitions which are impacted by its statutory responsibilities with regards to licensing. This will be referred to as an 'establishment' regulatory model in a subsequent section of this article.

Health Research Authority (HRA)

The HRA[802] was established as a Non-Departmental Government Body under the Care Act 2014. The primary objective of the HRA is:

> ' (a) to protect participants and potential participants in health or social care research and the general public by encouraging research that is safe and ethical, and (b) to promote the interests of those participants and potential participants and the general public by facilitating the conduct of research that is safe and ethical (including by promoting transparency in research)'.[803]

[800] *Human Tissue Authority. Home Page* (no date) Available at www.hta.gov.uk/
[801] *Human Tissue Authority. Licensing* (2021) Available at www.hta.gov.uk/guidance-professionals/licensing
[802] The HRA was initially established in 2001 as a Special Health Authority and subsequently a Non-Departmental Government Body via the Care Act 2014.
[803] *Care Act 2014*. Available at www.legislation.gov.uk/ukpga/2014/23/contents/enacted s 110 ss (2)

Moreover, the Care Act 2014 requires the HRA to publish guidance on 'requirements, whether imposed by enactments or otherwise, to which persons conducting health or social care research are subject'[804]. One of the ways in which the HRA fulfils this requirement is the publication of the HRA Approval assessment criteria and standards[805]. This document sets out the criteria against which applications for research taking place in the NHS[806] will be assessed and therefore must comply with to be approved[807]. Whilst the remit of the HRA is limited to England, the approval and assessment criteria which are published by the HRA include standards with must be complied with in all UK nations, notwithstanding the existence of some additional standards applying in individual UK nations. The standards which must be complied with for research to be undertaken in the NHS include requirements for there to be suitable governance procedures in place with regards to the management of tissue samples and patient information. For example, whether there will be a Material Transfer Agreement (MTA) in place for research projects which involve the transfer of tissue samples, such as when samples are transferred from a diagnostic archive for use in a research project[808]. An MTA is a document which defines the conditions under which a recipient is granted access to tissue samples and associated data[809]. Moreover, Laurie et al[810] and Dove[811] suggest that the HRA has a regulatory stewardship role which extends beyond the issuing of guidance and standards against which applications are assessed for compliance. In also fulfilling the requirement to facilitate research, which is safe and ethical, the HRA has a role to support and guide through to the research state. It

[804] *Ibid* s 111 ss 6 (b)
[805] Health Research Authority (2016) *HRA Approval: Assessment Criteria and Standards Document*. Available at www.hra.nhs.uk/documents/217/hra-approval-assessment-criteria-standards-document.pdf
[806] The document is published by the HRA but contains standards which apply across all 4 nations of the UK.
[807] *Health Research Authority. HRA Approval* (2021) Available at www.hra.nhs.uk/approvals-amendments/what-approvals-do-i-need/hra-approval/
[808] Health Research Authority (2016) *HRA Approval: Assessment Criteria and Standards Document*. Available at www.hra.nhs.uk/documents/217/hra-approval-assessment-criteria-standards-document.pdf
[809] National Cancer Research Institute (2009) *Samples and Data for Research: Template for Access Policy Development*. Available at tdcc-blog.azurewebsites.net/wp-content/uploads/2016/06/Initiatives-Biobanking-2-Access-template-1.pdf
[810] Laurie G et al. Charting Regulatory Stewardship in Health Research: Making the Invisible Visible. *Cambridge Quarterly of Healthcare Ethics* 2018 **27(2)** 333-347
[811] Dove E. (2020) *Regulatory Stewardship in Health Research.* Cheltenham: Edward Elgar Publishing Limited

does not merely act as a gatekeeper which decides who will enter the research state, it has a responsibility to encourage and facilitate entry into the research state, in a safe and ethical way.

Research Ethics Committee (REC)

Where a research project intends to use tissue which has been removed, or is to be removed, from patients accessing NHS services, there is a requirement for the research project to be reviewed by an authorised REC; and a favourable opinion must be in place before the research can take place[812]. Where the person from whom the tissue was removed was not asked to consent to the tissue being used for research purpose then approval from an authorised REC is a legal requirement under the HT Act 2004. Therefore, the REC holds a clear 'regulatory gatekeeper' role in this context. Where a research project proposes to access tissue samples stored within a diagnostic archive, the REC will require assurance that steps are being taken to protect the interests of the patients from whom the tissue was removed. For example, consideration will be given to how decisions will be made with regards to whether samples can be accessed, ensuring that there is no potential harm by depleting tissue samples which may require further diagnostic analysis[813]. Moreover, empirical work undertaken by Dove[814] suggests that the role of the REC is also facilitative and therefore RECs do also hold a regulatory stewardship role. Dove observed the deliberations of RECs and interviewed individual REC members to determine the role of the REC, within the regulatory stewardship context[815]. This work surmised that the function of the REC is broader than the ethical deliberation and resulting ethical opinion. In addition to this, the REC has a role both pre and post ethical opinion to advise, guide and support in relation to individual research projects[816]. Whilst this is more of an informal than a formal

[812] Health Research Authority (2021) *Governance Arrangements for Research Ethics Committees.* Available at www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/governance-arrangement-research-ethics-committees/

[813] National Cancer Research Institute (2009) *Samples and Data for Research: Template for Access Policy Development*. Available at tdcc-blog.azurewebsites.net/wp-content/uploads/2016/06/Initiatives-Biobanking-2-Access-template-1.pdf

[814] Dove E. (2020) *Regulatory Stewardship in Health Research.* Cheltenham: Edward Elgar Publishing Limited

[815] *Ibid*

[816] *Ibid*

role, as this is not something that is defined within the scope of the Governance Arrangements for Research Ethics Committees[817] (GaFREC), it appears to be the normative experience described by REC chairs and members[818].

In facilitating individual research projects which propose to access surplus tissue from a diagnostic archive, the roles of the HRA and the REC are therefore in relation to the transition of tissue samples used in research from purely diagnostic to a potential or actual research sample. This is because the provision in the HT Act 2004 which permits the use of surplus tissue, where the research is ethically approved and the researcher will not be in possession of information which could identify the person from whom the tissue was removed, is met by the roles undertaken by the REC and the HRA. The next section of this article will refer to this approach as a 'research project' regulatory model, which may subsequently transition to become an 'establishment' regulatory model, provided for by the HTA, where a diagnostic archive transitions to also function as a research tissue bank.

12.6. Collaborative Regulatory Stewardship – 'Passing the Regulatory Mantle'

So far, this article has considered the individual transitionary processes which occur and the different regulatory stewardship roles which exist when a diagnostic archive provides tissue samples for use in health research, and subsequently also functions as a research tissue bank. However, I will now consider this as a broader collaborative transitionary process within which these regulatory bodies interface with each other as part of a broader regulatory framework. Whilst the transitionary process from diagnostic archive to also functioning as a research tissue bank is not necessarily a linear process, as it involves different transitions of different people and objects triggered by different events at different times, there is an element of order to the transitionary process. Dove[819] refers to the concept of 'passing the mantle' when different regulatory stewards fill different regulatory spaces within a

[817] Health Research Authority (2021) *Governance Arrangements for Research Ethics Committees*. Available at www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/governance-arrangement-research-ethics-committees/
[818] Dove E. (2020) *Regulatory Stewardship in Health Research.* Cheltenham: Edward Elgar Publishing Limited
[819] *Ibid*

broader regulatory context. This metaphor of passing the mantle helps to visualise the importance of each regulatory body fulfilling its individual responsibilities whilst also working collaboratively with other regulatory bodies through a broad transitional process[820]. Here I will consider the transition from purely diagnostic archive to also functioning as a research tissue bank in the context of passing the regulatory mantle from a 'research project' regulatory model, provided by the REC and HRA, to an 'establishment' regulatory model, provided by the HTA via an HTA research licence.

Where a diagnostic archive provides tissue samples for use in health research where consent was not obtained at the time the tissue was removed, there are conditions which must be complied with for the activity to be lawful. The researcher must not be in possession of information which could identify the person from whom the tissue was removed, and the research project must be approved by an authorised REC. Furthermore, for all research projects which take place in the NHS, the project must be assessed and confirmed as compliant with NHS governance standards, published and (in England) assessed against by the HRA[821] before it can start. As set out earlier in this article, compliance with these standards requires for there to be governance arrangements in place, such as procedures to deal with requests to access tissue samples and MTAs. This 'research project' regulatory model therefore ensures that there are appropriate procedures and safeguards in place on a research project specific basis, to protect the interests of those whose tissue samples are stored in the archive and enables important research which requires surplus tissue from a diagnostic archive to proceed.

The HTA via the issuing of an HTA research licence creates an 'establishment' regulatory model for research tissue banks because the licence applies to the functioning of the research tissue bank rather than individual research projects. Moreover, the UK[822] has a voluntary scheme for ethical review of research tissue banks which means that a generic approval can be obtained which covers the research

[820] Laurie G et al. Charting Regulatory Stewardship in Health Research: Making the Invisible Visible. *Cambridge Quarterly of Healthcare Ethics* 2018 **27(2)** 333-347

[821] In England and Wales in collaboration with Health Care Research Wales. Other arrangements apply in Scotland and Northern Ireland

[822] Different procedures apply in Scotland

tissue bank and all research projects accessing tissue samples which are within the scope of the approval; meaning that each individual project does not require individual ethical review by an authorised REC[823]. This means that there is an 'establishment' regulatory framework in place for research tissue banks which regulates the activities of the establishment rather than the individual research projects. Although internal project specific governance procedures will still be applied by the research tissue bank. Therefore, if we consider the transition from a purely diagnostic archive to also functioning as a research tissue bank as a transitionary process, which is regulated by a 'research project' model, transitioning to an 'establishment' regulatory model, and supported by regulatory stewards passing the regulatory mantle, then we can better see how regulation can be proportionate to the activities being undertaken. Moreover, in considering the in-between state as a state of potentiality, rather than a state which has a clear research intent, then we can see how the 'research project' regulatory model would be more proportionate to the in-between state, as it provides a regulatory framework for the actual tissue samples which may have secondary research value. However, where there is a clear research intent, such as where an establishment advertises itself as a research resource, then an 'establishment' regulatory model would be more appropriate.

The intention of viewing these as two distinct regulatory models in the context of passing the regulatory mantle from one (research project) to the other (establishment), when a diagnostic archive transitions to also function as a research tissue bank, is to establish a regulatory framework which ensures there are no regulatory gaps, but also avoids unnecessary regulatory duplication. In the next section, this article will consider the implication that a research licence is required, where a diagnostic archive provides tissue samples on a regular basis, or where there are governance procedure in place to deal with requests to access tissue samples for research, in the context of a 'right touch' regulation approach. Moreover, here it will be suggested that a regulatory framework which recognises the in-

[823] National Cancer Research Institute (2009) *Samples and Data for Research: Template for Access Policy Development*. Available at tdcc-blog.azurewebsites.net/wp-content/uploads/2016/06/Initiatives-Biobanking-2-Access-template-1.pdf

between state during the transitionary process from purely diagnostic archive to also functioning as a research tissue bank and a regulatory stewardship role passing the 'regulatory mantle' would be more proportionate.

12.7. 'Right Touch' Regulation

The HTA strategy 2019-22 set out its strategic approach as complying with the principles of 'right-touch' regulation; that regulation should be risk proportionate, targeted, taking account of other professional bodies and regulators and using the minimum direct intervention necessary to ensure compliance and improvement[824]. The concept of 'right touch' regulation was developed by the Council for Healthcare Regulatory Excellence (CHRE), which became the Professional Standards Authority for Health and Social Care (PSAHSC) under the Health and Social Care Act 2012[825][826]. This work built on previous work undertaken by the Better Regulation Executive in 2000, which resulted in five key principles; regulation should be proportionate, consistent, targeted, transparent and accountable. The CHRE added a sixth principle, that regulation should be agile, based on the idea that regulation should be forward facing and should anticipate change, rather than focusing on preventing mistakes which had occurred in the past[827]. Whilst the remit of the PSAHSC is oversight of the regulation of registered health professionals, the principles of right touch regulation are intended to be transferable to other areas of healthcare regulation[828]. Right touch regulation means that regulation should be outcome focused, regulation should only be applied where it is necessary and simple solutions, rather than overly complex regulatory systems, should be applied wherever possible[829]. This approach

[824] *Human Tissue Authority. Our Strategic Approach* (2019) Available at archive.hta.gov.uk/our-strategic-approach-0

[825] Professional Standards Authority for Health and Social Care (2015) *Right-Touch Regulation 2015.* Available at www.professionalstandards.org.uk/publications/detail/right-touch-regulation-2015

[826] Became the Professional Standards Authority for Health and Social Care in 2012 under via the Health and Social Care Act 2012

[827] Professional Standards Authority for Health and Social Care (2015) *Right-Touch Regulation 2015.* Available at www.professionalstandards.org.uk/publications/detail/right-touch-regulation-2015

[828] *Ibid*

[829] Bilton D and Clayton H. Finding the Right Touch: Extending the Right-Touch Regulation Approach to the Accreditation of Voluntary Registers. *British Journal of Guidance and Counselling*. 2013 **41(1)** 14-23
Cayton H and Webb K. The benefits of a 'right-touch' approach to health care regulation. *Journal of Health Services Research & Policy.* 2014 **19(4)** 198-199

acknowledges that more regulation does not necessarily lead to better quality or safer practices, and in fact can result in additional and unnecessary cost; to those being regulated and also to society more broadly where over regulation restricts or prevents intended outcomes from being achieved.

So far, this article has put forward two key arguments. First, the ambiguity caused by the *implication* in the HTA code of practice on research that a research licence is required where a diagnostic archive provides tissue samples for use in health research, and where there are governance processes in place, has the potential for adverse consequences. This is because it risks either over-regulation due to an assumption that a HTA licence is required where this is not *necessarily* the case, or it risks a culture of avoidance, where tissue samples are not provided for use in health research due to a fear of falling foul of legislative sanctions. Second, the section in the HTA code of practice on research which sets out licensing requirements for diagnostic archives is not proportionate. This is because it does not sufficiently recognise the 'in-between' state which occurs when a diagnostic archive goes through a transitionary process from a purely diagnostic archive to also functioning as a research tissue bank. In not recognising the 'in-between state', the HTA code of practice on research creates a 'regulatory leap' rather than guiding through the three distinct stages of regulatory transition. Moreover, the legislative provisions and policy requirements for research involving tissue which was removed during a clinically directed procedure and is surplus to diagnostic requirements, where consent was not requested when the tissue was removed, already provide a sufficient regulatory framework.

I further suggest that in coming to these conclusions, the implication in the HTA code of practice on research, that a research licence is required where a diagnostic archive provides tissue samples for use in health research, and where there are governance processes in place, does not comply with the principles of 'right-touch' regulation. This is because it applies a regulatory solution which is not proportionate to the risk of the activities being undertaken, taking into consideration other legal provisions and policy requirements, it applies regulation where this is not necessary and it has the potential to cause unintended consequences.

The HT Act 2004 permits the sharing of tissue samples which are held in a diagnostic archive where consent for future research use was not requested, for research projects which are ethically approved and where the researcher is not in possession of information which could identify the person from whom the tissue was removed[830]. This provision was included in the HT Act 2004 to ensure that research using surplus tissue samples, where the identity of the person from whom they were removed was not known to the researcher, could continue to be undertaken[831]. This provision therefore enables the sharing of tissue, which is surplus to diagnostic requirements, within a regulatory framework which also protects the interests of the person from whom the tissue sample was removed; by ensuring confidentiality and that research projects accessing tissue samples are ethically acceptable. Moreover, the Care Act 2014 provides a responsibility of the HRA to protect research participants in health and social care, both actual and potential, and to promote the interests of society by promoting and facilitating research that is safe and ethical[832]. These provisions within the HT Act 2004 and the Care Act 2014, therefore aim to enable research in a way which protects the interests of actual and potential research subjects. If these legislative provisions are *sufficient* to achieve this intended outcome, then any additional regulation is 'over regulation' and therefore unnecessary.

In addition to a requirement that regulation is necessary, 'right touch regulation' also requires for consideration to be given to any possible *unintended* outcomes which may occur as a result of implementing regulation[833]. As previously suggested, a potential consequence is a culture of avoidance. This is particularly the case where regulatory requirements are overly complex or unclear. Right touch regulation requires for regulation to be clear and simple so that those being regulated, as

[830] *Human Tissue Act 2004.* Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 1 s 7 & 9
[831] *'Human Tissue Bill'* (2004) Hansard: House of Lords Debates 22 July c 369
[832] *Care Act 2014*. Available at www.legislation.gov.uk/ukpga/2014/23/contents/enacted s 110 (2)
[833] Professional Standards Authority for Health and Social Care (2015) *Right-Touch Regulation 2015.* Available at www.professionalstandards.org.uk/publications/detail/right-touch-regulation-2015

well as other stakeholders such as employers and the public, are clear about why regulation is necessary and how it can be complied with[834].

As previously suggested, the licensing requirement set out in the HTA code of practice on research, with regards to diagnostic archives providing tissue for use in health research, is ambiguous. Moreover, this ambiguity sits within a broader regulatory framework which is often considered to be complex and confusing[835]. Evidence suggests that this had led to an 'if in doubt, don't' attitude in the past[836], as well as the collection of new tissue samples for use in research rather than accessing existing samples because it is perceived to be easier from a regulatory perspective[837]. Therefore, the ambiguity and implication in the HTA code of practice on research that a research licence is required, where a diagnostic archive provides tissue samples on a regular basis or where there are governance procedure in place, has the potential for unintended consequences and is therefore not in keeping with the principles of right touch regulation.

12.8. Conclusion

This article has put forward two key arguments with regards to licensing of diagnostic archives which also provide surplus tissue samples for use in health research. First, the HTA code of practice of research is too ambiguous with regards to the transition from a diagnostic archive to also functioning as a research tissue bank. Whilst there is a clear definition of when an archive is also functioning as a research tissue bank, because it is advertised as such and invites applications for tissue samples, there is ambiguity where a diagnostic archive provides samples on request. This is because the HTA code of practice on research *implies* that a research licence *may* be required where this is not necessarily required to comply with the HT Act 2004. Second this ambiguity and implication that a research licence

[834] *Ibid*
[835] Gibbons S MC. (2012) Mapping the Regulatory Space. In Kaye J, Gibbons S MC, Heeney C, Parker M, Smart A (eds.) *Governing Biobanks: Understanding the Interplay Between Law and Practice* (pp 51 – 92) Oxford: Hart Publishing ltd.
[836] Furness P. The Human Tissue Act: Reassurance for Relatives, at a Price. *British Medical Journal*. 2006 **333(512)**
[837] Lawrence E et al. The Barriers and Motivators to Using Human Tissue for Research: The Views of UK-Based Biomedical Researchers. *Biopreservation and Biobanking.* 2020 **18(4)** 266-273

may be required where this is not necessarily the case has the potential to cause intended consequences. There is evidence that confusing or ambiguous guidance and standards can lead to an 'if in doubt don't' culture of avoidance, resulting in research not being undertaken or the collection of new tissue samples rather than using existing samples. Furthermore, there is also evidence of the HTA code of practice on research leading to the inference that providing tissue samples on a *regular* basis *requires* an HTA research licence, when this is not necessarily the case. This therefore risks regulatory duplication for what is a relatively low risk activity.

In justifying these claims, this article has built on previous work applying the anthropological concept of liminality in a health regulation context, to view a diagnostic archive transitioning to also functioning as a research tissue bank as a transitionary *process* which has an 'in-between' state. Moreover, this article has considered the regulatory stewardship roles of three key regulatory bodies, the HTA, HRA and RECs, in supporting the transitionary process by guiding through the transitionary process and working in collaboration by passing the regulatory mantle from an 'research project' to an 'establishment' regulatory model. The intention of viewing the regulatory stewardship roles supporting the transitionary process by passing the regulatory mantle, is to demonstrate a regulatory model which does not have gaps but is also proportionate as it avoids regulatory duplication. Finally, this article has suggested that the ambiguity in the HTA code of practice on research, and the potential unintended consequences of avoidance or duplication, are not in keeping with a 'right touch' regulatory approach. This is because a 'right touch' regulatory approach requires regulation to only be applied where necessary, taking account of other regulatory bodies, and to avoid unintended consequences.

PART 3: CONCLUSION

CHAPTER 13

Conclusion

13.1. Introduction

My thesis aims to establish regulatory approaches which, if implemented in practice, could help to enable all surplus tissue samples to be potential research samples - focusing on tissue samples stored in diagnostic archives where consent for secondary research use has not been requested or recorded. My rationale for this focus is twofold. First, this is an area of regulation relating to research involving human tissue which is not as widely discussed or established in practice, a gap which my thesis aims to address. Second, I aim to establish a more *normative* regulatory approach to the secondary research use of surplus tissue which aims to increase patient awareness of the potential research value of surplus tissue and provides greater choice, but does not require explicit consent where the law provides for this. A regulatory approach which increases patient awareness of the potential research value of surplus tissue arguably also has the potential to provide a more solid regulatory foundation which in turn *supports* more established biobanking practices. The key focus throughout my thesis has been increasing the availability of surplus tissue samples for secondary research purposes, due to the significant potential research value and therefore potential public benefit, whilst also protecting patient interests.

In chapter 4 (ss. 4.3) I set out the existing literature with regards to consent for the secondary research use of surplus tissues. This was important because consent is the fundamental principle which underpins the lawful storage and use of human tissue[838]. The HT Act 2004 does however provide for

[838] *Human Tissue Act 2004.* Available at www.legislation.gov.uk/ukpga/2004/30/contents explanatory notes paragraph 4

the secondary research use of surplus tissue in the absence of consent, where the research is ethically approved and where the research is to be carried out in circumstances such that the person carrying it out is not in possession of information which could identify the person from whom the tissue was removed[839]. The primary focus of my thesis is making surplus tissue samples available for secondary research purposes under this legal provision and therefore in the absence of consent. However, consent provides more than a lawful basis for the secondary research use of surplus tissue samples and associated patient information. Consent also demonstrates respect for persons by enabling autonomous choice - the opportunity and ability to make decisions with regards to options which are presented, based on understanding and individual moral principles[840]. It is this element of consent which I did not want to lose sight of in the broader context of my thesis, despite the focus being on the secondary research use of surplus tissue where consent was not a requirement for such activities to be *lawful*.

Providing a comprehensive overview of the current discussions in the academic literature with regards to various approaches to consent for the secondary research use of surplus tissue was important context and provided a basis for subsequent discussion. However, in the broader context of my thesis I think it is important to view consent as a concept which is made up of different component parts, not all of which necessarily have relevance in the context of the secondary research use of tissue samples which are stored in a diagnostic archive and surplus to diagnostic requirements. Consent as a concept is complex[841] with roots in both legal and moral contexts[842]. Consent establishes entitlements, creates obligations, shifts risks and responsibilities from one to another[843] and reflects the decision to accept a course of action as well as the authorisation for that course of action to

[839] *Human Tissue Act 2004.* Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 1 s 1 ss (9)
[840] O'Neil O. (2002) *Autonomy and Trust in Bioethics*. Cambridge: Cambridge University Press.
[841] Nelson-Marten P and Rich B. A Historical Perspective of Informed Consent in Clinical Practice and Research. *Seminars in Oncology Nursing*. 1999 **5(2)** 81-88
[842] Faden R R and Beauchamp T L. (1986) *A History and Theory of Informed Consent.* New York: Oxford University Press
[843] Johnston D. (2005) A History of Consent in Western Thought. In Miller F and Wertheimer A (eds.) *The Ethics of Consent: Theory and Practice.* Oxford University Press Scholarship Online

occur[844]. However, as suggested by Brownsword, a danger arises where consent is applied as a free standing, detached principle, rather than applied in support of other principles[845]. Whilst respect for persons whose tissue has been removed and is stored in a diagnostic archive is undoubtedly important, this does not in itself mean that using such tissue samples for research purposes without explicit consent is *necessarily* wrongful towards that person.

The HTA code of practice on consent[846] refers to obtaining 'consent' for the secondary research use of surplus tissue as being 'good practice'. Applying the word 'consent' may however be best avoided in this context because it can blur legal and moral contexts to such a degree that it becomes difficult to separate 'legal requirement' from 'good practice'. In the absence of a *legal* requirement for consent, an approach which applies ethical components of consent, but in a non-legal context may be a preferred approach[847]. Moreover, the HTA code of practice on research is explicit that 'the giving of consent is a positive act'[848] and therefore referring to 'consent' where the law is permissive of the secondary research use of tissue in the absence of consent adds further confusion when accessing tissue on the basis of there being no evidence of objection. This blurring of lines is something that appears to occur in practice, as I demonstrated in chapter 11. Here I highlighted the varied approaches across different NHS organisations with regards to the secondary research use of surplus tissue. This case study highlighted that some organisations provide tissue samples without a requirement for consent, some organisations always require evidence of consent and some organisations provide tissue samples where there is no evidence of objection.

In demonstrating this variation, I argued that a consistently applied approach to the secondary research use of surplus tissue would be fairer, as it would provide patients with equal opportunities

[844] Beauchamp T. (2010) 'Autonomy and Consent' in Miller F, Wertheimer A (eds.) *The Ethics of Consent: Theory and Practice* Oxford University Press Scholarship Online
[845] Brownsword R. The Cult of Consent: Fixation and Fallacy. *King's Law Journal.* 2004 **15(2)** 223-251
[846] Human Tissue Authority (2020) HTA *Code A: Guiding Principles and the Fundamental Principle of Consent.* Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20A.pdf Annex C
[847] The Human Tissue (Scotland) Act 2006 uses the term 'authorisation' rather than 'consent'
[848] Human Tissue Authority (2017) *HTA Code E: Research*. Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20E.pdf paragraph 39

in relation to the donation of surplus tissue for secondary research purposes. Moreover, I suggested that the approach which, if consistently applied across all NHS organisations, would best meet the overall individual as well as public interests would be for surplus tissue samples to be available for secondary research use where there is no evidence of objection. My rationale for this conclusion was that well-publicised mechanisms to register an objection, which are simple and accessible, allow the opportunity for patients to choose whether their surplus tissue samples are used for secondary research purposes. Providing patients with the opportunity to *choose* whether their surplus tissue samples are used for secondary research purposes is an important ethical component of consent. However, by providing this choice as an opportunity to object rather than a requirement to actively consent, this approach aims to maximise the availability of surplus tissue for secondary research purposes within a legal framework which is permissive of such activities in the absence of consent.

Enabling the availability of surplus tissue for use in health research is important. However, the ability to link tissue samples to associated patient information is also important to ensure the maximum value can be obtained from the secondary research use of such samples. Linking tissue with associated patient information in a research context is important because it allows insight into complex interfaces between health, lifestyle, environment and genes which would not be feasible from the tissue alone[849]. Linking tissue and data therefore strengthens the validity and utility of research using surplus tissue[850]. However, linking tissue with associated patient information creates additional issues relating to data protection and patient confidentiality. Chapter 5 therefore set out the position with regards to the secondary research use of patient information, in particular this section focused on the legal provisions with regard to the research use of personal data under the GDPR and the DPA 2018 and the common law duty of confidentiality.

[849] Dörr B S. (2014) Collection of Human Tissue Samples in Biobanks: Challenges to Human Rights and Human Nature. In Albers M, Hoffmann T and Reinhardt J (eds.) *Human Rights and Human Nature.* (pp 185-196) Dordrecht: Springer

[850] Knoppers B, Isasi R. Stem Cell Banking: Between Traceability and Identifiability. *Genome Medicine.* 2010 **2(73)** 1-7

The primary focus of my thesis is to establish regulatory approaches which enable the sharing of surplus tissue in the absence of consent. For such activities to be lawful under the HT Act 2004, the research must be ethically approved and carried out in circumstances such that the researcher will not be in possession of information which could identify the person from whom the tissue was removed. However, it was apparent to me that there was scope to explore this provision further within the context of data legislation more broadly, which became the focus of chapter 10. This rationale was in keeping with my aim to establish approaches which could be more enabling of surplus tissue being accessed for secondary research purposes in ways which achieve a balance between individual interests and public benefit. This is considered in more detail later (ss. 13.1.2).

In establishing regulatory approaches which, if implemented in practice, could better enable the sharing of surplus tissue samples for secondary research purposes, it was important to consider other areas of legislation or regulation which could impact on the overall aim of my thesis. Chapter 6 set out the concept of property and ownership in the context of human tissue. This is an area which has been the basis of much discussion in the literature, in some part due to the terminology 'ownership' and 'abandonment' being used in a 1995 report published by the Nuffield Council on Bioethics, 'Human Tissue Ethical and Legal Issues'. The question of whether tissue can be owned is an important question when considering the use of surplus tissue samples and it was therefore important to establish the scope of its relevance in the context of the secondary research use of surplus tissue.

Chapter 6 set out case law with regards to ownership of human tissue, culminating with the most recent UK cases of *R v Kelly and Lindsay*[851]*, AB and other v Leeds Teaching Hospital*[852] and *Yearworth v North Bristol NHS Trust*[853]. The case law indicates a legal position whereby there can be claims of ownership for bodily materials removed from the body, both by the person from whom the material

[851] R v Kelly [1998] 3 All ER 742: (1999) QB 621 (CA)
[852] AB and others v Leeds Teaching Hospital NHS Trust [2004] EWHC 644 (QB)
[853] *Yearworth and others v North Bristol NHS Trust* [2009] EWCA Civ 37; [2010] QB 1

originated (*Yearworth v North Bristol NHS Trust*[854]) and by the subsequent holder (*R v Kelly and Lyndsay*[855]). However, as suggested by Herring, any such claims are limited as it is not the nature of the material or tissue itself, but the circumstances around its removal and retention which lead to a successful claim of 'ownership'[856]. Moreover, as suggested by Wall, applying property law in the context of excised tissue does not sufficiently acknowledge the complexities associated with the *uses* of excised tissue[857]. This is because a property law approach focuses on exclusionary rights over tissue as a *thing* and provides insufficient flexibility with regards to possible *activities* for which the tissue may be used[858]. With this in mind, I concluded that in the context of the secondary research use of surplus tissue, the question of property rights as established via case law, has now to some degree been superseded by statutory duties imposed on tissue holders via the HT Act 2004. These statutory duties primarily relate to ensuring appropriate consent and licensing for the storage and use of body parts and tissue for scheduled purposes. Moreover, it should be noted that in the cases of *R v Kelly and Lyndsay*[859] and *AB v Leeds Teaching Hospital*[860], both came before the courts before the HT Act 2004 was enacted and therefore its provision with regards to the lawful use of body parts and tissue for scheduled purposes did not apply in these cases. My rationale for setting out this position was to establish the legal boundaries with regards to the secondary research use of surplus tissue, concluding that the *activity* of research is regulated for under provision in the HT Act 2004 and therefore questions of property and ownership in a common law context are unlikely to be of direct relevance to the core arguments in my thesis.

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[854] *Yearworth and others v North Bristol NHS Trust* [2009] EWCA Civ 37; [2010] QB 1
[855] R v Kelly [1998] 3 All ER 742: (1999) QB 621 (CA)
[856] Herring J. Why We Need a Statute Regime to Regulate Bodily Material. In Goold I, Greasley K, Herring J, Skene L (eds.) *Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century?* (pp 215 – 230) Oxford: Hart Publishing ltd.
[857] Wall J. (2014) The Boundaries of Property Law. In Goold I, Greasley K, Herring J, Skene L (eds.) *Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century?* (pp 109 – 124) Oxford: Hart Publishing Ltd.
[858] *Ibid*
[859] R v Kelly [1998] 3 All ER 742: (1999) QB 621 (CA)
[860] AB and others v Leeds Teaching Hospital NHS Trust [2004] EWHC 644 (QB)

Chapter 6 (ss. 6.2) considered the concept of 'abandonment' in relation to surplus tissue. Abandonment has particular meaning in relation to property law, referring to items where ownership has been relinquished entirely and irrevocably; and there is no ongoing interest in what happens to the item[861]. The term 'abandonment' is sometimes used in a human tissue context, as was the case in the 1995 report by the Nuffield Council on Bioethics, and therefore required further consideration in my thesis. I drew on work by Matthews who suggests that if the principle of abandonment is truly to be applied in the context of human tissue, then ownership rights could be taken by the first person to claim possession and the person from whom the tissue originated could not claim any ongoing interest[862]. However, when we further consider this concept in a research context and within the statutory framework which is now provided for by the HT Act 2004 (which was also not in effect when the Nuffield Council on Bioethics report was published in 1995), the question of abandonment arguably becomes less relevant. This is because the HT Act 2004 regulates the storage and use of tissue for research purposes and therefore questions relating to abandonment and ownership of tissue are also likely addressed via the statutory provisions in the HT Act 2004. With this in mind, I concluded that whilst questions of tissue ownership may continue to be brought before the courts in some contexts, the HT Act 2004 provides a sufficient legislative framework for the storage and use of surplus tissue where tissue is removed during a clinically directed procedure, stored in a diagnostic archive and subsequently used for research purposes.

A key argument in my overall thesis is that there are benefits to using surplus tissue for secondary research purposes, both on an individual and a societal level. Chapter 7 (ss. 7.1 – 7.5) explored these potential benefits, suggesting that even where there is no therapeutic benefit for patients from their surplus tissue samples being used for research purposes, there may be individual benefits with regards

[861] Goold I. (2014) Abandonment and Human Tissue. In Goold I, Greasley K, Herring J, Skene L (eds.) *Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century?* (pp 125 – 156) Oxford: Hart Publishing ltd.
[862] Matthews P. The Man of Property. *Medical Law Review.* 1995 **3** 251-274

to altruism, reciprocity and solidarity[863]. This assertion is based on previously conducted empirical research and public engagement events which established that in general, people are supporting of their surplus tissue being used for research purposes because they want to help other people[864]. Moreover, in doing so they feel some benefit in being part of a community and therefore feel less alone in their experience[865]. This was particularly evident with patients who had undergone surgical resection for the diagnosis and treatment of cancer. Here patients reported feeling solidarity with others who are going through similar experiences both now and in the future, and considered the secondary research use of their resected tumour to be something which helped that 'community' and therefore something which they considered to be positive[866]. Moreover, there is potential benefit from a culture of reciprocity, particularly in the context of healthcare systems such as that provided by the UK NHS. There is evidence to suggest that patients consider the opportunity to donate surplus tissue for research purposes as a positive thing because it provides opportunity to reciprocate for the healthcare which they have received and to demonstrate gratitude to the healthcare institution[867].

This is important because demonstrating that there is individual as well as public benefit in the secondary research use of surplus tissue supports my overall argument that all surplus tissue samples should have the potential to be research samples. This is because it helps to level the balance between the protection of individual patient interests and the broader public interest claim in the use of surplus

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[863] Ipsos Mori (2019) *A Public dialogue on genomic medicine: time for a new social contract?* Available at www.ipsos.com/ipsos-mori/en-uk/public-dialogue-genomic-medicine-time-new-social-contract

[864] Lewis C, Clotworthy M, Hilton S et al. Consent for the use of Human Biological Samples for Biomedical Research: A Mixed Methods Study Exploring the UK Public's Preferences. *British Medical Journal Open*. 2013 **3**
Vermeulen E et al. A Trial of Consent Procedures for Future Research with Clinically Derived Biological Samples. *British Journal of Cancer.* 2009 **101** 1505-1512
Hamilton S et al. Consent gained from patients after breast surgery for the use of surplus tissue in research: an exploration. *Journal of Medical Ethics*. 2007 **33** 229-233
Williams A M et al. Consent to Donate Surgical Biospecimens for Research: Perceptions of People with Colorectal Cancer. *Cancer Nursing.* 2016 **39(3)** 221-227

[865] Dixon-Woods M, Cavers D, Jackson C J et al. Tissue Samples As 'Gifts' for Research: A Qualitative Study of Families and Professionals. *Medical Law International*. 2008 **9** 131-150

[866] Soto C et al. Consent to Tissue Banking for Research: Qualitative Study and Recommendations. *Archives of Diseases in Childhood*. 2012 **97** 632-636
Williams A M et al. Consent to Donate Surgical Biospecimens for Research: Perceptions of People with Colorectal Cancer. *Cancer Nursing.* 2016 **39(3)** 221-227

[867] Lewis C, Clotworthy M, Hilton S et al. Consent for the use of Human Biological Samples for Biomedical Research: A Mixed Methods Study Exploring the UK Public's Preferences. *British Medical Journal Open*. 2013 **3**

tissue for secondary research purposes. However, the benefits of acting on altruistic interests and feelings of solidarity from being part of a community with a shared experience can arguably only apply where the person has awareness that their surplus tissue may be used for such purposes. This is important because my thesis focuses on the secondary research use of surplus tissue where consent may not have been obtained, as I considered this to be an area which has the potential for the greatest overall benefit by applying regulatory approaches which better enable the use of such tissue samples. Therefore, in the absence of a requirement for consent, there must be an alternative way to achieve the benefits associated with altruism, solidarity and reciprocity by raising awareness of the value and potential research use of surplus tissue samples. This is an issue which was considered in chapter 11. Here I suggest that a consistently applied approach to the availability of surplus tissue for secondary research purposes and any consent requirements would be fairer as it would allow equal opportunities with regards to the donation of surplus tissue samples - concluding that well-publicised mechanisms to register an objection, which are simple and accessible, would best achieve the overall individual and public benefits. This will be discussed further in ss. 13.3.

Ss. 7.6 set out work in the academic literature which considers whether patients have a *duty* to participate in health-related research. The basis of arguments in favour of such a duty are routed in the benefit which we all receive, both directly as patients and indirectly as members of a community, from the generalisable knowledge gained from research which advances science and medicine. I considered previous work which suggested that where patients choose to accept healthcare which is evidence based, and therefore necessarily will have involved research in which previous persons have participated or have been the subject of, then there is a duty to reciprocate by supporting healthcare research which will benefit other patients. One argument here is that not supporting healthcare research is 'freeriding' - accepting the benefits gained from research without any commitment to reciprocate[868]. I suggested that whilst there may be no individual duty to support health-related

[868] Caplan A L. Is there a duty to serve as a subject in biomedical research? *IRB: Ethics and Human Research.* 1984 **6(5)** 1-5

research, even by those who do reap the benefits of previous research, there may however be a social imperative to ensure that healthcare infrastructures are conducive to supporting and progressing health-related research for the broader benefit of society. This is particularly relevant within the context of the UK NHS as the benefits delivered by the health service and gained by patients are bounded within a single institution[869]. With this in mind, I suggest that the regulatory approaches which are proposed by my thesis could provide an opportunity to discharge any such duty on a societal level without placing significant burdens on individuals.

Chapter 3 set out approaches to ensuring that regulation in the UK is proportionate, based on the activities being undertaken which are subject to regulation and the actual risks posed. The principle of 'better regulation' has been a focus of the UK Government since 1997 and led to the establishment of the Better Regulation Task Force (BRTF) which aimed to improve the framework of regulation in the UK[870]. Whilst there have been a number of approaches to better regulation over subsequent years, I focused on an approach referred to as 'right touch regulation'. This approach was developed by the Professional Standards Authority for Health and Social Care as a risk-based approach to regulation which considers the achievement of desired outcomes to be of equal importance to managing risks. This approach therefore promotes a more balanced approach with regards to regulation, whereby the sharing of surplus tissue samples for secondary research purposes in the public interest would be considered to be of equal importance to the protection of individual interests - which is a key aim of my thesis. Moreover, the HTA states that its strategic approach is based on right touch regulation[871]. In achieving this, the HTA aims to assess risks, be proportionate and targeted in its approach to

Harris J. Scientific Research is a Moral Duty. *Journal of Medical Ethics*. 2005 **31(4)** 242-248

[869] Johns S. (2009) Is there an obligation to participate in medical research? In Corrigan O, McMillan, Liddel K, Richards M, Weijer C (eds.) *The Limits of Consent: A Socio-Ethical Approach to Human Subject Research in Medicine* (pp 115 – 132) Oxford: Oxford University Press.

[870] *Parliament. Chapter 8: Improving the Framework of Regulation* (2004) Available at publications.parliament.uk/pa/ld200304/ldselect/ldconst/68/6810.htm

[871] *Human Tissue Authority. Our Strategic Approach* (2019) Available at archive.hta.gov.uk/our-strategic-approach-0

regulation so that it uses the minimum intervention necessary to achieve compliance and to take the role of professional bodies and other regulators into account[872].

The right touch regulation strategic approach of the HTA, which was set out in the HTA strategy 2019-22[873] , was discussed in more detail in chapter 12. Here I argued that implication in the HTA code of practice on research, that a diagnostic archive may cease to be a purely diagnostic archive where it provides tissue samples for secondary research use on a regular basis or where there are developed governance or decision making structures for applying for tissue samples, was not in keeping with the principles of right touch regulation. This was based on the potential for unintended consequences due to the ambiguous implication that a diagnostic archive may also be functioning as a research tissue bank and therefore should be under the authority of an HTA research licence - where this is not *necessarily* required for such activities to be lawful under the HT Act 2004. First, the potential for avoidance by diagnostic archives of providing surplus tissue samples for research use for fear of falling foul of legislative sanctions. Second, a potential consequence of over regulation due to diagnostic archives inferring a requirement to obtain an HTA research licence where this is not *necessarily* required under the HT Act 2004.

I will now go on to provide more focused conclusions with regards to the two key arguments which formed the basis of my thesis. First, that all surplus tissue samples should have the potential to be research samples and second that individual patient interests should be balanced with public interest claims in health research which uses surplus tissue samples, rather than the balance being tipped too far towards individual patient interests. My thesis aims to establish regulatory approaches which if implemented in practice, could be conducive to all surplus tissue samples having the potential to be research samples, whilst also safeguarding individual patient interests. Each of the articles within my thesis establish and propose regulatory approaches which aim to better facilitate the availability and

[872] *Human Tissue Authority. Our Strategic Approach* (2019) Available at archive.hta.gov.uk/our-strategic-approach-0
[873] *Ibid*

use of surplus tissue for secondary research purposes whilst also protecting individual patient interests. In this section I bring together the key arguments which have been made throughout my thesis and set out how these approaches support my broader thesis aim and add to the existing academic literature.

13.2. Accessing Surplus Tissue and Protecting Privacy Interests

In chapter 10 I argue that a 'safeguarding' approach when linking surplus tissue with associated patient information could better enable the linking of surplus tissue with relevant patient information for secondary research purposes in the absence of consent - whilst also protecting patient interests. My rationale for addressing this issue as part of my thesis is that the real research value in surplus tissue is where samples are linked with associated information about the person from whom the tissue was removed, the tissue alone has limited research value[874]. Therefore, establishing regulatory approaches to increase the availability of surplus tissue held in diagnostic archives for secondary research purposes was not itself sufficient to maximise the research value of this potentially valuable research resource.

In addition to enabling the availability of surplus tissue samples, I also wanted to ensure that the regulatory approaches which I established through my thesis were conducive to linking surplus tissue with associated patient information for secondary research purposes. A golden thread which runs throughout my thesis is balancing the public interest in facilitating health research with protecting individual patient interests. With this in mind, chapter 10 proposes a regulatory approach which views the linking of surplus tissue and associated patient information for secondary research purposes from a more enabling perspective. This approach takes the position that the secondary research use of surplus tissue and relevant patient information should not be avoided *because* consent was not

[874] Regidor E. The use of Personal Data from Medical Records and Biological Material: Ethical Perspectives and the Basis for Legal Restrictions in Health Research. *Social Science & Medicine.* 2004 **59** 1975-1984

requested or recorded, but rather these valuable resources *should* be used for such purposes with appropriate safeguards to protect individual patient interests.

The basis for this argument is that data protection legislation provides for the secondary research use of patient information, under legal bases other than consent, where there are appropriate safeguards to protect the rights and freedoms of the patient. Chapter 10 suggests that provision in the HT Act 2004 for surplus tissue to be used in the absence of consent for ethically approved research, in 'circumstances such that the person carrying it out is not in possession, and not likely to come into possession, of information from which the person whose body the material has come can be identified'[875], was based on wording in the DPA 1998, which was in force when the HT Act 2004 was enacted. The wording in the DPA 1998, which defines personal data as data from which a person can be identified….. 'from those data and other information which is in the possession of, or is likely to come into the possession of, the data controller'[876]. However, additional provision in the DPA 1998 with regards to applying appropriate safeguards to protect patient interests was not wholly reflected in the HT Act 2004. This arguably resulted in a more restrictive approach to the secondary research use of patient information which is linked with surplus tissue for secondary research purposes under the HT Act 2004.

This provision in the DPA 1998 was often taken to be synonymous with anonymisation, confirmed by the ICO as a misinterpretation[877], and consequently appears to have been reflected in the HT Act 2004 as a requirement for 'consent or anonymise'. Data protection regulations (the DPA 1998 has since been repealed and replaced with the GDPR and DPA 2018) are explicit that personal data can be processed for secondary research purposes under legal bases other than consent[878], where there are

[875] *Human Tissue Act 2004.* Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 1 s 1 ss 9 (b)
[876] *Data protection Act 1998.* Available at www.legislation.gov.uk/ukpga/1998/29/contents Part 1 s 1 ss (1) – Personal data
[877] Clark S and Weale A (2011) *Information Governance in Health. Research Report. University College London*

[878] The UK position is that processing of healthcare data for secondary research purposes in the NHS should be: Article 6 (e) processing is necessary for the performance of a task carried out in the public interest or in the exercise of official authority vested in the controller and Article 9 section 2 (h) processing is necessary for the

'appropriate safeguards' in place to protect the rights and freedoms of the data subject. However, the HT Act 2004 does not include explicit provision for 'safeguarding' of personal data and therefore a blanket requirement of 'non-identifiability' is applied. In chapter 10 I argue that applying a 'safeguarding' approach to protecting the identity of patients when linking surplus tissue with associated patient information for secondary research purposes, could be more enabling of such activities without necessarily lessening the privacy protection provided by a 'consent or anonymise' approach.

In making this claim, I refer to a report published by the Academy of Medical Sciences in 2006 which referred to the use of safeguards other than anonymisation to ensure data security[879]. This report acknowledged that health research will often require access to identifiable information at some stage. Moreover, anonymisation is often not an absolute process as there are degrees of anonymisation which depend on the context of any particular situation. This may involve retaining a link to a person's identity via a unique code (pseudonymisation) which means that the data are identifiable to those with legitimate access but 'anonymised' to those undertaking research using the data[880]. However, the report further suggested that a requirement for pseudonymisation with a requirement for the researcher to not have access to the key offers minimal security advantage over coded identifiable data sets which are maintained under strict data security policies. With this in mind, chapter 10 proposes an approach of 'share and protect' as an alternative to an approach of 'consent or anonymise'. Here I suggest that viewing the secondary research use of surplus tissue linked with associated patient information from the perspective of 'share and protect, *could* be more enabling of important research activities.

purposes of preventative or occupational medicine, for the assessment of the working capacity of the employee, medical diagnosis, the provision of health or social care or treatment or the management of health or social care systems and services on the basis of Union or Member State law or pursuant to contract with health professionals and subject to the condition and safeguards referred to in paragraph 3.

[879] Academy of Medical Sciences (2006) *Personal Data for Public Good: Using Health Information in Medical Research.* Available at acmedsci.ac.uk/policy/policy-projects/personal-data

[880] Lowrance W. (2012) *Privacy, Confidentiality and Health Research.* Cambridge: Cambridge University Press

In making the claim that a 'share and protect' approach could be applied to better facilitate the use of surplus tissue linked with associated patient information, I suggested that this different perspective does not necessarily lessen the protection which would be provided for under a 'consent or anonymise' approach. This is because there would continue to be a requirement for appropriate safeguards to be applied to personal data when being processed for secondary research purposes. However, viewing the situation via the perspective of 'share and protect' approaches the situation from a more enabling positionof, how can surplus tissue linked with associated patient information be used for secondary research purposes in a way which also protects the privacy interests of patients. It should be clear that the 'share and protect' approach which is proposed in chapter 10 is not intended to be an *alternative* to obtaining consent for the secondary research use of surplus tissue and associated patient information. It does however acknowledge that tissue which is stored in a diagnostic archive may have significant research value and an absence of consent should not in itself be a reason not to utilise this valuable resource and to obtain the maximum value from the tissue samples - by linking with associated patient information where appropriate safeguards can be applied which sufficiently protect patient interests.

Chapter 10 suggests that the current application of the requirement in the HT Act 2004, for the person undertaking the research to not be in possession of information which *could* identify the person from whom the tissue was removed, is potentially too restrictive and does not sufficiently balance the public interest in health research with the protection of individual patient interests. This is because it does not consider broader safeguards which could be applied to protect patient privacy interests and does not consider the information *necessary* to achieve the research aim. In applying the 'consent or anonymise' approach it only considers two key questions. First, is there consent for research use? and second, will the researcher be in possession of information which *could* identify the person? If the answer to the first question is 'no', there is no consent in place, then any answer other than 'no' to the second question would mean that the research cannot proceed. There is no consideration of the potential for public benefit, what the research involves and what data would be required to achieve

the intended aim or what other appropriate safeguards could be in place to protect the interests of the individuals.

My thesis aims to propose a more enabling approach to linking surplus tissue with associated patient information for secondary research purposes in the absence of consent, an issue which I primarily address on a conceptual level. However, effectively implementing this regulatory approach in practice would additionally require a clear identity safeguarding framework to support data controllers and diagnostic archives to comply with expectations for the safeguarding the rights and freedoms of data subjects when linking surplus tissue samples with associated patient information. The GDPR is not explicit with regards to safeguards - referring to security measures[881], encryption and pseudonymisation[882] and technical and organisational measures, in particular to respect the principle of data minimisation[883]. The Health Research Authority does provide some technical guidance with regards to appropriate safeguards on its website[884]. Here it states that appropriate safeguards require consideration of whether the research will likely cause substantial damage or distress, ethical approval and ensuring that the research use is in the public interest[885]. Moreover, it provides further information about the technical and organisational measures which would be considered to comply with provisions relating to safeguarding in the GDPR. Here it states that suitable measures would include IT security and data protection policies, compliance with the 'Data Security and Protection Toolkit'[886] and organisational codes of practice or guidance which make it clear that the use of identifiable data is only used where necessary.

[881] General Data Protection Regulation (2018) Available at eur-lex.europa.eu/eli/reg/2016/679/oj recital 94
[882] *Ibid* Article 4 ss. 4 (e)
[883] *Ibid* Article 89 s. 1
[884] *Health Research Authority. Safeguards* (2018) Available at www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/data-protection-and-information-governance/gdpr-detailed-guidance/safeguards/
[885] *Ibid*
[886] *NHS Digital. Data Security and Protection Tools* (2018) Available at digital.nhs.uk/data-and-information/looking-after-information/data-security-and-information-governance/data-security-and-protection-toolkit

However, to effectively implement an identity safeguarding approach to the linking of surplus tissue and associated patient information in the absence of consent, there needs to be explicit reference to these safeguarding approaches also applying to data linked with tissue. In the absence of clear and authoritative guidance, the question of whether an identity safeguarding approach would be considered to comply with provision in the HT Act 2004 for the use of surplus tissue samples for secondary research purposes in the absence of consent remains unclear. Moreover, as I suggest in chapter 10, compliance with data protection legislation does not in itself mean that processing of patient data is lawful.

Health data is also considered to be 'confidential' data and is subject to the common law duty of confidentiality. The main legal basis under which confidential data can be processed is consent. Therefore, linking surplus tissue samples with associated patient information for secondary research purposes in the absence of consent may require either 'anonymisation' or an alternative legal basis to comply with the common law duty of confidentiality[887]. The 'Confidentiality: NHS Code of Practice'[888] uses the term 'anonymisation' in this context and therefore *prima facie* an identity safeguarding approach would likely not meet this standard. However, this document further states that, 'Where the purpose served is not to provide healthcare to patients and is not to satisfy a legal obligation, disclosure should be tested for appropriateness and necessity, with the aim of minimising the identifiable information disclosed and anonymising information *wherever practical*[889]. Moreover, this document also refers to 'privacy enhancing measures and anonymisation techniques', which may be considered to be met by technical and organisational measures such as IT security and data protection policies. However, as I suggest in chapter 10, the legal basis for a duty of confidentiality and all circumstances under which it is breached remain unclear, particularly in a research context as there is no clear legal precedent. In the absence of such a test case, a legal basis other than consent to set

[887] Department of Health (2003) *Confidentiality: NHS Code of Practice.* Available at www.gov.uk/government/publications/confidentiality-nhs-code-of-practice
[888] *Ibid*
[889] *Ibid* pg. 15

aside the common law duty, provided under section 251 of the NHS Act 2006[890], may be required where obtaining consent would not be practical.

To effectively implement a safeguarding approach when linking surplus tissue with associated patient information in the absence of consent, there would need to be clear and authoritative guidance, endorsed by regulatory bodies such as the HTA and HRA, to provide assurance to those undertaking relevant research activities. In the absence of such guidance, there is risk that key actors, such as data controllers, pathologists, researchers and ethics committees, will continue with inconsistent practices. Furthermore, in the absence of clear authoritative guidance, there continues to be a risk that such actors will 'err on the side of caution' and therefore the patient and public interest balance will continue to be tipped too far towards protecting individual patient interests, potentially to the detriment of the broader public interest. A survey undertaken by onCore UK in 2009 found that a requirement for clear and authoritative guidance, which is endorsed by regulatory bodies, was overwhelmingly stated as a key factor which was required to effectively achieve confidence in the secondary research use of tissue[891]. The need for authoritative guidance to support the implementation of the regulatory approaches proposed in my thesis is something that I will return to as an important requirement throughout my thesis conclusion.

The 'share and protect' approach which I propose in chapter 10 adds to the academic literature because it proposes a regulatory approach which is potentially more enabling of linking associated patient information with surplus tissue, where consent for secondary research purposes was not obtained, whilst also safeguarding individual patient interests. This is an original approach because it acknowledges the complexity of identifiability, which runs a spectrum from fully identifiable to fully anonymous and can change when combined with other information[892], as well as practical challenges

[890] *National Health Service Act 2006.* Available at www.legislation.gov.uk/ukpga/2006/41/contents/enacted s 251

[891] onCore UK (2009) *The Effect of Regulation and Governance on Research Led by Pathologists or Involving Pathology in the UK.* Available at www.pathsoc.org/news/30/oncore_uk_report_effect_of_regulation_governance_survey

[892] Lowrance W. (2012) *Privacy, Confidentiality and Health Research.* Cambridge: Cambridge University Press

with obtaining precautionary consent on a large scale[893]. This enabling approach therefore provides a practical solution to linking surplus tissue and associated patient information for secondary research purposes in the absence of consent.

13.3 A Consistent Approach to Enabling the Secondary Research use of Surplus Tissue Samples

Chapter 11 highlights inconsistency with regards to the availability of surplus tissue for secondary research purposes and requirements for consent to be provided for the sharing of such tissue across different NHS organisations - using the policies of 12 NHS organisations in England as a case study to demonstrate this point. I argue that there should be a consistent approach applied across all NHS organisation as this would be the fairest approach for individual patients and would also best achieve public interest claims associated with the secondary research use of surplus tissue. This claim was based on the different approaches implemented by different NHS organisation affording different patients different opportunities associated with the donation of surplus tissue for secondary research purposes - without being based on any reasoned decision-making process or valid ethical or legal principle of distribution[894].

This inconsistent approach therefore treats equal moral agents unequally without any justified moral reasoning. Moreover, in highlighting the inconsistency across NHS organisations I further suggest that public interest claims cannot be fully realised. This claim is based on the approach in the HT Act 2004 of allowing research use of surplus tissue where consent was not obtained, and the good practice standard of requesting consent which is set out in the HTA code of practice on consent[895], arguably both having a public interest claim. However, I suggested that in reality, rather than these *individual*

[893] Lawrence E et al. The Barriers and Motivators to Using Human Tissue for Research: The Views of UK-Based Biomedical Researchers. *Biopreservation and Biobanking*. 2020 **18(4)** 266-273
[894] Beauchamp TL and Childress JF (2013) *Principles of Biomedical Ethics: Seventh Edition*. New York: Oxford University Press
[895] Human Tissue Authority (2020) HTA Code A: Guiding Principles and the Fundamental Principle of Consent. Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20A.pdf

approaches promoting public interest, by facilitating the research use of surplus tissue (by not requiring consent) or by securing and maintaining trust (by requiring consent), this confused and disparate position fails the public interest claim on both counts because it is inconsistently applied across NHS organisations.

This claim was based on different approaches being implemented in different NHS organisations potentially bringing into question the sufficiency of approaches being implemented. For example, some NHS organisations have a policy which permits the secondary research use of surplus tissue samples in the absence of consent while others require consent to be in place for surplus samples to be used for such purposes. This therefore has the potential for the sufficiency of reliance on safeguards, such as ethical review and privacy protection, to be questioned where consent is not required - due to consent being a requirement in other NHS organisations. With this in mind, chapter 11 argues that an approach which is consistently applied across all NHS organisations would be fairer and would better balance individual patient interests with broader public interest claims in health research which uses surplus tissue.

I have not identified any other work in the academic literature which has suggested that the lack of consistency across different NHS organisations results in an unfair distribution of opportunities to donate surplus tissue for secondary research purposes. In identifying barriers to accessing surplus tissue, Lawrence et al[896] highlighted some variation across different organisations which provide tissue samples for secondary research purposes. However, this work primarily focused on challenges within existing infrastructures rather than a focus on the inconsistency of approach across different organisations and the potential consequence of such inconsistencies.

In suggesting that there should be a consistent approach which is applied across all NHS organisations, chapter 11 proposes that the approach which would best balance individual patient interests with the

[896] Lawrence E et al. The Barriers and Motivators to Using Human Tissue for Research: The Views of UK-Based Biomedical Researchers. *Biopreservation and Biobanking*. 2020 **18(4)** 266-273

broader public interest in health research using surplus tissue samples would be for samples to be available where there is no evidence that the patient has objected. In referring to a regulatory approach which enables the secondary research use of surplus tissue where there is no evidence of objection, I do not consider this to be a 'consent model', as the HT Act 2004 is permissive of such activities in the absence of consent and referring to consent in this context risks further blurring lines between 'legal requirement' and 'good practice'. Moreover, it should be clear that the secondary research use in this context must also be subject to safeguards provided under the HT Act 2004. These safeguards are for the research to be ethically approved and the research to be carried out in circumstances such that the person undertaking it is not in possession of information which could identify the person from whom the tissue was removed (or potentially subject to appropriate technical and organisational safeguards to protect patient privacy as proposed in chapter 10). However, whilst an opportunity to object to surplus tissue being used for secondary research purposes, as proposed in chapter 11, is not considered to be a 'consent model', it does aim to provide some of the components of consent - from an ethical rather than a legal perspective. This approach aims to allow some autonomous choice, to choose to donate surplus tissue and therefore to act on altruistic interests by not objecting or to choose not to donate by registering an objection. Moreover, such an approach could supplement the reasonableness test proposed by the Medical Research Council[897], by allowing tissue holders to confirm whether patients have registered an objection, thereby strengthening the reasonableness test with regards to whether individuals would likely refuse their permission for the secondary research use of their surplus tissue samples.

In proposing this approach, I further suggest that there should be a mechanism via which patients can record their objection which is well-publicised, simple and accessible. This is important to ensure that an absence of objection reflects actual choice rather than a mere lack of awareness or an inability for

[897] National Cancer Research Institute (2009) *Samples and Data for Research: Template for Access Policy Development.* Available at www.ukri.org/publications/human-tissue-and-biological-samples-for-use-in-research/

preferences to be expressed and recorded. Moreover, raising awareness of the potential research value of surplus tissue would mean that patients have the opportunity to act on their altruistic interests by knowingly allowing their surplus tissue to be used for secondary research purposes. However, ensuring awareness is not without its challenges and achieving true autonomous choice can be problematic.

Problems with ensuring awareness exist on a practical and logistical level and would require the investment of potentially significant resources to be effective. Comparison may be drawn with the introduction of the National Data Opt-Out, enabling patients to opt out of their data being used for research and planning purposes, which was initially introduced in England in 2018, with full implementation now delayed until 31 March 2022[898]. During discussion in the House of Lords, Lord Bethel, the (then) Parliamentary Under-Secretary of State for the Department of Health and Social Care, stated that the delayed roll out was to ensure that the opt-out system was fit for purpose and to ensure there had been an effective campaign to raise patient awareness[899]. The importance of ensuring that there are strong foundations which instil public trust and social acceptance is therefore evident in the approach being taken by the Government to this data sharing initiative.

The roll out of the National Data Opt-Out initiative is taking a cautious approach, ensuring that the mistakes highlighted by the previous care.data initiative are not repeated. The care.data initiative had a legal bases for the secondary use of primary care health record. However, even where the secondary use of patient data in an anonymised format may be lawful, care.data highlighted an additional requirement to ensure not only public awareness, but also public acceptance[900]. Ensuring that there is a 'social licence' supporting the secondary research use of surplus tissue may therefore be more enabling than an approach which relies purely on there being a lawful basis. With this in mind, whilst

[898] *NHS. Sharing your Health Records* (2018) Available at www.nhs.uk/using-the-nhs/about-the-nhs/sharing-your-health-records/

[899] Lord Bethell (2021) '*NHS Digital: Primary Care Medical Records'* Hansard: House of Lords Debates 8 June c. 1320

[900] Carter P, Laurie G T and Dixon-Woods M. The social licence for research: why care.data ran into trouble. *Journal of Medical Ethics*. 2015 **41** 404-409

an approach which permits the secondary research use of surplus tissue where there is no evidence of objection may be lawful, it would also be important to ensure that there is public awareness and acceptance, so that such activities are what patients expect and accept. Therefore, the regulatory approach which chapter 11 argues should be applied consistently across NHS organisation should be supported by mechanisms to register an objection which are well-publicised, simple and accessible.

In proposing that this approach should be supported by mechanisms via which an objection can be recorded that is well-publicised, I suggest that as well as promoting individual choice this approach could impact on the availability of surplus tissue for secondary research purposes more broadly than tissue samples which are stored within a diagnostic archive. My thesis aims for *all* surplus tissue samples to have the potential to be research samples, primarily focusing on enabling access to tissue samples which are stored within diagnostic archives. However, for all surplus tissue samples to be potential research samples then it is also necessary to facilitate the availability of tissue which is removed during a clinically directed procedure but does not necessarily go to the pathology department for diagnostic testing. Moreover, recognising the potential research value of surplus tissue samples prospectively rather than retrospectively provides the greatest opportunity to obtain consent from the patient for any surplus tissue to be transferred to a research tissue bank and therefore stored in a way which maximises the research value. This is because samples which are stored with a future research purpose from the outset so are likely to be a better quality for research purposes, are more likely to be linked with associated data with the consent of the patient and research tissue banks are more likely to be where researchers look when needing tissue samples for research purposes. Therefore, a regulatory approach which normalises the secondary research use of surplus tissue samples on a broader scale may additionally support more established research tissue bank practices.

When studying the views of children diagnosed with cancer, along with the views of their parents, in relation to tissue banking, Soto et al[901] identified that prior awareness and understanding may better facilitate discussions with patients and parents at what can be a very difficult time. With this in mind, a well-publicised mechanism via which patients can register an objection to their surplus tissue samples being used for secondary research purposes could also raise awareness of the value of surplus tissue and the importance of researchers being able to access such tissue samples for use in health-related research. Raising awareness on a normative level could help to normalise the secondary research use of surplus tissue samples, making approaching patients with regards to more specific biobanking practices easier for both patients and professionals due to prior awareness of the research value in surplus tissue. This may in turn have the potential to better facilitate *all* surplus tissue samples being potential research samples. This is an area which my thesis was unable to explore in more detail, due to the focus being the availability of surplus tissue samples stored in diagnostic archives, but would be an area which would benefit from further work to achieve the overall aim of all surplus tissue samples having the potential to be research samples.

In chapter 4 (ss. 4.3.4) I set out discussions in the academic literature with regards to the use of electronic platforms to record preferences with regards to the secondary research use of surplus tissue samples. Proponent of 'dynamic'[902] and 'meta'[903] approaches to consent, which use technology to record and update consent preferences, suggest that there is potential benefit in using electronic platforms to record patient preferences. This is because they provide greater flexibility for patients, as well as those needing to confirm a patient's recorded preferences when deciding whether to share tissue samples for secondary research purposes. Previous work undertaken by Shoaibi et al[904]

[901] Soto C et al. Consent to Tissue Banking for Research: Qualitative Study and Recommendations. *Archives of Diseases in Childhood.* 2012 **97** 632-636
[902] Kaye J et al. Dynamic Consent: A Patient Interface for Twenty-First Century Research Networks. European *Journal of Human Genetics.* 2015 **23** 141-146
[903] Ploug T and Holm S. Going Beyond the False Dichotomy of Broad or Specific Consent: A Meta-Perspective on Participant Choice in Research Using Human Tissue. *The American Journal of Bioethics*. 2015 **15(9)** 44-46
[904] Shoaibi A et al. The Association Between Method of Solicitation and Patient Permissions for use of Surplus Tissue and Contact for Future Research. *JAMIA Open* 2018 **1(2)** 195-201

exploring alternatives to paper-based consent recording indicated that more flexible approaches do have the potential to add value, although this may require varied approaches to meet the varying situations and requirements which exist. For example, an approach which includes both electronic and 'in person' opportunities to express preferences with regards to the secondary research use of surplus tissue would likely best meet the needs of the largest number of patients. Moreover, in ss. 4.3.4.3 I referred to the NHS App having the potential to be one mechanism via which patients could record an objection to the secondary research use of their surplus tissue. Whilst the NHS App is not new (it has been publicly available since 31 December 2018[905]), there has been a significant increase in the number of people who have downloaded the NHS App in recent months, due to the NHS App also functioning as a 'vaccination passport' providing evidence of vaccination against SARS-CoV-2 (COVID 19). Between 31 January 2020 and 24 August 2021, the number of signed up users of the NHS App who have access to the full range of services increased by 11,390,820 (from 131,321 to 11,522,141 signed up users)[906], and therefore now has the potential to reach a larger number of patients if used as a mechanism to record preferences with regards to the secondary research use of surplus tissue.

Whilst the NHS App could be one potential mechanism via which patients can record an objection to the secondary research use of their surplus tissue, challenges associated with the 'digital divide'[907] would likely mean that achieving the aim of mechanisms being simple and easy to access would require additional approaches, such as opportunities to update patient records with an objection when accessing healthcare services. In proposing approaches which enable patients to have sufficient awareness that surplus tissue can be used for secondary research purposes and an opportunity to object to their tissue being used for such purposes, I suggest that this could be more enabling of all surplus tissue samples having the potential to be research samples. This is notwithstanding the fact

[905] *NHS England. News* (2019) Available at www.england.nhs.uk/2019/01/nhs-app-begins-public-rollout/
[906] Data provided by NHS Digital in response to a freedom of information request
[907] Steinsbekk K S, Myskja B K and Solberg B. Broad Consent Versus Dynamic Consent in Biobank Research: Is Passive Participation an Ethical Problem? *European Journal of Human Genetics*. 2013 **21** 897-902

that providing such mechanisms will inevitably lead to some patients objecting to their surplus tissue samples being used for such purposes.

Chapter 11 proposed a regulatory approach whereby surplus tissue samples may be used for secondary research purposes where there is no evidence of objection, supported by mechanisms via which an objection could be recorded which are well-publicised, simple and accessible. However, the implementation of such a regulatory approach in practice would not be without challenges. The effective implementation of such an initiative would need to be supported by clear authoritative guidance from the HTA to ensure confidence from tissue holder and researchers. Moreover, it would also require a culture change within the NHS to be more openly accepting of surplus tissue being used for secondary research purposes without explicit consent. However, this regulatory approach would also need sufficient public engagement to ensure that surplus tissue samples are being used for purposes that patients expect and accept, a cautious approach akin to that being taken with the roll out of the National Data Opt-Out initiative would likely be prudent.

13.4 Proportionate Regulation When Diagnostic Archives Provide Tissue for Research

In chapter 12 I suggest there is a regulatory grey area with regards to the requirements for an HTA research licence where a diagnostic archive provides surplus tissue samples for use in health research. The HTA code of practice on research is explicit that a diagnostic archive is considered to also be functioning as a research tissue bank where it '…..invites applications for the release of samples, and/or in any way advertises the archive as a research resource'[908]. However, the HTA code of practice on research is less clear about whether a diagnostic archive which does not advertise itself as a research resource but does provides surplus tissue samples for use in health research would be considered to also be functioning as a research tissue bank. A clear distinction is important because

[908] Human Tissue Authority (2017) *HTA Code E: Research.* Available at content.hta.gov.uk/sites/default/files/2020-11/Code%20E.pdf paragraph 95

where there is a clear intention to function as a research tissue bank, this must be under the authority of an HTA research licence for such activities to be lawful under the HT Act 2004.

In chapter 12 I argue that the guidance issued by the HTA in the code of practice on research is not sufficiently clear on the matter and risks two potential adverse consequences. First, it risks avoidance of sharing tissue samples for secondary research purposes for fear of falling foul of legislative sanctions - the penalty under the HT Act 2004 for undertaking licensable activities without a license is imprisonment of up to 3 years, a fine or both[909]. Second, it risks over regulation due to establishments inferring that an HTA research licence is required for the sharing of tissue samples for secondary research use where this is not *necessarily* required for such activities to be lawful under the HT Act 2004. For each of these potential consequences, either avoidance of using surplus tissue which is stored in a diagnostic archive or over regulation, the balance between protecting individual patient interests and broader societal interests is not effectively achieved. However, by viewing a diagnostic archive becoming an establishment which also functions as a research tissue bank as a transitionary process which has an in-between state (where it is not a purely diagnostic archive but is not yet also functioning as a research tissue bank), then it is possible to apply a regulatory approach which is proportionate to the actual activities being undertaken. Moreover, a more proportionate regulatory approach which better facilitates the sharing of surplus tissue samples whilst also applying regulatory safeguards, such as ethical approval, tissue access policies and Material Transfer Agreements, arguably better balances the interests of individual patients and broader societal interests, a key aim of my overall thesis.

Chapter 12 proposes a regulatory approach which is more enabling of the secondary research use of surplus tissue whilst also safeguarding individual patients interest, by viewing the transitionary process from a purely diagnostic archive to also functioning as a research tissue bank being supported by 'regulatory stewards' passing the 'regulatory mantle'. The concept of regulatory stewardship was

[909] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 2 s 25

initially posited by Laurie et al[910] and recognises that different regulatory bodies have different roles to deliver research regulation within a broader regulatory framework. Furthermore, Dove[911] refers to the concept of passing the 'regulatory mantle' in the context of different regulatory stewards which hold different spaces within a broader regulatory context. This metaphor of passing the 'regulatory mantle' helps to visualise the importance of each regulatory body fulfilling its individual responsibilities whilst also working collaboratively with other regulatory bodies through a broad transitional process[912].

Chapter 12 applies the concept of regulatory stewards passing the regulatory mantle in the context of surplus tissue being accessed from diagnostic archives for secondary research purposes, transitioning from a purely diagnostic archive to also functioning as a research tissue bank. Where a diagnostic archive provides tissue samples on a research project basis in the absence of consent, this is regulated under provision in the HT Act 2004 which requires research projects to be ethically approved and for the research to be carried out in circumstances such that the person undertaking the research is not in possession of information which could identify the person from whom the tissue was removed[913]. Moreover, individual research projects which are being undertaken in the NHS are assessed and must comply with established NHS governance standards for the research to start[914]. I refer to this as a 'research project' regulatory model. A 'research project' regulatory model where diagnostic archives provide surplus tissue samples for secondary research use is facilitative of tissue sharing by being permissive of such activities, acknowledging that consent for secondary research use of surplus tissue is not always requested along with consent for the tissue removing procedure, whilst also protecting individual patient interests.

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[910] Laurie G et al. Charting Regulatory Stewardship in Health Research: Making the Invisible Visible. *Cambridge Quarterly of Healthcare Ethics* 2018 **27(2)** 333-347
[911] Dove E. (2020) *Regulatory Stewardship in Health Research.* Cheltenham: Edward Elgar Publishing Limited
[912] Laurie G et al. Charting Regulatory Stewardship in Health Research: Making the Invisible Visible. *Cambridge Quarterly of Healthcare Ethics* 2018 **27(2)** 333-347
[913] *Human Tissue Act 2004*. Available at www.legislation.gov.uk/ukpga/2004/30/contents Part 1 s 1 ss 9
[914] *Health Research Authority. HRA Approval* (2021) Available at www.hra.nhs.uk/approvals-amendments/what-approvals-do-i-need/hra-approval/

However, when a diagnostic archive has transitioned into the final state of also functioning as a research tissue bank, because it invites applications to access tissue samples or advertises itself as a research resource, this is regulated under the HT Act 2004 via a requirement for the storage or use of tissue for research purposes to be under the authority of an HTA research licence. The regulatory mantle therefore passes from 'research project' regulatory stewards (for example RECs and the HRA – in England) to 'establishment' regulatory stewards (for example the HTA). This is because the transitionary process through the in-between state of neither purely a diagnostic archive but not yet also functioning as a research tissue bank has moved into the final state, and therefore the regulatory focus transitions from the *activity* - i.e. research project, to the *establishment.* With this in mind, I suggest that an approach where the regulatory mantle is passed from a 'research project' regulatory model to an establishment 'regulatory model' better balances the broader societal interests, associated with facilitating the secondary research use of surplus tissue, with individual patient interests.

To effectively achieve this outcome, I suggest the HTA code of practice on research should be revised to remove any ambiguity that an HTA research licence may be required where a diagnostic archive provides surplus tissue samples for secondary research purpose but is not yet also functioning as a research tissue bank. The definition of when a diagnostic archive is also functioning as a research tissue bank should remain as inviting applications to access tissue samples or advertising itself as a research resource, as this is an unequivocal intention to provide tissue for health research purposes. My rationale is that by the HTA providing authoritative clarity on the matter via the code of practice on research, this would lessen the risk of secondary research using surplus tissue being stymied unnecessarily for fear of falling foul of legislative sanctions. Moreover, this approach would be more proportionate to the activities being undertaken and therefore avoids the risk of unnecessary regulatory duplication.

I have not identified other work in the academic literature which has challenged the approach set out by the HTA in the code of practice on research with regards to diagnostic archives providing tissue samples for secondary research purposes. There is however evidence to suggest that the implied need for a research licence, purely on the basis of samples being released from a diagnostic archive on a regular basis, is being inferred as a legal requirement and therefore an over application of regulatory requirements does currently happen in practice. In relation to barriers to the release of tissue samples for research purposes, Macklin et al make the following assertion, *'*If tissue is released from a diagnostic archive on a regular basis, it is considered a Research Tissue Bank and requires a licence'[915]*.* My thesis therefore fills this gap in the academic literature by proposing a regulatory approach which is clear and unambiguous with regards to when a diagnostic archive is also functioning as a research tissue bank and should therefore be under the authority of an HTA research licence.

13.5 An Overall More Facilitative Regulatory Approach

Each of the regulatory approaches which I have proposed throughout my thesis aim to better enable the secondary research use of surplus tissue which is stored in a diagnostic archive whilst also protecting individual patient interests. However, for this broader regulatory framework to be effective in achieving this overall aim, there needs to be clear and authoritative guidance from regulatory bodies such as the HTA and HRA which provides assurance to tissue holders and researchers that such activities are lawful - where appropriate safeguards are in place. This is important to ensure confidence that such activities will not be met with legislative sanctions. As suggested in the Nuffield Council on Bioethics Report – Human Bodies: Donation for Medicine and Research,

> ''Regulation' may prohibit, require or permit particular actions. Where regulation is permissive, its actual impact is likely to depend on the extent to which the permitted activity

[915] Macklin P et al. Barriers to the Release of Human Tissue for Clinical Trials in the UK: A National Survey of Cellular Pathology Laboratories on Behalf of the National Cancer Research Institute's Molecular Pathology (CM-Path) Initiative. *Journal of Clinical Pathology.* 2019 **72** 52-57

is supported, encouraged or, on the contrary, discouraged – and hence will be strongly influenced by the approach taken by relevant organisations.'[916]

Moreover, there needs to be clear information for patients to ensure that they are aware of the potential research value of surplus tissue samples, the possibility that their surplus tissue samples may be used for secondary research purposes and the safeguards which are in place to protect their interests. This is important to ensure that surplus tissue samples are being used for purposes which patients expect and accept, and therefore that there is a social licence for such practices.

Whilst arguably reactions to activities of tissue retention for research and teaching at Bristol Royal Infirmary and Alder Hey were perpetuated by a sensationalist media and politicians[917], any repetition of such a paternalistic and autocratic approach has the potential to limit rather than facilitate the secondary research use of surplus tissue. Moreover, it is important to learn from the reaction to the care.data initiative which saw over a million patients opt out from their primary care data being used for secondary purposes, including research. The failure of this initiative has been blamed on a lack of social engagement and 'social licence' which meant that patients lacked trust in public authorities. The more cautious approach ensuring an effective infrastructure and public awareness which is now being taken with the implementation of the National Data Opt-out scheme may be more successful. However, the full effect is yet to be seen due to the full roll out currently being scheduled for 31 March 2022. In learning from the past, it is therefore important to ensure that the regulatory approaches which I propose in my thesis are accepted by patients and provide mechanisms to object which are well-publicised, simple and accessible - to ensure that there is a genuine option for patients to object. Moreover, the practical regulatory framework which my thesis proposes would likely need to be supported by a broader culture change throughout the NHS to be truly effective in achieving the aim of enabling all surplus tissue samples to be potential research samples.

[916] Nuffield Council on Bioethics (2011) *Human Bodies: Donation for Medicine and Research*. Available at www.nuffieldbioethics.org/publications/human-bodies-donation-for-medicine-and-research paragraph 5
[917] Gillott J. (2014) *Bioscience, Governance and Politics*. Basingstoke: PALGRAVE MACMILLAN

Such a culture change would need to permeate throughout the NHS to ensure that all relevant people have awareness and confidence in the secondary research use of surplus tissue. Individuals who undertake tissue removing procedures should be able and confident to inform patients that their surplus tissue may be used for research purposes with appropriate safeguards and advise patients how they can object if they choose. Patients should have the awareness and confidence that their surplus tissue samples may have research value and be used for such purpose with appropriate safeguards in place to protect their interests, including mechanisms via which they can object. This would therefore ensure that patients can act on their altruistic interests and potentially benefit from the opportunity to reciprocate for the care and treatment received from the NHS and the opportunity to feel solidarity as part of a health community. Moreover, tissue holders and researchers should have the confidence, supported by clear and authoritative guidance, that they can share and use surplus tissue samples for secondary research purposes with appropriate safeguards to protect individual patient interests.

13.6. Concluding Remarks

My thesis has focused on key areas of regulation and proposes regulatory approaches which if implemented in practice could better enable the secondary research use of surplus tissue samples held in diagnostic archives. However, whilst these regulatory approaches may address some extant challenges in this area, it does not provide an entirely comprehensive solution to the problems which exist with the secondary research use of surplus tissue samples. One area of regulation and law which I have not explicitly addressed in my thesis is the secondary research use of surplus tissue samples where the persons from whom the tissue samples were removed lack the capacity to object to their samples being used for such purposes. In my thesis (chapter 11) I have put forward an argument that a consistent approach to the availability of surplus tissue samples for research purposes should be applied across NHS organisations because this would be fairer than the current disparate approach. Moreover, I suggest that this would be fairer because it would allow equality of opportunity for patients to choose whether their surplus tissue samples are used for such purposes and therefore to

knowingly act on their altruistic interests. However, there are additional complexities where individuals do not have the capacity to make such decision, whether this is because they are incapacitated or because they are young children. Due to limitations of space in my thesis this is not an area which I have explored. I do however acknowledge that this is an important issue which warrants further consideration.

The implementation of regulatory approaches would also not in itself resolve the extant challenges experienced by those involved with activities relating to the secondary research use of surplus tissue samples. Whilst a clear and authoritative regulatory framework which is more enabling of such practices may provide a foundation to facilitate the secondary research use of surplus tissue, there are ongoing resource limitations within the NHS which would likely also continue to be challenging. Therefore, additional support would likely be required for diagnostic archives to ensure that they have the resources needed to provide samples for secondary research purposes. This is another area which would benefit from further work to be able to effectively implement the regulatory approaches which have been proposed through my thesis.

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