The response reproduced below was submitted further to a consultation held by the Nuffield Council on Bioethics on its Report: *Pharmacogenetics- ethical issues*, during November 2002 – February 2003. The views expressed are solely those of the respondent(s) and not those of the Council.

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Q1 What do you think will be the likely economic impact of pharmacogenetics on the development of new medicines?

- I think the cost of pharmacogenetics would be very high for the foreseeable future but would decrease with time as the technology improves and becomes more reliable. A large degree of capital investment and time will be required to fund the research necessary to identify the genetic markers that indicate an individual's pre-disposition to certain types of drug-responses. This will be compounded by the fact that the genetics involved are likely to be very complex involving several genes, giving rise to the need to develop diagnostic tests that analyse more than one gene at a time. It is also likely that drugs from different 'families' of chemicals will be metabolised / absorbed by diverse mechanisms meaning that a vast array of these tests will be required before patients can be properly 'genotyped'. The conclusions drawn from pharmacogentic research should also be subject to regular scrutiny and re-validation which would also add to the costs. However, some costs could be reduced if treatments that have previously been withdrawn by regulatory authorities may become viable again if it was found that their apparently poor safety record could be dramatically improved by excluding some patients on the basis of their pharmacogenetic data.

Q2 Do you think that further regulatory measures will be needed to encourage the development of clinically desirable but economically unprofitable medicines?

- Yes, but this would need to be accepted on a global level – i.e. incorporated into ICH Guidelines and into law across the world.

Q3 In your view, should pharmacogenetic testing of participants in trials be a regulatory requirement for the development of medicines in the future?

- Yes, especially for safety reasons, but this issue would have to be approached very carefully as it could lead to the exclusion of some individuals from taking

part in research. It is not clear how it would be possible to predict individual's drug responses in advance for early phase studies for genetics as animal work and computer modeling would not be adequate to do this. It would also be incredibly different to have this measure in place for very novel agents under investigation.

Q4 Who should be responsible for providing a pharmacogenetic test? For individual therapy, should tests be available directly to patients over the counter or on the internet, or should they only be available through medical practitioners as part of a decision about the use of a prescribed medicine?

- The tests should only be available through practitioners.

Q5 What will be the implications of pharmacogenetics for pharmaceutical companies and providers of healthcare regarding legal liability for adverse reactions?

- The use of pharmacogenetics should not exempt the pharma companies and health care providers from any responsibilities regarding adverse reactions. There will always be the possibility of unexpected adverse drug reactions and not all would be explainable by genetic pre-disposition. It would also not be possible to identify all the possible genetic polymorphisms that could result in an adverse drug reaction (in 1999 over 800 mutations of the Cystic Fibrosis gene that affected the activity of the protein the gene codes for had been identified). Pharma companies and health care providers may feel forced to exclude patients who are genetically at 'high risk' of having a serious adverse reaction to avoid exposing them to an unacceptable risk but this would have to be weighed against possible benefits. A process of obtaining informed consent to receive treatments, in a similar manner to that used in current research using human subjects, may become necessary to provide evidence that patients have been fully informed of potential risks and benefits. Hopefully this would help

prevent groups of patients at genetic risk of adverse reactions being denied treatment for fear of court action being brought.

Q6 Should medicines which have been developed for administration in conjunction with a pharmacogenetic test be distributed to countries in which testing facilities are not available?

- Yes, as this is the current situation anyway. Information from previous and subsequent pharmacogenetic research should be made available to all offered the treatment and may be used to inform healthcare givers' decisions on provision / withdrawal of treatments. Pharma companies should be encouraged to carry out pharmacogenetic research in such countries.

Q7 How should predictions of efficacy and safety, as well as cost, be integrated in deciding whether to provide a particular treatment to patients in (a) a public healthcare system, and (b) a private healthcare system?

- a) Currently the demand for high quality, independent evidence of the health and cost effectiveness of treatments is increasing and NHS decisions are increasingly based on evidence of this type. The requirement for this evidence-based approach to NHS decision making is likely to become increasingly rigorous in future.
- b) It is likely that the private sector may follow the public sector lead into an increasingly evidence-based approach to decision making.

Q8 Do you think the application of pharmacogenetics might exacerbate inequalities in the provision of healthcare? Is it likely to challenge the principle of solidarity that lies at the basis of the provision of national healthcare in the UK? Will the benefits of pharmacogenetics only be affordable or available to the wealthy?

- No, not in the UK where most healthcare is provided in the public sector. It is unlikely that pharmacogenetics will improve or exacerbate current inequalities in the UK. In other countries that are more reliant on private sector care it is

more likely that healthcare inequality will be exacerbated by the use of pharmacogenetics.

Q9 In your view, is the storage of genetic information for the purpose of pharmacogenetic analysis categorically distinct from storage of other kinds of genetic information, for example information about susceptibility to disease?

- No, given that the functions of only a small fraction of human genes are known, it is likely that pharmacogenetic analysis could reveal information about an individual's genetic make-up that has more far-reaching consequences than knowledge of likely responses to drugs (i.e. genetic diseases, paternity etc.)

Q10 What level of anonymity should be accorded to genetic information stored as part of research in pharmacogenetics?

- This should be a decision made by research participants – there should be options given during the consent process. However, it may be advisable for insurance reasons for all such research to remain anonymous. This could be made clear in a patient information sheet and consent form.

Q11 What kinds of consent should be required for the collection of samples for research in pharmacogenetics? Should pharmaceutical companies which collect samples in the course of research in pharmacogenetics be able to use such samples for any purpose, or should consent of the donor be restricted to allow usage only for specific kinds of research?

- Samples taken from patients should only be used for purposes for which express consent has been given or if the patient has consented to the use of anonymised samples in future research beforehand. Additional research on patients' tissue should only be carried out in a manner that would prevent patients being identified.

Q12 Do you think that researchers should provide individual feedback about genetic information obtained from participants in research in pharmacogenetics?

- Yes, if the patient consented in advance, the information is reliable / of high quality and if adequate genetic counseling is provided. Care should be taken with regard to what the likely outcomes will be and whether insurance etc. could be affected.

Q13 What, in your view, would be appropriate methods of regulating scope, storage and access with respect to pharmacogenetic information used in clinical practice?

- Pharmacogenetic information should be subject to the same safeguards as all medical records at present. Any requests for access to such information for the purposes of research should also be subject to scrutiny by the appropriate Caldicott Guardian / Information Commissioner and, at their discretion, patient consent may be required. The information should only be used for the purpose that it was requested / consent was given for. It seems reasonable that pharmacogenetic information should form part of a patient's medical notes as it could feasibly inform treatment decisions throughout their life. As part of an electronic patient records such information could be very important for patient safety – i.e. if they were to receive emergency treatment.

Q14 Do you think that the ethical and legal issues raised by the use of pharmacogenetic tests in primary care differ from those raised by other forms of genetic testing? What about non-genetic tests, such as tests for cholesterol?

- In most cases, no. However, pharmaceutical companies and other researchers may wish to request access to patients' pharmacogenetic information for research purposes especially as patients will increasingly become 'grouped' by their responses to drugs. The current NHS Research Ethics Committee, Caldicott approval and Data Protection systems should help ensure that certain groups of patients do not become exploited as a result of their particular genetic make-up.

Q15 What might be the psychological implications for individuals of

pharmacogenetic tests? Are such tests likely to reveal information that is of relevance outside the context of testing for response to medicines?

- Information obtained from pharmacogenetic testing has the potential to cause psychological distress in patients especially those being treated for serious disease / conditions if they are denied treatment on the basis of risk to them. This may also be of great concern to patients suffering from psychological or psychiatric conditions.

Q16 What implications do you think pharmacogenetic tests might have for family members?

- Another potential area of concern would be the issue of paternity which frequently arises during genetic testing. Great care will be required to minimise the possibility of potentially damaging information being disclosed.

Q17 In your view, are controversies likely to arise about who ultimately decides which treatment is prescribed in light of a pharmacogenetic test?

- Yes, patients who have been shown to be at high risk of a serious adverse reaction to a treatment may still wish to receive that treatment if there is no current alternative. Patients should be given as much information as possible to aid them in the decision making process but the possibility of seemingly irrational decisions being made will always exist. It may be difficult for healthcare givers to prescribe medications that they know carry a greater than acceptable risk to patients if a patient is adamant that they should receive that treatment.

Q18 Should patients be able to refuse a genetic test to determine response to medicines but still expect to receive a prescription?

- Yes but see my response to Q17 above.

Q19 Do you think that the providers of health insurance should have access

to pharmacogenetic information? What about other parts of the insurance industry, for example life insurance?

- No.

Q20 Do you think that pharmacogenetics will increase the likelihood of the grouping of patients according to racial or ethnic groups for medical purposes? If so, what might be the ethical and social implications of such an outcome?

- Possibly. As well as racial / ethnic groups, there is also the possibility of a 'genetic underclass' being created as there is as much genetic variation within ethnic groups as there is between them. If this is allowed to proceed in an unchecked manner, then health inequalities between ethnic/genetic groups are likely to develop as well those that currently exist between areas of differing levels of deprivation. It will be difficult to convince pharmaceutical companies to invest in research into less profitable genetic groups. IRBs / NHS RECs may start to reject more research proposals if it becomes apparent that the profitable genetic populations are being 'over-researched'.