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Short report

"Broad" consent, exceptions to consent and the question of using biological samples for research purposes different from the initial collection purpose

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ABSTRACT

An important ethical issue regarding biological samples stored in biobanks is unforeseen future sample use, when no or limited subject consent is obtained. Biobanks of biological samples have significant future research potential, but may cause conflicts of interest regarding the consent obtained. Indeed, ethics, deontology, and jurisprudence generally advise that consent must be specific and circumstantiated. However, it is not possible to foresee all of the future circumstances in which the samples might be useful, nor is it possible to re-contact all subjects in order to gain consent for a new use. The main arguments for the use of "broad" consent are presented with a brief discussion of the conditions where it may be legitimate not to obtain consent. Particular attention is given to the expressed positions of national and international bioethics bodies.

Introduction

An important ethical issue regarding biological samples stored in biobanks is unforeseen future sample use, when no or limited subject consent is obtained (Giroux, 2007; Greely, 1999). Informed consent is ethically important to protect patients' interests, protect the confidentiality of personal information, ensure subject autonomy, define research and social interests in the general advancement of knowledge, and maintain public trust in researchers and institutions. Broad informed consent expands informed consent by allowing sample use in unforeseen future studies. Although there are several authoritative reviews of the peer reviewed literature regarding informed consent (Dupont, 2008; Elger, Biller-Andorno, Mauron, & Capron, 2008; Weir & Olick, 2004), there has been no formal analysis of the impact on the breadth of informed consent made by the published opinions of national bioethics committees of European and other nations (Petrini (in press) lists relevant opinions). This paper will review problems that arise when using samples for unforeseen purposes, describe ethical guidelines published by national bioethics committees that favor a broad interpretation of consent for sample use, and discuss exceptions to the need for consent. The author's proposals for ethically consistent broad consent will be compared to the published opinions of national bioethics committees. Finally, recommendations will be proposed for conditions in which broad interpretation of subject consent are acceptable.

The problem of using samples for initially unforeseen studies

Many samples stored in biobanks are collected in non-standard situations, where an awareness of the need to meticulously handle information and obtain consent is lacking. The issue of the permissibility of sample use therefore arises when the samples have been stored without the consent of the subject or with very broad consent for future uses (Greely, 1999). The problem for the potential use of the samples is widely noted and confronted in differently. Knoppers (2005) states "legal comparisons between regulations in different countries are laborious and defy generalizations" (Van Veen, 2006). When previously collected samples are used for unforeseen research purposes, various needs (sometimes conflicting) become apparent, including the confidentiality of personal information, subject autonomy, and research and social interests in the general advancement of knowledge, and maintaining the public's trust in researchers and institutions. These problems are recurrent in health research (Lako, 1986).

The practical difficulty is evident. Often, particularly when a significant time has elapsed between the collection of the sample and its potential use, it is extremely arduous or impossible to re-contact the subjects. Additionally, the choice, which best respects individual rights (i.e., using only samples for which a new informed consent is obtained from the subject), could considerably diminish the validity of a scientific study by introducing bias into the selection process.

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The obvious solution, which would not preclude the possibility of future research, might be to obtain a "broad" consent from all donor subjects. Broad consent is not universally acceptable. Multiple proposals review intermediate positions between the two extremes, from specific consent for an individual study to broad consent for potential future studies (Shickle, 2006).

Two main, general arguments justify the use of broad consent (Clayton, 2005). The first is that it is often very difficult or impossible to obtain consent for subsequent studies using previously collected biological samples. The second is the extremely small or entirely nonexistent risks to the donor subjects. Supporters of broad consent additionally refer to cases in which possible further contact might be inopportune or even harmful to the subject, due to personal or family situations. The major arguments against broad consent, on the other hand, appeal to a generic risk of undermining the meaning of consent, which by its nature presupposes precise information (Clayton et al., 1995).

Examples of institutions and laws favoring broad consent

"Broad" ("open", "blanket" or "generic") consent has been proposed authoritatively. The World Health Organization (1998, p. 13) considers it "the most efficient and economical approach". The Human Genome Organisation ethics committee (2002), the Commission of European Communities (2004), and the national bioethics committees of various countries, including the Danish Council of Ethics (1996), the French National Consultative Ethics Committee for Health and Life Sciences (2003), and the German National Ethics Council (2004), share this position.

The broad consent approach appears to conform to the Council of Europe's Convention on Human Rights and Biomedicine (Council of Europe, 1996a), in particular with point 137 of the Explanatory Report (Council of Europe, 1996b), where the use of biological samples without the subject's consent is allowed under certain conditions. The Council of Europe has confirmed this position (Council of Europe, 2006).

The Danish Council of Ethics is a representative example of national bioethics committee position that is particularly open to broad consent regarding biobanks. The *Health Science Information Banks – Biobanks* guidelines state specifically, "Common to these biological banks is the fact that, once approval has been obtained from the scientific ethical committee system and in special cases from the individual patients, the material collected is sometimes used for some purpose other than that intended when the material was collected" (Danish Council of Ethics, 1996, chap. 3). Further (chap. 4), "Information or material from a biobank can be passed on to, say, a new storage site with other potential applications". The Council clearly states that specific consent precisely indicating the intended uses of the material is not necessary for new use. Rather, it is sufficient to inform the subject of this possibility at the beginning. The guidelines also state (chap. 6),"By means of general written information, the individual patient should be informed that samples, given for diagnostic use may possibly be included in a biobank at a later juncture and used in a teaching context, research and so on".

The Danish Council's position raises concerns. The general principles of the primary international documents require explicit consent for each specific use and consider generic consent for hypothetical and unspecified uses to be insufficient. In contrast, the Danish Council of Ethics maintains that a subject's consent may not be necessary for the use of samples "for some other purpose" different from the original purpose, or for the transfer of the samples to other centers or to research projects different from the original. Inherently, restricting the use of samples to within the center where the samples were originally collected serves to reduce the ethical concerns of violating informed consent. Nevertheless, sharing of samples between institutions offers definite research benefits, assuming that viable policies are in place to protect informed consent. The document *Raccolta di campioni biologici a fini di ricerca: consenso informato* (*Collection of biological samples for research purposes: informed consent*) (Gruppo Misto, 2009), which was produced by the Italian Joint Commission, National Bioethics Committee—National Biosafety, Biotechnology and Life Sciences, contains a standardized consent form that can be used by different centers. This document protects informed consent by clarifying the conditions for the use of the samples and for the transfer of samples between centers.

The Spanish Law on Biomedical Research (Rey de España, 2007) has elicited interest beyond its national borders. Chap. 4 explicitly provides for the possibility of broad consent. The preamble specifies that the legislative framework focus on donor consent and on information that must be provided to donors in order to guarantee valid consent. The duty to protect single individuals is affirmed, but there is also an insistence that the demands of modern research, which has passed from the age of genetics to genomics and now post-genomics, be met. The law proposes a "flexible, intermediate" compromise between specific consent and open consent. During the initial consent, a subject may express consent for later research that is "related to the originally proposed research." Further, a different research team may carry out the later research than the one that initially collected the sample. It does not specify the relationship between the initial and later research.

The law also contains provisions for the use, for scientific purposes, of samples before the law's enactment. In such cases, the samples may be used if one of the following conditions is met: (1) the subject expressed consent; (2) the samples are anonymous; (3) consent is lacking, but obtaining consent involves an "unreasonable effort" (defined in article 3.i as "disproportionate waste of time, work or other costs"); or (4) the subject is deceased or unreachable. If one condition is met, approval from the competent ethics committee must be obtained. The committee must determine that (1) the research is of general interest; (2) the lack of data would make the research impossible or less efficacious; (3) there is no explicit objection to the research; and (4) the confidentiality of individual information is safeguarded.

Exceptions to consent

Generic consent permitting any research at all is considered unacceptable, not only by this author, but by bioethicists and bioethics committees throughout the world. Informed consent, a "prima facie" duty, is linked directly to the principle of autonomy. Ross (1939) defined "prima facie" duties as binding in all circumstances unless they conflict with duties of equal importance in a given concrete situation. In such a scenario, one should look to the "actual" duties to be fulfilled, which are derived from a balancing of the "prima facie" duties in the limited context of the specific case. Beauchamp and Childress (2001) state the conditions that justify "balancing" values and violating "prima facie" duties are: (1) there must be a realistic possibility of achieving the moral objective, (2) there can be no morally preferable alternatives to the violation of the "prima facie" duty in the specific circumstances, (3) the duty violation must be the smallest possible violation necessary for reaching the objective, and (4) the effects of the violation must be minimized.

The United States Code of Federal Regulations (Department of Health and Human Services, National Institutes of Health and Office for Human Protection, 1998), the informed consent requirement for research on biological materials may be waived if four criteria are met: (1) The research involves minimal risk to the subjects, (2) The

rights and welfare of the subjects are not adversely affected by the waiver, (3) The research could not be practicably conducted without the waiver, and (4) When appropriate, the subjects are provided with additional information about the research. Meisel (1979) identifies four categories of exceptions to the informed consent requirement: emergency, incompetence, waiver, and therapeutic privilege. First, in dangerous situations such as emergencies, a subject is considered temporarily unable to express consent and action can be taken under the assumption that the subject would provide consent if able to. This is an unlikely situation for biobanks. Second, the situation in which subjects who are incapable of expressing consent often arises during the collection, preservation, and use of biological samples. In "opt-in" systems, subjects incapable of expressing consent are generally excluded unless a legal representative provides valid consent. "Opt-out" systems, on the other hand, are more ethically problematic because they assume the subject understands the information, freely chooses, and takes action if he does not want to participate (Johnsson, Hansson, Eriksson, & Helgesson, 2008a, 2008b; Laurie, 2008). The third exception, waiver, does not constitute a violation of autonomy. Dworkin (1989) writes, "if a patient has knowingly and freely requested […] that he not be informed or consulted about his course of treatment then to seek to obtain informed consent would itself be a violation of autonomy". The fourth exception, "therapeutic privilege", is similar to waiver, but with a fundamental difference. The decision is made not by the subject, but by a third party who considers providing and asking information harmful to subject. Conflicts may arise if the subject's wishes and the third party's beliefs regarding the subject's best interest differ.

According to Hansson, Dillner, Bartram, Carlson, and Helgeson (2006), broad consent preserves autonomy so long as three conditions are met: (1) personal data are treated confidentially, (2) donors are guaranteed the right to withdraw consent, and (3) new studies are approved by an ethics committee. Doyal (1997) describes three arguments against informed consent, which he maintains are inadequate and paternalistic. First, an excess of information about the purpose, methods and risks can generate unnecessary concerns. Secondly, informed consent, while certainly necessary when subjects are exposed to considerable risks, may be unnecessary when the risk is negligible, especially if obtaining informed consent could diminish the methodological rigor of the protocol. Finally, the advancement of communal knowledge could be slowed unacceptably by excessive emphasis on individual rights. According to Doyal, ethics committees could authorize studies without informed consent in three situations: (1) studies with subjects who are incapable of expressing consent assuming certain requirements, (2) studies using only previously recorded clinical data, and (3) anonymously collected samples. Consent must be obtained in studies on the genetic predisposition to illness where the material is incompletely anonymous and where a possibility exists of contacting the subjects.

Helgesson, Dillner, Carlson, Bartram, and Hansson (2007) propose that genetic analysis on identifiable samples is acceptable without new consent so long as "the study is not particularly sensitive, and on the condition that (i) strict coding procedures are maintained, (ii) secrecy laws apply to any handling of sensitive information and, (iii) vital research interests are at stake." Thus, research on biological materials without informed consent and under certain conditions is in accord with article 137 of the Explanatory Report to the Convention on Human Rights and Biomedicine (Council of Europe, 1996a, 1996b). There is fierce debate (Lwoff, 2008), however. Some authors have contested the interpretation of Helgesson et al. (2007) of the Council of Europe's position because of risks and ambiguities (i.e., the vagueness of the expression "particularly sensitive") and that the proposal may be "detrimental […] on public trust in biomedical research" (Helgesson, 2008; Hofmann, 2008).

According to Regidor (2004), there are moral justifications "for using personal data without informed consent, from both medical records and biological materials, in research where subjects are not physically present in the study and will never have any contact with the study investigators." Regidor outlines "several misconceptions that form the basis" for "ethical restrictions on the use of personal data in most western countries". These include "the assumption of a deterministic model of disease causation in which the prediction of disease occurrence is based on a genetic association despite the fact that most genotypes for common disease are incompletely penetrant […], and the great lack of knowledge about research methodology revealed in some alternatives proposed to avoid using personal data", etc. Although Regidor's arguments stir interesting debate, some are questionable. For example, the author claims that the Declaration of Helsinki (World Medical Association, 1964–2008) recommends, "That only research that offers some benefit to study subjects is justified." However, others conclude the Declaration does not exclude *a priori* the possibility of pursuing research with "social" interest (Williams, 2008).

Conclusions

In circumstances, such as large-scale sample collections involving hundreds of thousands to millions of samples and associated data, it is impossible to contact each subject prior to each new data use. Further, additional contact with the subjects might disturb or cause unjustified concerns. The UK Human Genetics Commission (2000), for example, found many patients explicitly do not wish to be re-contacted for such consent. Contacting subjects for every new project also limits the usefulness of large-scale population databases. Nonetheless, multiple factors must be considered to determine whether re-contacting donors is appropriate, including the practicality of making contact, the nature of the study, the possible consequences for the re-contacted subject, etc.

In the author's opinion, generic consent permitting all research is certainly unacceptable. A potential solution is formulating the consent to refer to a particular "type" of research, as precisely specified as possible, and conducted in the center holding the sample. This ensures the consent is valid and the sample preserved beyond a particular study so that further similar studies on the same topic are possible later. Therefore, broad consent may be acceptable under the following conditions.

(1) Adequate sample coding procedures are employed.
(2) Adequate procedures for personal data protection are employed.
(3) The importance of the research aim is sufficient to justify conducting the study and is evaluated on a case-by-case basis by an ethics committee.
(4) The sensitivity of the data is evaluated on a case-by-case basis. Genetic information varies in sensitivity based on its significance, ranging from very stringent protection to a lesser degree of protection.
(5) Generic research results are always released without specifically identification of individual subjects.
(6) "Opt-out" consent is allowed for subsequent or secondary studies. Every subject must be guaranteed the possibility of withdrawing consent at any time.
(7) Participants must have adequate means of involvement, such as encouraging participant consultation or communicating information through the mass media prior to project initiation. The multiple modes of involvement should be complementary

as opposed to mutually exclusive. It is especially important that forms of direct participation also be available, for example by having population representatives serve on the ethics committees that will decide on the approval of the research before it begins.

(8) Measures to ensure transparency and supervision must be in place. Adequate supervisory, procedural, and technical systems are necessary to guarantee information protection. Further, it is highly advisable to have external and independent supervisory bodies monitoring procedural correctness.

In conclusion, "broad consent" is not like signing a blank check. Consent, even though it might not indicate a specific study, must nonetheless indicate the type of study that can be conducted legitimately.

References

Beauchamp, T., & Childress, J. F. (2001). *Principles of biomedical ethics*. (1st ed.: 1979) (5th ed.). Oxford and New York: Oxford University Press.

Clayton, E. W. (2005). Informed consent and biobanks. *Journal of Law Medicine & Ethics, 33*(1), 15–21.

Clayton, E. W., Steinberg, K. K., Khoury, M. J., Thomson, E. J., Andrews, L. B., Khan, E., et al. (1995). Informed consent for genetic research on stored tissue samples. *JAMA, 274*(22), 1786–1792.

Commission of European Communities. (2004). Ethical, legal and social aspects of genetic testing: research, development and clinical applications. Conference on the ethical, legal and social aspects of genetic testing, 6–7 May 2004, Brussels. Available from http://europa.eu.int/comm/research/conferences/2004/genetic/pdf/report_en.pdf.

Council of Europe. (1996a). *Convention for the protection of human rights and the dignity of the human being with regards to the application of biology and medicine: Convention on human rights and biomedicine*. DIR/JUR (96)14. Strasbourg: Directorate of Legal Affairs. Available from http://conventions.coe.int/treaty/en/treaties/html/164.htm.

Council of Europe. (1996b). *Convention for the protection of human rights and the dignity of the human being with regards to the application of biology and medicine: Convention on human rights and biomedicine. Explanatory report*. Council of Europe. Available from http://conventions.coe.int/Treaty/EN/Reports/Html/164.htm.

Council of Europe. (2006). *Recommendation Rec. (2006) 4 of the Committee of Ministers to Member States on research on biological materials of human origins*. Council of Europe. Available from http://www.coe.int/t/e/legal_affairs/legal_cooperation/bioethics/texts_and_documents/Rec_2006_4.pdf.

Danish Council of Ethics [Det Etiske Rad]. (1996). *Health science information banks – Biobanks*. Danish Council of Ethics. Available from http://www.etiskraad.dk.

Doyal, L. (1997). Informed consent in medical research: journals should not publish research to which patients have not given fully informed consent – with three exceptions. *British Medical Journal, 314*(7087), 1107–1111.

Dupont, F. (2008). *Recueillir, conserver et utiliser des échantillons biologiques humains à l'hôpital*. Ruel-Malmaison: Doin Editeurs/Éditions Lamarre.

Dworkin, G. (1989). *The theory and practice of autonomy*. Cambridge: Cambridge University Press. p. 118.

Elger, B., Biller-Andorno, N., Mauron, A., & Capron, A. M. (Eds.). (2008). *Ethical issues in governing biobanks*. Aldershot: Ashgate.

French National Consultative Ethics Committee for Health and Life Sciences [Comité Consultatif National d'Éthique pour les Sciences de la Vie et de la Santé]. (2003). *Opinion n. 77. Ethical issues raised by collections of biological material and associated information data: "Biobanks", "biolibraries"*. French National Consultative Ethics Committee for Health and Life Sciences. Available from http://www.ccne-ethique.fr/docs/en/avis077.pdf.

German National Ethics Council [Nationaler Ethikrat]. (2004). *Biobanks for research*. German National Ethics Council. Available from http://www.ethikrat.org/_english/publications/opinion_biobanks-for-research.pdf.

Giroux, M. T. (2007). L'utilisation secondaire du don à des fins de recherche: du consentement spécifique au consentement général. In C. Hervé, B. M. Knoppers, P. A. Molinari, & M. A. Grimaud (Eds.), *Systemes de Santé et circulation de l'information. Encadrement éthique et juridique* (pp. 29–41). Paris: Dalloz.

Greely, H. T. (1999). Breaking the stalemate: a prospective regulatory framework for unforeseen research uses of human tissue samples and health information. *Wake Forest Law Review, 34*(3), 737–766.

Gruppo Misto Comitato Nazionale per la Bioetica – Comitato Nazionale per la Biosicurezza, le Biotecnologie e le Scienze della Vita (Italian Joint Commission National Bioethics Committee – National Biosafety, Biotechnology and Life Sciences). (2008). *Raccolta di campioni biologici a fini di ricerca: consenso informato*. [*Collection of biological samples for research purposes: Informed consent*]. Italian Joint Commission National Bioethics Committee – National Biosafety, Biotechnology and Life Sciences. Avaliable from http://www.governo.it/biotecnologie/documenti/Consenso_Informato_allegato_Petrini_2009.pdf.

Hansson, M. G., Dillner, J., Bartram, C. R., Carlson, J. A., & Helgeson, G. (2006). Should donors be allowed to give broad consent to future biobank research? *Lancet Oncology, 7*(2), 266–269.

Helgesson, G. (2008). Reply to bypassing consent for research on biological material. *Nature Biotechnology, 26*(9), 980–981.

Helgesson, G., Dillner, J., Carlson, J., Bartram, C. R., & Hansson, M. G. (2007). Ethical framework for previously collected biobank samples. *Nature Biotechnology, 25*, 973–976.

Hofmann, B. M. (2008). Bypassing consent for research on biological material. *Nature Biotechnology, 26*(9), 979–980.

Human Genetics Commission. (2000). *Inside information. Balancing interests in the use of personal genetic data*. London: Human Genetics Commission. Par. 5.17. Summary document. Available from http://www.hgc.gov.uk/client/document.asp?docid=19.

Human Genome Organisation (HUGO). (2002). *Statement on human genomic databases*. Human Genome Organisation. Available from http://www.hugo-international.org/img/genomic_2002.pdf.

Johnsson, L., Hansson, M. G., Eriksson, S., & Helgesson, G. (2008a). Patients' refusal to consent to storage and use of samples in Swedish biobanks: cross sectional study. *British Medical Journal, 337*, a345.

Johnsson, L., Hansson, M. G., Eriksson, S., & Helgesson, G. (2008b). Opt-out from biobanks better respects patients' autonomy. *British Medical Journal, 337*, a1580.

Knoppers, B. M. (2005). Biobanking: international norms. *Journal of Law, Medicine & Ethics, 33*(1), 7–14.

Lako, C. J. (1986). Privacy protection and population-based health research. *Social Science & Medicine, 23*(2), 293–295.

Laurie, G. (2008). Evidence of support for biobanking practices. *British Medical Journal, 337*, a337.

Lwoff, L. (2008). Ethics of research on human biological materials. *Nature Biotechology, 26*(1), 29–30.

Meisel, A. (1979). The 'exceptions' to the informed consent doctrine: striking a balance between competing values in medical decision-making. *Wisconsin Law Review, 2*, 423–488.

Petrini C. A bibliography concerning informed consent and biobanking: documents from national and international bodies. *International Journal of Bioethics*. *Journal International de Bioéthique*, in press.

Regidor, E. (2004). The use of personal data from medical records and biological materials: ethical perspectives and the basis for legal restrictions in health research. *Social Science & Medicine, 59*(9), 1975–1984.

Rey de España. (4 Julio 2007). Ley 147/2007, de 3 Julio, de investigación biomedical. *Boletin Oficíal del Estado, 159*, 28826–28828.

Ross, W. D. (1939). *The foundations of ethics*. Oxford: Clarendon Press.

Shickle, D. (2006). The consent problem within DNA biobanks. *Studies in History and Philosophy of Biological and Biomedical Research, 37*, 503–519.

Department of Health and Human Services, National Institutes of Health and Office for Human Protection. (1998). *Code of Federal Regulations. Title 45. Public welfare. Part 46, 45 CFR 46. Protection of human subjects. Revised November 13, 2001. Effective December 13, 2001*. USA: Department of Health and Human Services, National Institutes of Health and Office for Human Protection.

Van Veen, E. B. (2006). Human tissue bank regulations. *Nature Biotechnology, 24*(5), 496–497.

Weir, R. F., & Olick, R. S. (2004). *The stored tissue issues – Biomedical research, and law in the era of genomic medicine*. Oxford: New Roy.

Williams, J. R. (2008). The declaration of Helsinki and public health. *Bulletin of the WHO, 86*(8), 650–652.

World Health Organization, Human Genetic Programme. (1998). *Proposed international guidelines on ethical issues in medical genetics and genetics services*. Geneva: World Health Organization.

World Medical Association. (1964–2008). *Declaration of Helsinki. Ethical principles for medical research involving human subjects*. World Medical Association. Available from www.wma.net/e/policy/b3.htm.