Ethical, Legal and Social Issues

Essentials of Genomics and Bioinformatics
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17 Ethical Aspects of Genome Research and Banking

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1 Introduction

Genetic research is increasingly used to cover a wide range of research activities. These activities extend from classical research into diseases following Mendelian patterns, to the search for genetic risk factors in common diseases, to the more recent interest in pharmacogenomics and finally, to the actual need for studies of normal genetic variation across entire populations. This all encompassing nature of the term genetic research would not be so problematic were it not for the fact that corresponding distinctions (if necessary) may not in fact be applied in the ethical norms applied to evaluate such research. In order to address this issue, we need to understand the ethical aspects of the different types of genetic research. Beginning then with a cursory overview of the types of genetic research (Sect. 2), we will then proceed to an introduction to the ethics norms of research in general (Sect. 3), before analyzing their further elaboration in the area of genetic research (Sect. 4). Particular attention will then be paid to the problems raised by DNA banking (Sect. 5), with the conclusion focussing on the issue of ownership of the samples in an increasingly commercial environment (Sect. 6). Finally, the term "banking" will be used to cover all stored tissue samples used in genetic research whether obtained following medical care or specifically for research.

2 Types of Genetic Research

Incredible progress has been achieved in our ability to discover and develop diagnostic tests for hereditary, single gene disorders with calculable mathematical precision to say nothing of a known degree of morbidity and mortality. The same progress has not been made in the treatment of these conditions. They are, however, prime candidates for gene therapy research. Often inherited not only through families but also following racial and ethnic lines, these latter features together with the quasi-certainty of expression have led to the development of ethical guidelines and legislation sensitive to both potential discrimination and to the possibility of stigmatization by association (COLLINS, 1999) (see Sect. 4).

Understanding of the role of genetic factors in common conditions such as, e.g., hypertension, cancer, and diabetes is more complex. Other than perhaps certain rare forms of these conditions that follow familial patterns, their expression is often determined by the interplay of environmental, socioeconomic, cultural and other influences. This poses interdisciplinary challenges for ethics review to say nothing of determining the appropriateness of legislation in this area.

Pharmacogenomics is seeking to understand the role of genetic variation (polymorphisms) in individual response (e.g., toxicity, efficacy, dosage, etc.) and requires the expansion of epidemiology studies to entire populations (whether ill, at-risk, or, not) so as to establish normal, genetic diversity. While anthropological, demographic and surveillance research was hitherto free from "genetic" taint, the same is not true of the study of population genetics. Interestingly most population studies of genetic variation do not require personal, identifying medical information but rather seek to use anonymized DNA samples (ROSES, 2000) (see Sect. 5).

Across this spectrum then, from certainty, to probabilistic percentages in common diseases, to individualized susceptibility, to the anonymized sample, the possibility of applying uniform ethical criteria is unlikely. The same difficulties may not be present, however, in the application of the larger ethical framework governing biomedical research generally.

3 Research Ethics

The existence of a myriad of rules of conduct concerning the protection of human research subjects has prompted the National Bioethics Advisory Committee (NBAC of the United States) to make international harmonization a priority (3rd Global Summit of Na-

tional Bioethics Commissions, Imperial College, London/England, Sept. 20–21, 2000). Globalization, the explosion of new technologies, the North–South divide, sensitivity to differing cultural and religious worldviews and to the lessons learned from the biodiversity debate, make such harmonization difficult but not impossible. The real test may well be that of ensuring that not only the public sector but also the private sector (which is the largest source of funding), abide by such a future international approach. The other challenge relates to an endemic problem, that of proper, ongoing oversight.

Following the adoption of the *Nuremberg Code* (1946–1949) and later of the *Helsinki Declaration* (World Medical Association, 1964, 1975, 1983, 1989, 1996, 2000), the main tenets of research ethics are both integrated into the biomedical world and yet evolving. The most common elements include respect for privacy and autonomy through the process of informed consent and choice, the right to withdraw, and the protection of the vulnerable.

The last decade has seen the emergence of new issues and additional elements such as: community consent, commercialization, statutory regulation of clinical trials, benefit-sharing, inclusiveness, and equitable access to research trials and benefits. There is also a much greater specificity in that particular areas or groups of persons are singled out such as those suffering from mental disorders, HIV/AIDS, and the disabled. Moreover, frameworks are being or have been developed for particular areas such as organ transplantation, reproductive technologies, or tissue banking, to name but a few (Le Bris et al., 1997).

The adoption of the European *Convention on Biomedicine and Human Rights* (Council of Europe, 1997) illustrates the difficulty, however, of finding common principles and positions when technologies are already well entrenched and different countries have adopted legislation. For example, no agreement could be reached in the *Convention* on embryo research, an area where guidance is again required now that stem cell and therapeutic cloning techniques are offering new breakthroughs. Indeed, September 7, 2000, the European Parliament narrowly passed a resolution (237 vs. 230 votes with 43 abstentions) condemning the deliberate creation of embryos for therapeutic cloning (European Parliament, 2000). If this difficulty in finding consensus continues, the same will hold no doubt in the actual and future elaboration of the specific procedural protocols pursuant to the *Convention.*

The *Convention* is notable, however, in its broadening of the inclusion criteria governing incompetent adults and children. Indeed, rather than excluding them from biomedical research in the absence of direct benefit, the *Convention* would permit inclusion with the consent of the legal representative even if the benefits were only indirect, that is, for persons of the same age or condition (art. 17). This evolution in biomedical ethics bears examination in the field of bioethics and genetics (Le Bris et al., 1997).

4 "Genethics"

At the international level, UNESCO adopted the *Universal Declaration on the Human Genome and Human Rights* in 1997 (United Nations Educational, Scientific and Cultural Organization, 1997). The *Declaration* is prospective in nature and embraces the concepts of human dignity and diversity of the genome as the common heritage of humanity, of non-commodification, of the need for international solidarity, and of concern over technologies such as germ-line interventions that could affect future generations (art. 24). It specifically prohibits human reproductive cloning (art. 11). This *Declaration* then, comes at the beginning of a technology and hopefully will serve to prospectively guide national approaches, thus ensuring a minimum of harmonization.

Also anticipatory in nature and 10 years in the making, the 1998 European *Directive on the Legal Protection of Biotechnological Inventions* (Council of the European Union, 1998) is not only a clarification (if not ratification) of existing trends but also innovates. The *Directive* reaffirms the non-patentability of human genes in their natural state and under the umbrella of public policy (an ethical filter also found in the *European Patent Conven-*

tion) prohibits techniques such as human cloning and germ-line intervention [art. 5(2)]. The preamble ("recital"), while not having legal force, is the first legal instrument to require that a patent application for an invention using human biological material must be "from a person who has had the opportunity of expressing [a] free and informed consent thereto, in accordance with national law" (para. 26). This means that at a minimum, participants in genetic research and banking must be notified of the possibility of eventual commercialization. In the absence of "national law", however, its impact will be weakened.

It is interesting to note that both international and regional instruments are strengthening barriers to access by third parties (e.g., insurers and employers). Notable in this regard is the European *Convention on Human Rights and Biomedicine* (Council of Europe, 1997) mentioned earlier which in limiting genetic testing to health purposes (art. 12) effectively limits requests for testing by insurers and employers.

A significant development is the creation of both a right not to know under the *Convention on Human Rights and Biomedicine* [art. 10(2)], and yet, a new exception for professional disclosure to at-risk family members for serious or preventable conditions where the patient or research participant refuses to do so. This is the position of the 1997 *Proposed International Guidelines* of WHO (World Health Organization, 1997), of the 1998 HUGO *Statement on DNA Sampling: Control and Access* (Human Genome Organisation, 1999a) and of the European Society of Human Genetics (2000). This is interesting in the banking context since ongoing access to banked samples (unless anonymized) could create a similar ongoing obligation for the researcher-banker as new tests become available.

Finally, another change in international "genethics" is the attempt to move away from traditional, categorical, wholesale prohibitions in the area of cloning and germ-line therapy. Yet unfortunately, while the International Bioethics Committee of UNESCO in its penultimate draft had agreed to keep the *Universal Declaration on the Human Genome and Human Rights* (United Nations Educational, Scientific and Cultural Organization, 1997) free from the mention of any specific technology, the aim being to guarantee its viability over time and its universality as well as to strengthen the impact of concepts such as human dignity and diversity if justification for prohibitions were needed. Nevertheless, the governmental representatives convened to approve the Committee's final draft sought (political?) refuge in inserting "technique-specific" prohibitions in the *Declaration* with regard to human cloning and germ-line therapy as mentioned earlier. It bears noting that the WHO in both its 1997 *Proposed International Guidelines* (World Health Organization, 1997), its 1999 *Draft Guidelines on Bioethics* (World Health Organization, 1999), and its resolution on *Ethical, Scientific and Social Implications of Cloning in Human Health* (World Health Organization, 1998) distinguishes between the different types of cloning. Both WHO and HUGO (Human Genome Organisation, 1999b) prohibit human reproductive cloning but encourage relevant research in the field of therapeutic cloning and stem cell research.

This is instructive in the banking context where as we shall see, former, similar wholesale proclamations about the DNA as "person" or as "property" have ultimately proved secondary to the need to ensure personal control whatever the legal qualification and this without impact as regards commercialization.

5 DNA Banking

The last 10 years have seen tremendous upheaval and uncertainty in the world of DNA banking and research. Indeed, 1995 saw the hitherto unfettered access by researchers to archived samples come to a halt with the report of a NIH study group on informed consent for genetic research on stored tissue samples suggesting that the proof of consent to research was required even for those samples already stored during routine medical care (CLAYTON et al., 1995). While generally, the ethical and legal norms governing banking had been moving towards a more informed choice approach with options in the case of samples provided in the research context *per se*, the im-

plementation of this approach would effectively have halted the largest "source" of DNA samples for genetic research to say nothing of epidemiological or public health research (even if the latter wished to use only anonymized samples). This conservative position was followed by a myriad of contradictory positions around the world (KNOPPERS et al., 1998).

Five years later, in May 2000, the UK's Royal College of Physicians Committee on Ethical Issues in Medicine published its recommendation on *Research Based on Archived Information and Samples* (Royal College of Physicians, 1999a) and the circle was closed. The College does not consider it necessary to obtain specific consent for:

- The retrospective use of existing medical records for analysis of disease prevalence, clinical features, prognosis, response to treatment, etc.
- The use of biological samples that have been previously taken during the course of medical diagnosis or treatment, at autopsy, or for research, and are in excess of requirement for their original purpose, e.g., "left over" portions of blood samples or tissue biopsies (Royal College of Physicians, 1999b).

Thus, according to this most recent report, irrespective of whether the person is still alive or has consented or not to the research in question, subject to certain conditions, medical research using biological samples may be conducted without the express consent of the individual patients or research subjects. Nevertheless, the material must be anonymized at the earliest possible stage consistent with obtaining the information necessary for the research. The minimum level of anonymization is that which precludes identification of individuals from the output of the research (Royal College of Physicians, 1999b).

Where does this position stand relative to international norms or to that of other countries? To answer that question, we will examine the varying responses in the time period of 1995–2000 with respect to samples already archived that were obtained during medical care or from autopsies, samples provided specifically for research, and finally, samples obtained for research but where other research is now proposed.

It should be mentioned at the outset that perhaps more confusing than the plethora of contradictory positions is that of the terminology used. Only terms such as "identified", or, "nominative", or, "personally identified" are understandable by all. In contrast, "identifiable" or "traceable" is used interchangeably with the term "coded", and, the term "anonymous" (i.e., never had any identifiers such as with specimens found in archeological digs), is often confused with "anonymized".

For the purpose of clarity, we will use the term "anonymized" (e.g., originally identified or coded/identifiable/traceable but now stripped except for some clinical or demographic data), and, the term "coded" (e.g., identifiable only through breaking the unique code given the sample in lieu of personal identifiers). We will examine international (Sect. 5.1) and regional (Sect. 5.2) positions on abandoned or research samples before turning to particular countries (Sect. 5.3).

5.1 International

Most international statements and guidelines on the ethics of genetic research do not address the specific issue of archived samples originating from medical care, the context of medical care being largely left to individual countries.

One notable exception is the 1998 *Statement on DNA Sampling: Control and Access* of the Ethics Committee of the Human Genome Organisation (HUGO) (Human Genome Organization, 1999a, rec. 2). The very mission of the Committee is to provide such guidance. Like the Royal College of the United Kingdom (Royal College of Physicians, 1999a) the HUGO Ethics Committee holds that:

> "Routine samples, obtained during medical care and stored may be used for research if: there is general notification of such a policy, the patient has not objected, and the sample to be used by the researcher has been coded or anonymized. Routine samples obtained during medical care and stored be-

fore notification of such a policy may be used for research if the sample has been anonymized prior to use."

WHO's 1997 *Proposed International Guidelines* did not take a position on leftover or "abandoned" samples except to say that "specimens that could be useful to families in the future should be saved and should be available" (World Health Organization, 1997, Tab. 10, guideline 10).

The relative absence of international guidelines specific to possible research uses for "left over" samples is regrettable for many reasons. The first, as already mentioned, is the need for large scale epidemiology, for the study of population variations (genetics), and for general health surveillance (an often forgotten obligation of the State). Such studies would be greatly facilitated if abandoned, anonymized samples were made available. The second is the application by default of the rules governing samples obtained for specific research projects, or, of the rules of consent to genetic research generally. The third is the extreme difficulty, if not impossibility, of fulfilling the ethical obligation of international collaboration due to the lack of international guidance and harmonization. This last deficiency is further exacerbated by the confusion surrounding the use of different terminology to describe the samples as mentioned earlier.

Turning to samples obtained specifically for research purposes, only two international documents have addressed the issue, HUGO and the WHO. As we will see, until very recently, both were in stark opposition to the more conservative national positions. Indeed, WHO's 1997 *Proposed International Guidelines* (World Health Organization, 1997, Tab. 10, guideline 10) maintains that "a blanket informed consent that would allow use of a sample in future projects is the most efficient approach" (Tab. 10). This is somewhat tempered by the assertion that "genetic samples from individuals must be handled with respect, should be taken only after the consent is obtained, and, should be used only as stated in the consent document" (p. 4). Other than the general need to preserve confidentiality, no distinction is made between coded or anonymized samples for research purposes.

Due to its mandate, the 1998 HUGO *Statement on DNA Sampling: Control and Access* (Human Genome Organisation, 1999a) specifically addresses the issue and holds that:

> "Research samples obtained with consent and stored may be used for other research if, there is general notification of such a policy, the participant has not yet objected, and the sample to be used by the researcher has been coded or anonymized. For the use of research samples obtained before notification of a policy, these samples may be used for other research if the sample has been coded or anonymized prior to use." (rec. 3).

While consent to specific research is a *sine qua non*, both international bodies do not require an explicit consent for other uses. As just seen, HUGO would require notification and the opportunity for objection as well as mandating anonymization if such prior notification did not take place.

5.2 Regional

Other than upholding the need for informed consent for all medical interventions including research, at the regional level, there is very little guidance on genetic research with regard to either archived samples left over after medical care or research samples.

Article 22 of the 1997 Council of Europe's *Convention on Human Rights and Biomedicine* (Council of Europe, 1997) maintains that:

> "When in the course of an intervention any part of a human body is removed, it may be stored and used for a purpose other than that for which it was removed only if this is done in conformity with appropriate information and consent procedures."

In the mean time, what is "appropriate" depends on national positions. The Council of Europe is currently preparing a protocol to the *Convention* specifically on genetic research. Thus, perhaps some guidance on the thorny issue of the use of archived abandoned sam-

ples, or, on research samples will be forthcoming (see also the European Society of Human Genetics, 2000, the Society is preparing a position paper on sampling).

5.3 National

The majority of countries still do not distinguish between archived and research samples or have positions on the issue of other uses. Thus, unless a new and explicit consent is obtained, neither abandoned samples taken during medical care or research samples can be used for other purposes than those outlined in the protocol.

Before addressing the topic of other uses of research samples, it bears mentioning that the issue has not arisen in the context of leftover samples from routine care in that generally, any research use would require a specific consent unless the sample is anonymized (KNOPPERS et al., 1998). For example, the Health Council of the Netherlands, in its report on the *Proper Use of Human Tissue* states:

> "If residual material is to be used for purposes of which patients are unaware, then – the argument runs – they should at least be informed and given the opportunity to object." (Health Research Council of the Netherlands, 1994).

Taking notice of the fact that obviously, consent is required for the actual obtaining of the sample in medical care or research, it is only in the last year that some national jurisdictions have distinguished between obtaining consent at the time of sampling for research and the issue of other uses. Generally, they are becoming less stringent in always requiring an explicit consent for further uses. To take but a few examples, Australia's 1999 *National Statement on Ethical Conduct in Research Involving Humans* (National Health and Medical Research Council, 1999a), "normally" requires a new consent from donors of archived samples (princ. 15.7). Yet, the possibility of waiver by an Ethics Committee for the obtaining of another consent is foreseen in the context of research samples (princ. 15.6).

Indeed, "[A]n HREC [Human Research Ethics Committee] may sometimes waive, with or without conditions, the requirement of consent. In determining whether consent may be waived or waived subject to conditions, an HREC may take into account:

- The nature of any existing consent relating to the collection and storage of the sample;
- The justification presented for seeking waiver of consent including the extent to which it is impossible or difficult or intrusive to obtain specific consent;
- The proposed arrangements to protect privacy including the extent to which it is possible to de-identify the sample;
- The extent to which the proposed research poses a risk to the privacy or well being of the individual;
- Whether the research proposal is an extension of, or closely related to, a previously approved research project;
- The possibility of commercial exploitation of derivatives of the sample; and
- Relevant statutory provisions." (princ. 15.8) (National Health and Medical Research Council, 1999a).

Similarly, Japan also seems to be moving in this direction, in that the Bioethics Committee of the Council for Science and Technology in its *Fundamental Principles of Research on the Human Genome* (Council for Science and Technology, 2000) mentions that "[i]f a participant consents to provide a research sample for a genome analysis in a particular research project and, at the same time, anticipates and consents to the use of the same sample in other genome analyses or related medical research, the research sample may be used for 'studies aimed at other purposes' " (princ. 8.1.a).

Finally, it bears mentioning the Council of Regional Networks for Genetic Services (Council of Regional Networks for Genetic Services, 1997) in the USA did not exclude blanket consent when it stated: "[...] Any deliberate act of the medical profession to separate entire specimens from identifiers may be viewed as usurping the patient's/subject's right to determine subsequence uses for tissue. Consent forms should provide options of blan-

ket consent (waiving the right to be asked for further specific consent), as well as the option to limit their uses".

In short, on the national level, three positions typify the move away from the strict rule of requiring a new consent for other uses of research samples. The first is that of requiring ethics review when foreseeing the possibility of either anonymizing or coding the sample without going back to the source provided there is only minimal risk and confidentiality is ensured (National Bioethics Advisory Commission, 1999, rec. 9f; Medical Research Council, 1999; National Health and Medical Research Council, 1999b). The second requires ethics review but samples must always be anonymized (Health Research Council of the Netherlands, 1994; p. 88; American Society of Human Genetics, 1996; Medical Research Council of Canada, Natural Science and Engineering Research Council of Canada, Social Science and Humanities Research Council of Canada, 1998) and, the third eschews the automatic exclusion of "blanket consents" to future research. Indeed, a majority of members of the National Bioethics Commission of the United States would allow the use of "coded materials" for any kind of future study without further specification as to what kind of research, or the need for further consent, or even anonymization (National Bioethics Advisory Commission, 1999, rec. 9). Coding raises, however, other issues such as that of recontact should subsequent findings become clinically significant.

The advantage of coded samples is that clinical data can be added over time and so scientifically they remain viable. The disadvantage for researchers over time is that at a certain point in time the combination of research and clinical knowledge will become significant enough to have medical importance in the situation where prevention or treatment is available. NBAC has recommended that in this "exceptional" circumstance recontact and disclosure should occur (National Bioethics Advisory Commission, 1999, rec. 14).

In the same vein, on the issue of access by relatives to such information, Japan's Bioethics Committee of the Council for Science and Technology holds that "in case the genetic information obtained by research may lead to an interpretation that a portion of the genetic characteristics of the participant is or, is supposed to be, connected to the etiology of a disease, this interpretation may be disclosed to his/her blood relatives following authorization by the Ethics Committee only if a preventive measure or a cure has already been established for the disease in question." (princ. 15.2) (Council for Science and Technology, 2000, this is similar to the position of the Human Genome Organisation, 1999a, rec. 5: "[S]pecial considerations should be made for access by immediate relatives. Where there is high risk of having or transmitting a serious disorder and prevention or treatment is available, immediate relatives should have access to stored DNA for the purpose of learning their own status. These exceptional circumstances should be made generally known at both the institutional level and in the research relationship.").

The scientific advantage of coded samples has to be weighed against the potential ongoing obligations that may emerge. Even if such potential obligations could be foreclosed in part by asking research participants in advance whether they would want to be recontacted or not in the event of medically significant findings, what is the longevity or validity of an anticipatory "yes" or "no"? No doubt, the courts will settle this latter question but in the meantime, the option should be presented. If not, automatic communication of at-risk information to participants may run afoul of the emerging right not to know and yet, the failure to do so, of an emerging duty to warn!

To conclude this section on banking, the following comments can be made with regard to the issue of other uses without obtaining another explicit consent:

(1) the wholesale prohibition against both blanket consent to future unspecified uses of research samples and against the use of leftover samples from medical care without a specific consent is increasingly nuanced (and may be on the wane);
(2) there is a need to re-examine the automatic anonymization of samples as the expedient solution to ethical and legal quandaries;

(3) a distinction should be drawn between refusal of access to third parties such as insurers or employers and the legitimate needs for communication to blood relatives; and
(4) discussion is required on the issue of recontact and communication of results in the situation of other research that yields medically relevant information.

It goes without saying that underlying these difficult choices is the ultimate question: to whom does the DNA belong in this commercialized research environment?

6 Ownership

Intimately linked to the issue of ownership is that of the legal status of human genetic material. Even though this issue is one of principle, surprisingly, different legal status – person or property – has not had a concomitant impact on the ultimate issue, that of control of access and use by others.

At the international level, there is an increasing recognition that at the level of the species, the human genome is the common heritage of humanity (for example see United Nations Educational, Scientific and Cultural Organization, 1997, art. 1; KNOPPERS et al., 1998). Contrary to common misunderstanding, it means that at the collective level, like space and the sea, no appropriation is possible by nation states. Other characteristics of this approach include peaceful and responsible international stewardship with a view to future generations and equitable access. In the absence of a binding international treaty (UNESCO's *Declaration* and the WHO's and HUGO's positions being only proclamatory in nature), it remains to be seen if this concept will come to legally binding fruition.

This position, however, is particularly important in that it serves to place new sequences that fail to meet the strict conditions of patenting into the public domain. While patenting is not the subject of this analysis, a strictly personal property approach to DNA samples, would theoretically require a specific personal consent to eventual patenting. Yet, likewise giving the DNA sample the status of "person" also mandates obtaining consent, or at a minimum notification of patenting, as already mentioned under the 1998 European *Directive* (Council of the European Union, 1998). At the international level then, this position in favor of both the common heritage approach at the level of the collective human genome and that of personal control over individual samples and information has slowly been consolidated. Indeed, the last few years have seen the emergence of a new concept in the international arena, that of benefit sharing. This approach, largely sponsored by HUGO but gradually taking hold in industry, mandates recognition of the participation and contribution of participating populations and communities. Founded on notions of justice and equity, it upholds the common heritage approach but encourages "giving-back" by profit-making entities such as, e.g., contributions to the healthcare infrastructure (Human Genome Organisation, 2000).

Turning to the regional level, the "gift" language of a decade ago, that was replaced with "source", "owner", and "subject" has returned (see, e.g., European Society of Human Genetics, 2000). Lest there be any misgiving, a gift implies the complete transfer of any property or personal rights a person may have. The individual would also give up rights to a share of the profits derived from any commercial application. The language of gift is not found in international instruments, the former emphasizing the common heritage concept (Human Genome Organisation, 1996) or the notion of "general property" or "public domain" (German Society of Human Genetics, 1997), thus obviating the issue of status but excluding private ownership and concentrating on "shared goods".

The European *Convention* (Council of Europe, 1997) mirroring both UNESCO and WHO, limits itself to prohibiting financial gain by stating: "The human body and its parts shall not as such, give rise to financial gain" (art. 21). The *Convention* does, however, maintain that: "When in the course of an intervention any part of a human body is removed, it may be stored and used for a purpose other than that for which it was removed, only if this is done in

conformity with appropriate information and consent procedures" (art. 22). It is not known whether the term "intervention" includes research but it goes without saying that if an "abandoned" sample obtained during routine care requires a specific consent for other purposes, including one could presume, eventual commercialization, the same would hold for samples specifically obtained for research.

At the national level, it should be stated at the outset that payment to a research participant for time and inconvenience or cost recovery by the researcher or institution (both being minimal in the case of DNA sampling), neither affords the status of property to a sample nor undermines the notion of gift. Furthermore, the notion of gift, while obviously involving transfer, may not necessarily create immediate property rights in the researcher. Indeed, in the absence of intellectual property which could be afforded to any invention, increasingly we will see that the researcher-"banker" is described as a "custodian". This is both a real and symbolic statement. Real, in that the current complex, public-private funding of research involves multiple economic partners in any eventual profits from patenting. Symbolic, in that the researchers involved may be bench scientists or clinician-researchers and so both may be simple guardians and fiduciaries of the samples for the research participants or patients and their families.

Even in Iceland, with its controversial presumed consent to the storage and use of health data, the recent *Act on Biobanks* (Iceland Minister of Health and Social Security, 2000) extends this notion of "non-ownership" to any company licensed by the Government to do research on accompanying biological samples: "The licensee shall not be counted as the owner of the biological samples, but has rights over them, with the limitations laid down by law, and is responsible for their handling being consistent with the provisions of this Act and of government directives based on it. The licensee may thus not pass the biological samples to another party, nor use them as collateral for financial liabilities, and they are not subject to attachment for debt".

The language of "donation" of human genetic material was particularly prevalent in the countries of civilian tradition (see, e.g., Network of Applied Genetic Medicine, 2000) but has also been adopted in common law jurisdictions. Indeed, the recent MRC interim ethical guidelines on *Human Tissue and Biological Samples for Research* have placed the onus on the custodian of a tissue collection to manage access (Sect. 3.2) (Medical Research Council, 1999). While the MRC recommends that tissue samples donated for research be treated as gifts (Sect. 2.1), the definition of custodianship "implies some property rights over the samples but also some responsibility for safeguarding the interests of the donor" (...) (Medical Research Council, 1999).

Likewise, even those American states that have adopted the *Genetic Privacy Act* (KNOPPERS et al., 1998) have not done so with original articles on the property rights of the "source". Theoretically, the implementation of this approach would have given every "source-owner" an opportunity to bargain for a percentage of eventual profits (if any). The result of all of this debate as well as of increased commercialization of genetic research, is that most consent forms now inform research participants that their sample, or products derived from it, may be commercialized and that they will not be entitled to a share of any eventual profits (CARDINAL et al., unpublished data). Ultimately, it is usually universities, research institutes and/or commercial entities that maintain "biobanks" and share in any profits that may ensue (KNOPPERS, 1999).

7 Conclusion

Genetic research is moving to the forefront of the bioethics debate. This is due in part to public interest in the role of genetic factors in common diseases and also to the possibility of tailoring drugs to individual genetic susceptibility. Ethical frameworks will have to make a corresponding shift from an emphasis on monogenic diseases and the stigma they carry to the "normalization" of genetic information in common diseases. This is all the more important in that the study of normal genetic variation (diversity) will require large population banks. A corresponding "normalization"

of the treatment of DNA samples and genetic information as medical information with increased protection will also be welcome.

For now, two issues have served to attract attention to the ethical issues surrounding genetic research and DNA sampling – consent to sampling and commercialization. We have seen that the issue of consent is characterized and stratified by the origin of the sample (medical or research) and by the type of information accompanying the sample as well as the issue of other research uses. The debate on sampling is moving towards a recognition of the need to distinguish between coded and anonymized samples. The trend to favor the latter with its lower risk of possible socioeconomic discrimination may well be short-lived. This is due to the fact that increasingly, if medical and research information is better protected generally, participants themselves may want to be "coded" and followed-up over time and be offered that choice. Furthermore, the anonymized samples themselves may lose their scientific utility over time considering the absence of ongoing clinical information. Researchers may also come to favor coding when the issue of responsibility for recontact is clarified.

On the issue of commercialization of research, while some clarification has been forthcoming in that raw sequences with no specific or substantial utility are seen as being in the public domain and not patentable *per se*. The issue of benefit-sharing raises the possibility of balancing legitimate returns on investment (profit-making) with concerns with equity and justice for participating families, communities, and populations. Influence on consent to sampling has been largely limited to ensuring a clear renunciation of any interest in potential intellectual property by the research participant. The next step may well be to also clarify the role of the researcher, the university (if applicable) and industry. The possibility for conflicts of interest are real and actual where the researcher is not only a clinician but the custodian of the sample and has a financial interest in the research.

As we move from the gene map to gene function, there is a need to understand normal genetic variation and diversity. This will require the participation of large populations. The lessons learned in the last decade with respect to the need to not only respect personal values and choices in the control of and access to DNA samples in genetic research but also to communicate clearly its goals, should serve to direct the next decade. Transparency and ongoing communication of any change in the direction of the research will do much to ensure public trust in the noble goals of genetic research.

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