

Chapter 6

Consent

Introduction

- 6.1 Respect for persons is a fundamental moral duty. In research relating to healthcare, this duty requires that we do not act against a person's wishes. His or her consent to participate in research must thus be obtained. The duty upon those conducting research ordinarily to obtain consent is widely recognised in national and international guidance and in legislation (see Box 6.1).¹ The three elements of consent reflected in ethics, national legislation and human rights law are that it must be informed, given voluntarily, and given by a person competent² to do so. In this chapter we will focus on two elements of consent which are particularly relevant to externally-sponsored research conducted in developing countries: the provision of information to participants in research; and the requirement that consent to research be given voluntarily. Appropriate means of documenting consent to take part in research will then be considered.
- 6.2 When externally-sponsored research is conducted in developing countries, a range of issues arise in seeking consent to take part in research. With regard to informing potential participants, concepts that are common in research, such as the idea of randomisation, or of using placebos, may be unfamiliar to the culture in which the research is being conducted. As regards the voluntariness of consent, in some communities it is common for a spouse or senior member of a family to assent to healthcare (and by extension, to research) on behalf of a woman or adult children (see paragraph 3.18). In addition, access to better healthcare and other benefits which may accrue from taking part in research may act as powerful inducements, casting doubt on the true voluntariness of a participant's consent.
- 6.3 In research, in addition to their responsibilities to individual participants, researchers are seeking to conduct scientifically sound research that will provide generalised information that can improve healthcare. When medical care is combined with research, researchers may make different choices about clinical measures than they would if the participants' best interests were their only concern. For example, during research, healthcare workers may administer placebos or take blood samples for tests that will not benefit participants directly, in order to obtain information. The potential conflict between the dual roles of healthcare providers in such circumstances means that the process for obtaining consent to research must be rigorous and that participants must be made aware of the dual purpose of research before being asked to consent to it. Conversely, when research does not contain any therapeutic component, this fact must also be made clear to prospective participants.

Information

- 6.4 A prospective participant in research must be provided with information about the proposed research before any consent to participate can be considered to be valid. The ethically significant requirement is that consent to research be *genuine*.³ Ensuring that consent is genuine

1 US Regulations make provision for waiver of consent under four conditions: (1) the research involves no more than minimal risk to the subjects; (2) the waiver or alteration will not adversely affect the rights and welfare of the subjects; (3) the research could not practicably be carried out without waiver or alteration; and (4) whenever appropriate, the subjects will be provided with additional pertinent information after participation (45 CFR 46.116d). The UK Medical Research Council 1998 guidance entitled 'Guidelines for Good Clinical Practice in Clinical Trials' paragraph 2.9 states that 'freely given informed consent should be obtained from every participant prior to clinical trial participation' though this does acknowledge that situations may exist where this is not possible (e.g. emergency settings) and in such cases, procedures agreed in existing guidelines should be followed provided favourable opinion has been given by the appropriate independent ethics committee. The UNESCO's Universal Declaration states that 'limitations to the principle of consent and confidentiality may only be prescribed by law, for compelling reasons within the bounds of public international law and the international law of human rights' (Article 9).

2 A person is considered to be competent if they are able to understand information about the proposed research.

3 Nuffield Council on Bioethics (1995) **Human Tissue: ethical and legal issues**: Paragraph 6.20, Nuffield Council on Bioethics, London.

BOX 6.1 Examples of guidance on consent

The Helsinki Declaration (2000 revision) requires that each potential subject must be adequately informed about:

- the aims of the study and methods to be used;
- the sources of funding and possible conflicts of interest;
- the institutional affiliations of the researcher;
- the anticipated benefits and potential risks and the follow-up of the study;
- the discomfort it may entail; and
- the right to abstain from taking part in the study, or to withdraw from it at any time, without any reprisals.¹

The CIOMS/WHO 1993 Guidelines set out, in some detail, the 'essential information' that must be provided to research participants.² These go further than the Declaration of Helsinki and include:

- the alternative procedures or treatments available;
- what responsibility, if any, lies with the investigator to provide medical service to the subject;
- provision of free treatment for injuries related to research.

A detailed list of the duties of investigators in obtaining consent which is properly informed is provided, including:

- encouraging the participant to ask questions;
- avoiding possible deception; and
- obtaining new consent if the conditions or procedures involved in the study change.³

1 World Medical Association (WMA) (2000) **Declaration of Helsinki. Ethical Principles for Medical Research Involving Human Subjects**, adopted by the 52nd WMA General Assembly, Edinburgh, Scotland, October 2000: paragraph 22.

2 See CIOMS in collaboration with WHO (1993) **International Ethical Guidelines for Biomedical Research Involving Human Subjects: Guideline 2**. This should be regarded as a minimum and the guidance in the commentaries on several of the other guidelines outlines circumstances where additional types of information should be conveyed.

3 CIOMS in collaboration with WHO (1993) **International Ethical Guidelines for Biomedical Research Involving Human Subjects: Guideline 3**.

requires care in detecting a lack of consent. The apparent genuineness of consent can be defeated by a number of circumstances, including coercion, deception, manipulation, deliberate misdescription of what is proposed, lack of disclosure of material facts, or conflicts of interest.

6.5 To obtain genuine consent, health professionals must do their best to communicate information accurately and in an understandable and appropriate way. The information provided to participants must be relevant, accurate and sufficient to enable a genuine choice to be made. It must include such matters as the nature and purpose of the research, the procedures involved, and the potential risks and benefits. National and international guidance sets out the factors which prospective participants must be informed of (see Box 6.1).

6.6 Requirements of particular relevance to externally-sponsored research conducted in developing countries include the need to ensure that participants be provided with information about the study in a language that they can understand, and at their level of comprehension.⁴ The importance of allowing potential participants the time to ask questions, obtain answers and to reflect and give due consideration to their participation is also emphasised.⁵

6.7 An awareness of the social and cultural context in which the research is to be conducted is required, so that communities and individuals can be informed of any

4 For example, the commentary accompanying Guideline 2 of the CIOMS in collaboration with WHO (1993) guidance explicitly states that 'Informing the subject must not be simply a ritual recitation of the contents of a form. Rather, the investigator must convey the information in words that suit the individual's level of understanding'.

5 See, for example, National Consensus Conference on Bioethics and Health Research in Uganda (National Consensus Conference (1997) **Guidelines for the Conduct of Health Research involving Human Subjects in Uganda**: p. 32; Indian Council of Medical Research (2000) **Ethical Guidelines for Biomedical Research on Human Subjects: General ethical issues**, 2i.

aspects of the research that may cause them particular concern. These may include such matters as the amount of blood to be taken, or whether participants will be physically examined by researchers of the opposite sex. The process of informing participants about research must also provide opportunities for individual participants to ask about such matters as whether the research may affect their ability to carry out their livelihood. Consent may sometimes need to be sought in the presence of another person, or group, so that the individual feels supported, and more able to ask questions or voice concerns. In other circumstances, privacy may be essential; for example if the prospective participant wants to discuss confidential issues, such as HIV status, with the researcher.

- 6.8 Healthcare professionals should respect the limits of individuals' understanding and capacity to deal with difficult information and allow time for them to reflect and ask questions. For example, participants may have little understanding of the biological processes that take place in their bodies, or have different beliefs about the causes of disease, which make it more difficult to comprehend the information given. If all reasonable care is exercised, genuine consent may be given.

Issues which may arise when informing participants about research

- 6.9 In some developing countries, during routine clinical care, information about a diagnosis of a serious disease such as cancer may be provided to a patient's family, rather than to the patient.⁶ In such circumstances, the requirement that genuine consent be given to participation in research into appropriate cancer treatments will conflict with standard medical practice, which is to withhold the diagnosis of cancer from a patient.
- 6.10 In some cultures it is customary for a physician to advise a patient which treatment to take, rather than discuss various treatment options. In Vietnam, for example, it has been suggested that: 'it is unacceptable for a physician to openly express uncertainty with regard to what is the best treatment.'⁷ In such circumstances, it has been argued that it is not appropriate to comply with the requirement that participants be informed about the options for treatment which are available, and that there is uncertainty about which will prove to be the best.⁸
- 6.11 In Chapters 3 and 4 we discussed the need to be sensitive to the cultural context in which research is conducted. However, this does not mean that cultural practices must be accepted uncritically. In the circumstances outlined above, there is a tension between the requirement that genuine consent to research be obtained from participants and cultural contexts in which giving certain information is not customary. The Working Party has considered these competing interests and has concluded that obtaining genuine consent to research from participants is vital in ensuring that respect for persons is promoted. Without appropriate information, participants in research may be harmed by being exposed to risks or dangers that they would prefer to avoid. In addition, they will be denied the opportunity to learn more about their condition, possible treatments, and any beneficial outcomes of the research. Consequently, when research is conducted in contexts in which the information about diagnoses and options for treatment is not normally provided, care and sensitivity will be required to design appropriate consent procedures, so that participants receive appropriate information about research and genuine consent may be given.

6 See, for example, Moazam F (2000) Families, patients, and physicians in medical decisionmaking: a Pakistani perspective, **Hastings Center Report**, November–December: 28–37 and Macklin R: The doctor–patient relationship in different cultures, in Macklin R (1999) **Against Relativism. Cultural Diversity and the Search for Ethical Universals in Medicine**, OUP, New York.

7 Love RR and Fost NC (1997) Ethical and regulatory challenges in a randomized control trial of adjuvant treatment for breast cancer in Vietnam, **Journal of Investigative Medicine**, 45(8) 423–31.

8 Love RR and Fost NC (1997) Ethical and regulatory challenges in a randomised control trial of adjuvant treatment for breast cancer in Vietnam, **Journal of Investigative Medicine**, 45(8) 423–31.

Understanding information

6.12 A number of methods have been used by researchers in developing countries to ensure that information about research has been provided to participants in an appropriate manner. These include:

- providing information to participants at meetings, so that they have an opportunity to discuss the proposed research with others and pose questions for clarification
- providing information through health workers (and particularly female health workers when the research will involve women), rather than physicians so that participants feel more able to discuss and ask questions
- providing information about a research project in various ways that are appropriate to the community (i.e. in parts of Africa, information has been supplied on audio or video tape, on the radio and through ballad singers)
- providing information over a period of time, so that prospective participants have time to consider it and raise questions.

We concluded in Chapter 3, that consultation with the community in which research is to be conducted will be required to determine which methods of providing information will be most appropriate for a given research project. In some communities, particular care will need to be taken to ensure that the methods of providing information and aiding understanding which are adopted will ensure that the information will reach all members of the community. For example, if public meetings are used, it must be borne in mind that young women may feel unable to ask questions during such a meeting.

6.13 Information about research should be provided in a form that is likely to be comprehensible to a prospective participant. In some circumstances, healthcare workers, some of whom may have been recently recruited, will be responsible for explaining the research to prospective participants. Clearly, researchers will need to provide appropriate training to ensure that healthcare workers understand the research and can pass on accurate and comprehensible information.

6.14 A number of methods have been used by researchers to assess whether participants in research have understood information provided about the proposed research. For example, prospective participants may be asked to pass a test before consenting to participate in the research. Such tests are designed to ensure that the relevant information about the research has been understood. Alternatively, following the provision of information, prospective participants may be asked to explain what they have understood about the research.

Complex and novel concepts

6.15 Some concepts used in research may be difficult to explain in a understandable manner, particularly in populations with entirely different beliefs about the causes of illness and little familiarity with biomedicine. In such circumstances, researchers will need to consult communities to determine how concepts can be explained in a comprehensible manner. One example is to incorporate local belief systems into the process of providing information. For example, the researchers might say: 'Although I as a doctor believe that the disease is caused by germs (i.e. a virus or bacterium), I understand that you believe that it is caused by a demon. I respect the fact that you have this belief and I should like you to try this medicine to remove the disease. Removing the disease is more important to us both than whether we think it is caused by germs or a demon.' Some biomedical researchers resist this approach on the ground that biomedical interventions should not perpetuate what they regard as 'unscientific' or 'superstitious' beliefs and

practices. However, in some circumstances it will be possible to strike a balance between such a stance and the harnessing of local beliefs in the interests of improving participants' understanding of research.

6.16 Participants in research in developing (and developed) countries may find concepts such as randomisation, genetic research and placebos incomprehensible.⁹ Indeed, many languages will not have terms for such concepts. Researchers in developing countries have demonstrated that such concepts can be successfully explained, but again, care will be required to do so (see Box 6.2).¹⁰

6.17 In many developed countries, in response to the interests of relatively sophisticated populations and following concerns about legal liability, detailed and complex information is provided to prospective participants, setting out possible risks accompanying research. In both developed and developing countries such information may be poorly understood and, to the degree it may be understood, unduly alarming, particularly in populations with little experience of discussing possible side-effects or risks accompanying treatment.¹¹ For example, during the Working Party's fact-finding meeting in India, one physician noted that in rural areas the trust in doctors was so great that if a doctor described six possible side-effects of a treatment then participants often expected to experience them all.¹² Consequently, collaboration will be required with local researchers and representatives to ensure that information about risks and the likelihood of their occurrence is provided to participants in a comprehensible manner.

BOX 6.2 Good practice in explaining research concepts¹

To illustrate the principle of randomisation and the possibility that one of the vaccines might fail, in one research project a familiar agricultural example was used: the evaluation of fertilizers or of seed varieties on randomised plots, a procedure familiar to farmers in the area.

Another study required the concept of immunology and the role of immune cells to be explained. Immune cells were likened to people who guard houses, as a type of watchman, with blood depicted as containing particular kinds of watchman.

¹ National Bioethics Advisory Commission (NBAC) (2001) **Ethical and Policy Issues in International Research; Clinical Trials in Developing Countries. Volume I**, National Bioethics Advisory Commission, Bethesda.

Voluntariness

6.18 As discussed above, for consent to be genuine, it must be freely given. In some societies in developing countries, it is considered inappropriate for an individual to be asked to consent to participate in research without the community, or leader(s) of the community, having been consulted first (see Chapter 3). In other groups, a family or leader(s) of the community may be

⁹ In one study in the UK an exploration of participants' understanding of randomisation showed that: (1) Most trial participants were able to recall and describe various aspects of randomisation, including the involvement of chance, comparison and concealed allocation, (2) The majority found the concept of randomisation difficult to accept and developed other accounts to make sense of their experiences, (3) The use of terms which have different meanings to lay and professional (such as trial and random) can cause confusion among participants, (4) Providing clear and accurate patient information is crucial, but to give truly informed consent, patients may need time to discuss the purpose of clinical trials and concepts such as randomisation. See Featherstone K and Donovan JL (1998) Random allocation or allocation at random? Patients' perspectives of participation in a randomised controlled trial, **BMJ**, 317 1177-80.

¹⁰ See National Bioethics Advisory Commission (2001) **Ethical and Policy Issues in International Research; Clinical Trials in Developing Countries. Volume I Report and Recommendations of the National Bioethics Advisory Commission**, Bethesda, Maryland, USA : 40-41, for description of innovative ways of presenting information to research participants.

¹¹ See Marshall PA (2001) The relevance of culture for informed consent in US-funded international health research, in National Bioethics Advisory Commission (NBAC) **Ethical and Policy Issues in International Research; Clinical Trials in Developing Countries**. See **Volume II Commissioned Papers and Staff Analysis** for a discussion of issues around disclosure of risk in informed consent.

¹² Personal communication, Working Party fact-finding meeting.

BOX 6.3 The role of the community when consent is sought

Some national codes specifically address the role of the community and its leaders in the process of informing participants about research and obtaining consent. For example, the guidance in Brazil recognises the need to be sensitive to cultures and communities and requires that in the case of communities with a separate culture, including indigenous populations, prior consent must be obtained from leaders of the community before consent from prospective participants is sought. The importance of making efforts to obtain the consent of each participant in a study is also emphasised.¹

Guidance on research in New Zealand recognises in research with Maori communities the tribe and extended family groups have some authority over their members' participation in research. The guidance, therefore, emphasises the need at all stages of a research project for consultation with the Maori communities who will participate in it.² However, this does not remove the need to obtain the consent of each participant in research.

Australian guidance requires that with research involving aboriginal and Torres Strait Islander communities there must be written evidence of the assent of the community, or justification why it has not been possible to obtain it.³ There must also be evidence of the process for obtaining the consent of each participant.

- 1 See, for example, Paragraph IV (3e) of the Brazilian Resolution No. 196/96 on Research Involving Human Subjects which states that 'in communities with a different culture, including Indigenous communities, prior consent must be obtained from the community, through its leaders, without foregoing, however, efforts to obtain individual consent.'
- 2 The Maori Health Committee of the Health Research Council of New Zealand (1998) **Guidelines for Researchers on Health Research involving Maori**.
- 3 National Health and Medical Research Council of Australia (1999) **Guidelines on Ethical Matters in Aboriginal and Torres Strait Islander Health Research**.

expected to make decisions about participating in research on behalf of women and older children, who would make their own decisions in other societies. An additional factor which may affect the voluntary nature of consent to research is any inducements accompanying invitations to participate in research. These are considered in turn.

The assent/involvement of the community

6.19 In some societies it would be considered culturally inappropriate for researchers to ask individuals to participate in research without consulting the community or permission from community leaders. Three such situations can be distinguished:

- consultation is required with the community before individuals are approached about research
- permission from a leader(s) of the community is required before any research is discussed with the community or individuals
- the leader of the community is considered to have the authority to enrol participants in research.

6.20 In each of these circumstances, to seek consent from an individual without seeking assent from leader(s) of the community, or creating public acceptance of research, may be considered disrespectful and may harm relationships within that community and between a community and researchers. The role of the community in the process of obtaining consent is specifically recognised in some countries' guidance on research (see Box 6.3).

6.21 The third of the situations set out in paragraph 6.19, where the leader(s) of the community or a senior family member customarily has the authority to make decisions on behalf of others, including whether they will participate in research, is the most problematic. In some developed countries, in limited circumstances and with strict safeguards, the law permits a proxy to consent to research on behalf of children and adults who do not have the capacity¹³ to make such

13 We use the term capacity to mean a participant who is competent to consent to research themselves, i.e. if they are able to understand information about the proposed research.

decisions themselves. However, as discussed in paragraph 3.18, the notion of consent on behalf of others is more widespread and ingrained within some cultures in developing countries.

- 6.22 We noted in Chapter 4 that we cannot avoid the responsibility of taking a view when the two aspects of respect – respect for culture and respect for persons – come into conflict with one another. We are of the view that the fundamental principle of respect for persons requires that participants who have the capacity to consent to research should never be subjected to research without such consent. Some prospective participants may choose to delegate to another, the decision about whether or not to participate in research. Where such delegation has not taken place, to allow others to make decisions on behalf of participants in research who have the capacity to consent themselves would be to deny that all people are moral equals and deserve to be treated in ways that promote their dignity and wellbeing. We conclude that assent from others may be necessary before research is conducted,

but that it is not sufficient: individual participants must receive appropriate information about the research and should be asked to give consent. To ensure that individual participants can make up their own minds without undue communal pressure, anonymity for those who wish to decline to participate in research should be assured. **We recommend that, in circumstances where consent to research is required, genuine consent to participate in research must be obtained from each participant. In some cultural contexts it may be appropriate to obtain agreement from the community or assent from a senior family member before a prospective participant is approached. If a prospective participant does not wish to take part in research this must be respected. Researchers must not enrol such individuals and have a duty to facilitate their non-participation.** A summary of the reasoning behind this conclusion is given in Box 6.4.

BOX 6.4 Summary of arguments about genuine consent

The principle of respect for persons requires that we do not conduct research without their consent.

BUT

Sensitivity to other cultures requires that researchers pay attention to the context in which research is conducted, including customs and traditions.

NONETHELESS

Sensitivity to other cultures cannot override the central requirement of respect for persons, which requires that we refrain from conducting research without consent. This is a fundamental principle, which it is important to promote so as to empower vulnerable populations.

THEREFORE

Genuine consent to research must be sought from all participants in research.

AND

There is also a duty to develop or implement innovative practices with regard to providing information and to ensure that consent to research is freely given.

Refusing to participate in research

- 6.23 One respondent to our public consultation from South Africa, asked, 'How can women – who are known, can be identified and found, and are dependent on the available health facilities which simultaneously function as research sites – be made to feel that their participation is voluntary?'¹⁴ The real significance of this question lies in the extent to which such women could feel free to say no to research. If consent to research is to be genuine, participants will need to be made

14 Response by the HIV/AIDS Vaccine Ethics Group (HAVEG) at the University of Natal, South Africa, to the Working Party's Consultation.

aware that they may choose to refuse to take part, or withdraw at any time and that this will not affect their future healthcare.¹⁵ Consultation with local communities and researchers will be necessary to design an appropriate consent process that takes account of these matters. When concerns arise about whether or not participants feel able to decline to participate, it may be appropriate to have some form of external audit of the process for obtaining consent and its outcomes.

- 6.24 The Helsinki Declaration cautions that, where a subject is 'in a dependent relationship with the physician or may consent under duress', consent should be obtained by an independent physician. However, where participants have great respect for physicians and little awareness that they can refuse to participate in research, it may be immaterial whether it is a physician whom they know or an independent physician who asks for their consent. Researchers must take account of this respect for physicians and develop means to ensure that participants know that they can refuse to participate in research. In some circumstances it may be easier for participants to refuse to participate if they are speaking to a healthcare worker or interpreter, rather than a physician. Care must be taken, therefore, to ensure that research workers and interpreters realise that their role is to provide accurate information in an understandable manner to prospective participants, rather than to enrol as many participants as possible.

Inducements

- 6.25 Participants in research in developing and developed countries have a range of motivations for taking part in research (see paragraph 3.21). One motivation that may be offered to prospective participants is a benefit, such as a financial payment, or healthcare in the future, or for a period of time, for themselves or their families. Inducements which research ethics committees in developing countries have considered acceptable include money in the form of payments for travel, inconvenience or work lost, food, photographs or film, and healthcare for individuals and their families during research.¹⁶
- 6.26 The point at which inducements become inappropriate is not always clear. Principle 11 of the 1991 CIOMS guidelines draws attention to the fact that 'it can be hard to draw the line between exerting pressure, or offering inappropriate inducements, and creating legitimate motivation'. However, it is possible to offer some guidance to assist attempts to draw this line. It should be remembered that without some prospect of benefit, either for themselves or others, most individuals would be unlikely to consent to participate in any research. We consider that researchers should, at the very least, aim to ensure that participants are not placed in a worse position by participating in research. The payment of reasonable expenses incurred by the participant, or remuneration for loss of earnings suffered is generally considered to be acceptable and may be necessary in developing countries where high unemployment means that participants are only able to take part in research programmes with such support.¹⁷
- 6.27 An inducement may persuade an individual to change his or her mind about entering a research project, but this in itself is not enough to make it inappropriate. For example, it may well be a rational choice not to take part in a research project, which may or may not provide any personal

15 A number of national laws and declarations, including the Helsinki Declaration make clear that potential participants in a research project should be told beforehand that they have the right to abstain from participation, or, if they do take part, to withdraw from the study at any time without reprisal. This principle was also included in the CIOMS/WHO 1993 guidance which emphasises the right of the subject to refuse to participate in the study, or withdraw from it without penalty or loss of benefit. Similar provisions have been imported into a number of the national ethical codes or laws.

16 Nuffield Council on Bioethics (1999) **The Ethics of Clinical Research in Developing Countries**, Nuffield Council on Bioethics, London: paragraph 44.

17 Principle 12 of the 1991 CIOMS guidelines states that it is acceptable to repay expenses incurred, and that promises of compensation and care in case of damage, injury or loss of income are not to be considered as inducements.

benefit, unless some extra benefit is provided. However, inducements can also change a prospective participant's mind in a less benign manner, so that their calculation of the costs and benefits of the research results in their decision that the benefit offered by the inducement outweighs all risks, however substantial. This could cause individuals to expose themselves to risks or potential harms that they would ordinarily view as unacceptable, and it is in such circumstances that the inducement would be inappropriate.¹⁸

6.28 The greater the inducement, the more likely it is to be inappropriate, because it may cause an individual to ignore or devalue his or her concerns about the risks involved in a research project. Special care must be taken, therefore, when research is accompanied by significant risks. The more serious the risks faced by a participant in research, the more closely the level of inducement should be scrutinised, to ensure that it is not inappropriate.

6.29 It is an inescapable fact that people who are ill may place great weight on a possible health benefit, even if the probability that it will occur is relatively low. This means that involvement in research which, of necessity, involves medical treatment, may amount to an inducement since the

participant will receive medical treatment for his or her condition and may thus be less likely to refuse. This does not necessarily mean that the individual has been exploited. However, when participants are ill and do not have alternative ways of receiving treatment, the possibility for exploitation is greater. The CIOMS guidelines note that 'someone without access to medical care may be unduly influenced to participate in research simply to receive such care'.¹⁹

6.30 Guaranteed healthcare or a payment offered to individuals on condition that they take part in a research project could be considered to be exploitative if otherwise there is a very low probability of receiving such a benefit. This contrast in benefits, depending on whether an individual enrolls in research is particularly important in developing countries (see Box 6.5). Research ethics committees should bear this in mind when assessing whether it is acceptable to conduct a research projects which may involve more than minimal risk. In such circumstances special care should be taken when determining the nature of additional healthcare to be offered to participants as an inducement.

BOX 6.5 Views on the benefits of taking part in research

'How useful is the issue of informed consent in the Philippines and other developing countries, since it is always the poor in trials who cannot afford the drugs on the market? It is their only realistic form of treatment and they are not truly free to decide not to participate.'¹

'When the project first ended, the staff told me about a new project I might join and I decided to enrol again. If there were no studies, I would not have the opportunity to take anti-HIV medication.'²

'The study staff gives good advice and when this project is over I hope I can enrol in another study. For that matter, I hope there will be new studies for me to participate in all the time. If there would be no more studies, I don't know if I would have the strength to go on, as I would not know where to get drugs outside of clinical trials.'³

- 1 See Kenyon G (2000) Informed consent means little when drug trials are only means of treatment, **Medscape.com**, 26 September.
- 2 HIV-NAT (The HIV Netherlands Australia Thailand Research Collaboration) (2000) **HIV-NAT. The HIV Netherlands Australia Thailand Research Collaboration. A model for HIV-AIDS clinical research in a developing country**, UNAIDS, Geneva: 42.
- 3 HIV-NAT (The HIV Netherlands Australia Thailand Research Collaboration) (2000) **HIV-NAT. The HIV Netherlands Australia Thailand Research Collaboration. A model for HIV-AIDS clinical research in a developing country**, UNAIDS, Geneva: 41.

18 The CIOMS 1993 guidance states that payments should not be so large or provision of medical services so extensive 'as to induce prospective subjects to consent to participate ... against their better judgement'.

19 CIOMS in collaboration with WHO (1993) **International Ethical Guidelines for Biomedical Research Involving Human Subjects**: Commentary on Guideline 4.

6.31 We suggest when assessing the acceptability of inducements to participate in research in developing countries, those designing the research and research ethics committees should pay particular attention to:

- *harmfulness*: whether there are potential risks to the participants' health from taking part in the research
- *proportionality*: whether the inducement being offered is in proportion to the risks and costs to the participant involved in the research
- *vulnerability*: whether guaranteeing substantial benefits for taking part in research is more likely to constitute an undue inducement because prospective participants are especially vulnerable, for example because they have a terminal or chronic illness.

6.32 The CIOMS guidelines note that the propriety of inducements must be 'assessed in the light of the traditions of the culture'.²⁰ For example, some cultures may have a tradition of gifts or exchanges which will make some forms of inducement more appropriate than others. The majority of respondents to our public consultation noted that many decisions about which inducements are appropriate will depend on local circumstances. In such cases, local knowledge will be essential in making appropriate distinctions. One respondent commented:

The level [of compensation] would have to be determined locally e.g. what is considered an appropriate sum to cover time and inconvenience in the US (say \$50) would be equivalent to several years earning in rural Uganda.²¹

We recommend that dialogue is needed with sponsors, external and local researchers and communities to ensure that any inducements to take part in research are appropriate to the local context, especially in circumstances where the research exposes participants to a risk of harm. Decisions about appropriate levels of inducement will need to be justified to local research ethics committees.

Recording consent

6.33 As regards consent to research, many of the concerns raised by respondents to our public consultation and by those who attended our fact-finding meetings related to the process by which consent was recorded. A common observation was that consent forms often seemed to be designed to protect sponsors of research, pharmaceutical companies and researchers, rather than to provide prospective participants with appropriate information. The most common criticisms were that information and consent forms were too long and contained language that was inappropriate at best, or confusing and misleading at worst (see Box 6.6).

6.34 As we have made clear, it is the substance of the process for obtaining consent which is important, rather than the procedures used to record or document the process. Wherever research is being conducted, an appropriate and transparent procedure for obtaining genuine consent is required. A written consent form is merely evidence of what was agreed. If a prospective participant in research is given a consent form to sign, without there being an appropriate process for receiving information and then giving consent, a genuine consent to participate in research will not have been given, irrespective of whether or not a form has been signed.

20 CIOMS (1991) *International Guidelines for Ethical Review of Epidemiological Studies*, CIOMS, Geneva: Principle 11.
21 Response by Dr Dilys Morgan to the Working Party's consultation.

6.35 The purpose of a consent form is to record what has been agreed between the researcher and participant. Consequently, a consent form will not protect participants in research from possible harm, except to the extent that it discloses information which may lead to a prospective participant choosing whether to take part in the research and run a certain risk. Likewise, a consent form is neither an appropriate nor effective medium for seeking to limit legal liability for any possible harmful consequences of research.²² Questions about liability for harm arising from participation in research should be agreed by the parties involved in designing, sponsoring and conducting the research before the research begins (these questions will be governed by law in some jurisdictions). Participants in research in developing countries will need to be made aware of who will be responsible for looking after them should they suffer any harm as a result of research participation, and, unless informed, may be less likely than participants in developed countries to realise that they have avenues of redress.

6.36 In paragraphs 6.4–6.7 we discussed the information which participants need to be given before their consent to research should be sought. Various forms of guidance give detailed indications of the matters about which participants should be informed.²³ It should always be remembered that such devices as information sheets and consent forms are intended to assist the consent process. Researchers will need to refer to the relevant guidance and consider which matters are relevant to their research and to the context in which the research is to be conducted, and how to express the information they seek to convey. Forms which are long, complex and inappropriate for the cultural context in which they are being used, are likely to confuse, rather than inform, participants in research, and should not be approved by ethics research committees. Some ethics research committees, such as, for example, the committee in The Gambia prefer that all consent forms be no more than one page in length, and

BOX 6.6 Consent forms: criticisms from researchers

'The mechanisms of obtaining informed consent in developed countries evolved in communities that are literate and generally aware of modern health practices. Researchers can therefore engage the potential subjects on the basis of pre-existing scientific knowledge and concepts. To use the forms that were designed in such circumstances to obtain informed consent in a non-literate community that operates on different concepts of health and disease, would be an exercise in self deception.'¹

'Insistence by regulatory authorities on the use of complex consent forms devised for use in litigious Western societies is inappropriate.'²

'Consent forms can be too long. Patients don't understand them. It is quality not quantity that is important ...'³

'When most of a population was illiterate, participants were very cautious, they [didn't] know what they were signing or whether it could be used against them. Many researchers therefore considered verbal consent to be very important but did not require written consent.'⁴

- 1 Response by Professor Adetokunbo Lucas to the Working Party's consultation.
- 2 Response by Professor Brian Greenwood to the Working Party's consultation.
- 3 Comment made during Working Party's Fact-finding meeting, Chennai, India, 21 January 2001.
- 4 Comment made during Working Party's Fact-finding meeting, Madison Hotel, Washington, USA, 23 March 2001.

22 In many jurisdictions there are legal restrictions on the ability of individuals (such as researchers) and institutions (such as sponsors of research) to limit liability for injury caused by their own fault. Thus, even if a clause attempting to limit liability is included in a consent form, it may have no effect. However, participants in research who have signed such a form may believe that they have waived their rights and be less likely to pursue treatment or compensation for harm caused by research.

23 For example, Guideline 2 of the CIOMS 1993 International Ethical Guidelines for Biomedical Research Involving Human Subjects specifies 10 pieces of essential information which should be given to prospective research participants, including: the aims and methods of the research, the benefits that might reasonably be expected to result to the research participant or to others as an outcome of the research, any foreseeable risks or discomforts, the extent of the investigator's responsibility, if any, to provide medical services to the research participant, confidentiality of participant data and arrangements for compensation for research-related injuries.

that appropriate language be used. Information sheets, which can be taken home and read, shared, translated and re-read, may be longer but still need to be written clearly.

Situations where consent forms are inappropriate

6.37 There are circumstances in which, while genuine consent to research can be obtained, it may be inappropriate to ask participants in research to sign consent forms, no matter how well designed. One obvious example is when research is being conducted in an illiterate population. The Working Party considers that it is not consistent with the duty of respect for persons to require a prospective participants to 'sign' a written consent form that they are unable to read.²⁴ Some forms of guidance explicitly recognise that written guidance will not be appropriate in all circumstances and set out appropriate safeguards.²⁵ In its recent report, the US National Bioethics Advisory Commission recommended:

US research regulations should be amended to permit ethics review committees to waive the requirements for written and signed consent documents in accordance with local cultural norms. Ethics review committees should grant such waivers only if the research protocol specifies how the researchers and others could verify that research participants have given their voluntary informed consent.²⁶

6.38 In other societies, literate participants may fear that signing forms may link them to particular organisations and leave them open to retribution from repressive regimes.²⁷ In some cultures, participants' only experience of signing forms may be in relation to tax documents or court proceedings. Thus, signing a consent form is likely to have negative connotations, making otherwise willing participants less likely to take part. In one research trial examining the consequences of domestic violence, it was considered inappropriate to ask female participants to sign a consent form before enrolling them in the research because of their concerns that signing a form would mean that a record of victims of domestic violence would be kept and this might lead to them suffering more harm.

6.39 If requesting that participants sign consent forms is inappropriate (see Box 1.1), other means of recording their genuine consent to participation in research is required to protect them from being enrolled in research that they have not consented to. In many circumstances, the research worker who is informing the participant will sign a form stating that the appropriate information was given and verbal consent received. An alternative is to record consent on audio tape. As an additional safeguard, it is desirable for an independent witness to observe the verbal consent. In some circumstances it may be more appropriate to have an independent witness to observe the process of providing information to the community and individuals, rather than observing the verbal consent to participate in research (see Box 6.7).

24 However, in such populations participants may find it useful to take written information sheets away with them for discussion with literate family members or colleagues, and for future reference.

25 For example, the Declaration of Helsinki (2000) (paragraph 22) states that where written consent cannot be obtained, verbal consent must be fully documented and witnessed. **The Guidelines for Good Practice in the Conduct of Clinical Trials in Human Participants in South Africa** (2000) in referring to vulnerable communities state that where a person is illiterate 'verbal consent ... should be obtained in the presence of and countersigned by a literate witness' (paragraph 3.5).

26 National Bioethics Advisory Commission (2001) **Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries. Volume I Report and Recommendations of the National Bioethics Advisory Commission**, Bethesda, Recommendation 3.11.

27 The 'Guidelines for the Conduct of Health Research involving Human Subjects in Uganda' note that a research participant's wish not to execute a written informed consent form should be honoured but the investigator must obtain oral informed consent and document such. NBAC (2001) recognises that this rejection stems from Uganda's past experience of torture and persecution of individuals found to be associated with particular enterprises and that individuals may consequently be reluctant to sign a form which associates them with certain activities.

6.40 **Information sheets and consent forms must be designed to assist participants to make informed choices. We recommend that the information provided should be accurate, concise, clear, simple, specific to the proposed research and appropriate for the social and cultural context in which it is being given. Where it is inappropriate for consent to be recorded in writing, genuine consent must be obtained verbally. The process of obtaining consent and the accompanying documentation must be approved by a research ethics committee and, where only verbal consent to research is contemplated, include consideration of an appropriate process for witnessing the consent.**

BOX 6.7 Witnessing verbal consent

Some forms of large-scale research in developing countries, such as research into vaccines, may involve many thousands of participants. In such circumstances information may be provided in a number of ways, including by television, radio and articles in newspapers. In addition, regional, local and community meetings may be held to discuss the research. If participants wish to take part in research, they will then attend one of a number of sites where the vaccine is to be administered. In such circumstances, where there is a limit to the resources and appropriately trained staff available, it may be more appropriate for the provision of information to be witnessed, rather than to attempt to provide witnesses at the field sites to confirm that each individual who attends wishes to participate in the research.