IRISH MEDICINES BOARD

GUIDELINES FOR PHARMACOGENETIC RESEARCH

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This guide does not purport to be an interpretation of the law and/or regulations relating to the authorisation and is for guidance purposes only.

1. SCOPE

This guideline includes requirements for clinical trials, where samples for pharmacogenetic research are to be taken.

2. PROTOCOL

The protocol must define:

2.1 Rationale; clinical relevance, risk-benefit (for the participant).

2.2 Study design: studies should include an estimate of power. In some cases the frequency of polymorphisms may not be known, or may be known only in a population with characteristics different from those that are in the study.

In these cases, the number chosen for the study should be justified on the basis of some hypothesis or other consideration, which must be clearly reported in the protocol.

2.3 The expected use of the DNA samples.

2.4 The method of preservation.

2.5 Who will be responsible for their preservation during different phases of the research.

2.6 What happens to the samples when the research is finished; whether or not they will be destroyed, if not, who keeps them for how long, and for what possible use.

2.7 The level of anonymity of the samples and the data.

2.8 When possible and applicable, the expected negative and positive impact which the study might have on the subject who furnished the genetic material, his family and society in general.

3. INFORMED CONSENT

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.

Minors and incapacitated subjects should only be included whenever it is highly predictable that there are only minimal risks. Consent from a responsible surrogate should be sought. Each ethics committee should evaluate the value of consent from such responsible surrogates.

The information given to the patient should include:

3.1 The possible risks and potential benefits for him/herself.

3.2 The rights of access to the results.

3.3 The procedures used to ensure the protection of confidentiality.

3.4 The type of information to be derived from the study and the information to be given to the subjects.

3.5 The possible implications, if any, for other members of his family of the genetic information gathered in the study.

(Appropriate counselling should be made available, when implications for subject or family result from the study.)

3.6 The possible options for future use of the collected data in other research.

3.7 The possibility to have samples destroyed after the conclusion of the study, to allow samples to remain anonymously in the bank, or to be informed of any future results using his/her sample.

3.8 The possibility that their sample may be used by the commercial sector.

4 ANONYMISATION

The choice of level of anonymisation should be made with specific reference to the protocol. The patient information leaflet should provide a clear explanation to the subject, with regard to the method of sample labelling. This should include the advantages and disadvantages of the method of sample labelling to be used in the study.

See EMEA guidelines *Understanding the terminology used in pharmacogenetics*-EMEA/3842/04/Rev 2/Draft -June 2005

Summary of the terminology of sample labelling;

Identified-There is a direct link between subject identity and pharmacogenetic data. The sample is labelled with a name, or other unique way of identifying the subject.

With this category of coding, it is possible to fully identify which person the pharmacogenetic information relates to. The advantages for the subject of this type of labelling, is that they can easily ask for feedback about pharmacogenetic information. The subject can also ask the company to destroy the sample, or stop it being used for further analysis. The regulatory authority can also check the accuracy of the information, supporting the claim that a specific pharmacogenetic profile is associated with a certain type of response to a medicine.

The disadvantage of using identified samples is that there is no extra protection for any data produced as a result of pharmacogenetic analysis.

Single/Double coded-Subject and data are linked indirectly via a coding system. In the case of double coding, this is via two sets of code keys. The investigator holds the key to the first code but does not know the second code assigned to the genetic results. The advantages of single and double coding are that they allow samples to be withdrawn with immediate effect, or to add, future potentially valuable clinical information, to the study. They allow the participant access to the results of the study, and also allow the regulatory authorities to check the accuracy of data from the study.

Anonymised- There was initially a link between the sample and results using a coding system. The duration of the link depends on the objectives of the study. At the end of this pre-specified period of time, the link between the data and results is broken, by destroying the code and the code keys. The advantage of this method of sample storage is that it provides an increased level of data protection, but once anonymised doesn't allow subjects to withdraw from further analysis, or to access result

Anonymous-There is no link between subject and pharmacogenetic data. Total anonymisation is a good approach when it is particularly necessary to protect the confidentiality of the information and the results. However it doesn't allow subjects to withdraw from the study, or to receive individual results from the study. The method of sample labelling also has the disadvantage that it doesn't allow regulatory authorities to check how accurate and reliable pharmacogenetic data for a study is.

REFERENCES

1. Medical research Council, Clinical trial guidelines, available at http://www.mrc.ac.uk/index/publications/publications-ethics_and_best_practice/publications-clinical_trials_guidelines.htm.

2. US National Bioethics Advisory Commission Publications, available at http://www.georgetown.edu/research/nrcbl/nbac/pubs.html

3. Corrigan OP. Pharmacogenetics, ethical issues:Review of the Nuffield Council on Bioethics Report. J Med Ethics 2005;31:144-148.

4. Genetic Research and Human Biological Samples. Sheikh Asim A. Health Research Board 2002.

5. EMEA report to the CPMP on the EMEA seminar on the use of pharmacogenetics in the drug development process.EMEA/CPMP/1483/00.

6. CHMP position paper on terminology in pharmacogenetics (EMEA/CPMP/3070/01)

7. Understanding the terminology used in pharmacogenetics (EMEA-3842-04)

8. Nuffield Council of Bioethics, at http://www.nuffieldbioethics.org