The Fifth Global Forum on Bioethics in Research: Report of a Meeting, April 2004

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The Global Forum on Bioethics in Research ("Global Forum") was established in 1999 to bring together individuals, public and private organizations involved in medical research from "North" and "South", to share views on bioethics issues in research. Each meeting has enabled individuals in developing countries to have significant input on ethical debates related to the conduct of international collaborative research. At each annual Global Forum, roughly two-thirds of the participants are from the developing world, representing 30 to 40 countries. Representatives from developing countries typically include individuals involved in medical research, bioethics and law from academic institutions, international health organizations, government agencies, pharmaceutical organizations, and community organizations.

At the 2004 Global Forum meeting in Paris, hosted by INSERM, participants addressed issues of benefit sharing related to developing country health research. During the meeting, several themes emerged in relation to this topic: the need for collaborations and partnerships between stakeholders in the North and the South; the need to respect traditional practices and social structures; the need to consider the complexities of community involvement in research; and the need to consider benefits not only in terms of financial gain, but also in terms of development of capacity, knowledge, experience and autonomy.

The meeting included three types of presentations: general discussions regarding benefit-sharing in research; case study presentations and discussions; and technical talks relating to intellectual property and research in the South.

Philosophy and ethics. Jean-Claude Ameisen, (President, INSERM ethics committee), emphasized the need for ethics rules and practices to evolve hand in hand with scientific progress. Drawing on examples from AIDS research and treatment, Ameisen highlighted the influence of AIDS activists in stimulating greater discussion of access to medical treatment, asserting that such discussions in the public health arena are consistent with a broad social commitment to ethical values. He also stressed the importance of broad-based social discussion about ethical issues.

Mario Stasi (French National Ethics Committee) reflected on gross inequalities in access to drugs and medical care in countries at different levels of development. He warned against conducting research that would disproportionately benefit the North, but that targets populations in the South for clinical testing and drew upon the example of a hepatitis B vaccine. He stressed the right to health as a human right [1]. He also emphasized the need for independent ethics committees in developing countries to evaluate research on behalf of their populations, as a key element of autonomous decision-making. Further, he indicated that scientific research protocols should be required to address the provision of direct benefits to individuals or communities involved in research.

Picking up on the theme of responsibilities to communities, Assetou Derme (Centre National de Recherche et de Formation sur le Paludisme, Burkina Faso) outlined the complexities inherent in defining a community. She outlined different aspects of the notion of 'community', including spatial, spiritual, political and sociological dimensions. Accordingly, the spatial dimension of a community consists of a geographical area or entity; the spiritual approach defines a community by religion; and a political community consists of those who are grouped together either by a common political philosophy or a political boundary. The sociological categorisation of a community involves a common community of practice; interdependence among individuals with distinct characteristics; or a common 'decisional field', meaning common culture or rule-following. Dr Derme pointed out that a community might be characterized by more than one dimension, and that communities change both in space and in time.

Dr. Derme also analyzed representation of community interests, beginning with the concept of authority, which she characterized as either legally authorized or authorized based on trust granted by members of a community. She posited that individuals who represent community interests can be defined using the various dimensions outlined above; for example, a spiritual leader may represent community interests in some settings, whereas a politically appointed leader may address other concerns. The internal social order of the community will often determine who the leaders are, which may also create potential conflicts of interest (e.g. the interests of the elite within a community may not coincide with the interests of the majority). There may be internal struggle for power or conflict within a community, such that one representative may not be able to satisfy the interests of all. Researchers, Dr. Derme recommended, should take particular care in establishing "equidistance" from different interest groups in order not to polarize communities with competing interests. Furthermore, she maintained that communities must define themselves, rather than be defined by outsiders, including researchers.

Dominique Lecourt, (Institute of Research for Development, Paris) discussed the double meaning of the word sharing—to divide, as in dividing up resources, and to unite together, as in sharing experiences. Building on this observation, he elaborated the inherent tension between a competitive model of sharing on the one hand, which would include discussion of distribution of profits, and, on the other hand, sharing in the sense of joint participation and collaboration. Dr. Lecourt lamented the increasingly competitive nature of science and medicine, and advocated that a more humanistic notion of sharing should be adopted in the context of research. Turning to the issue of informed consent, Dr Lecourt emphasised the need for consent as an ongoing process and highlighted that such processes should not always be based on the systems of the North [2].

Ambrose Talisuna (Ministry of Health, Uganda) identified three criteria for determining how benefit sharing should operate: benefits should be fair; collaborative partnerships are needed; and transparency is required. He compared this framework to the concept of benefit sharing contained in many international guidelines, namely the 'reasonable availability' standard, and proposed it as an alternative to this principle. The 'reasonable availability' standard requires that successful products tested in research must be made reasonably available to host communities and countries after the research is over; however, this standard might not apply in many research projects that don't test specific biomedical interventions (e.g. basic genetic research or epidemiology studies), and is often difficult to interpret and apply. In addition, alternative benefit sharing arrangements are sometimes preferable to the host country. Indeed, benefits may be related to the research or they may be public health benefits, employment, capacity development, long-term research collaboration or sharing of intellectual property. In conclusion, Dr. Talisuna suggested that an independent body, such as WHO, should collate benefit sharing agreements, so as to evaluate the different benefit sharing standards that emerge over time.

Case studies and discussion. Four case studies were discussed, focusing on research where intellectual property was or could have been generated from resources or knowledge held by developing countries. Details of all the case studies can be found on the 5th Global Forum's website [3]. Two cases concerned research on traditional medicinal plants, and two related to genetic research. In the debate stimulated by these cases, concerns arose that developing countries hosting the research, or indigenous groups within these countries, might not benefit sufficiently from the overall results of the research.

The case studies involving research on plants used as traditional medicines by indigenous groups centred on the experiences of the Maya people in Chiapas, Mexico, and the San people of southern Africa. In the southern African case, presented in the meeting by Roger Chennells, lawyer for the San people, a plant well known to the San as an appetite suppressant, the hoodia plant, was used by a government research institute to develop a new diet drug. This was initially carried out without any recognition or compensation to the San people for the knowledge that contributed to the development of this potentially profitable drug. After challenges from San political leaders, the government institute

arranged a benefit-sharing agreement with the San that would return a percentage of profits from the drug to their regional indigenous political organization, for use in local development activities.

The Mexican research project was presented by Luis Garcia-Barrios of the Mexican research institution Colegio de la Frontera Sur. The Maya ICBG project involved collecting and cataloguing botanical species of the Chiapas highlands and evaluating their use in traditional remedies. Despite the researchers' good intentions, there was a lack of overall political unity among the local indigenous population: one faction of the community objected to the research project; at the same time, many local indigenous representatives agreed to participate. Despite efforts by research organizations and sponsors to set up a benefit-sharing arrangement, including providing short- and possible long-term benefits to the local population, political controversy made the project untenable, and the research activities never started.

In discussing these cases, participants stressed the importance of indigenous populations taking part in research having legal and political representation, and consulting with communities widely regarding the structure and design of the research project. Many at the meeting felt that protection of indigenous cultures and customs should be part of benefit-sharing principles, and that strictly monetary benefits could be either helpful or harmful in this regard. Some remarked that indigenous communities have a moral obligation to share medicinal knowledge which may help others. Many participants pointed to the long history of exploitation of indigenous communities, sometimes by their own governments and sometimes by outsiders, and the lack of equal bargaining power and mistrust that ensues.

Throughout discussions of research on medicinal plants, participants distinguished between knowledge and intellectual property. Although individuals or groups may have knowledge, it is often difficult to determine whether this knowledge exists in the public or private domain. In addition, within a community, there may be disputes as to who the legitimate holder of the knowledge is, as well as great uncertainty about whether the knowledge, if shared, will result in profitable or more widely useful products. These complexities often make it challenging to assess what kind of benefits are fair in a proposed research project, or even whether any benefit will emerge. Significantly, participants pointed out that timelines of research projects do not always reflect the time and resources required by researchers and communities to consider these issues.

The cases dealing with genetic research databases elaborated on the Estonian Genome Project, presented by Ants Nomper (University of Tantu, Estonia), and a proposed genetic research project in the island of Tonga, described by the Reverend Simote Vea (Tonga Democracy and Human Rights Movement). The Estonian project, constructing a genetic database of the population of Estonia, was initiated by the government and gained a high degree of popular approval and cooperation. In contrast, the Tonga project, which aimed to collect blood samples from Tongans for genetic studies of factors relating to diabetes and obesity, was proposed by an Australian biotechnology company. Although it gained approval from the country's monarchic government, it met with resistance from

religious and pro-democracy groups and research was never initiated in Tonga (the biotech company subsequently formed agreements with other groups). Discussants of the cases pointed to differences in history, scientific infrastructure and familiarity with science, degree of democratic representation, and religious affiliations, between the two countries. They observed that the projects themselves had been initiated and designed with different stakeholders and partnerships. In the Estonian case, the national government initiated and retained control of the project, but allowed a private company to conduct the research and have a share of profits; however, the Tonga project was entirely proposed and designed by a small company, without public discussion or transparency.

Discussion of all the cases focused on questions of ownership, shared heritage, confidentiality and identity. A distinction was made between access and ownership. A population may be said to have an interest in the uses and possible misappropriation of genetic information gathered from its members; however, this does not necessarily constitute ownership in the sense of legal or political control. In the research context, the issue of access to samples is often more relevant than ownership of samples or genetic data. At the population level, it may be difficult to determine the boundaries of group interests and individual rights, as some individuals may object to genetic research and may decline to participate, but may be affected by findings based on participation by other members of the same population. Questions were raised regarding how one is to measure benefits, who has the authority to give consent for a project to proceed, and the potential social value of the databases.

A final case study centred around the well-documented case of genetic and epidemiological research carried out in the Anhui province of China, which proved not to benefit Chinese participants. The principal investigator of the study was subsequently reprimanded and the study suspended.

Technical presentations. Cristina d'Almeida (Fiocruz, Brazil) described Brazil's strategies for negotiating licensing agreements with pharmaceutical companies in order to establish production of needed anti-retrovirals used by the Ministry of Health in its national AIDS treatment program. This presentation underscored the importance of national governments in establishing intellectual property agreements and manufacturing capacity to benefit their own populations. Given the importance of establishing such agreements and implementing them, she voiced concern about the lack of intellectual property expertise in Brazil.

Legal and political considerations in conducting research in developing countries were addressed by John Kilama (Global Biodiversity Development Institute, USA). Dr. Kilama highlighted the importance of understanding the political context in countries where research is conducted, as well as national laws and authoritative bodies, and relationships between and among different communities and national governments. He also emphasized the importance of knowing the relationship between the group in authority and the community with whom the research is to be conducted, and understanding the relevance of trust, or lack thereof, between different stakeholders.

From the national to the local level, it is critical for researchers and sponsors to know and understand the capacities of institutions in the host country. Some mechanisms for ensuring that negotiations are balanced include ensuring that indigenous communities have skilled legal representation and comprise outside neutral observers, for example WHO delegates.

Cross-cutting themes. Throughout the Global Forum, participants voiced the need for collaborations and partnerships among and between stakeholders from both the South and the North. They agreed that effective partnerships would include good-faith negotiations about research design before research starts, and that communities and national governments should be included in such negotiations. Partnerships must also include respect for traditional practices and social structures, and transparency throughout the research process. In advocating partnerships, participants acknowledged the challenges in determining appropriate representation of communities and establishing a level playing field among partners with a wide range of resources. The Forum participants also stressed the need to consider benefits not only as financial gains, but as gains in capacity, knowledge, experience, and autonomy. Delegates also acknowledged the complexities of community structures, the relationship of traditional medicine to modern medical practices, and the importance of historical context in understanding the interactions of communities with local and national governments. Significantly, there was considerable focus on fair procedures, rather than evaluation of specific outcomes with respect to justice or equity.

Concluding comments were provided by Dr. Achille Massougmodji (University of Cotonou, Benin), Prof Zulfiquar Bhutta (Aga Khan University, Pakistan) and Dr Florencia Luna (Facultad Latinoamericana de Ciencias Sociales, Argentina). All three speakers reflected on the importance of social justice and democracy as values to be incorporated into bioethics discussions and to be integrated into concerns about the ethical conduct of research. Drawing upon previous discussions, Prof Bhutta and Dr Luna outlined several questions that should be addressed with respect to research in the South, including: What are the boundaries of the community and the state? How are "indigenous community" and "community ownership" defined? Who represents the community? Who has authority within the community? What does the concept of partnership mean? What does it mean to study a disease of relevance to the community? What is the accountability of research sponsors and regulators? Dr. Luna also noted the evolution of research ethics discourse, which initially focused on questions of autonomy and informed consent, and is increasingly addressing concerns of access to health care, exploitation and justice.

In the coming years bioethicists will continue to address complex ethical questions facing those who engage in health research in the developing world. Moral challenges continue to grow, as communities and organizations try to find ethically acceptable approaches to health-related research in a world with large disparities in health. The Global Forum represents an effort to involve experts from the South in developing these approaches. The 5th Global Forum was supported by a consortium of funding and non-funding partners: the Wellcome Trust, the Fogarty International Center, the Rockefeller

Foundation, the U.S. Centers for Disease Control, the European Commission, INSERM, UNESCO, COHRED, WHO and the UK Medical Research Council. The 6th Global Forum is scheduled for March 2005 in Malawi and will focus on "What happens after the research is over? Post-trial responsibilities of researchers and sponsors".

Endnotes

1. http://www.ccne-ethique.fr/english/avis/a_078.htm
2. http://www.ccne-ethique.fr/english/avis/a_038.htm
3. http://www.inserm.fr/Geneweb/GlobalForum.nsf/Accueil?readform