Consent Forms in Genomics: The Difference between Law and Practice

Paula Boddington, Liam Curren, Jane Kaye, Nadja Kanellopoulou, Karen Melham, Heather Gowans and Naomi Hawkins

Abstract

Consent forms are the principal method for obtaining informed consent from biomedical research participants. The significance of these forms is increasing as more secondary research is undertaken on existing research samples and information, and samples are deposited in biobanks accessible to many researchers. We reviewed a selection of consent forms used in European Genome-Wide Association Studies (GWAS) and identified four common elements that were found in every consent form. Our analysis showed that only two of the four most commonly found elements in our sample of informed consent forms were required in UK law. This raises questions about what should be put in informed consent forms for research participants. These findings could be beneficial for the formulation of participant information and consent documentation in the future studies.

Keywords

consent; ethical oversight; genomics; regulation; research governance

A central tenet of research ethics regulation is that researchers must obtain informed consent from research participants, as part of respect for the autonomy and bodily integrity of individuals. It is now also frequently recognised that informed consent is, or at least should be, a process, rather than an event limited to the one-off signing of a consent form. As part of an on-going exchange of information between researcher and participant, the consent form represents a crucial document that records what has deemed to have been agreed and

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understood by both parties. In the case of new research planned on participants’ existing samples or derived information, the consent form becomes a basis for deciding whether additional consent is required, or whether the existing consent covers the new research. The content of these consent forms and associated documents is increasing in significance as more secondary research is undertaken on existing samples and information, and samples are deposited in biobanks or repositories accessible by many different researchers.

Generally, the content of consent forms seems to be a mix of legal requirements, ethical principles, and accrued practice. There are no detailed national or international mandatory standards for the format of consent forms for research participants. Rather, what is included in a consent form will vary according to the particular research context. For new research projects, or where new technologies or approaches are used in research, consent forms may be formulated on the basis of previous experience and practice in other research — whether related or unrelated to the current project — and of content that has been successfully approved by a research ethics committee in the past. Therefore, there may be an incremental development of the content of informed consent forms that may inadvertently deviate from current legal requirements, but may also fail to address all of the concerns of the new research approach in question.

There is a danger then that consent forms could represent an accrual of past practice, not all of which is relevant or sufficient for current work, which would not foster a consistent, coherent and comprehensive approach that can be tailored to the requirements of current research. With this in mind, we reviewed a selection of consent forms and accompanying information for participants who have been asked to participate in research that included Genome-Wide Association Studies (GWAS). Consent for research using a GWAS approach is particularly useful as a case study, since the complexities of this kind of research, and indeed genomics research in general, brings into clear relief the opacity of the current consent framework.1 Our analysis involved review of a number of consent forms from across the UK and Europe, including forms drawn from one consortium of predominantly European countries, in order to identify and assess the constituent elements. Although these forms were from different countries, research consortia frequently pool data and samples across national borders. The aim of our analysis was firstly to establish whether their content and the accompanying information sheets conformed to the legal and ethical requirements for medical research in the UK, and secondly to examine issues that may arise from diversity amongst consent forms.

This review is not intended to be comprehensive but rather provide some insight into the type of issues raised in the consent process for research with a genomic focus. The purpose of our sample group is to be indicative of the issues that are addressed in GWAS informed consent forms — in many ways to give a flavour of what is being presented to potential research participants. It is not in any way representative. In terms of our legal analysis, we have restricted this to UK law for a number of reasons. First, we need to confine the scope of our analysis for the purposes of this study and our expertise lies in UK law. Second, it is at the national level where an action will commence and be judged at first instance, and, as the recent Gillberg v Sweden case makes clear, national legislation will have precedence over international declarations, such as the Declaration of Helsinki. Therefore, this study attempts to give a sense of what is actually found in informed consent forms for genome-wide association studies involving large consortium generally and how this may conform or differ with the legal requirements in the UK specifically.

In this paper, we provide an introduction to the nature of genomic research, the current legal requirements for consent and the content of the consent forms from our sample. In the final section of this paper, we focus on the four elements that were found in every consent form, to establish whether they are required by UK law. The most common elements were: a description of the project; a description of what was required of participants; the ability of participants to withdraw; and assurances that confidentiality and the anonymity of samples and data would be maintained. The intention is to help tease out how much current GWAS practice is in accordance with the legal requirements. These findings could be beneficial for the formulation of participant information and consent documentation in future studies.

1. The Nature of GWAS and Genomic Research

Advances in the quality and efficiency of sequencing methods, such as ‘Next-Generation Sequencing’ techniques, mean that it is now becoming cost-effective for scientists to sequence an entire genome rather than just parts of it. This will in turn increase the quality and richness of the data on many thousands of individuals involved in genomic research. Genome-Wide Association Studies are used to establish the associations between genomic variants and diseases or quantitative traits. In 2008, the results of this new approach first appeared in scientific journals, and now these studies have become more commonplace. GWAS typically require large numbers of participants who may, or not, have the disease that

2) [2010] ECHR 1676.
is being studied or who may vary in the quantitative trait in question. The DNA of participants is genotyped to identify a large number of genomic variants — presently usually just over one million variants per individual.

By comparing the results of genotyping large sections of DNA, it is possible to identify variants that may be associated with the disease or trait in question. In order to identify these small genetic contributions, such studies usually involve at least a thousand individuals and typically many more. The cost and effort involved in collecting samples de novo means that existing samples or the sequence data are re-used or re-analysed as much as possible to allow comparison with a new sample group. This secondary use of existing samples is always (in theory) dictated by the nature, and scope, of the original consent unless exceptional circumstances exist. Genetic information can be a powerful personal identifier and can provide information not just on the individual but also an individual’s relatives and related groups and populations. As such, it requires careful handling and indeed there are many legal and ethical requirements that demand this.

The need for large numbers of samples has led to the development of large international projects and research consortia focussed on specific research questions, such as the International Cancer Genome Consortium.4 These research collaborations can involve specialists from different disciplines who are based in a range of institutions and countries around the globe. Increasingly, different research contexts include GWAS as part of their protocol but there are no standard consent forms for participants. Indeed, different research consortia and institutional frameworks — including the varying requirements of research ethics committees — may result in differences in information and consent documentation, even within the same project where data and samples are pooled and shared. Furthermore, when genetic data are shared internationally, across jurisdictions where there may be different standards or requirements for informed consent procedures, further variation of clauses will feature in the consent documentation. The individual-specific digital information created by these international projects can be easily shared and may potentially be a valuable resource for many different research projects and purposes. Indeed, funders require that the sequence data produced by GWAS research be deposited in open access repositories so that it can be accessed by other researchers across international borders. Examples of such projects were the Wellcome Trust Case Control Consortium (WTCCC)5 in the UK and the Genetic Association Information Network (GAIN)6 in the USA. Examples of managed access data repositories established especially for

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the deposition of GWAS data are dbGAP\textsuperscript{7} in the US and the European Genotyping Archive within Europe.\textsuperscript{8}

2. Consent for Research: The Legal Requirements in the UK

The widely-held view that researchers must obtain ‘informed consent’ from research participants prior to the commencement of research grew out of established rules of good practice and ethics and has been codified in various ways in a variety of laws. There are two key legal instruments that apply to genomic research at an international level: the Council of Europe Convention on Human Rights and Biomedicine 1997,\textsuperscript{9} and its accompanying Additional Protocols (the Oviedo Convention), and the UNESCO Declaration on the Human Genome and Human Rights.\textsuperscript{10} Significantly, neither of these has been fully implemented into UK law. The OECD Guidelines for Human Biobanks and Genetic Research Databases 2009 are also influential in the formulation of international and national policies as regards the conduct of biomedical research. Whilst not legally binding, they represent an important political commitment for OECD member countries and they are taken into account when formulating national policy. The recent guidelines advise on the importance of withdrawal as a research ethics principle.\textsuperscript{11} They also stipulate best practice provisions and detailed guidance for its implementation in national practice.\textsuperscript{12}

Within the UK, legal requirements relevant to consent in genomic research (and all medical research involving human subjects) are based on a combination of key pieces of legislation such as the Clinical Trials Regulations,\textsuperscript{13} the Data Protection Act 1998 (DPA 1998), and the Human Tissue Act 2004 (HTA 2004) with its accompanying Codes of Practice.\textsuperscript{14} There are no specific statute-based laws for research on human beings in the UK.\textsuperscript{15} There is some limited case law

\begin{itemize}
\item \textsuperscript{7} Database of genotype and phenotypes (dbGaP): http://www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/about.html.
\item \textsuperscript{8} See http://www.ebi.ac.uk/ega/page.php.
\item \textsuperscript{10} UNESCO, “Universal Declaration on the Human Genome and Human Rights”, (11 November 1997).
\item \textsuperscript{11} “The operators of the HBGRD should inform participants of their right to withdraw, of the nature of and modalities for exercising that right, as well as the implications of and limits to exercising that right” (pt I, principle 4G).
\item \textsuperscript{12} Pt I, 4.13 and pt II, Annotations 32, 35, 42, 43, 44, 57, and 60.
\item \textsuperscript{13} Medicines for Human Use (Clinical Trials) Regulations 2004, SI 2004/1031.
\item \textsuperscript{14} The requirements for consent are found in the Codes of Practice of the Human Tissue Authority. The UK has not signed or implemented the Convention on Human Rights and Biomedicine 1997, nor does it have patients’ rights legislation as do other countries within Europe.
\end{itemize}
pertaining explicitly to consent in a research setting,16 which must be read alongside a mixture of more general statutes and common law principles in order to create a legal framework for research.

3.1. Clinical Trials Regulations

The Nuremberg code, which followed on from the Nuremberg trials, established the principle of voluntary, informed consent for research.17 This formed the basis for the requirement of informed consent, a notion which has been further developed in the Declaration of Helsinki, the World Medical Association’s statement of principles for medical research.18 While the Helsinki Declaration has ambiguous legal authority, it has become the basis for many national statutes and is used as a guide by practitioners and research ethics committees around the world. Informed consent as described in the Declaration of Helsinki forms the basis for the requirements of consent in the Clinical Trials Directive,19 which was transposed into UK law in May 2004 in the form of the Clinical Trials Regulations. The Regulations refer explicitly to the ‘ethical principles that have their origin in the Declaration of Helsinki’,20 and they were intended to apply only to clinical trials, not medical research more broadly. It is Department of Health policy, however, that the operating procedures required by the Directive and the Regulations ‘should also apply in general to the review by RECs (Research Ethics Committees) in the UK of all other research involving human participants within the NHS; and to the review under other legislation or on a voluntary basis of research outside the NHS’.21 The practical effect is that all medical research in the UK is now required to conform to these requirements; in other words, all types of

16) The most relevant judicial statements have addressed the relationship between autonomy and consent in the context of medical treatment rather than research, and have been informed by the ethical notion that informed consent ‘ensures that due respect is given to the autonomy and dignity of each patient’ (Chester v. Afshar [2004] UKHL 41, [2005] 1 AC 134 [18]).
17) The first article begins ‘The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision’ (Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10, (Vol. 2, US Government Printing Office, 1949) at pp. 181-182).
18) The requirement of informed consent is enshrined in principle 24 of the World Medical Association, “Declaration of Helsinki — Ethical Principles for Medical Research Involving Human Subjects”.
20) Schedule 1, pt. 2, para. 1. This extends beyond the Directive’s indication of the Declaration of Helsinki as an instance of good practice, arguably enshrining it in law.
research in the UK are being judged by standards that have been developed for clinical trials. It bears repetition that the Regulations are therefore the only formulation of the requirements for informed consent for research that can be found in UK law.22

3.2. **Data Protection Act 1998**

On its face, the DPA 1998 does not seek unnecessarily to interfere with, or indeed to prevent legitimate research using personal data. Exemptions apply to research, and other areas, typically serving to disapply, or limit, the effect of at least one of the eight data protection principles23 that must be adhered to by those processing personal data.24 In the case of research, section 33 of the DPA 1998 provides limited exemptions in respect of the processing, or further processing, of personal data for ‘research purposes’,25 although it does not exempt the qualifying data from all of the DPA 1998.26 Significantly, the requirement to process personal data fairly and lawfully persists in the case of research.

A common misconception about data protection law is that processing of personal data, be it in research or other contexts, cannot occur without some form of valid consent on behalf of the relevant individual. This is not always the case. At its most general level, compliance with the DPA 1998 in the UK is established by fair and lawful processing of personal data: something that can be achieved by compliance with any one of several legitimising conditions, of which consent is only one.27 Similarly, the ‘explicit consent’ for processing of sensitive personal data,28 such as data obtained through GWAS, is only one of a number of additional conditions needed to legitimise their processing.29 If the processing of sensitive personal data in GWAS is deemed necessary for the purposes of medical research,30 and the research is undertaken by a ‘health professional, or a person

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22) For an interesting discussion of the relationship between national law and instruments such as the Helsinki Declaration see *Gillberg v. Sweden* [2010] ECHR 1676.

23) Schedule 1, pt. 1.

24) S 4(4).

25) The term ‘research purposes’ is not defined in the DPA, however s 33 states that they include statistical or historical purposes.

26) The exemption involves a three stage process. Firstly, the proposed processing of the personal data in question must not be used to ‘support measures or decisions with respect to particular individuals’ nor must the research result in any substantial damage or distress to a data subject. Secondly, if this is satisfied, the personal data may be: (i) used for alternative purposes; (ii) kept indefinitely; and (iii) exempted from a data subject’s rights of access. Thirdly, despite the exemption, the requirement to process the personal data fairly and lawfully will persist, and so too will the obligation to provide fair processing information to the data subject.

27) Schedule 2.

28) Schedules 3 and 1.

29) Schedule 3.

30) *Ibid.*, para. 8(2) defines ‘medical purposes’ as including ‘preventative medicine, medical diagnosis, medical research, the provision of care and treatment and the management of healthcare services.’
who in the circumstances owes a duty of confidentiality . . . equivalent to . . . a health professional; \(^{31}\) then the additional requirement could, in a significant diversion from the Directive, be met without need for explicit consent. \(^{32}\) Unhelpfully, the DPA 1998 does not provide comprehensive guidance on what constitute different levels of consent, \(^{33}\) a situation that demands reliance upon a host of other guidance. \(^{34}\)

### 3.3. Human Tissue Act 2004

The HTA 2004 does not apply to the removal of tissue from living donors and as a result does not outline the consent requirements for involvement in research within the Act itself but instead this is elaborated in its codes of practice. The removal of tissue from the living is covered by common law principles and, if appropriate, the Mental Capacity Act 2005. The HTA 2004 does however apply to the storage and use of ‘relevant material’ derived from living people though the definition effectively excludes the uses and storage of DNA from oversight by the Human Tissue Authority which has implications for genomic research. ‘Relevant material’ is termed as ‘material, other than gametes, which consists of or includes human cells.’ \(^{35}\) Blood and tissue samples come under the definition of ‘relevant material’ because they ‘consist of or include human cells’, but extracted DNA is only part of a cell and therefore outside its scope. \(^{36}\)

The implication of this approach is that once consent has been obtained for one activity, such as the collection of a blood sample for a genomics study, the extracted DNA could be used for research and other purposes without any further consent required by the HTA 2004. However, in order to do so: the material must come from the body of a person (alive at the time of donation); the research

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\(^{31}\) Schedule 3, para. 8(1).

\(^{32}\) The DPA 1998 differs from the Data Protection Directive (Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data [1995] OJ L281/31) in its treatment of medical purposes. ‘Medical research’ is included within this definition (schedule 3, para. 8(2)), whereas Art. 8(3) of the Directive permits processing of sensitive personal data where ‘required . . . for the purposes of preventive medicine, medical diagnosis, the provision of care or treatment or the management of health-care services . . . by a health professional subject . . . to the obligation of professional secrecy . . .’.

\(^{33}\) The DPA 1998 does not provide any clues as to how explicit consent should be interpreted. Art. 2(h) of the Directive, the provisions of which should dictate any interpretation of the DPA, only goes as far as defining consent, in more general terms, as any freely given specific and informed indication of his wishes by which the data subject signifies his agreement to personal data relating to him being processed.

\(^{34}\) Guidance from the Information Commissioner’s Office (ICO) suggests that: consent should be informed (i.e. individuals must be made aware of the proposed uses or disclosures of personal data); individuals must have some degree of choice (i.e. there must not have been any coercion); and there must be some indication that consent has been given, be it express or implied. See Information Commissioner’s Office, “Use and Disclosure of Health Data: Guidance on the Application of the Data Protection Act 1998” (2002) p. 3.

\(^{35}\) S 53(1).

\(^{36}\) S 53(1).
must be subject to proper ethical approval; and the person from whom the material comes must not be identifiable. If these provisions are not satisfied, a researcher could be criminally liable for the offence of non-consensual testing of DNA. The HTA 2004 is silent on the specific requirements for informed consent from living people who participate in research although this is partially supplemented by the Codes of Practice on Consent (which we discuss further below).

3.4. Common Law

The common law of England and Wales derived from a body of precedent rather than legislation, can provide some guidance with regard to informed consent, but does not specify clear requirements applicable to research practice. Generally, consent need not be express in order to be valid, and consequently some form of consent is required for the disclosure of confidential information, though there is no established definition of what the nature of this consent should be. It has also been held that where individuals are aware that their consent is being sought, and are given a genuine opportunity to say no, implied consent is sufficient. For implied consent to be acceptable there must be some active communication between the parties signifying consent. For example, implied consent may be inferred only from some relevant action, such as putting out an arm to take a blood sample, and it cannot be inferred from mere silence or acquiescence, nor from the absence of any objection. Because there is currently no case law specifically concerning research or research participants, it cannot be said that ‘the so-called “doctrine of informed consent”’ is recognised by the common law. Therefore, it comes as no surprise that the standard of informed consent found in the Clinical Trial Regulations is higher than that required by the common law.

We have seen how research ethics regulation arose in the context of clinical research, and a pressing question for researchers is how far a duty of care arising within a clinical context might apply to biomedical research in other contexts, such as research in genomics. There is, however, case law which at least indirectly addresses the extent to which a duty of care is owed by a researcher to a research participant in a research project. Where a clinician or researcher fails to obtain consent from a patient or research participant, a claim may be brought under negligence. The duty of care owed by a clinical researcher to subjects of a clinical

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37) S 1(9)(a).
38) S 1(9)(b).
39) S 45.
43) J. Herring, Medical Law and Ethics, (OUP, 2008).
trial was found to be ‘akin to that of a doctor and patient one of close proximity’ in the Creutzfeldt-Jakob Disease (CJD) litigation, a large scale medical product liability case concerning human growth hormone. The programme had begun as a clinical trial (thus underlining its research aspect), but because of the number of child recipients it effectively became a therapeutic programme. The programme came to a sudden end after it became clear that three participants in the programme had died from CJD. In the resulting judgment, it was held that all the participants should be owed the same duty of care by ‘a pharmaceutical company, Government Department or other agency’. Whether this would apply to genomics research that was clinically focussed is uncertain.

A note of caution may be advisable given opinion on the impact of the Bolam test on standards of informed consent and on the steps to be taken to respect individuals’ autonomy. The application of this test means that a doctor ‘is not guilty of negligence if he has acted in accordance with a practice accepted as proper by a responsible body of medical men skilled in that particular art.’ This builds into the notion of a duty of care the capacity to change as practice changes, and it has been suggested that as ‘practitioners pay greater attention to individual autonomy, the application of the Bolam test will cause the law to pay greater heed to the concept of informed consent.’ We have seen from our examination of consent forms in genomics research that practice in many respects varies; Bolam may imply that a certain upward pressure to cohere with best practice may be present in English law.

4. Consent Documentation: Information and Forms

For this study, we examined 14 informed consent documents from 2004–2010, used in GWAS projects both in the UK and in other countries. Many of these studies collaborated as part of a single project, thus allowing benefits such as greater statistical significance through the combination of samples as well as enabling the comparison of risk across population groups. In these studies, a blood sample will have been provided, which is then analysed and sequenced in a laboratory to create sequence information that undergoes statistical and comparative analysis. It is a common part of research practice to de-identify the original samples by means of codes used in place of obvious personal identifiers. The consent forms and accompanying information sheets used in these studies are the procedural mechanisms by which an individual’s voluntary agreement to

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45) *Bolam v. Friern Hospital Management Committee* [1957] 2 All ER 118, [1957] 1 WLR 582.
46) Biggs, *supra* note 15, at p. 82.
participate in GWAS research is recorded.\textsuperscript{47} This documentation constitutes a record of what the participant was told at the time of recruitment and it determines the permissions that are attached to the samples or data collected. Its aim is to inform individuals of relevant information about what is involved in the research so that they can make an informed assessment of the risks and benefits of participation in the research before they consent to taking part.

In Figure 1, we show the results of our analysis of this informed consent documentation. The table shows the frequency with which elements of GWAS research involvement were found in the informed consent documents. In this table, ‘always’ means that this component was found in all consent documents; ‘usually’ means that it was found in over half; and ‘sometimes’ means that it was found in under half but in more than one quarter of the documents.

The consent forms that we analysed all included some general mention of the sample handling procedures and a description of the proposed use of the data arising from such samples. There was also always some description of the project and its aims; what is required of participants; an explanation that participation is voluntary and that withdrawal is possible at any time; and that samples and data will be kept confidential. However, there was no specific information on the fact that GWAS generate very detailed data on individuals. It was rare to find a discussion of the risks and benefits of the use of this approach in general, or of the personal implications of the research findings. Information on how long samples would be stored or who will use the data and samples after the current project is finished were not always found in the informed consent documents. Even less frequent in our sample forms are statements about the storage of samples and data and its future use; commercial involvement; contact details for questions and complaints; and details of relevant laws and regulations. The first of these three is especially important when considering the international nature of GWAS and the fact that the sequence analysis may be used for many different studies well into the future. This alone raises serious concerns as to how informed participants are before they get involved in a GWAS study, as the reality of how information may be used is not uniformly described in these forms. It is beyond the scope of this paper to explore all of these elements in greater detail, so we will concentrate on the four aspects that were found in all of the informed consent forms in our sample (Table 1).

Table 1. Content of Typical GWAS Consent Forms

<table>
<thead>
<tr>
<th>Frequency of appearance</th>
<th>Element of the consent form</th>
<th>Range of variation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Always</td>
<td>Description of the project and its aims</td>
<td>Levels of detail vary greatly. Always present are statements to the effect that the participant has been informed about the project and had an opportunity to ask questions. Names of the PI and contact details for any further queries are often included.</td>
</tr>
<tr>
<td>Always</td>
<td>Description of what is required of participants</td>
<td>Levels of detail vary greatly, but may include discussion of blood collection and other investigations, and access to medical records. There are also options to re-contact for participation in research in the future, and to contact family.</td>
</tr>
<tr>
<td>Always</td>
<td>Explanation that participation is voluntary; that participants may request withdrawal of samples and data at any time</td>
<td>Details of withdrawal vary. Some projects promise that both samples and data will be withdrawn retrospectively; some explain that data already processed cannot be withdrawn; some are silent on what ‘withdrawal’ actually means.</td>
</tr>
<tr>
<td>Always</td>
<td>Assurances of confidentiality of samples and data</td>
<td>Levels of detail and levels of confidence in the robustness of the privacy of the data vary. Sometimes assurances are phrased as absolute, sometimes as ‘to the best of our very high ability’. Occasionally, exceptions to confidentiality are mentioned, such as to prevent serious harm to a participant or others. Some explain implications of data and sample sharing for confidentiality, particularly when leaving the recruiting institution. Often, details of a country’s own data protection or health confidentiality laws are given.</td>
</tr>
<tr>
<td>Frequency of appearance</td>
<td>Element of the consent form</td>
<td>Range of variation</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-----------------------------</td>
<td>--------------------</td>
</tr>
<tr>
<td>Usually</td>
<td>Discussion of risks and benefits of research</td>
<td>Content varies considerably. Usually there is discussion of minor physical risks of blood extraction; sometimes psychological and social risks associated with genetic information and its sharing, or much more rarely, privacy risks e.g. in relation to employment and insurance. There is only occasionally mention that research may find unexpected family relationships. In these cases, potential participants are usually told that these findings will only be fed back if they are of clinical importance. Often, but not always, there is mention of the benefits of research as helping advance knowledge rather than as concrete or personal.</td>
</tr>
<tr>
<td>Usually</td>
<td>Statement about personal benefits of research and feedback</td>
<td>Projects that are part of the same network may nevertheless have variations in any promise of benefit. Feedback of individual findings may vary even within a project. Some recruits may be told they will be informed of findings when these are found to be of clinical significance. Some are offered retests in clinical settings.</td>
</tr>
<tr>
<td>Usually</td>
<td>Details about the length of time of storage of samples</td>
<td>Even within the same project, different recruits may be given different information about the length of time that samples will be stored and about what will happen after that time. They may be told that samples will be kept indefinitely. Some are told that immortal cell lines will be made from samples.</td>
</tr>
<tr>
<td>Frequency of appearance</td>
<td>Element of the consent form</td>
<td>Range of variation</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Usually</td>
<td>Statements about who will use the data and samples for the current project</td>
<td>Recruits are sometimes explicitly told that their samples are a gift.</td>
</tr>
<tr>
<td>Sometimes</td>
<td>Statement about storage and future use of data and samples</td>
<td>This information is sometimes but not always present. Options include no further use without re-consent; no further use without ethics committee approval; a limited range of possible future uses. This may be more or less specific, such as ‘heart disease and related conditions’ or ‘melanoma and nevus research only’.</td>
</tr>
<tr>
<td>Sometimes</td>
<td>Statement about commercial involvement</td>
<td>This is often absent. Recruits may be told there is no commercial involvement. If potential participants are told that commercialisation is a possibility, it is always made clear that there will be no personal benefit. In these instances they are occasionally asked to sign a waiver.</td>
</tr>
<tr>
<td>Sometimes</td>
<td>Contact details for questions and complaints</td>
<td>These are sometimes present.</td>
</tr>
<tr>
<td>Sometimes</td>
<td>Details of relevant laws and regulations</td>
<td>Often absent, but sometimes present as a general statement that the project is in accordance with law; or indication of relevant legislation.</td>
</tr>
</tbody>
</table>

5. Comparing Law and Practice

Four elements were found in every consent form that were in our sample. These were: a description of the project; a description of what was required of participants; the ability of participants to withdraw; and assurances that confidentiality and the anonymity of samples and data would be maintained. The central
question of our study was whether these common elements of informed consent forms were actually required by law or were they simply an accrual of past practice, some of which may or may not be relevant for GWAS studies. In this section, we compare these four elements with the legal requirements that are found within the Clinical Trials Regulations, the Data Protection Act 1998, and the Human Tissue Act 2004 with its accompanying Codes of Practice, and the common law. This analysis suggests that two of the most common elements — a description of the project and withdrawal from a study by research participants — are not required by law within the UK.

5.1. A Description of the Project

5.1.1. Content
In every informed consent form reviewed, the principal investigators who were leading the study and their institutions were named. The funders of the research and whether the project was part of a wider research consortium were detailed in the information form and participants were given information about the study and its aims — for example, that the study would generate information that would be useful for research on a particular disease. It is this information that is context-specific and the details differ according to each study and the country where the study is based. An issue of particular significance for GWAS is whether consent is obtained for the storage of the sample so that it can be used for new analyses and whether there is permission for the sample to either be transported to other countries or worked on by researchers who may be based in other countries. Of the 14 informed consent forms that we analysed, 11 of these mentioned storage for future use explicitly and only 9 mentioned the possibility of access by international researchers. Being mindful that a number of these consent forms were approved in other jurisdictions, the question arises of whether they would be in conformity with legal requirements in the UK.

5.1.2. Relevant Law
The basic requirement to inform research participants of the research project has its origin in the Declaration of Helsinki, which requires that they must be:

   adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, and any other relevant aspects of the study.48

This is sufficiently broad in that it could be interpreted to require researchers to inform a potential research participant of the details about storage and that other

researchers will be able to access the samples or information as part of consortium research; there seems to be scant reason to exclude these from the points listed above. This list of requirements is also found in the National Research Ethics Service (NRES) review process which, as noted before, follows the Department of Health policy in applying Clinical Trials Regulations to all research with human participants.\(^{49}\) This also shows that this is a mandatory requirement for compliance with these regulations and to obtain research ethics approval. Therefore, the informed consent forms from our sample were in conformity with NRES requirements.

The DPA 1998 requires that processing of personal data should conform with objective ‘fair and lawful’ processing provisions. One requirement is that individuals be provided with information about the person who is carrying out the processing and the purpose of the processing. However, medical research is subject to the section 33 exemption as long as it does not ‘support measures or decisions with respect to particular individuals’ (and the research will not result in any substantial damage or distress to a data subject). If these conditions are met, then data must still be processed fairly and lawfully but they could be used for another research purpose and they can be kept indefinitely. This means that data can be held indefinitely and used for secondary research purposes without the need to inform the research participant of this. The convention, which we found in the informed consent documentation that we reviewed, to give individuals a detailed description of the project, goes beyond the minimal requirements of the DPA 1998.

Likewise, neither the HTA 2004 nor the accompanying Codes of Practice require that individuals are given a detailed description of the research project. The HTA 2004 does not provide a definition of the various types of consent that are stipulated in the Act, nor does it detail what the specific requirements are when consent is given for different purposes. The Act specifies who must provide consent, for what purpose and for what kind of material but it does not specify how this should be done, nor any specific provisions to be included in consent forms. Similarly, the Code of Practice on Consent\(^{50}\) recommends that Patient Information Sheets should be provided about research projects but it does not stipulate what they should contain. The HTA 2004 does not apply conditions to the export of samples but it requires that samples that are imported into England, Wales or Northern Ireland have research ethics committee approval. The Human Tissue Authority Guidance suggests that, wherever possible, similar ethical approvals are obtained in the source country.\(^{51}\) However neither of these conditions is something about which participants must be informed. The Human Tissue

\(^{49}\) See Clinical Trials Regulations schedule 2, pt. B.

\(^{50}\) Human Tissue Authority, “Code of practice 1: Consent”, (September 2009).

Authority does not specify what potential research participants should be told but it effectively has delegated this role to research ethics committees (RECs) and to NRES guidelines that point to the Clinical Trials Regulations.\textsuperscript{52}

5.1.3. Implications for Practice
Despite the fact that, in the UK, detailed description of the research project is only required by law in cases of clinical trials, this information features prominently in all GWAS documentation. Informing potential research participants about the project has become part of good practice, reinforced by the expectations and review of research ethics committees, even though it is not a legal requirement.

5.2. Description of What Is Required of Participants

5.2.1. Content
In all of the consent forms there was a description of what was required from participants, such as physical intervention to collect blood, skin, DNA and, in some cases, to take photographs. Most studies involved a request for access to medical records as well as other clinical data. In some cases, participants were asked to consent to further research participation in the future and to authorise contact with other family members. Much of this focus was on the physical interventions at the beginning of the research process.

5.2.2. Relevant Regulation
The removal of a sample or a physical intervention as described in the informed consent forms in this study is covered under common law rather than the HTA 2004. The common law has established that informed consent is necessary for the removal of blood, tissue or for any other physical intervention, which, if carried out without consent, would constitute a battery. In the case of genetic information, this would likely be covered by the DPA 1998 and it would require that the individuals were informed of the fact that personal data were being used in research. To provide this type of information conforms to the requirements of the Declaration of Helsinki and the Clinical Trial regulations. Providing this degree of information is not a legal requirement determined by statute but it has become the norm because of the NRES guidance that requires that research ethics committees apply the Clinical Trial Regulations to all kinds of research.

5.2.3. **Implications for Practice**

It is therefore no surprise to see information about physical procedures and informational practices in all of the GWAS documentation. The first is required by the law in all situations not just research; and the second is a legal requirement in the case of personal data. Despite the fact that the data in question may not always be personal, we see a continuation of the general trend of informing potential research participants about requirements of their involvement in a project. Again, this is presumably in order to conform to the requirements of research ethics committees. The difficulty with research that involves consortia and the creation of rich datasets based on GWAS is that it is difficult to foresee all the possible uses of the data that could be made in the future. Therefore, it is difficult to satisfy this requirement at the beginning of the research process when all of the research uses are not known. However, not all of the informed consent forms from our sample provide detailed information on how data will be used and shared in the future and whether they will be deposited in a managed access biorepository such as dbGAP or the European Genotype Archive.

5.3. **Voluntariness: The Ability to Withdraw**

In clinical research, the ability to withdraw consent is mandated by the requirement that individuals exercise control over their bodily integrity; and it is relatively straightforward to ascertain what counts as withdrawal from the study in these terms. In research involving genomic techniques however, the basis of such withdrawal may be less clear as there may be lack of clarity about what is involved for withdrawal to be effective. It may in practice relate to the use of samples and/or data derived from these.

5.3.1. **Content**

In all of the consent forms that we reviewed as a part of this study, research participants were told that they could withdraw from the research project. However, there were real differences between the different consent forms in our sample as to what would happen if an individual decided to withdraw. The majority of projects promised that all samples and accompanying information would be destroyed. Others only promised that any identifiable samples and information would be destroyed. In other forms, it was not stated what would happen to existing samples and data. Some projects would return to participants to ask them what they wanted to happen to the samples and information. In one project, individuals were promised that DNA ‘would be destroyed at that very minute’ without the participants needing to give a reason. There is considerable variation amongst these commitments made to participants, a variation that is found in projects contributing samples and information within the same consortium. It seems likely that this variation in practice has arisen partly as a response
to different notions of what withdrawal means in genomics research: whether it refers to past use of data and samples; whether rights of bodily integrity were ever intended to cover use of material and data long since separated from the body, also by taking into account the, often considerable, practical difficulty of physically removing data or samples from genomics research studies.

5.3.2. Relevant Regulation

Withdrawal is included as a requirement in the Helsinki Declaration,\(^{53}\) and the notion that a research participant can discontinue his or her participation in research at any time without adverse consequences is a routine component of research ethics committee regulation in the UK. The ability for a participant to withdraw from research at any time, without providing a reason, is generally seen as an expression of the entirely voluntary nature of consent, according to well-established principles of voluntariness and autonomy.\(^{54}\) However, as it has been noted, the original context for this was consent to clinical research involving medical interventions and hence implicitly related to bodily integrity.

In the UK, as in the case of consent, the legal requirements on withdrawal are not found in one specific statute. Other than the Human Tissue Authority Codes of Practice, there exist at present no UK legal instruments on withdrawal of consent in medical research more broadly, i.e., other than in clinical trials. Similarly to the case of consent, the legal requirements for withdrawal from biomedical, including genomic, research in the UK are based on a combination of common law doctrines, DPA 1998 provisions, the requirements of the HTA 2004, and its Codes of Practice. In these instruments, the legal requirements for withdrawal of consent in research are not specified in any detail. Furthermore, and in the same vein as in consent, the law regarding withdrawal applies differently to blood and tissue samples, DNA samples, and to the data derived from them. The Human Tissue Authority considers withdrawal of consent as central to the application of the consent provisions of the HTA 2004.\(^{55}\) When consent is withdrawn, tissue needs to be disposed of, as set out in the Codes of Practice,\(^{56}\) and with qualifications.\(^{57}\)

We explained earlier that once consent from a living person has been obtained for a regulated activity, (e.g. the collection of a blood sample for a genomics study), the extracted DNA can be used for research and other purposes without

\(^{53}\) “The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal” (para. 24).


\(^{55}\) Supra note 50, Art. 23.

\(^{56}\) Human Tissue Authority, “Code of Practice No. 9 on Research”, (2009), Art. 72; and Human Tissue Authority, “Code of Practice No. 5 on Disposal of Human Tissue”, (2009).

\(^{57}\) Supra note 50, Art. 39.
any further consent under the HTA 2004, but for the qualifications of appropriate research ethics review and non-identifiability. Withdrawal of extracted DNA in research can be difficult depending on de-identification methods, and also on whether materials have been released and shared among multiple researchers. That said, as regards consent requirements affecting research use of DNA in the UK, unless the relevant exceptions that are explicitly defined by the HTA 2004 apply, it is an offence to analyse DNA without ‘qualifying’ consent — that is, consent for DNA testing for other purposes required by the Act.\(^{58}\) In the exception provisions, the decision from a donor stating a specific refusal to consent is of relevance since the exception provisions allowing non-consensual DNA analysis do not apply where there is an express refusal to consent, or where the analysis is for the purpose of medical research.\(^ {59}\) The introduction of these provisions led scholars to support the position that non-consensual DNA analysis offers ‘an opportunity to enforce withdrawal’ with regard to the storage and use of blood and tissue samples.\(^ {60}\)

In terms of the withdrawal of personal data from research projects, and indeed more general data processing activities, data protection legislation is far from clear as to whether a data subject can withdraw their consent. A right to revoke consent for the processing of personal data is generally assumed to exist under data protection legislation (albeit only through an objective view of ‘fair and lawful’ processing), yet this is addressed neither expressly nor adequately by the law. Examination of the evolution of data protection legislation at a European and British level suggests that a general right to withdraw consent was assumed to be inbuilt, despite the lack of clear provisions in both the European Data Protection Directive and DPA 1998.\(^ {61}\)

Withdrawal in the case of DNA-derived data is complicated. In the case of large research cohorts such as research biobanks, for example, it may not be possible to completely remove DNA-derived data. This is because once information has been generated, aggregated, and distributed, it is difficult to pull it back. In genomic research, researchers’ attention shifts from samples to data, in the context of fast moving technologies, and the retrieval of personal data is a rather nuanced affair. Withdrawing from participation in a large cohort study is a very different matter from withdrawing from a clinical trial, as it may not be possible completely to remove one’s data from the research.

In practical terms, a right of an individual to withdraw data about themselves would require the severing of any linkages to that individual’s personal data, yet

\(^{58}\) The offence of non-consensual DNA analysis is regulated under s 45 of the Act, as mentioned earlier.


\(^{60}\) Gertz, supra note 54.

the ways in which such right could be implemented remain elusive. This complexity is apparent in the field of GWAS and it is taken into account across data sharing policies for genomic research. In the US, if a research participant wishes to withdraw consent, it is possible to remove their coded data from the data repository but it is not possible to retrieve data already distributed for approved research use.62 In the UK, the UK10K project framework adopts a comparable position, arguing that it is impossible to guarantee complete withdrawal of individual data from all researchers who have accessed the data through the data-sharing repository.63

Emerging guidance raises the question of whether withdrawal of data in genomic research, especially large GWAS, is practical at all. Given the high number of participants, a truly burdensome amount of work could arise if researchers were to follow to the letter the promises that they make in consent forms. In the case where data and samples have been released and shared among different research centres, and also perhaps internationally, withdrawal could be very difficult. Concurrently, promises of retrospective withdrawal would be impossible to keep for aggregate or already published data.64

5.3.3. Implications for Practice

In our study, all the consent forms that we reviewed explained that participation was voluntary and that withdrawal was possible at any time. The details of how participants could withdraw varied: some projects stated, rather optimistically, that withdrawal would result in both samples and data being withdrawn, and withdrawn retrospectively; some said that already processed data could be withdrawn; some were silent on what withdrawal actually involved. This wide assortment of options reveals a multiplicity of approaches, not necessarily grounded exclusively in ethics or law, but possibly also in pragmatic and ad hoc considerations. They could be the result of differing degrees of awareness about the ethical and legal requirements as well as the technological complexity that is involved in implementing withdrawal options in genomics.

Moreover, the disparity of approaches reveals ambiguity and uncertainty about the nature of withdrawal across research contexts. There is no established

63) ‘[U]pon withdrawal, no new information will be collected, no further analyses of existing information will be performed within the project and existing information will be destroyed but […] it will not be possible to remove data or destroy it once it has been downloaded by other researchers through the European Genome-Phenome Archive (EGA)’ (UK10K Ethical Advisory Group, “UK10K Ethical Governance Framework”, (September 2010). Retrieved 9 May 2011 www.uk10k.org/assets/EF_UK10K_v21.pdf.
definition of what withdrawal should consist of, nor of what types of withdrawal would be appropriate depending on the context or type of research. However there is evidence that it is becoming more common for research ethics bodies to require that researchers provide, in the consent form, clarity of withdrawal options and their possible limitations, together with an explanation of any mechanisms for ongoing communication on the research to be done. A key question is how to develop best tailored practices for withdrawal because one-size-fits-all solutions are no longer sustainable. As to law, current options for implementing withdrawal in genomic research contain considerable uncertainties and it is not even clear if withdrawal for such research should be based upon a model developed in the clinical sphere. An opportunity for clarification may be the pending reform of data protection by the European Commission, in which an individual ‘right to be forgotten’ is being proposed. The extent to which such a right could provide a clear mechanism for implementing revocation rights in the context of medical research remains uncertain at the time of writing, as does the question of the advisability of such a nebulous right.

At a broader level, the difficulty with current regulatory frameworks, chiefly as regards ethical practices but also in law, is that the promise of withdrawal continues to be made but in practice to honour such withdrawal may be extremely time-consuming and expensive with a consequently deleterious impact upon research. Motivation to stick to the letter of such withdrawal agreements may therefore be poor. Such disparity could have potentially devastating implications for the long-term sustainability of medical research insofar as it can lead to lack of certainty, confusion, disenchantment, non-cooperation, and possible loss of public trust in research. At the same time, insistence on vague references to withdrawal, without meaningful implementation across emerging research initiatives that warrant large scale data aggregation and dissemination, could block the development of alternative, more sustainable ethical and legal options. In the quest for improving best practices in the governance of genomic research, it may be time to either refine the parameters of withdrawal across different research contexts, or to complement it with other, less limiting mechanisms. Otherwise, it would arguably be disingenuous to continue to promise withdrawal in those research contexts where it can no longer be kept, as well as it being a questionable practice to offer different standards, even within the same project, unless there are good reasons to do so.

65 Such guidance possibly owes to increasing awareness of the intricacies of genomic research, which, for example, were taken into account when the UK Biobank proposed detailed options for individual withdrawal (‘no further contact’, ‘no further access’, and ‘no further use’) (UK Biobank Ethics and Governance Council, “Ethics and Governance Framework”, (Version 3.0, October 2007), at p. 9. Retrieved 9 May 2011, www.ukbiobank.ac.uk/docs/EGFLatestJan20082.pdf.
5.4. Assurances of Confidentiality and Anonymity of Samples and Data

5.4.1. Content
All consent forms that we reviewed made a promise of confidentiality, and many
made reference to the fact that samples and data would be made anonymous.
However, the level of detail and explanation of confidentiality and anonymity
greatly varies; sometimes assurances are phrased as absolute assurances, in other
cases, consent forms refer to maintaining confidentiality ‘to the best of our very
high ability’. Occasionally, exceptions to confidentiality are mentioned, for exam-
ple to prevent serious harm to the participant or to others. In other cases, consent
forms include warnings that levels of confidentiality cannot be assured once data
and samples leave the recruiting institution; however it is extremely rare that
consent forms warn that different rules and approaches in relation to confidenti-
ality may apply outside the recruiting institution or in different countries. In a
number of cases, the consent form refers specifically to the data protection or
health confidentiality laws in that jurisdiction.

5.4.2. Relevant Regulation
The Clinical Trials Regulations state that “The confidentiality of records that could
identify subjects shall be protected, respecting the privacy and confidentiality
rules in accordance with the requirements of the DPA 1998 and the law relating
to confidentiality”.67 Establishing a breach of confidence at common law is gener-
ally cited as having the following three elements: the information must have the
necessary quality of confidence about it; it must have been imparted in circum-
stances importing an obligation of confidence; and there must be an unauthor-
ised use to the detriment of the party who originally communicated it.68 The duty
of confidence in the medical context is supported by Article 8 of the European
Convention of Human Rights (ECHR), according to the European Court of
Human Rights.69 In a more general sense, in the UK, the House of Lords has —
in the context of the tort of misuse of private information — effectively conflated
the duty of confidence with the rights under Art 8 of the ECHR.70 The UK
courts’ approach to balancing Article 8 and confidentiality in a medical context
(albeit with reference to medical records, not physical samples) was demonstrated
neatly in a recent case relating to disciplinary proceedings involving a dentist.71

Where genomic information is anonymised for use in research, it will not be a
breach of confidence to disclose the information to a third party.72 Against the

67) Clinical Trials Regulations schedule 1, s 11.
68) Coco v. AN Clark (Engineers) Ltd [1969] RPC 41 (Ch) 47.
background of the concerns that persist about whether genomic information can ever be sufficiently anonymised, given the increasing sophistication of methods of identification of individuals from within mixtures of DNA, what is clear is that a researcher who collects information in the research context is subject to a duty of confidence in relation to any such information that is not anonymous. The information could legitimately be disclosed to third parties in two situations; if the disclosure was authorised (including under the consent form); or if the disclosure was necessary in the public interest.73

Owing to the legal uncertainty as to the nature of consent, it is not entirely clear what would be required for such disclosure to be authorised in a consent form. At the very least, it would seem that participants should be informed that the information in question will be disclosed to third parties, and the broad purpose of that disclosure, such as for the purpose of further medical research. The test for the public interest exception that permits disclosure of confidential information in the medical context is however very restrictive. It involves balancing the competing public interests of the right of the public to know the information versus the public interest in maintaining confidentiality and the possible adverse effects of disclosure. In the case of disclosure of medical records in the public interest, courts in the UK have required that the disclosure be made only to those to whom it is necessary to tell to protect the public interest, only when the risk is real, rather than merely fanciful, and where there is an imminent risk of physical harm to the public. The limitations on disclosure suggest that there must be exceptional circumstances where another’s life is immediately endangered and urgent action is required or where there is a real risk of danger to the public.74

5.4.3. Implications for Practice

Medical research has traditionally relied on either confidentiality or the mechanism of anonymity in providing protection for participants (on the assumption that what is anonymous cannot be confidential).75 Indeed, without the protection of anonymity, more rigorous standards of ethical protection are generally required. However, genomics research now challenges the confidence historically attached to promises of anonymity. Such promises may no longer be possible following the development of increasingly sophisticated methods of statistical and genomic analysis which make the identification of individuals within large cohorts of genetic data or from increasing small amounts of DNA possible.76 As it becomes

74) Ibid.
possible to identify individuals in such cases, the use of anonymity as a tool to protect participants in research becomes increasingly untenable.\textsuperscript{77}

The cases about disclosure in the public interest have traditionally revolved around particular individuals, where there was a need to identify the person. These situations can be distinguished from the research context. In situations where information is passed on in the conduct of research, there is disclosure of information about an individual who could be identified in theory, but who in practice is unlikely to be identified because the researchers in question are required by contract not to attempt to identify the individual. In such a case, it might be arguable that the disclosure for research purposes, where the use is strictly controlled, is justified in the public interest but this may be stretching the principle too far.

We noted above that consent is not actually a prerequisite for legitimising the processing of personal data in (suitably ‘medical’) research; at least not as far as the DPA 1998 is concerned. For the sake of argument, let us assume that explicit consent, or indeed any consent, is absent in respect of some aggregate genomic data that are intended for use in a genomic research project. On the assumption that such data can be personal data,\textsuperscript{78} it is contended, based on the argument set out above, that these researchers will, if they intend to use the data without consent, effectively need to act under a duty of confidentiality towards the participants commensurate with that which would be owed by a clinician. But how realistic is this?

Anecdotal evidence suggests that the contracts signed by researchers to give them access to research data require very high levels of confidence, arguably even higher than the duty of a clinician. For example, there are very often promises not to attempt to identify, or re-identify, participants from the data. Thus, the explicit consent of a research participant may not actually be needed before any research is commenced; mere ‘standard’ consent may be sufficient. But again, it should be stressed that this is merely what the DPA 1998 implies.

Leaving aside for one moment the additional conditions needed to legitimise the processing of \textit{sensitive} personal data, there are (relatively weak) legal arguments that question the requirement for consent as a legitimising condition for the processing of \textit{any} personal data. For example, could a genomics researcher carry out primary research using personal data without the consent of participants on the grounds that the research was in line with the researcher’s \textit{legitimate}

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\textsuperscript{78} For a detailed discussion of this matter, see L. Curren, P. Boddington, H. Gowans, N. Hawkins, N. Kanellopoulou, J. Kaye, and K. Melham, “Identifiability, genomics and UK data protection law”, \textit{European Journal of Health Law} 17(4) (2010) 329-344.
interests.\textsuperscript{79} If research was conducted on the grounds that any incidental results that might have serious health consequences would always be reported back to participants, would consent be unnecessary on the grounds that such research was in the ‘vital interests’ of the participants?\textsuperscript{80} Finally, would it be possible to justify non-consensual research on grounds of the ‘public interest’ on the assumption that the research will eventually benefit the wider public?\textsuperscript{81}

None of these options would seem particularly compelling, and so it is safest to assume that some form of meaningful consent should be present in order to carry out primary research using personal data in compliance with the DPA 1998. When it comes to secondary research, i.e. the use of personal data in other research projects not initially communicated to a participant, the research exemption in the DPA 1998 does away with the need for additional consent. Claims made in some of the consent forms that ‘re-consent’ will be required before further processing of personal data occurs are above and perhaps beyond the requirements of the DPA 1998. Failing to adhere to such promises could, however, run the risk of being deemed unfair, and thus contravene the first data protection principle. Accordingly, re-consent would, if promised, seem necessary under the DPA 1998, despite the obvious practical burdens.

All the situations considered here, where consent could be dispensed with but personal data still be processed in compliance with the DPA 1998, would appear to clash with the approach taken by two influential regulatory actors: the (soon to be abolished) Ethics and Confidentiality Committee of the National Information Governance Board (NIGB);\textsuperscript{82} and the NHS (in its Code of Practice on Confidentiality).\textsuperscript{83} In the case of the NIGB, consent would seem only capable of being waived if the NIGB permits it i.e. in line with its statutory function.\textsuperscript{84} This would constitute a defence if an action for breach of confidence was commenced by a research participant. Therefore, to comply with the law, good practice in the UK is to anonymise information if possible. If not possible, then consent or a statutory exemption from the NIGB must be obtained.\textsuperscript{85}

\textsuperscript{79} Schedules 2 and 6(1).
\textsuperscript{80} Schedules 2 and 4.
\textsuperscript{81} Schedules 2 and 5(d).
\textsuperscript{84} Via s 251 of the NHS Act 2006, such that the common law duty of confidentiality to be set aside by the NIGB to allow the use of personal data (patient-identifiable information) so long as the use: is for the purpose of improving patient care, or is in the public interest; and, is for a medical purpose; and the purpose cannot be achieved using de-identified data; and seeking consent for the use of identifiable data is not practicable.
\textsuperscript{85} One area where data protection may have more of a role to play is in the cross border transfer of personal data. The collaborative efforts employed in GWAS mean that it is very common for the sharing of
6. Conclusion

What are the implications for practice of these findings? One important factor is that legal requirements that are only applicable to clinical trials are being applied more broadly to all kinds of research in the UK. This means that, in some cases, the standards required by research ethics committees may be higher than required by UK law and, in other cases, they may be lower. Informed consent for research per se is not a legal requirement but nonetheless it is universally adopted in practice. Two of the four key elements that we found in our sample of consent forms — a description of the project and the right of withdrawal — are not in fact required by UK law. They derive from the interpretation of documents such as the Declaration of Helsinki and from what has evolved through practice. This finding should not be taken to imply that any elements over and above the law are therefore extraneous. This exercise has aimed to make clear what is the case in current law — that for which there is established legal recourse — and what on the other hand is part of current practice — whether as part of ethical governance or not.

Our analysis has shown that the first most common element — the description of the project — is over and above the legal requirements found in the Data Protection Act and the Human Tissue Act. However, it complies with the requirements of the Declaration of Helsinki, which has been transposed into the Clinical Trials Regulations and, because of the NRES guidance, it is now required by all research ethics committees before research approval will be granted. Without involving the passing of statute or further regulations, this has effectively set the standard for medical research. This means that in the UK, research that is not a clinical trial is required to meet standards that are designed for clinical trials. This brings UK research in conformity with other jurisdictions. This is essential in the case of GWAS, which are carried out in large research consortia. The result is that the description of the project that we found in our sample consent forms meets a higher standard than is currently required by UK law for research that is not a clinical trial. In this aspect, the standard required by research ethics committees is higher than the legal standard.

In contrast, the common law and the Data Protection Act both require that people must be given information about what is involved in their participation in research. This was one of our four most commonly found elements in our sample. To ensure that the taking of a sample does not constitute a battery, an individual

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data (and samples) to take place amongst large, often international consortia. It is a fundamental aim of European data protection legislation to promote the legitimate movement of personal data within the European Economic Area (EEA) and to permit extra-EEA transfer to countries only where there is 'an adequate level' of protection (i.e. similar data protection provisions). The Research Exemption permits indefinite storage of personal data used for research but it does not exempt the parts of the DPA that exist to regulate the flow of personal data across borders. The law regulating this aspect of data protection is, however, not at all straightforward and, in the interests of brevity, beyond the scope of this article.
must give their consent prior to the event. This is the same for the use of data exception in the case of secondary use for research purposes. In this regard, the legal and ethical requirements are in alignment. In the case of our sample consent forms, some issues that were relevant to GWAS and the sharing of samples and data in consortia were not mentioned in all of the informed consent forms. During GWAS projects, samples and data will be shared by researchers in a consortium, which may involve transporting samples and data to other countries where they can be processed further. After a GWAS is completed, samples and data may be stored in a central repository such as dbGAP or the European Genotype Archive, which will be accessed by other researchers. While the majority of forms (11) did mention storage for future use explicitly, only 9 mentioned the possibility of access by international researchers. To be compliant with the law, good practice would require that these two aspects of the research should be mentioned in the informed consent form for GWAS projects.

Our analysis further revealed that there is a multiplicity of approach on what research participants were told about withdrawal from research projects. This variety reveals ambiguity and uncertainty about the nature of withdrawal across research contexts, which stems from differing degrees of awareness about ethical and legal requirements on withdrawal, as well as the technological complexity that is increasingly required in implementing withdrawal options in genomics. In the UK, there is no established definition of what withdrawal should involve, nor is there standard guidance on the kind of withdrawal that would be appropriate for different types of research. This absence causes uncertainty about the nature of withdrawal across research contexts, which is arguably detrimental for the protection of participants’ rights and for the sustainability of research. It is problematic to continue to make the promise of withdrawal without developing strategies for how best to keep that promise. We suggest that there is a need to clarify the legal and ethical requirements involved in enabling withdrawal, and possible ways forward include a systematic effort to abandon one-size-fits-all approaches and instead develop tailored, detailed practices for the implementation of withdrawal in particular research contexts.

It is also questionable whether genomic information, as a rich and essentially unique source of data, could ever be considered as anything other than identifiable. If such information is not anonymous, there may be more restrictions on sharing by virtue of the duty of confidence. We believe that those who draft consent forms should be very wary of making absolute assurances of anonymity and confidentiality in relation to genomic data, as it is increasingly clear that it is difficult, if not impossible, to anonymise genomic data with complete certainty. However assurances of diligent efforts to maintain anonymity and/or confidentiality of identifiable information may be right and proper. Good practice might suggest that participants should be informed that their information may be shared outside of the research project in some circumstances. Participants should how-
ever be told that the information is shared in such a way that they are unlikely to be re-identified. If the information shared is subject to a duty of confidence, then sharing it without justification could possibly give rise to a cause of action for those participants who could prove that they were damaged as a result of such a disclosure.

Consent forms are still paper-based and thus very static, and there may be scope to look for another model, for example utilising novel information technology. The lack of uniformity in consent forms is a manifestation not only of the different legal and ethical sources but also of the differing demands of different research projects, local differences, and developments in science and technology. Although a standard template for consent forms may iron out divergences that may exist even within the same project there are many reasons why this may be inadvisable, given that it would lack the flexibility to accommodate scientific developments and local circumstances. Accompanying online information with genomics-learning activities is increasingly used in major research projects; these may be used as an educational tool to enhance understanding of the contentious issues that we have identified, which include withdrawal from research, the sharing of samples and data over borders, and anonymisation.

86 For example, the EnCoRe Project is developing IT mechanisms to allow individuals to give and revoke consent to the use of their biological samples and associated data in biobanks. Retrieved 9 May 2011 www.encore-project.info/index.html.