GenEditorial

EDITORIAL ON THE ETHICAL, LEGAL AND SOCIAL ISSUES OF HUMAN GENETICS

(2007) 5:2 *GenEdit,* 1-9

CONSENT IN PHARMACOGENOMIC RESEARCH

Michael S. Phillips PhD[1], Yann Joly LLM[2], Tina Silverstein BA[3], Denise Avard PhD[4]

This article analyzes the emerging ethical and legal requirements for informed consent in pharmacogenomic research. It reviews how policies at the international, regional and national levels have responded to the ethical challenges raised by this new research area. It concludes that the pharmacogenomic policy framework is still in its infancy and needs to be further developed to answer the challenges raised by this important discipline.

Central tenets of the informed consent process have for a long time been the ethical and legal principles of autonomy and integrity. These principles explain the importance of obtaining voluntary, informed consent in medical research. However, the emergence of the genetic and genomic era has led a growing number of authors to note that the informed consent process is in need of updating and restructuring to effectively address new realities faced by genetic researchers and research participants.[1] This is because many research studies that have been made possible since the sequencing of the human genome are thought to have significance for the family unit, the community, and even society as a whole, as well as for individual research participants.

1. Director of Pharmacogenomics, The Genome Quebec and Montreal Heart Institute Pharmacogenomics Centre, Université de Montréal
2. Project Manager, Centre de recherche en droit public (CRDP), Université de Montréal
3. Research Assistant, CRDP, Université de Montréal
4. Research Director, CRDP, Université de Montréal

Ethicists have argued that an approach to consent that is concerned with both the societal and individual implications of participation in research[2] would facilitate the use of biological samples and would thus result in superior and more rapid advancements for the treatment of disease.

Pharmacogenomics, the study of the relationship between genetics and drug response, is one example of research that holds the potential for great societal benefit and may thus require an approach to consent that is based on communal values. This issue of GenEdit has sought--through comparative analysis of national, regional and international guiding documents--to discover whether ethicists and policy makers are emphasizing communal values, such as reciprocity, solidarity, universality and citizenship in their guidance of

 ISSN 1718-9314

pharmacogenomic research. The purpose of this study is not to develop a specific model of consent, but rather to provide an overview of emerging issues with regard to informed consent in this novel research area. In particular, it questions whether informed consent standards are being relaxed to encourage advances in pharmacogenomics; or whether they are being strengthened on account of the perception of new risks. It further questions whether there is sufficient guidance to direct pharmacogenomic researchers on how to fulfill their informed-consent related obligations.

Pharmacogenomics and consent: A comparative study

Pharmacogenomics has the potential to dramatically improve that way that drugs are both developed and prescribed. However, pharmacogenomics, like most new areas of medical research, also raises a number of ethical issues. Does this mean that pharmacogenomics should have its own ethical framework? Proponents of this research believe that it should. They argue that since pharmacogenomics is limited to studying drug-response, it does not entail the risk of generating potentially stigmatizing information about disease susceptibility, and should thus be subjected to less constraining rules as compared to genetic susceptibility research.[3] The validity of this argument remains subject of debate and to date, little consensus has emerged between the various stakeholders involved in pharmacogenomic research.[4]

Nonetheless, recognition of the increasing relevancy of pharmacogenomics in relation to drug discovery, clinical studies, and perhaps eventually the drug approval process, has resulted in much discussion on how to best deal with the issue of consent in pharmacogenomic research. In this study, we seek to uncover emerging trends on this issue from the guiding documents published at the national, regional and international levels. Part (A) will explain the methodology of the study. Part (B) will explain the results in relation to each contentious issue outlined in the methodology. Finally, in the conclusion, we will identify any noticeable trends that emerge in the existing guidelines and explain where more direction may be necessary to ensure that this research advances in an ethically sound and efficient manner.

(A) Methodology

Using the *HumGen International Database of Laws and Policies*,[5] *Medline*, *PubMed*, *Google*, *Google Scholar*, *Lexis Nexis* and the *WHO International Digest of Health Legislation*, policy documents and recommendations from five international organizations and coalitions,[6] three European regional organizations and 16 countries were identified.[7] Of these, surprisingly few documents, only 4 international,[8] 2 European,[9] and 7 national,[10] focused explicitly or implicitly on pharmacogenomics. Using these documents, we analyzed the emerging ethical trends around five key issues in the pharmacogenomics consent process, including: (i) scope of consent, (ii) duration of consent, (iii) confidentiality and coding of research samples, (iv) return of research results, and (v) consent to 'add-on' studies in the context of clinical trials.

(B) Results

(i) Scope of consent

The scope of consent refers to the breadth of research permissible in a given pharmacogenomic study. While some policies permit broad consent for unspecified purposes,[11] others take a much more restrictive approach, requiring clear and specific explanations of potential future research.[12] The majority of texts advocate compromise solutions so that the rights of research participants are respected but at the same time freedom of research is not curtailed by overly specific consent clauses.[13] For example, according to the European Pharmaceutical Industry Association, the scope of consent should

 ISSN 1718-9314

strike "a reasonable balance between describing the research…and not curtailing flexibility for future use."[14] The US *Consortium on Pharmacogenetics* advocates that a "reasonable policy is to obtain consent to a range of related studies over time."[15] Another proposed solution is to permit unrestricted use of donor samples only after the samples have been anonymized and are no longer traceable back to an individual. UK's *Nuffield Council on Bioethics* favours this approach, explaining that "it is permissible to request broad consent to the use of samples which are anonymous or anonymised."[16] Another approach mentioned in the Nuffield Council report is to permit the consent to future use only when it is contained in a separate consent form. Thus, we find that although there is to date no general consensus on any one specific approach to consent scope, intermediate solutions are favoured by the majority of existing guidelines discussing this issue.

TABLE 1:

Document	Recommendation on the scope of consent
International: Pharmacogenetics Working Group (2002): *Elements of Informed Consent for Pharmacogenetic Research*	"The specific purpose of the study should be clearly described including both short-term objectives and potential long-term applications"
International: Council for International Organizations of Medical Sciences (2005) *Pharmacogenomics: Towards improving treatment with medicines*	"For informed consent documents, it is recommended that "field of use" needs to be well described but that appropriate broad use may also be permitted"
Europe: European Federation of Pharmaceutical Industries and Associations (2006): *Key Messages Surrounding Pharmacogenetics*	"The consent process must strike a reasonable balance between describing procedures and purposes of the research in sufficient detail while not being overly restrictive and curtailing flexibility for future use of data samples based on evolving scientific knowledge and technology"
Belgium: Consultative Committee on Belgian Bioethics (2003) *Opinion (No 26) December 15, 2003 concerning the introduction of pharmacogenetics in experimental protocols*	Sample donors can consent to future, unspecified use of their biological samples
Italy: A collaboration of research groups (2002): *Italian Proposed Guidelines for the Evaluation of Pharmacogenetic Research*	"The collection of biological samples without a clear aim, or only for unidentified future use should be prohibited." However, the patient can authorize use for a study in the same research area if it is anonymized. If the sample is identifiable, new consent is required
United Kingdom: Nuffield Council on Bioethics (2003): *Pharmacogenetics: Ethical Issues*	"It is permissible to request broad consent to the use of samples which are anonymous or anonymized. Where samples… are coded or identified, broad consent… may be permissible, but should be sought separately from the initial consent"
Ireland: Irish Medicines Board (2006): *IMB Guidelines for Pharmacogenetic Research*	Consent documents should include "the possible options for future use of the collected data in other research"
United States: Consortium on Pharmacogenetics (2002): *Pharmacogenetics: Ethical and Regulatory Issues in Research and Clinical Practice*	"In most cases, a reasonable policy is to obtain consent to a range of related studies over a defined period of time"

(ii) Duration of consent

The duration of consent refers to how long samples and/or data will be stored, as part of the initial study or for future research use. So far, only 4 documents have been identified that address the issue of duration of consent in the realm of pharmacogenomic research. While no consensus can be drawn from such a small number of policy statements, those that discuss the duration of consent were in agreement that the length of time for which the samples could be stored and studied should be included in the informed consent document given to research participants. None of the policy statements, however, gave an indication of the appropriate length of time for sample storage. For example, the recommendation

 ISSN 1718-9314

from the Council for International Organizations of Medical Sciences (CIOMS) is very broad, suggesting that "the time range for storage of the samples *may* be for the duration of the study to many years thereafter."[17]

TABLE 2:

Document	Recommendation on duration of consent
International: Pharmacogenetics Working Group (2002): *Elements of Informed Consent for Pharmacogenetic Research*	Timelines for the destruction of samples must be included in the consent form, however, no specified length is prescribed
International: Council for International Organizations of Medical Sciences (2005): *Pharmacogenomics: Towards improving treatment with medicines*	"The time range for storage of the samples may be for the duration of the study to many years thereafter"
Belgium: Consultative Committee on Bioethics (2003): *Opinion (No 26) December 15, 2003 concerning the introduction of pharmacogenetics in experimental protocols*	The protocol must define the period for which the sample is kept in an identifiable, codified or anonymous form.
Ireland: Irish Medicines Board (2006): *IMB Guidelines for Pharmacogenetic Research*	The consent protocol must define "[w]hat happens to the samples when the research is finished; whether or not they will be destroyed, if not, who keeps them, and for how long…"

(iii) Confidentiality and coding of research samples

Procedures for protecting confidentiality and its corollary, the protection of personal information and genetic samples, are extremely important considerations in pharmacogenomic research.[18] A major step toward a more harmonized approach to confidentiality protection was reached in 2002, when terminology describing the storage of samples was agreed upon by the *Pharmacogenetics Working Group*[19] and the *European Federation of Pharmaceutical Industries and Associations*[20] and was subsequently adopted by the International Conference on Harmonization in 2006.[21] This helped standardize the way that samples are coded and handled, and further addressed the concerns noted in several pharmacogenomic research guidelines.

On the issue of confidentiality and coding of samples, many policy statements favour flexibility regarding the degree of protection that must be used with respect to biological samples. It is often advocated that the appropriate level of protection should be determined on a case-by-case basis. Decisions as to what level of coding should be used in a given study should be based on a number of factors, including: the nature of the research, the intended use for the samples, the length of sample storage, secondary uses, legal context, specific concerns raised by researchers, committees and sponsors, and selection of the greatest degree of privacy protection compatible with the objectives of the research. [22]

Only the use of "identified" and "anonymous" samples tends to be discouraged. Identified samples are discouraged because they offer research participants insufficient privacy protection. The use of anonymous samples is discouraged for a number of reasons. It is ethically problematic because participants will not be re-contactable and therefore results that may be relevant to their health will not be returnable to them. Anonymous samples also cause regulatory problems because a study conducted on anonymous samples cannot be audited or validated. Finally, the use of anonymous samples is technically problematic because of their limited scientific utility outside of the exploratory stages of research. In the majority of cases, samples can be coded, double coded or anonymized, provided that the chosen level of protection is justified by the researcher and that the participants are informed in the consent process.

 ISSN 1718-9314

TABLE 3

Document	Recommendation on coding and confidentiality
International: Pharmacogenetics Working Group (2006): *Returning Genetic Research Results to Individuals: Points to Consider*	Anonymizing samples is not recommended for ethical (participants are unable to withdraw or obtain results), as well as regulatory (results cannot be approved with anonymous samples) reasons
International: Pharmacogenetics Working Group (2002): *Elements of Informed Consent for Pharmacogenetic Research*	The precise level of coding depends on the study and must be included in the consent process
International: Council for International Organizations of Medical Sciences (2005): *Pharmacogenomics: Towards improving treatment with medicines*	"The informed consent document should describe sample storage and access, along with any applicable restrictions and legal requirements"
Europe: European Federation of Pharmaceutical Industries and Associations (2006): *Key Messages Surrounding Pharmacogenetics*	The choice of how to code samples depends on five factors: 1) nature of the research, 2) intended use of the data, 3) legal and regulatory constraints, 4) position of the IRB (Institutional Review Board) or EC (Ethics Committee), and 5) the needs of the study sponsor/investigator
Belgium: Consultative Committee on Bioethics (2003): *Opinion (No 26) December 15, 2003 concerning the introduction of pharmacogenetics in experimental protocols*	Samples should remain in a codified form until verification by a regulatory agency is no longer needed
Italy: A collaboration of research groups (2002): *Italian Proposed Guidelines for the Evaluation of Pharmacogenetic Research*	"The degree of anonymization of samples and data… must be described and justified. Each of these levels of anonymity has advantages and disadvantages and the evaluation of the best approach must be made on a case-by-case basis"
United Kingdom: Nuffield Council on Bioethics (2003): *Pharmacogenetics: Ethical Issues*	"We consider that to protect the privacy of participants, the greatest degree of anonymity should be imposed on samples, compatible with fulfilling the objectives of the research"
Ireland: Irish Medicines Board (2006): *IMB Guidelines for Pharmacogenetic Research*	The consent form must define "the level of anonymity of the samples and the data"
United States: Consortium on Pharmacogenetics (2002):Pharmacogenetics: Ethical and Regulatory Issues in Research and Clinical Practice	Coding samples (single or double) is preferable to both identified and anonymous samples. Double-coding is superior to protect confidentiality, but it is also costlier, thus it must be balanced against the risk to the subject if the information is disclosed

(iv) Return of research results

Many texts recommend that "aggregate" results should always be made available to research participants, while individual results should only be made available when they contain scientifically valid and clinically useful information. A few texts, however, argue that the individual has a "right to know" and that patients should be given the choice as to whether they want to know their individual research results regardless of the utility or validity of the information.[22] Despite these divergences, a majority of texts are in agreement that patients should be informed in the consent process as to whether results will or will not be made available.

Many of the policy statements analyzed suggest that returning individual research results may not be relevant in pharmacogenomic research. This position is based on the view that it is highly unlikely that pharmacogenomic research will reveal clinically useful information in its current exploratory phase. While this may have been accurate in the past, many current pharmacogenomic studies now have the potential to reveal clinically useful information. In the future, the likelihood that these studies will continue to produce relevant information will increase. As such, policy makers should move away from the idea that pharmacogenomics will remain exploratory and should begin to work on the premise that relevant information will arise out of these studies. Taking this into account, a more appropriate framework needs to be developed for determining when and how individually relevant results of pharmacogenomic studies should be returned to individual patients.

 ISSN 1718-9314

TABLE 4:

Document	Recommendation on returning results
International: Pharmacogenetics Working Group (2006): *Returning Genetic Research Results to Individuals: Points to Consider*	"If the research is exploratory a reasonable default position could be that no results will be proactively returned to an individual. Specific requests for results could first be addressed with information about the general findings from the study, followed by individual results if deemed appropriate by law"
International: Pharmacogenetics Working Group (2002): *Elements of Informed Consent for Pharmacogenetic Research*	"It is important to describe the intended types of pharmacogenetic results to be derived from a study and to inform the subject about the realistic expectations and health implications, if any, of these results. In many types of pharmacogenetic studies, overall results are derived from analysis of aggregate genetic data (ie, population analysis); interpretations of data may be generally applicable to populations but are not specifically applicable to individual subjects"
International: Council for International Organizations of Medical Sciences (2005): *Pharmacogenomics: Towards improving treatment with medicines*	"Given that pharmacogenomics is in its infancy, only occasionally will precise, useful validated information be obtained as a result of pharmacogenetic research"
Europe: European Federation of Pharmaceutical Industries and Associations (2006): *Key Messages Surrounding Pharmacogenetics*	Although unlikely in this stage of PGx research, if individually useful information will be obtained in the study, participants should be given the option to obtain those results
Belgium: Consultative Committee on Bioethics (2003): *Opinion (No 26) December 15, 2003 concerning the introduction of pharmacogenetics in experimental protocols*	The protocol must be clear as to if and how individual results will be shared, or whether only general results will be available
Italy: A collaboration of research groups (2002): *Italian Proposed Guidelines for the Evaluation of Pharmacogenetic Research*	"After the preliminary nature of the results and their lack of clinical usefulness have been explained, each subject has the right to request and be given access to all data related to his own genetic information… The degree and manner by which subjects will be given access to genetic data about themselves… must be described"
United Kingdom: Nuffield Council on Bioethics (2003): *Pharmacogenetics: Ethical Issues*	"While we are sympathetic to the view that patients should have the opportunity to receive useful and validated information about their medical treatment, we consider that only on rare occasions will such information be obtained as part of research in pharmacogenetics"
Ireland: Irish Medicines Board (2006): *IMB Guidelines for Pharmacogenetic Research*	The patient should be given the opportunity "to be informed of any future results using his/her samples"
United States: Consortium on Pharmacogenetics (2002): *Pharmacogenetics: Ethical and Regulatory Issues in Research and Clinical Practice*	"The obligation of the researcher to disclose potentially beneficial information to subjects who opt for disclosure extends only to reliable information"

(v) Consent to pharmacogenomic 'add-on' studies in clinical trials

Pharmacogenomic "add-on" studies refers to studies conducted alongside clinical trials, but that are not usually essential to participation in the main clinical study. The "add-on" can be distinguished on two fronts: the first type of "add-on" study asks permission to carry out genetic research on specific genetic variants that are expected to influence the drug(s) being investigated in the clinical trial. This genetic information is linked to personal and medical history and the sample is "identifiable". The second type of "add-on" study asks to store the samples after completion of the clinical trial for a long or unlimited period in order to carry out future, yet unspecified research. The question thus arises as to how one handles the consent form in the context of these research scenarios. Can a single consent form address both the clinical trial and pharmacogenomic sub-studies?

As shown in Table 5, the majority of policy statements recommend the use of a

 ISSN 1718-9314

separate consent form for the pharmacogenomic portion of studies. The purpose of a separate consent is to highlight the fact that participants are free to participate in additional studies, and that declining to do so will not impact their involvement in the main study. However, CIOMS noted, interestingly, that while this has been the standard for pharmacogenomics research due to its novelty, this standard will most likely change as pharmacogenomics becomes more integral to the drug development and approval process.[23] For example, while Health Canada advocates that a separate consent form be used when add-on studies are initiated separately from the main clinical study, they specifically make an exception for situations where participation in the pharmacogenomic portion of the study is "a condition for participation".[24] This will likely be the case when prior genotyping is used as part of inclusion criteria to address safety considerations for participation in a trial. It will be interesting to see how policies evolve as pharmacogenomics becomes more mainstream and whether the request to store samples for unlimited periods and for unspecified research will continue to require additional consent.

TABLE 5:

Document	Recommendation on Separate Consent
International: Pharmacogenetics Working Group (2002): *Elements of Informed Consent for Pharmacogenetic Research*	A separate consent form explaining the PGx component of the study should be provided unless participation in the clinical and PGx studies are both required aspects of participation.
International: Council for International Organizations of Medical Sciences (2005): *Pharmacogenomics: Towards improving treatment with medicines*	"A separate informed consent has become quasi-standard… However, as the field develops more studies are likely to include genotype as an integral part of determining a drug's profile and/or as an inclusion criterion, shifting the quasi-standard towards a single consent form"
Italy: A collaboration of research groups (2002): *Italian Proposed Guidelines for the Evaluation of Pharmacogenetic Research*	"It would be preferable that the subject submits one consent for the clinical study and the other consent for the genetic study. This permits the subject to participate in the clinical study without necessarily also participating in the PGx study"
United Kingdom: Nuffield Council on Bioethics (2003): *Pharmacogenetics: Ethical Issues*	Broad consent "should be sought separately from consent to the initial study. This separate consent may be obtained when the samples are initially taken, or at a later date"
Ireland Irish Medicines Board (2006): *IMB Guidelines for Pharmacogenetic Research*	"It is preferable that the subject submits one consent for the clinical study, and another consent for the genetic study. This allows the subject to focus on each aspect of the study, and also permits the subject to participate in the clinical study without necessarily also participating in the pharmacogenetic part"
Canada: Health Canada (2007): *Guidance Document: Submission of Pharmacogenomic Information*	"When clinical trial sponsors intend to collect samples for exploratory pharmacogenomic testing outside the scope of the main clinical trial, informed consent should be obtained separately from that of the main trial." However, a new consent is not needed where the pharmacogenetic test is "a condition of participation"
Belgium: Consultative Committee on Bioethics (2003): *Opinion (No 26) December 15, 2003 concerning the introduction of pharmacogenetics in experimental protocols*	"We recommend that data for the pharmacogenomic add-on study be given on a separate consent form to ensure that the patient is perfectly informed of the particularities of the pharmacogenomic study (translation)"

 ISSN 1718-9314

Conclusion

This comparative review of the informed consent process in pharmacogenomic research addresses several key issues associated with pharmacogenomic research including: scope of consent, duration of consent, confidentiality and coding of research samples, return of research results, and consent to 'add-on' studies during clinical trials.

While this informed consent analysis is framed in the context of pharmacogenomic research, it is underpinned by the informed consent process in genomic research in general. This analysis demonstrates that very few recommendations or guidelines specifically explicitly address the requirements for the informed consent process in relation to pharmacogenomic research. Moreover, the guidelines that do exist do not always adequately address the technological advances in genotyping that now allow for samples to be genotyped for millions of single nucleotide polymorphisms (SNPs) cheaply and simultaneously.[25] Given adequate facilities and expertise, and with little effort, this information will become unique and theoretically could always be identified.[27]

As this analysis has demonstrated, there is little consensus concerning the requirements of informed consent for pharmacogenomic research. In relation to the scope of consent, guiding documents propose a diverse range of solutions to balance the rights of research participants with the importance of allowing the progress of research. Duration of consent is rarely discussed in the majority of guidance documents.[26] The need to describe the timeline for the use and storage of the samples, and to include and explain this timeline in the consent process are the only recommendations made in the few documents that mention this issue.[27] In terms of confidentiality, there is tension between the desire to protect participants' personal information and the importance of maintaining a link with the participant identity to be able to access the phenotypic information necessary to conduct translational pharmacogenomic research. Little guidance exists primarily because this type of determination must be made on a case-by-case basis.[28] In terms of returning individual research results, it is recognized that there is a right to know (or not to know) results, particularly when such results become clinically relevant. There seems to be a consensus that returning pharmacogenomic research results to participants is premature at this exploratory stage because current results do not meet the standards of scientific validity and clinical usefulness. However, this will soon cease to be the case as studies become more advanced; and therefore the issue of returning individual results needs to be re-evaluated in the near future. Finally, concerning how consent should be handled for pharmacogenomic add-on studies, there is recognition that investigators need to obtain separate informed consent for pharmacogenomic studies that are added on to a main clinical study. This requirement could be abandoned as pharmacogenomics becomes more integrated and routine within the drug approval process.[29]

In summary, pharmacogenomic research presents a number of important ethical challenges for the informed consent process. This analysis indicates that further guidance is needed to address the ethical considerations if pharmacogenomics is to be well-received by policy makers and the general public. It has become increasingly difficult for pharmacogenomic researchers to navigate their way across generic recommendations for genetic research that may not be relevant in the context of pharmacogenomics and across an insufficient number of specific guidelines that would often need to be reviewed to reflect the new reality of a science in constant evolution. Many more studies and much more discussion, recommendations and guidance are needed to enable pharmacogenomic research to move forward ethically and efficiently.

 ISSN 1718-9314

** This research was supported by Genome Canada and Genome Quebec.*

[1] Knoppers BM, Chadwick R, "Human Genetic Research: Emerging Trends in Ethics" (2005) 6 *Nature Reviews: Genetics* 75.

[2] Chadwick R, Berg K, "Solidarity and equity: new ethical frameworks for genetic databases" (2001) 2 *Nature Reviews: Genetics* 318; Beskow LM, Burke W, Merz JF, et al., "Information Based Research for Population-Based Research Involving Pharmacogenomics" (2001) *JAMA* 286:18 2316; Network of Applied Genetic Medicine, *Statement of Principles on the Ethical Conduct of Human Genetic Research Involving Populations* (Montreal: Network of Applied Genetic Medicine, 2003).

[3] Sass HM, "Bioethical Issues in Genetic Screening and Patient Information" (2004) 12:*1 J Med Ethics, Law and History* 1; Middleton L, Freeman A, Brewster S, et al., "From Gene-Specific Tests to Pharmacogenetics" (2000) 3 *Community Genet* 198.

[4] Netzer C, Biller-Andorno N, "Pharmacogenetic Testing, Informed Consent and the Problem of Secondary Information" (2004) 18:4 *Bioethics* 349.

[5] A database containing over 3000 normative texts that discuss the ethical, legal and social dimensions of human genetics: http://www.humgen.umontreal.ca/int/.

[6] Word Health Organization, Council for International Organizations of Medical Sciences, UNESCO, Human Genome Organization.

[7] Australia, Belgium, Canada, Germany, India, Ireland, Israel, Italy, Japan, New Zealand, Singapore, South Africa, South Korea, Sweden, United Kingdom, United States.

[8] The Pharmacogenetics Working Group, Council for International Organizations of Medical Sciences, and the Human Genome Organization.

[9] European Commission, European Federation of Pharmaceutical Companies.

[10] Belgium, Italy, Germany, United Kingdom, Ireland, Canada, United States.

[11] Consultative Committee on Belgian Bioethics, *Opinion (No 26) December 15, 2003 concerning the introduction of pharmacogenetics in experimental protocols* (Brussels: Comité Consultatif de Bioéthique, 2003).

[12] Alberti MP, Barale R, Brignoli O, et al., *Italian Proposed Guidelines for the Evaluation of Pharmacogenetic Research* (Verona: Italian Society of Hospital Pharmacists, 2002); Study Commission on Law and Ethics in Modern Medicine, *Final Report for the German Bundestag* (Berlin: German Bundestag, 2002); Irish Medicines Board, *IMB Guidelines for Pharmacogenetic Research* (Dublin: Irish Medicines Board, 2006).

[13] See table 1.

[14] European Federation of Pharmaceutical Industries and Associations (EFPIA), *Key Messages Surrounding Pharmacogenetics* (Brussels: EFPIA, 2006).

[15] Consortium on Pharmacogenetics, *Pharmacogenetics: Ethical and Regulatory Issues in Research and Clinical Practice* (Minneapolis: Consortium on Pharmacogenetics, 2002).

[16] Nuffield Council on Bioethics, *Pharmacogenetics Ethical Issues* (London: Nuffield Council on Bioethics, 2003).

[17] Council for International Organizations of Medical Sciences (CIOMS), *Pharmacogenetics: Towards improving treatment with medicines* (Geneva: CIOMS, 2005).

[18] European Agency for the Evaluation of Medicinal Products (EMEA), *Position Paper on Terminology in Pharmacogenetics* (London: EMEA, 2002) Entered into operation June 2003.

[19] Pharmacogenetics Working Group, "Elements of Informed Consent for Pharmacogenetic Research" (2002) 2:5 *Pharmacogenetics Journal* 284.

[20] European Agency for the Evaluation of Medicinal Products (EMEA), *Position Paper on Terminology in Pharmacogenetics*, (London: EMEA, 2002) Entered into operation June 2003.

[21] International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, *Final Concept Paper E15: Terminology in Pharmacogenomics* (Geneva: ICH, 2006) available online: http://www.ich.org/LOB/ media/MEDIA3099.pdf.

[22] Joly Y, Knoppers BM, Nguyen, M-T "Stored Tissue Samples: Through the Confidentiality Maze" (2005) 5 *Pharmacogenomics Journal* 3.

[23] See Table 4.

[24] Health Canada, *Guidance Document: Submission of Pharmacogenomic Information* (Ottawa: Minister of Public Works and Government Services Canada, 2007); See table 4.

[25] Ragoussis J, **"**Genotyping technologies for all" (2006) 3:2 *Drug Discovery Today* 115.

[26] See table 1.

[27] See table 2.

[28] See table 3.

[29] See table 5.

 ISSN 1718-9314