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.

Mid Yorkshire Hospitals NHS Trust, Research & Development Committee, UK

The development of pharmacogenetics and other similar scientific advances will have a major impact on our ability to treat a wide variety of malignancies. We believe that the developments such as this will lead to more effective therapies and inevitably to increased costs. This will occur regardless of the UK's position (although it is important that a position is taken) because it is driven, as indicated by the document, by the largely US-based pharmaceutical industry and market.

Question 1
Development of new drugs should become cheaper which will lead to the development of a wider range of drugs and increased costs
Also of interest will be the economic impact on health economies through the need to test prior to treatment with the new medicines. Will potentially reduce costs by allowing marketing of drugs which have previously been shelved, and reducing the number of drugs invested in but not marketed. Some cost for the investment in developing tests. Consideration will need to include the potential development of a cohort of volunteers who are not representative of the whole population. There will need to be enough information available to determine and describe adequately the extent of variation in wider populations.

Question 2
Yes - there a large number of "orphan" diseases that have major impacts on the well being and survival of affected patients. It is important that society continues to development drugs for "uneconomic" diseases which have very limited therapies rather than just drugs for diseases where there may be many therapeutic options but which are profitable. Since the state will not resource the development of such drugs it will have be done by the pharmaceutical industry. In view of the fact that the pharmaceutical industry is driven by the "dollar" financial incentives are probably the only way to achieve this! If there is no regulation, the medicine will have a price tag that reflects its development costs.

Question 3
Only when genetic testing becomes part of routine life. Until then, not practical. Also, individuals should be able to refuse to be tested but still participate in trials, and still benefit from the research.

Question 4
Available through prescribing physicians as this is the only way that the correct analysis can be done for individual patients. This is all about "personalising" medicine. The major ethical and moral issue of allowing testing by non-physicians is that we are likely to end up with companies advertising for individuals to take a certain test. For example one extreme would be a gene analysis which a company could claim to be able to predict an individuals risk of developing

cancer. As the technology for such testing is becoming increasingly simple insurance companies could offer cheaper insurance if patients take a certain test! – frightening. There should be mandatory pre-counselling about the implications of testing in context of up to date information about regulatory authorities access to data – similar to requirements before HIV testing. Need concurrent legislation specific to the protection of this data, and who is licensed to hold data – similar to recent debates about tissue banks. Implications also for blood relatives of the patient need to be considered.

Question 5
If an adverse reaction occurs, how likely is it that it can be proved to legal standards that the reaction was / was not caused by the genetic variation? This information will need to be robust.
Healthcare providers - If a test is available and not offered or used, the patient should be able to claim for negligence, unless the provider can demonstrate that full disclosure of risks and implications was given in a manner the patient understood (principles of informed consent).
Pharmaceutical companies –should supply robust information about the reliability of their tests, their availability and costs, ownership and uses of the test material and results, and clear information about probabilities to enable informed decision-making. The reliability of predicting probability of adverse reactions will compound any lack of reliability of the test. However, details about the test will be commercially sensitive. There may be a potential for abuse if test is owned and marketed by the company that owns and markets the drug, but the two seem inextricably linked. I know of one company currently offering 'free testing', available to help determine suitability for a drug that they market. Will the pricing of tests should be subject to scrutiny?

Question 6
Depends on the individual drug, but broadly yes. If the lack of testing is due to economic factors in the country, again the principle of informed consent should apply. For the healthcare regulators of the country, the drug should only be marketed with a clear warning that a predictable reaction may occur, but that the test will not be available. The care providers, and the patient should also receive this information, and be informed where the test is available and whether they can access it at their own expense.

Question 7
Public system - Current systems such as NICE not always trusted by public. Suspicion of influence from lobby groups and companies. However, can't suggest a better alternative.

Private system – as long as such a system exists and is appropriately regulated, clinicians' professional codes and standards should suffice to ensure the patient makes an informed decision.

Question 8
Yes - a major source of variation is likely to be in the variation of individual doctors and their understanding of the technology. Yes if costs are increased, although there is no clear indication that costs will be increased. Also if development work takes place within restricted genetic pools. Need to ensure that cultural and religious views are considered. Are there any groups who would oppose genetic testing or storage of genetic data?

Question 9
No. It should all be subject to compliance with the data protection act.

Question 10
The level the donor agrees to in an informed consent process.

Question 11
Clarity of information is required at the point of sampling about the degree of linkage, ownership of the sample and data, how long the data will be stored and the purposes it will be used for. Donors may well be willing for anonymous samples to be used for further unspecified purposes. Donors should be aware at the point of sampling whether or not they will have access to information from linked samples.

Question 12
Yes. The information should also be available for the donor to use for other purposes e.g. if testing for a different variation is appropriate at a later date.

Question 13
Similar to the recent proposals for regulating tissue banks. Companies who collect genetic information should be required to register with a regulatory body. This would involve adherence to a code of conduct, and a fee to recoup the cost of random monitoring of practice by the regulators.

Question 14

No, similar issues apply for genetic and pharmacogenetic tests. Non genetic tests can have equally wide-ranging implications. However, a lack of confirmation that a finding is genetic reduces the implications for family members.

Question 15
Danger of fatalistic response, as many individuals may not understand the concepts involved and the limited implications of probabilities. It will be imperative to establish and communicate other likely factors influencing reactions to medicines. Genetic information may not be the most important factor in many cases.
Yes, other information may be revealed, and this increases the importance of a fully informed consent process, and a code of conduct for those handling this information.

Question 16
As described in the text, there will be implications for the use of medicines. There may also be implications for health insurance similar to that for the individual tested. The extent of the implications will be determined by the agencies who may or may not have access to the data e.g. police, government agencies.

Question 17
Yes. There will be natural variations in levels of understanding of the issues involved. There will also be natural variations in beliefs about risk-taking and cost. These suggest that consensus will sometimes be impossible to reach between individuals, prescribers and regulatory agencies.
Will licensing authorities take a view about restricting the use of a new drug if there is no safety information available for their 'genetic group'?

Question 18
It is essential that the patient has confidence in the testing process and trust in the company which will be processing and storing their data. If this is not achieved, then the patient should not be penalised in any way for refusing a test. Unfortunately, as testing will likely only indicate probabilities of reactions, in most cases I would support the patient's right to refuse a test.
However, if adequate regulation is established, and reliable tests provide a very high indication of adverse reaction, and public money is involved, then there are some cases where I would support withholding a prescription. For example if a reliable test would indicate a common genetic variation which means expensive drug administration is futile, or if a predictable adverse reaction will be severe enough to require extensive treatment at public expense.

Question 19
Access to information should be the subject of legislation. As insurers currently ask about lifestyle habits carrying significant health risks (including smoking and participation in extreme sports) I cannot see any difference in disclosing knowledge of additional risks, as long as the disclosure is by the individual. I would oppose insurers having access to information held by organisations. Individuals should disclose known risks to life insurance companies. I do not think insurers should be allowed to make their own determination of the level of risk associated with having a test performed.
The question of whether (and which) healthcare providers have access to the information should also be the subject of legislation. Although the background information give in the consultation document suggests it is likely that this information will be shared, I have no indication at present that commercial companies are making this information available.

Question 20 – racial and ethnic issues
I suspect that there will be a temptation to concentrate on the development of medicines which could be marketed to affluent groups or countries. It should be recognised that this happens already, with medicines developed for affluent markets while the treatment of some conditions in developing countries is neglected. The whole concept of pharmacogenetics is to target medicines to specific patient groups. It would be unfair to expect pharmacogenetics to be a vehicle for social reform.