attention to research ethics is given at the national and institutional level was sent to 15 representatives of the Clinical Research Strategic Network. This network comprised nine clinical research centres in Burkina Faso, Cambodia, Indonesia, Peru, RD Congo, Uganda, Zambia and Belgium, aims among others things at implementing essential ethical elements in clinical research. The survey was written in English and contained 21 questions about research ethics practices at the national level and within each institution. Eight institutions participated in the survey. In eight countries ethical approval is mandatory to carry out clinical research. However, research on human subjects is not regulated by a comprehensive law in at least two countries. Ethics committees (EC) are present in all eight countries, but their advice is only legally binding in seven. While the EC gives initial approval, it is often weak in the follow-up of the research, e.g. concerning follow-up of safety aspects or the possibility to interrupt the research based on ongoing results. Three institutions implement non-fault liability insurance for clinical trials. Two institutions only routinely execute the policy of the International Committee of Medical Journal Editors about registration of clinical research projects in a public database, as a prerequisite for publication. Most ECs do not have the possibility to follow up clinical research after the initial approval; also, there are no structural means to verify and ensure that the opinion of an EC is respected when the research is carried out, in both cases, probably due to lack of resources and at least in some countries due to the lack of a clear legislative framework regulating ethical review. Non-fault liability insurance seems to be a poor tool for academic researchers due to high costs and lack of model templates or guidelines. The International Committee of Medical Journal Editors about trial registration seems to be largely unknown. In general, more substantial investments are needed to strengthen national and institutional capacities in the field of clinical research ethics.

TIP2-02

Informed consent, decision-making capacity and vulnerability in resource constrained settings

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Through the informed consent procedure a potential research participant or their parent/guardian agrees to enroll in a research project. Specific guidelines address the consent of individuals with diminished or impaired decision capacity. However, to our best knowledge there are no guidelines for populations that are vulnerable due to socio-cultural or socio-economic factors, including language barriers, gender relations, community pressure, dearth of health care and poverty. In 2008 a Network of researchers from Belgium, Burkina Faso, Cambodia, Cuba, the Democratic Republic of Congo, Indonesia, Nepal, Peru, Uganda and Zambia was created to jointly build the capacity to conduct biomedical research that addresses the need of vulnerable populations, while complying with sound ethical and scientific standards. For understanding the ethical challenges concerning informed consent in resource-constrained settings, the network convened in Antwerp in December 2008 to critically review the process. The work methods included plenary presentations on informed consent process in various settings and break away sessions to review case studies. It was agreed that several critical issues must be considered when seeking informed consent in resource constrained settings, including the lack of access to adequate health care which could lead to vulnerability when making decisions on participation in biomedical research. There was no consensus as to whether illiteracy is *in itself* a vulnerability factor and more research is needed on this. With respect to waivers of informed consent, it was agreed that it should be exceptional and never justified by the poverty or illiteracy of a population. While the signature can be waived in exceptional circumstances, there was unanimity that the interview process could not. Another major issue is that Ethics Committees and researchers should find context-related ways to address the contradiction between legal age and social status, for entitling mature minors, e.g. minors married by customary law and minor mothers, to take free autonomous decisions on participation in medical research. Further, social scientists including anthropologists should be involved in the design and evaluation of consent tools for ensuring that the procedure is adapted to local values and contextual constraints -always within the limits of respect for fundamental universal ethical principles. There is an urgent need for clear guidance to prevent exploitation of populations whose participation in biomedical research is not based on a free choice but on the necessity to access otherwise inaccessible medical care or other benefits. This meeting was only a first step and several critical issues may not have been addressed; however, we believe that the issues raised offer an opportunity to start a debate leading to better guiding principles on the informed consent procedure for biomedical research in resource constrained settings.

TIP2-03

Rationalising international approaches to ethical review: examining and revising the ethical review practices for clinical research funded, sponsored or carried out by Northern organizations in developing countries

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Various international recommend that clinical research sponsored, funded, or supervised by Northern organizations in developing countries be submitted for ethical review in the countries where the research takes place and in the country of the sponsor. In December 2008 a Network of researchers from Belgium, Burkina Faso, Cambodia, Cuba, the Democratic Republic of Congo, Indonesia, Nepal, Peru, Uganda and Zambia met at the Institute of Tropical Medicine in Antwerp, to build capacity for conducting health research that addresses the need of vulnerable populations, and to address the topic of 'double ethical review'. The discussion was based on the experience of projects sponsored by ITM and carried out with partner institutions: protocols are routinely submitted to the ITM Institutional Review Board as well as to the ethics committee (EC) at Antwerp University Hospital and to the EC in the study's countries. The workshop agreed that 'double ethical review' presented some challenges. In national, regional and private reports from northern countries the 'requirement' has not been substantially considered and there is often a sense of paternalism. There is a need to develop a systematic approach to ethical review that promotes respect and trust among research partners and improves the efficacy of international ethical review practices. Communication and education that cross traditional

boundaries (both those of geography and power relations) are needed. The group proposed that at the moment clinical research sponsored or funded by Northern organizations in resource-poor settings should undergo double ethical review, to minimize the risk of double standards and practices linked to the North-South inequalities, and to bring together the complementarities of perspectives of the various ECs, for increasing the quality of the research and promoting better protections of subjects and populations. In a preliminary way, we suggest that protocols be submitted simultaneously to the ECs in the North and in the South indicating the names and contact information for all ECs involved in reviewing the study. If comments are received from one or more EC, the researcher should send a single letter of reply to all the concerned ECs, so that each one becomes aware of all comments. In addition, measures are needed to deal with unwarranted delays from one or more EC, rules should be established to address cases of disagreement, and clear commitment to the highest ethical and scientific principles should be developed by all parties.

TIP2-04

Ethics and clinical research in Democratic Republic of Congo (DRC)

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Clinical research involving humans is subject to national and international ethical guidelines, whose principles are summarized in the Helsinki Declaration. In developed countries, many efforts and investments are undertaken to enforce these principles, while it is generally considered that most developing countries lack the means to carry out adequate ethical review of clinical research, irrespectively of whether it is carried out by sponsors from developing or developed countries. To address this question, we used questionnaires and interviews addressed to researchers at the Kinshasa University Teaching Hospital and to some key policy-makers and presidents of Ethics Committees (EC) in the Democratic Republic of Congo. We also examined the researches carried out in the past five years at Kinshasa University Hospital. The survey was carried out from 13th of October to 1st of November 2008. We found that in DRC, clinical research is not governed by a structured legislative framework. A national EC was created in 2006, but it still lacks sufficient and secured resources to be fully operational. We identified two other operational ECs in DRC, located respectively at the School of Public Health and at National Control Program against Trypanosomiasis. 49% of researchers (84/164) had some knowledge of ethical guidelines and were aware of the localization of the EC at the School of Public Health. However, 49% of clinical researches (81/161) only were based on a written protocol. 47% of the researchers based on a written protocol (38/81) had been submitted to an EC and 79% had received a written approval. Five percent (9/164) received training in good clinical practice. Enforcement of ethical review in clinical research is not a priority in the DRC. In Kinshasa, most researchers have limited or very limited knowledge about ethical guidelines and ethical review and often conduct their researches without a written protocol. If we have this situation in the capital, what could be the case in the provinces? This topic needs to be improved very urgently, through investments to strengthen the ethical review and by changing the mentality of researchers, to ensure maximal protection of the study subjects and scientific soundness of the research.

TIP2-05

Research ethics and international epidemic response: the case of Ebola and Marburg hemorrhagic fevers

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Outbreaks of filovirus (Ebola and Marburg) haemorrhagic fevers [FHF] in Africa are typically the theatre of rescue activities involving international experts and agencies tasked with reinforcing national authorities in clinical management, biological diagnosis, sanitation, public health surveillance and coordination. These outbreaks can be seen as a paradigm for ethical issues posed by epidemic emergencies, through the convergence of such themes as: isolation and quarantine, privacy and confidentiality, and the interpretation of ethical norms across different ethno-cultural settings. Our aims were to specify the nature of ethical dilemmas arising during epidemic response, as a result of tensions between clinical care, public health investigations and research, to review existing frameworks relevant to research ethics in emergencies, to review statements about ethical issues raised during public health responses to past FHF outbreaks, and to propose new approaches to research ethics in the course of epidemicsWe did this through review and analysis of current normative documents on ethics in emergencies and analysing peer-reviewed publications describing past FHF outbreaks. We found that undertaking research during an ongoing outbreak poses considerable and specific ethical questions, often related to the blurred boundaries between research and public health practice. The scope of existing normative documents relevant to research ethics in emergencies has so far been limited by a main focus on informed consent and research ethics committees and lack of comprehensive regulatory documents endorsed at international level. Concerns over research ethics during past outbreaks of FHF have generally been poorly addressed or reported, suggesting a need for more systematic considerations of ethical issues related to the conduct of research in emergencies. For the longer term, we recommend the design of basic research protocols prior to emergencies, the establishment and strengthening of national or regional ethical research committees, and the advance involvement of potentially affected communities, including considerations to distinct ethno-cultural representations of illness and contagion.

TIP2-06

Clinical research in less economically developed countries: the ethical challenges

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The Directive 2001/20/EC on the implementation of Good Clinical Practices in the conduct of clinical trials applies not only in the EU but also in less economically developed countries. The clinical trials carried out in the later often contribute to the development of new drugs for usage in industrialized countries. The marketing authorization delivered by the European Commission can however be refused in cases of non respect of ethical principles as stipulated in the Directive 2001/20/EC. Our objective was to review the Directive 2001/20/EC focusing on the procedure for involvement of vulnerable people in clinical trials and its interaction to existing international legal norms. From the

