# 3

Ethics in international research

The purpose of this chapter is to discuss the potential ethical issues associated with international research. All research should be conducted in both a scientifically robust and ethically sound manner. Many, but not all, countries therefore have mechanisms to formally review research protocols. Impartial ethical review is designed to minimise physical or social harm to research participants. It also protects participants' rights to privacy and to choose freely whether to participate in research. In addition, ethical review provides a safety net for researchers, institutions and sponsors (Wagner, 2003). For example, ethical approval is often requested before the release of funds from sponsors of research, editors of scientific journals often ask for confirmation of ethical approval, and in drugs trials, regulatory authorities require it.

This chapter begins with an introduction to the principles and guidelines of research ethics. It outlines a description of the functions of research ethics committees and provides an example of a systematic approach to ethical review, including a series of questions that may help to clarify the researcher's thinking at the time of preparing a research protocol. Informed consent, an important requirement, is discussed in some detail. The chapter closes with a summary of the ethical responsibilities for the international researcher.

Principles, approaches and guidelines

The fundamental basis of research ethics is about ensuring that vulnerable people are protected from exploitation and other forms of harm (Schüklenk, 2005). In order for a scientific investigation involving human participants to be universally acknowledged as ethical, two conditions need to be met: a theoretically and methodically sound research design and voluntary informed consent (Marshall, 2005). In international studies additional contextual considerations arise. For example, undertaking research in socio-culturally or economically diverse locations will require a respect for the different approaches to ethical issues which will be in the context of differing priorities,
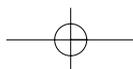
perspectives and environments (Benatar, 2002). In less-developed countries, it will be important that research results relate to the health priorities of the recipient country or to local capacity building, so justifying the best use of scarce resources. There is a wide literature on the place and complexities of research and development (R&D). However, specifically with regard to the topic of this chapter careful consideration of the links between health research and development can make for an intricate ethical situation (Robison, 1998; Olsen *et al.*, 2003).

Michael Heinrich, in his personal account describes the ethnobotanist as a link between diverse cultures which brings with it a diverse combination of ethical considerations (Personal account 3.1). For example, he raises ethical responsibilities that may arise as a consequence of the commercial exploitation of any potential pharmaceutical product in which, of course, the country of origin should benefit financially. More broadly, he highlights the significance of the partnership between 'provider countries' (i.e. of plant material and information on their uses) where knowledge resides, and outside researchers. He emphasises the importance of an appreciation of the place, contexts and consequences of the research process and outcomes for local communities.

A number of key documents have been produced by international bodies to identify ethical principles to research and guide their application with the aim of protecting human participants. The Nuremberg Code (1947) is the first, and historically the most important, international research ethical guideline. In 1964, the first Declaration of Helsinki was published by the World Medical Association, detailing regulations about research involving human subjects; there have since been five revisions, the fifth in Edinburgh (2000). Researchers in the USA are guided by the Belmont Report (1979) which is based on three ethical principles: justice (equal share and fairness), beneficence (the obligation to maximise benefits and minimise harms) and autonomy (respect for persons) (Dresden *et al.*, 2003). In 1991 and 1993 the Council for International Organizations of Medical Sciences (CIOMS, 2002) (founded by the World Health Organization and UNESCO) produced its own guidance for both clinical and epidemiological research (Schüklenk, 2005; Marshall, 2005). A number of other countries and bodies have also published their own sets of guidelines.

Focusing on international research, Salako (2006) described the three main issues highlighted by the Declaration of Helsinki, which is the most widely cited international ethical standard. The first is that researchers must be aware of the ethical, legal and regulatory requirements for research involving human participants in their own countries

PERSONAL ACCOUNT 3.1
MICHAEL HEINRICH

Ethnobotany and ethnopharmacy – multidisciplinary links between partners in developing countries and the 'West'

Pharmaceutical discoveries of the last decades based on the systematic evaluation of higher plants include, for example, camptothecan (and its derivatives), podophyllotoxin, vincristine and paclitaxel – all essential medicines in cancer chemotherapy – and galanthamine, a drug widely used in the symptomatic treatment of Alzheimer's disease (Balick and Cox, 1997; Heinrich and Teoh, 2004). These drugs are all derived from higher plants which were, and are, used by indigenous peoples as medicines. Norman Farnsworth (1990) estimated that 74% of the 119 drugs still derived from higher plants were discovered as the result of ethnobotanical research. Early explorers documented this knowledge and today such studies form one aspect of a multidisciplinary field of research – ethnobotany, defined as the study of the relationship between people and plants. It addresses broad issues of the human use of plants for food, clothing, ornament, ritual, building materials and religious uses. Ethnobotanists take detailed field notes and collect carefully documented plant samples – voucher specimens – that allow for precise determination of the plant species. Selected species are then studied pharmacologically and phytochemically in order to identify the active constituents.

Examples of early studies include those by the German Alexander von Humboldt (1769–1859), who conducted multidisciplinary studies in the Americas, and the French pharmacologist Claude Bernard (1813–1878), who studied the mechanism of action of curare, one of the plants 'discovered' by these explorers (Heinrich *et al.*, 2004). Two of the most famous British botanical explorers were Sir Hans Sloane (1660–1753), who studied plants most notably on Jamaica, and much later Richard Spruce (1817–1893), who worked in South America. In nearly all of these cases stakeholders from two or more countries (or two groups within one country) are involved (e.g. researchers and local informants).

However, while Spruce and von Humboldt simply 'explored' the unknown foreign countries, today the commercial potential of a country's biodiversity puts particular responsibilities on the ethnobotanist who often is a link between two cultures, two countries, and diverse views of understanding and interpreting the world. Such research is now based on mutually binding agreements and it is generally expected that the region or country of origin should receive some financial benefits if a commercially successful product is developed out of such a research collaboration.

Personal account 3.1 (continued)

More recently the systematic evaluation of indigenous pharmacopoeias in order to contribute to improved healthcare in marginalised regions has come onto the agenda of international and national organisations and of non-governmental organisations (NGOs). The World Health Organization estimates that 85% of the world's population depends directly upon local medicinal plants for medicine. Ethnobotanical and ethnopharmaceutical research can assist developing nations in assessing the safety and efficacy of plants used in traditional herbal medicine. An example is *Artemisia annua*, the source plant of the antimalarial sesquiterpene lactone artemisinin, which is now grown in some African countries and an extract is used in the treatment of malaria (Mueller *et al.*, 2000). This example also raises important questions about the widespread use of such extracts which may contribute to the development of resistance against the active compound. On the other hand, the huge problems with counterfeit 'licensed' medicines calls for solutions which involve local people, and the growing of medicinal plants may well be one such possibility.

In all these cases the original keepers of knowledge reside in what is now called 'provider countries' and thus ethnobotanical and ethnopharmaceutical research owes special debts to these keepers of knowledge, and novel ways of communicating this knowledge to future generations have become essential aspects of ethnobotanical research and practice (e.g. Vandebrock *et al.*, 2003; Rivera *et al.*, 2006). Today, more and more ethnobotanists come from developing countries, but in these cases, too, two cultures or sectors of a society meet.

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and any other countries where the research is being undertaken. Second, the research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results. Third, negative and positive results should be published or made otherwise publicly available. Within this, potential conflicts of interest should be disclosed: to research ethics committees, to patients when informed consent is sought, and in any research publication.

While these documents have a central role in guiding researchers regarding ethical principles, there is considerable variability in the socio-cultural environments and capabilities of institutions and communities where research is undertaken. Particular challenges may arise in balancing international ethical standards for research with local standards and the pragmatic considerations in carrying out the research. For example, potential conflicts may arise between universal standards and traditional customs for requirements such as informed consent (Marshall, 2005). Rashad *et al.* (2004) highlighted a range of difficulties that resulted from undertaking a research study in Egypt, for which the research protocol had undergone ethical review in the UK (see Box 3.1).

Rashad's experience illustrated the huge challenges of applying universal ethical principles and practices. When applying ethical guide-lines across international boundaries, there is a need to respect each culture within which the study is set. This includes sensitivity to cultural understanding and religious beliefs and attempting to minimise the imbalance of power (which is greater when principal investigators from a more developed country are recruiting participants from a less well-developed country) as this has the potential for exploitation (Olsen *et al.*, 2003; Kennedy *et al.*, 2006).

The importance of research ethics must explicitly include consider-ation of the community's interests as well as those of the individual (Dresden *et al.*, 2003). Researchers need to be creative in developing strategies to improve participants' understanding of the research aims, methods, risks and benefits. In addition, prompt and continuous feedback to participants and their communities should be carried out in ways that are culturally and linguistically meaningful (Marshall, 2005).

Box 3.1 An example of difficulties associated with imposing UK ethical requirements onto a study carried out in Egypt (taken from Rashad *et al.*, 2004)

- Until 1991, there were no national standardised ethical guidelines that could be applied to healthcare research in Egypt.
- Egypt has a scarcity of research ethics committees.
- Most research takes place within the public teaching hospitals, which are mainly used by patients from lower socio-economic sectors of Egyptian society.
- Egyptian doctors are regarded as a powerful professional group, so a paternalistic approach to care dominates resulting in reduced autonomy for research participants; there is an assumption amongst patients that the doctor will always act in their best interests; patients expect doctors to make decisions for them (influenced by cultural norms and beliefs). Unequal power relationship between health professionals and patients is pronounced in Egypt.
- Decision-making is commonly delegated to the most powerful figure in the context within which the decision is being made, e.g. father, teacher, employer.
- Low literacy levels exist amongst poor, uneducated women, who are frequently used as research participants in Egypt – this has potential implications for these women's abilities to make informed choices about participation.
- Confirmation of informed consent requiring a person's signature presents unique challenges as a signature has particular significance in Egyptian society and is usually only used in relation to major life events. Furthermore, requesting a written signature also implies a lack of trust in one's word.
- A cultural emphasis on politeness could increase an individual's perceived obligation to participate in research.

Conflicts can occur when the values and norms of the study population do not match those of the research team. However, a collaborative approach to setting a research agenda together can help ensure the appropriateness of the work and that limited resources are used to the best advantage of the countries involved. Providing the local community (such as local healthcare staff, community leaders or advocacy agencies) an early opportunity and a continuing mechanism to provide input into the purposes, goals and methods of research, could reduce the opportunities for exploitation in less-developed countries (Robison, 1998; Olsen *et al.*, 2003). However, the valuable involvement of community partners must not compromise the research team's autonomy and ability

to ensure that scientific integrity of the research is maintained and ethical principles are observed.

Research ethics committees

Research ethics committees are independent bodies who review research, particularly that involving 'patients', and they exist in many (but not all) developed countries. Benatar (2002) identified three functions of a research ethics committee. The first is the independent evaluation of research proposals: focusing on risk/benefit ratios, distribution of benefits and burdens, potential conflicts of interest, adequacy of information provided for potential research participants and the protection of freedom with regards to participants granting/withdrawing their consent and researchers' rights to publish. Second, they have a role to educate and assist all those involved in the process to understand and appreciate ethics. Third, they have a duty to monitor and audit research, and to provide accountability to the public.

In international research the structures, procedures and requirements for gaining ethical approval can vary significantly between countries. This was demonstrated by Hearnshaw (2004), who compared the processes required to gain ethical committee approval for an identical intervention study which aimed to improve the involvement of older patients in consultations with their general practitioners across 11 European countries (Austria, Belgium, Denmark, France, Germany, Israel, the Netherlands, Portugal, Slovenia, Switzerland and the UK). For example, in the UK, if research takes place involving human participants and/or resources within the UK's National Health Service (NHS), then independent review is sought through the National Research Ethics Service (NRES). In addition, there may be further requirements from other NHS committees and subgroups (e.g. management approval from NHS R&D offices), or institutions hosting the research (e.g. universities). International research undertaken entirely outside the UK (including that by UK-based researchers) is beyond the ethical review remit of the NRES and would require ethical approval in the country where the research will take place. If the research will be undertaken both within the UK and overseas, an NRES would only review the component of the study that actually takes place within the UK. Ethical approval for international studies gained in countries other than the UK does not nullify any requirements for ethical review in the UK, and vice versa (NRES, 2007).

In many countries processes are becoming more advanced and are continually evolving. It is, therefore, important to build the necessary time into a project to establish what is required in each participating country in terms of criteria, supporting documentation and costs, as well as the time it will take for a decision to be made. This can take several months. In her personal account, Mary Tully describes her experience and feelings regarding the differing requirements for independent ethical review for a study conducted in the UK and Sweden; two European countries for which it might be expected that requirements would be similar (Personal account 3.2).

PERSONAL ACCOUNT 3.2

MARY TULLY

Ethics committee approvals between different countries

I had conducted some work in the UK that explored how doctors in different specialities and of different grades viewed how the appropriateness of prescribing should be measured. As part of my visiting professorship to the University of Uppsala, Sweden, I had a new PhD student. Therefore, I had the opportunity to repeat my original work in another country, as views of appropriate prescribing and prescribing documentation may well depend on current healthcare debate and different healthcare systems (Ljungberg *et al.*, 2007).

In the UK, conducting qualitative interviews with hospital doctors, about their own prescribing and about prescribing in general, had required full NHS ethics committee approval, including attending the meeting. The committee had asked me to make amendments to the subject information sheet for the doctors before giving approval. In Sweden, therefore, I expected to have to make an application and, as vice-chair of an NHS committee, was interested to learn about the ethics committee application process in another country. My Swedish collaborators, however, said that research of this kind did not usually require approval. I pressed the matter and said that I would prefer to try even if they thought it was not needed, so that my PhD student (and I) could learn the system. However, I was told that an ethics committee application costs between Kr5000 and Kr16000 (approximately £385–1230), depending on the type of research – even if the committee later said an application had not been required. I did not press the matter any further! I had expected a variation in the system, but being so used to the free NHS ethics service, charging for this never entered my mind.

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In countries in which requirements are limited, members of the research team will want to be satisfied that the work is in accordance with accepted principles, that their own expectations regarding ethical standards are met and that they are satisfied that the research has undergone suitable external review and possible frameworks for review are discussed below.

The ethical review process

The independent review of research and its ethical acceptability takes time. The ethical issues in a research project have to be identified and considered. The potential risks and consequences have to be appraised and balanced against the potential benefits and a conclusion has to be drawn about the research as a whole. This often requires a delicate assessment; any decision may not be clear cut. Ideally, careful and reasonable thinking is required by the research ethics committee members who collectively understand the importance of different moral claims, and who can work constructively together to come to sound and reasonable conclusions (Foster, 2001).

A number of systematic frameworks have been developed for the review process. For example, in the USA, based on the Belmont Report, Robison (1998) detailed an ethical review process that focuses on three key features:

- Respect for persons (informed consent; voluntary participation; adequate awareness of benefits and possible risks)
- Beneficence (first do no harm; contribute to the general welfare/ health of study participants)
- Justice (equitable distribution of burdens and benefits of partici- pating in research).

Nicola Gray, a UK-based researcher, discusses in her personal account how when undertaking research in the USA, the Belmont Report represented a new framework for identifying and addressing ethical issues, and how this has continued to provide a stimulus for reviewing her work following her return to the UK (Personal account 3.3).

As a further example of a general framework which may be applied to judge the ethics of a research project, Foster (1996, 2001) highlighted three distinct approaches, together with a series of questions, which may be helpful to reflect upon when preparing a research protocol:

PERSONAL ACCOUNT 3.3
NICOLA GRAY

Undertaking health services research in the USA – ethics

To explore adolescents' views and experiences of using the Internet to find information about health and medicines, our study involved focus group discussions with middle and high-school students in the USA aged 11–18 years (Gray *et al.*, 2005). Ethical review was undertaken by the Research Subjects Review Board (RSRB) within the institution where I was placed for my Fellowship – the University of Rochester Medical Center, New York State. This review board deals with a breadth of research subjects similar to that of a local research ethics committee in the UK. At the time of my study, the chair and vice-chair of the RSRB were both pharmacists – a fact that was apparently common, considering the many drug trials undertaken within these university hospitals.

Key study personnel and any fieldworker who might be called upon to take consent from subjects are required to register with the RSRB. As our study was considered minimal risk, I completed the Ethical Principles in Research Program (EPRP); there is another level for interventions. The EPRP revolves around the Belmont Report (1978). Published in the wake of the Tuskegee syphilis experiment, in which 399 black men were purposely left untreated in order to study the late-stage disease (Jones, 1993), the report considers the difference between practice and research, and crystallises three basic principles of ethical research, which Tuskegee patently ignored, and their application within a research study with human subjects:

Basic principle	Application
Respect for persons	Informed consent
Beneficence	Assessment of risk and benefits
Justice	Selection of subjects

I have found this pithy and thought-provoking report to be invaluable since returning to the UK as a resource for pharmacy students and my own ethics applications.

The RSRB required a score of at least 80% on a short multiple-choice questionnaire submitted to their office. Successful completion resulted in an EPRP registration number being issued, and this had to be quoted for each fieldworker in the subsequent study application. The registration has to be renewed every three years and so, two years after my return, I had to renew my registration with Rochester as I was still analysing and writing up from study data.

After favourable ethical review, the original copies of information sheet and consent form submitted with the application and annotated with version number and date were taken, almost ceremonially, to the RSRB office where they were rubber stamped and signed by a RSRB officer. It was then obligatory to photocopy these documents, complete with stamp and signature, for distribution to potential subjects as verified copies of the original. Luckily the photocopier was in good condition so the quality of the copied leaflets was acceptable!

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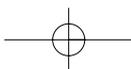
- Goal-based approach (validity of the research)
- Duty-based approach (welfare of the research participant)
- Rights-based approach (dignity of the research participant).

In using Foster's approach, equal weight may not always be given to all three and the decision will be based upon which concerns need to take precedence, a judgement made with each individual research project. This approach is discussed in further detail below.

Goal-based approach (validity of the research)

From a goal-based approach, an action is considered good if its goal, or outcome, is good. The outcome of a study cannot be of value (i.e. good) if the work is not conceptually or methodologically sound. Thus, in an ethical appraisal, the scientific merit of the work should be challenged. The research team should be able to defend the study design and methods as a sound approach to answering the research questions, or testing the hypotheses (see Box 3.2).

In the case of vulnerable groups (e.g. children, older people, people with mental health problems or special needs) special consideration must be given to the potential benefits of a study. Is the research necessary in this particular group of individuals, and is this the group who are likely to benefit? Can the results be generalised from the sample or study population to any other groups?

Box 3.2 Questions to ask yourself from a goals-based perspective

- For what reasons is the research being conducted?
- Is the research likely to provide new insights into a social phenomenon?
- How important is the research question?
- Is the research design optimal and will it answer the research questions posed?
- Are the research methods chosen to answer the question appropriate, rigorous and systematically applied?
- Have the data collection tools been tested or justified?
- How will the data be analysed?

Duty-based approach (welfare of the research participant)

The focus of the duty-based approach is whether or not the proposed research activities accord with moral principles. These considerations should take precedence over whether the outcome of the research activity is good. For example, even if a very important question may be answered by the research, it would be deemed unethical to deceive the research participants in order for the research to be undertaken (see Box 3.3).

For therapeutic research, where there are direct health benefits for participants (as compared to non-therapeutic research where there are no direct benefits for participants but there may be future benefits to those meeting the same inclusion criteria) the concept of *equipoise* should be considered (Choudhury and Knapp, 2006). For therapeutic research to be considered ethical, the participant must expect to receive treatment which is at least as good as the treatment they would have received had they not been enrolled in the research. That is, the new

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Box 3.3 Questions to ask yourself from a duty-based perspective

- What will participating in the research involve?
- In what ways will the research participants be treated?
- How much time might participating in the study involve?
- How intrusive might the interview or questionnaire be?
- What will happen to the information that is collected?
- To what risks will the research participants be exposed?
- Are the risks necessary and acceptable in the circumstances?
- Are there referral procedures to appropriate agencies in place if information that leaves an individual at risk, is revealed?

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treatment must be considered to be at least as good as 'the usual' treatment. Equally, the researcher must be uncertain whether the treatment that is being tested is actually better than standard or 'usual' care to which it is being compared. This has presented dilemmas in international research when studies have been carried out in countries with differing 'usual' standards of care compared with other participating countries or the country funding the research.

In research among vulnerable groups, particular attention must be paid to any risks, including those that may be viewed as relatively harmless. This is especially important when individuals may not be able to articulate concerns themselves.

Rights-based approach (dignity of the research participant)

Individual freedoms and recognised 'rights' of an individual within a given society are the focus of a rights-based approach. Therefore, the main concern is to establish and respect the views and feelings of prospective research participants. The rights of an individual to refuse participation in any research study must take precedence over any consideration of the wider public good. Value is afforded to the integrity, privacy, safety and human rights of the individual participant. In terms of confidentiality, there is a legal duty to keep patient information confidential and data should be secured against unauthorised access. Particular care should be taken in international collaborations where there are differing values and cultural norms; researchers must not dominate the relationship with research participants, and research participants must: (i) understand the nature and purpose of the research; (ii) have the opportunity to have their questions answered; (iii) give truly informed consent; and (iv) be able to make uncoerced decisions to participate (Benatar, 2002) (see Box 3.4).

Box 3.4 Questions to ask yourself from a rights-based perspective

- Will the research participant's consent be sought and how?
- How is consent dealt with in covert research?
- Are the participants being paid for their involvement?
- At what level may payment be considered coercive?
- Will the individual participant's dignity be protected?
- Will confidentiality be respected and assured by the researcher?
- What precautions are taken to safeguard all data collected?

Research involving competent research participants should only be conducted with their knowledge and consent. Researchers have an obligation to seek consent from all competent people. An individual's refusal to participate should always be respected. Once consent is given it is not necessarily enduring; individuals can withdraw from the study at any time. Consent must be maintained during long-term studies and reviewed if study procedures are altered (Choudhury and Knapp, 2006).

A number of challenges arise where consent cannot be provided by participants themselves and careful consideration must be given to the special legal issues relating to these cases. For example, in the UK, special procedures have to be followed if the proposed research involves the use of information from which NHS patients could be identified, but it is not possible to obtain their informed consent (NRES, 2007).

Combining these three approaches, Foster (2001) provides a framework for ethical review of research. A rights-based judgement is difficult when one cannot be certain of the wishes of an individual research participant; the duty-based approach could on balance regard the research as ethical if it was therapeutic and there was equipoise; a solely goals-based stance would view the research as ethical if it could be shown that ultimately more people would benefit than suffer.

The Foster framework will not necessarily result in any solution regarding the ethical acceptability of a study. In particular, in international studies, researchers should not anticipate a single best set of answers to the questions posed. Responses to individual questions may differ according to the research centre or setting. A judgement concerning the ethical acceptability of the research is made on balancing the risks and benefits of the project being undertaken.

Informed consent

Consent sets the limits for what the researcher can do with research participants or personal data (Simonsen and Nylenna, 2006). Informed consent has been defined as potential participants receiving information necessary to make an informed choice about participation in a study, understanding the information and making a voluntary decision regarding whether to participate (CIOMS, 2002).

Participants must receive *sufficient* information for their consent to be viewed as informed. Achieving informed consent is dependent on the researcher's ability to communicate, and the research participant's sense of freedom to choose. However, it must be acknowledged that there may be difficulties attaining full comprehension in any setting, and that this may be more challenging across diverse international collaborations. For
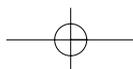
research being undertaken in a variety of locations, additional steps may include community level consultation and permission prior to seeking individual consent. Where the majority of potential participants cannot read or write (so signing consent forms cannot be expected), alternative methods of documenting the individual informed consent process should be adopted, e.g. a record of verbal consent through audio/video tape, or where the researcher signs a form stating that appropriate information was given and verbal consent received, which could be observed by an independent witness (Molyneux *et al.*, 2004; Choudhury and Knapp, 2006).

A study by Rivera *et al.* (2007) examined the level of detail that should be provided to potential research participants balanced against the participants' needs for information and capabilities to understand it. This research was undertaken with three independent groups of researchers based in Africa, Europe and North America. They found that researchers with different types of research backgrounds, from a variety of professional backgrounds, who held different cultural perceptions of informed consent, demonstrated low agreement on what should be included. The top priority was that potential study subjects should receive sufficient information about possible benefits of participating in a study and how it will be conducted. Consensus was achieved regarding the issue of publicising the names of community advisory board members or community representatives. Crucially, they also concluded that the amount of detail provided in the informed consent process should not be excessively comprehensive and information overload may actually hinder understanding.

Regardless of whether the consent form is presented in English, or in a translation, it can be meaningless unless it is explained by someone who fully understands the culture and concerns of the people for whom it is intended (McCabe *et al.*, 2005). Consent forms may require translation. As for other study documentation, forward and back translation methods can be adopted. Independent of the translators, further review may be required by language experts, disease/topic experts and study personnel to discuss any issues that may have arisen during the translation process and piloting of the translated documents. Sufficient time must be allowed both by the researchers and funding agencies to develop comprehensible material (McCabe *et al.*, 2005). For further information regarding the translation of research documentation see Chapter 4.

A number of considerations for adapting the informed consent process to cross-cultural settings have been identified (Robison, 1998; Molyneux *et al.*, 2004; McCabe *et al.*, 2005):
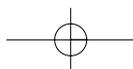
- Minimise legal and scientific jargon in the consent form.
- Consider the sequence of information presented in the consent form to facilitate logical translations into complex languages.
- Allow for community members' review and critique of forms.
- Identify conceptual and linguistic barriers to communicating effectively about research.
- Ensure that those administering consent forms are culturally competent to address questions and potential misunderstandings as the concept of research may be alien.
- Be aware of power relationship between the research team and the community which can impact on the informed consent process.
- The concept of the signed informed consent form may have additional issues regarding confidentiality, anonymity and the act of signing.
- Consider the local setting, for example if telephone support has been offered as a means of communication, offer alternatives for people without telephones.

The concept of informed consent may not translate culturally to all countries as individual rights and the patient–provider relationship can take on different meanings in different locations (Geller *et al.*, 2004). The autonomy of research participants will be influenced by the values held within their population. Researchers undertaking research in countries other than their own must be aware of, and respect, local customs and culture. For example, in some cultural environments, it may be customary to seek advice or permission from a spouse or head of household. In other settings, investigators may need to consult with local community leaders or elders before implementing a study. Notably, the spouse/head of household/community consent is supplementary and not a replacement for individual consent. Therefore this does not necessarily diminish the individual's ability to make his or her own choices, but approaches should be considered so that it is possible to obtain an individual's informed consent and preserve cultural norms and the spirit of the community. This approach may present its own difficulties, for example, it may be unclear who represents a community, conflict may arise when more than one individual/group represents the community's interests and/or community and individual interests may conflict (Geller *et al.*, 2004; Marshall, 2005; Salako, 2006; Choudhury and Knapp, 2006).

The understanding and operation of informed consent procedures are not universal. Consent procedures may be alien to some groups, for

example, the requirement of a signature may be interpreted as a legal obligation to participate. Barata *et al.* (2006) studied the perceptions of different minority groups (Portuguese Canadian and Caribbean Canadian immigrants) in understanding the informed consent process. Both participant groups identified the need for information. Consent letters were viewed as providing valuable information that participants used in their decision making process and actually encouraged participation. Verbal explanation of the study allowed participants to ask more questions. Researchers also found that establishing trust was culturally bound and that a fear of exploitation and mistrust was sometimes apparent. Where trust was present, it was associated with the view that the research was legitimate and safe.

This study highlighted the fact that different ethnic groups have different concerns which may require slightly different approaches to recruitment and methods to obtain informed consent. For example, Barata *et al.* (2006) recommended that recruitment and informed consent procedures may be enhanced if facilitated through a trusted community member. Providing study results to participants and other community members may help to demonstrate the benefits of health research, which was an important factor for prospective participants when deciding whether or not to take part. Viewing informed consent as a process rather than as a discrete event that ends with the signing of the consent form, could enhance the opportunities of the research team to promote trust between participants and researchers, before, during and after the study is complete.

Researchers need to respect the limits of participants' understanding and capacity to deal with difficult information, allowing time for reflection and questioning. For adults incapable of informed consent and for research involving children, assent should be sought and proxy consent from the legal representative, parent or guardian (Choudhury and Knapp, 2006). Informed consent must be fashioned to meet the needs, culture, and context of the community in which it is being used (Geller *et al.*, 2004).

Summary of ethical considerations for the international researcher

Peer review process

The first step in the ethical review process should be that undertaken by the research team, perhaps aided by senior research colleagues,
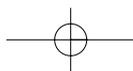
representatives of the potential participants and/or other stakeholders. A framework for review, as discussed above, may be useful for this. Only when ethical issues identified by the team have been addressed should independent review be sought.

Ethical review process

Researchers have the responsibility of complying with the ethical rules of the countries and institutions in which the research is taking place. If this is problematic due to the lack of ethical committees then appropriate alternatives should be identified. Review should be undertaken by individuals who are familiar with the laws, regulations and ethical requirements and expectations of the participating countries as well as having experience of the research process. In some countries, there may be diverse additional national and/or local requirements. Disagreements and resolving conflicts between decisions of committees in different countries can be a challenge. It is important that the scientific integrity of any international research project is not compromised by varying requirements, and adequate communication about these among research team members is crucial.

Protecting and respecting the community and participants

Awareness of, and sensitivity to, the social and cultural perspectives regarding the research objectives and procedures of the participating countries should be demonstrated. In addition, individual participants' autonomy should be respected. Scientific endeavour must not take precedence over the well-being of participants. The investigation should be discontinued if proven harmful. Participants should be volunteers and risks as low as possible, irrespective of potential future benefits.

Providing information to participants and obtaining informed consent

Information including the project's aims, methods, duration of an individual's participation and what it will involve, foreseeable benefits/risks, safeguards for confidentiality, freedom to abstain or withdraw from the study at any time, funding sources and institutional affiliations should be provided to research participants. Information must be conveyed in a way that is both effective and mindful of varying linguistic, social and cultural perspectives of the different population groups. There should
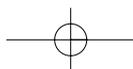
be opportunities for potential participants to ask questions. Once the information is understood, then researchers can request participation.

Voluntary informed consent must be obtained, based on the principle that competent individuals are entitled to choose freely whether or not to participate in research. Informed consent protects an individual's freedom of choice and autonomy. Researchers must not deceive or intimidate any participant. Excessive financial inducements to participate may compromise the extent to which decisions of whether or not to participate are genuinely voluntary. The acceptability and impact of offering inducements may also vary between settings and locations, and be influenced by local socio-cultural and economic factors. A distinction can usually be drawn between these payments and reimbursement for inconvenience, expenses incurred or time spent on the project. Any compensation should be approved by the ethics committees.

Conclusion

This chapter has introduced the central concepts of research ethics focusing on issues of concern and relevance in international research. International guidelines have been included to inform researchers of the ethical considerations for research involving human participants, however their application within individual countries does vary. Despite international guidelines, researchers need to allow time for establishing and meeting the requirements of all participating countries. In international collaborations, special consideration must be given to the value systems and cultural norms of local populations regarding the place and operation of the research proposed.

The Foster (2001) approach to ethical review provides one example of some of the issues to reflect upon when preparing an ethically sound research protocol for an international collaboration. It highlights the potential difficulties of balancing the benefits and concerns of different types of research, in order for ethical acceptability to be established. Most importantly, for all research involving human participants, a theoretically and methodically sound research design is required and voluntary informed consent must be obtained.

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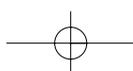
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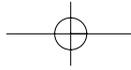
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