Translating pharmacogenetics research into practice: ethical and policy issues

18th - 19th September 2003

Hinxton Hall Conference Centre
The Wellcome Trust Genome Campus
Hinxton Hall, Cambridgeshire

Contents

Acknowledgements

Wellcome Trust:

Dr Bella Starling (Scientific Programme Officer, Biomedical Ethics)
Mr Martin Sexton (Policy Officer, Biomedical Ethics)
Mrs Georgie Penfold (Conference Administrator)

External advisors:

Professor Andrew Webster (Science and Technology Studies Unit, University of York)
Dr Paul Martin (Institute of Genetics, Biorisk and Society, University of Nottingham)

Disclaimer

The views expressed in this report do not necessarily represent the views of the Wellcome Trust, nor the views of any of the other organisations represented at the meeting.

Executive Summary

- This meeting recognised an opportunity for policymakers and ethics researchers to identify the potential ethical implications of pharmacogenetics before the science is fully developed and translated into clinical practice. Ethics research can help to identify policy options for the implementation of pharmacogenetics, and can assist policymakers in developing flexible responses.

- Policymakers should maintain the strategic capacity to respond to developments. It will be important to avoid a policy 'lock in' over pharmacogenetics, ie. a situation in which policy solutions are based on too narrow a range of assumptions about how the technologies will develop, leading to inappropriate policy solutions that cannot easily be revised.

- Dialogue should continue between regulators and the pharmaceutical and biotechnology industries to remove obstacles to the appropriate uses of pharmacogenetics in drug development. This should be supported by more public sector research on the economic barriers and drivers for developments in pharmacogenetics.

- Incentives may be needed to encourage the development of pharmacogenetics technologies that are based around existing drugs.

- Post-marketing surveillance of drugs should become more systematic and incorporate new technologies such as pharmacogenetics. This should be a key responsibility for industry as well as the public sector.

- The NHS will need to develop capacity in a number of key areas to manage the introduction of pharmacogenetics. These key disciplines include technology evaluation, clinical pharmacology, pharmacy, epidemiology, and health economics. Training in genetics should also be provided for other health professionals throughout the NHS.

- More research is needed on prescribers' behaviour, to understand how pharmacogenetic information may feed into clinical decision-making in practice.

- The introduction of pharmacogenetic tests into the NHS will provide an opportunity to re-evaluate the current regulatory framework for clinical testing in general. This will be a key question for clinical governance.

- Counselling in the NHS may need to be re-evaluated following the introduction of pharmacogenetics. A framework needs to be developed based on the impact of the information that will be generated by the test in question, rather than the fact that the information is derived from genetic analyses.

Purpose of the meeting

The Wellcome Trust's *Biomedical Ethics* programme seeks to build the knowledge base in this field, and to provide guidance and recommendations on the practical and policy implications of new biomedical research.

Pharmacogenetics, and its ethical, legal, social and public policy implications, has provided an important research focus within this programme. Following a call for proposals in 1999, the Trust funded five projects addressing a range of issues in this field (see Appendix 4). This research has now come to fruition and has produced a range of outputs. The Trust's *Biomedical Ethics* programme continues to consider applications for research in this area.

A workshop was held on 18 and 19 September 2003, drawing on the outcomes of these research projects. The meeting brought together some 30 participants, including researchers, policy makers and practitioners in various fields, as well as representatives of the Department of Health. The discussions focused on current understandings of pharmacogenetics, and how these might influence new technologies being 'translated' into the practical context of the clinic.

This question is particularly important in the light of the Government White Paper on Genetics, *Our Inheritance, Our Future*. The White Paper includes considerable discussion of the potential role of pharmacogenetics in the NHS and planned new investment to foster research that may help to secure the clinical delivery of pharmacogenetics in the long term.

The Workshop examined the development and potential deployment of pharmacogenetics, and explored the proposals raised in the White Paper, drawing on research supported by the Trust, and other evidence. The meeting also discussed the likely timescale of the various impacts of pharmacogenetics, and considered what factors might shape its introduction into the NHS and the implications for policy development.

There was also an opportunity for participants to comment on the draft call for proposals on pharmacogenetics research from the Department of Health.

Note: The meeting did not set out to reach consensus on all issues, but to identify points of substantial agreement and disagreement. This report is therefore a reflection of the discussions at the meeting, rather than a statement of consensus.

The Nuffield Council of Bioethics report "Pharmacogenetics: ethical issues"

As evidenced by funded research and this Workshop, pharmacogenetics has attracted considerable attention. In particular, the Nuffield Council on Bioethics (of which the Trust is a principal funder) published a report entitled "Pharmacogenetics: ethical issues" on 23 September 2003.

The discussions at the meeting on 18 and 19 September broadly echoed the findings of the Nuffield Council's report, but with a different focus. The Nuffield report is a detailed analysis of the various ethical issues that might arise as a consequence of pharmacogenetics.

The Trust meeting addressed some of those issues, but also looked in depth at some of the problems and tensions that may arise when pharmacogenetics is incorporated into regulatory decision-making and clinical practice.

Plenary discussion

1. Key messages from the meeting
2. The Department of Health's pharmacogenetics initiative
3. Suggestions for future activities.

1. Key messages from the meeting

Key messages for policy

There is a 'window of opportunity' to assess the potential social and public policy impacts of pharmacogenetics before it diffuses widely into healthcare practice. The clinical evidence base for pharmacogenetics is at a very early stage of development. It will be important to maintain momentum in the dialogue between social scientists and policy makers to address these impacts and issues.

It is likely that pharmacogenetics will be introduced into healthcare in a variety of ways and on a number of fronts, without a single predominant timeframe, business model, or method of service delivery. Policymakers therefore need to maintain strategic capacity to move with developments in pharmacogenetics and embrace significant levels of uncertainty. It is important to avoid a policy 'lock in'.

Key messages for regulation and innovation

Some concern was raised over the potential for clinical trials incorporating a pharmacogenetics element to develop over-complex consent procedures for participants. If separate consent processes are used for participation, access to medical records, and pharmacogenetics testing, this could lead to confusion and uncertainty for participants. Efforts to address this problem in commercial and academic research should continue.

One suggestion from the meeting to ensure the protection of patients in clinical trials was to hold DNA banks (particularly commercial banks) accountable to a public body, on issues of consent amongst other matters. It was also recognised, however, that there were limits to public oversight in this area because of issues of commercial confidentiality. Some approaches to protection of participants (eg. irreversible anonymisation of samples) will not always be possible due to the need to maintain audit trails to ensure regulatory compliance and good practice.

(NB. The public accountability of biobanks was also addressed in the 'Recommendations on the Ethical, Legal and Social Implications of Genetic Testing' made by the European Commission Expert Group in 2004.)

Methods should be developed to inform and counsel patients on the issues involved in taking a pharmacogenetic test in a range of contexts, including clinical trials. In many cases, this would require an approach that was different from traditional genetic counselling, as it was felt that pharmacogenetic testing usually did not raise the same issues as other forms of genetic testing eg. testing for risk factors for disease.

This point should be considered in the light of a broader evaluation of the evidence base for counselling for clinical testing in general. The meeting heard arguments that counselling methods are not rationally distinguished at present, and many types of clinical test are not currently accompanied by any counselling. There is no single framework that determines which patients receive counselling for which test. There is a need for more social research on this issue, as well as assessments of the likely impact of increased provision of counselling on NHS resources.

Frameworks of clinical governance will need to take account of pharmacogenetics. Many of the issues raised in pharmacogenetic testing are generic to clinical testing as a whole, but the introduction of pharmacogenetics technologies may trigger widespread changes to existing frameworks. Some participants felt that the current clinical testing regime in the NHS had a number of shortcomings and should be re-evaluated.

Clinicians and other practitioners may have difficulty absorbing the implications of pharmacogenetic test results. The regulatory system needs to recognise this, and improve its mechanisms for generating the necessary information. Advances also need to be made in the field of decision support systems, building on developments in other fields, such as computer-based algorithms used in diagnostic tests for breast cancer.

A more systematic approach is needed for post-marketing surveillance of drugs. One view was that the public would not find it acceptable if pharmacogenetics approaches are not deployed to detect and minimise adverse drug reactions (ADRs). This raises the question of who should bear the primary responsibility for surveillance of ADRs. More resources may need to be devoted to these issues by drug companies, as well as the health service. The meeting noted that the ‘yellow card’ system for monitoring ADRs is currently under review.

Key messages for NHS delivery

During the next few years, as the evidence base in pharmacogenetics expands, capacity should be developed in the NHS in a number of areas. One immediate focus should be on the evaluation of tests and products, particularly in clinical settings. Capacity building in service delivery should be addressed once there is more evidence of the effectiveness of pharmacogenetic technologies.

The NHS should carry out personnel and professional planning in a number of specialities, particularly clinical pharmacology, pharmacy, epidemiology, and health economics. Some participants felt that there should be clearer lines of accountability for these matters within the Department of Health. Training in pharmacogenetics will also be required for other health service professionals.

It might be instructive to compare pharmacogenetic testing with other forms of clinical and diagnostic testing being introduced into the NHS. This would help to identify the underlying

assumptions, practices, and utility of existing clinical testing procedures. Good practice in existing testing processes should be relevant to managing issues of sensitivity and specificity in pharmacogenetic tests. In common with other forms of clinical test, pharmacogenetic tests are unlikely to be 100% sensitive, ie. able to detect all individuals with a particular pharmacogenetic profile, nor 100% specific, ie. able to exclude all individuals without a particular profile.

One possible comparative case study might lie in the introduction of various forms of antenatal testing, which deploy a range of approaches to pre-test counselling and consent. The model of antenatal care may be instructive because it takes place in busy clinics where consent processes may be subject to considerable pressures of time. In addition, midwives do not always have in-depth knowledge of the tests that are being administered. Pharmacogenetic testing in primary care or community pharmacy might take place in a similar situation.

2. The Department of Health's pharmacogenetics initiative

The Department of Health advertised a call for proposals in pharmacogenetics research in October 2003, with a closing date in January 2004. This focused on research on ADRs of particular importance for the NHS. The call for proposals sought to attract multidisciplinary teams to work on projects that would help to establish the cost effectiveness of pharmacogenetic approaches to reducing ADRs. Participants at the meeting had an opportunity to comment on the call for proposals in draft form.

The meeting identified one priority area for advances in pharmacogenetics technology: the development of high throughput methods that are able to handle sequence data from thousands of cases. Resources could be used to establish points of comparison between different methods of analysis, and use these to compare the likely clinical utility of the outcomes of different studies.

The range of pharmacogenetic variation between patients, and therefore the size of the cohorts required for pharmacogenetics research, will depend on the magnitude of the effects of the various genes involved. As these effects will often be individually quite modest, large cohorts may be required. The Department should consider what role the Genetics Reference Laboratories could play, eg. in recruiting sufficient numbers of participants for Department-sponsored studies.

The Department of Health's programme should provide support to NHS-embedded researchers to look at NHS rollout issues and compare different approaches to incorporating pharmacogenetics into health service provision. There will be aspects of the process that are best studied by researchers working in close relationship with service providers.

The complexities of the likely influence of genetics on drug response need to be recognised. The Department of Health should not support research that adopts simplistic models of the relationships between genetic variants and ADRs.

Participants noted that pharmacogenetics research *per se* is not always especially demanding in terms of the scientific complexities involved: researchers should already be well equipped

scientifically to deal with these. The difficulties lie instead in creating a research infrastructure that will facilitate rapid developments in pharmacogenetics research and implementation. This points to the involvement of parts of the biotechnology sector, and the potential importance in this field of LINK programmes (the UK Government's principal mechanisms for promoting partnership in pre-commercial research between industry and the research base). Given the global level of interest in pharmacogenetics, it would be important to focus on what UK-based researchers are best placed to deliver.

3. Suggestions for future activities

- Gain insights from other settings on the barriers to uptake and the tensions that can arise when clinical testing is introduced in advance of a fully comprehensive evidence base. One possible example would be antenatal care.

- Develop new methods for evaluation of pharmacogenetics combining insights from Health Technology Assessment and other approaches.

- Look at the wider issues surrounding clinical testing – an interdisciplinary debate is needed.

- Develop a better understanding of consent in the full range of settings in which it is important (research, clinical practice, commercial activity etc).

Discussion groups

Discussion group 1: Clinical Trials & Drug Development

Main points

- Consent processes in pharmacogenetic trials should be as clear as possible. Patient information leaflets on pharmacogenetics should continue to be improved.

- An ethical governance framework should be elaborated to address the issues that will be raised by pharmacogenetic testing in trials. This could be on a national or regional level.

- A government-funded clinical directorate should be set up to co-ordinate all clinical trials in progress and to facilitate information exchange between relevant parties.

- A public-private partnership should be established to determine the incentives for companies or public institutions to analyse drugs for pharmacogenetic data purposes.

- Efforts should continue to link phenotypic data to genotypic information in clinical trials. Studies may need to become either more segmented or conversely more targeted (in terms of genotyping) with regard to the diversity of the trial population. This will be key to more effective detection of ADRs, and may also improve efficacy of treatments.

- Pharmacogenetics is likely to be more clinically efficacious in secondary care rather than in primary care in the first instance, because of the relative ease of implementing it through existing infrastructures.

- Education and training, perhaps provided through Genetics Knowledge Parks, should encourage greater engagement opportunities for clinical and academic collaboration.

- Public consultation is vital.

Discussion

<u>Informed consent in pharmacogenetic clinical trials</u>
A pharmacogenetic component to a clinical trial will add testing steps (eg. extra blood testing and genetic testing). As a result of these extra tests, additional informed consent is sought from trial participants, to cover consent specifically for pharmacogenetic testing and for banking of pharmacogenetic information. In some cases, consent might need to be given for three or four different procedures.

Some participants at the meeting were concerned that increasing the number of requests for consent during a clinical trial (eg. through incorporating pharmacogenetic investigations) might compromise the validity of the consent obtained. For example, by repeatedly having to consent to different procedures, a trial participant may become confused what it is they are actually consenting to in each situation.

In addition, individuals involved in clinical trials may confuse participation in the trial with provision of treatment. The introduction of pharmacogenetics into clinical trials may compound this confusion, as pharmacogenetic studies may be considered to be therapeutic. Research ethics guidelines advocate that a different risk/benefit assessment be deployed for non-therapeutic research, as the risks of participation cannot be offset against potential benefits.

A distinction needs to be drawn between the collection, storage and genetic research of a sample for specified research directly related to the patient's response of the drug undergoing clinical trial, and the banking of the sample for unspecified purposes unrelated to the trial.

Consent to a pharmacogenetic trial *per se* would obviously be sought prior to the trial. Another model suggested that governance of consent should move to the collective (eg. patient group) level: here, there may be circumstances where a drug may be perceived to be of particular value to a particular patient community (such as AIDS patients) where the terms of consent are defined through wider forms of negotiation and mutual reciprocity.

Public reaction to pharmacogenetic testing

In response to debate on the extent to which trial participants confuse research with treatment, it was suggested that more effort be devoted to producing patient booklets on pharmacogenetic trials. These would outline the nature of clinical trials, and, in particular, the non-therapeutic nature of pharmacogenetic trials.

Continuing on this theme, the group urged that public engagement is vital to the implementation of pharmacogenetics. There is a risk that pharmacogenetic data, by identifying the need for additional testing, may contribute to mistrust surrounding some medicines, by making some patients wary of taking drugs. However, by first establishing governance and ethical frameworks (with appropriate public consultation), consumer opinion on pharmacogenetics could be informed and encouraged.

DNA banking – consent, use of information and feedback

The group discussed issues concerning DNA banking, ie. long-term storage of data and samples for genetic evaluation beyond the initial time frame and scope of the original research study. What happens when pharmacogenetic data eventually lead to clinically validated information that may be relevant to individual trial participants? The group debated the relative merits of the approaches in trials sponsored by public and commercial organisations, with some participants arguing that publicly funded trials had better approaches to this question. It was very important for the terms of engagement over this complex issue to be agreed prior to the trial commencing.

The group stressed the necessity for all parties to exercise care in handling genetic information (including pharmacogenetic information). A particular concern was access to data by insurance companies. Although a moratorium is currently in place pertaining to the use of genetic information in underwriting insurance, the future is unclear. Some participants expressed concern that current safeguards were inadequate, speculating that there might be circumstances in future in which insurance companies could buy genetic information from other commercial organisations. Genetic information might also become available to insurance companies via other routes, for example, by the merging and acquisition of

companies across different sectors. (NB the Association of British Insurers has stated that data from genetics research should not be used for underwriting purposes.)

Registration of clinical trials

Although there is currently a National Research Register for clinical trials, it is incomplete. For example, it is often the case that information on clinical trials only reaches the public domain when they start recruiting patients. Often, pharmacogenetic information is not listed.

The case was therefore put forward for establishing a Government-funded clinical trials directorate, which would include public and private stakeholders. Such a directorate would serve as the main repository for clinical trial information. It could co-ordinate communication and intelligence sharing between clinical trials, and enforce appropriate consent-seeking procedures.

An alternative would be to establish institutions at the regional level to safeguard participants and promote the ethical procedure of pharmacogenetic trials, while considering the various commercial and public interests involved.

(NB The Department of Trade and Industry's Bioscience Innovation and Growth Team published a report in November 2003, a key recommendation of which was the establishment of a National Clinical Trials Agency. This recommendation was accepted in the Budget of 17 March 2004.)

Exclusion of trial participants

There are high hopes that pharmacogenetics will lead to better prediction of treatment outcomes and hence more effective allocation of resources. Conversely, the inclusion of pharmacogenetics in clinical trials may mean that fewer numbers will be needed for trials. Some participants were concerned that this would lead to the exclusion of 'poor metabolisers' and the potential marginalisation of certain other populations. This could create orphan patients. In this scenario, Government was urged to consider policy mechanisms to influence companies to specifically target trials at 'non-responders'.

Pharmacogenetics and secondary care

It was generally agreed by the group that pharmacogenetics is likely to impact first and foremost on secondary care practices rather than primary care situations.

Some participants felt that point-of-care testing is currently impeded by knowledge gaps surrounding genetics. Information consolidation and education is needed in secondary care systems to address the specific issues that pharmacogenetics raises, in particular genetic knowledge and its consequences for the patient. It was suggested that Genetics Knowledge Parks could help to address any knowledge gaps through education programmes and debates.

Other participants felt that resistance to uptake of genetic technology was not primarily due to lack of knowledge, and a more sophisticated understanding was required of the factors influencing take-up of genetic testing in secondary care.

Phenotypic and genotypic information in pharmacogenetic trials

It was suggested that one of the reasons why pharmacogenetics has yet to fulfil its promise is through the type of information gathered in clinical trials. Efforts should continue to bring

genetics and medicine closer together, and to integrate phenotypic data (including psychological data) in trials including a pharmacogenetic element. Increased phenotypic monitoring may help to address the incidence and causes of ADRs. To this end also, it was proposed that more efforts be devoted to the training of clinical pharmacologists and to bringing academics into clinical medicine more generally.

Incentives for pharmacogenetic testing of medicines

Who decides which drug to put forward for pharmacogenetic testing? The rationale behind including pharmacogenetics in a clinical trial considers pharmaco-economic information and socio-ethical factors. Care should be taken to carefully weigh up the benefit to patients against commercial profit-making factors.

Currently, all data derived from clinical trials are bound for consideration by the European Agency for the Evaluation of Medicinal Products (EMEA) or the Medicines and Healthcare Products Regulatory Agency (MHRA) in the UK. These regulatory agencies may be one avenue for making the decision to return to a trial for further pharmacogenetic investigation. However, repeated submissions to a regulator may diminish the incentives for pursuing commercial pharmacogenetic trials.

Although industry is carrying out some pharmacogenetics research on existing medicines, there may not always be sufficient incentives for companies to pursue pharmacogenetic testing in respect of marketed compounds, as it is likely to be time-consuming and expensive. Thus, Government may need to offer incentives for such trials.

How then, would Government decide which drugs should proceed to pharmacogenetic trials? Caution was expressed that Government should not be passing judgement on which drugs to trial for pharmacogenetic factors. Instead, a joint initiative of some sort, preferably a public-private partnership, should be set up to investigate the need for, and develop the incentives for, pharmacogenetics to fulfil public health needs.

Discussion group 2: healthcare delivery

Main points

- There are few, if any, ethical issues that are specific to pharmacogenetic testing; rather the issues that arise are typical of concerns across clinical testing in general.

- Clinicians will have a range of responses to pharmacogenetics. Some applications of pharmacogenetics will be welcomed; others will give rise to ethical concerns, which may make clinicians wary of using it.

- Drivers for demand could include: public and professional education demonstrating the benefits of pharmacogenetics (which will require building up an evidence base); investment in research (to establish an evidence base); and litigation.

- Capacity issues to be addressed include research, staffing levels and evaluation skills (such as epidemiology and health economics).

- There could be a role for pharmacists to issue prescriptions using pharmacogenetics tests, following referral from clinicians.

Discussion

The nature of pharmacogenetics

Pharmacogenetics is about probabilities, not 'individualised' medicine. This has clinical implications because a genetic test may only reveal a small probability that a particular drug may be safe or efficacious. There is a need for guidelines to be drawn up to enable practitioners to relate genetic test results to prescriptions.

Some participants felt that practitioners are already aware that tests in clinical practice, genetic or otherwise, are probabilistic in nature. Any additional tests (such as pharmacogenetic tests) will simply revise the prior probability of success of a possible treatment. It will be an important challenge to educate health professionals and the public that all tests are probabilistic, including genetic tests.

There is a need to unpack the critical issues raised by pharmacogenetics – which are generic to all medical testing? Which are pharmacological? Which are specific to genetics?

As pharmacogenetics enters clinical practice, it is likely that a range of practical difficulties will become apparent. A great deal can be learned from current practice in other areas, because most issues arising from pharmacogenetics are not specific to this new technology. For example, research on how clinicians and patients handle probabilistic information resulting from other tests may be useful. There may be complications specific to pharmacogenetics, however, eg. if patients refuse a pharmacogenetic test because they are concerned that they run the risk of not receiving a particular course of treatment.

One type of treatment where pharmacogenetics could be valuable is selective serotonin uptake inhibitors (SSRIs), used in the treatment of depression. These drugs are very closely related to each other, and the choice between prescribing one over another is largely arbitrary at the moment. These choices might be made more rational by introducing pharmacogenetic tests to determine the risk of ADRs or which drug or dose will be most efficacious.

Drivers of change

Clinical Trials and Litigation

Almost all clinical trials now involve a pharmacogenetics component looking at the relationships between genetics and good and bad responders to medication. ADRs and the fear of litigation may be a key driver for the uptake of pharmacogenetics into clinical practice.

Clinicians and Litigation

The perceived threat of litigation may also affect clinical practice. If a pharmacogenetic test is available but is not carried out for some reason, this could open up the possibility of legal action. The situation is likely to be unclear, however, due to the complexity of the law concerning medical negligence.

Targeting clinical specialities
There will not be a single rollout of pharmacogenetics; instead it will enter practice in a variety of ways. Given the existing culture and governance frameworks in oncology, for example, pharmacogenetics roll out in cancer treatment may well be easier in this speciality than in others. Similarly, within coronary heart disease, a culture of testing is already in place, into which pharmacogenetics could mesh.

Stratified Populations
For clinicians, pharmacogenetics will lead to more targeted medicine in which better informed decisions can be made about the most appropriate treatment, on the basis of a range of tests. This will tend to divide populations into ever-smaller sub-groups on the basis of the outputs of these tests. Whilst this may be important for minimising ADRs, the group felt that subdividing the population in terms of efficacy would be of doubtful value in most cases.

The prospect of stratified populations could provoke public concerns in a number of areas, such as the possible reintroduction of race as a biological concept, and differential treatment or prescribing for different races leading to unfair discrimination. The implementation of pharmacogenetic technologies should be sensitive to these perceptions and concerns.

Health-economic factors
The process by which most health technologies are introduced in the UK can be analysed in terms of supply-induced demand. Policymakers will need to consider the extent to which the supply of pharmacogenetic technologies should be promoted. Better evaluation frameworks are needed to determine this.

Some research suggests that in terms of drugs under development, pharmaceutical companies are still more interested in the 'blockbuster' drugs than in producing new drugs for subgroups of patients. Commercial research may leave certain gaps in important areas of research and development. Alternative sources of funding will have to come from the public and voluntary sectors.

Pharmacogenetics tests are likely to be fairly cheap and there may be hundreds of new tests. It may therefore be difficult to evaluate them comprehensively.

Other drivers
Consumer pressure from clinicians
- If evidence suggests that pharmacogenetics tests are beneficial, this will prompt GP demand. However, investment in evaluation will be essential in order to generate the evidence base.
- Clinicians want to give patients better treatments – i.e. driven by clinical outcomes. One serious ADR could have a significant influence on clinicians in terms of driving pharmacogenetics practice.

Consumer pressure from patients
- Genetically aware patients are already driving oncology practice by demanding increasingly individualised/personalised therapies for cancer.
- Patient groups are more focused on clinical outcomes than ethical problems.

Barriers to uptake of pharmacogenetics

A number of barriers to change were identified by the group:

- The pharmaceutical industry may be resistant to independent pharmacogenetic testing of on-patent drugs that could potentially lead to significant reductions in their market.
- There will be a pressing need for expert systems to assist practitioners in prescribing drugs (this problem is not confined to pharmacogenetic testing).
- Changes in the division of labour when GPs refer prescription judgements to pharmacists may lead to uncertainty over how pharmacogenetic tests should be administered and the results utilised.

Health service capacity

In order to implement pharmacogenetics, the NHS will need increased capacity in a number of specialities, including genetics, epidemiology, and health economics. It may be necessary to push supply in order to stimulate demand for these specialities, as existing demand may be insufficient to develop capacity in a timely fashion.

The NHS needs to recognise that, once this increased investment in capacity has been made, it will act as a significant driver for change in the nature of health services towards genetics-based medicine. Careful planning is required, but this will require an evidence base that is lacking at present.

Issues around genetic testing

Pre-test counselling for pharmacogenetics will need to be carefully considered. At present, genetic counselling is geared towards issues raised by testing for single gene disorders. Counselling needs to be re-considered and developed with pharmacogenetics in mind. It should be borne in mind however that some pharmacogenetics tests may also provide information on prognosis and susceptibility.

Discussion group 3: regulation and governance

Main points

- A range of approaches should be taken to developing the governance of pharmacogenetics, as there is no predominant clinical model or business model which could dictate a particular approach.

- Dialogue should continue between industry and regulators in order to establish how pharmacogenetics can best be incorporated into processes for drug trials and licensing. The public sector should support research on the economic aspects of pharmacogenetics, and the barriers and drivers affecting its take-up.

- Pharmacogenetics raises important issues of clinical validation and marketing, many of which are generic to medicine and clinical testing in general. It will be vital for practitioners to have access to appropriate information in a format that can be assimilated into their decision-making processes. Clinical governance frameworks need to evolve to address these problems in healthcare delivery.

- Safety rather than efficacy is likely to be the most significant issue for clinical governance in the short term.

- Pharmacogenetics is unlikely on the whole to raise the same ethical questions as other forms of genetic testing, such as testing for single gene disorders or other disease risk factors. However, it is also unlikely to be distinct in any fundamental way from other forms of clinical testing.

- Providing appropriate information on pharmacogenetic testing will have to take account of public perceptions of 'genetic exceptionalism' (ie. the belief that genetic information is fundamentally different to other kinds of biological or medical information).

Discussion

Four models of governance were presented to stimulate discussion:

1. 'Hierarchical': traditional bureaucratic model, which focuses on managing process;
2. 'Rational goals': a targets-based approach, which often collapses into model 1 when difficulties are encountered;
3. 'Self-governance': often subject to criticism, but positive outcomes can be achieved if it is possible to work with the culture in question;
4. 'Open system': potentially very flexible and responsive to change and uncertainty, but difficult to steer.

<u>Licensing of new therapies and tests.</u>
The current regulatory uncertainty surrounding pharmacogenetics technologies was identified as a significant issue. It appeared to participants that companies seemed to be waiting for guidance from regulators on what should be included in applications to license pharmacogenetics-related technologies. Conversely, regulators appeared to be waiting to see what information the companies are prepared to put forward, before offering guidance.

The discussion group felt that regulators and industry needed to further develop their dialogue to address these concerns. One particular area that needed to be examined was the size of study populations that would be needed to license pharmacogenetics-related products.

'Safe harbour' approaches can be useful in this regard. These are arrangements whereby companies discuss exploratory data with regulators on a confidential basis. This should help to expand the evidence base for pharmacogenetics technology, which is an important requirement. However, some participants were concerned that there might be potential for conflicts of interest in these developing arrangements.

Better economic models are needed to understand the barriers and drivers associated with innovation in this field. Industry may have its own proprietary models, but public sector research should also be undertaken. It would be important to know what kinds of information sharing and networks (including 'safe harbours') might facilitate or inhibit developments in pharmacogenetics.

Governance of clinical practice

It was felt that pharmacogenetics is unlikely to raise many new questions in most instances, but may highlight existing problems in testing and prescribing. Concerns were expressed that the current regulatory framework in the UK may not be producing enough of the right information to address these difficulties. Improvements would be needed both in the information provided by the agencies approving drugs and tests, and NHS guidelines.

In responding to pharmacogenetics at this stage of its development, clinical governance frameworks may need to give priority to measures to ensure protection of patients, rather than broader public health issues such as the comparative efficacy of different therapies.

Clinical governance will also need to take account of the fact that the gatekeepers (ie. those professionals who control access to services) for pharmacogenetics-related therapies will increasingly belong to specialisms other than clinical genetics.

A key issue would be practitioners' access to the appropriate information to enable them to make prescription decisions. In parallel with this, a better understanding is needed of prescriber behaviour. Understanding how health professionals use all available information, including pharmacogenetics data, to make decisions is as important as the availability of the information itself.

One concern discussed at the meeting was over medicines licensed for use only in conjunction with a pharmacogenetic test (without which patients could be exposed to risk of a severe ADR). This by itself does not protect patients from off-label prescribing without the use of the test. For high-risk medicines there might need to be additional safeguards e.g. use restricted to secondary care and by specifically trained and authorised personnel only.

A related issue is who is responsible for ensuring that a pharmacogenetic test has been carried out. What responsibility does someone administering a risky drug have to check that the pharmacogenetic test had been done and the result showed it was safe to proceed?

Governance of genetic testing

As previously stated, the discussion group's view was that pharmacogenetic testing should not be seen as distinct in any fundamental way from other forms of clinical testing. It was recognised however that the implementation of pharmacogenetic tests would be influenced in part by wider perceptions within society of the supposedly 'exceptional' nature of genetic information. The point was also made that the introduction of pharmacogenetics into the health service could facilitate the introduction of other genetic technologies.

The group discussed a number of possible exceptions to its general view that pharmacogenetics did not raise the same ethical issues as other forms of genetic test. There will be some cases where pharmacogenetics tests will provide information on issues such as disease susceptibility, in addition to predictions of drug response. Such cases could raise

issues similar to those that arise in other forms of genetic testing, such as confidentiality, implications for other family members, the need for counselling, and so on.

Another respect in which pharmacogenetics might prove to be different from other forms of testing is its potential to introduce new conflicts of interest into clinical practice. New actors will emerge, such as pharmacists, both in the supply of therapies and tests and in prescribing.

Appendix 1: Meeting Programme

Thursday 18 September 2003

10:00	Registration & coffee	*Foyer*
10:30	Welcome from Wellcome Trust *Clare Matterson, The Wellcome Trust*	*James Watson Pavilion*
10:35	Chair's introduction *Andrew Webster, University of York*	
10:40	Pharmacogenetics: current status and future challenges *Munir Pirmohamed, University of Liverpool*	
11:10	Translating pharmacogenetics into commercial and clinical practice *Paul Martin, University of Nottingham*	
11:40	Pharmacogenetics: Current policy issues for health systems, clinicians and patients *David Melzer, University of Cambridge*	
12:10	Discussion	
12:25	Lunch	*Foyer*
13:45	Pharmacogenetics and the White Paper *Dianne Kennard, Department of Health*	*James Watson Pavilion*
14:15	Breakout groups: (1) Clinical trials & drug development (2) Healthcare delivery (3) Regulation and governance	 *Loft Room 1* *Loft Room 2* *James Watson Pavilion*
17:15	Close	
18:00	Drinks	*Hall Foyer*
18:30	Dinner	*Restaurant*

Friday 19 September 2003

09:30	Chair's introduction to day 2 *Andrew Webster*	*James Watson Pavilion*
09:35	Pharmacogenetics and equity – stratifying drugs, diseases and patients *Nikolas Rose, LSE*	
10:05	Feedback from breakout groups	
11:00	Coffee break	*Cloisters*
11:30	Plenary session	*James Watson Pavilion*
12:30	Chair's closing remarks	
12:35	Lunch	*Foyer*
13:35	Depart	

Appendix 2: Abstracts

Plenary presentations

"Pharmacogenetics: current status and future challenges"

Professor Munir Pirmohamed
The University of Liverpool, Dept of Pharmacology, Ashton Street, Liverpool L69 3GE

Pharmacogenetics has a long history, dating back to the time of Pythagoras, with the term being coined in 1957. Its history is punctuated by a series of advances, but progress overall has been slow. Interest in the area was renewed following the completion of the first draft of the human genome, and since then there have been a number of important developments, which can be divided into three areas:

a) Increasing realisation that pharmacogenetics may be important in improving drug therapy has led to specific funding programmes from the National Institutes of Health (NIH) in the US, and in the UK, from the Wellcome Trust, and more latterly the UK Department of Health, as outlined in the White Paper *Our Inheritance, Our Future – Realising the potential of genetics in the NHS*. As important has been the investment from the pharmaceutical industry, which will act as a catalyst for future advances.
b) Genotyping technologies are improving rapidly and importantly, also becoming cheaper, both of which in the future may allow whole genome scanning to become a reality. However, it is important that such technologies are widely available, and it is essential that they are cheap.
c) Implementation of pharmacogenetics into clinical practice – this is the ultimate goal of pharmacogenetics, which unfortunately has lagged behind. There are few examples where drug prescribing is currently guided by patient genotype, for example, for the use of Herceptin in breast cancer, or determination of the activity of thiopurine S-methyltransferase (TPMT) activity before the use of azathioprine in the treatment of leukaemia. It is essential that much more emphasis is directed to this area.

The talk will largely concentrate on the third area, by providing examples of successes, but also outlining some of the scientific barriers that need to be overcome to realise the potential benefits of pharmacogenetics on healthcare delivery.

"Translating pharmacogenetics into commercial and clinical practice"

Dr Paul Martin
Institute for the study of Genetics, Biorisk and Society, University of Nottingham, NG7 2RD

This presentation summarises initial findings from a Wellcome Trust funded research project on *'The Clinical and Commercial Development of Pharmacogenetics'*, which will be competed by the end of 2003.

In the first part of the talk I will describe the way in which pharmacogenetics technology is being developed by the biotechnology and pharmaceutical industries. The project has identified a number of distinct options or 'visions' for the commercialisation of pharmacogenetics, which cover the entire process of discovering, developing and using medicines. In particular, there are two main divisions, between strategies aimed at improving efficacy versus safety, and strategies applied to new drugs and already licensed medicines. The research findings suggest that whilst large pharmaceutical companies are investing in pharmacogenetics to improve their internal processes of drug discovery and development, they are less interested in applications aimed at established products. The use of pharmacogenetics in the prescribing of already licensed medicines is therefore likely to be driven by small biotechnology firms, diagnostic companies and health care providers.

The second part of the talk will then describe research looking at the potential application of pharmacogenetics to the prescribing of a number of established medicines; Warfarin, Clozapine and 6-Mercaptopurine. Interviews carried out with clinicians, pharmacists and other NHS staff involved in the routine use of these drugs highlighted a number of key points:

1) There is a complex relationship between genotype, clinically important phenotypes and drug response;
2) Alternative (non-genetic) forms of diagnostic testing may be better in helping guide prescribing;
3) There was little clinical demand for pharmacogenetics testing;
4) Pharmacogenetics testing is likely to be only used as an additional prescribing tool.

In conclusion, the implications of the findings of the research for the development of 'personalised medicine' will be explored.

"Pharmacogenetics: Current policy issues for health systems, clinicians and patients"

Dr David Melzer
Institute of Public Health, Forvie Site, Robinson Way, Cambridge CB2 2SR

The Wellcome Trust-funded Cambridge pharmacogenetics policy study aimed to identify the important issues for health care stakeholders, and focussed on the availability of sound evaluation evidence for clinical decision-making. 86 experts were consulted internationally, including European and American regulators, academics, clinicians and patient advocates.

Genetic testing could help identify some patients at risk of serious adverse events, guide dose adjustments and help choice of the most effective drug for individual patients. However, there is substantial uncertainty over the science base and the rate at which clinical applications of pharmacogenetics are likely to emerge. While older drugs cause most adverse events, most of the published commentary on pharmacogenetics has focussed on new compounds. Ensuring a sound evidence base for test drug combinations will be a complex technical and regulatory challenge. The basis of test regulation in the US has been fundamentally different from that in Europe, where evidence of safety or efficacy was not required. How new European regulations work in practice needs monitoring. Clinical evaluations of tests offered by labs is an area of concern. Genetic research should be added to post marketing surveillance systems.

Without policy action, pharmacogenetics could produce a new generation of poorly evaluated tests and drugs. A number of choices exist for the timing and nature of the policy response. There is a need for public investment in evaluative expertise and in the 're-development' of old drugs.

"Pharmacogenetics and equity - stratifying drugs, diseases and patients"

Professor Nikolas Rose
The London School of Economics and Political Science, Houghton Street, London WC2A 2AE

I will consider a number of ethical issues raised by pharmacogenetics, taking 'ethical' in its widest sense, and begin by outlining the major ethical, legal, social, political, commercial and subjective issues that I think are raised by pharmacogenetics. I will then focus on two issues. The first is the prospect of pharmacogenetics acting as a 'wedge' for the generalisation of genetic testing into the doctor's surgery and its implications, as well as the varieties of forms of resistance that such a move might encounter. The second is the question of equity and the potential implications of pharmacogenetics for stratifying drugs, diseases and patients, especially on grounds of 'race'.

Discussion Groups

Group 1: Clinical Trials And Drug Development

Chair: Professor Andrew Webster
Lead participant: Dr Oonagh Corrigan

Clinical drug trials, and the research subjects on whom such trials are conducted, play a crucial role in drug development. Giving particular attention to the recent inclusion of pharmacogenetics add-on studies to conventional clinical trials, this session will examine the past, present and potential procedures involved in clinical drug trials, from the initial testing of new drugs in healthy volunteers through to subsequent phases involving patients. Questions will be raised for discussion in the subsequent breakout session that focus both on the socio-ethical impact for subjects taking part in clinical drug trials as well as issues relating to future patient populations.

Questions for discussion:
- Do current informed consent procedures address the problems posed by the banking of DNA samples for future as yet undetermined use by the pharmaceutical industry?
- Who will determine whether a newly developed drug should be licensed in conjunction with a pharmacogenetics test?
- Who will fund research for pharmacogenetics tests of existing medicines?
- What are the incentives if any for the pharmaceutical industry to do so?

Group 2: Healthcare Delivery

Chair: Dr Paul Pharoah
Lead participant: Dr Adam Hedgecoe

The Genetics White Paper seems to assume that pharmacogenetic products are not yet on the market, and that the NHS has a degree of 'breathing space' to decide how these drugs should be incorporated into clinical practice. While this is true for the 'classic' approach to pharmacogenetics (e.g. ADRs and CYP450), a commonly used broader definition that incorporates *non-inherited* tumour genetics allows us to look at how pharmacogenetics has already entered the clinic. An example of this kind of pharmacogenetics is the drug Herceptin, which is prescribed to women with metastatic breast cancer whose tumours have an amplified gene called HER2.

In talking to clinicians who have been using Herceptin over the past two years, a number of issues concerning clinical practice have become apparent. For example, clinicians rarely tell patients that their tumours are being tested for HER2 status, effectively undergoing a form of genetic testing.[1] Partly this is because the tumour is also being tested for a number of other, non-genetic, factors and it is impractical to discuss all these tests with every patient. But by

[1] Part of the complexity of pharmacogenetics is that this test does not tell us anything about the patient's own genetic make-up or that of their family, but simply gives information on genes driving the tumour's growth.

not informing patients of the HER2 test, clinicians are also protecting patients from the disappointment that results when they find out they are ineligible for they new drug.

This sort of well-intentioned paternalism raises important issues about informed consent in clinical practice. This will become even more important should pharmacogenetic tests become desktop 'black boxes', with minimal background information required to operate them. In a situation where a GP has little idea about what genes are being tested for when s/he submits a patient's blood sample to the lab (or black box), what kind of informed consent can we expect a clinician to get?

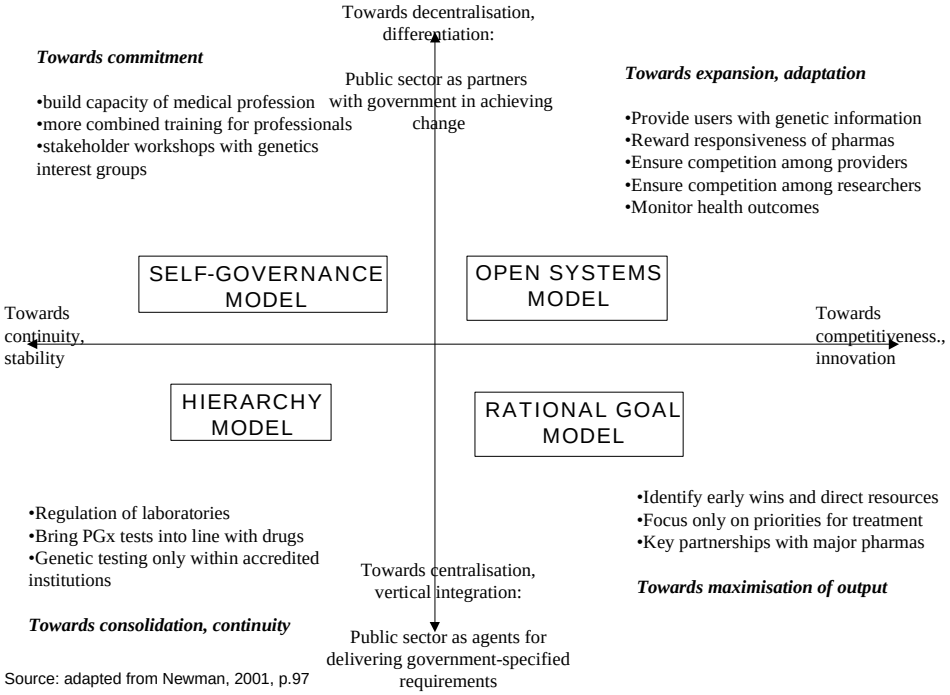
There is already a debate in the literature over the need for front-line clinicians to gain 'genetic literacy' if new technologies like pharmacogenetics are to be implemented. Unfortunately much of this discussion ignores the broader literature investigating public understanding of and reaction to genetics; a clear message is that better-informed publics are not necessarily more supportive of particular technologies. How much genetics does a clinician need to know to use pharmacogenetic drugs properly?

Group 3: Regulation & Governance

Chair: Dr Celia Brazell
Lead participant: Professor Tom Ling

The aim of Government and the Department of Health (as articulated in the Genetics White Paper) is to develop appropriate regulations and governance arrangements to ensure that the potential benefits of pharmacogenetics are secured while risks are managed. This requires a continuation of 'conventional' approaches to governance (accountability and performance management arrangements) and regulation (understood in the broad sense of creating a regime of agreed formal and informal rules supported by effective sanctions and rewards). However, it also requires new arrangements for meeting the ways in which pharmacogenetics takes government action into 'open systems' where the complexity of the interactions challenge these conventional approaches to governance and regulation.

Models of governance:



Source: adapted from Newman, 2001, p.97

Appendix 3: Participants

Dr David Bentley
Wellcome Trust Sanger Institute
Hinxton CB10 1SA
☎: 44 1223 494886
Fax: 44 1223 494969
Email: drb@sanger.ac.uk

Professor Martin Bobrow
University of Cambridge
Dept of Medical Genetics
CIMR
Hills Road
Cambridge CB2 2XY
☎: 44 1223 331154
Fax: 44 1223 331206
Email: lms28@cam.ac.uk

Dr Celia Brazell
GlaxoSmithKline
B60, G30
Greenford Road
Greenford
Middlesex UB6 0HE
☎: 44 208 966 2924
Fax: 44 208 966 3368
Email: cb30662@gsk.com

Mr Dave Carr
The Wellcome Trust
Policy Officer
183 Euston Road
London NW1 2BE
☎: 44 207 611 8220
Fax: 44 207 611 8742
Email: d.carr@wellcome.ac.uk

Dr David Coles
European Commission
DG Research (Ethics & Science)
SDME 6/41
1049 Brussels
Belgium
☎: 32 229 91194
Fax: 32 229 84694
Email: david.coles@cec.eu.int

Dr Oonagh Corrigan
Centre for Family Research
Faculty of Scoial & Political Sciences
University of Cambridge
Cambridge CB2 3RF
☎: 44 1223 331567
Email: opc22@cam.ac.uk

Professor Nigel Eastman
St George's Hospital Medical School
Dept of Forensic Psychiatry
Cranmer Terrace
London SW17 0RE
☎: 44 208 725 5567
Fax: 44 208 725 2475
Email: neastman@sghms.ac.uk

Dr Imogen Evans
Medical Research Council
20 Park Crescent
London W1B 1AL
☎: 44 207 670 5022
Fax: 44 207 636 6289
imogen.evans@headoffice.mrc.ac.uk

Dr Adam Hedgecoe
University of Sussex
Dept of Sociology
Falmer
Brighton BN1 9QN
☎: 44 1273 877633
Fax: 44 1273 673563
Email: a.m.hedgecoe@sussex.ac.uk

Mr Tony Horn
Department of Health
653C Skipton House
80 London Road
London SE1 6LH
☎: 44 207 972 5645
Email: anthony.horn@doh.gsi.gov.uk

Mr James Jarrett
University of East Anglia
School of Health Policy and Practice
Norwich NR4 7TJ
☎: 44 1603 593960
Fax: 44 1603 593904
Email: j.jarrett@uea.ac.uk

Miss Dianne Kennard
Department of Health
653C Skipton House
80 London Road
London SE1 6LH
☎: 44 207 972 1606
Email: dianne.kennard@doh.gsi.gov.uk

Dr Graham Lewis
University of York
SATSU
York YO10 5DD
☎: 44 1904 433055
Fax: 44 1904 434702
Email: gl12@york.ac.uk

Professor Tom Ling
Anglia Polytechnic University
Sociology & Politics
East Road
Cambridge CB1 1PT
☎: 44 1223 363271 x2035
Email: t.ling@apu.ac.uk

Mr Rohantha Liyanage
The Wellcome Trust
Project Manager, Education
183 Euston Road
London NW1 2BE
☎: 44 207 611 8850
Fax: 44 207 611 8269
Email: r.liyanage@wellcome.ac.uk

Dr Paul Martin
University of Nottingham
IGBiS
Law & Social Sciences Building
Nottingham NG7 2RD
☎: 44 115 951 5419
Fax: 44 115 846 6349
Email: paul.martin@nottingham.ac.uk

Ms Clare Matterson
The Wellcome Trust
Director, Medicine, Society & History
183 Euston Road
London NW1 2BE
☎: 44 207 611 8424
Fax: 44 207 611 0665
Email: c.matterson@wellcome.ac.uk

Dr David Melzer
IPH
Forvie Site
Robinson Way
Cambridge CB2 2SR
☎: 44 1223 330332
Fax: 44 1223 330330
Email: dm214@medschl.cam.ac.uk

Dr Helen Middleton-Price
North West Genetics Knowledge Park
7th Floor St Mary's Hospital
Hathersage Road
Manchester M13 0JH
☎: 44 161 276 6095
Fax: 44 161 276 6145
helen.middleton-price@cmmc.nhs.uk

Ms Eileen Neilson
Royal Pharmaceutical Society of Great Britain
1 Lambeth High Street
London SE1 7JN
☎: 44 207 572 2217
Fax: 44 207 572 2501
Email: eneilson@rpsg6.org.uk

Mrs Georgie Penfold
The Wellcome Trust
Conference Organiser
183 Euston Road
London NW1 2BE
☎: 44 207 611 8442
Fax: 44 207 611 8237
Email: g.penfold@wellcome.ac.uk

Dr Paul Pharoah
Strangeways Research Laboratory
Worts Causeway
Cambridge CB1 8RN
☎: 44 1223 740166
Email: paul.pharoah@srl.cam.ac.uk

Professor Munir Pirmohamed
The University of Liverpool
Dept of Pharmacology
Ashton Street
Liverpool L69 3GE
☎: 44 151 794 5549
Fax: 44 151 794 5540
Email: munirp@liv.ac.uk

Dr Tim Root
Chelsea & Westminster Hospital
London Specialist Pharmacist Clinical Governance & Technical Services
Regional Pharmacy Offices
369 Fulham Road
London SW10 9NH
☎: 44 208 846 6853
Fax: 44 208 846 6860
Email: tim.root@chelwest.nhs.uk

Professor Nikolas Rose
London School of Economics and Political Science
Dept of Sociology
Houghton Street
London WC2A 2AE
☎: 44 207 955 7533
Fax: 44 207 955 7405
Email: n.rose@lse.ac.uk

Mr Martin Sexton
The Wellcome Trust
Policy Officer, Biomedical Ethics
183 Euston Road
London NW1 2BE
☎: 44 207 611 8791
Fax: 44 207 611 8254
Email: m.sexton@wellcome.ac.uk

Dr Andrew Smart
The Ethox Centre
University of Oxford
Institute of Health Sciences
Old Road
Oxford OX3 7LF
☎: 44 1865 227087
Fax: 44 1865 226938
Email: andrew.smart@ethox.ox.ac.uk

Dr Bella Starling
The Wellcome Trust
Programme Officer, Biomedical Ethics
183 Euston Road
London NW1 2BE
☎: 44 207 611 8536
Fax: 44 207 611 8254
Email: b.starling@wellcome.ac.uk

Dr Nicholas Steel
Institute of Public Health
Robinson Way, Cambridge CB2 2SR
☎: 44 1223 330325
Email: ns246@cam.ac.uk

Ms Jessica Watkin
Policy Adviser, Biomedical Ethics
The Wellcome Trust
183 Euston Road
London NW1 2BE
☎: 44 207 611 8837
Fax: 44 207 611 8254
Email: j.watkin@wellcome.ac.uk

Professor Andrew Webster
SATSU
University of York
York YO10 5DD
☎: 44 1904 434740
Fax: 44 1904 434702
Email: ajw25@york.ac.uk

Dr Anthony Woods
The Wellcome Trust
Programme Manager, Biomedical Ethics
183 Euston Road
London NW1 2BE
☎: 44 207 611 8686
Fax: 44 207 611 8254
Email: a.woods@wellcome.ac.uk

Dr Ron Zimmern
Public Health Genetics Unit
Director
2 Worts Causeway
Cambridge CB1 8RN
☎: 44 1223 740200
Fax: 44 1223 740200
Email: ron.zimmern@srl.cam.ac.uk

Appendix 4: Research on the ethical, social, legal and public policy aspects of pharmacogenetics funded through the Wellcome Trust Biomedical Ethics Programme

"Information Policy for Pharmacogenetics"
Dr David Melzer, Dr Ron Zimmern and Professor Don Detmer, University of Cambridge
Professor Tom Ling, Anglia Polytechnic University

"The ethical and socio-cultural implications of innovative genetics-based drug development. The application of pharmacogenetics in clinical drug trials - A case study."
Dr Oonagh Corrigan, University of Cambridge

"The Clinical and Commercial Development of Pharmacogenetics: Issues For Patients, Professionals and Public Policy"
Dr Paul Martin and Dr Alison Pilnick, University of Nottingham
Professor Andrew Webster and Dr Graham Lewis, University of York
Dr Andrew Smart, University of Oxford

"Pharmacogenomics and the genetic reclassification of common disease"
Dr Adam Hedgecoe, University of Sussex

"Ethical factors in psychiatric drug development: an archival study of the ethical factors that influenced the development and production of Prozac in Eli Lilly & Company Ltd"
Dr Mariam Fraser, Goldsmiths' College
Dr David Healy, University of Wales College of Medicine
Professor Nikolas Rose, LSE

Further details of these projects can be found on the Biomedical Ethics pages of the Wellcome Trust website:

http://www.wellcome.ac.uk/en/1/pinbio.html