Obtaining informed consent for research involving tissue samples and data is the Damoclean sword for both researchers and participants. It has become the focal point of research ethics review. Over time, and strongly influenced by models of consent from clinical drug trials, core elements have been developed that form the template for most research in Canada (Box A). Protection of the interests and inclusion of children, minors and incompetent adults find expression in the clarification of the role of legal representatives and of assent mechanisms but the ambit and mechanisms involved in ratification remain unclear (Box B). Whether research is retrospective or prospective, the juxtaposition of informatics and genomics, together with the need for access to normal and affected tissues and to ongoing data (medical, phenotypic, environmental, epidemiological ...) (Box C), are posing new challenges. Issues are emerging that were not foreseen in the current guidelines governing research.¹

Indeed, the twin ethical and legal principles of autonomy and privacy are being challenged by: (1) requests for access to tissues/data collected from now deceased persons; (2) the creation of biobanks (including registries and longitudinal studies as well as surveillance for public health); (3) the need for withdrawal mechanisms; (4) an expectation that individual results should be returned to participants; and (5) benefit-sharing issues. These challenges require a rethinking of consent to research and the accompanying provisions for confidentiality.

1. Tissue and Data Collected from Deceased Persons

Are access requests to use samples and data from deceased individuals subject to health information and privacy laws? Currently, such legislation applies only to identifiable living persons.² Often the general consents signed upon admission to a hospital contain provisions concerning the use of archived samples removed during routine medical care for quality assurance programs or for “in-house” research in university hospitals with appropriate confidentiality protections. Moreover, until recently little thought was given to access to such samples and data by other researchers whether from the public or private sector. But, in the absence of explicitly “giving” one’s body for research upon death, prior, free and informed directives by patients for end-of-life decisions usually do not contain specific instructions for research purposes. In the case of incompetent adults and children, those legally mandated to provide proxy consent for medical care or for research may not have authority for the research use of samples after death. Prospective studies can obtain such prior authorization but in the absence of anonymization or a legislative provision concerning the powers of family members or authorized medical personnel in the context of research,³ this area is an ethical and legal minefield with no apparent resolution or harmonization of practice across Canada. It would be strange indeed if incineration of samples and destruction of data were to be, due to lack of clarity, the legally and ethically expedient solution rather than either double coding (see infra 7) or anonymization of the data with REB oversight.

2. Biobanks/Repositories as Resources for Future Research

Contrary to the usual trajectory of single or multicentre research protocols, or even of individual collections of samples and data that simply grow in size and purpose over time or are merged with others to create a larger cohort to answer a specific research question, modern biobanks are created as research resources. They are usually longitudinal in nature,
have specific governance structures and may serve one or more large projects comparing phenotypic and genotypic information over time as well as receive requests for access for individual research projects.

Biobanks are the focal point of many of the challenges mentioned earlier. Moreover, as just mentioned, these banks often require broad consent from donor participants to facilitate research involving their samples and data over time (see infra 6). Subject to ethics review and requiring procedural and independent governance of a more centralized nature, additional unique features of these banks also include the potential profiling of the populations or sub-populations as patterns of disease susceptibility emerge over time. Another distinction is that they are organized in a systemic way so as to be searchable and usable for validation purposes in other studies. Together, all these unique features impact the elements for obtaining consent.

First, in the context of biobanks, consent is usually broad and is preceded by a period of public consultation and engagement (see infra 6). This has led some to argue that beyond the initial informed consent to the banking of biological samples, the term used to describe agreement to future, yet unspecified uses (subject to ethics oversight) should be “authorization.” Second, the interest being societal and long term, the process usually will involve the use of coded or double-coded data (see infra 7), which allows for withdrawal (see infra 3). Third, to maintain public trust and participation, strict conditions on access and use by third parties is required. Fourth, in that same vein, ongoing communication with participants is essential to ensure that secondary uses based on authorization are authenticated via oversight mechanisms. Most of these issues are slowly being discussed and possible solutions envisaged. Yet, others including the possibility of transfer, sale, termination or even bankruptcy of the resource to say nothing of destruction are far from resolution. The longitudinal nature of biobank research requires: prior and constant communication with the public and individual participants (where so wished) in exchange for the trust that broad consent implies, a balancing of public and private interests in access to data, in resolving ownership in the case of transfer, sale or bankruptcy and in the examination of the interests and rights of future generations.

The lessons learned from the experience of registries and traditional longitudinal, epidemiological studies may prove to be instructive. They themselves are, however, under attack from new consent and personal data legislative requirements. Long accepted (if not foreseen by legislation) as a legitimate public health tool, they may no longer be exempt. Such legislation often fails to make the necessary distinction between these epidemiological tools and other research involving humans, such as clinical trials.

Likewise, unless strictly considered as included under the “statistical” data gathering powers of the State, infectious disease epidemics such as SARS exposed the lamentable lack of public health powers for ongoing surveillance. The public often presumes that such surveillance studies are ongoing as part of the duty of the State to prevent, promote and protect the health of its citizens. Obviously, even health ministries need a legislative mandate or independent review prior to waiving consent requirements for surveillance programmes. Moreover, widespread public notification of such surveillance programmes with proper confidentiality mechanisms should be a sine qua non.

3. Participant's Right to Withdraw

The primacy of consent necessarily carries with it the right of withdrawal. In clinical studies involving drugs, devices, or procedures, this is less problematic than in biobanks and impossible where samples and data are anonymized or destroyed. Such limits on withdrawal require further clarification during the consent process to ensure an understanding of their ramifications. Limited then to identifiable samples (including double-coded), withdrawal can mean that any remaining samples will be destroyed, or anonymized, or future uses of data halted. Data already included in aggregated data sets are not affected. This right can be exercised at any time during a trial or presumably, for the lifetime of a biobank or repository. In the case of the latter however, the very nature of the study presumes consent to long-term participation and follow-up. Can it be made a condition of participation that samples/data be maintained for a period of time? The only choice open to potential participants is not to enroll. Or, options can be offered but this may prove to be cumbersome and to unduly lengthen the consent form, to say nothing of the open-ended legal obligations such options may create. Advance notification of a particular approach should, at a minimum, provide information on the rationale applied and clearly state that samples and data will be kept for an extended period of time.

4. Return of Results to Participants

Whether research participants are entitled to the return of research results even when those results have no known clinical significance is a contentious issue. While there is
recognition of the need for ongoing communication of general results with participants (if so desired), and of the need to not limit such “return” to the publication of general, aggregate results in scientific journals, the return of specific, individual results is problematic, if not impossible. Research results are not clinical diagnostic results. Where such an option is offered, it is important to not be misleading in order not to raise false hopes or to communicate information that is not understandable or creates confusion or fear. Usually the return of specific, individual results is limited to situations where the results are scientifically validated and of clinical significance and some form of prevention or treatment of the condition in question is available. Even then it is probably preferable to communicate such results to the treating physician to ensure appropriate counselling.11

5. Benefit-Sharing

The concept of benefit-sharing arose in the arena of non-human biological diversity. It formally transposed to human genetic research by the HUGO Ethics Committee (2000) Statement on Benefit-Sharing12 and has been extended to international clinical trials. Traditionally, publication of results was seen as a form of benefit-sharing. Increasing commercialization has led some to argue that benefit-sharing should be a percentage of financial return on eventual net profits following successful patenting to all the populations or communities involved, or a contribution to the health care infrastructure that made it possible. Benefit-sharing is much broader than financial return. It may include a whole host of other things, including knowledge sharing, infrastructure development, and capacity building.13 At a minimum, benefit-sharing demands that there be some form of information prior to participation and also recognition of participation. Even where the potential for patenting exists, exemption for research uses and the requirement of non-exclusive licensing have been suggested as a means of balancing public and private interests so as to ensure that the benefits are broadly accessible for further use and improvement.

6. Consent

What emerges then from this brief overview of consent revisited is not only the addition of biobank issues but also of the use of tissues and data from deceased persons, benefit-sharing, the development of the duty to return results, and a new typology of consent terminology or mechanisms such as broad consent and authorization. Possible foreseeable future uses should be described insofar as possible and be consistent with the overall aims of the bank. Furthermore, the notion of a waiver of consent by REB’s for anonymized, surveillance studies or even double-coded studies is resurfacing in the context of discussion of what is minimal risk, impracticability and unreasonableness.14 While the issue of waiver of information in the clinical setting is a decision between physician and patient, it is doubtful whether a research participant can legally waive his or her right to information.

It is my opinion that broad consent to longitudinal studies, with authorization for future studies together with the protections of ethics review, ongoing communication of the project and the communication of general results is not a waiver of informed consent. It is a form of consent that is true to the very nature of biobanks. Furthermore, if these protections are met, re-consent is not necessary unless the REB considers, for example, that the proposed secondary research deviates from the original goals of the biobank. Finally, in addition to consent with authorization for future uses, there remains the option of simple notification with the possibility of opting out. This is usually limited to situations where the research envisaged is in conformity with the known mission of an institution or programme (i.e. teaching or educational purposes in university hospitals or for quality assurance). Notification with no opting out should be reserved for public health purposes and subject to legislative mandate.

7. Confidentiality

Obviously, the level of consent required is directly proportional to the degree of confidentiality that is offered to research participants. In hypothesis-driven research such as clinical trials or candidate gene hunting, risks to confidentiality are greater and the nature and risks of the study itself mandate being able to trace the participant if so desired. In contrast, anonymization, irresponsibly de-identifies the data in such a way that there can be no tracing of the individual.15 The long term viability and scientific usefulness of biobanks
requires some form of data linkage. Double coding has emerged as a tool that allows for withdrawal and promotes confidentiality and ongoing research. It involves a single code put on the initial data and samples being replaced by a second code by a data custodian before being sent out to another researcher for secondary uses consistent with the initial consent. The researcher can return relevant research data to the custodian who in turn can inform the clinician for improved patient care. The clinician can also continue to download clinical data to the custodian to enhance research outcomes. It is my opinion that this maximum protection of double-coding with a third party keyholder — a “fiduciary” or “data steward” — offers adequate safeguards in the case of broad consent for longitudinal studies, provided there is independent ethics review and governance of such projects.

Conclusions

It is my opinion that underlying the ongoing debate on a form of “consent” that respects confidentiality and autonomy in the research setting is the very societal nature of the novel directions taken by public resources or infrastructures such as biobanks. For a decade there has been tension between the reification and sacralization of human tissue and accompanying data. As exemplified by the “grid,” the increasing complexity of choices and issues, and the legalistic nature of informed “choice” and the consent “process” could undermine the very act of communication and consensualism so necessary to ethically sound research. Moreover, in the future, can truly public resources and infrastructures such as population biobanks, be built to gird a universal health care system — one that promotes open access where the applicable norms are extrapolated only from personal data or health information legislation? The latter presumes that personal privacy is inimical to participating as a citizen in the public interest. In revisiting consent, researchers should not only consider the issues raised in the grid set out below but also the challenges they pose to mindsets forged by the polarization of setting up consent and confidentiality barriers for individuals that impede their participation as citizens in society for the benefit of others, including future “others” without an explicit consent in every case.

Bartha Maria Knoppers is a Professor and Senior Researcher at the Université de Montréal Law Faculty, Centre de recherche en droit public (CRDP). The author wishes to thank Lori Sheremeta, Timothy Caulfield and Mylène Deschènes for their invaluable contribution to this paper.

This research was funded in part by the CIHR (Christian Dechepper, MD, Laboratory Director, Clinical Research Institute of Montreal (IRCM) under CIHR grant #NFD-62300), Genome Quebec/Genome Canada /Genome Prairie.

2. An Act Respecting Health Services and Social Services, R.S.Q. S-4.2 s. 23 “The heirs, legatees by particular title and legal representatives of a deceased user are entitled to be given communication of information contained in his record to the extent that such communication is necessary for the exercise of their rights in such capacity. The same applies to the person entitled to the payment of a benefit under an insurance policy on the life of the user or under a pension plan of the user. The spouse, ascendants or direct descendants of a deceased user are entitled to be given communication of information relating to the cause of death of the user, unless the deceased user entered in writing in his record his refusal to grant such right of access. Notwithstanding the second paragraph, persons related by blood to a deceased user may be given communication of information contained in his record to the extent that such communication is necessary to verify the existence of a genetic or hereditary disease.”
3. An Act Respecting Health Services and Social Services, R.S.Q. S-4.2 s.19.2 “Notwithstanding section 19, the director of professional services of an institution or, if there is no such director, the executive director may authorize a professional to examine the record of a user for study, teaching or research purposes without the user’s consent.”


Grid: Research Involving Humans (Data/Samples)
B.M. Knoppers

A. Consent: Core Elements
- Names of Researchers
- Sponsors/Collaborators
- Description of the Project
- Objectives
- Length of Project/Conservation
- Risks/Harms (psych./physical econ./social) (indiv./collective)
- Benefits (personal/social future)
- Confid. Mechanisms/Access
- Secondary Uses
- Data Linkage
- Commercialization
- Return of Results/"Right" Not to Know
- Right of Withdrawal
- Compensation
- Person to call/Gen’l Info.

B. Children
Minors/Incompetent Adults
- Legal Representation
- Assent
- Ratification?

C. Samples/Data
- Restrospective/Prospective
- Archived (Medical Care)
- Archived (Research)
- Living/Dead Indiv.

1. Deceased Persons
- Expressed Wishes
- Access by Family Members
- Confid. Mechanisms
- Secondary Uses

2. Biobanks/Repositories
- Public Engagement
- Broad Consent/Authorization
- Longitudinal/Surveillance
- Coding/Anonymization
- Labelling of Pop.
- Access/Use
- Database
- Ongoing Communication Mechanisms
- Future Generations?
- Transfer/Sale/Termination
- Audit/Governance

3. Withdrawal
- Identifiable
- Destruction
- Anonymization

4. Return of Results
- General
- Specific
- When?
- To whom?

5. Benefit-Sharing
- Transparency/Negative Results
- General/Specific Results
- Communities/Pub/Health Care Systems
- Long/term Benefits
- Non-exclusive licensing

6. Consent
- Specific
- Re-consent
- Broad consent
- Presumed
- Notific/Opting Out
- REB Waiver

7. Confidentiality
- Identified
- Coded/Double-Coded
- Anonymization

* Verify that your protocol is in accordance with applicable provincial and national legislation.