Research ethics workshop – Wellcome Trust/KEMRI Programme
Kilifi, Kenya, 12 March 2004

Meeting report

General comments

- During the scientific meeting preceding the workshop, a high level of enthusiasm was expressed for the day.
- The workshop was well attended: approximately 42 people attended the morning session (35-40 anticipated); 32 remained for the afternoon session
- The audience was mainly composed of scientific researchers, both Kenyan and British, with some field workers and community liaison officers
- Most of the audience were based in Kilifi; some were from KEMRI in Nairobi
- The experience of research ethics in the audience was very varied: some researchers had no previous engagement with research ethics issues; some had extensive knowledge of research ethics principles and issues, particularly in the Kilifi context
- Overall, the workshop was very well received (see feedback). In particular, the presentations by Dr Doug Wassenaar and Dr Nhlanhla Mkhize were praised.
- The discussion of case studies in small groups was considered stimulating (see case study discussion); most participants would have preferred more time devoted to this aspect of the workshop, and to the subsequent plenary session.
- In addition to providing a training opportunity for less experienced researchers, the workshop provided an occasion for forging South–South links in this field.

Suggestions for improvement

- Because of the varied experience of the audience, the workshop would benefit from having an optional, more detailed, pre-session on the principles of research ethics.
- Following on from this point, more time to be devoted to case study discussions
- Earlier pre-circulation of the case studies: on this occasion the workshop pack was circulated the day before the workshop; some would have preferred more time to consider the case studies.
- The case studies used on this occasion had no obvious ethical resolution. In future, such case studies could be supplemented by simpler cases, as a springboard for discussion of the more complex studies.

1. Workshop timetable

Time	*Topic*	*Lead*
9.15-9.20	Welcome and introduction	Dr Norbert Peshu Director, KEMRI Centre for Geographic Medicine Research
9.20-10.00	Issues in the ethical review of health research in developing countries	Dr Doug Wassenaar Director, SARETI, University of KwaZulu-Natal
10.00-10.40	Overview of principles in health research in developing countries	Dr Doug Wassenaar Director, SARETI, University of KwaZulu-Natal
10.40-11.00	*Break*	
11.00-11.45	Social Reality, Clinical Reality and Culture: implications for moral and ethical decision-making in health-related research	Dr Nhlanhla Mkhize Dept of Psychology, University of KwaZulu-Natal
11.45-12.30	Consent, communication and understanding?	Dr Sassy Molyneux Training Fellow Wellcome Trust-KEMRI Research Programme, Kilifi
12.30-13.00	Plenary Discussion and the Wellcome Trust's 'Ethics of Research in Developing Countries' grants scheme	Dr Bella Starling Programme Officer Biomedical Ethics The Wellcome Trust
13.00-13.50	*Lunch*	
13.50-14.00	Introduction of cases, format of group discussions	Dr Doug Wassenaar Director, SARETI, University of KwaZulu-Natal
14.00-15.00	Group discussions	All
15.00-15.15	*Break*	
15.15-15.30	Group discussions	All
15.30-16.00	Plenary feedback	Dr Bella Starling Programme Officer Biomedical Ethics The Wellcome Trust
16.00-16.15	Summing up	Dr Kevin Marsh Director Wellcome Trust-KEMRI Research Programme, Kilifi

2. Case study discussions (incorporating plenary discussion)

Case study 1: Reimbursement of participants in international health research

Briefing for participants

Acknowledgement: Dr Doug Wassenaar

Many authors have pointed out the complexities of research conducted in developing countries sponsored by developed countries.

One of the many related complexities concerns the payment of research participants for participation in health research. There is little consensus in terminology and guidance documents on this issue, and great variation in practice. Some authors argue that payments should only be made to healthy volunteers – on a scale that reimburses them for travel and time, in addition to a midday meal if necessary. Other authors argue that healthy and 'patient' participants should be reimbursed equally for time, travel and discomforts/complexity of procedures/samples. Other still argue that payment should be a simple, uniform daily rate.

Further complications arise in studies and trials which have developed and developing country arms. Paying the developing country cohort the same monetary amount (e.g. US $ 30 per visit) as the developed country cohort might be regarded by a local ethics committee as an undue inducement to the developing country persons to participate.

- Is there a difference between payments, inducements, undue inducements, incentives and reimbursements? If so, how do these terms relate to each other?
- With reference to an ethical framework, discuss whether healthy volunteers and 'patients' should be reimbursed equally in health research.
- Should inducements and reimbursements be considered 'benefits' of participation in research – e.g., should they be included when the research ethics committee does a risk/benefit analysis of a protocol?
- With reference to an ethical framework, how can the issue of standard reimbursements in both arms of a multinational study be resolved without undue inducement on the one hand and exploitation on the other?
- A hypothetical research centre in a developing country has become a well-funded site for local and multi-national collaborative health research. The centre has an active community development policy and programme, developed in close collaboration with local community members. This comprehensive policy includes employment and training opportunities for community members. It excludes health care beyond that offered by the various studies hosted by the centre.

The centre has experienced increasing problems with various externally funded projects based at the centre, with regard to uneven reimbursement of research participants. Some studies pay a set rate per visit, while others pay a different rate, with additional payments for discomfort and a bonus for trial/study completion. This has led to complaints to various investigators and the centre's management team. Research participants have become aware that reimbursement rates differ for different studies. The centre is considering adoption of a new policy that requires all studies to pay participants a standard rate for transport only, calculated slightly above actual local rates. No extra payments to participants will be allowed by projects based at the centre. Surplus funds from research grant provisions for payment of participants will be deposited

in the Centre's community development fund rather than paid to study participants. This fund will be is spent/allocated in consultation with representatives of the local community.

- With reference to an ethical framework, discuss the merits and demerits of the Centres' new policy.
- Similarly, discuss whether this policy would be fair to participants in collaborative studies where there is an arm at the centre and an arm in a developing country.

Discussion

The group offered the following definitions for reimbursement, incentive and inducement. Reimbursements were defined as purely monetary concerns, but which incorporate an element of obligation, ie. participants are earning money for availing themselves for research purposes. Reimbursements ensure that the research participant was not worse off for having participated. Generally, the group felt that reimbursements were acceptable in research, but that they could be considered as incentives. Incentives and inducements were considered not just monetary in nature; however, inducements were felt to confer distinct monetary advantages to the research participant. The term 'inducement' had more negative connotations than the term 'incentive'. Some in the group felt that it was unethical to offer incentives for research. The distinction was drawn between inducements and *undue* inducements. Much discussion centred on whom should determine what is an undue inducement – the researcher, the research ethics committee?

Most in the group felt that it would be unethical – with reference to the eight benchmarks of ethical research in developing countries – to offer different reimbursements or incentives to patients and healthy volunteers involved in research. It was acknowledged, however, that patients might benefit more from participating in research, by receiving healthcare.

The group felt that research ethics committees should not consider reimbursements as part of the risk:benefit ratio of a protocol. Reimbursements, in the form of compensation for travel and time, were not felt to be benefits of research. Anything over and above reimbursements (ie. incentives and inducements) would be considered a benefit, but should not be financial in nature and should be made explicit to the research participant.

The group felt that a policy of paying research participants a standard rate in developed and developing countries, but retaining that part of the payment not considered a reimbursement in a community fund as described, to be ethically acceptable.

Case study 2: Comprehension and consent in Kilifi

Acknowledgement: Dr Sassy Molyneux

Background on The Wellcome Trust-KEMRI Research Programme, Kilifi and Nairobi:

Research studies in Kilifi on the Kenyan coast focus on clinical, basic and epidemiological aspects of malaria and other diseases of childhood, while work in Nairobi targets the pharmacology and therapeutics of antimalarial drugs, as well as malaria epidemiology, control and health policy. The Programme is integrated with the KEMRI Centre for Geographic Medicine Research.

The Wellcome Trust-KEMRI Research Programme also collaborates closely with the Kenyan Ministry of Health.

Briefing for participants

In the multidisciplinary research unit in Kilifi on the Kenyan Coast, parents sign consent for themselves or their children to be recruited into studies that cover the spectrum of types of biomedical research. Every study and consent form is reviewed in advance by independent national and international committees. A recent study exploring participant understanding of three ongoing studies (one field-based and two hospital-based), revealed low levels of understanding of the details of studies, with participants joining primarily because they trust in researchers' aims and activities, and because they are eager to access current or future benefits associated with research. The research institution is broadly appreciated, not because of the contributions of information to global knowledge about health and disease, but because of the benefits that accrue to the local population from research related activities. A range of interrelated issues were identified as contributing to these findings, loosely grouped into conceptual and linguistic barriers, the critical and complex role of communicators (fieldworkers and nurses) in consent procedures, and unit community relations.

A series of activities aimed at tackling some of the factors behind the shortfalls in informed consent have been initiated in this setting:

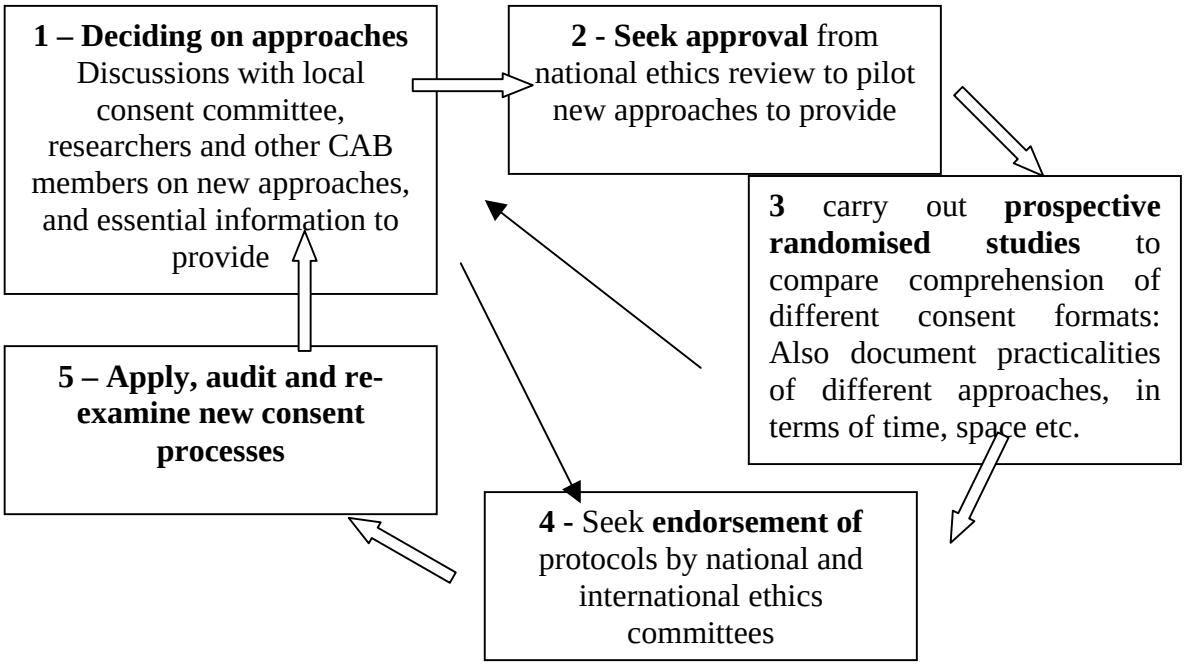
- Increased information, education and communication with the general community
- Involvement of local researchers and fieldworkers in developing and reviewing consent forms
- Improved interpersonal communication
- Developing standardised pre-tested IEC materials to feed into the above processes

Why consider alternative approaches to informed consent?
Informed consent is a central principle in the ethics of biomedical research, and at the time of the above-mentioned study, researchers were not achieving anything like full comprehension of all study details by all research subjects. Therefore, the unit is striving towards improved informed consent through a range of activities. However:

- there are significant impediments to achieving full comprehension of current informed consent even in settings where levels of education and income are far higher than here.
- there are specific situations in which understanding and genuine consent are inherently difficult to achieve, regardless of how carefully communication processes are designed and supported (for example where research involves seriously sick children).
- In some cases one small blood sample is being used for several studies in order to minimise the total number of blood samples taken. Individual study information is repetitive, time-consuming and possibly confusing.

What can be done?
One suggestion would be to seek alternative approaches to consent, such as requesting 'assent' only on admission for emergency research, developing a 'step-like' or 'continuous' consent process for other in-patient studies, and some form of 'unified consent' for immunological studies.

The following steps could be taken:



As unit members, community members, ethical advisors and research funders, discuss:

- Are new approaches to consent worth considering at all? On what basis?

Assuming some piloting of new forms is decided upon:

- Which alternative forms of consent should be prioritised for piloting and why?
- Are the steps outlined above appropriate and feasible? Should any be altered/added?
- Which on-going or planned studies would be suitable for piloting of asset, unified consent, and step-wise consent?
- How would outcome be measured in a prospective study?
- If comprehension of a new and old informed consent for one study is identical, what should be done?

Discussion

The group felt that increased comprehension of research would be beneficial amongst research participants and the community more generally. The community-based programme was supported, as was the need to continue to promote feedback during the research or at the end of a study, and to consider alternative consent approaches. A first step regarding the latter would be to ask the community through the channels identified whether changes are required, what they most want to know, and how this is best explained in different settings.

Discussion then focused on ward-based studies. In some cases, for example, some paediatric care research, it is impossible to obtain full informed consent. In this situation, the group felt that it was ethical to consider a two-step system: 1) a preliminary 'assent' stage at the time of admission consisting of a very pared down description of the research, followed by 2) a more detailed description of the research and consent seeking process at a later stage. This suggestion was based on a belief that giving simplified clear sets of messages at the outset and revisiting and expanding on these messages would lead to improved study understanding. Points raised, however, included:

- the definition of emergency research and what information would be needed in each of the two stages (mothers' perspectives are likely to differ from researchers', and many of the cases admitted in Kilifi would be considered emergencies in settings such as UK). Consultation with community representatives and researchers is required.
- permission to proceed with prospective randomised studies to compare assent with current informed consent requirements was considered problematic. The unit may be considered as trying to take short cuts as opposed to improving information and communication by review committees. It was suggested that a hypothetical comparison of assent and current approaches be carried out in the community to provide some preliminary data/support of the benefits of simplified consenting approaches.
- That simplified consent processes should mean giving less and less information for convenience sake was stressed, and lead to comments on the importance of monitoring process and impact.

In addition to, or instead of assent, another possibility raised was giving basic clinical and study information again on the child's discharge from the ward, when information is more readily received.

In plenary discussion a suggestion (deliberately controversial/challenging to current thinking) was to consider emergency case-control studies as carefully monitored standard clinical care, given that there is equipoise over the appropriate management of patients. This would suggest no study related assent or informed consent but good basic clinical communication. However this would apply only to a minority of clinical studies and would require significant discussion with the national ethics committee; a committee that currently prefers to remain entirely independent of researchers.

Emergency paediatric research was highlighted as an area of particular ethical concern and voices pushed for an immediate consultation of this area, in particular including research ethics committees in Kenya.

Case study 3: Responsibility in research

Briefing for participants

Acknowledgement: Dr Doug Wassenaar

A local consultant has been hired by an international reproductive health research organization to conduct research on family planning service delivery. Her job is to design and manage a clinic-based study to measure standard indicators of quality of care. She realizes that a critical component of the research with be observation of client–provider interactions.

With her intimate knowledge of the local health system, the consultant realizes that the observers she must hire and train will need to strike a balance between neutral observation and advocacy for client welfare. In fact, during the pre-test of the observation data collection instrument, she observed many instances of poor quality care. For example, some providers failed to mention side effects of the clients' chosen method or they answered clients' questions erroneously. She did not intervene in these situations. However, she began to worry about how her observers should handle more serious problems they might witness, such as providers' failure to wash their hands between pelvic exams or before insertion of an IUD.

Questions:

- What guidelines would you give observers for safeguarding client welfare? Is there a point at which intervention is warranted?
- How should neutral researchers react when they observe mistakes, lapses, and misinformation in the context of a study to assess quality of care?
- Quality of care assessments and performance evaluations are often exempted from the informed consent standards applied to clinical research. What, if any, informed consent procedures should be required of clients? Of providers?

Discussion

The group questioned whether this study constituted human subjects research and felt that such observational research did not require fully informed consent on behalf of the clients. However, the researcher should seek informal assent from clients, and offer them the right to refuse and withdraw from the study. It was unclear whether consent should be sought from providers to be included in the study.

The group felt that, before issuing guidelines, the aims of the study in question should be more clearly elaborated. This would help to decide whether any intervention was warranted. In addition, the group felt that the magnitude of the clients' risk would define the need for intervention, ie. if the risks were relatively small, intervention might not be required; greater risks might require intervention. In this example, the study wouldn't directly introduce harm to the research participant, but would cause harm by omission (non-disclosure of side effects, non-washing of hands).

If intervention were recommended, concern was expressed that the scientific validity of the research would be compromised. Moreover, intervention would affect the participation and trust of clinicians in the research protocol (and therefore undermine the aims of the research to assess quality of care) and consequently the provision of healthcare services in the community. One suggestion was to alter the research design to incorporate training stages for providers at regular intervals during the research, rather than recommending intervention.

Importantly, the design of this case study example does not require any intervention as part of the design. The need for intervention is perceived as a personal obligation on the part of the researcher. The group recommended that researchers try to balance the well being of the individual versus the wider community in reaching any decision to intervene in such a situation.

3. Feedback

Q1. What were your expectations of the workshop? (9 answers)

- ❑ To learn more about research ethics
- ❑ Practical issues to be discussed rather than just theory
- ❑ Understanding global concerns surrounding ethical issues
- ❑ Principles and current norms of ethics
- ❑ Solidification of ethical issues in the Unit
- ❑ Comparative views of ethical review in different countries/contexts
- ❑ Expected to understand issues around 'payment'/incentives in research and how ethical it is to give incentives to participants especially in a rural poor setting like Kilifi
- ❑ Overview of ethical decision-making in research
- ❑ Discussions of informed consent, post-trial issues, standards of care, Wellcome bioethics programme

- (1) Highlights on key ethical issues from various perspectives (researchers vs researched; funders vs funded); (2) discussion of these issues; (3) resolution of issues
- We were not given info about the workshop until the previous evening – so 'signed up' without a clear idea. Overall assumed this would provide an introduction to principles of ethics in research and discussion of problems specific to the Unit

Q2a. To what extent did the workshop meet your expectations? (9 answers)

Exceeded my expectations	5
Met my expectations	4
Failed to meet my expectations	

Q2b. Please comment on your answers to Q2a (9 answers)
- Good facilitation
- General good discussion
- Apart from the time constraints, lots of issues tried to meet my expectations
- Many issues were addressed head-on – in contrast to some meetings where no one dares to say that the emperor has no clothes!
- I understood issues on 'payment' and how to incorporate them in the research design without damaging/influencing the risk:benefit ratio
- I felt that the presentations gave a very full and thought-provoking introduction to this area
- This went beyond the content of most ethics workshops I have attended
- (1) and (2) in Q1 were well done but there were grey areas in (3)
- Presentations were extremely useful

Q3a. How useful did you find the presentations? (9 answers):

	Not at all				Very
Presentations			1	3	5
Breakout groups				4	5
Plenary discussion			1	4	4

Q3b. Please comment on your answer to Q3a (8 answers)
- Good facilitation
- The first two talks could have been combined into one to leave more time for practical discussion
- All were quality presentations that covered thought-provoking issues
- I dreaded the breakout but it was very interesting and stimulating discussion
- The groups were excellent because they helped members discuss issues critically and brainstorm through potential problems and solutions
- All excellent
- In breakout groups it was difficult to participate in all case studies
- More time to allow a quick discussion on each case study appropriate
- More time needed to prepare group work for plenary – much of value in discussions did not reach plenary
- Also more time for plenary discussion – awareness of limited time (I think) discouraged much exploration

Q4a. How satisfied were you with (7 answers):

	Not at all				Very
Pre-event administration			3	4	
Meeting pack			2	3	2

Venue			1	4	2

Q4b. Please comment on your answer to Q4b (4 answers):

- There could be more resources provided that describe specific aspects of ethics – ie. specified ethical issues
- I appreciated the inclusion of recent papers in the pack
- Did not read the unanswered two questions (ie. the case studies that the breakout group did not get around to discussing)
- Venue appropriate within one of the other research units in developing countries
- More information at an earlier stage on aims of workshop

Q5a. To what extent do you agree that this workshop was a useful means of discussing ethical issues in health research in developing countries? (8 answers)

Disagree strongly				Agree strongly
			5	3

Q5b. Please comment on your answer to Q5a (3 answers):

- Useful workshop
- Probably not all key issues were discussed but those discussed were very relevant to current research experience in developing countries
- Useful preliminary discussions

Q6. Are there any important issues that were not covered in the workshop? (5 answers)

- Practical examples of community participation in research – examples that have been successful
- No
- Ethics of international property rights
- Knowledge transfer
- Research and capacity building ethics
- Nothing on post-trial issues and standards of care, but they have been discussed enough elsewhere
- Ethics should be seen from higher level 'mission of the funding agencies'

Q7. In what ways, if any, could future meetings of this kind be improved? (6 answers)

- A full training course on ethics
- None
- Move the time
- Couple more hours of participatory involvement
- Could have done with more time scheduled
- Increased presentations from donors to spell out their perspectives
- Representation from community
- Possibly shorten presentations and extend discussions – alternatively 1.5 days?