

# The ethical aspects of biomedical research in developing countries

*Proceedings of the Round Table Debate\**

**Brussels, October 1<sup>st</sup>, 2002**

Secretariat of the EGE

European Group on Ethics in Science and New Technologies to the European Commission

**- February 2003 -**

---

\*Report written by Katerina Sukovski, a trainee with the Secretariat of the European Group on Ethics in Science and New Technologies to the European Commission from October 1<sup>st</sup>, 2002 to February 28<sup>th</sup>, 2003.

***Europe Direct is a service to help you find answers  
to your questions about the European Union***

**New freephone number:  
00 800 6 7 8 9 10 11**

A great deal of additional information on the European Union is available on the Internet.  
It can be accessed through the Europa server (<http://europa.eu.int>).

Cataloguing data can be found at the end of this publication.

Luxembourg: Office for Official Publications of the European Communities, 2003

ISBN 92-894-5064-9

© European Communities, 2003  
Reproduction is authorised provided the source is acknowledged.

*Printed in Luxembourg*

PRINTED ON WHITE CHLORINE-FREE PAPER

## Table of Contents

---

---

Introduction .....	1
Agenda.....	3
Moral Pluralism Søren HOLM .....	7
Norms, Values and Trans-Cultural Medical Ethics Monica KONRAD .....	11
Ethics of clinical collaboration with developing countries: controversial issues Reidar K. LIE.....	21
ICMR's approach concerning the ethics of clinical research in India Vasantha MUTHUSWAMY .....	27
HIV/AIDS clinical research in Africa: ethical aspects Nicolas MEDA .....	33
Ethical issues in the pneumococcal conjugate vaccine clinical trials in the Philippines: the ARIVAC experience Hanna NOHYNEK .....	43
Ethical aspects of conducting clinical trials in developing countries: Experiences of GlaxoSmithKline (GSK). Nadia TORNIEPORTH.....	51
Discussion .....	59
Curriculum Vitae of the Speakers.....	71
Participants.....	87
Secretariat of the EGE .....	95



# Introduction

---

The European Group on Ethics (EGE)<sup>1</sup> is an independent, pluralist and multidisciplinary body, which advises the European Commission on ethical aspects of science and new technologies in connection with the preparation and implementation of Community legislation or policies.

The Group is composed of twelve independent experts appointed by the Commission for their expertise and personal qualities.

The Group is presently preparing its 17<sup>th</sup> Opinion on “***the ethical aspects of biomedical research in developing countries***”. This reflection work has been requested on behalf of the European Commission. The EU Sixth Framework Research Program (FP6), adopted on the 3<sup>rd</sup> of June 2002, defines thematic priority fields for 2002-2005, open to collaboration also for non-EU countries. Within the FP6, a European and Developing Countries Clinical Trials Partnership aiming at joining efforts to combat poverty linked diseases, such as AIDS, malaria and tuberculosis, is being set up and will involve developing countries.

In preparing its opinions, the EGE is open to broad consultation, involving experts, representatives of European institutions and other international institutions as well as representatives of civil society. The objective of the Round Table organized by the Group is to promote transparency dialogue between parties representing different interests.

The round table organized by the European Group on Ethics was held on October 1<sup>st</sup>, 2002, in order to stimulate dialogue and reflection on the ethical aspects raised by clinical research in developing countries. The following report is a summary of the presentations and discussions which took place.

Christiane Bardoux  
Secretary of the EGE

---

<sup>1</sup> More information on the EGE is available on the website:  
[http://europa.eu.int/comm/european\\_group\\_ethics](http://europa.eu.int/comm/european_group_ethics)







## ***Presentations***

---

---



**Søren HOLM**

Dr. Søren Holm

University of Manchester & University of Oslo



# Moral Pluralism

---

Søren HOLM

This presentation represents a philosophical perspective on the ethical implications of clinical research through the discussion of the nature of moral pluralism. Moral pluralism is the idea that moral values and/or moral judgements are not universal and that moral nihilism is false. It is thus a rejection of moral universalism, but a rejection that keeps open a space for moral discourse.

There are a number of different forms of moral pluralism. These differ with regard to how 'deep' the pluralism is supposed to be. The most common form of moral pluralism is the so-called '**cultural relativism**' which typically claims that moral values and moral judgements differ between cultures (as an empirical statement this is fairly uncontroversial). It also implies that there is no deeper/higher level of moral thinking that can show the moral values of a given culture to be wrong which entails a rejection of foundationalism in ethics. And finally, that we should be tolerant of the moral values and judgements of other cultures.

According to cultural relativism moral discussion and criticism is thus possible within a culture, but not between cultures except in the areas where they share values. This concept may sound attractive because it seemingly supports cultural tolerance and offers a platform from which to criticise cultural imperialism of a moral nature. On closer analysis, however, it is easy to see that there is no valid argument from cultural relativism to cultural tolerance. If our culture values intolerance, then we would presumably be right when we were intolerant!

## Problems with cultural relativism

Cultural relativism also entails other problems. First, it is at risk of collapsing into a more comprehensive relativist position, where moral values and judgements are simply seen as personal expressions of taste or emotion. There is no argument to stop at cultures and not move to sub-cultures, groups, families, individual, etc.

Second, it potentially undermines the idea of universal human rights, and the possibility of rightful criticism of human rights breaches, at least as moral rights. We might claim legal rights, but if cultural relativism were really true, we would not be able to derive universal rights through a moral construct

And finally, cultural relativism follows from the view that we cannot compare the "quality" of different cultures, but we can perhaps compare the features of those cultures. For example, some countries treat people with mental illness "better" than others, without saying that that makes one culture universally "better". Therefore, our inability to compare cultures does not mean we can not compare their features.

This, however, requires that we can delimit “a culture”, and again we cannot say that cultures are equivalent to countries. Who can make a rightful claim to be a culture? Often this is done through self-identification: I decide whether I belong to a given culture. This, however, does not solve the problem. For example, imagine in Europe that we had a culture making a living out of crime, and this culture managed to export itself to other parts of the world. Those who identified with the feature of crime would identify to the culture and not to the nation state or region they belonged to. One can take this reasoning further: should we tolerate killing or stealing within a given cultural grouping in our society if that is part of that group’s culture?

Moreover, there is a risk of marginalising sub-cultures within the culture. Who decides what the culture thinks? What moral practices are right? We should be careful of reifying cultures: making them into things, which they are not.

### **Are there any more viable forms of moral pluralism?**

First, we have what could be called “procedural pluralism”. This is the idea that the moral goals and values are universal in some sense, but that the ways in which we try to reach these goals are, and have to be different in different cultures. For example, self-determination may be agreed upon on, but the methods for documenting this self-determination may differ in that the person has made a choice for himself or herself. In this, values, judgements, goals are the same, but the methods for reaching them may differ in different cultures

Second, is what could be called “limited pluralism”. The idea that there are a few universal moral values, but that most of morality is culturally determined. But here too we could come to disagreement about what these Universal values are, and even when there is agreement, we are then tempted to use these agreed upon universal values (few and far between) to make derivative values such as human rights.

Finally, “negotiated universalism” is when we have to work with people with other cultures, we negotiate the values we are going to build on. We do not try to convince that our values are right, but rather we negotiate a set of values/procedures for the given context. We can see a lot of different types of human rights this way. For example, the Bioethics Convention is hardly satisfying from a moral philosophical point of view, but exemplifies a negotiated set of values that most member states of the Council of Europe can agree to. So maybe we cannot get any further than this, but with partners we can negotiate for a set of shared values.

**Dr. Monica KONRAD**

Cambridge, United Kingdom

School of Advanced Study

University of London



# **Norms, Values and Trans-Cultural Medical Ethics**

---

**Monica KONRAD**

## **Introduction**

Professor Vice-President and members of the EGE, thank you for the invitation to speak at today's Round Table. I am pleased to be here in my capacity as a medical anthropologist. The focus of today's discussion is of direct relevance both to social anthropological concerns and to medical anthropology more specifically. Let me briefly preface my comments by saying a little about the kind of work medical anthropologists do.

Medical anthropology deals with the relationship between culture, taken in the broadest sense, and various aspects of health and illness. Medical anthropologists spend periods of field research in settings across all parts of the world. This means that our research inevitably generates cross-cultural data, thereby creating opportunities for new knowledge to be built up from comparative analysis.

Our aim always -- as trained 'professional strangers' -- is to gain an in-depth understanding of the cultural values, beliefs and experiences informing the local health practices we study. At times this may also include analysis of the cultural processes of moral action. Increasingly so, anthropologists are turning their focused attention to the contextual nature of moral decision-making and the cultural embeddedness of moral systems, including the field of bioethics.

## **Towards a transcultural medical ethics**

So the question of how biomedical research can be conducted as international collaborations between different countries is of direct relevance to medical anthropology. In thinking about how we create normative and regulatory frameworks with broad applicability, it is important to consider the following: What is a 'trans-cultural medical ethics' and how can it be truly effective in the future as a genuine 'health for all' development policy?

This question deserves attention for many reasons. There are today a number of health priorities that were not at the fore of the thinking that shaped the original guidelines of the [World Medical Association's] *Declaration of Helsinki* in the 1960s. First, the effects of globalisation and the changing geopolitical and socio-economic landscape. This is of direct relevance to global epidemics and emerging drug-resistant viruses; to the health effects of warfare and ethnic genocide on migration and resettlement; also to the implications of the new biotechnologies, especially in the field of genetics and human reproduction. And additionally the impact of the new information and communication technologies with telemedicine delivery systems. Some of the close connections between international health ethics and globalisation were brought home when Tore Godal, Executive Secretary of the Global Alliance for Vaccine and Immunisation (GAVI)

commented on the possible diversion of funds away from routine vaccine production to vaccine development against bioterrorism in the light of 9/11 (International AIDS Vaccine Initiative [IAVI] Report 2002). Also of relevance: the emergence of new collaborative partnerships and cross-regional networks set up specifically to combat poverty-related diseases such as the European and Developing Countries Clinical Trials Partnership (EDCTP) that Octavi Quintana Trias will talk to us about later today. Initiatives such as the Millennium Development Goals and the network 'clusters' that are shaping global public private partnerships deserve special mention too.

All these developments indicate why a trans-cultural medical ethics now seems particularly timely. We currently have at our disposal a particular conceptual framework that has underpinned much of Western-derived bioethics during the latter half of the 20<sup>th</sup> century. But, as moral philosophers and ethicists themselves have observed, this framework may not be sufficiently accommodating to pose a range of culturally inflected questions, nor to secure certain desired-for solutions within a global context. Principlism and the '4-principles approach' developed by Beauchamp and Childress (1994) with its stress on the respect for persons through (1) autonomy (2) beneficence (3) non-maleficence and (4) justice, including equity, was not originally formulated with the explicit remit of tackling the socio-political effects of multiculturalism - either within the USA or elsewhere. Nor, in its founding conceptualisation, was it particularly sensitive to the challenges facing cross-cultural field research in international health. Nonetheless, it is these very principles that have provided general guidance for many regulatory bodies involved in formulating ethical guidelines for biomedical research. And it is these principles that continue to inform the work programmes of various international agencies, inter-governmental and non-governmental bodies (e.g. WHO, the UN, The Council for International Organisations of Medical Sciences (CIOMS), Médecins sans Frontières (MSF), International Red Cross). So, we need to ask careful and non-hurried questions about the extent to which the framing conceptions and premises of Western bioethics can continue to provide a primary source of ethics evaluation beyond the resource rich countries for which they were originally devised. How do we best start to ask these questions?

If we say that a trans-cultural medical ethics may establish certain unconditional minimum requirements such as the inalienability of 'human dignity', it does not *necessarily* follow that such a position is homologous with moral fundamentalism or absolutism *per se*. Namely, the view that certain ethical principles are timelessly and universally applicable as immutable standards. Nor is a trans-cultural medical ethics *necessarily* exactly the same as the critical project of cross-cultural *anthropological* analysis. And if we do not *necessarily* equate cultural relativism with uncritical acceptance of the moral norms of any given culture -- as Soren Holm has just outlined to us -- then we are also better placed to see how a trans-cultural medical ethics, built upon *ethical pluralism*, depends upon continuous dialogue, negotiation and reflection between different agents and parties.

Modulating between different varieties of fundamentalism and relativism to establish new bioethics models with global relevance is demanding conceptual work. It requires nuanced thinking. What I want to stress today is that these important conceptual

questions have no instantly accessible, straightforward answers. Our conceptual efforts need to be shaped by on-the-ground empirical investigation and guided by the weight of specific contexts witnessed in real time: observing real situations, real people, real dilemmas. Adding another layer of collaborative networks to those I mentioned a moment ago would seem to promise a constructive way forward. A global bioethics needs a multidisciplinary taskforce. Ethicists and moral philosophers, medical anthropologists, health-allied professionals, international lawyers and human rights specialists: shouldn't we also be thinking about ways of working creatively alongside each other on specific research projects? I believe something along these lines has been shaping up by way of the informal partnerships of *The Global Forum on Bioethics in Research*.

Now various commentators have been critical of the existing international regulations on biomedical research. It has been said that they are too complex, over-general, insufficiently specific and cross-referenced. (Tröhler & Reiter-Theil 1998). Also that the essentially normative, aspirational and decontextualised frameworks of the instruments endow them with a rigid, non-proactive character (Christakis 1996:263; see also Tröhler & Reiter-Theil 1998 on medical ethics codification). These critiques all point to the significance of the gap between norms as idealistic stipulations and their actual implementation in practice. Which in turn points to the recognition that international declarations need to be responsive to local needs and circumstances, rather than simply 'top-down' formulations of 'first principles'. 'Bottom-up' approaches, as I have been saying, depend upon the collection of fresh empirical data. A trans-cultural medical ethics that incorporates such grass-roots perspectives would have many agendas. One surely would be to ask and document how what is learnt in practice can shape future ethics guidelines. How does decision-making and problem-solving on the ground, especially during clinical practice and across multi-site project-based partnerships, feed back into the modification of new guidelines, norms and values?

Basically, this question amounts to a plea to consider the implementation of guidelines in terms of a *shift* from contents based protocol to procedure based negotiations. To do this within a joint sponsor-host collaborative framework, it may be helpful to bear in mind the notion of 'procedural justice'. Bioethicist Ruth Macklin (1998:133) has advocated a version of procedural justice for future transcultural research in human subject experimentation that is based on '...a different yet important expression of fairness, and relat[ing] to the *process according to which* decisions are made and actions are carried out' (emphasis added). Macklin and colleagues (Kahn *et al* 1998) identify the need to move beyond simply ensuring informed consent agreements to what they call a 'balancing conception of justice' (*ibid*: 4), namely one as preoccupied with benefits as it is with concepts of risk, burden and harm. Suggesting that the dilemmas facing the ethics of subject recruitment can be conceptualised in terms of benefit and not simply according to risk criteria, *procedural justice* crucially places emphasis on processes of decision-making. Let's consider this notion of procedural justice by introducing some points about informed consent from the perspective of critical ethical pluralism.

## **Ethical pluralism and procedural justice: questioning autonomy as paradoxes in consent**

Cultural differences in beliefs about the nature of personhood and the location of decisional authority for consent have been problematic for some recent investigators conducting international health research. In some settings, the internationally agreed-upon standard for individual informed consent that derives from the norm of autonomy can seem inappropriate since important decisions are often made in conjunction with families or by entire communities. Patients asked to enrol in a medical study might then be sceptical of an investigator who did not involve their immediate or extended kin in the decision-making process. As one commissioned submission to the US National Bioethics Advisory Council Report (2001) observes, research projects may need to adopt a 'multistep consent process'. For research involving children, this might begin with community consent followed by individual parental consent. Village elders might also be invited to sit in on sessions with juniors because of community suspicions that children may be abducted and used as servants, or subjected possibly to organ harvesting (see Sugarman *et al* 2001). The process of consent as the acquisition of community trust thus takes place over several encounters. It is in this basic sense 'procedural'. And it may well vary in its specific practice between different rural and urban settings (requirements for community consent generally being stronger in rural areas).

However, securing study approval from community leaders, tribal elders, or household heads is no *substitute* for individual consent, regardless of the particular cultural setting. This is the [minimum requirement] position adopted by The Nuffield Council of Bioethics Report (2002) and its emphasis on the importance of individual autonomy within the context of community consent. That said, we need to know more about how different members of communities really see themselves as genuinely involved in such decisions, as well as how different communities think of themselves as inter-related and inter-relating members. This is where the in-depth, time-sensitive and detail-rich work of cultural and anthropological analysis may play a very constructive part within the setting of epidemiological and other collaborative health research. For example, local norms associated with marriages involving multiple wives may comprise additional cultural factors that influence recruitment strategies and the process of informed consent acquisition. In genetic epidemiological studies, for instance, investigators might want to enrol family members who are genetically related to each other. When a man has conjugal relations with more than one wife, but researchers only want to recruit the wife who is genetically important to the study on account of known biologically related offspring, medical personnel must navigate the potentially disruptive social consequences for extended family households. One can easily anticipate that incoming researchers would not be hearing the whole story about intrahousehold disputes between the various wives simply by talking to the husband in question. Nor for that matter could it always be easy to obtain a full account from the tribal chief or head of the local council from whom one 'part' of a multi-step consent may already have been obtained. But an anthropologically focused research study, working alongside people from the local community, would aim to treat these different viewpoints as culturally significant data in their own right.

The philosophical question here is this: how do we reconfigure a system of consent(s) not predicated exclusively on the value of subject autonomy. To understand ethical pluralism as culturally specific forms of procedural justice, further empirical work is required to address the relevance of consent procedures in the light of non-western cultural norms (for instance, taking into account varying local understandings relating to norms of personhood and other manifestations of personal identity).

In its Report published earlier this year, the Nuffield Council of Bioethics introduces the concept of 'genuine' consent, thereby refining further the previous stipulations in the CIOMS/WHO guidelines (1993) for 'informed' consent (see Nuffield Council of Bioethics 2002:77). But what exactly is 'genuine' consent? What are the specific criteria for its evaluation? How do we take on board issues of information provision during clinical sessions? Lines of miscommunication might be manifest as problems to do with language barriers and translation, such as the introduction of terms for which there are no indigenous concepts, like 'placebo' or 'randomisation'. One 'incoming' (externally-sponsored) anthropological researcher from North America notes that amongst the Yoruba-speaking trial participants recruited to a genetic epidemiology study she co-conducted in Nigeria, people did not understand the terms 'genotyping' and 'candidate genes' because there is no local Yoruba term for 'gene' (Marshall 2001). How does procedural justice unfold here as 'fair' strategies for risk communication? Behind this question lie numerous others, each of which requires further empirical analysis.

One of the basic principles of the Declaration of Helsinki (WMA 2000) states:

*Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific literature.*

On the face of it, this all sounds sensible. But, can people consider themselves as *genuine* participants in trials when they do not understand the defining concepts and rationales motivating the studies? In a certain sense this question applies to all human experimental studies in medicine, but it has additional salience in the context of international collaborations. Can we think of developing country recruits as real participants in a genetic study when subjects' own predominantly a-genetic understandings of 'inheritance' mean that they also hold non-western notions of disease transmission? Or to turn that question around. How do Western researchers working in developing countries themselves respond when trial participants who have not had educational schooling in the germ theory of disease causation report that they can explain the sudden death of a relative as the effects of witchcraft and evil spirits?

And another dimension: is it enough simply to say at recruitment stage that 'this clinical trial might lead to a cure sometime in the future' and leave it at that? How, if at all, is the future defined in consent procedures? What specificity of information is given about delayed benefits and how are the different phases of trials explained? Is it understood -- implicitly or explicitly -- by the trial participant that a cure will impact during one's lifetime, or that direct health benefits shall only accrue at some unspecified time for future

generations? How can and how should Western researchers ethically 'explain' the rationale of their research and seek to clarify the problem of so-called 'therapeutic misconception' (see Nuffield Council of Bioethics 2002:46)? Also, how is the sequential relationship in real time to expected drug development made explicit? The issue of the financial commitments by pharma to drug manufacturing for diseases that offer little promise of large commercial return: how is this explained during the consent procedure, indeed if at all? Given that such issues may be unknown even to the sponsor and host researchers themselves both before, during and even after the completion of a successful trial, what then is the basis of so-called 'genuine consent'?

Now at the same time as one wants to ask these kinds of detailed questions, recent evidence suggests that the detailed documentation of written consent forms may be *too* cumbersome for some potential trial recruits. For those unaccustomed to official documentation, the requirement to make a personal signature or undergo thumb printing as proof of voluntary consent are acts that may cause suspicion and intimidation because they are seen as excessively legalistic. Persons with low literacy levels may be frightened of the repercussions of signing a document because this may be associated with previous police tactics (Sugarman *et al* 2001). Or it may be associated with past experiences that resulted in forms of victimisation, such as loss of personal property or land, when 'legal' documents were used against them (Marshall 2001). Also, in the context of guerrilla warfare, the use of written informed consent might pose a risk to participants by linking them to particular institutions.

It is true that several of the recent national guidelines recommend that informed consent documents be developed in collaboration with local colleagues, and that special attention be paid to potential problems in translation of particular concepts. Also, that a degree of flexibility be exercised with regards to written consent documents for those unaccustomed to receiving documentation of any important transaction. These are constructive starting points. But we need to go still deeper than this. It is not just western researchers who need to 'educate' others in biomedical constructs and related scientific terminology. Such educational attempts will be at best meaningless, and at worst seen as yet another form of 'health ethics imperialism', unless a genuinely intercultural and multilateral learning process unfolds on the ground. Incoming researchers from developed countries need to understand and respect how cultural beliefs concerning the cause and treatment of disease may differ radically from Western views about disease aetiology, rather than see alternative explanatory systems of ill-health as beliefs that simply threaten the viability of a proposed biomedical research study. A positive extension of this would be the setting up of projects aimed at the effective integration of different health knowledge systems and traditions. The recent debates on international health ethics have tended to forget that certain so-called 'developing' countries have their own indigenous stocks of ancient health wisdom. In terms of education and training, India has one of the largest formally recognised traditional medicine sectors in the world. Currently, the Department of the Indian Systems of Medicine & Homeopathy (2001) is seeking to promote medical pluralism so as to combine approaches from modern biomedicine with Ayurveda, Unani, Siddha, Yoga & Naturopathy. And it's worth noting also that several ingredients of Indian medicines have found application in many allopathic drugs used in the conventional

treatment of cancer, blood pressure, heart disease and diabetes -- the major Western killers.

Which brings me to my last point. Many of the issues I have mentioned bear directly upon the collection of human biological samples and the problem of the ownership of genetic resources in the context of the Human Genome Diversity project, and other genomics ventures. The ethics and equity of IPR claims relating to international 'bioprospecting' can be taken right back to issues of consent and information provision at the point of blood and other tissue sample collection from various indigenous peoples. Many indigenous groups see the patenting of human life as a violation of their integrity and against their own traditions and norms. So, policies are required to protect the *collective rights* of indigenous peoples, as proposed for instance by the Indigenous Peoples Council on Biocolonialism and the [generically formulated] Indigenous Research Protection Act.

### **Final words**

In conclusion, further thinking is required to develop interdisciplinary collaborations between bioethics, clinical medicine, medical anthropology and human rights. With the objective of establishing a culturally sensitive and plurally-inflected bioethics research agenda for 'global health'. That way we can start to flesh out specific cases. And start to show how a shift from the rigidity of pre-given, content-based international ethical standards to processes of negotiated settlement -- as procedure-based protocols -- may not only change the language in which we talk about norms and values, but give more people better, healthier lives. Because ultimately it is the terrible health inequities between rich and poor countries that we must work to eliminate. Thank you.

## References

- Beauchamp, T.L. & Childress, J.F. (1994) *Principles of Biomedical Ethics*, Oxford: Oxford University Press.
- Christakis, N (1996) 'The distinction between ethical pluralism and ethical relativism: implications for the conduct of transcultural clinical research'. In Harold Y. Vanderpool (ed) *The Ethics of Research Involving Human Subjects. Facing the 21<sup>st</sup> Century*, Frederick, Maryland: University Publishing Group.
- CIOMS/WHO (1993) *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, available at: [http://www.cioms.ch/frame\\_1993\\_texts\\_of\\_guidelines.htm](http://www.cioms.ch/frame_1993_texts_of_guidelines.htm)
- Department of Indian Systems of Medicine & Homeopathy (2001) *Draft National Policy on Indian Systems of Medicine*, Ministry of Health & Family Welfare Government of India, New Delhi, available at <http://indianmedicine.nic.in>
- IAVI Report (2002) 'New models for vaccine delivery: an interview with Tore Godal, International AIDS Vaccine Initiative, available at [http://www.vaccinealliance.org/tg\\_interview.html](http://www.vaccinealliance.org/tg_interview.html)
- Kahn, J., Mastroianna, A.C., & J. Sugarman (eds) 1998 *Beyond Consent: Seeking Justice in Research*, Oxford: OUP.
- Macklin, R. (1999) *Against Relativism: Cultural Diversity and the Search for Ethical Universals in Medicine*, Oxford: OUP.
- Marshall. P. (2001) 'The relevance of culture for informed consent in US-funded international health research' in National Bioethics Advisory Commission (US) Report: *Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries*, Bethesda, MD: NBAC. (Volume II: Commissioned Papers).
- National Bioethics Advisory Commission (US) Report: *Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries*, Bethesda, MD: NBAC (Vols I & II). Available at: <http://bioethics.georgetown.edu/nbac/pubs.html>
- Nuffield Council of Bioethics (2002) *The Ethics of Research Related to Healthcare in Developing Countries*: London: NCB.
- Sugarman, J, Pokin, B, Fortney, J. and Rivera, R. (2001) 'International perspectives on protecting human research subjects' in National Bioethics Advisory Commission (US) Report: *Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries*, Bethesda, MD: NBAC. (Volume II: Commissioned Papers).
- Tröhler, U. & Reiter-Theil, S. (1998) (eds) *Ethics Codes in Medicine: Foundations and Achievements of Codification since 1947*, Aldershot: Ashgate.
- WMA (2000) *Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects*, adopted by the 52<sup>nd</sup> World Medical Association General Assembly, Edinburgh, Scotland, October 2000. Available at: [http://www.wma.net/e/policy/17-c\\_e.html](http://www.wma.net/e/policy/17-c_e.html)

**Reidar K. LIE,**  
**M.D., Ph.D**  
University of Bergen, Norway



## **Ethics of clinical collaboration with developing countries: controversial issues**

---

---

**Reidar K. LIE**

The controversies surrounding clinical trial collaborations with developing countries have mainly been concerned with two issues: the level of care owed to participants in clinical trials and the obligations, if any, to trial communities after successful testing.

After the debate surrounding the perinatal HIV transmission studies, there has been a controversy whether it is ever permissible to use a lower, local level of care in the control group than is available in resource rich settings. Those who defended a local level of care argued that this was necessary because otherwise the results from the trial would not be applicable to the host country. Those who defended a universal standard of care argued that useful results could be obtained using a universal standard, even if it might involve higher costs and take longer time. In the international literature there has been a great deal of confusion about the issue of scientific necessity of a local standard of care. Nevertheless, it can easily be shown that in cases of an unknown, variable placebo effect, equivalence trials cannot show that an intermediate treatment is better than placebo, if the trial results in non-equivalence between the two treatments. Thus, there can be no question that there are real scientific reasons for wanting to conduct trials with a lower standard of care. The crucial issue is therefore whether there are other, overriding moral concerns, which would make such trials impermissible, in spite of the fact that they might be the only way to obtain useful results. If one can argue that they sometimes are permissible, the second crucial issue is under what conditions they are permissible. Can we allow different levels of care in trials depending on different economic conditions?

The main criticism has been that in allowing studies that could not be done in developed countries, we would be exploiting developing countries and would be allowing an ethical double standard. And secondly, that there is a clinical obligation to identifiable individuals to provide known proven treatments.

Against this, in a defence against these criticisms it has been argued that it is sometimes necessary, in order to obtain knowledge necessary in resource poor settings, to do trials with a different level of care. Such trials should be permissible if one can introduce safeguards to avoid exploitation. Such trials would have to be done in full openness and after wide consultation.

The second controversial issue concerns the obligations to trial communities after successful testing. In resource rich settings, one would normally expect that a successful product would become available to those who need it. In resource poor settings this is often not the case. Recently, attention has also been brought

to a practice of conducting trials in resource poor settings, which cannot be done for ethical reasons in resource rich settings, but where the results are known not to be useful in the host country. One recent example is the preventive malarone trials in African countries, resulting in licensing of this drug for the prevention of malaria in travellers and expatriates. Because of such cases, a number of recent international guidelines and documents have required that research can only be morally permitted if there is some likelihood that it will benefit the community in which it takes place. Some have defended a stronger requirement of explicit prior agreements with a detailed plan for how the results will be useful for the host community. In spite of the current popularity of these notions, there are very few, if any, examples of successful prior agreements. There is a danger that the preoccupation with prior agreements will deflect attention from the fact that it is the size of the benefit to the host population that is important, not whether the benefit concerns availability of the product after successful testing. In addition, one needs to address the issue whether “reasonable availability” should be a condition for approval of protocols?

There are many International Guidelines that address these issues. Where the Helsinki Declaration establishes a universal standard, NBAC, Nuffield and UNAIDS foresee allowable differences; and the CIOMS guidelines do not allow for these differences *per se*, but the accompanying commentary does.

Between them there seems to be agreement with respect to the necessary conditions of placebo use and reasonable availability. First, the results of the trial should be relevant to the study population/country in which the study is carried out and that there is a reasonable likelihood that the new intervention will be implemented. Unfortunately, this was not the case for the short course treatment.

And secondly, at the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic, and therapeutic methods identified by that study, as required by the Helsinki Declaration This is also reflected in other guidelines.

There is no agreement on a requirement for the availability to general community. According to the previous version of the CIOMS guidelines, as a general rule, the sponsoring agency should ensure that, at the completion of successful testing, any product developed would be made reasonably available to the inhabitants of the underdeveloped community in which the research was carried out. Exceptions to this general requirement should be justified, and agreed to by all concerned parties before the research is begun. Whereas, the current Helsinki Declaration stipulates that medical 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 of the research.

Moreover, there is consensus and agreement that this issue needs to be addressed. The notion of “prior agreements” is gaining some popularity, however

one should not underestimate the complexities of this issue. Focusing on prior agreements might divert resources from more important concerns.

## **Conclusion**

Therefore, it is clear that when focusing on prior agreements, all the complexities of prior agreements need to be addressed. Against this, one might want to maintain that more emphasis needs to be placed on the risks and the benefits of the research project itself, as well as the benefits that are to be provided immediately, including health benefits during the study period.



**Dr. Vasantha MUTHUSWAMY**

Senior Deputy Director General of the Indian Council of Medical Research,  
New Delhi, India



# ICMR's approach concerning the ethics of clinical research in India

---

---

Vasantha MUTHUSWAMY

Established in 1947, the Indian Council of Medical Research (ICMR) was set up in order to foster a research culture in India, improve and develop infrastructure and foster community support. As one of the oldest medical research bodies in the world, ICMR is the apex body in India for the formulation, co-ordination and promotion of biomedical research. With an institutional network incorporating 21 permanent institutes and six regional centres, ICMR has developed into a formidable funding agency for supporting medical research in the country. It's primary role is the development of infrastructure, capacity building, peer review, monitoring, evaluation procedures, etc.

The major challenges facing the ICMR and public health in India remain the double burden of communicable and non-communicable diseases. Clinical trials are therefore oriented towards TB, leprosy, viral diseases, malaria, leishmaniasis, HIV/AIDS, as well as cancer, cardiovascular, mental health, haematological disorders. (see graph). These health concerns are primarily due to the realities of a population without access to safe water, health services and sanitation.

## The establishment of ethical standards

In 1980, the *Policy Statement on Ethical Considerations involved in research on Human Subjects*<sup>2</sup> was established. However, the growing demands made by the critical issues in the area of biogenetic research, as well as mandatory trials for new drugs have developed a need to update these guidelines. Moreover, new technologies and diagnostic procedure have further underlined this need most notably with respect to issues such as ART, organ transplants, xenotransplantation, human genome and use of foetal tissue.

These guidelines were therefore revised in 1996, during which time an ethics committee was constituted under the chairmanship of Justice Sh.M.N. Venkatachalia. The Central Ethics Committee on Human Research (CECHR) comprised of 27 members, and 5 Sub-committees of experts, was set up for drawing up the guidelines in respective areas.

The major areas identified by the Committee were:

- Clinical evaluation of drug/devices/diagnostics/vaccines/herbal remedies
- Epidemiological research
- Human Genetic Research

---

<sup>2</sup> Mainly dealt with issues such as ethics committees, informed consent, clinical trials, research on children, the mentally disadvantaged and those with diminished autonomy ; traditional medicine ; and publications.

- Transplantation research including foetal tissue transplantation
- Assisted Reproductive technologies

The final Revised guidelines were released in September 2000, entitled “*Ethical Guidelines for biomedical research on human subjects*”. The general principles outlined by these guidelines, known as the ICMR code, are as follows:

- Essentiality
- Voluntarism, Informed consent, Community Agreement
- Non-exploitation
- Privacy and Confidentiality
- Precaution & Risk minimisation
- Professional Competence
- Accountability and Transparency
- Maximisation of public interest and distributive justice
- Institutional arrangements
- Public domain
- Totality of responsibility
- Compliance.

Unfortunately, these guidelines are not binding. For example, did the recent controversial Phase I and II clinical trials for anti-cancer drug treatments done in India not follow certain procedures laid down in these guidelines. There is no National Biomedical Authority in place for monitoring which is now being suggested. The Ethical Review Procedure is however mandatory and must be done by either the IEC. It is done to ensure sound ethical & scientific decision-making and to promote ethically viable priority research. As well, with respect to public health, this procedure is put in place to provide public assurance, and to safeguard welfare & rights of participants. In so doing, establish regular monitoring of clinical trials.

The main ethical issues involved in the Ethical Review Procedure are:

- the Informed Consent Process,
- Compensation for participation,
- Selection of Special Groups as research Subjects,
- Essential Information on Confidentiality for Prospective Research Subjects,
- Compensation for Accidental Injury,
- International Collaboration,
- Relations with Media & Publication Practices.

### **Ethical concerns in clinical research in India**

There are however many concerns and issues surrounding these procedures. First, research ethics are a relatively new speciality in India, which impacts on ethical review. The process therefore remains relatively unknown and rudimentary in general. It has been said that only Ethical Review can make a difference, but can ethics committees make a difference?

The inherent difficulties associated with informed consent remain high illiteracy rates and the existence of many languages in India. This coupled with overburdened health professionals leaves little time for explanation.

Moreover, bioethics education is not currently a part of the present curriculum; there is a need for legislation to regulate human experiments; and the issues surrounding Community consultation must be addressed. These issues include a community benefit agreement, product availability, and the ethics of priority setting. These require a greater involvement of those close to communities, as well as that of voluntary agencies, and village leaders.

International Collaboration also requires greater attention. Community participation and that the protection of vulnerable populations should be requirements for all capacity building initiatives done through international collaboration. The careful planning of clinical trials can ensure this. The discussion on standard of care highlighted the necessity to insist on best possible care through the study of the situation within country, according the best nationally available health care, and not care set by international standards. The burden and benefits of these issues should be assessed in the framework of equal respect for the rules and regulations of both countries.

### **Initiatives and strategies**

Some strategies being developed to address these concerns include the preparation and dissemination of guidelines, the organising of public debates, workshops as well as regional initiatives, such as FERCAP (Forum for Ethics review Committees in Asia-Pacific), FERCI (India), FERCIT (Thailand), FEHRIN (Nepal), etc.

Moreover, legislation has been developed in order to protect research participants in India. The possibility of malaria trials at the Mekong region have spurred the development and implementation of national legislation for ethics committees over the last year at Laos and Cambodia. Currently, Nepal and Philippines have their own guidelines, where as Vietnam and Indonesia are in the process of developing such guidelines. This is with the hope that all countries will have appropriately functioning ethics committees.

More specifically, ICMR has developed certain specific initiatives in order to better address these issues. These initiatives include the establishment of a Central Ethics Committee at Headquarters to look at research proposals with national significance and also to help the Regional IEC's in various issues. These include: the strengthening the increasing demand for infrastructure development, capacity building, monitoring mechanism, safety issues, and innovative initiatives; the establishment of the Pre-clinical toxicology units, Clinical Pharmacology units, Clinical Trial centres.

Regarding education and training, the initiatives include Research Methodology workshops, Clinical trial training courses, biostatistics courses, and training in human & animal ethics and in modern biology. In this, FRCAP, has developed workshops for ethics review committee members for WHO ethical guideline implementation, while Industry is also getting involved by sponsoring ethics workshops.

## **Conclusions**

To ensure that India becomes a leading nation in Good Clinical Research, greater attention must be paid to promoting clinical research. The gap between the developed and developing worlds needs to be narrowed in order to ensure global justice, particularly with respect to the widespread availability of proven interventions in developing countries. The emphasis is to ensure that Research ethics should be made an integral part of all biomedical research. As such every stakeholder should consider research participants as central players, who should be protected from any harm for which an appropriate legislation should be in place to ensure the above.

### **Networks of Centres of Advanced Research**

Pre clinical Toxicology Units (PCT) : National Institute of Nutrition (Hyderabad), Institute of Pathology (New Delhi), Industrial toxicology Research Centre (Lucknow), Institute for Research in Reproduction (Mumbai), Post Graduate Institute (Chandigarh).

ICMR Institutes having Animal Facility : RMRIMS, Niced, RMRC, TRC, RMRC, IIH, IOP, CJIL, VCRC, NIV, NCLAS, IRR.

Clinical Pharmacology Units (Phase I and Phase II trials) : Tuberculosis Research Centre (Chennai), KEM Hospital (Mumbai), Nizam's Institute (Hyderabad).

Traditional Medicine research : CAR for Natural products, CDRI (Lucknow), Clinical Pharmacology Centre for TRM – Nair Hospital (Mumbai), Standardisation & Quality Control of Traditional Remedies : RRL (Jammu) and NIPER (Chandigarh)

**Dr. Nicolas MEDA MD, PhD**

Chief, Department of HIV/AIDS & Reproductive Health  
Centre MURAZ, MoH Biomedical Research & Training Institute,  
Bobo-Dioulasso, Burkina Faso



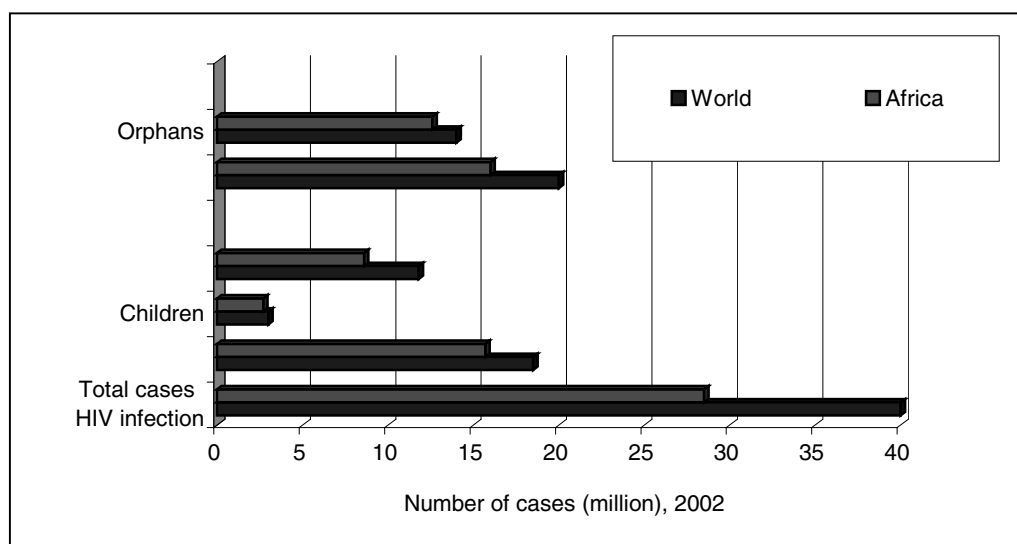
## HIV/AIDS clinical research in Africa: ethical aspects

Nicolas MEDA

It is impossible to begin to discuss this topic without giving an indication of the scale and the seriousness of the problem in the African region. Nearly 30 million people today live with the AIDS virus in Africa. About 16 million people have already succumbed to AIDS leaving behind as many orphans.

The total statistics from around the world do not even approach those from Africa. Moreover, if AIDS has imposed itself as the most serious threat to public health in Africa, it has also become the most serious obstacle to durable human development in the region.

### HIV/AIDS situation in Africa, 2002



There is no question as to the necessity of the need for clinical research as a necessary step in the advancement of medical knowledge in order to provide quality health care to the public. We should also recognise that Africa is clearly where HIV/AIDS medical research should become a priority, and everyone (national decision-makers, development, scientific and community partners) should recognise this. More than anywhere else, it is in Africa that issues such as prevention, access to healthcare, treatment and finally the care of people infected are the most desperate.

In this line, major advances have been obtained on the field in Africa. With the principal support of the European Commission, research has shown that treating sexually transmitted diseases (STD) will significantly reduce the incidence of HIV in

the general population<sup>3</sup>. With the support of the French Nationale Agency for AIDS Research (ANRS)<sup>4</sup>, the American National Institut of Health and the Centre for Disease Control and Prevention (CDC), research has proven that short-course antiviral drugs can diminish by half mother to infant transmission of the AIDS virus.<sup>5</sup>

Moreover, with this same financial support from the ANRS and the CDC, we now know that cotimoxazole, commonly known as BACTRIM and very inexpensive, diminishes by almost half the severe illnesses and even death in tuberculosis infected and non-infected individuals living with HIV. This work was done in the Ivory Coast.

And finally, through research done in Kenya and Tanzania, we are today convinced that the counselling and HIV testing services provided to the individual, and what is more, to the couple, changes sexual behaviour. Thus, reducing by 46% the incidence of sexually transmitted disease, including HIV/AIDS.

These recent advances in medical research in Africa are already being applied and are saving lives. All the United Nations agencies as well all the development partners have taken the examples cited as points of reference for program financing.

However, if we were to apply one of the many ethical guidelines established around the world to these projects, none of these studies would have been conducted. Which is why the main part of my presentation will address the following: « we want the research results in Africa », « we reject the research necessary to obtain the results we need ».

This is why the foundation of my presentation will seek to defend the following hypothesis: if the ethical rules dictated by the dominance of the western atheism, said to be liberated from dogmas, are imposed on all as revelations of truth, we can therefore consider that instead of promoting human rights, these rules represent an obstacle to scientific progress in Africa. My scientific perspective on ethics has been formed by culture, the value system of a given society, religion, the level of education, of development, of experience, and also contains and an emotional and an intuitive dimension.

This is the reason that the real foundations of ethics in medical research in developing countries must be based on the African context and the reality of North-South relations today. Outside of this frame of reflection, this meeting would be nothing more than another meeting where good people sat around a richly ornamented table to say good things but which would have no influence on the everyday reality of the African population.

---

<sup>3</sup> Treating STD syndromes reduces HIV incidence by 42% in adult general population and is cost effective. Grosskurth et al. Lancet 1995, Gilson et al. Lancet 1997.

<sup>4</sup> L'Agence Nationale française de Recherches sur le SIDA (ANRS)

<sup>5</sup> Using short course ARV regimens in the perinatal periode reduces MTCT of HIV by nearly 50% at 6 months and is cost-effective. Dabis et al. Lancet 1999, Gay et al. Lancet 1999, Creese et al. 2002.

There are essentially five fundamental principles in 'universal' ethics that served as the basis for the putting in place of different rules, regulations and laws. My presentation will review, one by one, these different principles and build on the reality of these different principles in the medical research devoted to HIV/AIDS in Africa.

### **The principle of the respect of the Science Dignity**

The first of these principles is for me the respect of the dignity of science. This respect necessitates that questions with respect to public health are given priority and addressed with the necessary scientific rigour. This includes the relevance of the study question for medical progress and public health, the quality of the study protocol, the adequacy of technical facilities and funds, and the qualifications of scientific investigators.

The reality in Africa is somewhat different. In Africa good science is equated with imported research, where local researchers are not involved in the scientific protocols. Moreover, these protocols are not evaluated independently. This therefore leaves room for the « the kingdom of promotional studies », where the low capacity of local investigators in the design, conduct and publication of scientifically relevant studies are targeted by the private sector. The pharmaceutical industry is thus conducting purely promotional research in collaboration with doctors from public hospitals in order to prepare glossy brochures colour prospecti responding to questions of little social value.

In Africa, the best clinical research is generally those projects which are conducted by researchers from the North in collaboration with scientists from the South, due to the weak methodological capacity of local researchers as well as the weak economy. For example, let us randomly take the ten most renowned journals, and look at the first author of published AIDS clinical research. The number of African researchers will virtually tend towards zero, if it is not simply zero.

In the field, the African media daily 'reports' rumours and information on traditional treatments with miraculous curative powers with respect to HIV/AIDS. Moreover, many traditional practitioners and unscrupulous persons abuse the distress created by AIDS. The fact that the population is generally uninformed in regard to HIV natural history, enables these persons to prove the absolute efficiency of traditional (or non-traditional) products, whose efficiency and safety have never been tested. And often, this is done with the benediction of the local authorities, always ready to value traditional or local medicine over the too expensive modern medicines.

## **The principle of Individual Autonomy**

The respect of human dignity, centred on enlightened consent is the principal ethic which has been the most valued. It is the basis for the Nuremberg code. It is useless to spend time on the main ideas behind this principal. Let us rather look at the reality of the application of this principle in Africa.

Autonomy in the choice to participate in the study through a clear understanding of the study protocol indicated by the signature of informed consent. This is done in order to ensure the protection of the confidentiality of collected data or private information known in the context of the study. The situation in Africa, plagued by poverty, has introduced vulnerability and coercion into the debate.

Can we speak of the autonomy of women in a precarious social position? Which autonomy of choice can exist in the context of poverty when faced with the privileges offered by the study? How can one protect confidentiality in a social situation where HIV/AIDS is highly stigmatised? Is the individualistic approach of ethics appropriate in a context where communitarianism governs society?

In discussing Africa, we evoke a context of vulnerability marked by increasing poverty, cumbersome sociocultural traditions and high illiteracy. In an environment where there is little available treatment for AIDS, and where participating in a clinical trial may be considered a privilege (where participants are given the benefit of a standard of care significantly better than the rest of the population) what value does freedom of choice have?

What freedom of choice does a woman have in this decision when she herself is convinced that only her partner or husband can authorise such and such act in life (DITRAME experiment)? What autonomy does individual consent have in a rural environment where the village chief is responsible for the relationship with the outside world? To what extent can notions of random parallel, crossed or plan factorial trial double blind versus placebo be understood when almost 70% of the population is illiterate? At this stage we only have questions.

## **The principle of Beneficence**

The third principal is that of beneficence. It is in the respect of this principle that the scientist is subjected to the most difficult questions in research: How to treat the individual, in the form of direct benefit and evaluate long term collective benefit? If a certain treatment is evaluated to have an interesting potential benefit and is comparable to the standard treatment in place, a priori, ambivalence is respected.

The ethical conflict remains how to maximise benefits and minimise harm: how to treat a patient (care) and evaluate a treatment (research)? How does one respect the equipoise between a new promising method, with good results in the preliminary

animal and Phase I/II studies versus the established standard of care? What is the place of placebo?

The situation in Africa is that of poverty, one which cannot afford a high standard of care. As we saw with the Harvard MTCT trial in Thailand, those results are for rich countries. However, the MTCT and Cotrimoxazole clinical trial results are widely utilised in Africa. Microbicides trials have the right to use placebo groups. However, where there is no standard of care, or where the existing standard of care is inaccessible (culturally, technically, logistically, financially, etc.), should research be forbidden? Is it ethical, in the name of universal moral values, to prevent downtrodden populations to fight to identify interventions that would be accessible to them?

One has only to consider the short-course trials of antiviral drugs in Africa. I personally led this type of trial in Burkina Faso. The use of placebo as a standard of comparative treatment was contested without taking into account its social and scientific value, as well as the adaptation of the study to the local context. The disputed studies produced scientifically irrefutable results that all the agencies across the world, and particularly the European Commission, recommend in AIDS programmes in the South.

The standard of care which we are discussing with respect to the principle of beneficence is not a simple question of will but that of what the power to buy at the level of the State or that of the individual can buy. The reality can not be hidden by a declaration, a rich person and a poor person do not have the same standard of care. To impose such standards, in order to respect ethics, would prevent much needed clinical research, to an African would appear as unjust and immoral.

### **The principle of Justice**

Let us consider this principle of Justice which appears as one of the five pillars of so-called universal ethics. There are many components to this principal, and I will only cite one rule: *Ethically, all patients having participated in a study must be assured, at the end of the study, of diagnostic, therapeutic and preventive treatment which the study showed to be superior.*

This principle implies the equitable distribution of the risks, the burden and most importantly, the benefits resulting from research. It also implies that post-trial benefits are seen in rich and poor countries, and that North-South collaboration establishes good principles of research partnership. The reality is that the poverty at country and population levels precludes any large application of research results for prevention and care of HIV. In the case of external funding, the location of research activities or resulting programmes depends on political and economical interests and geostrategy. For example, which EU funds will be allocated to Togo? Which for Zimbabwe?

How many Africans have access to the positive aspects of HIV/AIDS clinical research financed by the North? Less than 1% of those living with HIV in developing countries who require treatment have access to ARV. Very few pregnant women benefit from short term ARVs to save their child's life.

The question is above all linked to the weak purchasing power of the populations and states in Africa. But when international solidarity intervenes in order to benefit the African population, the principle of Justice remains in this room on the rue Froissart. Where is USAID in Africa? Will the European Commission give even one penny to the populations of Zimbabwe, Togo or the Ivory Coast? What is the responsibility of African governments, rich countries, funding agencies, "North" & "South" researchers? It seems clear that without international solidarity it is quite impossible to apply the Justice principle in the post-trial period.

### **The principle of Independence**

And finally, we will end with the fifth principle which is that of independence. It is not easy to prove the credibility, good faith, conformity to ethical rules and the application of standards in the good practices for clinical, biological and statistical research when we refuse to submit to the criticism and control by external scrutiny. This is why the role of the different ethical, scientific, regulatory and pilot committees is preponderant in clinical trials. (e.g. Scientific Review Committees, Ethical Review Committees, Data & Safety Monitoring Board, Study Steering Committee, Study Scientific Committee)

In Africa, we are always looking for this type of committee, particularly when only local researchers conduct the research. Who is responsible for this void? Why is this criticism of the lack of ethical committees done in such an insidious manner when researchers from the North are implicated? Why is this same concern not raised when researchers from the South are working in their corner?

By talking about ethics in clinical research in Africa without taking into account the state of poverty, culture, social value systems, religion, illiteracy levels, development levels, and local experience is to contemplate the gender of angels. In Africa, many countries do not have committees for local or imported studies.

Without government awareness of duties to protect human rights, it is difficult to imagine the creation of competent ethical committees. The actual practices have many limitations with respect to the ethical rules in medical research in Africa. How do the standards of ethics, established under the domination of the Western value system represent a universal standard? Why are governments and civil society in Africa inert in the face of questions and challenges of ethical dilemmas in the field of medical research in Africa? Why are the technical abilities and methodological capacities of Africans, with respect to clinical research devoted to AIDS, so

underdeveloped after decades of scientific collaboration between the North and South? Is there a real vision of development in the North/South exchange with respect to HIV/AIDS research? What is the North doing to promote human rights in the HIV/AIDS research that it finances in the South?

It is almost pretentious to talk about the right answer to the ethical challenge that is HIV/AIDS research in Africa. But in my humble opinion, there is substance in the results that we have today that will allow us to abandon the rhetoric wrapped in dogmatism, even imperialism, to engage in a pragmatic path to the contextualisation of medical ethics.

A principal I would like to introduce is the obligation of international solidarity in the defence of the right to health and human rights in the South. International solidarity can amplify pressure on governments and civil society in Africa in order to take into account ethics in HIV/AIDS research. International solidarity can also truly become a way to development in the formation and support of the immense capacity in the South for medical research. Without international solidarity, I do not see how African populations can benefit from the positive results of HIV/AIDS research conducted by agencies financed by the North. And what role, what leadership can the European Commission provide or play in order to overcome these major challenges that can guarantee African populations, and what is more -to those infected with AIDS, the power to enjoy the basic right to health?



**Dr. Hanna NOHYNEK MD PhD**

Department of Vaccines

National Public Health Institute

HELSINKI - Finland



# **Ethical issues in the pneumococcal conjugate vaccine clinical trials in the Philippines: the ARIVAC experience**

---

---

Hanna NOHYNEK

Since July 2000, the ARIVAC consortium has been conducting a Phase III effectiveness study of an unlicensed pneumococcal (Pnc) conjugate vaccine (PCV) in the Philippines. Unlike most other PCV trials which have concentrated on invasive Pnc disease, the main endpoint of this study is pneumonia, which kills approximately 4 million children annually, and thus constitutes a major public health disease burden. An estimated cohort of 12 190 infants will be enrolled over a period of three years. The vaccine is given according to the national immunisation programme at 6, 10, and 14 weeks, and the children are being followed up until the age of 2 years.

The study is a Phase III, randomised, double blind, controlled, clinical trial (RCT) to determine the effectiveness of an 11-valent PCV in preventing radiologically proven pneumonia in young children. It is being conducted in 6 municipalities on the island of Bohol, the Philippines. The trial commenced in July 2000 and will last until 2005, with a decade of preparatory work.

In addition to the main endpoint, the trial will answer several other research questions such as overall Pnc disease burden, cost-effectiveness of PCV, herd immunity effect, vaccine type invasive disease, immunogenicity and safety of PCV, and the vaccine impact on the nasopharyngeal carriage of pneumococci.

Pneumonia was chosen as the primary endpoint diagnosis because of its importance as the major global public health disease burden in children under five years old. The Philippines was chosen as the study site because of the availability of data arising from long-term baseline studies on ARI case management and on the causes of pneumonia, sepsis and meningitis. The island of Bohol was chosen because of its infrastructure supporting the trial and the research friendly environment, both on professional and political level. This study is so far the only Phase III study being planned with any Pnc vaccine to take place in Asia. It is carried under the multiparty international co-operation by the ARIVAC consortium, which includes Finland, France, the Philippines, the United Kingdom, Australia, and the United States.

Studies of this scope and size tend to be complex, loaded with numerous research questions and expensive; there are many ethical issues raised during the course of the work. The main ethical points which the trial team is or has been dealing with are the process of informed consent, the availability of care during the trial, the availability of the product after the trial is over, the long term safety follow-up of the trial subjects, and finally the sponsor's responsibility for securing funding.

## **The process of informed consent**

Informed consent (IC) is a PROCESS by which a subject voluntarily confirms his or her willingness to participate in a trial or research after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. IC is documented by means of a written, signed and dated informed consent form.

The practical dilemma with informed consent is how to give the vast amount of new information needed for the parents and the extended family to fully understand what their child isare getting involved in when becoming a trial subject. In the ARIAC consortium, we see this informing as a process evolving over a long period of time rather than just the face to face contact with the enrolling physician and the parental signing of their consent. The process starts with educational posters put up in the community on pneumonia and vaccine preventable diseases, and continues in the well baby clinic meetings where the trial is being discussed. A leaflet is given to parents, then a study nurse pays a home visit to discuss the trial details with all those family members who need to know, and are involved in making decisions for the baby, which in this Asian setting often includes the grandmother and father. Only then the final discussion during the enrolment and signing of the consent form will follow. Despite this extensive process, not all parents fully understand and/or remember. We have evaluated the outcome of the process in focus group discussions;it is evident that the concept of randomisation and placebo are the most difficult ones to grasp.

It is most important to provide the opportunity to ask questions, and discuss in prenatal clinics the trial brochure, and information sheet. Only through repeated questions and answers do the participants truly understand what they are getting into. These provisions are put in place so that all relevant information is available for the parents to make a fully informed decision. We also ensure that there is opportunity for prospective participants to ask questions and discuss concerns with a knowledgeable research team member, one to two weeks prior to the first study visit or during a postpartum visit. And most importantly, to allow time to discuss the information sheet with significant others. This process is put in place in order to create an atmosphere allowing requests for additional information.

The international Data Safety Monitoring Committee, concerned that the process was too long and the information sheets too complicated requested for Informed Consent quality checks. In 2001, the IC process was therefore evaluated through external interviews with consented (N=536) and non-consented (N=130) mothers. These interviews showed that few mothers understood that placebo does not provide protection. Most mothers could not have decided on participation prior to discussion, and that most mothers sought advice from family members or neighbours prior to consenting, a clear indication for the need to involve community participation and information.

### **The availability of care during the trial**

During the clinical trial the ARIVAC patients receive free physician's attention, free diagnostic tests (blood culture, cerebrospinal fluid culture CSF, white blood cell count, oxymeter), free chest radiograms and free access to oxygen, and antimicrobials, but only if they attend the Bohol Regional Hospital or the 3 private hospitals in charge of case evaluation for pneumonia, sepsis, and meningitis.

To avoid discrimination and to support unforced decision to participate in the trial, chest radiograms, blood and CSF culture, clinical chemistry tests and basic antimicrobials are provided for all the children <5 years of age admitted to the 4 collaborating hospitals for the trial endpoint diseases (i.e. pneumonia, sepsis, meningitis) and living in the 6 trial municipalities regardless of their participation in the trial. One might argue that this makes the trial more expensive, but the availability of care to all children from the trial area has been deemed ethically a more just solution than discriminating on the basis of trial enrolment.

This decision was made in response to criticism that parents were not truly given a free choice to participate.

### **The availability of the product after the trial is over**

In January 2001, after less than a year of an intensive fact-finding and consultation, the manufacturer decided to stop the clinical development of the study vaccine (11PCV). The reason was that 11PCV was shown to be very immunogenic when given with the conventional diphtheria whole cellular pertussis vaccine, but did not perform nearly as well when given with acellular pertussis vaccine.

In the light of the estimated risk of possibly not succeeding in the licensure of the product should the FDA requirements for immunogenic equivalence in comparison to the presently licensed 7-valent PCV-the manufacturer in January 2002 decided not to pursue the commercialization of the product. Immediately the availability of the product after the trial would be over became a major concern to the trial team. This led to extensive consultative process with the Ethical Review Board in Manila, the provincial and municipal health officers, the Ministry of Health, and the Data Safety Monitoring Board. The ARIVAC consortium for its part agreed that the trial should continue as its main aim was to find answers to relevant public health questions (vaccine effectiveness in true field conditions, burden of pneumococcal disease, cost effectiveness, herd immunity) rather than to be a pivotal licensure study. All research questions were still valid, as this is the only PCV trial in Asia, where Pnc disease burden information is very much needed and to aid in the decision making on PCV implementation into national programmes.

When the community advice was sought by the consortium, the major reason why the local municipal health officers decided that the trial should be allowed to continue

was the immediate benefits brought to the community, i.e. steady availability of the EPI and study vaccines and treatment during hospitalisation.

Two ethical issues arose from this event. First, what and how to inform the ARIVAC trial participants, trial staff and the community of the manufacturer's decision? The informed consent was changed and a question answer sheet developed in order to standardise the messages given by the study nurses and physicians to the community on this new development. In addition, the intention was to publish a news piece on recent developments in the Bohol Bulletin, but this initiative was given up in fear of media possibly misunderstanding the course of events and their rationale. Second, what product would the sponsor (the ARIVAC consortium) provide to the participants and community after the trial is over ? The negotiation process to resolve this issue has started. However, in my opinion, addressing this site specific issue should not deviate the scientific and public health community away from initiating the long term decision making process via feasibility, disease burden and cost effectiveness studies along with the phase III studies, so that by the time the effectiveness data of the product is available, the decision makers, funders and donor community are better prepared to implement the new product in national programs, provided effectiveness has been proven.

Another question on the availability of the product after the trial is over is whether the community as a whole should be given this benefit. How does one define the community? Is it only those municipalities which participated in the trial, is it the whole island, region or possibly the nation? From the point of view of the funders of the study, requests of this magnitude may be economically hard to come up with, and may in long run be counterproductive. The ARIVAC consortium has started negotiations over this issue , but nothing definite has as yet been decided.

### **Long term safety surveillance**

Once the trial is over, there are two ways of dealing with the placebo group: one can decide not to give them any further extra benefit in the form of the study vaccine or its equivalent or one can decide to give them this benefit. Those who argue for the benefit want to believe that the vaccine is safe also in long term and see no scientific or ethical reason to extend the long-term follow up time. Those who are increasingly weary of long term non-specific effects of any vaccine are strongly against treating the placebo group, and advice following up this group to rule out any deleterious effects. For them, it is unscientific, unethical and unjust to give the placebo group the study vaccine. Moreover, most studies do not have the power to look at rare adverse events. In statistical terms, the power calculations demonstrate that in order to detect a two-fold increase in any adverse event from 5 to 10% incidence , 1000 study subjects are needed. An increase from 1 to 2 % can be observed with 5000 trial subjects. And as rare event as 0.1-increasing to 0.2 % will explode the sample size to 50 000, a size of a trial very few of researchers and funders can afford..

The ARIVAC consortium is not strongly for treating the placebo group also from the epidemiologic point of view that by the age of 2 years, most study children have passed the riskiest age for Pnc disease. A dose of PCV would thus not provide so much preventive benefit that it would be justified. Another question is how the long term safety follow up should be arranged by the study team provided the trial as such no longer exists and the trial staff and enhanced active surveillance usually cannot be supported by the local health care infrastructures.

If the product is licensed and thus enters into phase IV, it is the national AEFI surveillance system and manufacturers whose responsibility safety surveillance falls under . It becomes a different issue if the product is not brought to the markets. Clinical development cost is already very high- If we want to add the burden of extended safety follow up to the manufacturers, it could be counterproductive in the long run.

### **Sponsor's responsibility for secure funding**

In the case of this phase III trial, the ARIVAC consortium which consists of different academic institutions and the manufacturer jointly sponsors the study . According to the ICH guidelines, the sponsor takes responsibility of the initiative, monitoring and/or financing of a clinical trial. Thus, it is the sponsor's responsibility to secure the funding basis of the trial, preferably already prior to the start of the trial. If the sponsor is the manufacturer alone, often times there is enough venture capital to provide the funding basis. However, if the sponsor is from the public domain, and relies on funding agencies, the situation becomes more complex. This is the case with the ARIVAC study where EU DG Research is the main funder . The EU funding contracts usually allow only 2-3 year funding periods . These funding periods are in striking contrast to the mean durations of clinical trials. Discovery to development alone represents an average of 7 to 13 years. Baseline studies, finding the facts and phase I and II trials were started in 1990. The ARIVAC consortium has had 5 separate EU contracts in place. The amount of insecurity arising from the evaluation and negotiations in the middle of an ongoing trial is in striking contrast to the general requirements of planning ahead and the good conduct of clinical trials. The present EU funding reality raises the last ethical dilemma the ARIVAC consortium has had to deal with: is it ethical even to start a study with a contract from a public domain funder if there is no guarantee for further funds to take the trial to its planned end?

### **CONCLUSIONS**

RCT is the gold standard to test vaccine efficacy and effectiveness on ethically sound ground. In order to successfully undertake clinical trials, and especially in developing countries, a 3 dimension interphase, i.e. public – private - regulatory is essential in most advanced vaccine development.

From the nature of any product development it follows that the developmental work will take more time, will be increasingly more costly, and professionally more demanding if we want to maintain high ethical standards. Also, if we want to keep clinical product development in the public domain and maintain independence from private industry, we need to practice creative thinking. .

**Dr. Nadia TORNIEPORTH, MD, DTM&H**

Director, Clinical Development,  
GlaxoSmithKline Biologicals,  
Rixensart, Belgium



# **Ethical aspects of conducting clinical trials in developing countries: Experiences of GlaxoSmithKline (GSK).**

---

---

**Nadia TORNIEPORTH**

This presentation will highlight some of my practical experiences while conducting clinical trials in developing countries. GSK has ongoing active collaborative research programs into diseases of the developing world. Personally, I have been involved in research concerning the development of vaccines against malaria, tuberculosis and pneumococcal infections. Although I am not here to speak on behalf of industry, I would like to share with you the specific product development perspective that I have gained during this period.

It should be strongly emphasised that any research, regardless of locale, should always be conducted according to recognised ethical standards. Clinical research must be conducted according to principles of the International Conference on Harmonisation Good Clinical Practice (ICH-GCP), and national and international guidelines to safeguard the rights and safety of trial participants worldwide. The research should take into account local laws and regulations as well as ethical and cultural practices.

Clinical research in developing countries is conducted for a number of different reasons, foremost to respond to local health needs of disease endemic countries. It can also be translational research to test the effectiveness or implementability of interventions, to respond to national regulatory requirements, which may require clinical trial experience in different ethnic groups or in a number of different health care settings.

Whatever the reason, conducting clinical trials in developing countries is never an easy or inexpensive option. The lack of infrastructure and complex ethical and regulatory requirements can make conducting clinical research in developing countries a formidable challenge. Therefore, it is necessary to pay particular attention to the local context in which research will take place, and obtain guidance from local experts, committees and institutions as necessary. This must be done as part of an interactive learning experience if the research is to be implemented successfully.

## **The local context**

In the developing world in particular, local experts, community leaders and ethics committees have an important role in advising on the social, economic and cultural context in which the research will be carried out. This includes guidance on the appropriate reimbursement to be offered to trial participants. Independent ethics

committees should play an active part in the review and oversight of the informed consent process that may include consultations at several community levels but should ultimately result in informed individual consent.

This can represent quite a challenge to sponsors and researchers who need to comply with regulatory requirements according to “Western standards” in complex local settings, for instance in poorly educated or illiterate populations.

The social, economic and cultural context in the host community must therefore be considered. Guidance must be sought and dialogue established with the lay and scientific community, the ethical review committees, governmental and non-governmental organisations in a continuous and mutual learning process.

### **The role of the Ethical Review Committee (ERC)**

Appropriately constituted and competent ethics committees do not always exist where disease burden is highest. Independent international co-operative projects dedicated to developing best practices in the ethical review of biomedical research by strengthening regional and in-country capacity are welcomed by industry as they are essential in ensuring competent guidance by local ethics committees.

The ethical review committee should be a competent and independent review board with knowledge of the local context and would ideally even conduct site visits to oversee procedures. The reality can look different. A worldwide survey has identified frequently encountered issues that would affect the quality of ethical review. These include:

- The inadequate representation of the scientific and lay communities on ethical review committees in particular with respect to their composition by gender or religion.
- Without standard operating procedures there may be a lack of transparency.
- Conflict of interest or interdependence between the members of the ethics committee may be a problem. If you are familiar with the importance of authority, for instance in some African countries, and see that some ethics committees have the head of the hospital on the board but also his subordinates, then you can understand what issues may arise from this.
- Inadequate documentation is the most frequent problem we as sponsors have to deal with.
- The lack of resources, time, and space. This frequently results in inadequate ethics committee monitoring of study conduct and follow-up systems.
- The inadequate training of ERC members: new members are expected to learn on the job and often receive little or no specific training on important issues.

In addition the increasing complexity of collaborative research involving multiple institutions and sponsors can challenge the ethical review system. Currently, this

represents a complex process of multiple reviews, which should be facilitated by dialogue between external and host country ERCs. In a project we recently initiated between partners in Africa, the US and Europe, multiple rounds of ethical review took several months to complete. While the requirements and decision making of the local ERCs were relatively clear, it took a major educational effort to familiarise external institutional review boards ("IRBs") with the ethical aspects of conducting clinical trials in developing countries. This process really needs to be simplified.

### **Capacity building for ethical review**

Effective capacity building should be measured by its sustainability and as such should be developed in close partnership with the various stakeholders in any given research program. Capacity building for ethical review must not only focus on strengthening the local ethics committee but also must encourage and foster the interactive and mutual learning process between developed and developing countries.

Standard operating procedures (SOP) for ethics committees are available, and should be used to ensure harmonisation of ethical review procedures. Harmonisation can save time with respect to much needed research to reduce disease burden. Currently, quality assurance systems, auditing and accreditation of ERCs are being developed and cautiously put in place to ensure transparency. However, responsibilities and the authority of this quality assurance need to be defined.

#### *How can the sponsor ensure adequate ethical review?*

CIOMS clearly indicates the increased responsibility of the sponsor to build capacity in ethical review. However, in order to maintain the independence of ERCs, the mechanisms to do so may actually be limited, as there is limited interaction between the sponsor and the ERC.

Providing dedicated funding for local governments as some have suggested may not necessarily be the ideal solution. So what mechanisms are available if quality ethical review is to be established in developing countries? ERC training needs may not be communicated to the sponsors - should the assessment of ERC performance be done through external review?

In one situation we encountered recently, we solved this problem by asking the chairman of the independent data safety monitoring board to talk to the ERC to assess possible training needs. So in my view, the initiatives mentioned by the *Strategic Initiative for Developing Capacity for Ethical Review* (SIDCER - WHO) are extremely important and welcomed to support, strengthen and allow independent review and assessment of ERCs. Independent initiatives & training to strengthen ethical review capacity should therefore be encouraged and supported.

## **Capacity building for clinical research**

Training of local investigators and the strengthening of local expertise and infrastructure for the conduct of clinical trials according to ICH Good Clinical Practice (GCP) and regulatory requirements are a pre-requisite for clinical research in developing countries and are an important capacity building measure.

Clinical research capability determines the quality and ultimately the regulatory acceptance of data, so where the capability does not exist, targeted development should be implemented to ensure that these standards are put in place. However, active participation of the local community and the local government are paramount to ensure that such measures will remain sustainable. It is extremely important for local research institutions to establish career development plans for their staff so that qualified staff can be retained and the learning is not lost.

### **Informed consent:**

In compliance with ICH GCP, legal and regulatory requirements, informed consent must be based on an understanding of the society in which the study takes place but should adhere to universal principles.

We should remember to consider the very specific local requirements within a broader framework. The ethical issues surrounding the use of appropriate language, community versus individual consent, as well as illiteracy, oral consent and the impartial witness should all be considered. Moreover, any reimbursement provided must be consistent with the principle of voluntary consent.

The community itself can teach us valuable lessons. The informed consent process will – in some cultures – need to involve the larger community, local village chiefs, family members... Sufficient time and flexibility should be built into the process to accommodate the local customs. However, this can only complement and never replace individual informed consent.

Legal requirements can lead to a lengthy and complicated informed consent document difficult to comprehend for any person. Local ethics committees have repeatedly complained that value of and understanding by study populations may be limited, which led to the other extreme: the request for a one page informed consent, simplifying the language, taking out what the population might not have understood anyway.

Given the real difficulties to ensure informed consent I do agree that all attempts should be made to simplify the language in the informed consent - without however applying a double standard. All relevant elements according to ICH-GCP should be provided to study participants in their information. It is our challenge to find the appropriate wording to communicate this information. When dealing with illiterate

populations, oral consent or thumb printed consent in the presence of an impartial witness may be obtained. In practice there may be issues: how impartial is the impartial witness, if he is reimbursed for the time spent supporting the study on the time spent on the study? And can he really assess whether the information was understood?

But paramount for any clinical research, any recompense provided must be consistent with the principle of voluntary consent. Again, this raises questions – does the provision of free medical care for a participant during a clinical trial constitute appropriate clinical care? In areas where medical supplies are scarce this may be an established practice, approved by the local ERC and yet constitute a strong incentive for participation. There is no definitive answer, we must always challenge established practices and confer with the local ethics committee on a case by case basis while applying international and national regulatory and legislative requirements and following the research methodologies outlined in ICH-GCP guidelines.

### **The standard of care**

This applies similarly to decisions taken regarding standard of care provided to trial participants that need to be aligned with sustainable health care practice in the respective country and must not constitute undue inducement for participation.

The design of a clinical trial protocol is not necessarily an issue specific to developing countries. Scientific considerations have to be taken into account irrespective of where a study will be performed. However, the standard of care in a particular context is the subject of much debate today, in particular since the Declaration of Helsinki was last revised. I think we can all agree that sound scientific ethical and clinical judgement must guide the design of clinical trials. Moreover, clinical trials *“cannot be justified ethically unless capable of producing scientifically reliable results”* (CIOMS 2002).

Difficulties are often encountered with respect to the understanding of concepts such as randomisation and placebo. Regulatory agencies such as the European Committee for Proprietary Medicinal Products (CPMP) and the U.S. Food and Drug Administration and the scientific community maintain that randomised controlled trials remain the gold standard when demonstrating the efficacy and tolerability of a new product.

Randomised, controlled trials are designed to generate scientifically reliable results while avoiding a distribution bias of risks/benefits:

*“The judicious use of placebo remains essential to demonstrate the value of new medicinal products”* (CPMP 2001)

The choice of active control or placebo/escape treatment as comparator will depend principally on the level of risk to participants, and whether the design will yield scientifically reliable results. Any choice of comparator, especially within the context of developing countries must be determined in close consultation with local experts and health authorities and ideally be aligned with locally sustainable health care practice.

### **Post trial considerations**

All post-trial considerations must be determined before a study takes place. Early dialogue with representatives of the scientific and lay communities as well as local governments will be essential to manage expectations as to possible trial outcome and the provision of any post-trial medications. Currently, however, deliberations may take more than a year. A transparent and more efficient process must be established. We must keep in mind that it is a long road to product licensure – the fact that one trial shows a research intervention to have merit does not necessarily mean that the specific intervention has been proven successful.

The shared responsibilities must be defined upfront. A reasonable balance must be found which does not jeopardise clinical research in developing countries but shows a positive way forward – exemplified by an increasing number of public-private partnerships for the development of products against developing world diseases.

### **Conclusions and Recommendations**

Clinical research in developing countries requires special consideration of ethical aspects to safeguard the rights and safety of research participants. I believe that strengthening ethical review capacity is critical in this process. I further strongly believe that dialogue and the sharing of experiences between stakeholders should be encouraged to ensure research priorities in the developing world are addressed.

## ***Discussion***

---

---



## Summary of the Discussion \*

---

The Round Table discussion was characterised by a dynamic exchange of ideas, which sought to put forward, some of the more complicated issues surrounding the ethics of clinical trials in developing countries. Inspired by the morning and afternoon panel, the discussion focused on issues ranging from negotiation and moral pluralism, to capacity building and placebo control trials. The essential themes evoked during these discussions are presented below.

### **Cultural relativism and the need for negotiation**

When conducting biomedical research in developing countries, the question of differing values was raised in light of cultural relativism. Are there universal values in research or does research need to be adapted to the existing value systems and cultures locally? This question needs to be addressed both from the point of view of the researchers and the local community. Moreover, issues such as the impact of research on culture lead to other lines of thought: what possibility is there for cultures to be enriched by Science? And on the other hand, in what way could Science benefit from local culture?

In order to better address these issues, a need for sociological and cultural studies was expressed in order to examine the relationship between research and the local community. This would in fact introduce direct input from the developing countries into the debate and expose the disparities between international standards and local realities. We must, however, also note that there is very little empirical evidence to show the existence of cultural differences in a medical research context. To support this argument, a study conducted on South East Asian countries showed that more differences existed between these countries than between Asia and the West.

The differing interpretations and perceptions, within the context of cultural relativism, of concepts and beliefs render negotiation an essential tool in the interaction between the researchers and the community. As we cannot proceed only on the basis of established guidelines, input from cultural anthropologists would be extremely beneficial. Researchers must familiarise themselves with the culture they will be working with: discuss with people, understand the traditions, etc. This also includes confrontation and dilemma, nuanced with the intricacies of different points of view. There are so many different ways of meeting different groups or communities, and there is a need to use all the levels of encounter: confrontation, sharing stories, histories and really establishing a living community or conduct with the societies. These differences in values, as well as the '*capacity of cultures to resist to technoscience*' are the main arguments for the need for negotiation.

---

\* The summary of the discussion has been prepared by Katerina Sukovski, Trainee within the Secretariat of the European Group on Ethics in Science and New Technologies.

The emphasis must be on the negotiation process between all concerned parties. In a conference room, the framework for that process can be set up, establishing the means for capacity building in developing countries and for the acquisition of value knowledge. In this respect, negotiation will be a continual process, which must be left to a certain extent to researchers and the developing countries (government, local researchers and the community). Moreover, this means that all actors will come around the table with a set of values and not consider universal values. However, although an interesting venue to explore, while each actor tries to promote his/her own values and trying to come to an agreement, the obstacle becomes the balance of power between all these actors. This process could help solve such questions as for example, what would be considered the conditions for a fair negotiation process between the funding agency and a developing country in which a trial is supposed to take place?

Any negotiation that is developed is going to go beyond anything that is agreed upon in a conference room. One must keep in mind that requiring scientists to conduct research according to standards established by Northern countries may be a quick and easy political strategy, but this will not be effective for global health for a number of reasons. First, it will exclude developing countries from access to this research, a benefit in and of itself. Secondly, it will promote 'unethical' behaviour, where researchers will shop around for an ethical committee, which will approve their protocols. This is well-documented common practice in some places. And finally, it assumes that guidelines established by Northern countries are always relevant, which is often not necessarily the case. These are reasons that negotiation is necessary. However, there are many critical questions with respect to negotiation, which need to be addressed. How will this negotiation process meet the standards of procedural justice?

And finally, the issue of what has been referred to as cultural imperialism needs to be addressed in this process. Emphasis must be put on the process, based in North-South dialogue, and not a Northern top-down approach. One must consider what are the ethical issues and what are the needs of the population and their point of view. This dialogue must not degrade into a form of paternalism. Often, researchers from developing countries, and specifically, local researchers feel that they are passive recipients of protocols, which is most often the case. They receive finalised protocols from Europe, which are submitted to them for administrative approval. They feel that they are cosmetic partners. This concern needs to be addressed within the context of the negotiation process.

Therefore, the importance of cultural relativism may not simply lie in identifying cultural differences, but in interpreting these differences. Perhaps through their interpretation, these differences will diminish, allowing space for partnership and participation through common values and common rules.

## **Informed consent**

The ethical aspects of 'informed consent' can be considered from the point of view of the individual, as well as that of the community. Again here, the importance of the role of the community can be seen. First, considerations of how 'informed' consent actually is with respect to language and cultural barriers must be taken into account. If there is no word for 'gene' or 'informed consent' in the local language, how can one explain the process? It must be kept in mind that issues surrounding the understanding of informed consent are not proper to developing countries, and are often associated with studies done in industrialised countries as well. However, it has been suggested that given the relationship between North and South, the lack of understanding with respect to scientific research and principles of informed consent may be exploited in developing countries, at the expense of local communities. What safeguards, if any, need to be put in place?

Moreover, when personal consent is requested from one member in one tribe or in one village, we're putting forth a cultural question: we're asking if this person has the authority to actually answer, on their behalf and that of the community. The relationships between members of the community, as well as differing conceptions of autonomy therefore require a better understanding of the local context so that the principles underlying informed consent are respected. Moreover, given the greater role of the community, we cannot ignore the possibility of segregation or discrimination that may exist within the community between the participants and the rest of the community? What criteria must be established in order to evaluate this positive or negative community influence?

In these negotiations, with respect to the community, could interested consent play a greater role than informed consent? Considering the expected advantages, could this concept of interested consent be useful? Considering the socio-economic divide, to what extent does inducement play a role in informed consent? What impact would the promise of financial gain or improved health care have on the participants and the community as a whole? Is inducement actually wrong and is it equally wrong for all kinds of trials? We pay doctors to do trials, and research methodologists to design them. Is inducement therefore always wrong?

Given the context, could more standards or monitoring be required in order to ensure that the requirements for informed consent are upheld? The danger of introducing a double-standard raises concern when considering extensive monitoring of informed consent procedures as a requirement in developing country research, when not routinely done in Northern settings. Currently, research ethics committees review protocols, but they do not monitor the research, don't do site visits, don't review consent. If this is to be made a requirement, it should be universal. However, the infrastructure and resources required to do this properly are almost impossible to achieve. This may be a good idea in certain types of trials, but impossible as a universal rule, as it would require an enormous amount of resources. In the following section we will take a closer look at the challenges and obstacles facing local ethical

review committees, and therefore better understand the difficulty in implementing such requirements.

### **Ethical Review Committees (ERC)**

The nature and role of local Ethical Review Committees evoked much discussion. First the role of the local ERC is to evaluate ethical considerations with respect to the study and its impact in the community.

Unfortunately, due to the limited resources available to implement and maintain local ERCs in developing countries, these bodies are often non-existent or limited in their capacity to effectively carry out evaluations. It is in this light that the question with respect to the competence of local ERC was evoked. Often, clinical trials are given great importance whereas other issues such as control by health authorities, adequate study design, and its interpretation in practises are inadequately discussed.

However, there was a suggestion put forward on the possibility of having a type of DSMB (Data and Safety Monitoring Board) extended to more than data and safety, which would deal with ethical problems and post trial considerations. This committee could be composed of people from the North and South, including lay persons and ethicists.

Many low-income countries do not have the resources for ethical considerations and community participation. If these systems are not in place, what needs to be done in order to conduct these trials? Do we wait for a system to be put in place before initiating any trials? Or do we negotiate a working model with all stakeholders involved?

The central role of ERC in clinical research in developing countries lies specifically in the nature of their function. As an intermediary between the scientific and local community with respect to ethical concerns, the increasing number of guidelines requiring ethical review have accorded more and more importance to ERCs. It is for these reasons that the strengthening of ethical review has become an important aspect of capacity building, the subject of the following section.

### **Capacity Building: who can build capacity? what kind of capacity is needed?**

The question of 'who can build capacity?' is closely linked to that of 'who is funding capacity building?'. Many debates during the discussion centred on the ethics of who should be involved in this process.

It was suggested that the sponsoring agency should be responsible, there is therefore a need to define the 'sponsoring agency'. If defined by the private sector, such as the pharmaceutical industry, is it ethically sound for industry to be funding

capacity building and ethics in developing countries? On the other hand, funds for capacity building are scarce, and more than just workshops and conferences are needed, such as the ability to maintain infrastructure in the long term. Therefore, if the public sector is going to take on the responsibility of 'sponsoring', it needs to clearly identify and define its level of participation and commitment.

The industry perspective maintains that it provides a good partner for capacity building, highlighting that there is a lot of skill there. The question is rather what capacity is being built? In addition to the need to work jointly, the point was raised that often, once the training is completed, the individuals often go to work in Western countries (i.e. USA), and that this too is a form of capacity building which is continually being depleted. In what way can the training and skills targeting developing countries be maintained in the long term?

Moreover, there are many levels to capacity building in research with respect to developing countries. Although fundamentally due to the socio-economic divide, the gap between developed and developing countries in scientific research and health care standards is growing exponentially in the face of diseases such as HIV/AIDS, which have exploded on the African continent. Before discussing these levels, we must first illustrate the context in which this capacity is necessary. For this, the case of HIV/AIDS in Africa can best demonstrate the complete market mismatch between the needs of developing countries and the economic reality of vaccine development. The pharmaceutical industry has had an important role in the development and research of vaccines with respect to HIV/AIDS. If, however, the industry is demanded to make vaccines available at their own cost in all the countries where the clinical trials take place, the pharmaceutical industry will withdraw from these markets. However, vaccines are only made available to the poorest countries 15 to 20 years after their introduction to the West. What measures need to be taken to ensure that the few pharmaceutical companies that are investing in AIDS vaccines or others do not withdraw from the markets because the sets of rules and regulations have become too strict? We should not forget that we are working in a globalised economy, and as such, take into account the multiple levels and degrees involved.

Moreover, when discussing developing countries, there is a tendency to mainly discuss Africa. However, countries in transition are also developing countries: low brut national product (less than \$5000), very small public funds for research, less than 1% of this sum. The very strong influence of the manufacturers on research-whether the pharmaceutical industry, medical devices or equipment- is mainly due to the fact that they are the main or sometimes the only source of funding.

This creates a conflict of interest on the side of researchers, because the main source of their research funding comes from the manufacturers. What is more, the competence and the power of ERCs, if they exist at all, are often unsatisfactory, and the implementation of the legislation is insufficient.

Therefore, when discussing capacity building, we should consider the government (legislation), local researchers as well as the local community. It should be noted that some of the national guidelines, such as in South Africa, mention the explicit need for capacity building and what they refer to as community consultation. This includes the involvement of the local community health workers, a stress on local education and training, and the need for the presence of local independent witnesses or an ombudsperson, in specific clinical situations. This, however, raises questions as to what actually is happening on the ground? Who is documenting this? Who is recording this? What verification, what procedural mechanisms are in place to document all the negotiation that is happening?

The capacity needs of local researchers, although evoked, were discussed to a lesser extent. With respect to research protocols, there has been a tendency to involve local researchers in only Phase III and IV trials. This exclusion from Phase I and II trials needs to be addressed, as well as the need to ensure that local researchers participate in all stages of the clinical trial process. This is necessary not only from a capacity building perspective, but from an ethical point of view which stresses partnership.

While discussing the needs of developing countries, the type of research needs of the population of the country must also be considered. If we look at the global pharmaceutical research budget, tropical diseases have a small insignificant share of that budget. We also know that diseases of developing countries are not given enough attention. This should be a major concern. No ethical guidelines will change this. For instance, Sweden has a traditional window for research co-operation, which includes budgets, capacity building, trying to promote building domestic capacity in research (i.e. tropical diseases). More attention must therefore be accorded to developing co-operation with respect to these needs.

In discussing the issue of ethics of research in developing countries, attention must be given to the definition of priorities, and the place of capacity building in this discussion. Too often the advantages to industrialised countries are stressed, rather than the interests of the developing country.

### **Standard of Care: is first class health care undue inducement?**

Although, all would agree that it is extremely important to insist upon well-being when providing health care and referring to health care standards, the ethical concerns stemming from the impact of this standard of care with respect to the clinical trials has sparked debate. Some would argue that when there is research between the North and the South in a partnership situation, then the standard used in the North should be used in the South. Some would argue that this is not a decision that should be made by Northern researchers or ethicists, but by the developing country.

Still others would argue that this level of standard of care would impact on the trial results, and constitute undue inducement. In resource poor settings, there can be many forms of inducement. For example, during an HIV vaccine trial in Bangkok, participants received 10 Euro for transportation. This is a very small amount, and can not be considered inducement, although the transportation cost was actually 10% of that amount. The argument made was that this induced drug users in the study, but in reality, much more is needed to maintain a drug habit. In fact, the real inducement lied in the entitlement to health care clinics. It appears that the main motivation for participants was the promise of being taken care of if they got sick, which was perceived as something much greater than its actual cost.

Although the debate with respect to the standard of care continues, the danger of establishing a double standard remains in the background. Would it be a form of paternalism to enforce such standards of care on research coming from the North when there same standards are not applied to local researchers conducting clinical trials?

There is, however, general agreement that the health needs of local community should be taken into account. One would hope that in developed countries there is an awareness of the health needs of developing countries and the desire to develop these needs.

The standard of care is a particularly difficult issue in that it involves not only the scientific community and the advancement of Science, but also the health care and health needs of the community. In this context, the obvious benefits of improved standards of health care in certain trial communities can quickly become the topic of political debate when national health care standards are insufficient to meet the health needs of the general population. Given the discrepancy between the standard of care between the North and the South, there were questions raised during the discussion as to the obligations and the nature of these obligations to improve global health in general.

And finally, the cost of such improved standards of care can not be neglected. Given that current conditions in developing countries offer obvious financial advantages in the research and development of vaccines, would standards imposing universal standards of care be a deterrent to further research and development?

### **Placebo Control Trials: best available or best-proven treatment?**

The ethical concerns raised by the use of placebo control trials emanate from the fact that placebo control trials are used in order to establish standard treatment. However, given the controversy surrounding the Helsinki Declaration revisions the debate over best proven and best available treatment remains at the core of clinical trial design in developing countries, where, for the most part, the best proven treatment is not

available to the population. The best illustration of this would be the HIV transmission trials done in Africa and Thailand.

The Clarification Note of the WMA<sup>6</sup> **Declaration of Helsinki** states: “*extreme care must be taken in making use of a placebo-controlled trial and that in general this methodology should only be used in the absence of the existing proven therapy*”.

This *existing proven therapy* may not however be available to the populations in need; can placebo trials then be justified? Very often, the placebo control trials done in these countries are very difficult to defend, such as placebo controls on schizophrenic or major depression patients. It is clear from an ethical point of view that the local context in terms of treatment availability and access to health care has an important place in this debate.

Moreover, the requirements of the American FDA are often cited as reasons for the continuation of this practise, because it does not permit any new drug that does not have such a control. The role of regulatory bodies with respect to drug licensing needs to be elucidated and also taken into account in this debate.

When discussing developing countries we should keep in mind that underdevelopment has several levels. Placebo control trials are a scientific tool used in research, but it is the reality of the impact of this research on trial communities, as well as the relevance of these trials to the local community which are taken into account when discussing ethical concerns. The debate did however echo general agreement that treatment availability at a local or regional level should be taken into account.

## **Patent issues**

Patent issues, although highly technical and legal in nature, have made their way into the ethical debate with respect to their place in prior agreements, and as obstacles to access to treatment, and the development of new treatment in developing countries.

The International AIDS Vaccine Initiative (IAVI) Price Agreements were put in place under certain conditions for the co-funding of HIV vaccine development. If a vaccine were found to be effective, the company would agree to make it available to developing countries at production costs plus a 10% profit. If IAVI disagrees with the estimate, it can then ask another company to produce the vaccine. IAVI claimed to have solved the problem of intellectual property rights, the following two examples will show that this is in fact not the case.

IAVI was set up to try to get passed the standard kind of paradigm: that something is licensed to Europe or the US, and after one or more decades it might become available in developing countries, and for HIV vaccines, this is unacceptable. Hence,

---

<sup>6</sup> World Medical Association.

there are attempts to change that paradigm, by working directly in developing countries. These attempts are however facing many obstacles.

In the first case, in IAVI vs. Kenya, the UK researchers submitted a patent application without involving the Kenyan researchers. When faced with the anger and frustration of the Kenyan researchers, IAVI was ill equipped to deal with the situation. Eventually, IAVI recognised that the memorandum of understanding was inadequate and apparently now there is a new agreement in place that does involve intellectual property rights, but the content is still unknown. This highlights the complexity of prior agreements and the importance of property rights in research.

In the second case, IAVI and a North Carolina (NC) company, there was a dispute about the ownership of the patent rights of a vaccine candidate, and it is not certain that the NC company had the patent right over this vaccine. If the company that develops the vaccine does not have the intellectual property rights it would have to pay a license fee, which would become part of the 'production costs', again showing the possible deficiency of this type of agreement.

However, with respect to patents, it is important to keep in mind who owns patents - and someone will ultimately own a patent -and it may not be clear until years of litigation and counter claims who really owns the various patents. It's not an ethical issue of whether someone owns a patent. The issue is what is done with the patent and whether the development of a vaccine is allowed in the most cost-effective way for these countries or whether the patent is used to block that development?

The intellectual property issues are complex, but it is thought that the eventual outcome should be that there is no profiteering or just simple obstructiveness that will block the availability of the vaccines in the countries where they are most acutely needed. However, looking at how patents are going to be controlled and how to prevent them from being a block to distribution is not a substitute for looking at ethical issues within a trial, including benefits to participants.

### **Traditional medicine**

With respect to the cultural dimension, the role of traditional medicine was evoked in order to understand its impact on the ethical considerations discussed.

To what extent is traditional medicine, including traditions stemming from Buddhism and Hinduism incorporated into education and ethics in these countries? Are there any contradictions in theory and in practice of these teachings?

In India, for example, when discussing bioethics, it is modern bioethics. There are no theologians except those based in Christianity. Bioethical teachings are mostly dominated by Western influence.

In Africa, traditional practices are transmitted from one generation to another, one family to another, based on non-referenced practises. For example, in the village they say that eating a certain form of bark is good for you. This, of course, is not published in a medical journal. In a given context, the importance of spirituality and its relationship to health through traditional medicine, is also considered an important aspect of treatment.

Issues with respect to forms of treatment were also discussed: Are there criteria to distinguish between traditional forms of treatment and the non-traditional forms of treatment? The referral to non-traditional implies that there is a different treatment model, and what is the hierarchy between these models? Can traditional forms of treatment actually be made subject to scientific investigations?

In India, there are five systems of traditional medicine, and there are more traditional medical practitioners than non-traditional practitioners. Where quality checks have been done, modern practises have not necessarily been shown to be superior to traditional practices. What is more, a number of cases have shown the equality if not the superiority of traditional medicine. Especially in cases involving chronic illness or illnesses related to ageing, traditional medicines are shown to be as effective with less or no side effects. Specific medicines used for ageing are now undergoing modern techniques of evaluation, to prove that traditional medicine has value.

It should be noted that traditional medicine is a community-based practise, and therefore has an important role in any medical practise and should be taken into account, not only with respect to clinical trials, but to capacity building as well.

## **Conclusion**

In general, the discussion provided many lines of thought and reflection with respect to ethical considerations in research in developing countries. The main themes, outlined here, have been summarised in order to provide a foundation for further thought and reflection in this area. The end comments of participants and panellists focused primarily on the need for practical solutions, and pragmatism. Although ethical principles are at the centre of these discussions, it is their transformation into policy that is most significant in the field, and for the participants of the clinical trials.

The role of International Guidelines were also evoked with respect to many of these issues, but the inconsistencies and divergence in these have often further complicated ethical discussions. Moreover, post-trial considerations must also not be neglected, as they also constitute a part of the clinical trial, and although mentioned, were not extensively discussed.

The general sentiment emerging from the discussion can be summarised as follows: there are many difficulties associated with working in development, the most important is that the intervention does not create more problems than those already existing, and secondly it generate a positive impact.

## ***Curriculum Vitae***

---

---



## Curriculum Vitae

# Søren HOLM

### **Professor University of Manchester & University of Oslo**

Søren Holm is Professor of Clinical Bioethics at the University of Manchester and Professor of Medical Ethics at the University of Oslo. He holds degrees in medicine, philosophy and health care ethics and works clinically as a doctor one day a week treating patients with ovarian cancer.

His doctoral thesis was concerned with the question whether American biomedical ethics could be transferred to Europe without modification.

He has written over 100 papers and several books on various issues in bioethics.



# Dr. Monica KONRAD

## Cambridge, United Kingdom

**Monica Konrad** is a medical anthropologist and active researcher in the life sciences. She has carried out field-based research projects since the early 1990s linked to the cultural and ethical implications of the new reproductive and genetic technologies.

She has an interdisciplinary training in the social sciences with degrees in politics, sociology and social anthropology and gained her Ph.D. from the London School of Economics & Political Science (1996). Her doctoral thesis addressed the subject of anonymous egg donation and the kinship of IVF transplantation cultures between British donors and recipients. She has held teaching and research posts at the University of Sussex, Goldsmiths College, University of London, and is currently Associate Fellow at the School of Advanced Study, University of London. Recent publications explore the interface between culture, biotechnology and bioethics in relation to predictive genetic testing technologies. (Konrad, M. (2002) 'Pre-symptomatic networks: tracking experts across medical science and the new genetics'. In C. Shore & S. Nugent (eds) *Elite Cultures: Anthropological Perspectives*, London: Routledge, pp.227-48).

Forthcoming publications in the journals *Anthropology & Medicine* and the *Journal of the Royal Anthropological Institute* explore the relationship between new diagnostic and prognostic knowledge in clinical genetics, and moralities of information disclosure at the familial level. Monica Konrad is currently researching transcultural medical ethics and comparative medical moralities relating to the new genetics, planning future research collaborations in this area, and developing new teaching materials addressing the 'anthropology of genetics'. She contributed a written submission to the UK Nuffield Council on Bioethics Consultation Paper informing the final Report (2002) on *The Ethics of Research Related to Healthcare in Developing Countries*. Memberships of professional bodies: International Network on Feminist Approaches to Bioethics; the British Association for Advancement of Science; Genetic Interest Group; Human Genetics Alert; British Fertility Society; London Forum for Arts in Health; Royal Anthropological Institute; Association of Social Anthropologists of the Commonwealth; European Association of Social Anthropologists; Anthropology in Action.



## Curriculum Vitae

---

# Reidar K. LIE

**M.D., Ph.D**

**University of Bergen, Norway**

Mag.art. (Philosophy), University of Bergen, 1982

M.D., University of Bergen 1983

Ph.D. (Philosophy), University of Minnesota, Minneapolis, 1987

Born November 26, 1954

## EDUCATION

University of Bergen, Mag.art. (Philosophy), September 1982.

University of Bergen, M.D. June 1983.

University of Minnesota, Minneapolis, Department of Philosophy. Ph.D. July 1987.

## PROFESSIONAL DEVELOPMENT

Assistant professor, Department of Medical Humanities, School of Medicine, East Carolina University, Greenville, North Carolina, 1987 - 1989

Director, Centre for Medical Ethics, University of Oslo 1989 - 1995

Professor of Medical Ethics, University of Oslo, 1992 - 1995

Professor of Philosophy, University of Bergen, 1995 -

Adjunct Professor, Thammasat University, Bangkok, Thailand, 2000-

## MAJOR FUNDED RESEARCH PROJECTS

- Director of a 5 year research and competence building project in Medical Ethics, funded by the Norwegian Research Council, 1989-1994. A total of 7 Ph.D. students were associated with this project, all of whom have successfully defended their dissertations. Funded by the Norwegian Research Council, US\$ 1,000,000
- ETHICA - Ethics and Health: An International and Comparative Arena. Core project is a collaboration between the University of Colombo, Sri Lanka and the University of Bergen, Norway in ethics and health policy. Funded from 1996-2006. Co-director. Funded from Norwegian Council for Higher Education's Programme for Development Research and Education, US\$ 500,000
- SEAHEN - South East Asian Health Ethics Network. Consultant on a WHO-SEARO region project with the aim of creating a network in the region as well as initiating research projects. Funded from 1997 - 1998 by World Health Organisation, South East Asian Regional Office, New Delhi, US\$ 200,000
- EUROPEAN ETHICS NETWORK - EU funded Socrates project with the aim of producing European textbooks in applied ethics as well as preparing a European Mastersprogram in ethics. Co-coordinator of the Bioethics part of this project. Funded from 1997 - 1999, by European Commission, Brussels US\$ 3,000 (Bergen part).

- EURO ELSAV - BIOMED project on ethical, legal and social issues in vaccine development, coordinated from Rome. Responsible for a sub-project on ethical issues in international collaborative vaccine trials within this general project. Funded from 1998 - 2000, by European Commission, Brussels. US\$ 60,000 (Bergen part)
- HUMAN RIGHTS, EQUITY AND HEALTH SECTOR REFORM. TDR/WHO funded project involving three countries, Bangladesh, Sri Lanka and Thailand. Funded 1998-1999. Funded by World Health Organization, Geneva, US\$100,000
- CTC-ETHICS - Ethical issues in clinical trial collaborations with developing countries. EU funded, 2000-2002. Director. Funded by European Commission, Brussels, US\$ 300,000
- EVIBASE. Ethical issues in evidence based medicine. EU funded project 2001-2002. Funded by European Commission, Brussels, US\$ 50,000

## SERVICE

### *International consultancies*

- Member of drafting group for UNAIDS Guidance Document on Ethics and HIV vaccine trials, 1999
- Member of UNAIDS team to assess plan for HIV vaccine development in Kenya, South Africa and Zambia, 1999-2000
- Member of UNAIDS team to do an ethical review of phase III HIV vaccine trial in Bangkok, Thailand, 2001

### *International Research Review Committees*

- Review of research proposals for funding under the Quality of Life Programme, European Commission, 1999-2001
- Ethics review of funded research, European Commission, 1998-2001
- Review of research proposals for funding, Belgian Research Council, 2001

### *National Committees*

- Member of a Commission of the Ministry of Health on Psychiatry and Lobotomy in Norway, 1991-1992
- Member of a Commission appointed by the Social Security Court on definition of disease for the purpose of sickness certification. 1994

### *Other WHO consultancies*

- Organised one-week training workshops for faculty of medical and nursing schools funded by WHO-SEARO in Sri Lanka and Nepal. A total of five workshops between 1996 and 1998
- Organised three day training workshops for members of research ethics committees in Geneva, Brazil, South Africa and India 1998-1999, funded by UNAIDS
- Organised one week training workshops in Thailand and Indonesia, 2000-2001

# Dr. Vasantha MUTHUSWAMY

**Deputy Director General of the Indian Council of Medical Research, New Delhi, India**

Dr (Ms) Vasantha Muthuswamy, MD, DGO,  
Senior Deputy Director General and Chief,  
Division of Basic Medical Sciences  
Indian Council of Medical research (ICMR), New Delhi

Dr. Muthuswamy is a trained gynaecologist and obstetrician from Madras, India. After pursuing a research career in the area of Maternal and Child health and Contraception at Bangalore and Mumbai, she is now in Charge of research in Basic Medical Sciences for the past 20 years at the ICMR headquarters, New Delhi. Her areas of activity include genetics, genomics, drug development including traditional medicine etc.

For the last 6 years she has been deeply involved in the area of biomedical ethics both for animal and human experimentation. A visiting Fellow at the Kennedy Institute of Ethics at Georgetown University, Washington DC Dr. Muthuswamy is responsible for revising the **"Ethical guidelines for biomedical research on human subjects"** brought out by the ICMR in 2000 after four years of intense deliberations by the Justice Venkatachaliah committee.

She has been member of ethics committees of various national and international organisations such as UNAIDS, HPTN, EC, AIIMS, VP Chest Institute, ICMR Central ethics committee, National Brain Research Centre etc. Since January 2000, she has become the Secretary General of the Forum for ethical review committees in the Asia-Pacific region (FERCAP) and conducted workshops on research ethics at India, Thailand, Nepal, Pakistan, Indonesia, Philippines, Laos and Cambodia. She is currently visiting faculty at the Thammasat University, Bangkok and involved in introducing teaching of bioethics at medical colleges and Universities all over the country and capacity building of ethics committee members all over India.

She has been associated with development of various national and international guidelines on Ethical issues.

As Chief of the Basic medical Sciences, she is involved in funding, infrastructure development and capacity building in all areas of Drug development including Traditional medicine Research. As Secretary of the Toxicology Review Panel of the Council, she is closely involved in all regulatory requirements of drug research in the country.



## Curriculum Vitae

---

# Dr. Nicolas MEDA

## MD, PhD

Dr. MEDA, medical epidemiologist and senior researcher, is the Director of Centre MURAZ (Burkina Faso Ministry of Health Institute of Training and Biomedical Research) Department of HIV/AIDS and Reproductive Health. He is also the field coordinator of French National Agency for AIDS Research activities in Burkina Faso. He has extensively conducted multicentre clinical trials in the area of Mother-to-Child Transmission of HIV. He is the author of more than 50 articles published in international journals.

## PERSONAL INFORMATION:

Date of birth: December 7, 1962  
Place of birth: Dissin, Burkina Faso  
Nationality: Burkinabe

## PROFESSIONAL EXPERIENCE:

Assistant Director of Research and Head of Centre MURAZ Department of HIV/AIDS	March 2002-present
Short-term Consultant / Professional, Regional Programme on AIDS Regional Office for Africa, World Health Organization, Harare, Zimbabwe	April 2001 February 2002
Senior Research Scientist, Centre MURAZ, Burkina Faso Training and Biomedical Research Institute	since July 1997
Assistant Research Scientist, Centre MURAZ, Burkina Faso Training and Biomedical Research Institute	October 1994 to June 1997
Clinician, Gynaecology & Obstetrics Department Ministry of Health Sourô Sanou National Hospital, Bobo-Dioulasso, Burkina Faso	October 1989 to September 1994

## OTHER WORKING EXPERIENCE

Participation and scientific contribution to more than fifty workshops, seminars, international conferences, focusing on Reproductive Health, HIV/AIDS and Health systems development.

## ACADEMIC TRAINING:

Doctorat d'Université (Ph.D.) en Epidémiologie Université de Bordeaux II, Bordeaux	June 1997
Diplôme d'Etudes Approfondies (DEA) "Epidemiology and Public Health"	October 1993

Université de Bordeaux II, Bordeaux  
B.A. in Statistics and epidemiology  
Institute of Statistics, University of Paris VI

June 1991

Doctorat d'Etat en Médecine (Medical Degree)  
Université de Ouagadougou, Burkina Faso

June 1990

### **CONTINUING EDUCATION**

May 1994 – June 1994

Diploma of the International Course on STDS & AIDS, Main topics: detection and management of STDs and HIV infection focusing in developing countries. Alfred Fournier Institute, Paris, France, WHO Collaborative Centre on STDs.

September 1995

Certificate on Data analysis in Epidemiological Research. Main topics: Advanced methods in data analysis in epidemiology. Free University of Brussels, School of Public Health, Belgium.

### **AUTHOR:**

Publications mainly on reproductive health and HIV infection in children and adults in peer reviewed medical journals (52) and book's chapters (3). More than 60 oral communications.

### **MAJOR AREAS OF INTEREST:**

Epidemiology, ethics and public health interventions on maternal and child health  
Epidemiology, ethics and control of human immunodeficiency virus (HIV) infection  
Health information systems and monitoring of primary health care programs  
Epidemiologic surveillance and monitoring and evaluation of public health programmes

### **CONSULTANCIES:**

Around twenty expertises and missions in different African countries in area of HIV/AIDS, Reproductive Health and Health systems development requested by French Ministry of Cooperation, World Bank, UNAIDS and WHO.

# Dr. Hanna NOHYNEK

**Department of Vaccines  
National Public Health Institute  
HELSINKI - Finland**



Hanna Nohynek completed her medical studies in Helsinki, Finland, and is presently working as a Senior Scientist at the Department of Vaccines for the National Public Health Institute. She is the scientific project coordinator of the ARIVAC trial, a phase III study of an 11-valent pneumococcal conjugate vaccine being conducted by the international ARIVAC consortium on the island of Bohol in the Philippines. The study is funded by the European Commission DG Research INCO programme, Bill and Melinda Gates Children's Vaccine Programme at PATH, the Finnish Academy and the Finnish Foreign Ministry, and WHO Vaccines and Biologicals. For more details, visit [www.sph.uq.edu.au/arivac/](http://www.sph.uq.edu.au/arivac/)

Hanna Nohynek did her PhD work on the serodiagnosis of childhood pneumonia, which she has studied in Finland, Russia, and the Philippines. In collaboration with the Research Institute of Tropical Medicine in the Philippines, she has coordinated 6 phase II trials on a number of vaccines (*Haemophilus influenzae* type b, meningococcal conjugate, and pneumococcal conjugate among infants, and pneumococcal polysaccharide among pregnant mothers and infants). She is also a member of the National Public Health Institute Advisory Board for Vaccines, Editor in Chief of the Finnish Vaccinators Manual ([www.ktl.fi](http://www.ktl.fi)), a founding member and chairman of the Steering Committee of the Finnish Global Health Course initiated in 1999, a partner in the DG Research funded project CTC-Ethics, a Working Group member of the European Developing Country Clinical Trial Platform (EDCTP), a Steering Committee member of the EU DG SanCo funded European Programme on Intervention Epidemiology Training (EPIET), and has served as technical advisor to the EU, WHO, GAVI and the Finnish Ministry of Foreign Affairs. She has taught on several vaccinology and infectious disease epidemiology related courses in Finland, Sweden, Russia, Estonia, France, Thailand and the Philippines and belongs to the scientific faculty of the Fondation Merieux initiated Advanced Course on Vaccinology, in France, since 1999. She has published 21 original scientific communications in peer reviewed journals, presented original data in 68 international scientific meetings, edited several manuals and textbooks both in Finnish and English languages, and serves as a peer reviewer to several international scientific journals.



## Curriculum Vitae

---

### Dr. Nadia TORNIEPORTH

**Director, Clinical Development,  
GlaxoSmithKline Biologicals,  
Rixensart, Belgium**

#### PROFESSIONAL EXPERIENCE

*1997-2002 Clinical R&D, prophylactic vaccines, SmithKline Beecham/GlaxoSmithKline Biologicals:*

**Apr 2002-present**                      **Director, Clinical Development,** Pediatric Pneumococcal Vaccines and Emerging Diseases, GlaxoSmithKline Biologicals, Rixensart, Belgium: *Project Director, MVI/GSK public-private partnership for pediatric development malaria vaccine; clinical development tuberculosis vaccine; pneumococcal conjugate vaccine development; new technologies (adjuvants, prime-boost).*

Since 2001: GSK Biologicals representative, IFPMA contact group on ethics in biomedical research

**Jan 2001-Mar 2002**                      **Associate Director & Director, Clinical Development,** Emerging Diseases: *Project Director, MVI/GSK public-private partnership for pediatric development malaria vaccine; clinical development tuberculosis vaccine; New technologies (adjuvants, prime-boost)*

**Jan 2000-Dec 2000**                      **Associate Director, Clinical Development,** Travelers' & Hepatitis Vaccines, Adult Development Unit: *early clinical development malaria vaccine, Phase III – IV development of travelers and hepatitis vaccines (adult and paediatric studies).*

**June 1997-Dec 1999**                      **Manager & Senior Manager, Clinical Development,** Travelers' Vaccines, Adult Development Unit, SmithKline Beecham Biologicals, Rixensart, Belgium,: *Phase I-II clinical development malaria vaccine, Phase III – IV development of travelers vaccines (registration of Hepatyrix™); ETEC epidemiology (Travelers' Diarrhoea Worldwide).* Additional responsibilities for Clinical Development of Travelers' & Hepatitis Vaccines, Adult Development Unit, September – December 1999: *Phase III clinical development hepatitis vaccines.*

#### **1992-1997 Academic and field research in infectious diseases/tropical medicine:**

**May 1996-May 1997**                      **Assistant Professor,** Overseas Staff, Section International Medicine and Public Health, Dept. of Infectious Diseases and Tropical Medicine, University of Munich, Germany: *Resident physician, International Collaborative Study on Travelers' Health, Montego Bay, Jamaica/W.I (healthcare, food safety surveillance, training and data management)*

**1995-96**        **Instructor in Medicine**, Division of International Medicine and Infectious Diseases, Cornell University Medical College, New York, NY: *TBNetwork Coordinator: Laboratory-Based Surveillance of Tuberculosis Transmission in New York City; Epidemiology of Nosocomial Infections.*

**1992-94**        **Research Fellow (Molecular Biology)**, Division of International Medicine, Cornell University Medical College, New York, NY: *Molecular Pathogenesis of Enteropathogenic Escherichia coli; Molecular Epidemiology of Pathogenic Escherichia coli Infections in Brazilian Children.*

**1988-91**        **Resident in Internal Medicine**, University Hospital of Ulm, and Technical University Hospital, Munich, Germany

## **POSTGRADUATE TRAINING**

**Diploma in Tropical Medicine and Hygiene (D.T.M.&H.)**, London School of Hygiene and Tropical Medicine, London, United Kingdom, 1987

**Medical Mycology**, "Centraalbureau voor Schimmelcultures", Baarn, The Netherlands, 1990

**Advances in Human Genetics**, Cornell University Medical College, New York, NY, 1993

**Principles of Epidemiology / Introduction to Biostatistics**, Graduate Summer Program in Epidemiology, Johns Hopkins School of Hygiene and Public Health, Baltimore, MD, 1994

**Sub-specialisation "Tropical Medicine"**, Bavarian College of Physicians, Munich, Germany, 1997

## **EDUCATION**

**1987**    **Doctoral Dissertation ("*magna cum laude*")**        , Department of Infectious Diseases and Tropical Medicine of the University of Munich, Germany

**1986**    **M.D.**, Medical School of the Ludwig-Maximilians-University, Munich, Germany

**1979**    **Baccalauréat Européen**, European School, Bergen, The Netherlands

**LANGUAGE SKILLS:**    German (mother tongue), English, Dutch, French (fluent)

## ***Participants***

---



## Members of the European Group on Ethics (EGE)

Prof. Catherine LABRUSSE – RIOU  
Centre de Recherche en Droit Privé  
Université de Paris I Panthéon-Sorbonne  
Paris, France

Dr Nicos C. ALIVIZATOS  
Professor of Public Law  
University of Athens  
Athens, Greece

Prof. Göran HERMERÉN, President  
Philosopher, Professor of Medical Ethics  
Faculty of medicine, Lund University  
Sweden

Prof. Rafael CAPURRO  
Professor of Information Management and  
Information Ethics at Fachhochschule  
Stuttgart, Hochschule der Medien  
University of Applied Sciences  
Germany

Dr. Yvon ENGLERT  
Head of Fertility Clinic, Free University of  
Brussels (ULB), Professor of Medical  
Ethics and Deontology  
Brussels, Belgium

Prof. Anne McLAREN  
Geneticist, Research Associate at  
Wellcome CRC Institute  
Cambridge – United Kingdom

Dr. Linda NIELSEN  
University of Copenhagen  
Faculty of Law, Institute of Legal Science  
Copenhagen, Denmark

Dr. Pere PUIGDOMÈNECH ROSELL  
Research Professor, Department for  
Molecular Genetics, Director of Institut de  
Biologia Molecular de Barcelona, CSIC  
Barcelona – Spain

Dr. Stefano RODOTA  
Professor of Civil Law, University of Rome  
Chairman of the Italian Data Protection

Authority, Chairman of the European  
Group of the Data Protection Authorities  
Roma - Italy

Dr. Günter VIRT  
Professor of Theology, Institut of Catholic  
Moral Theology  
University of Vienna  
Vienna - Austria

Dr. Peter WHITTAKER  
Biologist, Professor of Biology, Head of the  
Biology Department  
National University of Ireland  
Maynooth - Ireland

## Secretariat of the EGE

Ms Christiane BARDOUX

Ms Joëlle BEZZAN

Ms Anne-Sophie COIFFET

Ms Brigitte GRATTON (stagiaire)

Ms Agueda OLLERO MONTIEL

## Speakers

Dr. Soren HOLM  
Philosopher  
Institute of Medicine, Law and Bioethics  
University of Manchester - UK

Dr. Monica KONRAD  
Doctor  
Institute of Commonwealth Studies  
School of Advanced Study  
University of London – UK

Dr. Reidar K. LEI  
Philosopher  
M.D., Ph.D  
Department of Philosophy  
University of Bergen - Norway

Dr MUTHUSWAMY  
Senior Deputy Director General  
Indian Council of Medical Research  
New Delhi – India

Dr. Nicolas MEDA  
Head, Department of HIV/AIDS  
Centre Muraz/Ministry of Health  
Burkina Faso, West Africa

Dr. Hanna NOHYNEK  
MD PhD Project coordinator  
National Public Health Institute, Dept  
Vaccines  
Helsinki - Finland

Dr Nadia TORNIEPORTH  
M.D., D.T.M. & H.  
Director  
Clinical Development - Emerging Diseases  
GlaxoSmithKline Biologicals s.a. (GSK)  
Rixensart - Belgium

### **European Commission**

#### DG Research (RTD):

Mr. Octavi QUINTANA TRIAS  
Director - Health

Mme Laurence CORDIER  
Scientific Officer

Dr. Anne DEGRAND-GUILLAUD  
Directorate Ageing/Poverty Diseases

Prof. Arnd HOEVELER  
Chef d'Unité – Poverty Related Diseases

Ms Anna KARAOGLOU  
Principle Administrator

Ms Line Gertrud MATTHIESSEN-GUYADER  
Directorate Biotechnology,  
Agriculture & food, Strategy & policy

Dr. Barbara RHODE  
Head of Unit - Ethics & Science

#### DG Development:

Ms Lieve FRANSEN  
Unit Human & Social Development

Mr Juan GARAY AMORES  
Unit Health, AIDS and Population

#### DG Enterprise:

Dr Birka LEHMANN  
Pharmaceutical Unit

#### DG SANCO (Health & Consumer Protection):

Mr Jean-Jacques RATEAU  
Advisor on Consumer Information

### **European Parliament**

#### Committee on Development & Cooperation:

Mr. Paul LANNOYE  
MEP

Ms Christina PLATZER  
Assistant to Ms Karin SCHEELE  
MEP

Mevr. Marieke SANDERS-TEN HOLTE  
2ème vice-Président  
MEP

#### Committee on Industry, External Trade, Research and Energy:

Ms Erika MANN  
MEP

Dr. Elly PLOOIJ – VAN GORSEL  
MEP

Mr John PURVIS  
MEP  
and his Assistant : Ms Sally TAYLOR

## **International Organizations**

Prof. Juhana E. IDANPAAN-HEIKKILA  
Secretary-General  
Council for International Organizations of  
Medical Sciences (CIOMS)  
C/o WHO  
Geneva, Switzerland

Ms Laurence LWOFF  
Council of Europe  
Bioethics Division  
Strasbourg, France

Ms Zara MERALI  
Technical Officer  
World Health Organization – WHO  
Geneva, Switzerland

## **National Instances**

Mr André BEAUCHAMP  
Membre de la Commission de l’Ethique de la  
Science & de la Technologie  
Quebec - Canada

Dr. Matthias BECK  
Dr. Med. Dr. Theol.  
Institut für Ethik und Recht in des Medizin  
Wien, Austria

Prof. Sadek BELOUCIF  
Professeur d’Anesthésie-Réanimation  
Membre du CCNE  
Comité Consultatif National  
D’Ethique pour les Sciences de la Vie  
et de la Santé  
Paris, France

Mr Christian BYK  
Secretary General  
International Association of Law,  
Ethics and Science  
Paris, France

Prof. Francesco D’AGOSTINO  
Comitato Nazionale per la Bioetica  
Roma, Italy

Mme Edith DELEURY  
Membre de la Commission de l’Ethique de la  
Science & de la Technologie  
Quebec - Canada

Mme Diane DUQUET  
Membre de la Commission de l’Ethique de la  
Science & de la Technologie  
Quebec - Canada

M. Jean-Claude MILMEISTER  
Chargé d’Etudes de la C.N.E.  
Commission Nationale d’Ethique – C.N.E.  
Luxembourg – Grand-Duché-de-Luxembourg

Mme Michèle JEAN  
Membre de la Commission de l’Ethique de la  
Science & de la Technologie  
Quebec - Canada

M. Jean-Philippe LAVOIE  
Conseiller en Ethique  
Ministère de la Recherche, de la Science  
Et de la Technologie  
Quebec - Canada

Mr Harald SCHMIDT  
Assistant Director  
Nuffield Council on Bioethics  
London - UK

Prof. Maxime SELIGMANN  
Professeur Emérite – Membre du CCNE  
Comité Consultatif National d’Ethique pour  
Les Sciences de la Vie et de la Santé  
Paris, France

Prof. Daniel TARSCHYS  
National Council on Medical Ethics  
Ministry of Health & Social Affairs  
Stockholm – Sweden

## **Representatives of Industry**

Ms Rebecca DOWNING  
Consultant  
Weber Shandwick – Adamson  
Brussels, Belgium

Mr Jean-Pascal DUCRET  
Directeur Impact Malaria  
Sanoti - Synthelabo  
Gentilly, France

Mr Thomas GALLACHER  
Member of IFPMA Ethics Group  
International Federation of Pharmaceutical  
Manufacturers Associations  
Global Head, Medical Policy  
& Standards Dept  
GlaxoSmithKline R & D  
Middlesex, UK

Mr Benjamin GANNON  
EU Affairs Advisor  
GlaxoSmithKline  
Brussels, Belgium

Mr Joachim HOMBACH  
Director Government Affairs  
GSK Biologicals  
Rixensart, Belgium

Mrs Magdalena RODRIGUEZ DE AZERO  
Manager  
European Vaccines Manufacturers  
Brussels, Belgium

Dr. Henrietta UKWU  
Member of IFPMA Ethics Group  
International Federation of Pharmaceutical  
Manufacturers Associations  
Pennsylvania, USA

#### **Representatives of associations**

Mr Georges BINAME  
Président  
Association belge de Bioéthique  
Brussels - Belgium

Pr. DETILLEUX  
CPME Ethics Subcommittee President  
Standing Committee of European Doctors  
Brussels, Belgium

Dr Pat FAST  
Medical Director  
International AIDS Vaccine Initiative  
New York, U.S.A.

Dr. Georges LIENARD  
Secretary General  
European Humanist Federation – EHF  
Brussels, Belgium

Mr Adrian C. VAN BELLEN  
Board Member  
Dutch Genetic Alliance of Parent / Patient  
Organizations – VSOP  
Bennebroek – The Netherlands

Dr Frans VAN DEN BOOM  
European Director  
International AIDS Vaccine Initiative  
Amsterdam, The Netherlands

Ms Kamau WANJIKU  
STOP AIDS ALLIANCE  
Brussels, Belgium

#### **Representatives of religion**

Rev. P. Edouard BONE  
COMECE – Commission of the Bishops'  
Conferences of the European Community  
Brussels, Belgium

Mgr. Athanase CHATZOPOULOS  
Evêque d'Achate  
Représentation de l'Eglise de Grèce  
Auprès de l'Union Européenne  
Brussels, Belgium

Mr Albert GUIGUI  
Conférence des Rabbins Européens  
Brussels - Belgium

Mr Faustino SAINZ-MUNOZ  
Nonce Apostolique auprès des CE  
298 Avenue Brugmann  
B – 1180 Bruxelles

Ms Katharina SCHAUER  
Secretariat of the COMECE  
Commission of the Bishops'  
Conferences of the European Community  
Brussels, Belgium

Ms Monica LÜCKE  
EVANGELISCHE KIRCHE in Deutschland  
Brussels - Belgium

### **Academics**

Professor Donna DICKENSON  
Centre for the Study of Global Ethics  
The University of Birmingham  
Birmingham, United Kingdom

Prof. Michel DUPUIS  
Responsable de l'Unité d'Ethique Biomédicale  
Faculté de Médecine UCL  
Brussels, Belgium

Prof. Guy LEBEER  
Université Libre de Bruxelles – ULB  
Brussels, Belgium

Prof. Freddy MORTIER  
University of Ghent  
Ghent, Belgium

Prof. Didier MOULIN  
Faculty of Medicine  
Université Catholique de Louvain  
Cliniques Universitaires Saint Luc  
Brussels , Belgium

Dr. Claude Michèle POISSONNET  
Médecin de Prévention  
Coordinateur de la Préfecture de Police de Paris  
Service de Médecine de Prévention  
Hopital des Gardiens de la Paix  
Paris, France

Prof. John Alexander RAEBURN  
University of Nottingham  
Centre for Medical Genetics  
Nottingham City Hospital NHS Trust  
Nottingham, United Kingdom

Ms Sujatha RAMAN  
Institute for the Study of Genetics, Biorisks  
And Society – IGBIS  
Nottingham – United Kingdom

Dr. Monique VERON  
Médecin du Travail - Coordonnateur National  
Centre National de Recherches Scientifiques  
et A.P. – H.P.  
CNRS  
Paris, France

Dr. Heather WIDDOWS  
Centre for the Study of Global Ethics  
The University of Birmingham  
Birmingham, United Kingdom



***Secretariat of the EGE***

---



## Secretariat of the European Group on Ethics



**Ms Christiane Bardoux**

Tel: 32 (0) 2 295 45 47  
Fax: 32 (0) 2 299 45 65  
E-mail: [christiane.bardoux@cec.eu.int](mailto:christiane.bardoux@cec.eu.int)



**Ms Joelle Bezzan**

Tel: 32 (0) 2 296 19 48  
Fax: 32 (0) 2 299 45 65  
E-mail: [joelle.bezzan@cec.eu.int](mailto:joelle.bezzan@cec.eu.int)



**Ms Marie Chirol**

Tel: 32 (0) 2 296 25 84  
Fax: 32 (0) 2 299 45 65  
E-mail: [marie.chirol@cec.eu.int](mailto:marie.chirol@cec.eu.int)



**Ms Patricia Mommens**

Tel: 32 (0) 2 296 84 74  
Fax: 32 (0) 2 299 45 65  
E-mail: [patricia@mommens@cec.eu.int](mailto:patricia@mommens@cec.eu.int)

### Mailing address

European Commission  
Group of Policy Advisers  
BREY 10/128  
B – 1049 – Brussels - Belgium

### Office

European Commission  
Avenue d'Auderghem 45  
B – 1049 – Brussels - Belgium

### Web site

[http://europa.eu.int/comm/european\\_group\\_ethics](http://europa.eu.int/comm/european_group_ethics)



European Commission

**The ethical aspects of biomedical research in developing countries**

**Proceedings of the Round Table Debate**

Luxembourg: Office for Official Publications of the European Communities

2003 — vi, 97 pp. — 21 x 29.7 cm

ISBN 92-894-5064-9