

PHARMACOGENETICS RESEARCH NETWORK RECOMMENDATIONS FOR MODEL INFORMED CONSENT LANGUAGE, TERMS, AND PROCEDURES

Introduction/Statement of purpose

The Pharmacogenetics Research Network (PGRN) has developed recommendations for potentially useful model language for informed consent documents for pharmacogenetics studies. The model consent language presented below should be considered a working draft/starting point that is modifiable by local investigators to suit their particular study and IRB needs. It should be noted that the language and information below represent general recommendations. This should not be viewed as a comprehensive document, and special situations of the project, the intended use of the data, local IRB requirements, and/or state law may govern the actual content of a consent document for a pharmacogenetics study. **Specific requirements regarding consent language and/or use of extant samples for genetics or pharmacogenetics varies across IRBs, so you should contact your local IRB for specific recommendations regarding required language.**

Issues not addressed in this model consent language document

It is acknowledged that there are several areas that are not fully addressed in this document. First, is that the Food and Drug Administration has some specific consent requirements that may apply, if generated data are to be used to support drug approval or a label change. If this is the intent of your study, consultation with an expert in these guidelines is recommended. Research that voluntarily complies with a set of FDA-recommended privacy protections (which are described in FDA's April 25, 2006 Guidance document at <http://www.fda.gov/cdrh/oivd/guidance/1588.html>) may be allowed to use certain types of stored specimens without informed consent. However, FDA's earlier December 19, 1999 Guidance (available at <http://www.fda.gov/cdrh/comp/ivdreg.html>) is still in effect for research that does not comply with this set of privacy protections. FDA's 1999 Guidance requires informed consent in some situations where consent is not required under the Common Rule and current OHRP policies.

This document also does not fully address the evolving area of data derived from genome-wide studies, particularly as it relates to posting of such data to public databases, such as PharmGKB. There are currently a variety of opinions on this topic, but yet no consensus on how such data should be handled. Many ethicists, investigators and institutes within NIH are working to define the appropriate scenarios and venues for sharing of such data. **As such, the proposed model consent language does not explicitly address the issue of whole genome data.**

Model consent sections

This document is divided into four sections:

- 1) Use of extant samples and consent language that would be considered acceptable for pharmacogenetics studies and posting to PharmGKB for "coded" extant samples
- 2) Model consent procedures and language for pharmacogenetic studies and posting to PharmGKB
- 3) Model consent language for issues surrounding intellectual property arising from pharmacogenetics studies
- 4) Miscellaneous consent provisions an investigator may wish to consider.

In all cases, the actual model consent language is shown in italics.

PGRN RECOMMENDATIONS FOR MODEL INFORMED CONSENT LANGUAGE, TERMS, AND PROCEDURES

USE OF EXTANT SAMPLES

Extant samples are samples that already exist in investigators' freezers or in tissue repositories, having been collected in the past either with no informed consent for research use of the specimen, or with an existing research consent (either express or implied) that does not cover the currently planned use of the specimen. The following definitions were originally proposed by the Trans-Industry Pharmacogenetics Working Group to describe the various types of extant samples that might exist.

Categories for Genetic Research Samples/Data

- **Identified Samples/Data** are those labeled with personal identifiers such as Name or Social Security Number. Use of a clinical trial subject number does not make the sample/data identified.
- **Coded Samples/Data** are those labeled with a clinical trial subject number that can be traced or linked back to the subject only by the investigator. Samples do not carry any personal identifiers.
- **De-Identified Samples/Data** are double coded and labeled with a unique second number. The link between the clinical study subject number and the unique second number is maintained, but unknown to investigators and patients. Samples do not carry any personal identifiers.
- **Anonymized Samples/Data** are double coded and labeled with a unique second number. The link between the clinical study subject number and the unique second number is deleted. Samples do not carry any personal identifiers.
- **Anonymous Samples/Data** are those that do not have any personal identifiers, and the identity of the subject is unknown. Anonymous samples may have population information (e.g., the samples may come from patients with diabetes) but no additional individual clinical data.

One of the most common types of extant sample/data used in genetic/pharmacogenetic studies are de-identified samples/data. In 2004, the Office of Human Research Protections (OHRP) issued a *Guidance on Research Involving Coded Private Information and Biological Specimens*. This Guidance allowed that research on de-identified samples/data be treated as **not** "human-subjects research" (i.e., such research will not be subject to the informed consent and IRB-review requirements of the Common Rule), if certain conditions are met. To qualify, the investigators need to receive the data and specimens in a coded form *and* there needs to be assurance that investigators cannot obtain access to the code. OHRP would consider this latter condition to be met, for example, if: (1) the investigator and the holder of the code key enter into an agreement prohibiting release of the code key to the investigator at any time during the research subjects' lifetimes, or (2) if there are IRB-approved written policies and operating procedures for a repository or data management center that prohibit release of the key to the investigators. For more specific information about these requirements, please refer to the following resources:

OHRP August, 2004 Guidance on Research Involving Coded Private Information or Biological Specimens: <http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf>

Guidance on Research Use of Stored Data or Tissues:
<http://www.hhs.gov/ohrp/humansubjects/guidance/reposit.htm>

OHRP Human Subjects Decision Charts:
<http://www.hhs.gov/ohrp/humansubjects/guidance/decisioncharts.htm>

OHRP Policy Guidance (by topics): <http://www.hhs.gov/ohrp/policy/index.html#tissue>

Additional helpful discussion is provided in the 4/2006 version of NIH's PHS 398 Part II *Supplemental Instructions for Preparing the Human Subjects Section of the Research Plan*: <http://grants.nih.gov/grants/funding/phs398/HumanSubjects.doc> (pages 3-5 discuss OHRP's August, 2004 Guidance).

Suggestions of language that may be deemed acceptable consent language for conducting pharmacogenetic analyses and/or posting data on PharmGKB from extant samples that are defined as “coded”.

Example language in the consent documents for extant coded samples that would generally be considered acceptable for future research and posting data to PharmGKB are shown below:

I agree that some blood/urine/DNA samples may be kept at XXX institution (or by Dr XXX) for use in future research to learn about, prevent, treat or cure diseases.

I agree that my blood/urine/DNA samples and other relevant information may be shared with other researchers, as long as my sample and other information is coded in a way that makes it very unlikely that my data could ever be traced back to me.

For samples that meet the definition of de-identified, anonymized, or anonymous, they would typically be categorized as “not human subjects research”, and so would not be subject to IRB regulations or consent requirements.

MODEL PROCEDURES AND CONSENT LANGUAGE FOR PROTECTION OF CONFIDENTIALITY FOR SUBJECTS WHO PARTICIPATE IN PHARMACOGENETICS RESEARCH STUDIES.

It is the intent of the PGRN investigators and NIH staff that as much data as possible should be placed on the PharmGKB Website and made available to interested researchers. Inadvertent release of data that would identify any potential individual or participant would seriously jeopardize the research effort and undermine the goals of the pharmacogenetics researchers. Protection of individual research subjects' confidentiality thus must be primary, and takes precedence over the dissemination of information. At the present time, non-identifiable data, such as aggregate data on polymorphisms, their position and allele frequency, and aggregate pharmacokinetic or pharmacodynamic data such as would appear in a manuscript can appear on PharmGKB without privacy concerns. Genotype or phenotype data on individual subjects requires that the individual samples are submitted to PharmGKB as de-identified or anonymized data. PharmGKB has approval from Stanford's IRB that specifically requires only de-identified or anonymized data be accepted. **Therefore, elements that represent personal health information (PHI), as defined by HIPAA, should not be submitted to PharmGKB.** The 18 elements that are considered PHI under HIPAA are shown below.

HIPAA de-identification requires removal of 18 types of data or certification by statistician that reidentification risk is very small. The 18 types of information are: (1) names; (2) all geographic subdivisions smaller than a state, except for the initial three digits of the zip code if the geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; (3) all elements of dates except year, and all ages over 89 or elements indicative of such age; (4) telephone numbers; (5) fax numbers; (6) e-mail addresses; (7) Social Security numbers; (8) medical record numbers; (9) health plan beneficiary numbers; (10) account numbers; (11) certificate license numbers; (12) vehicle identifiers and license plate numbers; (13) device identifiers and serial numbers; (14) Uniform Resource Locators (URLs); (15) Internet Protocol (IP) addresses, (16) biometric identifiers; (17) full-face photographs and any comparable images; and (18) any other unique, identifying characteristic or code, except as permitted for re-identification in the Privacy Rule.

MODEL CONSENT LANGUAGE: Confidentiality and posting of data to PharmGKB

Confidentiality: Participation in research may cause a loss of privacy. All information gathered about you in this study will be used with information from other participants. Your name will not be used in published results and data from the study will not be reported in a way that can be linked to your identity. All your personal and medical data will be considered confidential. Once you have completed the study, all of the data collected on you will be coded in a manner that contains none of your personal identifiers. Only Dr. XXX and his/her designees will have access to the keys to the code, so as to minimize the risk of loss of confidentiality of genetic testing results. The keys to the code will not be shared with researchers who are not part of this research project.

The data obtained for your participation in this study, including your genetic data may be deposited into the Pharmacogenetics Research Network Database (PharmGKB) or another appropriate database on the World Wide Web. The PharmGKB database is a central repository for genetic and clinical information about people who have participated in research studies in pharmacogenetics. Its aim is to aid researchers in understanding how genetic variation among individuals contributes to differences in responses to drugs. Researchers for further studies in other patients may use information on this database. However, the database will not receive from our research staff any information that identifies you. All the data we send to the database will have identifying information removed. In addition, in order to obtain access to these data, users of the database must document that they are scientific researchers. These researchers must agree to the usage policies of the PharmGKB at the time they register and their use of data can be monitored by the database.

MODEL CONSENT LANGUAGE: Subjects' rights to intellectual property resulting from pharmacogenetics research.

Sample language that makes clear to subjects will not retain intellectual property rights in genetics investigations in which they participate are proposed below.

By consenting to participate in this study, you authorize the use of your tissue samples and data for research. Your tissue samples will be kept by Institution XXX or by a third party designated by Institution XXX (such as another university or a private company). If you later decide to withdraw from the research study, you may do so. You may also request that your samples and information about you are destroyed. If possible, we will honor your request, however, this may not be possible. Once you contribute data and tissue samples, they may no longer be in an identified form that would let us locate them and destroy them, or they may already have been supplied to other researchers or databases, or there may be other reasons why Institution XXX needs to retain the samples for further study and validation of results. Therefore, when you contribute data or tissue samples to this study, you should assume that it will not be possible for you ever to get them back. By signing this form, you are consenting to allow Institution XXX to retain your tissue samples and data on a long-term basis and to make decisions about how your samples and data will be used in the future.

If commercial products or other valuable discoveries result from this research project, these products and discoveries could be patented, licensed, or otherwise developed for commercial sale by Institution XXX or its designees. If this should occur, we will not provide financial compensation to you, or share with you the patent rights, other ownership rights, or rights to control any resulting commercial products and discoveries that may result from this research project.

Specific language for cell lines

Cells obtained from your body may be used to establish a cell line that may be shared in the future with other researchers that may be of commercial value. A cell line is one that will grow indefinitely in the laboratory. Cell lines may be useful because of the characteristics of the cells and/or the products they may produce. If commercial products or other valuable discoveries result from this research project, these products and discoveries could be patented, licensed, or otherwise developed for commercial sale by Institution XXX or its designees. If this should occur, we will not provide financial compensation to you, or share with you the patent rights, other ownership rights, or rights to control any resulting commercial products and discoveries that may result from this research project.

MISCELLANEOUS CONSENT PROVISIONS

Re-contact of subject based on research findings. Depending on the local IRB regulations, the investigator may wish to clarify that the Institution or investigator is not taking on any obligation to re-contact research participants/specimen contributors, in the event that the research discovers information that would be relevant to a subject's future health. For example:

It is possible that, in studying tissue samples and data from you and others, researchers may discover information that would be potentially relevant to your future health. In the event that this occurs, there are no plans to make this information available to you, since the tissue samples may have been coded in a way that makes it difficult to trace the result back to a specific person, and since the results of scientific research of this type are often based on group data, and therefore represent a general risk, but not a specific diagnosis of risk for an individual."

Re-contact of subject for additional data/sample in current study or future studies. If there is any possibility that PGRN researchers may need to harvest more samples from particular individuals whose tissues have shown interesting results, or if they may wish to invite the subject to participate in a future study, it would be wise to seek the subjects' consent to be re-contacted in the future:

Please indicate whether you would or would not be willing to be recontacted in the future to ask you whether you are willing to contribute additional specimens for study or to participate in other studies. By checking below, you are not agreeing to contribute more specimens or participate in future studies. Rather, you are simply agreeing to let our researchers get in touch with you in the future, to ask whether you would be willing to contribute more tissue samples or participate in another study at that time:

I am willing to be recontacted by Institution XXX about possible future contributions of my tissue samples for use in research or participation in future studies.

I do not want to be recontacted to ask me to contribute more tissue samples in the future or to participate in future studies.