

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.

Royal College of Physicians, Committee on Ethical Issues in Medicine

Pharmacogenetics raises fears in many people. Much of this is the instinctive response to any new development in the basic science of genetics whose public image is coloured by images of Frankenstein, mutants, cloning and so on. Some of these fears are legitimate: genetic information has implications not only for individuals but for those to whom they are related. My consent to the release of information has implications for others who have not consented. The Nuffield Council's consultation on pharmacogenetics is extremely welcome as an attempt to examine a number of the issues. We note that it coincides with an increasing number of articles and reviews in the medical literature on pharmacogenetics and pharmacogenomics.

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

This is an empirical question and not therefore one for the RCP's Committee on Ethical Issues in Medicine (CEIM).

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

Again this is an empirical question. We do believe that the development of economically unprofitable medicines ('orphan medicines') will need positive encouragements – and should receive it - but cannot comment on whether such measures already in place are sufficient.

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

Given that such testing offers the possibility of maximising safety (& therefore non- maleficence), yes.

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?

Where the therapy is provided by a medical practitioner, it would seem logical for that individual to provide such testing. That does not exclude alternative providers. There may be considerable anxieties about quality of provision over the internet and the counselling that might be needed to accompany such testing. Our preference would therefore be to limit the provision of testing to accredited professionals (e.g. pharmacists, doctors etc). The public will need accessible information on the standard of testing available.

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

It will need to be made clear that normally such tests will only provide probabilistic information. Adverse reactions cannot therefore be excluded with certainty. As in other areas of medical practice, the notion of reasonableness in the amount and quality of information provided will be likely to dictate the liability – both in law and ethically.

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 – at least such distribution should not automatically be excluded. If a medicine is cheap and valuable for a major disease, while its side effects' risks identified by testing are (relatively) minor it would seem highly unethical to ban the use of the drug from a poorer country. Because a country cannot afford the best is no justification for only allowing it the worst: no treatment at all. We note that in some poor countries, samples can be sent away for tests – a member of the RCP CEIM has knowledge of this in Bangladesh where samples can be sent away to Singapore. So while the drug may be available easily – perhaps over the counter without even a prescription- testing may be available for the wealthy. Extreme differentials in wealth are morally offensive but while they exist, both between and within countries, banning health care facilities does not seem an appropriate response.

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?

The answer is dependent on the economics of testing. The avoidance of side effects and the greater use of efficacious medicines (thus saving waste in giving greater numbers ineffective therapies) should save costs. This would be attractive to any system, public or private. But new technologies have often increased costs. Rationing is a reality in public healthcare systems and a level of probability of response to a costly therapy will have to be defined for funding by the public purse. Treatments are frequently offered at present for which patients only have a likelihood of responding at well below the 10% level. (Cardiopulmonary resuscitation is a well known example).

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?

This will depend on the costs of the new technology and the degree to which it increases overall healthcare costs. Previous experience may make one anxious about this but pessimism should not be assumed.

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?*

In most genetic research in clinical trials in the UK, genetic information is anonymised at an early stage and no feedback is offered. It will ultimately be published in aggregated form. Most ethics committees are satisfied with these arrangements and agree with guidance provided by the Medical Research Council. In the case of pharmacogenetic information, there is a direct therapeutic implication and the information must be available to individuals. To this degree, the storage of such information is distinct.

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

In the research context, the current arrangements are appropriate. Unlinked anonymisation makes feedback unnecessary and there is no duty of care. The information is not relevant at this stage as its significance is unknown. All this requires consent of course, as at present.

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 for 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?

Currently, most patients consent for studies to be carried out in the broad area of interest of a current project, acknowledging that new techniques may develop. Provided samples are unlinked and anonymised this is ethically sound – as in MRC guidance.

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

See above responses. Unless there are likely implications for a patient, samples may be best anonymised with no feedback, with consent.

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

The Human Genetics Commission might be empowered to take on this role. It is likely that a body with ethical & genetic expertise would be desirable.

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 test for cholesterol?

Probably not: cholesterol may have implications for the family too, so may many other biochemical tests.

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?

An individual who is identified as a non-responder to a variety of medicines may well feel much the same way as an individual with various other social, educational or medical shortcomings. The answer to the second part of the question seems to be speculative at the present time.

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

Rather similar ones to current genetic tests, at least in principle.

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

Yes. Those controversies exist already as medicine is practised in a consumerist society.

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

The question is a consumerist one versus professional integrity. If the harm was likely to be great without the test, many would take the view that it would be unethical to prescribe, no matter how much the patient wanted the drug. More marginal risk/benefit situations would be more controversial. At least in principle, an automatic right to a treatment cannot be assumed.

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?

This should be legally regulated if health care were to be provided in a social insurance system – as in many other European countries and as has been proposed by some analysts for the UK. Given that access to health care should be on the basis of need, access to pharmacogenetic information would be likely to discriminate in the provision of care on other grounds than need. Against this, there would be no discrimination in the public system – another argument in the view of many for the moral superiority of state health care.

In the private sector then, matters are different. If I choose to belong to an insurance scheme, I expect to pay according to risk – as in any other form of insurance. This may include pharmacogenetic information. Provided there is health care available from the state, it is accepted that other forms of insurance, such as life insurance, may be affected by pharmacogenetic information. But this is no different from the present situation in that various disease entities and risk factors affect insurance premiums and availability. For life insurance, we believe

that insurance should not be terminable by the insurer on the basis of change in individual circumstances.

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?

Yes, on balance this does seem likely. In order to maintain equality of access to healthcare, positive measures will be needed to ensure that this has no adverse consequences. We already target certain high risk ethnic groups for health education in the UK (e.g. diabetes in Asians). Pharmacogenetics does raise the possibility that certain groups (majority or minority) could find themselves without the therapies enjoyed by other sections of society. Given that major pharmaceutical companies are multinational, one hopes this will not discourage the development of alternatives. Given the nature of the international market however, this could imply the need to encourage new 'orphan' drugs.