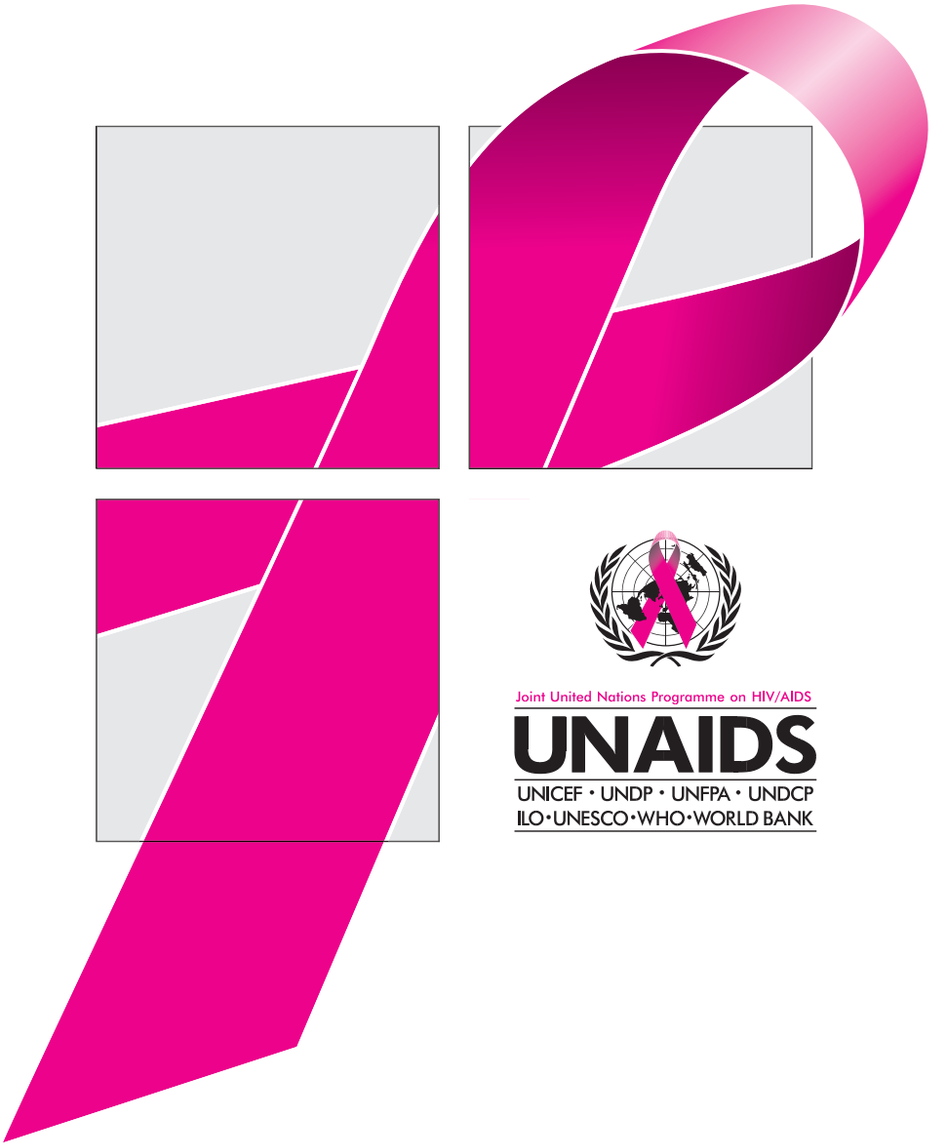
Meeting on care within the context of HIV/AIDS-related research in developing countries

Summary of issues and conclusions



Joint United Nations Programme on HIV/AIDS

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UNAIDS BEST PRACTICE COLLECTION

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26–28 May 1999

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Geneva, Switzerland
January 2002

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Executive summary

On 26-28 May 1999, a meeting was held at UNAIDS, Geneva, with the following theme: “Care within the context of HIV/AIDS-related research in developing countries.” The objective of the meeting was to develop a framework of care that guarantees that the health needs of participants in HIV-related research in developing countries are given precedence, and that their personal and social integrity are fully protected. The meeting also sought to clarify the appropriate roles and responsibilities of research partners with respect to the care of participants in HIV/AIDS-related research. The meeting was guided by the general ethical principles expressed in the Declaration of Helsinki (World Medical Association) (1996) and the International Ethical Guidelines for Biomedical Research Involving Human Subjects (Council for International Organizations of Medical Sciences)(1993). The meeting was attended by representatives of community and patient organizations, research organizations, research sponsors, ethics committees, governmental and inter-governmental organizations, and academia.

Those at the meeting confirmed that respect for the individual and the community should be at the core of HIV-related research in developing countries, and that participants must be provided with a context of care that fully addresses their dignity and responds to their physical and psycho-social health needs. The meeting confirmed that the health and well-being of participants must be the primary concerns during HIV-related research and that they should prevail over any other concerns, including the interests of science.

The meeting confirmed that an ethical framework of care should be provided during HIV-related research in developing countries. This framework of care should be grounded in the ethical principles of respect for individuals, justice and beneficence. In the research situation, this framework of care should deepen the ethical imperative that respect for the individual be safeguarded, the relationship of trust between participant and researcher/physician be maintained, and the well-being of the participant ensured at all times. The meeting also confirmed that the human rights of the participants, including the rights of patients/participants, should be protected within and by the framework of care that is implemented during the research. Thus, those providing care and overseeing the research may have both an ethical and legal duty to ensure care.

The meeting confirmed a comprehensive framework of care that addresses the total well-being of the participant in the context of the research, including physical, psychosocial and spiritual well-being. Any care that is provided should also be sensitive to, and located in, the cultural and local contexts of care and caregivers.

Those present at the meeting agreed that researchers have a responsibility to fully explore the expectations of the participants regarding care during the design of the proposal, during the informed consent process, and throughout the research. They also have a responsibility to ensure that the care provided and/or unrealistic, uninformed expectations of care do not comprise undue inducements to participate in the research. Participants should be fully informed as to the nature and content of the care to be provided, its duration, and those who will benefit from it. Furthermore, researchers should be as pragmatic and flexible as possible in their response to changing care needs and expectations as the research progresses.

It was agreed that researchers have the responsibility to discuss with the wider community (from which participants are drawn) the nature of the research and the expected benefits (short- and long-term), risks, and the level and duration of care that will be offered. A process of consultation with the community should be commenced during the design of the research and should continue throughout the research. This consultation should include people living with HIV/AIDS who may also serve as other types of resource persons during the research. The community should be involved in the design of any care package to be offered.

The meeting did not agree on the standard of care to be provided to study participants. However, it was recognized that, in the context of developing countries, the standard of care must, at the very least, involve the best available care that is practicable under local circumstances. It was also agreed that the community must be involved in determining and agreeing on the standard of care to be employed. Researchers must include this issue in the consultation with the community during the design and implementation of the research.

The meeting agreed that sponsors should be encouraged to develop policy regarding the provision of care in HIV-related research and should demand of the researchers whom they sponsor the inclusion of a care component in the research. Sponsors should also negotiate with the host government to ensure that proposed research and care plans are consistent with the public health priorities of the host country. Sponsors should also, in consultation with researchers and the host government, contribute to the strengthening of local infrastructure, provision of training and education, and enhancing the capacity of local support groups.

The meeting proposed a comprehensive care package to be considered for HIV-related interventional research. Any such package should be discussed with, and approved by, the community in which the research occurs, and be tailored to local circumstances and to the needs of women and children, as appropriate. The meeting agreed that, in considering the provision of care, the proposed comprehensive care package should be assessed in terms of whether it constitutes an undue inducement, is feasible, is capable of being funded, and is sustainable.

The comprehensive care package posited by the meeting comprises the following elements: counselling, preventive measures (e.g. male and female condoms), treatment for STIs, tuberculosis prevention and treatment, prevention/treatment for opportunistic infections, nutrition, palliative care, pain control, spiritual care, community support, family planning, home care, and antiretroviral therapy, when it is readily available outside the research context or when the infrastructure permits its being made available to research participants. The meeting agreed that researchers should implement a monitoring process to ensure that the proposed comprehensive care package is actually implemented throughout the research.

The meeting stressed that host governments must be informed regarding any research to be carried out in their countries and communities, and that host governments should participate in its development and implementation, particularly with regard to ensuring an ethical process, as well as protection of the human rights of participants, and legal redress in case of violation. In compliance with international human rights instruments, the meeting agreed that host governments should ensure that care is sustained for study participants after the research is concluded.

Introduction

On 26-28 May 1999, UNAIDS convened a meeting on 'Care within the context of HIV/AIDS-related research in developing countries'. The meeting responded to a widely recognized need to address the issue of the nature of the care provided to participants in HIV/AIDS-related research in developing countries. Within a framework of respect for the value and dignity of the human being, those at the meeting examined the meaning and dimensions of the provision of care during research into the epidemiology, prevention and treatment of HIV/AIDS. They also examined the roles of research institutions, investigators, health-care professionals, counsellors, participants, sponsors, communities and governments in the context of the ethics of research and the rights of the participant/patient.

The meeting was part of a series of UNAIDS consultations on the ethics of vaccine trials and biomedical research. It attempted to address issues that had arisen in the context of ongoing research, in meetings sponsored by UNAIDS and other institutions, and in discussions in international publications. It was attended by representatives of community and patient organizations, research organizations, research sponsors, ethics committees, governmental and inter-governmental organizations, and academia. The meeting was guided by the ethical principles expressed in the Declaration of Helsinki (World Medical Association) (1996) and the International Ethical Guidelines for Biomedical Research Involving Human Subjects (Council for International Organizations of Medical Sciences) (1993).

The overall objective of the meeting was to assist in developing a framework of care that guarantees to participants that their health needs are given precedence, and that their personal and social integrity is fully protected in the context of HIV/AIDS-related research in developing countries. The specific objective of the meeting was to clarify the appropriate roles and responsibilities of research partners with respect to the care of participants in HIV/AIDS-related research. The following is a summary of the main issues discussed and conclusions reached at the meeting. Based on this summary, comments to it, and developments subsequent to the meeting, UNAIDS, in partnership with its collaborators, will consider the development of a guidance document regarding the provision of care in HIV/AIDS-related research.

The framework of care

The meeting considered a broad framework of care–one that is both rooted in, and serves to protect, the essence of the human personality and dignity. Such a framework of care includes the notion that care is that which is received from outside the individual and nurtures both body and soul. At the same time, care is what lies at the core of the individual in that what one 'cares about' serves to define the individual.

In the context of biomedical research, the framework of care must remain grounded in the established ethical principles (respect for individuals, justice and beneficence) elaborated in numerous ethical codes. A meaningful framework of care should heighten awareness of how these ethical principles actually inform the special relationship between a physician and patient, and a researcher and trial participant, in the context of 'patient care', 'clinical care' and 'standard of care'. In the research situation, the ethics of care should deepen the imperative that persons be treated with dignity, that respect for the individual be safeguarded, and that the relationship of trust between participants and researchers be protected and maintained.

The meeting recognized that it is inherently difficult to define 'care'. This is because: there are many different dimensions to care; care can only be defined in the context in which it is provided; and the nature of care is likely to change and evolve as the research goes forward.

However, all research should be conducted in a caring relationship, and care in the research context should be comprehensive, including both psycho-social and clinical care. Researchers should also be aware of, and sensitive to, relevant cultural perceptions of care and sources of care, including family, traditional healers, faith healers, etc. Where possible, care provided during research should draw support from these contexts. It was also noted at the meeting that there is a need to balance a view of care that may be paternalistic with a perspective of care that is informed by the concept of rights.

The meeting discussed how, in the context of biomedical research, there can be tension regarding the relationship of trust between researcher/physician and the participant, due to the fact that the researcher/physician has in mind not only the interests of the participant, but also the interests of science. In spite of this, he must place the interests, well-being and care of the participant at the forefront of the research endeavour.

It was agreed at the meeting to include surveillance, epidemiology and other non-interventional and observational studies in the consideration of the nature of care in biomedical research, particularly as the majority of biomedical research activities are not interventional studies, such as clinical trials. It was noted, however, that these types of studies raise significantly different care issues and responses, particularly regarding the obligations of researchers and sponsors (see below).

It was also noted that 'participants' in research could be defined broadly to include individuals, local and national researchers, clinics and institutions, host community, local regional and national government and funding sources. However, in this summary, 'participants' will be used to refer to individuals consenting to participate as volunteers in the research. The other participants mentioned above will be referred to explicitly. It was recognized that each has differing types and levels of responsibility.

Care and the rights of patients/participants in biomedical research

Most of the discussion at the meeting focused on the ethical imperatives regarding the provision of care during research. However, the meeting also discussed the provision of care through the perspectives of human rights and patients' rights, and recognized that these perspectives are becoming more and more relevant to the issue of the well-being of patients and participants in research. The meeting considered the human rights set forth in international instruments, which are legally binding on those governments that have acceded to them. Of principal interest are the rights to nondiscrimination, information and participation. Additionally, there is Article 7 of the International Covenant on Civil and Political Rights, which states that "No one shall be subjected to torture or to cruel, inhuman or degrading treatment or punishment. In particular, no one shall be subjected without his free consent to medical or scientific experimentation." There is also the right to health, as set forth in Article 12 in the International Covenant on Economic, Social and Cultural Rights.

Though international human rights instruments legally obligate governments to take measures to protect health and provide health care, these obligations are subject to the principle of 'progressive realization' within available resources, which places an onus on states to strive for their realization over time and encourages other states to provide international cooperation and assistance towards that end.

Where there is some sort of redress for violations of these rights, this must occur, in the first instance, at the national level and be based on national laws that reflect international human rights law. Furthermore, there must be legal mechanisms in place. This can be a major problem in developing countries when governments do not have the means or the political will

to meet their legal obligations. Increasingly, international efforts are geared towards supporting governments to protect and fulfill the rights for which they are legally accountable.

There has also been rapid development of the concept of patients' rights, which have been specifically elaborated in a host of declarations, recommendations, resolutions, codes and guidelines. Though most of these create ethical rather than legal obligations, they do serve to guide conduct, establish responsibility, and act as a source of meaning for the more generally worded international and national human rights law. Furthermore, developments in the area of patients' rights indicate that the discussion about well-being and health is moving beyond the ethics of the doctor/patient relationship to the much broader concepts of the right to health, the right to health care, and the right to an environment that allows people to realize their full potential for health.

This discussion serves to bring together the professional obligations of health-care workers with the legal obligations of governments and law enforcement to respect, protect and fulfill human rights in the health and research contexts.

The meeting agreed that there is a need to translate the concepts involved in ethics, patients' rights and human rights into concrete modalities in the context of HIV/AIDS-related research and care. This is particularly necessary with regard to securing the rights of participants in such research in developing countries. It should also be clarified what constitutes 'damage' in the research context, and what legal mechanisms should be set in place, or referred to, as a means of protecting participants' rights during research.

The expectations and experience of participants regarding care in HIV-related research

The meeting recognized that participants have expectations concerning the research context in which they participate and that these significantly influence the behaviour and experience of participants during the research. Common expectations of participants include that they will receive some care and health benefits, that personal information will be kept confidential, that they will be counselled regarding how to avoid HIV (and STI) infection or live with HIV/AIDS, that transportation and other out-of-pocket expenses will be paid. Participants may also have unrealistic expectations of benefits, and little understanding of risks emanating from the research. In particular, the equipoise that is necessarily at the basis of randomized control trials may not be fully understood by participants, and there may be particular difficulty in explaining placebo controls to participants who expect that their participation will indeed benefit them. Furthermore, expectations are likely to differ depending on the source that created the expectations (e.g. research staff, family, community, government officials), as well as on the level of knowledge and sophistication of the participant.

It was noted that expectations of care often induce people to consent to participate even when they are not clear as to the nature or duration of the care that will be provided. This is particularly true in very low-resourced countries or communities where almost anything can amount to an inducement. The ethical question is whether these expectations amount to undue inducement. If there has been insufficient attempt to explain the level of care, and expectations are allowed to remain unrealistic, undue inducement may have occurred.

The meeting noted that seldom is there a full exploration by the researcher/investigator/physician of participants' expectations or their personal feelings, motivations and experience before and during the research. Furthermore, as the research progresses, contact between researchers and participants increases, and care issues and expectations of care often change and evolve. This evolution is seldom given sufficient attention by researchers.

The meeting noted a number of factors regarding the experience and expectations of participants in HIV-related research in developing countries that may cloud expectations of care and hinder fully informed and consensual participation. These included: lack of knowledge about HIV/AIDS in the community in general and among those engaging in risky behaviour, little understanding or low awareness of the impact of HIV/AIDS, lack of knowledge about medication and treatment in general and in relation to HIV/AIDS, widespread stigma and discrimination, little or no access to medication, low standard of health, low standard of education, low economic status, few local resources, and inadequate health-care infrastructure or trained personnel.

However, in some communities, particularly where HIV prevalence has been high for some time, there is a great deal of experience with HIV/AIDS. In such communities, people, including those living with HIV/AIDS, may be more able and willing to mobilize around research initiatives; participate as informed, motivate partners; and, in certain situations, make particular demands regarding the standard of care to be provided. Researchers, sponsors and government officials should encourage and support such community involvement, but often do not. The fear expressed is that the research will be blocked or overwhelmed by communities' expectations or needs.

The meeting agreed that researchers have a responsibility to fully explore participants' expectations throughout the research. Furthermore, researchers should be as pragmatic and flexible as possible in their response to changing care needs and expectations. Researchers also have the responsibility to ensure that participants are properly informed and that their expectations are appropriate. In research involving a placebo control, particular care should be taken to ensure that participants fully understand the dynamics and possible personal consequences of such research.

The meeting agreed that researchers also have the responsibility to discuss with the wider community (from which participants are drawn) the nature of the research and the expected benefits (short- and long-term), risks, and the level and duration of care that will be offered. In this regard, researchers should ensure an appropriate level of involvement by the community in the design and follow-through of the research. It was also pointed out that governments have a responsibility to become informed regarding any research to be carried out in their countries and communities, and to participate in its development and implementation, particularly with regard to ensuring an ethical process, as well as protection of their citizens' human rights, and legal redress in case of violation.

The standard of care

Throughout the meeting, there was focus on the difficult issue of the standard of care to be achieved in HIV-related research in developing countries. This was particularly true during the discussion of the role of research institutions and sponsors in caring for participants as these institutions and sponsors would most likely bear the costs of the care. It was recognized that the debate on the standard of care is driven by glaring differences and inequities in resources between developed and developing countries. With regard to HIV/AIDS therapy, differential access to antiretrovirals, as well as basic drugs for opportunistic infections and pain relief, is most significant. From the point of view of developing countries and variations among them, 'standard of care' might not only involve issues of access to drug therapies, but also to such elements as technology, infrastructure, and trained health-care personnel, including counsellors for psychosocial care.

Furthermore, it was recognized that inequities exist not just between countries, but also within them. In the developing world, this often takes the form of an urban/rural divide. Even where guidelines are provided with regard to the standard of care, there may be resis-

tance to implementing these guidelines (as well as an inability to do so) among the poorly-resourced health-care workers in the countryside. It was pointed out that the injustice of unequal access to health care, including life-prolonging interventions, is as relevant to other diseases as it is to HIV/AIDS.

The meeting discussed the different possible standards of care. The majority at the meeting agreed that, at a minimum, researchers have the duty to provide, or refer participants to, the best available care that is practically attainable under local circumstances. It was recognized that it is very difficult to define “practically attainable”.

Some, however, felt that participants should be provided with the best proven therapy available anywhere. Concern was expressed that this position would essentially halt international research collaborations, because most of the resources would necessarily go towards drug treatments. It was pointed out that provision of the best proven therapy might also create ethical dilemmas in developing countries, e.g. such care might become an undue inducement to participate; it might create inequities *vis à vis* other people living with HIV/AIDS who are not in research and have no such access; and it might influence participants to undertake more risky behaviour. Furthermore, it was noted that the best proven therapy often simply cannot be implemented in developing countries. It cannot be funded, compliance cannot be obtained, nor is the necessary lab, storage and other infrastructure and personnel support available.

However, many research initiatives in developing countries have been carried out providing the standard of care that equals the prevailing standard of care. It was felt that as this means no care, in many circumstances, this is ethically unacceptable, particularly given that participants take risks during research. Finally, it was stressed that the situation regarding access to care, as well as developments in the content of HIV care and treatment, is a rapidly evolving one. This mandates that the standard of care adjust with the evolution of HIV/AIDS treatment and its availability.

It was cautioned that outside parties should not decide what is best for a country or community that is not their own, in terms of the standard of care. Instead, communities should be involved in, and perhaps even spearhead, attempts to define a locally acceptable and applicable standard of care. This was not only necessary from the ethical point of view of avoiding exploitation of communities, but also from the point of view of communities being able to attract health-related research and interventions that they desperately need and want. It was recognized that it is often difficult to identify representatives of communities, and that it may be necessary to empower these to represent communities effectively (e.g. by building up community advisory boards). There was also recognition that local ethics boards may not exist, may not function well, or may be extremely varied in terms of roles and responsibilities (education, standardization, approval, monitoring, policy development, coordination).

Still it was agreed that there should be in-depth consultations within communities about the nature of the care to be provided in a particular research initiative. Such care must comprehensively address the research context and must be defined locally in a process of consultation involving the sponsoring agency (industry, government, health agency), host country principal investigator, sponsoring agency principal investigator, study participants, community representatives and ethics boards of sponsors and host countries. This process of consultation should begin during research design and should continue throughout the research. It should also provide clear guidance and outline roles and responsibilities, including funding, regarding any care to be provided after the research is concluded.

The role of professionals in the provision of care during research

The meeting confirmed that investigators in interventional biomedical research have a clear duty to obtain informed consent. In the context of developing countries, the following minimum was described. Informed consent may not necessarily mean that the prospective participant should be informed of all details of the research and its methodology, as this may overwhelm and confuse the participant. Rather, it is essential that s/he be informed of the purpose of the research, the nature of the risks and benefits, the availability of the research product if the research is successful, and the type of care that will and will not be provided, e.g. for medical problems unrelated to the research.

Information should be presented in simple language and in the native language of the participant. It should not only be read to the participant but should be presented in the context of a dialogue, with ample time for questions and answers. Written consent is preferable, but oral consent, in the presence of a witness, may suffice where the participant is illiterate. It was noted that the investigator has a potential conflict of interest in being the one to obtain the informed consent in that s/he may influence the participant unduly. However, the investigator is also the one who can best explain the trial and answer questions.

It was also noted that, to maximize compliance and to guarantee good-quality care, participants should live within easy access to the health-care/research facility, and should be provided full transportation costs. In the case of a possible research product, there should be a clear undertaking to have the product available free or at a preferential cost to the participants who undertook the risks involved in the research. This most often involves a commitment from the sponsor/drug company. Where this cannot be obtained, the research should not be carried out.

The meeting agreed that, if one is to protect the health of the participant in research, one must consider the total well-being—both physical and psychosocial—of the participant. Thus, medical care alone may not be sufficient. However, protecting the health of the participant is a particular challenge in developing countries where there are low literacy rates, weak economies and infrastructure, high doctor/patient ratios, and lack of applicable guidelines.

The meeting noted that the research setting presents potential conflicts of interest for doctors conducting research. Conflict of interest was defined as “a set of conditions in which professional judgement concerning the primary interest tends to be unduly influenced by secondary interests.” The meeting confirmed that, in research involving human participants, the primary interest is to safeguard and promote the well-being of such participants. Secondary interests might include contributing to generalizable knowledge, obtaining funding, getting promoted, or gaining respect from colleagues. Doctors/researchers must take care to be aware of these possibly conflicting interests and keep the participant’s well-being at the centre of the research. Factors that the doctor/researcher must remember include the following:

- ethical principles (respect, beneficence and justice) (including those in the Helsinki Declaration, CIOMS and other guidelines) must be respected;
- confidentiality must be maintained;
- informed consent must be obtained and legal notions of negligence and unlawful touching (assault and battery) borne in mind;
- the study must be scientifically designed;
- the study must have sufficient value;

- the study must be conducted honestly;
- the community must be consulted;
- the findings must be reported promptly and accurately;
- the public health consequences must be justifiable.

Doctors/researchers should also assess the proposed research in terms of care with regard to whether:

- the proposed care is feasible;
- the proposed care is available outside the study area (problem of possible undue inducement);
- funding for the costs of the proposed care is available;
- the proposed care is sustainable.

The meeting discussed the roles of other actors in research settings. It was pointed out that the people the researchers/doctors/sponsors think are important in the research setting might not be the ones the participants think are important. People who may have a significant impact on the nature and quality of the experience of participants during the research include receptionists, porters, domestics, cooks, administrators, telephone operators, nurses, drivers and counsellors. All staff in the research should be prepared and empowered to act in a competent and caring manner throughout the research. This is facilitated if staff members are provided clear roles and responsibilities, sufficient information and clarification regarding the research, adequate resources, realistic limits, feedback, and explanation of post-research strategies.

The meeting recognized that counselling is an essential component in the provision of care during HIV-related research, including the breaking of bad news and psychosocial support extended afterwards. The role of counsellors should start at the beginning of the research and continue throughout and beyond, particularly as continuity in counselling is important and the implications of HIV testing do not end when the trial ends. Furthermore, counsellors can be supportive of other staff involved in the research project, providing peer support for stress, distress, accidents and burnout.

Though there are often insufficient resources in developing countries for counselling, it is essential that counsellors be well prepared. This means that they understand and are supported to maintain counselling privacy, they are well-informed about treatment and research conditions so that they can be useful to their clients, they are clear on the limits of what can be done (and the participants/community have also been informed of the limits), and their roles as counsellors are well-defined, but also involve a mix of functions to reduce the possibility of their own burnout.

Counselling and other psychosocial interventions should be subject to the same ethical principles as other care and research interventions. Quality-control and correct ‘dosage’ are necessary to the maintenance of minimum standards regarding the provision of counselling. Recruitment of counsellors should be done carefully with ethical issues, continuity and sustainability in mind. For instance, those from the community may be best placed to serve the community as they know it and its culture so well, but participants may hesitate to go to someone from the community for fear of loss of confidentiality.

The meeting discussed the involvement of associations of people living with HIV/AIDS in HIV-related research. It was agreed that, where appropriate, these should participate as partners in HIV-related research, and could play a number of important roles. For instance, as part of the community response to HIV/AIDS, associations of people living with HIV/AIDS can provide input into research design, implementation, monitoring and follow-up. In particular, they can monitor, advise and assist regarding issues such as providing information on the trials to the community, providing information in the informed consent process, recruitment of participants, provision of care, and the dissemination of research results. Currently, members of some such associations are represented on local ethics boards. Challenges to their involvement include a low level of training in some locales and continuing problems with stigma and discrimination if HIV status is revealed.

The role of sponsors in the provision of care during research

The meeting considered the role of sponsors in biomedical research, with a focus on industry sponsors. One standard that sets forth the role of sponsors is the ICH Guidelines. It was recognized that, although these guidelines list necessary obligations for sponsors in the conduct of research, they do not address the issues raised at this meeting regarding care and its content. It was further recognized that there is no commonly accepted answer among sponsors (or others) to the question: “Where does the responsibility to care for others begin and end in the research context?” Industry sponsors often have no developed policy in this respect; yet they have demonstrated interest in the issue.

The meeting recognized that there are opportunities, which have been seldom used, to build bridges between those in need and industry sponsors. Such opportunities might help to clarify the content of care and the role and responsibilities of sponsors in providing this care. The meeting felt that there is a need to push for more focus on these issues among industry sponsors; and there is a need for leadership in this area, in particular, to establish an agenda for discussion, and to create forums in which to discuss this agenda and find areas of collaboration.

At a minimum, however, the meeting confirmed that sponsors should be in discussion with host governments and communities to ensure that the proposed research is consistent with the public health priorities of the host country. Furthermore, they should explore with governments, local researchers, and local research institutions how sponsors can help to strengthen local infrastructure, training and the capacity of local research and support groups. Although there was no agreement on the obligations of sponsors to fund care after the research is concluded, it was agreed that this issue should form a part of the discussion with the host government and community in terms of the duration of the care package that is provided.

The proposed comprehensive care package for HIV-related interventional research

The meeting agreed that a comprehensive care package should be implemented during any HIV-related interventional research in developing countries. Furthermore, it was agreed that, from the outset of the research design and during implementation, there should be local involvement and decision-making in developing the comprehensive care package, and plans for sustainability should be included. Any comprehensive care package should be tailored, as appropriate, for children and with attention to the differences between male and female participants. It was also stressed that, as the research develops, it might be necessary to add or subtract care package components, and that it was more important to maintain quality and responsiveness in the care package than to adhere strictly to a checklist. Items to be included in a comprehensive care package should be described in the research protocol and should be made known to trial participants so that they will know what to expect.

The following comprehensive care package was discussed (see Appendix I: Consensus and non-consensus for final version):

- counselling
- preventive measures, e.g. condoms
- STI treatment
- treatment of adverse effects related to the research
- nutrition
- palliative care
- TB prophylaxis
- pain control
- psychosocial care
- spiritual care, including at the end of life
- community support for the individual participants.

Various problems were noted regarding the ability to implement such comprehensive care packages in developing countries, e.g. participants' difficulty in understanding the care package, participants' unwillingness to learn of their HIV status, difficulty in coordinating TB prophylaxis, and insufficient resources for proper counselling. Special efforts would need to be made to overcome these.

It was also stressed that a system should be developed to monitor provision of the comprehensive care package, and other issues of well-being, during research trials. It was agreed that this might best be done by an independent body or person, such as an ombudsperson, to whom the participant could go with complaints and problems. This committee or ombudsperson could investigate the matter without necessarily identifying the source.

Care in epidemiological and non-interventional research

It was pointed out that surveillance, epidemiological studies and other non-interventional research have produced substantial biomedical and social benefits in the fight against HIV/AIDS, including important biological and epidemiological risk factors for transmission and disease progression. These, in turn, have provided the basis for interventional developments for prevention and treatment. However, while health departments and research institutions carry out surveillance and/or collect epidemiological information, they seldom provide, nor are they obligated to provide, HIV-related or other health care, beyond possibly referrals, to those reporting with HIV/AIDS. Usually, HIV-related care is provided by the local institution or facility at the best available local standards. On the other hand, sponsors of such research often do, and should, provide, where necessary in a developing country, diagnostic tests, equipment, supplies, training of personnel and other infrastructure development.

It was noted that, in such studies, an assessment of the nature and extent of care to be provided might be done on the basis of: (1) the objective of the study; (2) the level and duration of contact with the study participants; and (3) an evaluation of the availability and accessibility of medical care in the research area. Examples were given of benefits provided that may have an immediate impact on care in the area, such as the provision of a study clinic for research purposes, a counselling service for those who wish to know their HIV status, health education activities, and treatment for STIs.

Moreover, it was confirmed that it is necessary to conduct an ethical review of non-interventional studies, whether or not participants are aware that they are participating in a research programme. It was stressed that, even if the participants themselves are not made directly aware of the study, the community as a whole should be made aware that such a study is taking place. Furthermore, in surveillance studies in developing countries, there is particular difficulty in maintaining confidentiality. Systems should be set in place to protect confidentiality; and the risk of stigma, for the individual or for the community, should be guarded against.

Considering care in research design

When formulating care plans, it was agreed during the meeting that the following are key considerations:

- There should be a presumption of care, which should be defined as the research is designed and progresses.
- The type of care should be based on a broad definition of care.
- The care provided should be sustainable.
- The limits of the care should be clearly defined in terms of duration, type, and the beneficiaries (e.g. participants, their families, partners, the community, the catchment area).
- The provision of care should be governed by the principle of distributive justice, e.g. those that take the risks should benefit from the care provided, the type of care should address those risks and other adverse effects arising from the research, and any research results/products should be made available to the community from which participants came.
- The contents of care should include, at a minimum, drugs, counselling and psychosocial support.
- The elements of the care package should be made in consultation with government, should involve the community, people living with HIV/AIDS, and representatives of people from less empowered groups where these are participating in the research.
- The research design should spread and define responsibilities, in terms of care, among the host government, sponsors, researchers, ethics boards, international agencies.
- The research should benefit the community in terms of training, education, strengthening of infrastructure and the local culture of science and research.
- Sponsors should consult with the host government to ensure that research plans are consistent with the health-care priorities of the communities involved.
- A system to monitor the provision of care and its quality should be put in place, should operate throughout the research and should be easily accessible by participants.

Conclusion

Some possible follow-up steps considered at the meeting include: a UNAIDS position paper or guidelines on the provision of care during HIV-related research, further consultation and possible collaboration with CIOMS on the subject, and commission of a separate paper by a health economist that could address questions regarding cost-effectiveness.

Appendix I

Consensus and non-consensus

The following are areas on which the participants at the meeting reached consensus, as well as areas in which no consensus was reached. The views expressed are not necessarily those of UNAIDS.

Consensus

I. Sponsors should request that plans for research clarify how care for participants will be dealt with in the community in which the HIV research will be conducted. Researchers should elaborate specific plans for the type of research they propose to conduct.

II. A recommended comprehensive care package should include, but not be limited to, some or all of the items listed below, depending on the type of research and the setting. Arriving at the package is a dynamic process, and new items may be added as circumstances warrant. When research participants are women or children, items in the comprehensive care package (such as those listed below) should be modified as appropriate.

- Counselling
- Preventive measures, e.g. male and female condoms
- Treatment for STIs
- Tuberculosis prevention and treatment
- Prevention/treatment for opportunistic infections
- Nutrition
- Palliative care
- Pain control
- Psychosocial care
- Spiritual care
- Community support
- Family planning
- Home care
- Antiretroviral therapy, when it is readily available outside the research context or when the infrastructure permits its being made available to research participants.

III. In deciding on a recommended comprehensive care package, researchers, sponsors and the host government should consider the following:

- Are the ingredients of the package available outside the study area?
- Is it feasible to implement the care package in the near future? If so, researchers and sponsors should negotiate with the host government for plans for its sustainability.

- If the care package is implemented in an efficacy trial, will it be used when operationalizing the findings of the trial?
- Who will pay for this care?
- What is the likely public health impact of the care package?

IV. Researchers have an obligation to devise a process of consultation with the community in order to determine what items of care might be needed during the course of the study. This consultation should begin before the research starts and continue throughout the process. Researchers should identify constituencies in the population from which the participants will be drawn. People living with HIV/AIDS and less empowered groups should be involved in this process to ensure that their needs are considered in the total care package.

V. Sponsors should negotiate with the host government to ensure that the proposed research and accompanying care plans are consistent with the public health priorities of the host country.

VI. Researchers should devise a monitoring process to ensure that the proposed care package is actually being carried out during the research. This function could be carried out by a DSMB, REC or other oversight body established for this purpose. Researchers should describe procedures for establishing this mechanism in the research proposal.

VII. Sponsors and researchers, in consultation with the host government and the community, should strive to determine how the proposed research can contribute to the strengthening of local infrastructure, provision of training and education, and enhancing the capacity of local support groups.

VIII. In compliance with their international human rights obligations, host governments should ensure that care is negotiated into research proposals, and is sustained after research is concluded. Governments should recognize their dual responsibility to promote and protect public health and to respect, protect and fulfill human rights under international human rights law.

Non-consensus

There was no consensus on the following: the specific obligations of the host government and whether to include such obligations in the meeting's conclusions; the care package that accompanies a research project should be reviewed and approved by the local or national ethical review committee in the location where the research will be carried out; there must be agreement between the local or national ethics review board and the sponsor's ethical review board, and any differences must be negotiated before the research is done; and this process should be in compliance with international ethical guidelines governing research.

The following issues were identified as some that should be further explored:

- the full significance, in terms of the care to be provided, of the distinction between non-interventional and interventional research;
- the nature of the care to be provided at the end of the trial, and its duration;
- the relationship between providing care or other benefits and the concept of 'undue inducement to participate', including whether there is a difference between care as an inducement and other types of benefits as inducements.

Appendix II

Background documents

- *A world of research subjects* (1998) The Hastings Center Report, Vol. 28:6.
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- Edgar H, Cruz-Coke R (1996) *Draft Report: Access to Treatment, Experimentation on Human Subjects and Ethics.* Paper presented to the International Bioethics Committee (IBC), UNESCO, Paris, 3-4 October 1996.
- *Ethical and Social Aspects of AIDS in Africa.* A consultant's report by Julia Hausermann, commissioned by the Commonwealth Secretariat.
- International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH) (1996) *Guideline for Guidance on Good Clinical Practice* (CPMP/ICH/135/95).
- Practical and Ethical Dilemmas in the Clinical Testing of Microbicides (1998), a report on a symposium sponsored by Women's Health Advocates on Microbicides (WHAM) and The Population Council.
- Science, ethics, and the future of research into maternal infant transmission of HIV-1. Perinatal HIV intervention research in developing countries workshop. *The Lancet,* 1999; 353:832-835, with follow-up letters to the editor.
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Japan, October 1975; 35th World Medical Assembly, Venice, Italy, October 1983; 41st World Medical Assembly, Hong Kong; and the 48th General Assembly, September 1989. Somerset West, Republic of South Africa, October 1996.

- World Medical Association (1995) *World Medical Association Declaration of Lisbon on the Rights of the Patient*. Adopted by the 34th World Medical Assembly, Lisbon, Portugal, September/October 1981 and amended by the 47th General Assembly, Bali, Indonesia, September 1995.

The Joint United Nations Programme on HIV/AIDS (UNAIDS) is the leading advocate for global action on HIV/AIDS. It brings together eight United Nations agencies in a common effort to fight the epidemic: the United Nations Children's Fund (UNICEF), the United Nations Development Programme (UNDP), the United Nations Population Fund (UNFPA), the United Nations International Drug Control Programme (UNDCP), the International Labour Organization (ILO), the United Nations Educational, Scientific and Cultural Organization (UNESCO), the World Health Organization (WHO) and the World Bank.

UNAIDS both mobilizes the responses to the epidemic of its eight cosponsoring organizations and supplements these efforts with special initiatives. Its purpose is to lead and assist an expansion of the international response to HIV/AIDS on all fronts: medical, public health, social, economic, cultural, political and human rights. UNAIDS works with a broad range of partners—governmental and NGO, business, scientific and lay—to share knowledge, skills and best practice across boundaries.

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In May 1999, UNAIDS convened a meeting on 'Care within the context of HIV/AIDS-related research in developing countries' as part of a series of consultations on the ethics of vaccine trials and biomedical research. The meeting's objectives were to develop a framework of care for participants in HIV/AIDS-related research in developing countries, as well as to clarify the appropriate responsibilities of the research institutions, health-care professionals, sponsors, communities and governments in the context of research ethics.

This report is a summary of the issues discussed at the meeting and the conclusions reached, which included the agreement that the participants' health and well-being must be the primary concern during HIV-related research and that this concern should prevail over any other concerns, including the interest of science. Based on this summary and the subsequent developments, UNAIDS (in partnership with its collaborators) will consider the development of a guidance document regarding the provision of care in HIV/AIDS-related research.

Joint United Nations Programme on HIV/AIDS

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